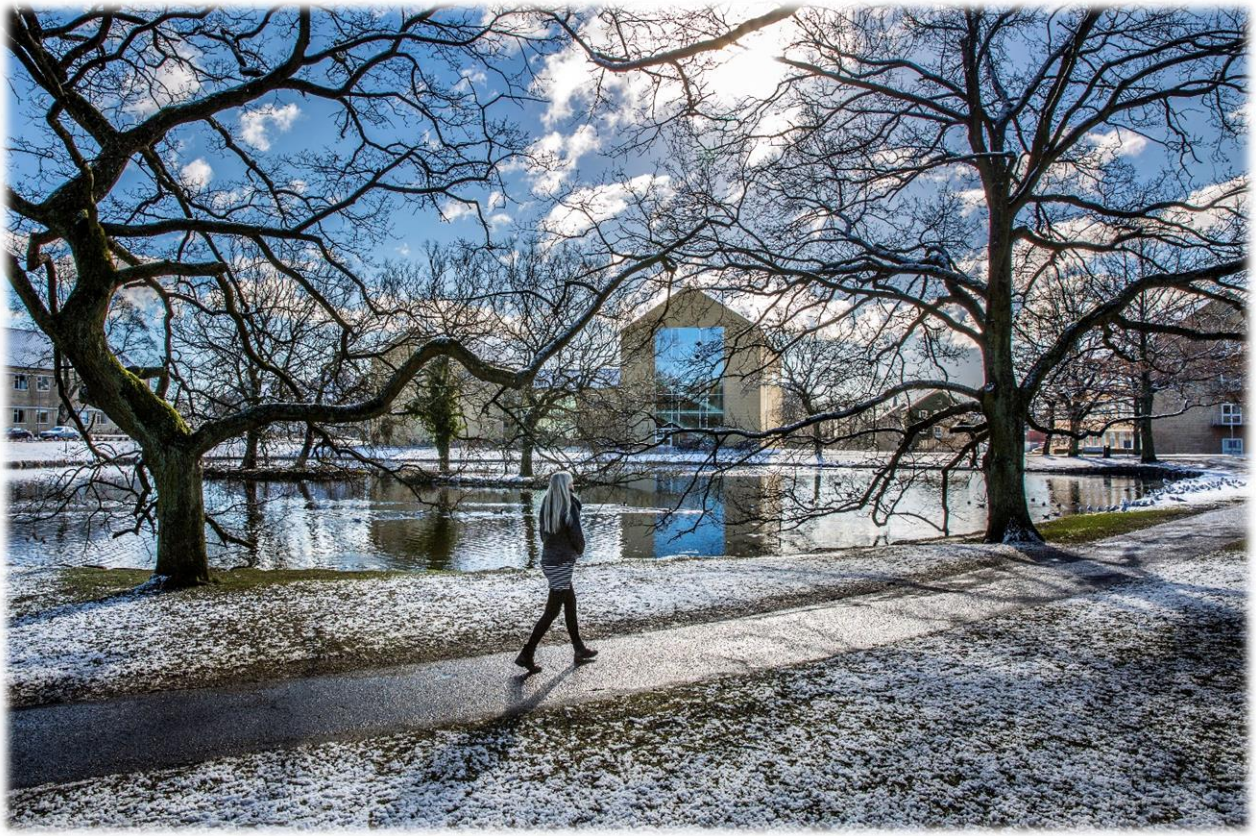
PHD DAY
HEALTH

ABSTRACTS

17 JANUARY 2025



AARHUS
UNIVERSITY

PHD DAY 2025 PROGRAMME

17 JANUARY 2025, THE PER KIRKEBY AUDITORIUM, THE LAKESIDE LECTURE THEATRES

8.30 **Welcome by Organizing Committee Chair and by the Chair of the PhD Association (in Per Kirkeby)**
Anders Etzerodt, Associate professor, Department of Biomedicine, Aarhus University
Livie Yumeng Li, PhD student, Chair of the PhD Association at Health, Aarhus University

8.40 **Keynote lecture by Professor Jens Juul Holst Department of Biomedical Sciences and Senior Group Leader at Novo Nordisk Foundation Center for Basic Metabolic Research, The Faculty of Health and Medical Sciences, University of Copenhagen (in Per Kirkeby)** (45 min)
Introduced by Organizing Committee Chair Anders Etzerodt, Associate professor, Department of Biomedicine, Aarhus University

9.25 **Short break with coffee/tea and fruit**

9.50 **Fogh Nielsen Prize Competition** (60 min)
Per Kirkeby, The Lakeside Lecture Theatres

11.05 **First round of sessions**
The Lakeside Lecture Theatres, Anatomy (build. 1231), Public Medicine Auditorium (build. 1262/101), building 1264 (209 and 310) and Bartholin (build. 1241)

12.35 **Break with lunch and networking**

13.30 **Keynote lecture by Professor Aasa Feragen, Section for Image Analysis and Computer Graphics, Technical University of Denmark (in Per Kirkeby)** (45 min)
Introduced by Organizing Committee Chair Anders Etzerodt, Associate professor, Department of Biomedicine, Aarhus University

14.30 **Second round of sessions**
The Lakeside Lecture Theatres, Anatomy (build. 1231), Public Medicine Auditorium (build. 1262/101), building 1264 (209 and 310) and Bartholin (build. 1241)

15.40 **Coffee, cake and see you later**
The programme for the day ends on different locations

18.30 **Dinner and award ceremonies**

DGI-Huset, Aarhus C

Festive speech: Stine Sofia Korreman

Practical information

- There will be a name tag for you if you are signed up for a presentation or as chair/co-chair. You can collect this at the reception on the lowest level in the Lakeside Lecture Theatres.
- Lunch is served at two locations: the Lakeside Lecture Theatres and in building 1231 on the ground floor.
- A photographer from Aarhus University will be present at the event. Photos taken at the event will only be used in Aarhus University contexts, for example as publicity for/in the invitation to a similar event. If you do not wish to be photographed, please contact the photographer.

The Organizing Committee, PhD Day 2025

- Anders Etzerodt, Associate professor, Department of Biomedicine, Chair PhD Day 2025
- Anika Kofod Kousgaard Petersen, PhD student, Department of Forensic Medicine, Co-chair PhD Day 2025

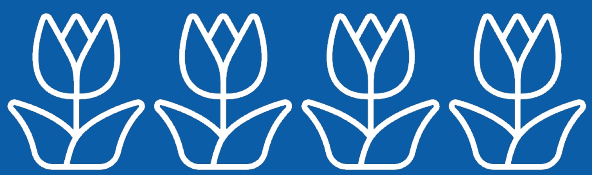
- Alma Becic Pedersen, Professor, Department of Clinical Medicine
- Anders Schram, PhD student, Department of Clinical Medicine
- Emil Ammitzbøll Weissmann, PhD student, Department of Clinical Medicine
- Helene Hallas, PhD administrator, Graduate School of Health
- Henning Grønbæk, Clinical professor, Department of Clinical Medicine
- Johan Palmfeldt, Associate Professor, Department of Clinical Medicine
- Luana Barreto Domingos, PhD student, Department of Biomedicine
- Mayuri Sandesh Charnalia, PhD student, Department of Clinical Medicine
- Merete Bjerrum, Associate professor, Department of Public Health
- Pernille Lajer Sørensen, PhD student, Department of Biomedicine
- Reimar W. Thomsen, Professor, Department of Clinical Medicine
- Rikke Horsted Bundgaard, PhD administrator, Graduate School of Health
- Rubens Spin-Neto, Associate professor, Department of Dentistry and Oral Health
- Salma Karim, PhD student, Department of Clinical Medicine

Social Media: Facebook: PhD Association Health

Hey there, PhD minds so bright,
Do you crave change, to spark the light?
At AU Health, let's lift the game,
Join our cause, and make a name!

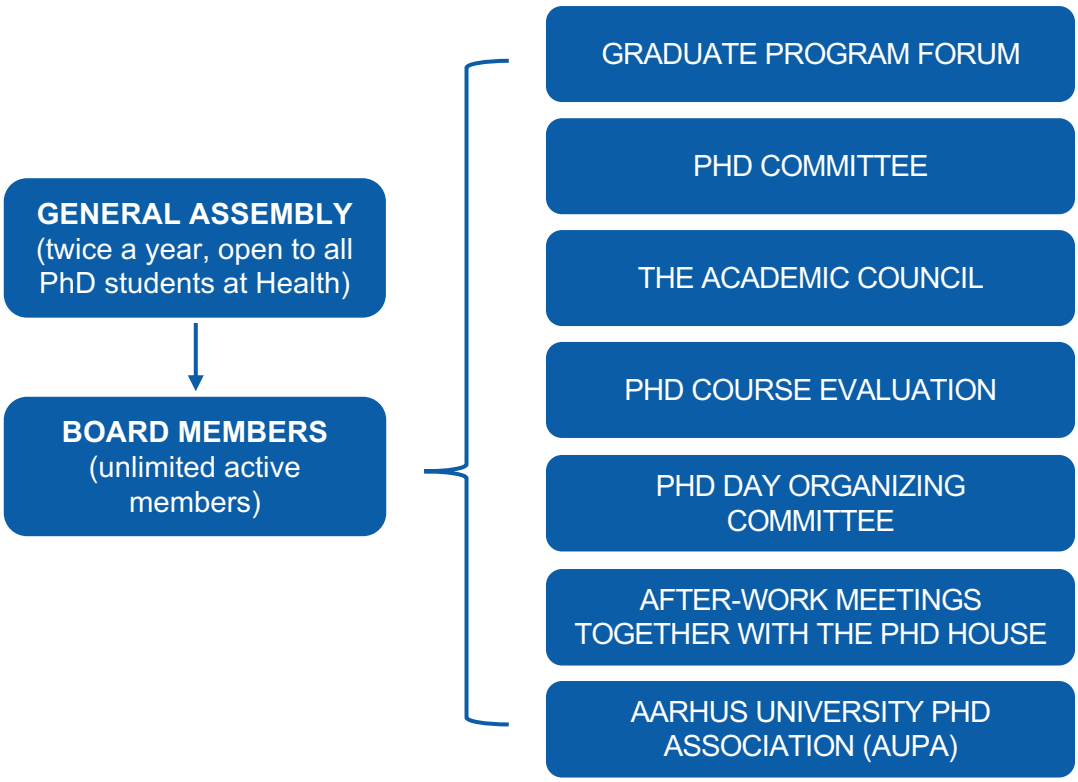
The PhD Association calls to you,
For brighter paths and visions through.
Follow us on Facebook, LinkedIn too,
Stay informed on what we do!

Events and stories, together we grow,
A place for all, let the spirit flow.
All are welcome, your voice is key,
Join us now, and shape the way!



PhD Association
Health, Aarhus University

for all PhD students at the Faculty of Health



We aim to create better education and better conditions

for PhD students at the Faculty of Health

*Find us on **Facebook** or **LinkedIn** at:*

PhD Association Health

Check out our webpage: **phdassociation.dk**

ALL PHD STUDENTS CAN JOIN!

NorDoc
NORDIC DOCTORAL TRAINING IN HEALTH SCIENCES

is going to launch its

8th Nordic PhD Summer School

At University of Oslo, 18-19 August 2025

More information **very soon** at https://www.nordochealth.net/

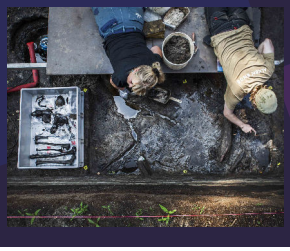
Attend PhD courses in the NorDoc network for free

PhD courses at the 21 NorDoc partner institutions are **free of charge** for all PhD students at Health. The graduate school offers **financial support to cover your travel and accommodation costs.**

AU Career PhD & JR

Career services for PhDs and Junior Researchers






Would you like to get ahead and engage in career development during you PhD or postdoc?

Do you know which career path to choose when finishing your PhD or postdoc?

Do you know which specific competences companies value when hiring researchers?

Are you aware of your many opportunities?

Our services

- Career events
- Interaction with industry
- Individual career counselling
- Support in your career development
- Assessing your competencies and strengths
- Feedback on CVs and cover letters
- Mentor programme

Vibeke Broe
Ph.D. Career Consultant
Phone: +45 2942 6029
Email: vibr@au.dk

Miriam Kobbersmed
Ph.D. Career Consultant
Phone: +45 93522564
Email: mkob@au.dk

AU CAREER PHD & JR

AARHUS
UNIVERSITY

Aarhus University's **Alumni Network**

- A universe of knowledge and relations

Your knowledge matters - stay in touch

Sign up for **free membership** and join 40,000 other alumni, students, PhDs and employees - get access to benefits, life-long learning and the opportunity to contribute with knowledge, experience and network.

alumner.au.dk/en/become-a-member

Nov 2024

AU **LIBRARY**
HEALTH SCIENCES

- Systematic literature search designed for your specific project
- Tips and tricks for PubMed, Embase, Cinahl, Covidence etc.
- Citation searches in Scopus and Web of Science
- EndNote – courses and support
- ORCID, Journal Impact Factor, H-index, and Pure
- Copyright and Open Access
- Courses in PubMed, EndNote etc.

Come by the library, phone or email us and we will help you.

AU Library, Health Sciences
Victor Albeck Building
Vennelyst Boulevard 4
DK-8000 Aarhus C
Tel. +45 2265 0073
sundhedsvidenskab.aul@kb.dk

Opening Hours
Monday – Thursday 9 a.m. - 5 p.m.
Friday 9 a.m. - 3 p.m.

library.au.dk

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Upgrade your teaching and supervision practices

Course: The Reflective Teacher

The course is about the role of the teacher in student-centred teaching. You will gain knowledge, skills, and competences in pedagogical principles related to being a university teacher who can reflect on your own and colleagues' teaching practices. You will also develop and complete the first draft of your teaching portfolio.

https://ced.au.dk/en/courses/the-reflective-teacher

Course: The PhD student as supervisor for undergraduate students

Are you acting as co-supervisor for undergraduate students' bachelor projects, written assignments, master's theses, or research year assignments? Then you play an important role as a near-peer supervisor, guiding students in their learning. This course will prepare you for the role.

https://ced.au.dk/en/courses/the-phd-student-as-supervisor-for-undergraduate-students

AU Educate – Inspiration for your teaching

At AU Educate, you can find inspiration for your teaching and learn more about relevant topics in university teaching. Learn from the practice of others and try new teaching activities. The content will serve as the perfect remedy for your professional teaching development.

https://educate.au.dk/en/

About the

Centre for Educational Development

The CED offers AU teaching staff free competency development, consultation services, and collaboration on higher education pedagogy, educational technology, teaching, and education.

Visit us:
ced.au.dk

Contact us:
ced@au.dk
+45 21 55 14 19

Your occupational health and safety organization

Your Safety
Our Commitment

AARHUS UNIVERSITY
HEALTH

CONNECT

REGION MIDTJYLLANDS DATASTØTTECENTER

10 TIMERS GRATIS RÅDGIVNING TIL DIN FORSKNING

HVAD?

RÅDGIVNING OM BRUG AF SUNDHEDSDATA I FORSKNING

HVEM?

FOR FORSKERE OG KLINIKERE PÅ AU OG I REGION MIDTJYLLAND

HVORDAN?

SE MERE PÅ: WWW.CONNECT.AUH.DK

AARHUS UNIVERSITET

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AUH

AARHUS UNIVERSITET
HEALTH

THE CARDIOVASCULAR NETWORK




NETWORK STRATEGY

Cardiovascular research at AU and the hospitals in Region Midt contributes to **patient** welfare and health

Interdisciplinary cardiovascular research to address societal changes

Cardiovascular research and degree programmes of the highest **international** quality

Development of talents within cardiovascular research

WHAT DO WE OFFER?

- Annual meetings
- Summer schools
- Seminars & workshops
- Networking
- Interdisciplinary collaboration
- Project bank
- PhD programme
- PhD courses

Join our network

Visit our website

Experiments

Research in cardiovascular function and disease mechanisms with cells, isolated organs and animal models.

Patients

Research in prevention, diagnostic tools, and therapy of cardiovascular diseases in patients.

CONTACT

Anja P. Einholm
Network Coordinator
Phone: +4593508408
E-mail: ape@au.dk

www. health.au.dk/en/the-cardiovascular-network

AARHUS UNIVERSITY HEALTH

THE FOOD AND NUTRITION NETWORK

Join the Food and Nutrition Network at AU Health

Food and Nutrition is relevant for both clinical outcome and research in health and disease. As this field of research often requires a multidisciplinary approach as well as expertise (methodological and/or clinical), the network offers a unique opportunity to collaborate and develop new skills. The network stimulates and connects research and teaching activities within food and nutrition at a pre- and post-graduate level.

A wide array of technologies and research methodologies are available through the network ranging from experiment clinical-, epidemiological-, biomedical- to qualitative approaches. Stimulation of research collaboration across the Faculty of Health and other faculties at Aarhus University as well as method development and increased awareness of and accessibility to already existing research methodologies are important scopes of the work.

Among the pertinent research questions that are addressed by the network are:

- What are health consequences of the green transition?
- What are the potential health benefits from novel food products and food processing technologies?
- How do we prevent obesity and associated negative impact on well-being?
- How do we prevent malnutrition, sarcopenia, and cachexia among vulnerable subjects?
- What is the physiology behind consumption and ingestion of food and nutrition?
- How does disabilities and disease conditions impair normal consumption and ingestion of food?

The network serves as a platform for larger research projects initiated from within the network or through external invitations. This involves communicating with funding institutions, connecting researchers, and stimulating food and nutrition research among peers at AU Health.
The network also serves as a forum for coordination of established network activities in food and nutrition research outside AU Health.

Join the Food and Nutrition Network if you are interested in the activities within the network, wish to broaden your horizon within food and nutrition, or are interested in collaborations! The network is relevant and open for scientists at all levels.

To join the network, please visit https://health.au.dk/en/the-food-and-nutrition-network

AARHUS UNIVERSITY HEALTH

THE INFLAMMATION NETWORK

Join the Inflammation Network

Inflammatory and infectious diseases continue to be significant global health challenges. As a society, our quest for understanding the interplay between inflammation and the development of autoimmunity and cancer, uncovering biomarkers, and deciphering the molecular mechanisms of infectious and inflammatory diseases remains paramount. The Inflammation Network is where multidisciplinary collaboration leads to the formulation of the right questions and the discovery of answers.

Scan this to join via our website

Our network comprises an extensive group of researchers, each with a keen interest in various aspects, including immune-mediated diseases, diagnostic methodologies, epidemiological insights, inflammatory markers, intracellular immune pathways, human genetics, and a deep comprehension of cell populations and tissue structures. Our steering committee also includes **two dedicated PhD student representatives** Lotte L. Eriksen and Marvin Werner and one **dedicated postdoc representative** Fernando Valentim Bitencourt.

What´s in it for early career researchers?

The Inflammation Network opens doors for early career researchers, providing an invaluable opportunity to expand your research network. These connections can pave the way for enduring professional relationships that may prove instrumental in shaping the trajectory of your future research endeavors. Researchers at all stages of their careers, including those who are still pursuing education, play an integral role within the Inflammation Network. **PhD student** Morten Kelder Skouboe, a member of the research group at the Department of Biomedicine, shares his perspective:

"I've signed up to get a better idea of what's going on in other areas, and perhaps to get a clearer understanding of how my research skills can be used in other research groups working on things that I find really exciting".

Save the date and sign up!

Mark your calendar for **our 5th Inflammation Network Day**, scheduled for **March 13 2025**. A day filled with insightful talks that bridge the realms of basic and clinical research in inflammation, infection, and autoimmunity. Our program features excellent keynote speakers who will delve into topics such as infection immunology, the microbiome, tumor immunology, and autoimmunity. You can also expect numerous talks from junior researchers!

Scan this to read more and register for 5th Inflammation Network Day

Our focus the next couple of years

- Continuous promotion and bridging of basal and clinical research within diseases related to inflammation, infection, and immunopathology
- Internationalisation, including Circle U. initiatives
- Engagement of younger researchers in the network, including the steering committee
- Establishment of focus groups related to specific topics, methodologies, and diseases

Network vision

Strengthen Aarhus University's position

Bridge university-based research departments, faculties & clinical medicine

Improve recruitment and visibility

Increase funding opportunities

HOW TO JOIN? https://health.au.dk/en/the-inflammation-network/join-the-inflammation-network

THE PERSONALISED MEDICINE NETWORK

WHO ARE WE?

Members include junior and senior researchers and clinicians across many fields, including genetics, epidemiology, molecular biology, bioinformatics, pharmacology, law and ethics, and more!

READ MORE
& SIGN UP HERE

SCAN ME

WHAT CAN WE OFFER?

- Biennial international conferences with international and national experts
- Annual meetings
- Regular seminars
- Specialised focus group meetings
- Up-to-date news on upcoming events, PhD courses, and grant funding opportunities
- Collaboration with the National Academies: Danish Cardiovascular Academy, Danish Data Science Academy, Danish Diabetes & Endocrine Academy, and Neuroscience Academy Denmark

AARHUS UNIVERSITY
HEALTH

THE TRANSLATIONAL CANCER NETWORK

AARHUS UNIVERSITY HEALTH

AARHUS UNIVERSITY HOSPITAL

VISION & STRATEGY

- **Accelerating translation of scientific discoveries into tangible clinical applications**
- **Bring basic science into clinical practice and vice versa**
- **Involve the public and patients in our translational research through communication and outreach**
- **Encouraging an environment of open dialogue and mutual understanding**

THE NETWORK OFFERS:

- Interdisciplinary collaborations
- Seminars & workshops
- Annual meetings
- Summer schools
- PhD courses

SCAN TO JOIN THE NETWORK

linkedin.com/showcase/the-translational-cancer-network

Are you WORKING within the field of cardiovascular physiology, related clinical divisions, or do you have a professional interest in the cardiovascular health?

Danish Cardiovascular Academy

dcacademy.dk

Become a member of the DCAcademy network:

- Recieve latest news and information from DCAcademy (~6 times a year)
- Stay updated on DCAcademy grants, events, and courses

← click or apply camera for details

Apply for DCAcademy grants:

- DCAcademy PhD scholarships (1/3, 2/3 or full scholarships)
- DCAcademy Postdoctoral fellowships (2 year)
- DCAcademy Clinical Postdoctoral fellowship (or 20 % over 5 years)

Deadline - 21 of February 2025, 12:00 PM

← click or apply camera for details

Register for DCAcademy events:

- DCAcademy Postdoctoral Winter Meeting 2025
- Cardiometabolic Networking Summit 2025
- Neurovascular coupling in metabolic brain diseases. The DCA & NAD event.
- DCAcademy Summer Meeting 2025
- Diet and Cardiovascular Health: From Fatty Acids to Foods and Dietary Patterns
- Integrative Human Cardiovascular Control 2025
- Vascular-Adipose Link: Exploring the Intricacies of Health and Obesity

← click or apply camera for details

Dcacademydk @DCAcademyDK Danish Cardiovascular Academy

founded by novo nordisk foundation
HJERTE FORENINGEN

Danish Diabetes and Endocrine Academy
Funded by the Novo Nordisk Foundation

Danish Diabetes and Endocrine Academy

Are you an early-career researcher within the research fields of diabetes, metabolism and/or classical endocrinology? Are you seeking funding for your research, excellent education activities or new collaborations?

Check out Danish Diabetes and Endocrine Academy (DDEA):

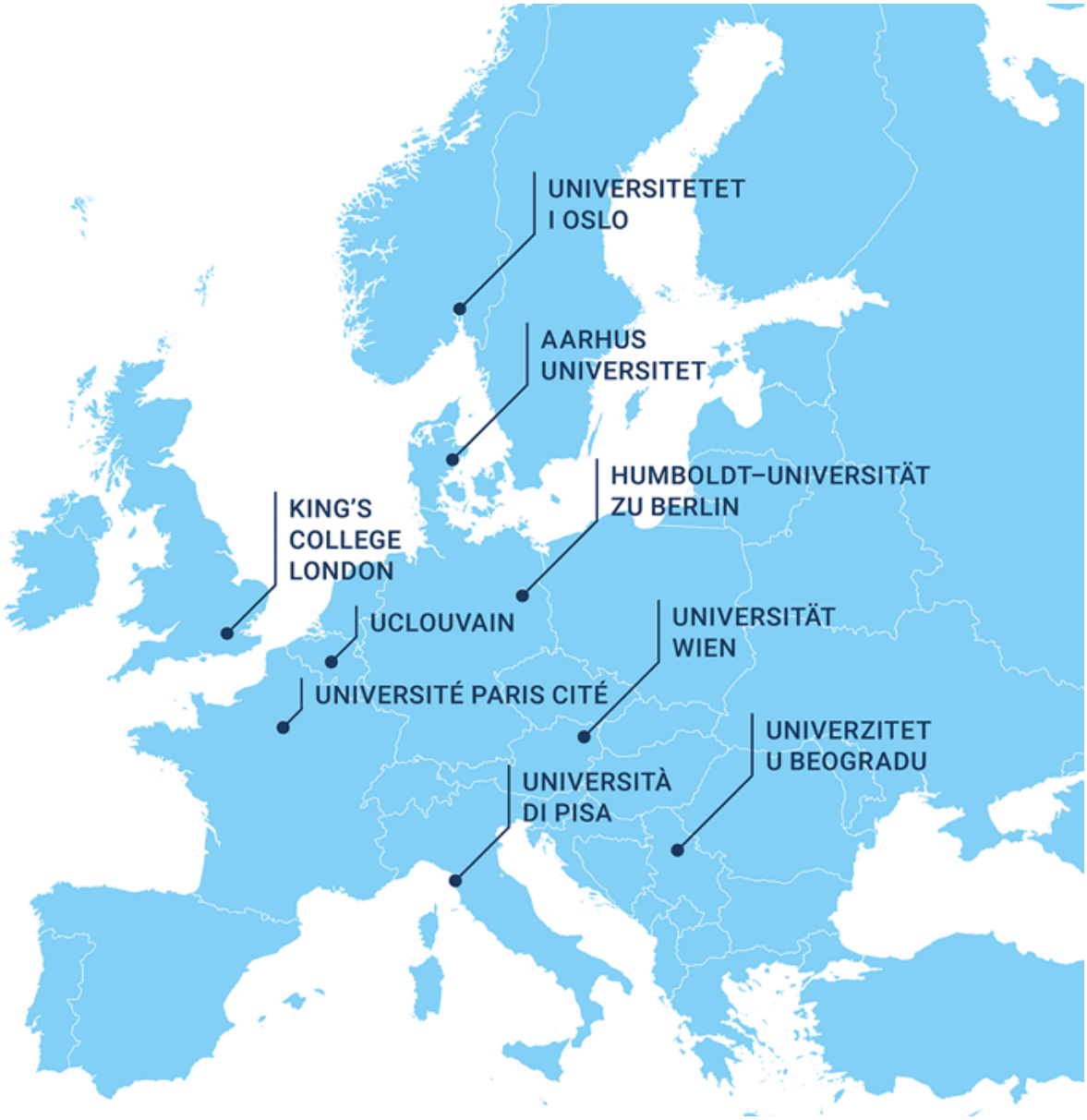
- 20 February, Aarhus, DK – Meeting on **Vascular-Adipose Link: Exploring the Intricacies of Health and Obesity** *In collaboration with Danish Cardiovascular Academy (DCA)*
- 12-13 March, Korsør, DK – Meeting on **Diabetes and the Bio-psycho-social Model in a Life Course Perspective**
- April 7 – Copenhagen, DK – Meeting on **Endocrinology from Cradle to Adulthood**: Joint Meeting by Paediatric and Endocrine Societies
- April, DDEA Website **– Call for DDEA PhD Scholarships and Postdoc Fellowships**
- May, TBD, DK - **Intermediate Course on Reproducible Research in R**
- 26-27 May Odense, DK; **PhD Course on the Patient a Resource in Research**
- 2-3 June, Faroe Islands, FO; **Symposium on Emerging Strategies in Obesity Prevention and Treatment**
- 25-25 August, Ebberup, DK - **DDEA PhD Summer School on Diabetes, Metabolism & Endocrinology**
- 6-9 October, Kibæk, DK **Postdoc Summit**
- 20-23 October, Korsør, DK - **PhD Course** on**Basic Cardiometabolic Research**
  Co-organised with the Danish Cardiovascular Academy
- December, TBD, DK - **Advanced Course on Reproducible Research in R**

And many other interesting symposia and networking events that we encourage PhD students with an interest to participate in.

Read more and sign up at www.ddeacademy.dk

Circle U.
European University Alliance

Co-funded by the
Erasmus+ Programme
of the European Union



Learn more at

www.circle-u.eu

Or contact AU Academic Chair for Global Health,
Professor Christian Wejse

PHD DAY 2025

Session overview and chairs

Session Overview

11.05-12.35 – First round of sessions

PhD Innovation Workshop:	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**
Session 1:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Session 2:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Session 3:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Session 4:	Anatomy (Building 1232), 1st floor **Big Anatomy Auditorium**
Session 5:	Anatomy (Building 1231), 2nd floor, **Room 214**
Session 6:	Anatomy (Building 1231), 2nd floor, **Room 216**
Session 7:	Anatomy (Building 1231), 2nd floor, **Room 220**
Session 8:	Anatomy (Building 1231), 2nd floor, **Room 224**
Session 9:	Anatomy (Building 1231), 2nd floor, **Room 228**
Session 10:	Anatomy (Building 1231), 2nd floor, **Room 232**
Session 11:	Anatomy (Building 1231), 4th floor, **Small Anatomy Auditorium**
Session 12:	Building 1262, 1st floor, **Room 101 – Public Medicine Auditorium**
Session 13:	Building 1264, 2nd floor, **Room 209**
Session 14:	Building 1264, 3rd floor, **Room 310**
Session 15:	Bartholin (Building 1241), 1st floor, **Room 114 – Auditorium 4**
Session 16:	Bartholin (Building 1241), 1st floor, **Room 119 – Auditorium 3**
Session 17:	Bartholin (Building 1241), 1st floor, **Room 125 – Auditorium 2**
Session 18:	Bartholin (Building 1241), 1st floor, **Room 135 – Auditorium 1**

14.30-15.40 – Second round of sessions

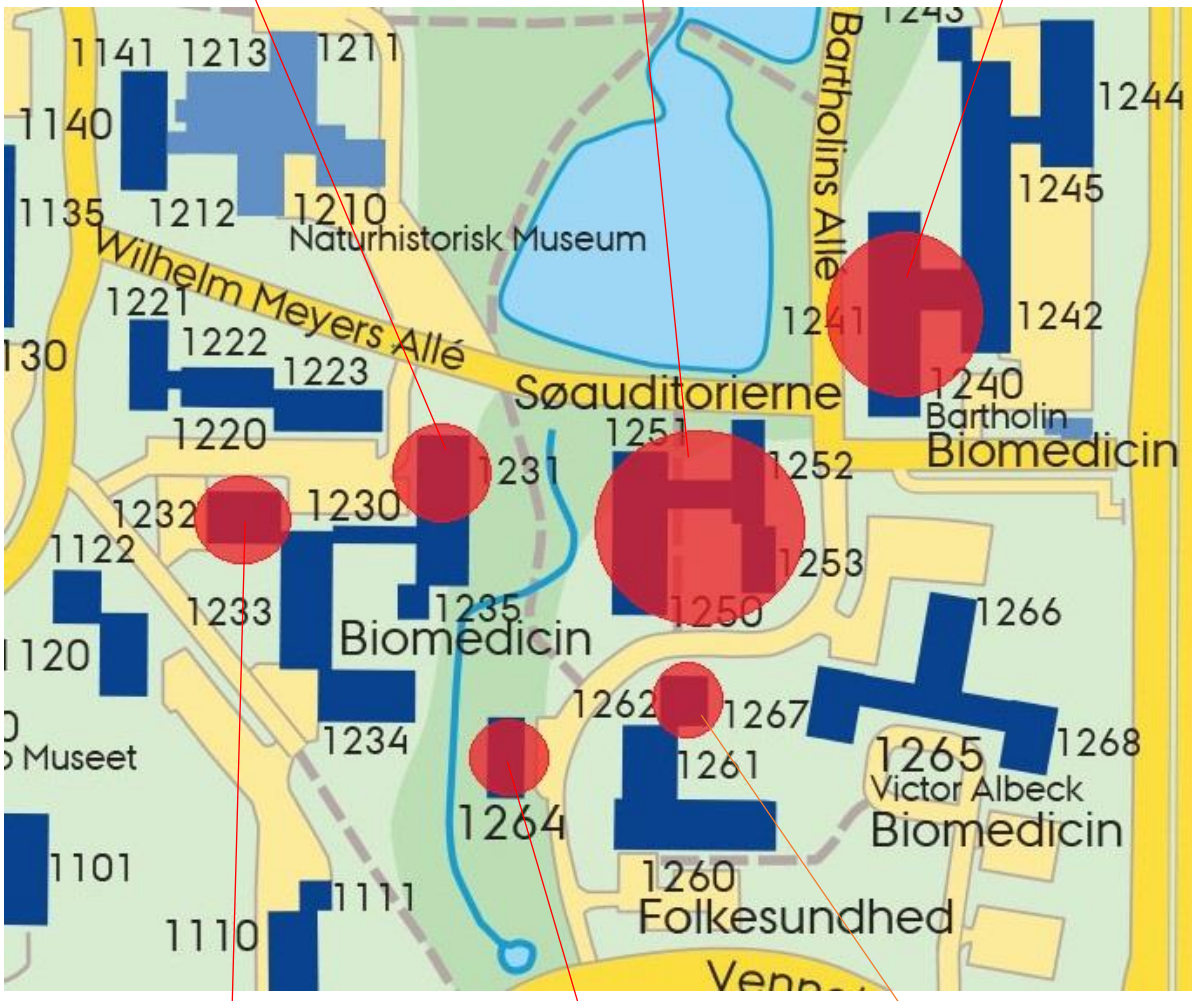
Session 19:	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**
Session 20:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Session 21:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Session 22:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Session 23:	Anatomy (Building 1232), 1st floor **Big Anatomy Auditorium**
Session 24:	Anatomy (Building 1231), 2nd floor, **Room 214**
Session 25:	Anatomy (Building 1231), 2nd floor, **Room 216**
Session 26:	Anatomy (Building 1231), 2nd floor, **Room 220**
Session 27:	Anatomy (Building 1231), 2nd floor, **Room 224**
Session 28:	Anatomy (Building 1231), 2nd floor, **Room 228**
Session 29:	Anatomy (Building 1231), 2nd floor, **Room 232**
Session 30:	Anatomy (Building 1231), 4th floor, **Small Anatomy Auditorium**
Session 31:	Building 1262, 1st floor, **Room 101 – Public Medicine Auditorium**
Session 32:	Building 1264, 2nd floor, **Room 209**
Session 33:	Building 1264, 3rd floor, **Room 310**
Session 34:	Bartholin (Building 1241), 1st floor, **Room 114 – Auditorium 4**
Session 35:	Bartholin (Building 1241), 1st floor, **Room 119 – Auditorium 3**
Session 36:	Bartholin (Building 1241), 1st floor, **Room 125 – Auditorium 2**
Session 37:	Bartholin (Building 1241), 1st floor, **Room 135 – Auditorium 1**

BUILDING LOCATIONS

Anatomy (1231)
Session 5-11 and 24-30

Lakeside Lecture Theatres
PhD Workshop
Session 1-3 and 19-22

Bartholin (1241)
Sessions 15-18 and 34-37

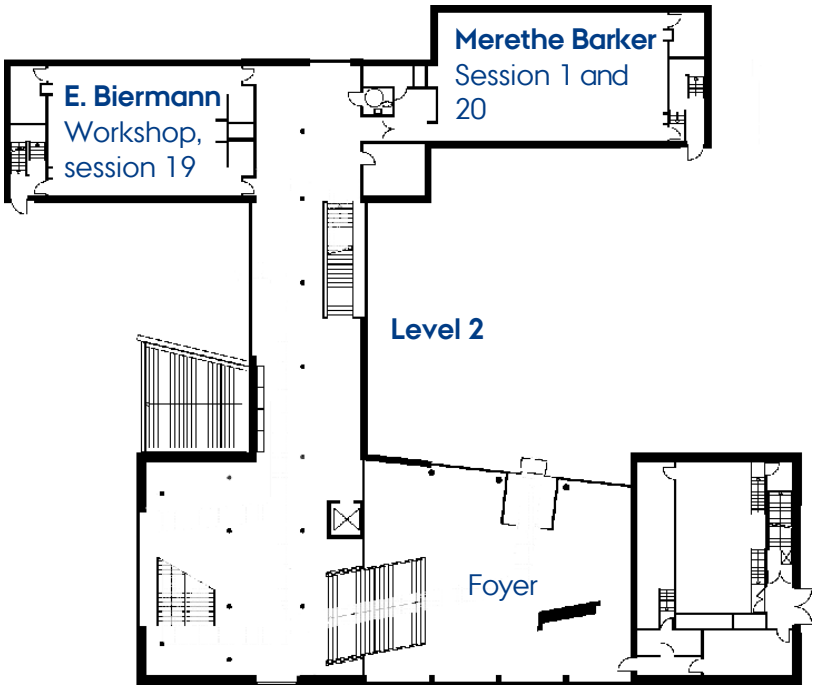


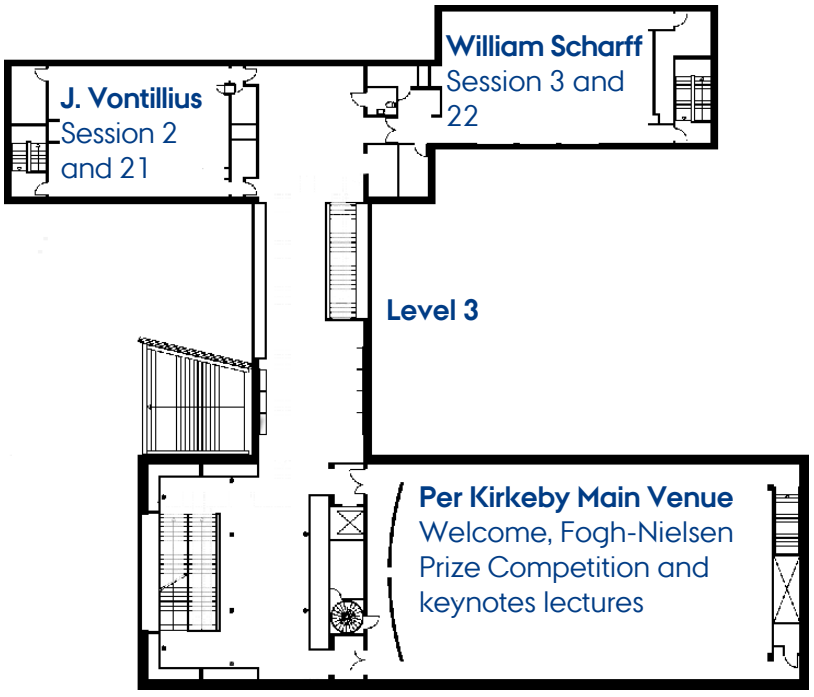
Anatomy (1232)
Session 4 and 23

Building 1264
Sessions 13-14 and 32-33

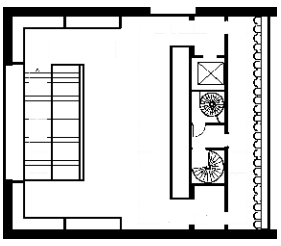
Public Medicine Auditorium (1262)
Session 12 and 31

Lakeside Lecture Theatres





Level 4



Session Chairs

Find yourself, abstract titles, and abstracts belonging to your session by searching the file (Ctrl+F)

Fogh-Nielsen Competition – 9.50 to 10.50

Chair: Ida Vogel

Co-chair: Anika Kofod Petersen

First Round of Sessions – 11.05 to 12.35

Session	Senior chair	Co-chair
1 - Basic medical research 1	Ole Halfdan Larsen	Maithri Prasad Aspari
2 – Surgery 1	Thomas Baad-Hansen	Josefine Beck Larsen
3 - Mental health 1	Christine Parsons	Oliver Kjærlund Hansen
4 - Endocrinology	Jens Bruun	Lukas Ochsner Ridder
5 - Bladder and kidney disease	Sebastian Frische	Kathrine Pedersen - **CANCELLED**
6 - Diabetes and cardiometabolic disease	Esben Søndergaard	Anders Mellemkjær
7 - Qualitative research and public health	Knud Ryom	Julie Hauer Vendelbo
8 - Imaging diagnostics	Marta Diaz Del Castillo	Karolina Klucznik
9 - Neuroscience 1	Kathrine Agergård Kaspersen	Emil Winkel
10 - Neuroscience 2	Poul Henning Jensen	Ina Grønkjær Laugesen
11 - Public health 1	Annett Dalbøge	Anitha Malling Tind
12 - Cardiovascular disease 1	Kasper G. Lauridsen	Christel Gry Aagren Nielsen
13 - Immune mediated diseases 1	Klaus Eyer	Lise Filt Jensen
14 - Rehabilitation	Julie Duval Jensen	Majbritt Jeppesen

15 - Cancer 1	Pia Kirkegaard	Anne Andresen
16 - Epidemiology	Alma Becic Pedersen	Camilla Kjersgaard
17 - Cancer diagnostics 1	Deirdre (dee) Cronin Fenton	Kristoffer Moos
18 - Drug risks and benefits	Natalya Fedosova	Søren Dabelsteen Isidor

Second Round of Sessions – 14.30 to 15.40

Session	**Senior chair**	**Co-chair**
19 - Basic medical research 2	Niels Okkels	Trine Rasmussen
20 - Reproductive health	Niels Uldbjerg	Anna Melgaard
21 - Neuroscience 3	Lise Kirstine Gormsen	Johannes Høgfeldt Jedrzejczyk
22 - Infectious disease biology	Jesper D. Gunst	Malene Risager Lykke
23 - Surgery 2	Katrine Emmertsen	Josephine Olsen Kipp
24 - Basic medical research 3	Gregers Wegener	Aisha Shigna Nadukkandy
25 - Cancer 2	Torben Stamm Mikkelsen	Christina Glismand Truelsen
26 - Public health 2	Dorte Rytter	Sofie Sejer Skoubo
27 - Health statistics	Jacob Johansen	Rasmus Klitgaard
28 - Diagnostics and technology	Thien Vinh Luong	Line Kristensen
29 - Mental health 2	Katherine Louise Musliner	Amalie Lambert Mørkved - **CANCELLED**
30 - Qualitative research and mental health	Anna Louise Skovgaard	Michella Runge K Bjerregaard
31 - Public health 3	Henrik Kolstad	Danni Chen
32 - Immune mediated diseases 2	Bent Winding Deleuran	Xiangning Ding
33 - Paediatrics	Konstantinos Kamperis	Nicolai Kjældgaard Kristensen

34 - Cardiovascular disease 2	Leila Louise Benhassen	Thomas Jensen
35 - Cancer 3	Maja Ludvigsen	Theresa Jakobsen - **CANCELLED**
36 - Dentistry	Rubens Spin-Neto	Shirin Haghshenas Bilehsavar
37 - Cancer diagnostics 2	Mette Madsen	Marvin Werner

Session Overview

Find abstract titles and abstracts by searching your name or session (Ctrl+F)

Fogh-Nielsen Competition – 9.50 to 10.50

1. Anne Kraushaar Martensen
2. Kirsten Woolpert
3. Martin Qvist Rasmussen

First Round of Sessions – 11.05 to 12.35

Session 1 - Basic medical research 1

Pitch
1. Ellen Hayhurst Appel - CANCELLED

Flash talk
2. Karina Rewitz
3. Pavani Rekulapally
4. Monja Rene Müller
5. Laura Elgaard Iisager Jensen
6. Saeideh Tavajoh
7. Anna Bøgh Lindholm
8. Maria Hønholt Jørgensen
9. Ditte Kamille Rasmussen
10. Ditte Marie Storm

Oral presentation
11. Clàudia Río-Bergé

Session 2 - Surgery 1

Pitch
1. Jacob Schade Engbjerg
2. Hannah Inez Houborg

Flash talk
3. Rasmus Roost Aabling
4. Christian Lind Nielsen
5. Laura Houstrup Matthiesen
6. Louise Schmidt Grau
7. Martin Mølhave
8. Tanita Drejer Jeppesen
9. Andreea-Alexandra Bach-Nielsen
10. David Kocemba

Oral presentation
11. Ida Kaad Faurschou

Session 3 - Mental health 1

Pitch
1. Marie Sønderstrup-Jensen
2. Emilie Roger Andersen
3. Katrine Bødkergaard Nielsen

Flash talk
4. Leonardo Melo Rothmann
5. Alisha Silvia Mercedes Hall
6. Ziping Zhang
7. Anne Marie Ladehoff Thomsen
8. Frida Hæstrup
9. Anette Faurskov Bundgaard
10. Jette Steinbach

Oral presentation
11. Camilla Termansen Erichsen

Session 4 - Endocrinology

Pitch
1. Laura Woidemann Trans
2. Victoria Bøttker
3. Thoranna Hlif Gilbertsdottir
4. Emaan Ghias
5. Ivonne Bedei
6. Thomas Hvid Jensen
7. Mohamed Hassan

Flash talk
8. Camilla Mains Balle
9. Trine Züricho Lyksholm
10. Ibrahim Alzaim
11. Julie Bondgaard Mortensen

Oral presentation
12. Hendrik Nicolaas Lourens

Session 5 - Bladder and kidney disease

Pitch

1. Kristine Aarup
2. Anne Sophie von Wowern
3. Ina Karstoft Ystrøm
4. Xabier Sørtvedt

Flash talk

5. Sandra Hansen
6. Peter Engholm Hjort
7. Benjamin Bach Green
8. Cristina Ballester I Bergadà
9. Malene Söth Andersen
10. Nathalie Demuth Fryd

Oral presentation

11. Nanna Østergaard Johnsen

Session 6 - Diabetes and cardiometabolic disease

Pitch

1. Tine Storebjerg Knudsen
2. Sarah Maria Thornhøj Eriksen
3. Jens Hohwü Voigt
4. Anna Dons-Jensen - CANCELLED

Flash talk

5. Natasha Amran Laursen
6. Vivi-Nelli Mäkinen
7. Ida Borreby Pedersen
8. David Haldrup
9. Natasa Brkovic Zubanovic
10. Mathias Flensted Poulsen **Oral presentation**
11. Katrine Høyer

Session 7 - Qualitative research and public health

Flash talk

1. Mette Eklund
2. Sissel Due Jensen
3. Kirstine Guld Frederiksen
4. Lene Gissel Rasmussen
5. Emil Weissmann Jensen
6. Stina Bollerup
7. Rikke Bjerre Lassen
8. Sarah Cecilie Tscherning
9. Charlotte Hald

Oral presentation

10. Helene Rask Dalby

Session 8 - Imaging diagnostics

Pitch

1. Kamilla Kørup Trosborg
2. Emma Paydari
3. Kasper Holst Hansen
4. Teresa Kirkegaard Jensen
5. Morten Hulbæk Fog

Flash talk

6. Niels Lech Pedersen
7. Giorgia Marino
8. Niels Abild Jespersen
9. Kristine Wiborg Høgsbjerg
10. Maja Kanstrup Jørgensen

Oral presentation

11. Nadia Iraqi

Session 9 - Neuroscience 1

Pitch

1. Sia Eleni
2. Louise Hill-Madsen
3. Caroline Vangsøe
4. Janne Auning Hansen
5. Chen Zhang

Flash talk

6. Silvia Genovese
7. Peter Andreas Andersen
8. Frederikke Lynge Sørensen
9. Simon Arvin
10. Jacob Drachmann

Oral presentation

11. Line Amalie Aarestrup Hellemose

Session 10 - Neuroscience 2

Pitch

1. Maria Hovmann Andresen
2. Emil Breinholt Sørensen
3. Tim-Simon Burmeister
4. Gaia Fanella
5. Emilie Dam Rosenberg

Flash talk

6. Fatemeh Yarmahmoudi - CANCELLED
7. Naja Helt Andersen
8. Jesper Helbo Storgaard
9. Johanne Aarup Lauritsen
10. Elizaveta Melnikova

Oral presentation

11. Lara Marziani

Session 11 - Public health 1

Pitch

1. Fridtjov Smith-Gahrsen Tvedten
2. Jacob Friso Wierema
3. Lise Kjær Schou
4. Sofie Bech Vestergaard
5. Nanna Emilie Nørgaard Eg

Flash talk

6. Anne Sofie Baymler Lundberg
7. Frederik Teicher Kirk
8. Bjarke Godske Baisner
9. Grace McKinney
10. Jesper Fjølner

Oral presentation

11. Fardous Reaz

Session 12 - Cardiovascular disease session 1

Pitch

1. Elena Jørgensen
2. Kathrine Abildskov Friis
3. Line Hjorth Stjernholm Nielsen
4. Anna Holtz Hansen
5. Lene Halkjær
6. Anne Lind Malte

Flash talk

7. Simon Graff
8. Yumeng Li
9. Tarannum Ara
10. Henriette Ladegård Skov

Oral presentation

11. Louise Bjerregaard Henningsen

Session 13 - Immune mediated diseases 1

Pitch

1. Agnete Overgaard Donskov
2. Nicolai Olesen Haahr
3. Nathalie Jäck

Flash talk

4. Nanna Sutter Rolighed
5. Kerstin De Keukeleere
6. Camilla Charlotte Mærsk-Møller
7. Sofie Rahbek Dorset
8. Maya Dyveke Schou
9. Giacomo Schmidt Frattari

Oral presentation

10. Yan Hu

Session 14 - Rehabilitation

Pitch

1. Frederik Bonde Jensen
2. Katrine Schilling Andersen
3. Johanne Kolind Bech

Flash talk

4. Trine Arnam-Olsen Moos
5. Katrine Astrup Sørensen
6. Mette Nørtoft Nielsen
7. Ann Louise Hanifa
8. Rikke Daugaard
9. Sedsel Kristine Stage Pedersen

Oral presentation

10. Johan Kløvgaard Sørensen

Session 15 - Cancer 1

Pitch

1. Lotte Krog Eriksen
2. Danny Mortensen
3. Naja Lange
4. Randi Kræmmer Nielsen
5. Stine Bisgaard Greve
6. Elisabeth Solmunde
7. Johanne Hollands Steffensen

Flash talk

8. Ida Ravnsbæk Johannsen
9. Ane-Kersti Skaarup Knudsen
10. Janni Mølsted Siemer

Oral presentation

11. Jonas Busk Holm

Session 16 - Epidemiology

Pitch

1. Cæcilie Laigaard Skejø
2. Nanna Makholm Østergård
3. Søren Korsgaard
4. Sissel Jessen Weissert

Flash talk

5. Sofie Kejlberg Al-Mashhadi
6. Christine Mailandt Ljungberg
7. Sidse Høyer
8. Mette Vestergård Pedersen
9. Anne Østergaard Nannsen

Oral presentation

10. Tina Lund Leunbach

Session 17 - Cancer diagnostics 1

Pitch

1. Sarah Søltoft Rasmussen
2. Lea Elisabeth Bank Kristensen
3. Emma Roger Andersen
4. Signe Bülow Therkildsen
5. Martin Kjær Simonsen
6. Mathias Hald
7. Simon Nørregaard Agersnap
8. Sarah Eckholdt Jensen

Flash talk

9. Lærke Rosenlund Nielsen
10. Anne Vittrup Jakobsen

Oral presentation

11. Sebastian Søby

Session 18 - Drug risks and benefits

Pitch

1. Sofie Lindman Juul
2. Anna Vingborg
3. Julie Loft Nagel
4. Ali Hussein Jaber Mejren

Flash talk

5. Ida Marie Marquart Løber
6. Marlene Schouby Bentestuen
7. Christian Byskov Nielsen
8. Abarajitha Thiyagarajah
9. Signe Dalsgaard Justesen

Oral presentation

10. Casper Homilius

Second Round of Sessions – 14.30 to 15.40

Session 19 - Basic medical research 2

Pitch

1. Andreas Møller Lind
2. Mette Skovbo Self
3. Anne Grosbøl Jensen
4. Jacob Hørlück Janns
5. Simon Bøje Fammé

Flash talk

6. Lena Anastasia Magdalena Nielsen
7. Virginia Fochi
8. Anne Mette Gissel Jensen
9. Lærke Bay Marcussen - **CANCELLED**

Oral presentation

10. Charlotte Nygaard

Session 20 - Reproductive health

Pitch

1. Johanne Berntsen
2. Maria Gabriela Barslev Jensen
3. Mette Jørgensen Langergaard
4. Karen Omann Binderup
5. Stine Bundgaard

Flash talk

6. Laura Bjerre Andersen
7. Lea Kirstine Hansen
8. Asli Sena Kücükyildiz
9. Helena Hørdum Breum Andersen - **CANCELLED**

Oral presentation

10. Josefine Tang Rørbech

Session 21 - Neuroscience 3

Pitch

1. Andreas Lund Pedersen
2. Julie Bjørn Bay

Flash talk

3. Saba Molhemi
4. Josefine Jul Jarbæk Nielsen
5. Nayereh Ghazi
6. Simon Kjær Simonsen
7. Andreas Færgemand Laursen
8. Benjamin Yamin Ali Khan

Oral presentaion

9. Ana Teresa Lourenço Queiroga

Session 22 - Infectious disease biology

Pitch

1. Maja Skjærbæk Sønderby
2. Sofia Sedó Korsgaard
3. Anders Birk Andersen
4. Jannifer Jasmin Thavarajah
5. Eva Anna Marianne Baerends
6. Laura Marie Aalkjær Danielsen
7. Maria Lange Pedersen
8. Nanna Pi Lauritsen
9. Siri Nana Halling Svensgaard
10. Rasmus Alstrup Nielsen

Oral presentation

11. Aimi Danielle Munk Hamilton

Session 23 - Surgery 2

Pitch

1. Rasmus Ilkjær
2. Christine Krogsgaard Schrøder
3. Mathias Høgsholt

Flash talk

4. Frederik Nicolai Foldager
5. Simon Storgaard Jensen
6. Karoline Assifuah Kristjansen
7. Kim Morgenstjerne Ørskov
8. Helle Joon Christiansen

Oral presentation

9. Christian Jessen

Session 24 - Basic medical research 3

Pitch

1. Nicolai Matias - **CANCELLED**
2. Vasileios Theologidis
3. Daniel Zornow Kruse
4. Marc Gjern Weiss
5. Cecilie Munch Johannsen
6. Jesper Frank Andersen
7. Amalie Dyrelund Broksø

Flash talk

8. Madison Clark
9. Pernille Lajer Sørensen **Oral presentation**
10. Ditte Emilie Munk

Session 25 - Cancer 2

Pitch

1. Jesper Huitfeld Jespersen
2. Mostafa Hossam Mahmoud M Khairy
3. Mette Kathrine Nygaard
4. Diana Faibish
5. Katharina Wolter
6. Cecilie Poulsen
7. Sofie Krarup Thomsen

Flash talk

8. Ronja Tügel Carstensen
9. Mathilde Søbye Blaavand

Oral presentation

10. Tobias Stemann Lau

Session 26 - Public health 3

Pitch

1. Freja Hauberg Hallen
2. Louise Birk Suder
3. Michelle Vestergaard Stadelhofer
4. Kristoffer Torp Hansen
5. Elisabeth Due Andersen
6. Cecilia Hee Laursen
7. Christian Emil Sejersen Brinck

Flash talk

8. Trine Brøns Nielsen
9. Asbjørn Frederik Kloppenborg

Session 27 - Health statistics

Pitch

1. Bertram Lahn Kirkegaard
2. Mathilde Diekema
3. Maria Louise Køpfli
4. Frederik Skovbo

Flash talk

5. Janus Rønn Lind Kobbersmed
6. Sky Rohrer - **CANCELLED**
7. Merete Ajstrup
8. Paul Jaques Gilbert Maublanc

Oral presentation

9. Mia Aagaard Doherty

Session 28 - Diagnostics and technology

Pitch

1. Anders Valentin Abildgaard Nielsen
2. Josefine Rosenskjold Madsen
3. Johannes Ulrich Wittig
4. Marius Eldevik Rusaas

Flash talk

5. Amalie Lykke Olsen
6. Helene Bei Thomsen
7. Sie Fensman
8. Siria Pasini

Oral presentation

9. Nora Spraakman

Session 29 - Mental health 2

Pitch

1. Yawei Ma
2. Christina Krogner Caspersen
3. Anna Westh Stenbro
4. Josefine Klakk Jeppesen
5. Lea Nørgaard Sørensen

Flash talk

6. Nina Friis Bak Fuglsang
7. Kirstine Bundsbæk Bøndergaard
8. Sara Kolding

Oral presentation

9. Thomas Tandrup Lamm

Session 30 - Qualitative research and mental health

Pitch

1. Johanne Farø

Flas talk

2. Athanasia Kontouli
3. Anne Poulsen
4. Inger Dorf
5. Manja Rothenberg
6. Cecilia Pihl Jespersen
7. Eileen Dorte Shanti Connelly

Oral presentation

8. Anne Wilhøft Kristensen

Session 31 - Public health 3

Pitch

1. Alexander Jahn Jensen
2. Anne Kristine Lundgård Christensen
3. Thea Emily Benson
4. Nanna Pedersen Larsson
5. Aurélie Mailhac

Flash talk

6. Christina Bisgaard Jensen
7. Marie Hauge Pedersen
8. Marie Dahl Jørgensen

Oral presentation

9. Mette Fogh

Session 32 - Immune mediated diseases

Pitch

1. Thea Hoffmann Nielsen
2. Nanna Mørk Vammen
3. Celine Thiesen
4. Lykke Mo Ran Skaarup
5. Samantha Nelson
6. Maja Louise Hansen

Flash talk

7. Christoffer Søvsø Våben
8. Josephine Gladov

Oral presentation

9. Fredrikke Tove Birgitta Dam Larsen

Session 33 - Paediatrics

Pitch

1. Rasmus Saul
2. Natalie Vestergaard Olesen
3. Lise Fischer Mikkelsen
4. Ann-Kristine Mandøe Svendsen
5. Bjarke Bøttger
6. Sigrid Agersnap Bom Nielsen

Flash talk

7. Mads Andersen
8. Sofie Axelgaard

Oral presentation

9. Anders Schram

Session 34 - Cardiovascular disease 2

Pitch

1. Maya Sanjuan Jensen
2. Archana Kulasingam

Flash talk

3. Maja Brøgger Thomassen
4. Jacob Hartmann Søby
5. Nina Stødkilde-Jørgensen
6. Malene Glud
7. Malene Højgaard Andersen

Oral presentation

8. Henrik Laurits Bjerre

Session 35 - Cancer 3

Pitch

1. Mette Møller Steiniche
2. Signe Hedebo Hansen
3. Malene Krabbe Østergaard

Flash talk

4. Christoph Felix Kollmann
5. Henriette Nymark Friis
6. Stine Mary Vissing
7. Silke Dahlbom Nielsen

Oral presentation

8. Asbjørn Kjær

Session 36 - Dentistry

Pitch

1. William Astrup Kaaber
2. Sara Volf Jensen
3. Karina Herholdt Petersen
4. Hossein Mohammad Rahimi Khansari
5. Sanyam Jain
6. Sukeshana Srivastav
7. Nicole Renner

Flash talk

8. Nicoline Hjort Larsen

Oral presentation

9. Anika Kofod Petersen

Session 37 - Cancer diagnostics 2

Pitch

1. Maiken Mondrup hjelt
2. Eva Ferlev Jensby
3. Mathilde Aalling
4. Casper Urth Pedersen
5. Deema Radif

Flash talk

6. Karoline Andersen

Oral presentation

7. Laura Andersen

PHD DAY 2025

Abstracts

Fogh-Nielsen Competition

Electrical stimulation as prevention of postoperative ileus

Anne Kraushaar Martensen, Department of Clinical Medicine, Departement of Surgery

Anne K Martensen1,2, Thomas Nielsen3, Anne B Bruun2, Mette M Sørensen4, Lene H Iversen1,2, Jonas A Funder1,4

1Department of Clinical Medicine, Aarhus University, Denmark, 2 Department of Surgery, Aarhus University Hospital, Denmark, 3 Department of Electrical and Computer Engineering, Section of Biomedical Engineering, Aarhus University, Denmark, 4 Department of Abdominal and Plastic Surgery, University Hospital of Southern Denmark, Vejle, Denmark

Background:

Postoperative ileus (POI) is a common complication following cytoreductive surgery (CRS), with no effective treatment available. Preclinical studies suggest electrical stimulation of the gastrointestinal tract may reduce POI duration. This study evaluates the safety and feasibility of stomach electrical stimulation in patients undergoing CRS.

Methods:

Patients scheduled for CRS were considered eligible. At the end of surgery, before closing the abdomen, a pacing wire was attached to the stomach, externalised through the abdominal wall, and connected to a pacemaker. Participants were randomised 1:1, with the pacemaker activated in the intervention group and inactive in the control group. Daily during hospitalisation, patients completed a diary assessing gastrointestinal function. The pacing wires were removed once normal gastrointestinal function was restored.

Results:

63 patients were eligible, and 27 patients (43%) consented to participate. Seven were excluded during surgery. To date, nineteen patients completed the intervention, 9 in the control group and 10 in the intervention group. The pacing leads were easily removed in all patients. The treatment was well tolerated. Both groups reported brief intra-abdominal muscle spasms. In the intervention group median number of days till first stool was 2,5 (range: 0-6), in the control group it was 4 (range: 3-6) (p=0.04).

Conclusion:

This study confirms that electrical stimulation of the stomach is both safe and feasible in the clinical setting. The intervention was well tolerated, supporting further clinical studies into electrical stimulation as a potential treatment for POI.

Themes: Surgery, Surgery
Keywords: Prevention, Postoperative complications, Ileus

Endocrine therapy adherence and effectiveness in premenopausal breast cancer patients

Kirsten Woolpert, Department of Clinical Medicine, Department of Clinical Epidemiology

K.M. Woolpert1, D.P. Cronin-Fenton1, P. Damkier2,3, A. Kjærsgaard1, S. Hamilton-Dutoit4, B. Ejlertsen5,6, R.F. MacLehose7, P. Christiansen5,8, R.A. Silliman9, T.L. Lash1,10,11, T.P. Ahern12, & L.J. Collin1,10,11,13

1 Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Denmark, 2 Department of Clinical Pharmacology, Odense University Hospital, Odense, Denmark, 3 Department of Clinical Research, University of Southern Denmark, Odense, Denmark, 4 Department of Pathology, Aarhus University Hospital, Aarhus, Denmark, 5 On behalf of the Danish Breast Cancer Group; Department of Oncology, Rigshospitalet, Copenhagen, Denmark, 6 Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, 7 Division of Epidemiology & Community Health, University of Minnesota School of Public Health, Minneapolis, MN, USA, 8 Department of Plastic and Breast Surgery, Aarhus University Hospital, Aarhus, Denmark, 9 Section of Geriatrics, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, USA, 10 Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA, 11 Winship Cancer Institute, Emory University, Atlanta, Georgia, USA, 12 Department of Surgery, The Robert Larner, M.D., College of Medicine at the University of Vermont, Burlington, Vermont, USA, 13 Department of Population Health Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, USA

Introduction

Tamoxifen is guideline treatment for most premenopausal breast cancer patients. Therapeutic efficacy arises in part from biotransformation of tamoxifen by CYP2D6, CYP2C19, and CYP3A4 enzymes. Pharmaceutical inhibition of these enzymes may impact breast cancer recurrence, but previous studies may have been biased by not accounting for longitudinal associations between CYP-inhibiting medication use and recurrence hazard.

Methods

We enrolled 5,959 premenopausal breast cancer patients in Denmark (2002– 2011), divided into estrogen receptor-positive (ER+) tumors treated with tamoxifen, and ER-negative (ER–) tumors not treated with tamoxifen. We defined time-varying medication exposures to each enzyme inhibitor based on the proportion of overlap with the tamoxifen treatment period. We estimated associations of concomitant medication use with recurrence (hazard ratios [HR] and 95% confidence intervals [95%CI]) using: (1) Bayesian joint modeling and (2) Cox regression.

Results

With Bayesian joint modeling, women with >50% overlap in tamoxifen and CYP2D6-inhibiting medication use had increased recurrence compared with non-users (HR: 1.24, 95%CI: 0.96, 1.58). No association was seen for CYP2C19-inhibiting medication- and tamoxifen-use with recurrence (>50% vs. 0%, HR=1.0, 95%CI: 0.69, 1.40), but Cox models yielded positive associations (>50% vs. 0%, HR=1.45, 95%CI: 1.07, 1.96), even in ER– patients who were never prescribed tamoxifen (>50% vs. 0%, HR=1.93, 95%CI: 1.03, 3.62).

Conclusion

We observed improbable estimates using Cox regression in this study. With Bayesian joint modeling, we saw a slight increase in recurrence among ER+ users of CYP2D6-inhibiting medications.

Themes: Epidemiology, Cancer
Keywords: drug interactions, tamoxifen, pharmacoepidemiology

Megalin-targeting antibody-drug conjugates for treatment of epithelioid mesothelioma

Martin Qvist Rasmussen, Department of Biomedicin, Infection and Inflammation

MQ Rasmussen1, H Hager2, JH Graversen3, M Madsen1, SK Moestrup1,3

1 Department of Biomedicine, Aarhus University, Aarhus, Denmark, 2 Department of Pathology, Aarhus University Hospital, Aarhus, Denmark, 3 Department of Molecular Medicine, University of Southern Denmark, Odense, Denmark

Background

Megalin is a large endocytic membrane receptor involved in ligand uptake in absorptive epithelial cells. In healthy adults, megalin displays a highly restricted expression pattern, with kidney proximal tubule epithelial cells being the major site of expression. Megalin is also expressed in several epithelial cancer types, particularly in epithelioid mesothelioma, an asbestos-related cancer arising from mesothelial cells in the pleural cavity, for which there is a poor prognosis and limited treatments. Megalin is localized to the apical cell surface (facing the pleural cavity) of mesothelioma cells. Based on these observations, we now investigate megalin as a target for drug delivery in mesothelioma, which can be reached by local administration to the pleural cavity.

Results

Mouse monoclonal antibodies demonstrating specific binding to megalin were developed and used to demonstrate cell surface location of megalin on mesothelioma cells, which exhibited a highly polarized phenotype with megalin concentrated in the apical membrane. Moreover, the antibodies underwent internalization and trafficking to intracellular vesicles in megalin-expressing cancer cells. Megalin-targeting antibody-drug conjugates efficiently killed megalin-expressing cancer cells in vitro. The cytotoxic effect was completely absent after genetic inactivation of the megalin gene.

Conclusion

Megalin-targeting antibody-drug conjugates were generated and showed potent and selective killing of megalin-expressing cancer cell lines in vitro. These data encourage future preclinical development of megalin-targeting antibody-drug conjugates for cancer treatment.

Themes: Cancer, Molecular biology
Keywords: Cancer, Molecular target, Antibody-drug conjugates

FIRST ROUND OF SESSIONS

SESSION 1 - Basic medical research 1

Utilizing reprogrammable ADAR-based RNA sensors for novel intracellular cytokine detection - CANCELLED

Ellen Hayhurst Appel, Department of Biomedicin, Personalised Medicine

K. Mikkelsen1, R.O. Bak1

1 Department of Biomedicine, Aarhus University

Cytokines are small proteins secreted mainly by cells in the immune system. Because they are continuously secreted, tracking their expression in real time within live cells is challenging. Traditional methods require fluorescent tagging or cell fixation for intracellular antibody staining, which results in cell death. Here, we use the RADAR tool as a novel approach for intracellular detection of cytokine mRNA transcripts in live cells.

RADAR (RNA sensors using ADAR) is a new RNA-based sensor that is programmed to detect other RNA transcripts by binding to these via base complementarity, upon which the sensor is edited by the enzyme adenosine deaminase acting on RNA (ADAR). ADAR edits an adenosine within a user-designed UAG stop codon in the sensor, converting it to the base inosine, which is read as guanosine. This change converts the stop codon into a sense codon, releasing a downstream user-defined cargo for translation, for instance a reporter protein.

By transfecting HEK293T cells with RADAR, ADAR, and a cytokine-overexpressing plasmid, we successfully detected various cytokine mRNAs in real-time by using the RADAR system with a fluorescent cargo for flow cytometry or a luciferase-based cargo for luminescence. Furthermore, next-generation sequencing confirmed the stop codon conversion by RNA base editing. With further optimisations in RADAR specificity and sensitivity, we aim to shift plasmid-based RADARs to mRNA and/or lentiviral -vector-based RADARs for implementation in primary cells. From there, the RADAR system has strong potential for tracking or influencing cells based on mRNA detection, both in vitro and possibly in vivo.

Themes: Molecular biology, Genetic engineering
Keywords: RNA sensing, Immunology, RNA editing

Real-Time Visualization of Copper Uptake in HepG2 Cells Using the Ligand Tracer Method

Karina Rewitz, Department of Clinical Medicine, Afdelingen for Lever- og Mavetarmsygdomme AUH

Mikkel Holm Vendelbo 2, Mie Ringgaard Dollerup 2, Mia Koldby Blum 1, Peter Ott 1 and Thomas Damgaard Sandahl 1

1 Department of Hepatology and Gastroenterology, Aarhus University Hospital, 2 Department of Nuclear Medicine and PET-Centre, Aarhus University Hospital

Background: Copper (Cu) is necessary for various cellular processes, including mitochondrial respiration, connective tissue production, and neurotransmitter synthesis. The high-affinity copper transporter CTR1 mediates the primary copper uptake. Traditional copper uptake studies compile data from separate experiments with varying substrate concentrations, potentially missing dynamic processes. With the Ligand Tracer method, we aim to visualize real-time changes in cellular copper influx.

Methods: The Ligand Tracer White features a beta-emission detector and a rotating platform holding a standard Petri dish. HepG2 cells were plated 48 hours before experiments. Each 135-minute experiment included interventions every 15 minutes, involving the addition of 1 uM copper chloride (Cu(II)Cl) and radioactive 64Cu at a constant tracer-to-trace ratio (TTR). The petri dish, inclined at 30 degrees from the vertical, alternates between immersing cells in radioactive media (for 30 s.) and positioning them under the detector (for 30 s.). When submerged in media, cells take up Cu(I) and 64Cu. The activity of 64Cu is recorded as counts per second (CPS) and given a constant TTR, CPS reflects the total intracellular copper levels.

Results: Preliminary data indicates that increasing copper concentrations steepens the slope of each segment, reflecting elevated uptake rates until saturation is reached. The Km was 2.212 +- 0.856 uM, which aligns with the existing literature. Introducing silver, a known competitive substrate for CTR1, reduced copper uptake significantly.

Conclusion: This in vitro Ligand Tracer assay demonstrates its potential for studying real-time copper uptake into cells.

Themes: Molecular biology, Gastroenterology and hepatology
Keywords: Copper uptake, Ligand Tracer, Wilson Disease

New players involved in the establishment of phagophore-endoplasmic reticulum membrane contact sites (peMCSs)

Pavani Rekulapally, Department of Biomedicin, 4 minute flash talk

Pavani Rekulapally1, Ruben Gomez Sanchez 2, Fulvio Reggiori*1

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Autophagy is a cellular degradation process essential for maintaining homeostasis. The formation of the phagophore, a membrane cisterna, and its elongation and closure into a double-membrane autophagosome is essential for sequestering cytoplasmic material for lysosomal/vacuolar degradation. Recent studies in yeast Saccharomyces cerevisiae have shown that membrane contact sites (peMCSs) between the phagophore and the endoplasmic reticulum (ER), the formation of which is primarily mediated by the Atg2-Atg9-Atg18 complex, facilitate the lipid transfer required for the phagophore elongation. Interestingly, the loss of Atg2 or Atg9 does not inhibit the phagophore connection with the ER, suggesting the involvement of additional unidentified proteins in peMCSs formation. Here, we report new candidate proteins that may participate in the formation of peMCSs, identified through a meta-analysis of proteomic and genetic datasets focused on Atg2 and Atg9. Fluorescence microscopy experiments revealed that approximately 25-30% of new potential candidate proteins colocalize to the phagophore. We are currently investigating the functions of these proteins in the orchestration of peMCSs formation.

Themes: Molecular biology, Imaging techniques
Keywords: Autophagy, Membrane contact sites,

The role of ubiquitination in the mechanism and regulation of aggrephagy

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In a healthy organism, cytoplasmic protein aggregates are recognized and degraded by the autophagosomal-lysosomal system, in a selective process known as aggrephagy. With our novel system of particles induced by multimerization (PIM), we can track the formation of GFP-RFP-tagged PIM-aggregates, measure their lysosomal delivery by aggrephagy and recruitment of aggrephagy factors, and their subsequent lysosomal degradation. We recently showed that the degradation of PIM aggregates takes place through three main mechanisms. The first one is classical macroautophagy, which includes the involvement of the autophagy machinery, including the autophagy regulator FIP200. The second only utilizes FIP200 from the classical autophagy machinery. The third mechanism involves neither the autophagy machinery, nor FIP200, but it requires TBK1 and selective autophagy receptors like p62 and TAX1BP1. Employing super-resolution microscopy, I showed that there is a specific time-dependent ubiquitination pattern on PIM aggregates, composed of mainly M1-, but also K48- and K63-containing ubiquitin chains. By inhibiting the E3 ubiquitin ligase LUBAC, which is essential for M1-ubiquitination, PIM degradation is decreased, suggesting a pivotal role of this specific ubiquitin modification during aggrephagy. We plan to conduct a siRNA-based screen for E3 ubiquitin ligases to unravel which other ubiquitin modifications play a key role in aggrephagy. By understanding how protein aggregates get degraded via aggrephagy, we might be able to understand the etiology behind pathological accumulation of toxic aggregates in neurodegenerative diseases.

Themes: Molecular biology, Neurodegenerative disorders
Keywords: Autophagy, Protein aggregation, Ubiquitination

Integrative Analysis of Methylation Alterations and Copy Number Variants for Biomarker Discovery in Renal Cell Carcinoma

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Clear cell renal cell carcinoma (ccRCC) cases are increasing worldwide, with about 20% being detected at an advanced disease stage and another 15% experiencing relapse after curative treatment of their localized disease. A few studies have proposed circulating tumor DNA (ctDNA) as a promising prognostic tool in ccRCC, but analyses have been challenged by the trace amounts of ctDNA shedded by ccRCC tumors.

In this project, we aim to investigate ctDNA as a more precise method for risk stratification and as a sensitive marker for relapse detection. We have analyzed the genomic and epigenomic landscape of tumor (n = 118) and normal (n = 45) tissue samples from 118 ccRCC patients across disease stages using the sensitive cell-free methylated DNA immunoprecipitation sequencing (cfMeDIP-seq) method and compared these profiles to blood samples from 20 healthy donors. We have identified characteristic copy number alterations in ccRCC tumor tissue, including significant losses in chromosomes 3p and 14q as well as gain in chromosome 5q, distinguishing them from donor and normal tissue samples. Additionally, within chromosome 3p, we confirmed significant losses at the gene level in the three well-known tumor suppressor genes VHL, PBRM1, and SETD2.

Our future work includes the identification of differentially methylated regions and the development of a tumor-based cfMeDIP-seq classifier for ctDNA detection. ctDNA will be assessed in plasma from 100 localized ccRCC patients collected before and after surgery using this tumor-based cfMeDIP-seq classifier.

Themes: Molecular biology, Cancer
Keywords: Renal cancer, Biomarker, cfMeDIP-seq

Inflammatory resolution in cardiometabolic health and disease

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Background & Aims:

Approximately 30% of obese individuals are protected against conditions like diabetes, dyslipidemia, and hypertension. This study investigates the mechanisms behind why some obese individuals remain metabolically healthy, focusing on the role of inflammatory resolution. By exploring resolution pathways, we aim to better understand susceptibility to cardiometabolic diseases.

Methods:

We classified both lean (L) and obese (O) participants as either metabolically healthy (MH) or unhealthy (MU); recruiting 5-20 individuals per group and sex. Biological samples were collected to examine inflammatory parameters across lean and obese participants. We used flow cytometry and proteomic profiling (using Olink's Proximity Extension Assay) of plasma, along with a "blister model" of inflammation where immune cells and fluid from induced blisters were sampled. We also tested the effect of lipoxins on neutrophil-platelet aggregation ex vivo.

Results:

Obese individuals exhibited higher systemic low-grade inflammation, with elevated CRP levels than lean participants. The unhealthy obese group had significantly higher counts of total leukocytes, neutrophils, and B-lymphocytes. Olink plasma and blister fluid analyses revealed distinct biomarker profiles across different phenotypes and changes between inflammatory and resolving time points in the blister model, respectively. Ex vivo treatment of blood samples with lipoxins significantly reduced the number of platelet-positive neutrophils.

Conclusion:

These results underscore the important role of inflammation in the progression of cardiometabolic diseases among obese individuals and potential therapeutic effect of lipoxin.

Themes: Molecular biology, Molecular biology
Keywords: Inflammation, Obesity, Cardiometabolic diseases

Characterization of primary porcine retinal endothelial cells and pericytes co-isolated with a developed method

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Background: The prevalence of diabetes is increasing globally, impacting millions of people worldwide. Diabetic retinopathy (DR) is a common microvascular complication of diabetes and a leading cause of vision impairment. Current treatments against DR are directed towards the advanced disease stages and do not address the mechanisms driving disease progression. Consequently, there is a need to identify potential targets for early-stage intervention. Although there are gaps in the understanding of DR pathogenesis, recent studies have shown that early stages of DR are largely driven by angiogenesis-related proteins primarily derived from endothelial cells (ECs) and pericytes (PCs).

Aim: To achieve monocultures of primary porcine retinal ECs (ppECs) and PCs (ppPCs) for translationally relevant in vitro analysis of retinal vascular function.

Results: We have developed a simple protocol that allows the co-isolation of monocultures of ppECs and ppPCs. Important optimization steps of the protocol included seeding density, toxin inclusion and specialized culture conditions. Cells have been characterized by immunofluorescent staining and qPCR analysis of cell-specific proteins and genes, respectively. The results validate the claimed cell types, thus supporting the model for further exploration of retinal vascular function.

Perspectives: Due to the anatomical and physiological similarities between porcine and human eyes, porcine eyes are highly valuable for experimental research. In vitro studies in primary vascular cells isolated from porcine eyes will provide significant insight into vascular barrier properties, enabling comparisons between the diseased and healthy retina.

Themes: Molecular biology, Endocrinology
Keywords: Method development, Primary cells, Laboratory science

Advancing Clinical Implementation of ctDNA Detection Through External Quality Assessment

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In cancer patients, circulating tumor DNA (ctDNA) is shed from tumors and constitutes a small fraction of the total circulating cell-free DNA. ctDNA contains unique cancer-specific characteristics, such as mutations and methylation patterns, making it a promising blood-based biomarker. However, for ctDNA to be implemented in routine clinical practice, laboratory workflows, including detection methods, must be standardised and harmonised.

We established a setup for external quality assessment (EQA) to heighten and harmonise the quality of ctDNA detection in all parts of Denmark. We developed a protocol for producing ctDNA reference samples with common driver mutations, including actionable variants. In the first two EQA rounds 265 reference samples with varying ctDNA levels, were sent in a blinded manner to 16 national and international laboratories for analysis using their standard protocols. Laboratories reported whether they deemed each sample positive for ctDNA, the ctDNA levels measured, and selected details of the methods used for ctDNA detection.

Laboratories were evaluated for their sensitivity and ability to correctly identify samples positive for ctDNA. True positive rates for each laboratory ranged from 41.6% to 100%. Successful detection of ctDNA in at least one sample with the lowest ctDNA level was achieved by 7 laboratories. Among the laboratories analysing negative samples, 50% reported at least one false positive, with false positive rates ranging from 8% to 75%.

This EQA provides a framework for quality assessment of ctDNA detection and certification of ctDNA methods, contributing to the standardisation of practices across laboratories.

Themes: Molecular biology, Cancer
Keywords: ctDNA, External Quality Assessment, Reference Material

Megalin ablation causes impaired heterophagy relevant in age-related macular degeneration

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Age-related macular degeneration (AMD) is the most common cause of blindness in the Western world. The pathophysiology of this disease involves accumulation of undigested remnants of photoreceptor outer segments (POS) in the retinal pigment epithelium (RPE). These remnants can accumulate if the lysosomal system is dysfunctional, which is a known consequence of megalin deficiency in other tissues including the kidney. My working hypothesis is that megalin deficiency cause compromised lysosomal function which contributes to AMD risk.

We differentiated induced pluripotent stem cells into mature RPE monolayers and used short hairpin RNA to knock megalin expression down. Downregulation of megalin was verified by q-RT-PCR, Western blotting and immunocytochemistry. Cells were fed with bovine POS, and trafficking and degradation were evaluated by immunocytochemistry and Western blotting. Aptamer-based proteomics of cell lysate was used to evaluate intracellular changes following megalin ablation. Analyses of tissue from our inducible megalin knockout mouse model was done by immunohistochemistry and Western blotting.

Megalin-knockdown in RPE cells caused slower trafficking of POS to lysosomes as well as delayed degradation of POS particles. Proteomics revealed downregulation of several key pathways including heterophagy. In mice, rhodopsin, which is part of POS, accumulated in the RPE in line with our in vitro data. Furthermore, we found a delayed activation of lysosomal cathepsin D, which also indicates lysosomal malfunction.

We conclude that megalin downregulation induces a lysosomal phenotype resulting in delayed degradation of POS, which could contribute to AMD risk.

Themes: Molecular biology, Imaging techniques
Keywords: Age-related macular degeneration, Megalin, Retinal dystrophy

Vascular and metabolic dysfunction in adipose tissue: a dangerous duo in obesity

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Adipose tissue (AT) functionality is dependent on a continuous exchange of nutrients and hormones, which is regulated by the AT vascular barrier and AT blood flow (ATBF). The ATBF is controlled by innervation as well as by an interplay between adipocytes (among other AT cells), and the cells constituting the AT vasculature. Importantly, in people living with obesity and/or insulin resistance, the ATBF is disturbed during fasting and in the post prandial state, which exacerbates cardiometabolic complications. We hypothesize that impaired cellular crosstalk within AT drives ATBF dysregulation and cardiometabolic complications in people living with obesity.

The aim of this project is to identify cellular determinants of ATBF functionality and investigate their correlation with clinical features like obesity. We will thoroughly analyse transcriptomic data, captured at the single-cell level, from human AT samples that showcase both functional and dysfunctional AT states. Our study groups include individuals with insulin resistance, those with normal glucose tolerance, those assessed for ATBF (obese both before and after lifestyle intervention), and a control lean and obese group. Key determinants of ATBF, identified either in clinical studies or in the transcriptomic data, are further explored in vitro in primary cells from human AT (endothelial cells, smooth muscle cells, and pericytes) and ex vivo in whole-mount stainings of human AT. In short, we plan to elucidate the molecular mechanisms and cellular crosstalk that governs the ATBF.

Themes: Molecular biology, Endocrinology
Keywords: Adipose tissue, Vasculature, Obesity

ER-phagy-related proteins: enemies or allies of virus infections?

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The selective autophagy of the endoplasmic reticulum (ER), ER-phagy, involves the lysosomal degradation of ER fragments. ER-phagy contributes to the cell homeostasis, and it also appears to be a mechanism against pathogens, including viruses. The ER is a key organelle exploited by multiple viruses to promote their propagation, so ER-phagy may affect their replication with pro-viral or anti-viral effects. So far, only two direct associations have been described in molecular detail, i.e., the one between the ER-phagy receptors FAM134B and ATL2 and SARS-CoV-2, and the one between FAM134B and dengue and Zika viruses. Thus, virus-ER-phagy interactions remain largely unexplored, and previous studies only focused on specific viruses and/or ER-phagy components. We applied a systematic approach to investigate the extent to which ER-phagy and viruses interact. We designed a siRNA library targeting each gene specifically involved in ER-phagy and used it to study the relevance of ER-phagy in the replication of ten viruses from eight different families. Our screen identified several ER-phagy-related genes that appear to promote or prevent viral replication. Interestingly, ER-phagy may play a role in the life cycle of herpes simplex virus 1 and coxsackievirus B3, while specific genes may have ER-phagy-unrelated functions in the replication of the other tested viruses. Follow-up experiments will elucidate the mechanistic aspects of some of these interactions, providing new insights into the role of ER-phagy and ER-phagy-associated proteins in viral infections as well as the subversion strategies adopted by viruses, which could be key for the future development of anti-viral therapies.

Themes: Infectious Diseases, Molecular biology
Keywords: Selective autophagy, Endoplasmic reticulum, Viral hijacking

SESSION 2 - Surgery 1

Is the Tip-Apex-Distance associated with the risk of reoperation after osteosynthesis with DHS in femoral neck fractures?

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Dynamic hip screw (DHS) fixation is a common surgical procedure for femoral neck fractures (FNF). Tip-apex distance (TAD), is a radiographic measurement used to assess the position of the screw in the femoral head. Studies suggest that a TAD > 25 mm is a risk factor for screw cut-out. Failure of the DHS (e.g. cut-out) often results in reoperation. This study investigates the association between TAD and postoperative complications following DHS osteosynthesis of FNF.

A retrospective review was conducted of all patients undergoing DHS treatment for FNF at Regional Hospital Randers between 2015 and 2021 (n=325). Patients were identified through the Central Denmark Region's Business Intelligence portal using diagnosis code DS720. The primary outcome measure was a composite of complications identified on radiographs (e.g., cut-out) and reoperation within 2 years. Radiographs were evaluated for TAD and postoperative complications/reoperations. The Mann-Whitney test was applied to assess the data.

The overall complication and reoperation rate was 14.5 % within 1 year, and 16.0% within 2 years. The median TAD was 16.3 mm (IQR 13.8;18.7)), with no significant difference (p = 0.56) between patients with and without complications < 1 year, TAD 16.3 mm (13.7;18.7) vs. 16.7 mm (14.1;19.2). No significant difference was found between patients with and without complications < 2 years (p=0.99), TAD 16.3 mm (13.7;18.7), and 16.6 mm (14;18.5). Interestingly, there were 53/325 TAD > 20 mm and 6/325 TAD >25 mm.

We report no association between TAD and complication rates following DHS fixation for FNF. The relatively few TAD outliers did not result in an increased risk of complications.

Themes: Surgery, Surgery
Keywords: Hip Fractures, Dynamic Hip Screw, Complication- and Reoperation Rate

Tonsillectomy versus Tonsillotomy in the treatment of Recurrent Acute Tonsillitis: A Randomized Controlled Non-inferiority Trial

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BACKGROUND: Recurrent acute tonsillitis (RT) is frequent condition among young adults causing episodes of throat pain, fever, sick leave and impaired quality of life (QOL). Tonsillectomy (TE), the complete removal of the tonsils, is the only current well-documented treatment, and 4000 surgeries performed annually in Denmark for RT. TE is efficient, but associated with significant morbidity (e.g. pain and risk of postoperative bleeding). Recent studies suggest that tonsillotomy (TO), the partial removal of the tonsils, may be equally effective as TE but with significantly less morbidity. The current study aims to clarify whether TE is as effective as TO in the treatment of RT.

METHODS: This is a two-armed, randomized, controlled, non-blinded trial allocating RT patients for TE or TO. We will include 250 patients aged ≥15 years with RT (≥5 tonsillitis episodes in one year ≥3 tonsillitis episodes per year for two years). Primary outcome measures are the number of sore throat episodes and QOL scores 12 months after TE vs. TO and postoperative pain scores after TE vs. TO.

DISCUSSION: The study has the potential to alter the surgical approach to one of the most prevalent diseases in young adults in Denmark and globally by reducing the pronounced postoperative pain and substantial risk of bleeding without compromising the benefits of intervention. Our results may be directly implemented in clinical guidelines and improve the management of numerous future RT patients.

Themes: Surgery, Infectious Diseases
Keywords: tonsillectomy, tonsillotomy, recurrent acute tonsillitis

Allogenic mesenchymal stem cell intraarticular injection for knee osteoarthritis therapy, an RCT explorative mode-of-action study

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Background: Knee osteoarthritis is a progressive chronic inflammatory degenerative disease characterized by the gradual breakdown of cartilage in the knee joint, leading to pain and reduced mobility. Current treatments rely on pain relievers, physiotherapy, and joint replacement in severe cases. These treatments primarily focus on symptom relief rather than halting disease progression. Mesenchymal stem cell (MSCs) injections into the knee represent a novel treatment approach that not only offers pain relief but also reduces inflammation and has cartilage-regenerative properties.

Objective: To evaluate the pain-relieving and cartilage-regenerating effects of MSC treatment in patients with knee osteoarthritis.

Method: In a randomized placebo controlled clinical trial, 80 patients with mild to moderate knee osteoarthritis will be included. Of these, 40 patients will receive MSCs injections into the knee, while the other 40 will receive saline (placebo). All participants will be monitored for two years with clinical examinations and MRI scans to assess the effect of MSCs on the osteoarthritic knees.

Perspective: MSC therapy for osteoarthritic knees has the potential to delay or even prevent the need for joint replacement surgery, and it is anticipated that this technique could eventually be applied to other osteoarthritic joints.

Themes: Surgery, Diagnostics & technology
Keywords: Adipose derived mesenchymal stem cells, Regenerative Medicine, Knee osteoarthritis

Vascularized fibular grafting following tumor resection demonstrates acceptable long-term outcomes in Denmark: a national retrospective cohort study

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Background and purpose: Vascularized fibular grafting following tumor resection is an essential treatment option in limb salvage surgery. This study aimed to assess the surgical and oncological outcomes of patients treated in Denmark between 2010 and 2022.

Methods: We present a retrospective review of a national cohort comprising 27 patients. The indications were 13 cases of Ewing sarcoma, 12 cases of osteosarcoma, and 2 cases of giant cell tumor. The median age at surgery was 16 years (IQR: 10-18), and the median follow-up was 82 months (IQR: 32-101). Patients were analyzed overall and stratified into upper and lower extremity groups based on tumor location.

Results: The primary rate of graft union was 63%, and after secondary procedures, the overall rate of graft union was 67%, with a median time to union of 13 months (IQR: 9-17). The reoperation rate was 74%, while the limb salvage rate was 93%, with two patients undergoing amputation during follow-up. The 5-year overall survival rate was 81% (95% CI: 61-92). Patients with upper extremity tumors were more likely to attain graft union (92% vs. 47%, p=0.02) and less likely to undergo multiple reoperations (17% vs 60%, p=0.047) than patients with lower extremity tumors.

Conclusions: Vascularized fibula grafting remains a valuable option in limb salvage surgery with acceptable long-term outcomes. However, especially in lower extremity cases, a low rate of graft union and multiple reoperations are to be expected.

Themes: Surgery, Cancer
Keywords: Orthopedic Oncology, Sarcoma, Limb-Salvage Surgery

Reoperations after Percutaneous Needle Fasciotomy for Dupuytren's Contracture – A retrospective cohort study

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Background:

Dupuytren's contracture is a progressive hand disease causing finger flexion contracture. Percutaneous Needle Fasciotomy (PNF) is a minimal invasive surgical procedure using a thin needle to release the Dupuytren cord until the finger can be extended.

The purpose of the study was to estimate the reoperation rate after PNF due to recurrence, defined as any subsequent treatment in a previously PNF-treated finger.

Methods:

This is a register-based, follow-up study on PNF-treated patients at Silkeborg Regional Hospital, Denmark, between 2007-15. The first PNF procedure within the study period was defined as index procedure. Succeeding data relative to the PNF index procedure were extracted from the Danish National Health Registries in 2018 to identify possible reoperation procedures.

Medical records were reviewed to validate reoperations performed at Silkeborg Regional Hospital (Silkeborg subcohort). We evaluated the reoperation rate in the Silkeborg subcohort with further best/worst case scenarios on the total cohort.

Results:

A total of 2,257 unique patients (3,331 PNF-treated fingers) were identified. Of those, 1,724 (76%) patients (2,511 (75%) fingers) were included in the Silkeborg cohort. The reoperation rate in the Silkeborg cohort was 28% at a median follow-up time of 6.8 (IQR: 4.6-9.3) years. The reoperation rate in the total cohort was estimated to be between 21% and 46% at median follow-up time of 7.2 (IQR: 4.9-9.5) years.

Conclusion:

This study provides valuable information about reoperations after PNF, which may be useful to patients and providers when discussing the options and making decisions regarding Dupuytren's contracture management

Themes: Surgery, Epidemiology
Keywords: Reoperation, Dupuytren, Fasciotomy

Dorsal genital nerve stimulation in patients with faecal incontinence and faecal urgency - a feasibility study with the novel UCon neurostimulator

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Background: The UCon neurostimulator is a novel device providing dorsal genital nerve (DGN) stimulation. DGN stimulation has shown effectiveness in treating faecal incontinence (FI) in experimental studies. The aim was to explore the safety and the efficacy of the UCon neurostimulator in FI/faecal urgency (FU). We hypothesized that DGN stimulation with UCon would be feasible and safe, while reducing FI and strong FU episodes.

Method: A prospective two-centre feasibility study in Denmark. Inclusion criteria: ≥18 years reporting FI ≥1/week and/or strong FU ≥3/week along with a St. Mark's Incontinence Score (SMIS) ≥9.

The UCon neurostimulator is connected via adhesive electrodes placed at clitoral hood/root of penis. Home stimulation, time-limited (30 minutes/day) or urge/on-demand (60 sec. session), was performed daily for four weeks. Safety was evaluated based on device-related serious and adverse events.

Evaluation of efficacy was based on a 14-day bowel habit diary and SMIS.

Results: Forty patients consented to participate (39 women) with a median age of 62 years (interquartile range 54-69 years); 26 completed the study. Drop-out rate during the intervention was 23.5% and no serious device-related adverse events were seen. FI episodes (n = 19 with ≥1 episode/week) 14 patients (74%) had ≥50% reduction (p = 0.005). FU episodes (n = 14 with ≥3 episodes/week) 6 patients (43%) had ≥50% reduction (p 0.001). SMIS (n = 26) was significantly reduced from 16.0 (13-18) to 11.5 (9-15) (p 0.001).

Conclusion: Use of the UCon neurostimulator was both feasible and safe. A 4-week stimulation period demonstrated, with significance, positive results in the treatment of FI and FU.

Themes: Surgery, Diagnostics & technology
Keywords: faecal incontinence, dorsal genital nerve electrical stimulation, new device

Evaluating Tonsil Surgery Quality in Denmark: Completeness of Data in the Danish Tonsil Database

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Background: Tonsil operations, including tonsillectomies, tonsillotomies, and adenoidectomies, are among the most common surgeries worldwide. While Norway and Sweden use national databases to control and improve surgical quality and reduce complications, Denmark lacks a similar national instrument. The Danish Tonsil Database was created to address this gap by monitoring and optimizing tonsil surgeries. This study aims to validate completeness of records from 2017 to 2024 by comparing them to data in the National Patient Register.

Methods: The Danish Tonsil Database, a population-based clinical registry, was established in the Central Denmark Region in 2017 and expanded to include the Region of Southern Denmark and the North Denmark Region in 2022. Tonsil operations identified from surgical lists in ENT departments were registered with corresponding operative techniques and demographic data, then compared to procedural codes in the National Patient Register. Completeness was assessed through binary outcome comparisons, calculating agreement rates as percentages.

Results: A total of X1 tonsil operations were registered, categorized as follows: X2 tonsillectomies, X3 adenotonsillectomies, X4 tonsillotomies, and X5 adenoidectomies. Results of comparisons with the National Patient Register are pending.

Discussion: Pending results, this study is expected to support the development of national quality improvement programs in Denmark aimed at enhancing surgical outcomes in tonsil operations. Similar initiatives in Norway and Sweden have demonstrated effectiveness in reducing postoperative bleeding rates, underscoring the potential impact of a validated registry on surgical outcomes.

Themes: Surgery, Surgery
Keywords: Tonsil operations, Quality assessment, National database

A novel expansible aortic annuloplasty ring for aortic valve repair

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Up to 50% of patients with aortic insufficiency (AI) who undergo aortic valve replacement experience valve-related complications within 10 years, compared to only 12% when aortic valve repair is performed. A subvalvular annuloplasty ring is essential to avoid recurrent AI when performing aortic valve repair, but none have proven superior in material, shape or position. Therefore, our group developed a physiological, expansible open aortic ring with a heterogenous design; the Aortic Phlex-ring (A-ring).

In this study, we evaluate its performance in an acute porcine model.

An 80 kg porcine model was used to study aortic root motion, hemodynamics, and valve performance before and after A-ring implantation, using epicardial echocardiography, sonomicrometry, and pressure catheters. After median sternotomy and extracorporeal circulation, the A-ring was secured around the aortic annulus with six U-sutures, achieving a mild reduction in annular diameter during systole.

Results show that the aortic root dynamics of the A-ring were similar to those of the native aortic root. It maintained aortic root distensibility and haemodynamic performance during the cardiac cycle. Moreover, the A-ring downsized the aortic annulus diameter as intended.

The A-ring showed physiologic expansibility comparable to the native aortic annulus. The results of these studies are promising. They underline that the A-ring has the potential to become a future adjunct for aortic valve repair. This affords us with a basis for continued functional testing aiming to develop a new surgical device and create the foundation for improving the overall treatment of AI.

Themes: Surgery, Animal Models
Keywords: Annuloplasty ring, Aortic insufficiency, Cardiothoracic

A systematic review on surgical treatment of recurrent rectal prolapse

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Background

Management of recurrent rectal prolapse (RRP) often depends on surgeon preferences due to limited scientific evidence. The choice of redo procedure is dependent on the technical aspects of previous surgeries. This review evaluates different procedures in RRP treatment, aiming to create an evidence-based treatment algorithm.

Methods

A systematic review of RRP surgery literature was conducted following PRISMA guidelines. English-language studies from 2004 and on were included. Primary outcomes were re-recurrence rates, functional outcomes, and quality of life (QoL). The secondary outcome was a description of how surgical choices were made.

Results

Fourteen studies were analyzed, of which 12 were retrospective cohort studies including 871 patients. The main procedures were ventral mesh rectopexy (24.11%), Altemeier (18.83%), and Delorme (11.94%). Re-recurrence rates reached up to 42.86%, with outcomes varying across studies. Functional data, such as constipation and incontinence, were sparse, with one study reporting a median Wexner score change of 8.0. QoL data were also limited, with two studies reporting means of 81/100 and 8.0/10, respectively. Four studies described procedure selection, mostly based on surgeon experience or predefined rules. Developing a definitive algorithm was not possible, though a potential pattern in procedure choices was identified.

Conclusion

Evidence on RRP treatment is growing, but studies are small and focus more on surgical than functional outcomes. Re-recurrence rates are high, and procedure choice often depends on surgeon preference. Larger, international studies are needed to create a treatment algorithm for RRP.

Themes: Surgery, Qualitative research
Keywords: Recurrent rectal prolapse, Surgery, Systematic review

Diagnostic Accuracy of Selective Nerve Root Blocks in lumbar degenerative disease

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Introduction:

Over 500 million people annually require spine care for conditions like lumbar disc herniation and spinal stenosis, leading to pain and reduced quality of life. Selective nerve root blocks (SNRB) aim to diagnose pain-causing nerve roots, guiding potential surgical decompression. However, the diagnostic accuracy of SNRB is debated. This study evaluates the diagnostic accuracy of SNRB to predict surgical outcomes.

Methods:

We reviewed studies on SNRB as a diagnostic tool with reported post-surgery outcomes, sourced from 9 major databases. Inclusion criteria were: (1) Adults ≥18 years with radiculopathy; (2) Pre-operative SNRB under fluoroscopy or CT with anesthetic or corticosteroid, followed by surgery; (3) Outcome data on pain, disability, quality of life, or health scores. Studies were excluded if using SNRB solely as therapy, case reports, and prior reviews. Sensitivity, specificity, and predictive values are reported, with a pooled estimate via a random effects model and a GRADE assessment.

Results:

We identified 10,357 eligible studies and screened 126 full-text articles, ultimately including 26 studies. Only 7 studies provided all values for calculating pooled sensitivity and specificity. We found a pooled sensitivity of 0.88 (95% CI: 0.80-0.92) and specificity of 0.57 (95% CI: 0.27-0.83).

Discussion:

We found moderate evidence that SNRB is a useful diagnostic tool for identifying patients likely to benefit from surgical intervention. We found very low level of evidence for specificity, SNRB is not a good tool to rule out surgery in patients with a negative response.

Themes: Surgery, Diagnostics & technology
Keywords: Radiculopathy, Spine, Diagnostic Nerve Root Block

Preliminary Results on Risk of Reoperation After Incision and Drainage for Pilonidal Sinus Disease from 2010-2021 - A Danish Population-Based Cohort Study

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Background: Pilonidal abscesses are typically treated with lateral incision and drainage (I&D), leaving any midline disease untreated, which carries a risk of recurrence. This study aimed to assess the rate of reoperations following I&D as the initial treatment for pilonidal abscesses.

Methods: Using data from nationwide Danish registries, we identified patients with a pilonidal sinus disease (PSD) diagnosis who underwent I&D as their initial surgery for PSD between 2010 and 2021. The patients are hereafter followed until reoperation.

Results: A total of 8,975 patients were included, with a median age of 24 years (IQR 19-31); 64% were male. During follow-up, 30% underwent reoperation, with 62% occurring within the first year. Reoperations included repeat I&D (52%), pit-picking (15%), cleft lift surgery (9%), and wound management procedures (10%).

Conclusion: Preliminary findings suggest that I&D effectively resolves pilonidal abscesses in a large proportion of patients. If midline manifestations are minimal, patients should be informed of a 30% risk of recurrence and not necessarily undergo further follow-up. Additional results will come, identifying factors that influence the risk of reoperation.

Themes: Surgery, Epidemiology
Keywords: Pilonidal sinus disease, Proctology, Reoperation

SESSION 3 - Mental health 1

Candidate pathways and biomarkers in OGT-CDG - a novel intellectual disability syndrome

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Intellectual disability (ID) affects 1–3% of the global population and is marked by impairments in cognitive and adaptive functions. Recently, a syndromic form of ID, termed OGT-CDG, has been linked to missense mutations in O-linked N-acetylglucosamine transferase (OGT), a glycosyltransferase essential for mammalian development. OGT catalyses the co- and post-translational modification O-GlcNAcylation, where O-GlcNAc is added to serine/threonine residues on more than 7,000 nuclear and cytoplasmic proteins. It is a process involved in critical cellular functions, including transcription and metabolism, and recent studies have highlighted OGT's role in neuronal development and function. However, the mechanisms driving OGT-CDG pathogenesis and its neurobiological connections with other syndromic and non-syndromic ID forms remain poorly understood.

Here, we investigate the role of OGT in neurodevelopment, with a focus on understanding how OGT mutations contribute to the pathogenesis of OGT-CDG. Through data mining, we aim to identify key stages and regions in brain development vulnerable to OGT disruptions. Utilising spatial transcriptomics in OGT-CDG mouse models, we define affected neurodevelopmental pathways, while multi-OMICs analysis of patient blood samples will further reveal OGT-CDG-associated biosignatures. These insights have the potential to enhance our understanding of the pathoaetiological processes underlying OGT-CDG and their links to other forms of ID – potentially leading to new diagnostic markers, therapeutic targets, and ultimately improving the lives of the patients suffering from this debilitating disorder.

Themes: Neuroscience, Omics
Keywords: Neurodevelopment, Intellectual disability, Bioinformatics

The impact of vortioxetine on the kynurenine pathway in flinders sensitive line rat model of depression

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Depression affects millions of individuals globally, and while selective antidepressants are the standard treatment, a significant proportion of individuals do not respond adequately. Recent attention has been directed toward the kynurenine pathway, which is increasingly recognized for its potential role in depressive disorders. Metabolites within this pathway, such as quinolinic acid and kynurenic acid, exert neurotoxic and neuroprotective effects, respectively. An imbalance between these metabolites is hypothesized to contribute to the pathophysiology of depression, through mechanisms such as inflammation and neuronal damage. Recent animal studies support this notion. Importantly, emerging evidence suggests that the antidepressant vortioxetine may help restore balance within the kynurenine pathway, offering a novel therapeutic strategy.

This research study aims to investigate the function of the kynurenine pathway in a rat model of depression, specifically the Flinders Sensitive Line rats, compared to non-depressed Flinders Resistant Line rats. Moreover, the study will assess the potential of antidepressant treatment to correct the proposed kynurenine pathway imbalance in these animals. We will analyze behavioral outcomes through behavioral tests, including the Novel Object Recognition Test, Forced Swim Test, Open Field Test and Social Interaction Test. Biochemical analyses of blood and brain tissue will be conducted using ELISA, Western Blotting, HPLC, and PCR to quantify relevant kynurenine pathway enzymes and metabolites. This research aims to enhance understanding of this pathway in depression, potentially unveiling novel therapeutic targets and improving treatment.

Themes: Neuroscience, Mental health
Keywords: kynurenine pathway, depression, flinders

Mental health in the Danish National Health Survey: Representativeness and implications

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Background: The Danish National Health Survey (DNHS) contains information that is usually not available in administrative registers, such as lifestyle factors. In this study, we explored whether DNHS participants are representative of the general adult Danish population with regard to a range of health conditions, including mental disorders.

Methods: By linking registers and surveys, we compared the 2017 DNHS participants with the general population (aged 16+ years). We estimated period prevalence ratios (PPRs) of having received a diagnosis of 202 different health conditions within ICD-10 subchapters in the 5 years prior to the survey using log-binomial regression. We used Cox regression to estimate 3.5-years hazard ratios (HRs) of (1) receiving a diagnosis or (2) dying after survey participation. In all analyses, sampling weights were applied.

Results: The weighted survey participants (N=183,208) were representative of the general population (N=4,697,913) with regard to most diagnoses but mental disorders were slightly underrepresented (PPR: 0.86 [0.85; 0.88]), especially organic disorders (PPR: 0.55 [0.52; 0.59]), intellectual disabilities (PPR: 0.66 [0.59; 0.75]), substance use disorders (PPR: 0.78 [0.75; 0.80]) and schizophrenia (PPR: 0.79 [0.74; 0.83]). The hazard of receiving a subsequent mental diagnosis or dying was also lower among survey participants compared to the general population (HR: 0.87 [0.85; 0.89] and 0.77 [0.75; 0.79], respectively).

Conclusion: DNHS participants are overall healthier than the general population and people with prior mental disorder diagnoses are underrepresented. Hence, we suggest updating sampling weights to account for mental disorders.

Themes: Epidemiology, Mental health
Keywords: Register- and survey-based data, Representativeness, Inverse probability weights

Signature Model for people with Cocaine Use Disorder: integrating neuroimaging, DNA methylation, and clinical outcomes

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Substance Use Disorder (SUD) is associated with complex changes in neurobiology, which are often worsened in populations facing significant social vulnerabilities. This study aimed to develop a comprehensive model that integrates clinical data, structural neuroimaging, and DNA methylation to analyze the characteristics that distinguish individuals with SUD.

In this cross-sectional study, individuals with Cocaine Use Disorder (CUD) (n = 80) and healthy controls (n = 57) from a developing country underwent clinical evaluations and structural neuroimaging. Some participants also underwent DNA methylation assessments. All analyses were conducted during detoxification treatment. Structural neuroimaging, using a T1-weighted GE HDxt 3T scanner, was performed to identify brain signatures, focusing on changes in brain volume and cortical thickness. DNA methylation analysis was carried out using the Infinium MethylationEPIC v1.0 BeadChip on blood samples to uncover epigenetic sites that correlate with observed neurobiological changes, clinical features of CUD, and significant life events.

The proposed model aims to identify clinical markers that differentiate the groups and provide insights into potential underlying mechanisms. It is crucial to determine whether DNA methylation and neural markers act as predictors or mediators, as this will advance hypothesis-driven research and inform future studies.

Themes: Neuroscience, Bioinformatics
Keywords: Addiction, Signature Model,

Investigating the Familial Co-aggregation of Psychiatric, Somatic, and Behavioral Outcomes with Borderline Personality Disorder in a Swedish Birth Cohort: Shared Genetic or Environmental Factors?

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Borderline or emotionally unstable personality disorder (BPD) is characterized by marked instability in emotions/self-image/ interpersonal relationships and acts of self-harm. Previous studies have shown that BPD is associated with many negative health outcomes, and that this is partly due to genetics. We aimed to provide an overview of the familial co-aggregation of various phenotypes with BPD, as well as estimate the genetic vs. environmental contributions to the observed associations.

In a cohort of 2.7 million individuals born in Sweden 1973–2001 and their relatives, we ascertained 44 phenotypes (20 psychiatric, 18 somatic, and 7 behavioral) using diagnoses from the National Patient and Cause of Death Registers up until 2020. We calculated odds ratios for different relative pairs adjusted for sex and birth year and family cluster-robust standard errors. Then, we used bivariate structural equation modeling to estimate the proportion of each association explained by shared genetics, shared environment, and unique environment/error using full and half-siblings.

Individuals with BPD were at increased risk for a wide range of phenotypes. Associations were strongest for psychiatric disorders, with within-individual adjusted odds ratios (aOR) of 5.47–43.9, but also greatly elevated for most somatic and behavioral phenotypes. Having a relative diagnosed with BPD was also associated with an increased odds of having most phenotypes, and the strength of association typically decreased with decreasing degree of genetic relatedness. With few exceptions, common environmental factors explained small to none of the observed associations. Instead, shared genetics and unique environmental factors/error explained the associations to an equal degree.

This study shows that a wide range of phenotypes co-aggregate with BPD in families in a large register-based study. The findings will guide future research of the shared etiology of BPD and other phenotypes.

Themes: Mental health, Epidemiology
Keywords: Borderline personality disorder, Comorbidity, Family study

Medication Use in Severe Anorexia Nervosa: A Danish Register-based Study

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Anorexia nervosa (AN) is a serious psychiatric disorder with high mortality and follows a complex clinical course. Severe AN represents a subgroup of patients with prolonged illness duration and poor outcome. Previous research reported increased medication use in AN patients, but prescription patterns in severe AN remain unexplored.

Utilising Danish registers, our study sample includes ~7,700 individuals diagnosed with AN. We assigned cases to severe AN or non-severe AN groups based on register-based AN severity scores. First, we compared the difference of medication use between groups and examined trajectories for all medications across 5 to 10 years post-diagnosis. Second, we used latent class analysis to identify the common comorbidity profiles among severe AN patient, forming groups for between-group comparisons with Benjamini-Hochberg correction.

Our analyses revealed an increased odds of pharmacotherapy among severe AN patient across various medication classes. Notably, high odds for specific prescriptions were observed for alimentary tract and psychotropic medications. Conversely, lower rates of contraceptive prescriptions were observed in severe AN group than non-severe AN group. After accounting for comorbidities, we found that patients with severe AN were prescribed a range of medications, varying from various comorbidity profiles. Subgroup analysis further indicated that AN patients without comorbidities were also prescribed various mediations.

Our findings emphasise the need for further investigation into specific medications in severe AN patients, highlighting the complexity of severe AN, and the importance of considering distinct comorbidity profiles.

Themes: Epidemiology, Mental health
Keywords: Pharmacoepidemiology, Eating disorders, Danish registers

Pubertal timing and tempo and anxiety disorders in Danish adolescents: a population-based cohort study

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Background: Anxiety disorders affect up to 20% of adolescents, including social anxiety disorder (SAD) emerging around puberty. Earlier pubertal timing has been associated with anxiety disorders particularly in girls. Studies in boys and on pubertal tempo are sparse.

Aim: To examine the associations between pubertal timing and tempo and anxiety disorders and self-reported SAD.

Methods: The study population consisted of 13 208 adolescents (6941 girls and 6267 boys) from the Danish National Birth Cohort (DNBC). Self-assessments of Tanner stages were collected every six months throughout puberty. Pubertal timing and tempo were modelled as continuous and categorized (earlier/faster, average, later/slower) variables. Primary outcomes included self-reported SAD from the 18-year DNBC follow-up and diagnosed anxiety disorders from the Danish National Patient Registry. Secondary outcomes included contacts with psychologists and/ or psychiatrists, and redeemed prescriptions psychotropic medication from Danish registries. Logistic regressions were used to estimate adjusted odds ratios with 95% confidence intervals.

Results: Earlier pubertal timing and faster tempo in girls were associated with higher risk of anxiety disorder and self-reported SAD compared to average timing and tempo while later timing and slower tempo were associated with lower risk. In boys, associations were less consistent with the primary outcomes including only self-reported SAD.

Conclusion: If associations of earlier pubertal timing and tempo are causal, future research may focus on targeted preventive interventions for adolescents that show early signs of puberty and early onset of anxiety disorders such as SAD.

Themes: Epidemiology, Mental health
Keywords: Puberty, Anxiety disorders, Cohort

Temporal stability of an electronic health record-driven prediction model for type 2 diabetes among individuals with mental illness

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Clinical prediction models, including those for psychiatry, aim to improve diagnostic classification and patient outcome prediction. Despite initial promise, there is an increasing body of literature raising concern about real-world applicability and validation of generalizability before such models are implemented in clinical practice. Changes in medical standards, patient demographics, and treatments over time can lead to performance drifts in these models, making it essential to investigate temporal stability (i.e., maintained performance of a prediction model on new data) prior to clinical implementation. Accordingly, this study examined the temporal stability of a previously trained model for prediction of incident type 2 diabetes (T2D) in individuals with mental illness. The original model, a hyperparameter-tuned XGBoost model, was trained on EHR data from the Psychiatric Services of the Central Denmark Region from 2013 to 2021. The model was trained to - based on sex, age, and mean HbA1 within the past two years - predict whether a patient will meet criteria for T2D in the 2 years following each physical contact to the Psychiatric Services. In this study, we reused said model, fitted exclusively on patient data from 2013 to 2017, and examined how well it generalized to patient data from the years 2018-2022, respectively. AUROC scores showed minor variations in the model's ability to predict T2D across years (a linear model estimated a performance decrease of 0.006 (SE 0.0005) per year). The high temporal stability of the T2D prediction model bodes well for clinical implementation, where it may support early detection and interventions to reduce the risk of T2D.

Themes: Statistics, Mental health
Keywords: Machine learning, Clinical prediction models, Generalizability

A longitudinal study comparing cognition between both biological parents and their offspring in families with parental schizophrenia or bipolar disorder

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Background: Neurocognitive deficits are core features of schizophrenia (SZ) and bipolar disorder (BP), and research has found that cognitive impairments are early vulnerability markers for these disorders. Studies comparing patients and their first-degree relatives show, that first-degree relatives generally display cognitive impairments that lie in between the respective patient group and controls. However, to our knowledge, no study has investigated the association between cognition in parents and their offspring simultaneously with the same methodology in a longitudinal manner in families with parental SZ and BP. Therefore, this study aims to investigate the association between parent and offspring intelligence, processing speed and verbal working memory in a developmental perspective from the offspring were seven to 15 years old, and to assess whether this association is influenced by parental SZ or BP.

Methods: The study is part of the Danish High Risk and Resilience Study – VIA 15, a longitudinal nationwide cohort of families with either 0, 1, or 2 parents diagnosed with SZ or BP. At first assessment (VIA 7), 522 Danish children aged seven and their parents participated. Both biological parents were assessed with the same neuropsychological tests as their offspring. In VIA 15, the second follow-up, 427 families participated, responding to a retention rate of 82% of the original cohort.

Results:Data analysis is ongoing. Preliminary results will be presented at the PhD Day.

Conclusion: Assessing the association between parent and offspring cognition in a developmental perspective can add to our understanding of the mechanisms underlying SZ and BP.

Themes: Epidemiology, Mental health
Keywords: Neurocognition, Familial High Risk, Longitudinal study

Blood is thicker than water: Improving genetic prediction of psychiatric disorders

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Background: Genetic studies have transformed our understanding of health and diseases. However, most large-scale genetic studies are based on individuals of European genetic ancestry, and findings from these studies don't always transfer well to other ancestries. For example, research has shown that polygenic scores, which represent genetic risk as a single score, are up to 78 % less affective for individuals of African genetic ancestry compared to individuals of European genetic ancestry (Martin et al., Nat Genet 2019). This difference in prediction accuracy can introduce bias and increase health disparities in clinical practice. This study investigates whether family history is a more robust alternative to polygenic scores.

Methods: I predicted risk of seven psychiatric disorder in more than 130.000 individuals using data from the iPSYCH2015 case-cohort study and Danish registers. The outcome of interest is the prediction accuracy of two different family history measures and polygenic scores as a function of genetic distance.

Results: Our results show that family history is more robust than polygenic scores when predicting the case-control status in individuals of non-European genetic ancestry.

Conclusion: By evaluating the prediction accuracy of family history and polygenic scores along the genetic ancestry continuum, this study provides valuable insight into the development of unbiased and transferable prediction models. Our results can help decrease health disparities and social injustice present in current clinical prediction models.

Grants: This work was supported by Danish Data Science Academy (ID: 2023-1420).

Themes: Bioinformatics, Mental health
Keywords: Mathematical genetics, Trans-ancestry prediction, Clinical prediction

Brain activity as a promising tool for diagnosing schizophrenia

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Schizophrenia is a disorder with several underlying causes, and patients suffer from a variety of symptoms, grouped as positive, negative and cognitive. It is possible to treat some of the symptoms, but no treatment is available for the cognitive symptoms. The cognitive symptoms affect close relationships, work, and quality of life. The dorsolateral prefrontal cortex (dlPFC) is a brain area that regulates some cognitive functions, and this brain area is abnormally activated in schizophrenia.

This project elucidates disruptions in brain connectivity in the dlPFC in schizophrenia using resting-state functional magnetic resonance imaging (fMRI) data from healthy individuals and individuals with schizophrenia to study how this affects cognitive functions. We also assess whether brain activity in the dlPFC can be used to diagnose schizophrenia.

We found that the functional connectivity, calculated as the statistical correlation between the dlPFC and the rest of the brain, is dysfunctional in schizophrenia. Specifically, the dlPFC has disconnections to areas that regulate learning, memory, and attention, and disruptions in these functions can be viewed as cognitive and negative symptoms in schizophrenia. Individualised functional abnormality scores were determined and classified from the brain activity, which showed a clear difference between healthy and schizophrenia individuals for the left dlPFC.

Our results suggest disruptions in brain connectivity in the dlPFC in schizophrenia, which may affect cognitive functions. Our results further show that the functional abnormality score for the left dlPFC can be used as a biomarker of schizophrenia when compared to healthy controls.

Themes: Neuroscience, Mental health
Keywords: Schizophrenia, Biomarkers, Disease mechanisms

SESSION 4 - Endocrinology

The molecular mechanism of augmented renal HCO3- excretion during respiratory alkalosis

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Background: During respiratory alkalosis, the kidneys increase urinary HCO3- excretion by a mechanism that is yet unknown. This is evident during hypoxia-driven respiratory alkalosis at high altitudes. Recent studies show that the ability to increase renal HCO3- excretion during metabolic alkalosis depends on pendrin and Cystic Fibrosis Transmembrane Regulator (CFTR) in the collecting duct (CD) β-intercalated cells (β-IC). Also, secretin is shown to activate HCO3- excretion in β-ICs that express the receptor (SCTR) basolaterally.

Methods: Two protocols are performed in WT and KO mice to assess the role of pendrin, CFTR and SCTR for the ability to increase renal HCO3- excretion during respiratory alkalosis.

1. In anaesthetized, mechanically ventilated mice, hyperventilation-induced respiratory alkalosis is assessed by monitoring of real time urine pH and HCO3- excretion via bladder catheterization.

2. Intermittently-Closed-Flow Respirometry is performed during hypoxic and control conditions of 12.5% and 20.5% O2, yielding ACRCO2 and ACRO2.

Preliminary results: In pilot studies with Intermittently-Closed-Flow Respirometry in pendrin mice, acute hypoxia caused an increase in ACRCCO2/ACRO2 in WT and KO mice, and, thus, hyperventilation. However, KO mice were unable to produce alkaline urine, exhibited reduced hyperventilatory response and a much larger decrease of body temperature. This indicates augmented alkalosis-induced inhibition of ventilation due to failure of renal base elimination and consequently lower oxygen availability.

Preliminary conclusions: These results indicate that renal compensation to respiratory alkalosis relies on pendrin activity in the β-ICs of the CD.

Themes: Urology & Nephrology, Endocrinology
Keywords: Renal HCO3- excretion, Respiratory alkalosis, Acid-base balance

Blood glucose levels in pregnant non-diabetic women during treatment with betamethasone for fetal lung maturation

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Background: At premature birth, one of the main problems is immature lungs in the newborn. In case of threatening preterm delivery, treatment with betamethasone is recommended to stimulate formation of surfactant and accelerate fetal lung maturation. In pregnancies with diabetes, administration of betamethasone often leads to significant hyperglycemia, which is known to inhibit the formation of surfactant, and if the women deliver while glucose is still high there is risk of neonatal hypoglycemia. Only few studies have examined blood glucose changes in non-diabetic pregnant women treated with betamethasone.

Aim: To examine and describe the pattern of changes in maternal blood glucose in non-diabetic women threated with betamethasone for fetal lung maturation.

Method: A prospective observational study, aiming to include 25 non-diabetic singleton pregnancies receiving betamethasone due to threatened preterm birth between gestational weeks 24+0 and 34+0. Blood glucose levels will be measured with continuous glucose monitor (CGM). Additionally, blood and urine samples will be collected. After delivery, an umbilical cord blood sample will be obtained and information about hypoglycemia and/or the need for early feeding of the infant will be collected.

Results: This study is ongoing, with enrollment beginning in November 2024.

Conclusion: The study will improve the understanding of how betamethasone affects maternal blood glucose levels in pregnant women without diabetes. If it is found that administration of betamethasone causes significant hyperglycemia, it may be important to measure and treat hyperglycemia during betamethasone treatment to prevent neonatal complications.

Themes: Gynecology and obstetrics, Endocrinology
Keywords: Preterm birth, Blood glucose, Steroids

Prenatal Exposure to Arsenic in Drinking Water and Type 1 Diabetes

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Objectives: According to the Word Health Organization, inorganic arsenic (As) "is the most significant chemical contaminant in drinking-water globally." Its toxic effects are well documented across many countries, which has led to a national guideline value of 5 µg/L As in drinking water in Denmark. However, recent evidence indicates that chronic low As exposure (<10 µg/L) may be a risk factor for diabetes. Therefore, this study aims to investigate the association between prenatal drinking water As exposure and type 1 diabetes (T1D).

Methods: This follow-up study links prenatal As exposure from household drinking water with information on T1D diagnoses from The National Patient- and Prescription Registry. All singleton births from 2002-12, located from The Danish Medical Birth Registry, and living in a household using a public water supply, were included. Cox proportional hazards models were used with age as underlying time scale and adjusted for sex, calendar year, mother's age, smoking status, BMI, parental T1D status, education and income.

Results: A total of 563,871 births were included. Preliminary analyses show a positive association between prenatal As drinking water exposure and T1D. In adjusted models using <1 µg/L as reference, a monotonically increasing association was observed: HR (95%CI) were 1.11 (0.98-1.25), 1.35 (0.93-1.97) and 2.16 (1.22-3.83) for 1-5, 5-10 and ≥10 µg/L, respectively.

Conclusion: We find prenatal drinking water As exposure to increase risk of T1D in public supply users at relatively low levels, even under national guidelines, demonstrating that As might be an important modifiable risk factor for diabetes.

Themes: Public health, Endocrinology
Keywords: Drinking Water, Arsenic, Diabetes Mellitus, Type 1

Exploration of a novel group of lactoylated amino acids as biomarkers and signaling molecules in metabolic diseases.

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The regulation of appetite and satiety is a complex process that is influenced by several molecular and cellular factors. Extensive research has been conducted into conventional biomarkers of satiety, such as glucagon-like peptide-1 (GLP-1), however, studies show that energy metabolites like lactate, may also be involved in appetite regulation. Recently, small molecule adducts of lactate have been gaining increasing attention as both signaling entities and possible biomarkers of clinical relevance. L-Lac-Phe, an adduct of L-lactate and phenylalanine, formed by mass action after exercise, has been shown to increase satiety in rodents and has proved to be a biomarker of metabolism and disease.

Literature suggests that there exist novel amino acid adducts, related to energy metabolism, which are potentially involved in satiety regulation, like L-Lac-Phe. Using reactivity-based metabolomics and proteomics, we aim to detect and quantify these novel biomarkers and profile their formation kinetics as well. Additionally, the mechanism by which L-Lac-Phe and, most likely, other modified amino acids promote satiety has not been elucidated yet and warrants investigation. Determining this mediation could provide insights into the complex interplay between metabolism and satiety signaling. This research is therefore crucial for establishing metabolic biomarkers and developing sensitive methods to detect and quantify them in humans. Ultimately, we may move towards developing potential treatments for the prevention and management of metabolic disorders such as obesity.

Themes: Omics, Endocrinology
Keywords: Lactoylation, amino acid adducts, appetite regulation

NIPT for Monosomy X and genetic variants of Turner syndrome - performance and phenotype

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Abstract: NIPT for Monosomy X and genetic variants of Turner syndrome - performance and phenotype

Objective: Non-invasive prenatal testing (NIPT) has been used for screening of Turner syndrome (TS), with most research not reporting on the specific karyotypes. Limited data exist regarding NIPT's performance in detecting variant karyotypes of TS, such as mosaicism and structural abnormalities. This study aims to evaluate NIPT's potential in identifying these karyotype variants, explore the specific phenotype, and analyze associated clinical outcomes.

Methods: A total of 1,103 cases with suspected or confirmed TS, diagnosed between 2000 and 2024, were collected from a database built via surveys distributed to ultrasound specialists across Germany. Out of these, NIPT was performed in 108 cases, which were included in the analysis. NIPT results were compared to confirmatory diagnostic tests (e.g., karyotyping) to assess Performance. The study also investigates genotype-phenotype correlations and clinical outcomes in the identified karyotype variants.

Results: Results to be added upon completion of the analysis

Conclusion: Conclusion to be added upon completion of the analysis

Themes: Gynecology and obstetrics, Endocrinology
Keywords: Turner Syndrome, Turner Syndrome variants, NIPT, Performance of NIPT and Phenotype

Polyamine treatment in elderly patients with coronary artery disease (Poly CAD)

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Background: As life expectancy rises, chronic conditions such as ischemic heart disease (IHD) and diabetes become more prevalent emphasizing the importance of healthy ageing. Spermidine, found in whole grains and vegetables, has been associated with longevity and improved cardiovascular health in epidemiological studies. Pre-clinical studies suggest that prolonged spermidine intake may reduce left ventricular hypertrophy, yet clinical data remains sparse.

Aim: To study the cardiovascular benefit of treatment with spermidine.

Hypothesis: One year treatment with spermidine reduces left ventricular hypertrophy as compared with placebo (rice flour, cellulose).

Design: Randomized, double-blind, placebo-controlled trial of 180 (>65 years old) patients with IHD. Participants will receive either 24 mg of spermidine or a placebo daily for one year. Study visits are planned at baseline and at one year follow-up.

Endpoints and Methods: The co-primary endpoints are the change in: (i) left ventricular mass (g) from baseline to one year (cardiac MRI) and (ii) maximal aerobic capacity (cardiopulmonary exercise test). Secondary endpoints: blood pressure (24-hour ambulatory blood pressure), arterial stiffness (pulse wave velocity), cytokine expression, physical activity (accelerometry), quality of life (Heart QoL), and cognitive function (CANTAB, eMOCA).

Clinical Perspectives: As of November 2024, 141 patients have been randomized. Enrollment is expected to end by the end of first quarter of 2025. Spermidine could represent a low-cost adjunct therapy to conventional treatments for ischemic heart disease, potentially reducing disease progression and improving quality of life.

Themes: Cardiology, Endocrinology
Keywords: Ischemic heart disease, Ageing, Cardiovascular

Defining the Vascular Niche of Human Adipose Tissue Across Metabolic Conditions

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The proper functioning of human adipose tissue, a major regulator of whole-body metabolism, requires a healthy vasculature. While notable heterogeneity within the vascular compartment has been previously reported, the function of these cells in health and disease is understudied. We aimed at constructing a comprehensive atlas of human subcutaneous adipose tissue (SAT) at the single-cell level, integrating seven publicly available datasets with an in-house single nucleus RNA sequencing one. We evaluated different integration methods following rigorous quality check and used optimal computational frameworks to construct the atlas, which comprised 329,774 cells (68,503

vascular cells) from lean, obese, and obese diabetic donors. Extensive analyses of the vascular populations were performed including differential gene expression, gene set enrichment, and cell-cell communication. We further characterized a previously undescribed endothelial population displaying features of endothelial-to-mesenchymal transition. To further investigate this population, we profiled human SAT using single-nucleus multiome sequencing, enabling simultaneous transcriptomic and epigenetic profiling. Using this dataset, we aim to understand the changes in gene regulatory networks evoked by metabolic disease. To that end, we aim to perform peak-gene linkage analysis, conduct DNA sequence motif enrichment, and use in silico transcription factor perturbation. Integrating these approaches will provide a comprehensive view of the transcriptomic landscape of individual cells and the regulatory mechanisms that govern their functions.

Themes: Bioinformatics, Endocrinology
Keywords: Single-cell, Multiome, Computational Biology

Estrogen Replacement Therapy in Women with Turner Syndrome: A Randomized Controlled Trial

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BACKGROUND: Turner syndrome (TS) typically presents with gonadal dysfunction, causing hypergonadotropic hypogonadism and estrogen deficiency. Estrogen receptors are distributed throughout the female body and have broad beneficial effects, making estrogen deficiency in TS associated with adverse cardiovascular, endocrine, and physiological consequences. Due to gonadal dysfunction, patients with TS generally undergo hormone replacement therapy (HRT) from puberty to menopause, using either oral or transdermal estrogen treatments. Although HRT is widely used, evidence on the optimal route, dosage, and monitoring of estrogen therapy in this population is very limited.

AIM: To compare the long-term effects of oral versus transdermal HRT in women with TS.

METHODS: This study is a 14-month, phase IV randomized controlled crossover trial involving 50 women with TS aged 18-50 years and 50 healthy, age-matched female controls. TS participants are randomized to receive either oral or transdermal HRT for six months, followed by crossover to the alternate treatment for another six months, with doses individualized to normalize gonadotropin levels. The study will evaluate cardiovascular, coagulation, endocrine, and physiological endpoints.

PERSPECTIVES: Findings are expected to guide optimization of HRT in TS patients and may also provide insights for women with ovarian insufficiency more broadly. Results will hopefully contribute to improved national and international HRT guidelines for TS patients.

Themes: Endocrinology, Pharmacology
Keywords: Turner syndrome, Hormone Replacement Therapy,

Exogenous Ketosis increases Renal Function and Sodium Excretion in Healthy Subjects

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INTRODUCTION: Renewed interest in the physiological role of ketone bodies (KB) has emerged. Various animal studies have suggested that kidney ketosis leads to renoprotection due to anti-inflammatory and anti-fibrotic effects. Yet only few clinical studies have examined renal effects of ketosis, and there are no clinical studies dealing with the effects of ketosis on sodium- and water balance.

Therefore, we aimed to examine the effects of exogenous ketosis on renal function and sodium excretory capacity in healthy subjects.

METHODS: A randomized, placebo-controlled, double-blind, crossover study. Sixteen healthy participants received a drink with KB and placebo three times a day for five days in a randomized order. Effect variables were measured on the last day of the interventions. Normally distributed variables were compared by paired t-tests or mixed models for repeated measures.

RESULTS: Mean GFR increased during ketosis compared with placebo, with a mean difference of 6 ml/min (p=0.007, 95% CI: 2.0, 10.1). Moreover, ketosis increased the fractional excretion of sodium with a mean relative difference of 28% (p=0.02, 95% CI: 1.04, 1.58), while the fractional excretion of potassium was decreased with a mean relative difference of -36% (p=0.009, 95% CI: 0.47, 0.87).

CONCLUSION: Ketosis affects kidney function by increasing GFR and sodium excretion and decreasing potassium excretion. These findings suggest potential advantages for kidney health, but further research is needed to assess its therapeutic value in chronic kidney disease before making clinical recommendations.

Themes: Urology & Nephrology, Endocrinology
Keywords: Ketosis, Metabolism, Nephrology

Defining the vascular niche of human adipose tissue across metabolic conditions

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Adipose tissue physiology and homeostasis depend on a healthy vascular network. Vascular malfunction is a hallmark of obesity, and vascular endothelial dysfunction, in particular, precipitates metabolic diseases, including obesity and type two diabetes. Although single-cell transcriptomic approaches have defined atlases of human white adipose tissue (WAT) cells, the associated adipose vascular cells remain relatively undefined. Specifically, there is limited information on their heterogeneity, their function, and their roles in metabolic disease. To address this gap, we profiled paired human subcutaneous and visceral adipose tissue from 15 donors with a wide range of metabolic states using snRNA-seq, creating an atlas comprising 275,000 cells of which 64,205 belong

to the vascular niche. We identified ten blood endothelial cell, eight lymphatic endothelial cell, and six mural cell populations exhibiting divergent gene signatures and provided extensive description of their putative functions. We also identified a heterogenous population, termed sub-endothelial cells, that possibly arise through endothelial-to-mesenchymal transition (EndMT) and that exhibit immune, adipogenic, or fibrotic gene signatures in a depot-dependent manner. We compared the abundance and the transcriptomic signatures of these cell populations across metabolic states and provided an exhaustive description of metabolic disease-associated patterns. This atlas, along with the accompanying analyses establish a solid foundation for future investigations into the biology of the WAT vascular niche in metabolic health and disease.

Themes: Omics, Endocrinology
Keywords: Adipose tissue, Vasculature, Endothelial cells

Prevalence of metabolic dysfunction-associated steatotic liver disease in individuals born with low-birth-weight – a clinical screening study

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BACKGROUND: The thrifty phenotype hypothesis suggests that individuals born with low-birth-weight (LBW) have a higher risk of developing cardiometabolic diseases later in life, a hypothesis that has been supported by epidemiological and clinical studies. Recently, a higher prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) has been shown in healthy males born with LBW. We aim to validate a higher prevalence of MASLD and associated dysmetabolic features in individuals born with LBW by performing a clinical screening study.

METHODS: Recruitment is ongoing of healthy individuals aged 34-49 years and born with LBW or NBW. Birth weight information is obtained from the Danish Birth Register. Clinical examinations include anthropometrics, blood samples, body composition (DXA) and measurement of liver fat content and stiffness by vibration-controlled transient elastography (FibroScan). Participants with indicates of liver steatosis and/or fibrosis are examined by magnetic resonance spectroscopy. Gene expression analysis will be performed for frequent variants to adjust for genetic risk of relevant diseases. The aim is to recruit a total of 300 participants (LBW n=250 and NBW n=50) in collaboration with Steno Diabetes Center Copenhagen. We expect to have examined 50 individuals in Aarhus by December 2024 and preliminary data from these individuals are expected to be presented on the ph.d. day 2025.

PERSPECTIVES: This project may help identify a subset of individuals at high risk for cardiometabolic diseases that may benefit from preventive strategies. This knowledge may be useful in guiding clinicians in making personalized risk assessments.

Themes: Gastroenterology and hepatology, Endocrinology
Keywords: Steatotic liver disease, Low birth weight,

Overview of Demographic Data, Gender Identity, Gonadal Status and External Genitalia Score (EGS) in 23 true Ovotesticular DSD patients from a single centre in South Africa

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Introduction: The incidence of DSD in the general population is between 1 in 4500-5000 births, with true Ovotesticular DSD the rarest. Here we report on demographic data, AMH levels, external genitalia score, gonadal status as well as gender identity in 23 patients from South Africa.

Methods: A retrospective study evaluated data and patients were diagnosed with OT-DSD based on gonadal biopsy or discordance between pelvic ultrasound, karyotyping and hormonal profiles. Data was obtained anonymously and analysis performed.

Findings:

Mean age 7 years 8 months

Mean delay in diagnosis 26,9 months

Karyotyping 46XX (22/23)

QF-PCR for evidence of Y-chromosome material QF-PCR NEGATIVE (19/19)

Mean External Genitalia Score 4 (22/23)

Gonads status on biopsy Unilateral Ovotestis: 30% (6/20), Bilateral Ovotestis: 68% (13/20), Not biopsied: 1 patient

Mean Anti-Müllerian Hormone (ng/ml) 21,97 ng/ml (15/23)

Concordance/Discordance in gender identity between parents and child 84% Concordance, 16% Discordance (19/19)

Evidence of DSD in siblings None (16/23)

Employment status of parents Mothers: 45% Unemployed, Fathers: 45% Unemployed

Province in South Africa Mpumalanga 76,2%, Gauteng 23,8%

Conclusion: This is a unique population of 46XX OT-DSD patients originating from a small rural area. Most patients have a delay from birth until first contact with a specialised centre. The absence of Y-chromosome material is peculiar, while gonadal biopsies showed the presence of either unilateral or bilateral ovotestes. A large portion of parents are unemployed, which might be an additional risk factor for OT-DSD. Further genetic and epigenetic evaluation is needed to fully understand this condition.

Themes: Urology & Nephrology, Endocrinology
Keywords: Disorders of Sex development, Endocrine disrupting chemicals, Paediatric Urology

SESSION 5 - Bladder and kidney disease

The role of LAPTM5 in renal lipid metabolism in mouse models with kidney disease

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Chronic kidney disease is a global health issue affecting almost 700 million people worldwide and more than half of these patients have dyslipidemia. However, the mechanisms leading to dyslipidemia during kidney disease are yet to be clarified. LAPTM5 has previously been known as a proinflammatory marker associated to both decreased and increased expression in different pathophysiological events, and in preliminary studies we have observed an increase of LAPTM5 in mice with kidney disease.

To investigate the role of LAPTM5 five mouse strains were used; 1) wild type, 2) Podocin knockout(P KO), 3) LAPTM5/Podocin knockout(LaP KO), 4) LAPTM5 knockout and 5) Megalin/cubilin/podocin knockout. LAPTM5, expression of inflammatory markers and proteins in renal cortex were measured with q-RT-PCR. Plasma lipids and markers indicating the extent of kidney disease were measured by MRC, Harwell. LAPTM5 and renal lipid accumulation will be visualized with immunohistochemistry and lipid staining. The type of lipids accumulated will be determined by lipidomics.

Our results show that LAPTM5 is upregulated in P KO mice, and that this upregulation is dependent on the endocytic receptors megalin/cubilin. LAPTM5 does not seem to alter the extent of kidney disease, any of the inflammatory markers or enzymes investigated. However, plasma triglycerides are increased as well as glycerol and free fatty acids are altered in LaP KO mice compared to P KO mice. This indicates an association between LAPTM5 and lipid metabolism in mice with kidney disease. Further results are pending and required to investigate the mechanism and role of LAPTM5 in renal lipid metabolism in kidney disease.

Themes: Urology & Nephrology, Molecular biology
Keywords: LAPTM5, Chronic kidney disease, Dyslipidemia

Intraoperative Ultrasound Assessment of Regional Lymph Nodes to Optimize the Lymph Node Dissection Template in Bladder Cancer

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Background: Muscle invasive bladder cancer can be treated curative with surgery, a radical cystectomy with urinary diversion and pelvic lymph node dissection (PLND). PLND is important for staging and can increase the long-term survival, however the extent of the template is still being questioned. Furthermore, there is a slight concordance between the cN-stage obtained from the pre-operative FDG-PET/CT and the pN-stage (golden standard) from the post-operative pathological assessment, in which only 13.5% present with pN+. The majority of the patients is therefore treated with a unnecessary PLND, which is time consuming and increases the risk of bleeding.

Purpose: to optimize the PLND with the use of intraoperative ultrasound to identify lymph nodes suspected of malignancy.

Methods: a consecutive series of robot-assisted cystectomies due to bladder cancer at AUH, from November 2024 till Summer 2025, will make use of ultrasound intraoperatively. Ultrasonographic suspicion of a metastatic lymph node will be evaluated or conferred with a radiologist with high level of clinical and sonographic competence. Lymph nodes will be sent for pathological assessment as “ultrasound positive (UL+)” or “ultrasound negative (UL-)” to evaluate the feasibility of the ultrasound with a specificity and sensitivity analysis.

Perspectives: this study aims to optimize the PLND which in the future require a randomized controlled trial exploring overall survival, intraoperative injury, time of PLND, and related postoperative complications of ultrasound-guided PLND versus standard PLND. Furthermore, it can be tested in other cancer operations involving PLND.

Themes: Urology & Nephrology, Imaging techniques
Keywords: Bladder Cancer, Lymph Node Dissection, Ultrasound

PhD project: Consequences of Persistent Hyperparathyroidism in Kidney Transplant Recipients

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Kidney transplant recipients have a markedly increased risk of long-term complications, including fractures, compared to the background population. Disturbed mineral metabolism is common post-transplant and may convey negative effects on skeletal health and overall survival. However, the consequences of these disturbances remain uncertain causing a tendency towards treatment nihilism. The current project aims to improve the evaluation and treatment of disturbed mineral metabolism in kidney transplant recipients by filling important knowledge gaps regarding the consequences of persistent hyperparathyroidism on skeletal health after kidney transplantation.

In this project, the comprehensive Danish health-registries will be used to build a large, well-characterized cohort of kidney transplant recipients across 20 years to investigate long-term skeletal outcomes. In a second cohort of Belgian kidney transplant recipients the availability of detailed bone phenotyping will allow for an in-depth investigation of risk factors of bone loss post-transplant. Finally, an explorative study will utilize bone-biopsy material and investigate the potential pathophysiological links between phosphate metabolism and skeletal responsiveness to PTH in the post-transplant period.

The combined knowledge from this project should contribute to more individualized estimates of patient-risk and encourage further research into optimal treatment regimens of disturbed mineral metabolism after kidney transplantation.

Themes: Urology & Nephrology, Epidemiology
Keywords: kidney transplantation, mineral and bone disorders, fracture risk

mCCDcl1 cells as an in vitro model for the cellular remodeling of the kidney collecting duct during Li-induced nephrogenic diabetes insipidus

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Lithium (Li) is widely used for the treatment of patients with bipolar disorder. However, up to 40% of the patients develop Li-induced Nephrogenic Diabetes Insipidus (Li-NDI). Li-NDI is characterized by urine-concentrating defects, due to insufficient water reabsorption in the kidney collecting duct (CD). Studies in rats have shown that Li treatment induces a downregulation of the water channel, AQP2, and a cellular remodeling of the CD. In addition, the subcellular localization of E-cadherin and beta-catenin changes in a subset of CD cells during the remodeling. The cell line, mCCDcl1, has previously been used to study CD cell physiology and expresses cell-type markers for both Intercalated-(IC) and Principal Cells (PC). mCCDcl1 cells also show downregulation of AQP2 upon Li exposure.

The aim is to evaluate the potential of mCCDcl1 cells as an in vitro model for Li-induced cellular remodeling. By immunocytochemistry and western blotting, we will investigate whether Li treatment induces changes in expression levels of IC and PC markers and changes in both expression and localization of E-cadherin and beta-catenin. By pharmacological inhibition, the project will also investigate whether any observed changes are mediated by ADAM10 shedding of E-cadherin.

Preliminary results suggest that E-cadherin and beta-catenin localize to the basal plasma membrane domain of mCCDcl1 cells, and that expression of the IC marker, H-ATPase, decreases when cells are treated with Li for 48 hours. The possibility of using mCCDcl1 cells as an in vitro model for the cellular remodeling may contribute to the investigation into new avenues of treatment and prevention of Li-NDI.

Themes: Urology & Nephrology, Imaging techniques
Keywords: Lithium, Remodeling, Cell-contacts

Bile Acids – Renal Friend or Foe?

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Bile acids (BAs) are essential for fatty acid digestion. However, high concentrations of hydrophobic BAs can be cytotoxic, raising concerns about their role in kidney injury. Research on BA nephrotoxicity largely relies on murine models. This is despite differences in BA composition between humans and mice, with hydrophobic BAs being more abundant in humans. To address this gap, this study compares the effects of hydrophobic BAs lithocholic acid (LCA) and chenodeoxycholic acid (CDCA) on human and mouse kidney tissues using precision-cut kidney slices (PCKS). Human PCKS (hPCKS) were prepared from nephrectomized kidneys (n=5) and mouse PCKS (mPCKS) from kidneys of C57BL/6 mice (n=5). Both were cultured for 24, 48, and 72 hours with or without LCA or CDCA. Viability was assessed via ATP levels, while fibrotic response was analyzed using qPCR and Western blotting. LCA exposure significantly decreased ATP levels and reduced RNA and protein concentrations in mPCKS, indicating cytotoxicity in mice. Consequently, LCA-exposed mPCKS were not further analyzed. CDCA did not affect mPCKS viability, and neither LCA nor CDCA impacted hPCKS viability. Solvent-exposed hPCKS and mPCKS developed fibrosis at 48 and 72 hours, a typical response in PCKS known as "culture activation". Notably, fibrosis was absent in CDCA-exposed mPCKS and LCA- and CDCA-exposed hPCKS, indicating antifibrotic effects of BAs. Western blotting confirmed that CDCA significantly reduced fibronectin in mPCKS, while LCA- and CDCA-exposed hPCKS showed a non-significant trend toward reduced fibronectin. These findings reveal species-specific BA responses, supporting the need for human models in BA nephrotoxicity studies.

Themes: Urology & Nephrology, Molecular biology
Keywords: Bile acids, Chronic kidney disease, Translational models

The impact of PDD on recurrence and progression in BCG-treated NMIBC patients: a nationwide follow-up study

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Background and objective

In non-muscle invasive bladder cancer (NMIBC) patients, Photodynamic diagnosis (PDD) is an integrated part of the diagnostics work-up and follow-up. Animal studies suggest that PDD can potentially affect response to Bacillus Calmette-Guérin (BCG). This study investigates the association of PDD on recurrence and progression risk in BCG-treated NMIBC patients.

Methods

We conducted a nationwide cohort study, using Danish register data. We included patients treated with BCG for a primary NMIBC between 2009-2022. Patients were followed until death, cystectomy, or December 31st, 2023 and compared according to PDD-status at first TURBT. We calculated cumulative incidences and relative risks for recurrence and progression and estimated crude and adjusted odds-ratios for BCG-response depending on PDD-status.

Key findings and Limitations

We identified 4318 patients with a first time NMIBC diagnosis treated with BCG. There were no differences in initial BCG-response across exposure groups. Age adjusted relative risk of recurrence was 0.88 (0.79 – 0.97) and 0.97 (0.89 – 1.05) at 1 and 5 years for the PDD-group compared to the non PDD-group. Age adjusted relative risk for progression was 0.93 (0.73 – 1.19) and 1.01 (0.84 – 1.21) at 1 and 5 years for the PDD-group.

Limitations were limited information regarding size and number of tumors from registers and a potential detection bias with more tumors diagnosed at the time of diagnosis in the PDD group.

Conclusions and clinical implications.

The present study did not support the hypothesis that PDD modulates the BCG-response in NMIBC patients.

Themes: Urology & Nephrology, Epidemiology
Keywords: Non-muscle invasive bladder cancer, BCG, PDD

The renal urinary concentration mechanism: Towards a detailed model of Aquaporin-2 shuttling

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Aquaporin water channels (AQPs) play a critical role in water homeostasis by facilitating water diffusion across cellular membranes following an osmotic gradient. AQP2 localizes to the apical plasma membrane and subapical intracellular vesicles in principal cells of the renal collecting duct. Stimulation with the antidiuretic hormone Arginine Vasopressin (AVP) mediates AQP2 accumulation in the apical plasma membrane which increases water permeability and thus water reabsorption. AQP2 shuttling and expression are dysregulated in multiple diseases associated with water balance disorders including chronic kidney disease, nephrogenic diabetes insipidus and congestive heart failure. A major challenge in studying the AQP2 vesicle population is the small size of the vesicles of approximately 40 nm. Thus, conventional fluorescent microscopy with a lateral resolution of approximately 250 nm cannot resolve individual AQP2 vesicles. Consequently, comprehensive information regarding the AQP2 vesicular population remains elusive. The recently established 4.5x Expansion Microscopy (ExM) technique represents a notable advancement, enhancing resolution to the range of 60-70 nm.

In this project, we aim to deepen our understanding of AQP2 vesicle shuttling by visualizing AQP2 vesicles via ExM. We have successfully expanded both cells and tissue and by using spinning disk confocal microscopy coupled with deconvolution and image processing, we can now resolve the AQP2 vesicular population. A better understanding of the shuttling mechanism of AQP2 could provide new insights leading to new treatment options and an improvement in the quality of life of patients affected by AQP2 dysregulation.

Themes: Urology & Nephrology, Imaging techniques
Keywords: Aquaporin 2, Expansion microscopy, Water balance

mRNA therapeutics delivery during machine perfusion of donor kidneys

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Introduction

Kidney transplant success is often hindered by complications like graft fibrosis, primarily caused by ischemia-reperfusion injury (IRI). Post-transplant fibrosis impairs graft function but also shortens graft survival. To address this, improved organ preservation techniques and methods for organ repair are crucial. Normothermic machine perfusion (NMP) of donor kidneys before transplantation offers a platform for ex-vivo delivery, minimizing systemic effects. Synthetic messenger RNA (mRNA) encoding therapeutic proteins is a promising biopharmaceutical due to its cost-effectiveness and good safety profile. This study assesses the feasibility of mRNA therapy during kidney-NMP.

Materials and methods

mRNAs encoding a secretive protein (human erythropoietin, hEPO) and an intracellular red fluorescent protein (mCherry) were used as proof-of-concept molecules. Porcine kidneys (n=9) were perfused on NMP using an erythrocyte-based perfusate for 6-12 hours at 37°C. After 30 minutes of NMP, the kidneys were infused with either DSPE (1,2-Distearoyl-sn-glycero-3-phosphoethanolamine) or TPGS (D-alpha-tocopheryl polyethylene glycol 1000 succinate) based lipid nanoparticles carrying 150 µg mRNA into the renal artery. Perfusate, urine and tissue samples were obtained during perfusion for protein expression analysis. The same protocol was used in human donor kidneys (n=7). Ex vivo mRNA delivery during kidney-NMP was tested through porcine auto-transplantation with a 2-week follow-up (n=3).

Results

Perfusion characteristics were not affected by mRNA treatment. Porcine hEPO mRNA-treated kidneys exhibited increased hEPO protein levels in perfusate and urine already 1 hour after mRNA delivery, reaching 4-6 IU/mL. mCherry protein was detected in porcine kidneys 3 hours after mRNA administration and in human donor kidneys 7 hours after mRNA administration. mRNA delivery by TPGS based LNPs resulted in higher and earlier

protein expression compared to DSPE based LNPs. Protein expression of transplanted porcine kidneys is currently being analyzed.

Conclusion

mRNA therapy during NMP was shown feasible paving the way for ex-vivo therapy of kidney grafts, in which production of therapeutic proteins in the kidney will persist after transplantation. Future studies will validate this strategy focusing on mRNAs encoding vascular endothelial growth factor (VEGF) as an anti-fibrotic treatment.

Themes: Urology & Nephrology, Urology & Nephrology
Keywords: mRNA, kidney transplantation, machine perfusion

Bladder cancer risk following cancer negative cystoscopy – a population based cohort study

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Background: Cystoscopy is the key diagnostic tool in bladder cancer diagnosis, but knowledge about short- and long-term bladder cancer incidence following a cancer negative cystoscopy primarily exist for the hematuria subgroup. We aimed to describe short- and long-term bladder cancer incidence following a cancer negative cystoscopy in comparison with the general population.

Method: We conducted a nationwide cohort study in 2005-17 of all first-time cystoscopy patients. We set the index date at 12 months after cystoscopy. We excluded individuals below age 18 years at the index date, with any prior cancer diagnoses (except non-melanoma skin cancer) or periods with missing lookback data. We individually matched the exposed cohort to cystoscopy-unexposed individuals at the index date by age, sex and municipality. For bladder cancer, we required stage and date-concomitant diagnoses to be recorded in both the Danish National Patients Registry and Pathology Registry. We followed individuals to the earliest of: emigration, death, 31.12.2018 or bladder cancer diagnosis, and computed cumulative incidences (CIP) of bladder cancer with death as competing event.

Results: We included 172,163 cancer negative cystoscopy patients and 1,719,169 cystoscopy unexposed individuals. The exposed cohort had slightly more comorbidities. In five and 10 years of follow-up, the exposed cohort had a bladder cancer CIP of 0.25% (95% CI: 0.23-0.27) and 0.36% (0.33-0.39) compared with 0.16% (0.16-0.17) and 0.26% (0.25-0.26) in the unexposed cohort.

Conclusion: Individuals with a cancer negative cystoscopy at baseline have higher CIP of bladder cancer than the background population in 14 years of follow-up.

Themes: Urology & Nephrology, Diagnostics & technology
Keywords: Bladder cancer, Cystoscopy, Diagnostic accuracy

GreenBladder - Early Detection of Bladder Cancer in Residents in Greenland Using a Urinary Biomarker

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Introduction

The incidence of bladder cancer (BC) in Greenland is significantly lower than in Denmark. However, a disproportionately high mortality rate indicates potential underdiagnosis and diagnostic delay of BC in Greenland. This may partly be explained by limited access to specialized healthcare services and the non-specific symptoms associated with BC. Early detection and treatment are vital, emphasizing the need for novel diagnostic strategies. A proposed solution is the use of urinary biomarkers.

This study evaluates the Xpert Bladder Cancer Detection test, a BC-specific urinary biomarker, to assist in prioritizing patients for cystoscopy, particularly in areas with limited access to urological services.

Methods

Greenlandic citizens over 18 referred for cystoscopy participated in this study, undergoing the Xpert test alongside their scheduled cystoscopy. Conducted across five Greenlandic cities via a mobile clinic, this study allowed direct comparison with cystoscopy outcomes.

Results

Of 198 participants, one-third were referred due to macroscopic hematuria, with a median referral-to-cystoscopy wait time of 218 days (range 4-2,338 days). Seven BC cases were confirmed. The Xpert test showed a sensitivity of 71.4% and specificity of 88.8%, with a positive predictive value (PPV) of 19.2% and a negative predictive value (NPV) of 98.8%. Among hematuria patients, sensitivity rose slightly to 75.0% with a PPV of 23.1% and an NPV of 97.8%.

Conclusion

The Xpert Bladder Cancer Detection test shows promise for triaging BC patients and addressing extended diagnostic wait times. However, false negatives underscore the need for careful interpretation in clinical practice.

Themes: Urology & Nephrology, Diagnostics & technology
Keywords: Diagnostic biomarkers/Urinary Biomarkers, Bladder Cancer, Greenland

Thrombocytes Constitute an Effective Clearance System for Uropathogenic Escherichia Coli in a Murine Model of Urosepsis

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Sepsis is a life-threatening condition where pathogens trigger a lethal host response. Thrombocytopenia, a key diagnostic marker for sepsis, correlates with higher mortality rates. Beyond coagulation, thrombocytes now appear to play a role in modulating the immune system and directly mediating pathogen killing. In a murine model of sepsis, we found that thrombocyte numbers decrease before onset of coagulation. This study examines the fate of circulating thrombocytes during sepsis.

Experiments were performed on anesthetized male Balb/cJRj mice (8-10 weeks), injected with E. coli (O6:K13:H1) 330·106 iv. In vitro studies were conducted on human blood. Thrombocytes and E. coli were measured by flow cytometry.

We observed a 37% thrombocyte reduction ($p<0.05$) 30 minutes post-injection, paralleled by a 95% decrease in bacterial counts ($p<0.05$). Imaging flow cytometry revealed that E. coli was rapidly scavenged by thrombocytes, forming complexes that were cleared from circulation. In vitro data confirmed thrombocytes' role as primary scavengers in sepsis. Thrombocytes gradually induced bacterial death, though not sufficiently to achieve a significant reduction within 30 minutes.

Preliminary findings suggest that E. coli is mainly deposited in the liver, potentially facilitated by thrombocyte-Kupffer cell interaction to encounter a more efficient bacterial killing. However, further investigation is required. These results strongly highlight thrombocytes as key players in the early clearance of E. coli during sepsis.

Themes: Infectious Diseases, Urology & Nephrology
Keywords: Sepsis, Thrombocyte, E. coli

SESSION 6 - Diabetes and cardiometabolic disease

Pre-Pregnancy Care for Women with Pre-existing Diabetes – A Prospective Cohort Study

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Background: Women with pre-existing diabetes (PED, type 1 or type 2 diabetes) face a 3-5 times higher risk of adverse pregnancy outcomes compared to the general population. Pre-pregnancy care (PPC) may be a key strategy in reducing this elevated risk.

Method: To investigate this, we will undertake a prospective cohort study to assess the impact of PPC in women with PED. The study population will consist of women of childbearing age living in the Central Denmark Region with PED. We aim to recruit 100 participants through outpatient diabetes clinics and electronic invitations via e-boks. They will have access to individualized PPC, focusing on pregnancy planning, optimal glycemic control, folic acid supplementation, and avoidance of potentially teratogenic medications. For those who conceive, first-trimester HbA1c levels will be compared between PPC participants and non-participants. The non-participant group will be drawn from The Danish Diabetes Births Registry 2 and include approximately 530 pregnant women with PED who did not receive PPC.

Perspectives: This project addresses an important clinical challenge. It evaluates a feasible intervention that aims to improve glycemic control in early pregnancy, potentially leading to better outcomes for both mothers and their children.

Themes: Endocrinology, Gynecology and obstetrics
Keywords: Pre-existing diabetes, Keywords: Pre-existing diabetes, pre-pregnancy care,

Cardiovascular, Renal, and Skeletal Complications in Patients with Post-Surgical Hypoparathyroidism (CARE Hypo)

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Background: Hypoparathyroidism (HypoPT) is a rare disorder characterized by hypocalcemia with low levels of parathyroid hormone. The most common cause of HypoPT is following neck surgery, whereas about 25% are due to non-surgical causes. The classical actions of PTH are well recognized, but its effects on other target tissues, such as the cardiovascular system, are not as well identified. Renal complications in patients with HypoPT are remarkably common, however, the reported complication rates differ significantly between studies, most likely due to differences in study design and methodology. Regarding skeletal health, patients with HypoPT do most often have a high BMD, however, several, but not all, studies point towards a high risk of vertebral fractures.

Aim: The overall aim of the project is to investigate cardiovascular, renal, and skeletal indices in patients diagnosed with Post-Surgical Hypoparathyroidism (PS-HypoPT)

Methods: A cross-sectional clinical based study on 50 patients diagnosed with PS-HypoPT compared to 50 healthy controls from the general population matched on age and sex. Outcomes will be investigated by DXA, 24-hour urine sample, tonometry, 24-hour blood pressure measurement, and CT scan of the heart, kidney, and skeleton.

Perspectives: Hopefully, the study will bring novel knowledge to the field of calcium metabolism in the heart, kidney, and skeleton.

Themes: Endocrinology, Endocrinology
Keywords: , ,

Effects of intact and disrupted milk fat globule membrane on postprandial metabolic response to high-fat.

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Background

Dietary guidelines recommend low-fat dairy to limit consumption of saturated fat. This recommenda-tion is based on studies of single nutrients showing a direct link between saturated fat and increased risk of cardiovascular disease. However, evidence from observational studies indicate that consump-tion of specific full-fat dairy, is associated with lower risk of type 2 diabetes, obesity, and cardiovascu-lar disease This unexpected benefit may be linked to the milk fat globule membrane (MFGM), which encapsulates triglycerides. The intactness of MFGM might influence metabolic health. Past studies have been unable to isolate the effects of MFGM structure due to confounding from nutrient differ-ences. The aim of the study is to investigate the effects of MFGM content and intactness on postpran-dial metabolic response to a high-fat meal.

Methods

A randomized, double-blind, controlled, crossover study will be conducted with 12 healthy partici-pants aged 18-40. Participants will undergo three test days with at least a one-week washout periods. At the test days, subjects will consume two high-fat meals composed of milk fat with intact MFGM, destroyed MFGM, or without MFGM. The primary outcome is postprandial triglycerides levels, while secondary outcomes include others metabolic markers: hormones, energy expenditure, ventricu-lar emptying rate etc.

Perspectives

We hope to clarify MFGM's role in metabolic health, offering insights into how structural variations in dairy fats impact human metabolism. The findings could challenge current dietary recommendations surrounding full-fat dairy and support a nuanced approach to dairy fat consumption in nutritional guidelines.

Themes: Endocrinology, Endocrinology
Keywords: Human metabolism, Substrate utilization, Postprandial lipids

Effect of Treatment with Finerenone on Renal Target Organ Damage in Patients with Type 2 Diabetes – A Randomized Trial - **CANCELLED**

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Background:

Diabetic nephropathy remains the most common cause of chronic kidney disease, and markedly increases the risk of cardiovascular disease. Hence, there is an urgent need for an improved understanding of the underlying disease mechanisms to reduce the risk of chronic kidney disease and cardiovascular disease.

The new drug finerenone reduces renal and cardiovascular disease in type 2 diabetes patients with chronic kidney disease. The mechanisms behind the protective effects of finerenone are unclear and especially the effect of combination therapy with the first-line diabetes drug class sodium-glucose cotransporter-2 inhibitors (SGLT2-Is) remains elusive.

Purpose:

In this 26-weeks placebo-controlled double-blinded randomized trial, we investigate the effects of finerenone versus placebo on renal, cardiovascular, and retinal target organ damage in 80 high-risk SGLT2-I treated type 2 diabetes patients with chronic kidney disease and albuminuria. This study mainly focuses on the renal outcomes and tests the hypotheses that finerenone 1) reduces albuminuria, 2) reduces kidney fibrosis, and 3) improves renal oxygenation to a greater extent than placebo.

Perspective:

The long-term goal for diabetes patients and researchers is to ensure that diabetic individuals have the same opportunities as those without diabetes. This study will advance our understanding of the mechanisms behind the increased risk of kidney failure and cardiovascular disease in diabetic patients. Gaining insight into these fundamental causes is essential for developing new treatments that can reduce the risk of complications.

Themes: Endocrinology, Urology & Nephrology
Keywords: Type 2 diabetes, Chronic kidney disease, Finerenone

Clinical Experience with Denosumab Discontinuation

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Summary: In patients receiving long-term treatment with denosumab, denosumab discontinuation via sequential treatment with zoledronate, resulted in a minor decrease in bone mass density (BMD) of 0-2.5% within the first year, and stabile BMD in the second year. Thus, showing that repeated treatments with zoledronate limit the loss of BMD, when discontinuing denosumab.

Purpose: Discontinuing denosumab (DMAb) rapidly decreases bone mineral density (BMD) and increases the risk of multiple vertebral fractures. We wanted to examine if the recommendation stated in the ECTS position paper on DMAb discontinuation can prevent the bone loss in a clinical setting.

Methods: We conducted a retrospective cohort study based on medical records of patients referred for DMAb discontinuation. We administered zoledronate (ZOL) 6 months after the last DMAb injection and 3, 6, 12 and 24 months thereafter if p-C-terminal collagen crosslinks (CTX) increased above 0.5 µg/l or BMD decreased (≥5% at the hip, ≥3% at the spine) at month 12 and 24.

Results: We included 66 women and men discontinuing DMAb after a mean treatment duration of 6.7 ± 2.7 (mean ± SD) years.

BMD decreased 12 months after the initial ZOL treatment by 2.5 ± 4.2% and 1.9 ± 2.5% at the LS and TH, respectively (n=44) ($p \leq 0.001$ for all). There was no significant change in FNBMD (0.0 ± 5.1) ($p > 0.05$). No significant change in BMD was seen from month 12 to month 24 at any site ($p > 0.05$ for all).

Conclusion: Adhering to the recommendation in the ECTS position statement, a mean of 3 infusions of ZOL limited the bone loss 12 and 24 months after DMAb discontinuation and thereby preserving most of the BMD gained during DMAb treatment.

Themes: Endocrinology, Pharmacology
Keywords: Osteoporosis, Bisphosphonates, Denosumab

Fracture Liaison Service at Aarhus University Hospital – Two-year experiences

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Introduction: In 2018 the Danish Health Authority recommended to implement fracture prevention programs in all Danish hospitals. With governmental fundings being limited, the fracture prevention program at Aarhus University hospital (AUH) was implemented as an integrated part of an endocrinology outpatient clinic. The aim of the implementation was to identify fragility fractures subsequently improving secondary fracture prevention.

The fracture prevention program is an adapted model of the Fracture Liaison service ("AUH FLS"). A nurse practitioner has the initial role of post-fracture assessment and recommendation for further investigation or treatment, supported by a bone specialist at the department.

Here, we report our early experience with a fracture prevention program implemented in Aarhus, Denmark.

Methods: A retrospective single-center cohort study was conducted. We retrieved information from the hospital registries. Eligible patients were those of ≥50 years of age, who sustained a fracture of the hip, pelvis, spine, distal forearm, or shoulder.

Results: Twenty-four months after the implementation, a total of 2625 patients with a fracture were identified. 48% (n=1274) were invited to a DEXA scan. 21% of the patients attending AUH FLS were diagnosed with osteoporosis. 65% were eligible for treatment with an anabolic agent.

Conclusion: At Aarhus University Hospital, the implementation of the fracture prevention program has systematized the identification of patients presenting with a fragility fracture. We believe that the program might have resulted in more patients being diagnosed and treated for osteoporosis.

Themes: Endocrinology, Pharmacology
Keywords: osteoporose, ,

Register-based Cohort Study on the Non-specific Effects of Influenza Vaccination in Delaying Autoimmune Comorbidity in Individuals with Type 1 Diabetes

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Background: Individuals with type 1 diabetes (T1D) are at heightened risk for developing additional autoimmune disorders, particularly autoimmune thyroid disease (17-30%) and coeliac disease (8%). Both diseases are linked to adverse outcomes in T1D; abnormal thyroid hormone levels can impair glycaemic control, while celiac disease is associated with an increased risk of microvascular complications. This study aims to investigate the potential benefits of influenza vaccination in delaying the onset of these comorbid autoimmune diseases in individuals with T1D.

Methods: We will conduct a nationwide cohort study of all Danish citizens aged 1-64 years diagnosed with T1D, recorded from 2015 to 2022. Using national health registries, we will assess data on influenza vaccination, comorbid autoimmune disease incidence, and predictors of comorbid autoimmune comorbidities. Individuals will be followed from date of T1D diagnosis or cohort entry (2015) until the diagnosis of subsequent autoimmune disease, death, emigration, or end of follow-up.

Statistical analysis will employ time-to-event analysis and Kaplan-Meier estimate.

Perspectives: To our knowledge, this is the first study to explore whether influenza vaccination can delay the onset of additional autoimmune diseases, such as celiac disease and autoimmune thyroid disease, in individuals with T1D. If influenza vaccination proves beneficial in reducing the incidence or postponing the onset of other autoimmune disease, it could impact clinical care and risk of long-term complications in individuals with T1D.

Themes: Endocrinology, Epidemiology
Keywords: Type 1 Diabetes, Influenza Vaccination, Comorbid Autoimmune Diseases

Effects of extensive Weight loss on Insulin resistance and Lipid-kinetics in people with obesity and fatty liver Disease - The WILD study

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Background

Obesity drives the development of metabolic dysfunction-associated steatotic liver disease (MASLD) and dyslipidemia. A central pathophysiologic feature of dyslipidemia is proposed to be increased serum concentrations of very-low-density lipoproteins and triglycerides (VLDL-TG).

We wish to study the VLDL-TG kinetics in obese patients with MASLD before, during and after a weight loss intervention induced by either Roux-en-Y Gastric Bypass (RYGB) or high dose Semaglutide treatment.

Methods

Currently, we have recruited 16 of 24 female patients with MASLD referred to bariatric surgery from our out-patient clinic at Steno Diabetes Centre Aarhus. The patients will be randomized to either RYGB or Semaglutide treatment.

Anthropometrics, blood samples, DXA-, MR-, and Fibroscan, subcutaneous fat- and muscle biopsies and VLDL-TG-, palmitate-, and glucose kinetics during fasting and hyperinsulinemic euglycemic clamp will be registered at 3 time points:

1) Baseline, before treatment initiation, 2) After a weight loss of 10 % of baseline weight,

3) 8 months after treatment initiation.

Primary end point

Changes in VLDL-TG kinetics during weight loss and after 8 months of treatment initiation.

1. Differences between the two groups

2. Changes in relation to the degree of weight loss/resolution of MASLD

Significance of the project

The WILD study is both a study of the natural history of VLDL-TG kinetics during weight loss and a randomised clinical study on the effects of RYGB versus Semaglutide treatment. We

hope to elucidate the resolution of insulin resistance, dyslipidemia, MASLD and changes in hepatic secretion of VLDL-TG particles during extensive weight loss.

Themes: Endocrinology, Gastroenterology and hepatology
Keywords: Obesity, Lipid kinetics, Metabolic dysfunction-associated steatotic liver disease

Does co-administration of lactate to a meal affect postprandial nutrient absorption and fat disposition?

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Objectives: Fermented dairy products have been linked to a decreased risk of type 2 diabetes and cardiovascular disease, possibly due to lactate produced during fermentation. Lactate may influence fat absorption and metabolism, but the mechanisms are not well understood. The incidence of type 2 diabetes is rising and is associated with an increased risk of dyslipidemia and cardiovascular disease. This study aims to investigate whether adding lactate to a meal improves postprandial lipemia and reduces ectopic lipid storage, and to validate the use of the 18F-FTHA-PET-CT method for meal fat absorption and distribution.

Methods/Design: In a randomized, double-blinded, placebo-controlled crossover study, including 16 individuals above 50 years with pre-diabetes (HbA1c 39-47 mmol/mol), participants will receive a liquid meal labeled with an 18F-FTHA radioisotope, with either lactate or placebo. 5 hours after the mixed meal test, they will undergo a 1-hour PET-CT scan to measure fat partitioning. The primary endpoint is fat uptake in the heart, while secondary endpoints include fat uptake in other organs. The 18F-FTHA method will also be validated in 8 healthy individuals to assess intraindividual variation.

Perspective: This study will provide insights into the effects of lactate on postprandial fat absorption and distribution in individuals with pre-diabetes. The results could support dietary strategies to improve metabolic health and potentially reduce the risk of dyslipidemia, cardiovascular disease and type 2 diabetes. Additionally, validating the 18F-FTHA method may establish a noninvasive method for evaluating fat distribution for future metabolic research and clinical use.

Themes: Endocrinology, Diagnostics & technology
Keywords: Lactate, Fat-metabolism,

An activin type II receptor ligand trap prevents loss of cortical bone strength and cancellous bone mass in a mouse model of severe disuse osteopenia

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Background: Muscular disuse is a potent catabolic stimulus for bone. The use of TGFβ superfamily antagonists has a compelling rationale in the setting of disuse since activin and myostatin inhibition is known to stimulate both bone and muscle anabolism. This study evaluated a research version of KER-065 (RKER-065), a modified activin type II receptor ligand trap, in a mouse model of severe disuse induced by botulinum toxin A (Btx), to assess its effects on bone preservation.

Methods: Sixteen-week-old C57BL/6JRj mice were assigned to Baseline (n = 10), Ambulating+Vehicle (Amb+Veh, n = 12), Amb+RKER-065 (n = 12), Btx+Veh (n = 12), and Btx+RKER-065 (n = 12). Btx was injected into right quadriceps and calf muscles on day 1, and either RKER-065 (10 mg/kg) or vehicle was administered ip. twice weekly. Bone properties were analyzed via DXA, μCT, and mechanical testing.

Results: Btx+Veh mice exhibited significant muscle volume loss of the lower right hindlimb (-44%) and declines in femur BMD (-19%), cortical strength (-17%), cancellous BV/TV (-53%), and femoral neck strength (-45%) compared to Amb+Veh. The deterioration in cortical and cancellous structural and mechanical parameters was countered by RKER-065. In disuse mice, RKER-065 significantly improved whole-femur BMD (+15%) and cancellous BV/TV (+141%), restoring these parameters to Amb+Veh levels. Cortical strength was fully preserved, while femoral neck strength (+41%) and muscle volume (+21%) was partially restored compared to Btx+Veh.

Conclusion: Taken together, these data support the potential of KER-065 to offset osteopenia induced by muscle disuse.

Themes: Endocrinology, Pharmacology
Keywords: , ,

Faecal microbiota transplantation for patients with diabetes type 1 and severe gastrointestinal neuropathy (FADIGAS): a randomised, double-blinded, placebo-controlled trial

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Background: Diabetic gastroenteropathy is associated with nausea, vomiting, bloating, pain, constipation, and diarrhoea. We tested faecal microbiota transplantation (FMT) for patients with type 1 diabetes and gastroenteropathy.

Methods: In a randomised, double-blinded, placebo-controlled pilot trial, adults with type 1 diabetes and moderate-to-severe gastrointestinal symptoms were randomised (1:1) to encapsulated FMT or placebo. All received FMT as a second intervention. The primary endpoint was number of adverse events of severity grade 2 or more assessed by the CTCEA following the first intervention. Secondary endpoints included gastrointestinal symptoms and quality of life.

Results: Between June 2021 and May 2023, we randomised 20 patients to FMT or placebo. Following this intervention, 26 adverse events of grade 2 or more occurred. Four patients in the FMT group reported seven adverse events and five patients in the placebo group reported 19.

The most frequent adverse events were diarrhoea, bloating, and abdominal pain. No serious adverse events were related to the treatment. Patients who received FMT reduced their median GSRS-IBS score from 58 (IQR 54–65) to 35 (32–48), whereas patients receiving placebo reduced their score from 64 (55–70) to 56 (50–77) (p=0.01). The IBS-IS score improved from 108 (101–123) to 140 (124–161) with FMT and 77 (53–129) to 92 (54–142) with placebo (p=0.02). The PAGI-SYM declined from a median of 42 (28–47) to 25 (14–31) after FMT and 47 (31–69) to 41(36–64) after placebo (p=0.03).

Conclusion: FMT was safe and significantly improved clinical outcomes for patients with type 1 diabetes suffering from debilitating bowel symptoms.

Themes: Gastroenterology and hepatology, Endocrinology
Keywords: Diabetic gastroenteropathy, Faecal microbiota transplantation, Microbiota

SESSION 7 - Qualitative research and public health

Midwives' perspectives on working in a specialized unit for pregnancy loss - A qualitative study

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Background:

Caring for parents bereaved by late pregnancy loss (second or third trimester) is a complex task. On the one hand, healthcare professionals experience high levels of meaningfulness in this work. On the other hand, they feel unprepared and struggle emotionally. Experience, support, and education are factors of great significance when working in this field. It is suggested that the care should be provided by healthcare professionals experienced in bereavement and grief. To improve the quality of care, Denmark is gradually shifting towards care in specialized units for loss. Latest in Maj 2022, where a specialized unit for loss was established at Gødstrup Hospital. Midwives dedicated to this field were employed providing a unique opportunity for this study where we explored work-motivation and experiences among midwives who have actively chosen to work in this field.

Methods:

Qualitative method

Semistructured interviews with 7 midwives employed at Unit for Loss, Gødstrup

Interviewed in April 2022 (before startup) and again in August 2023.

A reflexive thematic analysis was performed using a hermeneutic-phenomenological approach.

Results and Conclusion:

Will be presented at the PhD-day

We anticipate having a description of results and conclusion ready soon and expect to submit the article in December 2024

Potential impact:

This study provides valuable insights into key factors influencing work motivation and experiences among midwives working in a demanding field. It sheds light on aspects such as the experience of working closely with death and grief and contributes useful perspectives to the debate on sustainable working conditions for midwives.

Themes: Gynecology and obstetrics, Qualitative research
Keywords: Midwife, specialized unit for loss, specialized unit for loss

Managing the new wave of weight loss medication in general practice: A qualitative study

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Background and aim: The introduction of Wegovy (semaglutide) in Denmark in late 2022 generated substantial media attention and public demand. As general practitioners (GPs) are responsible for most prescriptions, this study aimed to explore how Wegovy is managed in general practice, focusing on prescribing practices and follow-up.

Material and methods: A focused ethnographic study was conducted in the spring of 2023, involving direct observations in three Danish general practices and follow-up interviews with seven doctors and four nurses. Observations spanned four weeks per clinic and included observations of consultations and taking part in lunch breaks and in-house meetings. Field notes were recorded contemporaneously during observations and supplemented afterwards. All interviews were audio-recorded for subsequent analysis.

Results: The study documented 273 consultations, of which 28 involved discussions about Wegovy. Most patients who requested Wegovy were prescribed the drug, with only two exceptions based on medical criteria and patient decisions. Analysis revealed four key discourses: a fundamental trust in medical science, the emphasis on health and individual responsibility, the negotiation of weight loss costs, and patient-led shared decision-making.

Conclusion: The study highlights the complexities faced by GPs in managing the introduction of Wegovy. The findings reveal the diverse factors influencing the prescription process, including medical, economic, organizational, and moral concerns, and offer insights into the broader implications of introducing new obesity treatments in primary care.

Themes: Endocrinology, Qualitative research
Keywords: General Practice, Obesity, Weight loss medication

Needs for nutritional support in patients receiving palliative chemotherapy: A qualitative study

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Background: Malnutrition has negative effects on outcomes, including quality of life, physical function, treatment tolerance and survival in patients with cancer. Nutritional support might prevent and treat malnutrition and improve wellbeing and quality of life. Yet, little is known about how nutritional support should be organized to meet the demands of the patients.

Aim: To explore experiences, perceived needs, requests, and preferences for nutritional support in patients with cancer receiving palliative chemotherapy.

Methods: Semi-structured, face-to face interviews were conducted with 10 patients with colorectal-, lung- or pancreatic cancer who had received palliative chemotherapy for 2-6 months at Gødstrup Hospital. Interviews were audio-recorded, transcribed verbatim and analysed using qualitative content analysis.

Results: Five themes were identified; “Limited focus on nutrition”, “Important knowledge from the start”, “Nutrition is my responsibility”, “The dietitian as a nutritional lifeline” and “Meet me where I am”. Participants describe limited focus on nutrition during treatment. While some did not perceive a need for nutritional support, others expressed a desire for more information and emphasis on nutrition. Even though participants consider nutrition their own responsibility, they see the relevance of the dietitian supporting them.

Conclusion: Patients with cancer receiving palliative chemotherapy request focus on nutrition, knowledge and individual support to manage own nutrition.

Themes: Cancer, Qualitative research
Keywords: Nutrition, Cancer, Dietetics

Social Prescribing Initiatives Connecting General Practice Patients with Community-based Physical Activity: A Scoping Review with Expert Interviews

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Aims: WHO states that physical inactivity is one of the leading behavioural risk factors for disability and mortality in Europe. Social prescribing holds promise as a possible solution, by connecting patients from general practice to community-based physical activity. Although research within social prescribing exists, the process of connecting general practice patients towards community-based physical activity is not well investigated. This scoping review aimed to summarize and synthesise knowledge on social prescribing provided by health professionals in general practice towards community-based physical activity.

Methods: A systematic search for literature in PubMed, Embase, Scopus, SportsDiscus and other sources was conducted to identify initiatives connecting general practice to community-based physical activity. Semi-structured interviews were then conducted with subject-specific experts. Finally, preliminary findings from the literature and the interviews were used in a co-creation process with experts to synthesise and finalize the results of a thematic analysis across data sources.

Results: Based on 19 records, five expert interviews and subsequent co-creation, we identified three themes: a) Barriers and facilitators; b) organisational perspectives; and c) value-based considerations.

Conclusion: This review illuminates the complex nature of social prescribing programs that connect general practice patients to community-based physical activity. But it also presents practical and fundamental considerations when applying social prescribing across different settings.

Themes: Public health, Qualitative research
Keywords: Social prescribing, Co-Creation, Review

'I' as a Teacher? – Analyzing how I-positions Promote and Challenge Teacher Identity among Early Career Academics in Health Professions

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What challenges do you face in being the teacher you want to be? Teacher identity formation among early career academics (ECAs) in Health Professions Education (HPE) is a dynamic process shaped by multiple roles. Integrating teaching into identities as 'researcher' and 'clinician' is challenging and complicated by a competitive environment where teaching is often underprioritized. Solicited audio diaries and pre/post interviews were collected from 10 ECAs over one semester to examine how I-positions promote and challenge a teacher identity that values teaching. I-positions, derived from Dialogical Self Theory, describe various standpoints an individual identifies with, suggesting identity consists of multiple selves. Preliminary results indicate the ECAs identify with several I-positions that value teaching, such as 'I as a caring teacher,' 'I as a responsible teacher,' and 'I as an experimental teacher,' each committed to providing quality teaching. In contrast, I-positions like 'I as a researcher' and 'I as a clinician,' along with an 'I as busy' position arising from tight schedules, may challenge teaching-valuing I-positions. Some ECAs describe an 'I as alone' position, lacking a teaching community to discuss and share experiences. These findings indicate persistent tensions between teaching and research/clinical roles, challenging teaching quality in a demanding academic culture. Consequently, institutions may unintentionally challenge identities that value teaching by creating a high demand for internal motivation and personal commitment to deliver quality teaching, which may be undermined without adequate support and institutional recognition.

Themes: Health Education, Qualitative research
Keywords: Teacher Identity, Health Professions Education, Audio Diaries

National scale-up of telehealth in Denmark: The role of translation in large-scale implementation processes

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Background:

Health systems face economic pressure due to rising chronic patient numbers and healthcare staff shortages. Telehealth has emerged as a promising solution, but large-scale implementation remains a key challenge. Actors working on macro (national) and meso (organisational) levels play a crucial role in large-scale implementation yet remain understudied. Hence, this study investigates the first national implementation of telehealth for patients with Chronic Obstructive Pulmonary Disease (COPD) on meso- and macro-level.

Methods:

An in-depth qualitative study was conducted using data from interviews with 16 stakeholders in key administrative roles across governmental, regional, and municipal levels, along with 45 documents, including policy papers and meeting minutes. Data were analysed using thematic analysis and translation theory as a lens.

Results:

The analysis revealed that large-scale telehealth implementation is complex, requiring significant translation by stakeholders across a meso- and macro-level. Three themes emerged around this translation work: (i) navigating the complexities of large-scale implementation, (ii) balancing fidelity and local adaptation, and (iii) ensuring legitimacy and local buy-in. This translation work led to variations in telehealth models implemented across local contexts.

Conclusion:

Large-scale telehealth implementation is complex and time-consuming, requiring significant translation work and adaptation across contexts. Meso- and macro-level actors act as translators, aligning political visions with local needs to ensure legitimacy. The need for translation must thus be carefully balanced with the need to ensure intervention fidelity.

Themes: Public health, Qualitative research
Keywords: Implementation, Telehealth, Public Health

Multidisciplinary Teams for Patients with Chronic Conditions: A Scoping Review of Patient Perspectives and Experiences

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Aim: To identify, summarize, and analyze studies of patients' perspectives on and experiences with multidisciplinary team (MDT) meetings for patients with chronic conditions.

Introduction: MDTs bring different health professionals together to assess, plan, and manage patient care jointly. However, little attention has been drawn to how patients with chronic conditions experience MDT meetings and their perspectives on them.

Inclusion criteria: Literature describing patient perspectives and experiences of MDTs for adult patients with diabetes, heart disease, stroke, cancer, chronic respiratory diseases, osteoporosis, asthma, or rheumatoid arthritis. Literature about effects of MDTs on health outcomes are excluded.

Methods: JBI guidelines are followed. PubMed, Embase, CINAHL, PsycINFO, JSTOR, Scopus, and MedNar are searched without limitations on publication language. Year of publication is restricted to the 1980s and forth since MDTs were initiated in this period. Data extraction, charting, and analysis are guided by a template developed following the study aim.

Results: 16 articles have been included. Preliminary results show that patients are not necessarily aware of MDT existence, want to participate in team discussions, and value MDT work in their treatment.

Conclusions: A small amount of literature about patient experiences with and perspectives on MDT meetings exists. Recognizing patient experiences and perspectives and further investigation in this topic area can contribute to potential improvement of MDT activities, such as the acknowledgement of patient preferences and the patient's involvement in treatment decisions.

Themes: Public health, Qualitative research
Keywords: Chronic conditions, Multidisciplinary Team conferences, Patient perspectives and experiences

Developing a complex intervention to improve guidance for researchers involving patient partners in a research process

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Background: Research funders, policymakers and patients are increasingly calling for the involvement of patients and their relatives in research processes. However, it remains unclear how researchers can best involve patient partners and what the impact of their involvement is. This PhD project aims to develop an intervention to improve the partnership between researchers and patient partners across different patient groups in Denmark.

Method: A complex intervention framework guides four studies, each answering a unique research question.

Study 1: How can patient partners be effectively involved in the research process? A scooping review will be informed by the approach of Levac et al.

Study 2: How can researchers be supported when planning to involve patient partners in a research process? Interviews will be conducted with researchers who involve patient partners in a research process.

Study 3: How to improve research guidance for best practice in involving patient partners in the research process in Denmark? A course will be developed and tested using questionnaires. A prototype guide will be developed, and Delphi tested with relevant stakeholders.

Study 4: How can stakeholder involvement in a steering group influence a research process? A steering group of relevant stakeholders will be established to support the PhD project. Initially interviews will be conducted, and the meetings will be evaluated through questionnaires.

Perspectives: By improving guidelines for researchers involving patient partners, the PhD project has the potential to influence future national guidelines and to improve the quality of health care research in accordance with the needs of the stakeholders.

Themes: Public health, Qualitative research
Keywords: Patient and Public Involvement (PPI), Public Involvement, Guidance for researchers

Interventions and Communication Strategies for Sharing End-of-Life Care Preferences Among Independent Living Older Adults During Healthcare Transitions: A Scoping Review

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Background: End-of-life care preferences of independent-living older adults (life expectancy < 12 months) are poorly communicated during healthcare transitions, leading to unwanted, costly interventions.

Aim: To map evidence on interventions and communication strategies for sharing end-of-life care preferences of independent living older adults (>65 years) during healthcare transitions.

Methods: A scoping review based on Joanna Briggs Institute's framework examined studies (2014–2023) from six databases. Eligible studies addressed how healthcare professionals identify, communicate and document end-of-life care preferences during healthcare transitions for independent living older adults.

Results: Fifteen studies from seven countries, mostly non-randomized, were included. Interventions varied from structured facilitator-led programs to informal discussions, often including professional training, structured advance care planning (ACP), multidisciplinary meetings, or decision aids. Some combined approaches, such as face-to-face meetings with written follow-up, while others relied on written documentation only. Proactive ACP and multidisciplinary and comprehensive communication seemed to impact hospital admissions, alignment with care preferences, and out-of-hours consultations, though standardization was limited, and long-term effects were unexamined.

Discussion: Comprehensive ACP interventions, including multidisciplinary communication and proactive identification of care needs may improve outcomes during transitions. The lack of standardization highlights the need for focused research to establish sustainable, effective ACP models for this group.

Themes: Public health, Qualitative research
Keywords: Advance Care Planning, Geriatrics, Healthcare Transitions

Impact of colonic diverticulosis on daily life. The DIVIPACT study.

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Knowledge of the symptoms and impact of colonic diverticulosis in the general population remains sparse. We aimed to establish a cohort of subjects with colonic diverticulosis to characterise subjects with and without symptoms and investigate diverticulosis's impact on daily life.

Subjects with contact to a hospital in The Central Denmark Region due to colonic diverticulosis (K572-9) from 2010 to 2022 received a comprehensive online survey in their Digital Post during April and May 2023. The survey included questions regarding background information and several validated questionnaires concerning quality of life, pain and bowel, urinary, and sexual function. Additionally, subjects were asked to accept a review of their medical records.

Of 29,624 eligible subjects, 20,961 (74%) responded. Responders had a median age of 70 years (IQR: 63-77), females constituted 52%, the median BMI was 27 (IQR: 24-30), and 11% were smokers. Of the responders, 13% (n = 2,791) had seen their general practitioner due to flare-ups. Concerning the impact of colonic diverticulosis on daily life, 11% (n = 2,264) answered that they had missed work or other important obligations during the last two weeks due to diverticulosis. Almost half of responders (45%, n = 9,441) reported that their bowel function impacted their quality of life. Concerning overall quality of life, 8% (n = 1,677) reported their quality of life to be bad or very bad.

Diverticulosis is asymptomatic in most subjects, but some develop symptoms that impact quality of life. We have established a huge cohort of subjects with diverticulosis and will further investigate symptom burden and quality of life.

Themes: Surgery, Gastroenterology and hepatology
Keywords: Diverticulosis, Quality of Life, Survey

SESSION 8 - Imaging diagnostics

Deuterium Metabolic Imaging for the investigation of Alzheimer's Disease

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Background: Alzheimer's disease (AD) is the most common cause of dementia, characterized by amyloid and tau protein accumulation along with structural and metabolic changes of the brain. Among these changes, impaired glucose uptake has been identified using FDG-PET.

This study aims to further explore the glucose metabolism in healthy and AD-affected brains using deuterium metabolic imaging (DMI), a magnetic resonance imaging (MRI) technique that traces deuterium (2H) labeled substrates such as glucose and its conversion into metabolites (glutamine, glutamate and lactate).

Methods: This prospective clinical study will include 20 AD patients and 30 healthy controls. The controls will be aged 50-85 years and evenly distributed with respect to sex. All participants will ingest 75 g of [6,6′-2H2]glucose before being scanned on a 3T clinical MR scanner. The scan will include conventional MRI with T1-weighted imaging for anatomical assessment, and DMI with magnetic resonance spectroscopy imaging for metabolic assessment.

Results: A normative atlas of the healthy brain glucose metabolism will be generated by spatially normalizing the signal intensities of 2H-water, 2H-glucose, 2H-glutamine+glutamate, and 2H-lactate across brain regions to a standard brain template and modelling the impact of age and sex. This atlas will serve as a reference for comparison with the DMI scans of AD patients.

Perspectives: Discovering significant metabolic differences between AD patients and controls could enhance AD diagnosis and disease management. Additionally, the generated atlas is expected to be a valuable resource for future research into neuronal diseases.

Themes: Neuroscience, Imaging techniques
Keywords: Alzheimer's disease, Brain metabolism, Deuterium metabolic imaging

Deciphering calcium signaling crosstalk between breast cancer cells and cancer associated macrophages

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Breast cancer is the most common malignancy in women globally. It is curable in 70-80 % of patients with early disease, but advanced breast cancer is incurable. In recent years, there has been increased attention to the different cells in the tumor microenvironment (TME), including macrophages, which are the most abundant immune cells in breast tumors. The TME can promote macrophages to become immunosuppressive tumor associated macrophages. Different signaling pathways play a role in the crosstalk between cancer cells and macrophages, but limited research has investigated the role of calcium signaling in the crosstalk between these two cell types, although it is known that calcium signaling is involved in many macrophage functions and cancer processes. Therefore, this project aims to develop co-culture models to explore calcium signaling in breast cancer cells and cancer associated macrophages.

Mice expressing a genetically encoded green calcium sensor and a calcium insensitive protein (GCaMP6f-TdTomato) were generated via Csf1r-Cre. Bone marrow cells from these mice were isolated and differentiated to bone marrow derived macrophages. To create a syngeneic model, we utilized the mouse breast cancer cell line EO771 expressing a red calcium sensor (jRCaMP1b).

We have created direct and indirect co-cultures. The direct co-culture model was used to image calcium signaling during physical interactions between breast cancer cells and macrophages, while the indirect co-culture model using a transwell system allowed investigations of gene expression changes of calcium signaling proteins in each cell population via RT-qPCRs. The preliminary results from this work will be presented.

Themes: Cancer, Imaging techniques
Keywords: Breast cancer, Macrophages, Confocal imaging

Structure of biofilm-forming functional amyloid PSMa1 from Staphylococcus aureus

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Biofilm protected pathogenic Staphylococcus aureus cause chronic infections that are difficult to treat. An essential building block of these biofilms, are functional amyloid fibrils that assemble from phenol soluble modulins (PSMs). PSM 1 cross-seeds other PSMs into cross-β amyloid folds and is therefore a key element in initiating biofilm formation. To date, there is no highresolution cross-β biofilm-forming functional amyloid structure available amongst the 469 amyloid entries deposited in the EMDB. Here we present a 3.5 Å resolution density map of the major PSM 1 fibril form revealing a left-handed cross-β fibril composed of two C2-symmetric U-shaped protofilaments whose subunits are unusually tilted out of plane.

Finally, we provide mechanistic insights into the PSM functional amyloid formation and conformation transformation on the path from monomer to fibril formation. Details of PSM 1 assembly and fibril polymorphism suggest how S. aureus utilizes functional amyloids to form biofilms and helps future researchers to establish a framework for developing therapeutics against infection and antimicrobial resistance.

Themes: Infectious Diseases, Imaging techniques
Keywords: Bacterial Biofilm, Cryo-EM, Amyloids

Aquaporin-5 as a potential new target in breast cancer treatment

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Multiple aquaporin water channels are expressed in breast cancer and especially aquaporin-5 (AQP5) has been associated with spread to lymph nodes, worse prognosis, and reduced survival in breast cancer patients. The precise mechanisms by which AQP5 promotes breast cancer pathogenesis are mostly unknown. However, AQP5 is predominantly localized intracellularly in tumor cells, suggesting that AQP5 contributes to breast cancer spread and progression via cellular signaling rather than transcellular water transport. Therefore, downregulation of AQP5 could be a potential treatment strategy.

This study aims to investigate AQP5 as a potential new therapeutic target in breast cancer treatment. Therefore, the ectopically intracellular localization of AQP5 will be examined along with the pathways that are upregulated by AQP5 to facilitate breast cancer progression and spread. Moreover, I will test FDA-approved drugs, that have been shown to reduce the protein levels of AQP5 for their ability to downregulate AQP5 in breast cancer cells and thereby counteract AQP5-mediated signaling in breast cancer cells. Since AQP5 has also been shown to affect the sensitivity of conventional chemotherapy drugs, I also will test the AQP5-downregulating drugs in combination with conventional chemotherapy treatments. This study is expected to contribute to a better understanding of AQP5 in breast cancer and possibly lead to new treatment options for breast cancer patients in the future.

Themes: Cancer, Imaging techniques
Keywords: Breast Cancer, Aquaporin-5, Microscopy

Inflammatory Amyloids in Phenylketonuria

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In classic phenylketonuria (PKU), the most common inborn error of amino acid metabolism, genetic defects in the phenylalanine hydroxylase (PAH) enzyme cause elevated levels of L-phenylalanine (Phe) in the blood (bPhe). Poorly regulated bPhe leads to severe neurodegeneration in the unborn fetus and during infancy but also adversely affects the central nervous system (CNS) later in life. However, the biochemical basis of the PKU-induced neurodegeneration remains unclear. At PKU- relevant concentrations, Phe may form amyloid fibrils resembling those found in Alzheimer's and Parkinson's Disease (AD and PD). Some evidence suggests Phe fibrils possess an amyloid imprinting activity on other proteins, e.g., albumin, a process here named Phe fibril-imprinted amyloidogenesis (PIA). This project will investigate the hypothesis that PIA particles are formed and are a target for pro-inflammatory phagocytosis. We will use Thioflavin T staining and absorbance measurements. With a PKU mouse model, we will investigate whether high bPhe levels lead to an inflammatory phenotype and correlate these findings with patient serum. Furthermore, the high bPhe levels are hypothesized to inflict amyloid brain pathology and vascular damage in brain blood vessels in PKU mice. Brains collected from PKU mice will be investigated with several scanning modalities. Taken together, these techniques might lead to an improved understanding of the neuropathology of PKU.

Themes: Neurodegenerative disorders, Imaging techniques
Keywords: Phenylketonuria, Neuroimmunology,

Perfusion MRI in stroke: Investigating the relation between relative transit time heterogeneity (RTH) and stroke subtypes in ischemic stroke

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Background:

MRI is essential in diagnosing and managing ischemic stroke. Perfusion-weighted imaging (PWI) with gadolinium contrast provides vascular characteristics, such as cerebral blood volume, flow, and derived values like relative transit time heterogeneity (RTH), which serve as a metric for capillary dysfunction. Emerging theories suggest that capillary dysfunction significantly contributes to stroke pathophysiology, rather than being solely a flow-limiting condition. This study will examine the relationship between RTH and ischemic stroke subtypes classified by the TOAST criteria: large artery atherosclerosis, cardioembolic, small vessel disease, and other causes.

Methods:

A cohort of 140 patients with acute ischemic stroke was enrolled in the prospective study, "Exploring Vascular Contributions to Cognitive Impairment and Dementia (ENIGMA)," between April 2021 and August 2024. Each patient underwent an MRI scan within 24 hours after admission. We will calculate perfusion parameters, including RTH maps, for each patient. Regions of interests (ROIs) will be placed on these maps and compared with normal-appearing contralateral ROIs to quantify capillary dysfunction. This will enable correlation analyses between RTH and specific TOAST stroke subtypes, aiming to identify markers for different stroke etiologies and enable early risk stratification of ischemic stroke patients.

Conclusion:

We anticipate that RTH levels will differ between ischemic stroke subtypes, with the highest values expected in patients with small vessel disease. Such findings could improve early stroke risk stratification and inform personalized treatment strategies and thereby enhance patient outcomes.

Themes: Neuroscience, Imaging techniques
Keywords: Neuroradiology, Neuroscience, Ischemic stroke

In vivo explorative study of immune pathways in response to HSV-1 infection using Imaging mass cytometry for spatial analysis

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This study aims to investigate how the immune system reacts against Herpes Simplex Virus Type 1 (HSV-1) upon its invasion of the central nervous system (CNS), leading to some rare cases of Herpes Simplex Encephalitis (HSE).

This work addresses gaps in our understanding of CNS-specific immune responses to viral infection, advancing the current knowledge of HSE pathogenesis using an advanced spatial imaging technique, for spatial single-cell analysis of the complex cellular interactions in the brain environment.

Using Imaging Mass Cytometry (IMC), we want to investigate different genotypes (cGAS -/- and TMEFF1 -/-) where the host exhibits increased susceptibility to infection at the early stages.

Our 34-marker panel is designed to include markers for a deeper understanding of HSE pathology, including signaling pathways (e.g Viperin), oxidative cell damage (e.g.4HNE) and immune cell infiltration (e.g CD45 and CD68), correlated with early-stage HSV-1 infection.

By uncovering these interactions, upon tissue localization and time of infection, these findings will deepen our understanding into the dynamics of antiviral immunity and viral neuropathogenesis of

HSV-1.

Themes: Infectious Diseases, Imaging techniques
Keywords: Mouse model, Brain, Virus

Determination of the mechanisms of ketone body-induced beneficial cardiac effects in patients with chronic heart failure

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Background: Growing evidence supports a beneficial effect of the ketone body 3-hydroxybutyrate (3-OHB) in heart failure. Our research group recently found a persistent increase in cardiac output and lowering of pulmonary capillary wedge pressure during rest and exercise in patients with heart failure with reduced ejection fraction after ketone treatment compared with an isocaloric comparator.

Hypothesis: In patients with heart failure with reduced ejection fraction (HFrEF) a 2-week ketone body supplement will increase myocardial 3-OHB uptake. This is reflected in altered myocardial mRNA expression encoding ketolytic enzymes and ketone transporters. Changes in myocytic protein, metabolomics, and mRNA expression can be defined and related to the cardiac hemodynamic effects of 3-OHB.

Methods and aims: This is a randomized, double-blind, placebo-controlled crossover trial, in which 12 patients with HFrEF will be investigated on parameters including: 1) myocardial uptake of 3-OHB, 2) myocardial oxygen consumption (MVO2), 3) myocardial external efficiency (MEE), and 4) myocardial blood flow (MBF). Examinations will be performed before and during acute ketosis.

Assessments also include skeletal muscle biopsies, Swan-Ganz measurements with coronary sinus blood sampling, and endomyocardial biopsies for single nucleus mRNA sequencing (Sn-mRNA-seq), proteomics and metabolomics.

Results: Data are analyzed using appropriate statistical methods, and correlations will be explored when applicable.

Perspectives: Understanding the mode of action of ketone bodies in heart failure is crucial for delineating the specific pathways involved in the beneficial myocardial effects of ketones.

Themes: Cardiology, Imaging techniques
Keywords: Heart failure, Metabolism, Clinical research

Validating the ESTRO target consensus: pattern of breast cancer failures in the DBCG Skagen trial 1

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Purpose: The phase III DBCG Skagen trial 1 (NCT02384733) randomized 2080 node-positive Danish breast cancer patients (2015-2021) to receive either 50Gy/25fr or 40Gy/15fr for loco-regional radiotherapy. Target volumes were delineated by ESTRO guidelines, with a pre-specified report on the loco-regional pattern of failure to assess guideline feasibility in high-risk breast cancer patients. This analysis presents the first validation of the ESTRO guidelines with prospective data.

Methods: Loco-regional failure with or without distant failure as the first event was defined from all available imaging and matched with the planning CT scan, and classified as inside the CTV, inside the high-dose volume, as marginal misses, or outside.

Results: At a median follow-up of 4.5 years, locoregional recurrence occurred in 53 patients: 29 with isolated locoregional failure and 24 with concurrent distant failure. Nearly all locoregional failures were detected within the high-dose volume, with only two exceptions. Specifically, all 29 cases of isolated locoregional failure were entirely within the high-dose volume. "Among the 24 patients with concurrent distant failure, two had nodal failures located at the edge of the high-dose volume.

Conclusion: Loco-regional failures largely occurred within the high-dose volume, supporting the feasibility of the ESTRO guideline and indicating no need to expand nodal targets. The full cohort pattern of failure analysis in the DBCG Skagen trial 1 will be performed.

Themes: Cancer, Imaging techniques
Keywords: Breast cancer, Radiotheraphy, Delineation

Advanced molecular imaging of patients with primary biliary cholangitis

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Background

Medical cholestatic conditions such as primary biliary cholangitis (PBC) can lead to malabsorption of lipophilic substrates from the intestines and, in the liver, cirrhosis. The effect of medical treatment is monitored by liver blood tests, which do not necessarily represent the functional degree of cholestasis. Position tomography (PET) with the radiolabeled conjugated bile acid tracer [N-methyl-11C]cholylsarcosine (11C-CSAR) can be used to quantify hepatobiliary secretion of bile acids and bile flow.

Aim

The aim is to investigate patients with PBC with functional 11C-CSAR PET/CT before and after standard treatment (ursodeoxycholic acid) or before and after treatment with second-line therapy (bezafibrate) to gain new insight into the functional effects of the treatment.

Methods

Patients with PBC are recruited from the outpatient clinics in Aarhus and the regional hospitals in the Central Region of Denmark. A 45-minute functional 11C-CSAR PET/CT of the liver and biliary system with blood concentration measurements of 11C-CSAR in arterial and hepatic venous blood is performed before and after treatment initiation. By analyzing the time course of radioactivity in blood and tissue using a tracer model, we can calculate bile acid clearance levels. So far, three patients have been included.

Perspectives

This study will improve our understanding of PBC and its treatment by quantifying treatment effects on in vivo hepatobiliary bile acid secretion and associated functional outcomes. We aim to extend our understanding of why some patients progress to cirrhosis while others do not, examining the underlying pathophysiological mechanisms contributing to these differences.

Themes: Gastroenterology and hepatology, Imaging techniques
Keywords: Bile acids, Autoimmune, PET/CT

Interscan Reproducibility Of Computed Tomography Derived Plaque Quantification Using A Semi-automated Analysis Software

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Background Coronary computed tomography angiography (CCTA) enables detailed quantification and characterization of coronary atherosclerotic plaque. However, studies on interscan reproducibility of plaque quantification are limited in number and size.

Purpose The study aimed to assess the interscan reproducibility of CCTA-derived plaque volume measurements and the implications of clinical and technical factors on interscan reproducibility.

Methods A total of 101 patients with known coronary artery disease (CAD) underwent two CCTA scans within 1 hour using identical CT acquisition protocol. Coronary plaque volume measurements were quantified using a contemporary semi-automated plaque analysis software.

Results There was no statistically significant difference in median plaque volumes between the first and second scan. The direct correlation was excellent for volumes of non-calcified plaque (NCP), calcified plaque (CP), and total plaque (TP) across all analyses, while moderate for low-density non-calcified plaque (LD-NCP) volumes. Bland Altman analyses demonstrated high interscan agreement across plaque subtypes, except for LD-NCP volumes. Interscan reproducibility of CP volumes was affected by CT image quality with better agreement in scans with the highest image quality score or lowest image reconstructive iteration level. Limits of agreement were significantly narrower for NCP, CP, and TP volumes in lesions located in LAD compared to non-LAD lesions.

Conclusions The use of a semi-automated plaque analysis software holds potential for monitoring disease progression or regression in patients with CAD, provided high CCTA image quality.

Themes: Cardiology, Imaging techniques
Keywords: Coronary artery disease, Coronary computed tomography angiography, Coronary plaque quantification

SESSION 9 - Neuroscience 1

Neuroepigenomics of THC and CBD Exposure during Pregnancy in the Developing Brain

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The landscape around cannabis use is dramatically changing, swifting the clinical interest towards substance abuse during pregnancy and the long term effects on the offspring. Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) can cross the placental barrier and influence the long-term molecular and behavioral outcome of the offspring, in a sex-dependent manner. Only a limited number of studies utilizing animal models have evaluated prenatal Δ9-THC exposure and offspring adverse outcomes, with most of them focusing on males. Most importantly, the vast majority of data available is over 30 years old. Despite notable activity in recent years attempting to address the mechanisms underlying the effects that reach adolescence, the gap in our knowledge is still evident. Here, we aim to understand the cellular, molecular and phenotypic outcomes of THC and CBD exposure during pregnancy employing a translational science approach using mice and brain organoids models. Tissue collection will be performed in different developmental stages, followed by behavioral assessments of cognition and social behavior at adolescence. We will perform whole-genome analysis from fluorescence-activated cell sorting (FACS) isolated neurons of the prefrontal cortex (PFC) and hippocampus. This will target neural progenitors, as well as excitatory and inhibitory neurons. Epigenetic markers, specifically 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) at CpG sites, will be identified using long-read Nanopore sequencing. The results of this study will shed light on the epigenetic pathways implicated in cannabis consumption during pregnancy and the protracted offspring neurodevelopmental outcomes, revealing new targets for the development of personalized therapies.

Themes: Neuroscience, Molecular biology
Keywords: Cannabinoids, Neurodevelopment, Epigenetics and Neurocognitive Outcomes

Genetic and epigenetic background of inner ear dysfunction in Turner Syndrome

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Background: Sensorineural hearing loss (SNHL) affects approximately 6-8% of the population in developed countries. It is highly disabling and impacts choices regarding education, employment, and overall quality of life. Up to half of women with Turner syndrome (TS) suffer from SNHL, but the underlying cause remains unknown similar to half of the cases in the general population. SNHL may be of epigenetic origin, i.e. a result of altered DNA methylation.

Hypothesis: Turner Syndrome represents an ideal model for studying epigenetics related to SNHL.

Purpose: To investigate epigenetics in individuals with TS with SNHL vs. TS without SNHL as well as a comparison with healthy controls.

Population: 50 women with TS and SNHL, 50 women with TS without SNHL and 50 healthy controls.

Methods: A case-control study. Evaluation of hearing and vestibular function with pure tone audiometry, video head-impulse-test (v-HIT), vestibular evoked myogenic potentials (VEMP) and computerized dynamic platform (CDP). MRI and CBCT will be performed for structural assessment; and epigenetic profiling will be performed to establish a link between epigenetics and inner ear dysfunction.

Sub-studies: The correlation between epigenetic profiles and SNHL in TS compared to healthy controls; the vestibular function in TS and controls; and the connection between structural malformations and inner ear dysfunction will be investigated.

Perspectives: The project will generate basic knowledge of SNHL and pave the way towards future biologic treatment modalities.

Themes: Neuroscience, Genetic engineering
Keywords: Epigenetics, Sensorineural hearing loss, Turner Syndrome

Cytoprotective effect of conditioned extracellular vesicles in stroke

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Globally, stroke is the second leading cause of death with 85% of cases attributed to ischemic stroke. This condition deprives brain regions of oxygen and glucose, leading to rapid cell death and severe tissue damage in the brain. Since the blood-brain barrier is compromised, brain endothelial cells are the first line of defense impacted during stroke.

Remote ischemic conditioning (RIC) is a non-invasive therapy that promotes neuroprotection by stimulating the release of extracellular vesicles (EVs) and other protective signals. RIC-conditioned EVs, capable of crossing the blood-brain barrier, hold promise for stroke therapy due to their role as intercellular signaling mediators and their miRNA content capable of reprogramming the recipient cell. However, the protective mechanism, especially of EV subpopulations from endothelial and red blood cells, remain to be fully elucidated.

This study isolates RIC-conditioned EVs from endothelial and red blood cells using cell-type specific antibodies and MACS nanobeads technology. In addition, RIC-conditioned EVs cytoprotective effect are evaluated in an oxygen-glucose deprivation assay mimicking acute ischemic stroke in vitro using human brain endothelial cells.

Unveiling the mechanisms of RIC-conditioned EVs could inform the development of new therapies to reduce stroke damage and improve patient outcomes.

Themes: Neuroscience, Molecular biology
Keywords: Ischemic stroke, Extracellular vesicles (EVs), Remote Ischemic Conditioning (RIC)

Comprehensive Heritability Atlas of More Than 300 Phenotypes in the Danish Population: Insights from family and genotype data

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Heritability, the proportion of phenotypic variance attributable to genetic variation, is essential for understanding genetic influences on human health. Traditional twin studies estimate heritability by comparing monozygotic and dizygotic twins, but these studies are resource-intensive and subject to recruitment biases. Large-scale population registers offer a more comprehensive and unbiased way to assess heritability across diverse traits, even in the absence of zygosity information. This study aims to create an atlas of heritability using Danish health registers along with estimates of single nucleotide polymorphism heritability (h_SNP^2).

Data from Danish national registers were used to identify twin and sibling pairs born between 1977 and 2021. International Classification of Disease diagnostic codes were mapped to phecodes. Heritabilities were estimated by fitting a linear mixed model with the resulting variance components used in a modified Falconer's formula.

We used the 140,000 genotyped individuals from the Lundbeck Foundation Initiative for Integrative Psychiatric Research cohort to perform genome-wide association studies and used LDpred2-auto for h_SNP^2 estimation.

In total, 83,850 twins and 1.4 million siblings were included in the study. Heritability estimates were computed for more than 300 phenotypes, allowing for detailed comparisons across disorders. h_SNP^2 was estimated for a range of neurological and psychiatric disorders.

This study provides the most comprehensive atlas of heritability in the Danish population to date, highlighting both narrow-sense genetic heritabilities as well as specific contributions from common variants for specific disorders.

Themes: Neuroscience, Public health
Keywords: Heritability, Genetic architecture, Phecodes

Crosstalk in the Peripheral Nerve Microenvironment of Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency: Implications for Mitochondrial Fatty Acid Oxidation and Neurorehabilitation

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Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) is essential for mitochondrial fatty acid oxidation (FAO), where it converts long-chain 3-hydroxyacyl-CoA esters into the corresponding 3-ketoacyl-CoA esters. Of great concern, peripheral neuropathy (PN), manifesting as axonal neuropathy with demyelination, is found specifically in LCHAD deficiency (LCHADD), while rarely reported in other long-chain FAO disorders. Given that myelin is rich in lipids, myelination and maintenance is expected to be particularly vulnerable to inborn errors of FAO. This indicates that the accumulation of disease/gene-specific fatty acid metabolites may be responsible for PN demyelination. Additionally, the secondary mitochondrial dysfunction that seems more pronounced in LCHADD, such as LCHADD products destabilizing the respiratory supercomplexes, could be involved. To unravel the molecular pathogenesis of PN demyelination in LCHADD, our project plan to construct the first “LCHADD PN in a dish” model using human stem cell-derived sensory neurons and Schwann cells. Phenotypical examination, mitochondrial bioenergetics, combined with proteomics, metabolomics and lipidomics will be integrated to investigate the pathological mechanisms. Currently, we have successfully designed and cloned gsRNA plasmid, aiming to knock in the common LCHADD variant c.1528G>C in healthy embryonic stem cells. And we have successfully differentiated healthy stem cells into Sensory neurons and Schwann cells.

Themes: Neuroscience, Genetic engineering
Keywords: Fatty acid oxidation disorder, Peripheral neuropathy, Mitochondrial dysfunction

Can music have an impact on the neurological fundaments of sleep?

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Music has been used as a sleep aid since ancient times, and today many adults report it among other strategies to facilitate sleep (Bjorvatn et al., 2023; Trahan et al., 2018; Brown et al., 2017; Morin et al., 2006).

Although several studies have found a positive effect of music on sleep quality using subjective measures (Jespersen et al., 2022; Chen et al., 2021), little attention has been paid on the impact of music on sleep quality assessed through objective measures.

Polysomnography (PSG) represents the gold standard for the objective assessment of sleep, measuring different parameters and assessing both brain activity (through EEG) and physiological measures. Nevertheless, sleep studies using PSG return mixed and unclear results, raising doubts about the efficacy of this technique alone. Indeed, PSG corresponds poorly with the subjective perception of sleep as reported by participants, and thus gives us just partial understanding of brain activity during sleep.

Recently, new directions in sleep studies suggested using the full spatiotemporal resolution of BOLD signals to find large-scales networks activated during sleep. This involves the use of simultaneous EEG and fMRI on participants falling asleep to explore brain network transitions during sleep onset (Stevner et al., 2019).

We aim to investigate the neural mechanisms underlying the effect of music on sleep quality by using this methodology, and thus exploring the effects of music on whole-brain networks involved in listening to music during sleep initiation.

We expect music to facilitate sleep initiation and consolidation, as reflected in both EEG patterns and fMRI whole-brain networks dynamics.

Themes: Neuroscience, Public health
Keywords: Sleep, Music, Brain networks

Pain and Sensory Disturbances in Patients with Nerve Root Lesions Confirmed by Magnetic Resonance Imaging

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Background: Clinical examination combined with magnetic resonance imaging (MRI) form the diagnostic gold standard when diagnosing patients with disease affecting the nerve roots. However, the dermatomal maps that underlie clinical assessment are based on old and flawed studies. We aim to examine pain and sensory disturbances in patients with nerve root lesions and propose revised dermatomal maps.

Methods: Patients with radiculopathy and MRI verified compression of one or two nerve root segments were included in a cross-sectional study. Medical history was obtained including pain drawing and pain-related questionnaires. Sensory disturbances on the symptomatic extremity were mapped using light touch, pinprick, pin scratch, warm roll (45 °C) and cold roll (20 °C) by an examiner blinded to affected nerve root segment. Sensory changes reported during examination were categorized as “reduced”, “absent”, “increased with pain”, “increased without pain”, and “different”, and marked on patients’ skin with pens and photographed. In a subgroup of patients, we will quantify mechanical and thermal detection- and pain thresholds, and record contact heat and dermatomal somatosensory evoked potentials.

Results: All patients reported sensory disturbances in the affected limb to at least one modality. Combined sensory loss and gain was the most prevalent finding (53 %), followed by isolated sensory loss (47 %).

Conclusion: Areas of sensory disturbances deviated considerably from existing dermatomal maps indicating that a proposition for revised dermatomal maps is warranted. The study is ongoing, and the results are preliminary.

Themes: Neuroscience, Diagnostics & technology
Keywords: , ,

Whole-brain 3D mapping and quantification of pathological alpha-synuclein aggregate spreading and toxicity in a mouse model of early-stage Parkinson's disease

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Progressive spreading of alpha-synuclein (αSyn) aggregates in the brain plays a key role in the prodromal phase of Parkinson's disease (PD). Several preclinical models of synucleinopathies have been developed for studying the neurotoxicity of prion-like αSyn aggregate spreading, but remain to be explored with regards to early pathological events that could be targeted to delay or prevent progression of PD. Using 3D whole-brain light sheet fluorescence microscopy (LSFM), the present study aimed to provide a 3D map of progressive pathological Syn spreading and tyrosine hydroxylase (TH) expressing neurons and projections in the Syn pre-formed fibril (PFF) mouse model of PD. Wildtype mice received unilateral intrastriatal injections of α-Syn PFFs. Mice were terminated at 1 to 26-weeks post injection and whole-brains were dual immunolabelled for pS129- Syn and TH, optically cleared and scanned using LSFM. Distinct spatiotemporal phases of endogenous Syn aggregate spreading was observed over time. The phases included progressive spread of Syn aggregates to primary and secondary seeding regions based on their interconnectivity to the injection site. In parallel, TH expression was downregulated in the nigrostriatal pathway, suggesting axonal damage in terminal areas preceding dopaminergic neuronal loss in the Syn PFF mouse model. The anatomical complexity of Syn aggregate spreading in the model underscores the unique applicability of whole-brain 3D LSFM imaging to fully capture spatiotemporal dynamics in Syn and TH expression, making the model instrumental for the evaluation of therapeutic modalities that may prevent Syn aggregate spreading and dopaminergic neuronal loss.

Themes: Neuroscience, Neurodegenerative disorders
Keywords: Synucleinopathy, 3D Imaging, Preclinical model

Fast dopamine and serotonin dynamics in the human brain

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The neuromodulators dopamine and serotonin are critical for healthy function. They regulate the excitability and plasticity of neuronal populations; support a variety of behavioural and cognitive processes; are implicated in a range of neuropsychiatric conditions; and are often targeted pharmacologically. Yet, our understanding of the neuromodulatory basis of human health has been impeded by an inability to measure fast neuromodulator dynamics in the human brain. Here, we report preliminary results from a project in which we use a recently developed electrochemical method which – for the very first time – allows us to record sub-second dopamine and serotonin dynamics in the conscious human brain. The recordings are made in essential tremor and Parkinson's disease patients who are undergoing awake brain surgery for the implantation of a deep brain stimulation electrode. During the electrochemical recordings, the patients perform simple behavioural and cognitive tasks which have been designed to reveal why dopamine and serotonin are so critical for healthy function. The recordings are made for research purposes only with fully informed patient consent.

Themes: Neuroscience, Neurodegenerative disorders
Keywords: human decision making, dopamine and serotonin, parkinsons and essential tremor

Lack of regional differences in hypoxia-induced vasodilation and hyperperfusion in retinal arterioles in vivo

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Purpose:

In vision-threatening retinal vascular diseases, the retina exhibits a distinct pattern of lesions. In the macular region, exudates and edema dominate, while the retinal periphery suffers from capillary occlusions leading to ischemia. The underlying reason for this contrasting pattern remains unclear, but differences in blood flow regulation might play a role. However, it remains unknown if hypoxia-induced vasodilation in the retina follows similar regional differences.

Methods:

In 28 examinations of healthy young participants, oxygen saturation, vessel diameter, and blood flow were measured in the upper temporal peripapillary arteriole and in its branches extending towards the macular area and the retinal periphery. The measurements were performed before and during breathing of a hypoxic gas mixture containing 12.5% oxygen.

Results:

Hypoxia significantly reduced the systemic oxygen saturation from (mean SD) 97.6 1.2% to 85.4 4.4% ($p<0.001$), and the saturation in the studied arterioles from 95.3% 5.4% to 86.7% 7.8% ($p<0.001$). Systemic hypoxia induced a significant dilatation of 7.9% 14.8% ($p<0.001$) and increased blood flow by 43.9% 62.8% ($p<0.001$) in retinal arterioles, but no significant differences were observed in the response when comparing peripapillary, peripheral and macular arterioles ($p=0.6$ for diameters and $p=0.4$ for blood flow).

Conclusions:

The preliminary results suggest that hypoxia-induced vasodilation and hyperperfusion are similar across retinal regions. This argues against regional differences in the hypoxia-induced vascular response, and does not seem to contribute to the different manifestations of retinal vascular diseases in the retina.

Themes: Neuroscience, Diagnostics & technology
Keywords: Ophthalmology, Retinal autoregulation, Blood flow

Early interdisciplinary intervention (GAIN), to reduce persistent post-concussion symptoms in adults: Results from a stepped-wedge cluster randomised controlled trial

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Background:

Concussion is a common condition, and 20,000 Danes gets a concussion every year. The majority recover within the first weeks, but 30 % of patients develop persistent post-concussion symptoms (PPCS), which are associated with reduced quality of life and high societal costs. Evidence for effective interventions is sparse. Recently, a novel interdisciplinary intervention, Get going After concussIoN (GAIN), showed effective in reducing PPCS in young adults (15-30 years). However, more research is needed to test the effect of GAIN in different settings and in a broader age group.

Objective:

In a stepped-wedge cluster randomised controlled trial (ClinicalTrials.gov ID NCT04798885) to test the effect of GAIN compared to enhanced usual care (EUC) in reducing PPCS in adults 2-4 months after injury, when delivered in a municipality setting by a larger group of health professionals.

Method:

In total, 310 consecutively recruited patients (18-60 years) with PPCS were randomised to either 1) the intervention GAIN, based on principles from cognitive-behavioral therapy and graded exercise therapy, or 2) EUC, including 30 minutes of information and reassurance about concussion. The primary outcome was reduction of symptoms. Secondary outcomes

included psychological distress, and health-related quality of life and mental and physical functioning.

Results:

Results of linear regression analysis using an adjusted random effects model and pertaining to data obtained at trial endpoint will be presented.

Conclusion:

This trial evaluates the effect of an early intervention (GAIN) on PPCS in adults. It may have the potential to prevent symptom chronification and long-term disability.

Themes: Neuroscience, Rehabilitation
Keywords: brain concussion, post-concussion symptoms, mTBI

SESSION 10 - Neuroscience 2

Middle Cerebral Artery Remodelling as a Response to Alzheimer's Disease Proteins

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Introduction

Alzheimer's Disease (AD) frequently coexists with cerebrovascular diseases in the elderly. Disruption of cerebral vasculature appears to trigger pathological vessel remodeling, limit cerebral perfusion, and contribute to cognitive impairment in AD patients. AD is defined by accumulation of Amyloid-beta (Aβ40 and Aβ42) oligomers and tau fibrils in neuronal tissue, disrupting synapses and inducing cell death. Furthermore, these proteins accumulate within arterial walls, implicating a direct impact on vascular function, although their specific effects are poorly understood.

Methods

We investigated the effects of AD-associated peptides on vascular function of middle cerebral arteries (MCA) from mice (C57Bl/6NRj). Arteries were incubated with varying concentrations of Aβ40, Aβ42, and human tau fibrils in a wire myograph. We assessed MCA contraction and relaxation before and after incubation using U-46619 and acetazolamide (ATZ) on vessels preconstricted with U-46619.

Results

Preliminary findings indicate that incubation with tau and a combination of all three proteins increases MCA baseline tension and attenuated the vessel's response to U-46619 but increased relaxation. When stimulated with ATZ, vessels from both groups dilated below baseline levels.

Conclusion

Our study demonstrates that tau fibrils induce vascular disturbances, a phenomenon previously described primarily for Aβ oligomers. Notably, the combination of the three peptides, resembling a model of patient pathology, has a prominent effect on vascular function. These results highlight the influence of AD proteins on vascular functionality, potentially affecting blood flow dynamics in AD progression.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Alzheimer's Disease, Wire myograph, Amyloid and Tau

Impact of Alzheimer's co-pathology in Lewy body dementia

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Introduction: Recent advancements in antibody therapies targeting amyloid-β have shown promising results in reducing pathology and slowing cognitive decline in Alzheimer's disease (AD). Given that 50-80% of patients with Lewy body dementia (LBD) exhibit co-occurring AD pathology, it raises the possibility that these therapies could also benefit LBD patients. Research suggests a potential synergistic interaction between α-synuclein, the hallmark protein in LBD, and amyloid-β – yet many critical aspects of how these co-pathologies contribute to both cognitive and non-cognitive symptoms remain unexplored.

Methods: This prospective study began primo October, including patients with clinical diagnoses of AD or LBD. We aim to enroll 100 participants over the next two years. Participants will undergo lumbar puncture, skin biopsy, blood sampling, and detailed neuropsychological assessments. MRI and cholinergic PET scans will be performed, the latter using a novel tracer with high affinity and specificity for cholinergic neurons. Biomarker status will be determined through α-synuclein testing in skin and cerebrospinal fluid using seed amplification assays, and plasma will be analyzed for p-tau217. Participants will be invited to annual follow-ups for up to seven years.

Conclusion: Our study will compare LBD patients with and without co-pathology. We anticipate that LBD patients with co-pathology will show more severe cognitive and non-cognitive symptoms at baseline and experience a more rapid cognitive decline. These findings could improve patient selection and outcome measures in future drug trials, while enhancing our understanding of co-pathology in neurodegenerative diseases.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Lewy body disease, Alzheimer's disease, Co-pathology

Harnessing the Vagus nerve immunomodulatory capacity as therapeutic intervention in Parkinson's disease

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Parkinson's disease (PD) is marked by neuronal α-synuclein (AS) aggregates, immune activation, and neurodegeneration affecting both the peripheral and central nervous systems (PNS & CNS). The vagus nerve (VN) is proposed as a critical entry point for AS pathology towards the CNS. Notably, not all patients exhibit early signs of PNS involvement, highlighting the heterogeneity considered in the novel brain-first/body-first theory. In this context, AS pathology is present in the VN earlier in body-first PD than in brain-first PD. Importantly, the VN facilitates bi-directional communication along the gut-brain axis and plays a crucial anti-inflammatory role primarily mediated by acetylcholine (ACh). We hypothesize that harnessing the VN's anti-inflammatory capacity can have therapeutic relevance in PD. In collaboration with JHU and DTU we aim to assess whether chronic electrical VN stimulation can serve as a valid therapy for early-stage brain-first PD patients with functional VN. For body-first PD, where VN impairment may limit stimulation efficacy, we propose to restore the anti-inflammatory effects via ACh replacement through advanced microbiome therapeutics (AMT).

To model distinct characteristics of PD, we inject pre-formed fibrils of murine AS into the striatum or the VN of rats. We evaluate the therapeutic effects of our interventions on motor impairments and immune modulation. Post-mortem analyses focus on immune markers, neurodegeneration, and AS pathology patterns in both the central nervous system and peripheral tissues. This research aims to elucidate the therapeutic potential of the VN and its impact on disease progression and immune response in PD.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Neuroinflammation in Parkinson's disease, Immune modulation, Vagus nerve stimulation

Disclosing the most effective therapeutic transcranial magnetic stimulation strategy for reducing cortical excitability in Amyotrophic Lateral Sclerosis (ALS)

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BACKGROUND: Recent evidence suggests that cortical motor hyperexcitability is a key pathogenic mechanism in the development of ALS, leading to the degeneration of upper motor neurons (UMNs) and, subsequently, of lower motor neurons (LMNs) through glutamate-mediated excitotoxicity. Cortical excitability can be assessed using paired-pulse Transcranial Magnetic Stimulation (TMS), with the Short-Interval Intracortical Inhibition (SICI) protocol showing significant early alterations in ALS patients.

OBJECTIVE: This study aims to evaluate the effectiveness of continuous Theta Burst Stimulation (cTBS) and transcranial Static Magnetic Stimulation (tSMS) applied over the primary motor cortex as neuromodulation strategies for reducing cortical excitability in healthy subjects and ALS patients.

METHODOLOGY AND STUDY DESIGN: This study will recruit healthy controls, patients suspected of having ALS, supported by neurophysiological examination, and patients who already have an ALS diagnosis according to the Gold Coast criteria. The study design is prospective, cross-over, randomized, single-blind, and sham-controlled. It consists of two arms: 1) real cTBS versus sham cTBS; 2) real tSMS versus sham tSMS. Both healthy controls and ALS patients will participate in both arms. All enrolled subjects will undergo clinical and neurophysiological assessments before and after the neuromodulation intervention.

ENDPOINTS: The primary endpoint will be the average SICI measured between 1–3 ms. Secondary endpoints will include Motor Evoked Potential (MEP) amplitude, resting motor threshold (RMT), stimulus-response curve, short-interval cortical facilitation (SICF), and safety evaluations.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: ALS, Neuromodulation, Transcranial Magnetic Stimulation

A framework to establish classes of pathogenic SORL1 variants allowing tailored personal medicine for Alzheimer's disease.

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None (for now)

None (for now)

Alzheimer's disease (AD) is the most prevalent form of dementia, a distressing condition known for its deterioration of memory and cognitive functions. Sortilin-related receptor 1 (SORL1) was recently described as the fourth causal AD gene. SORL1 encodes the multidomain protein SORLA and variants across its domains increase the risk of developing AD. The group of domains that harbor the largest number of pathogenic variants are the CR-domains. This could be attributed to multiple highly conserved residues which can be categorized into three groups: calcium cage variants, odd numbers cystines, and Axn-turn variants. Genetic and cell biology data suggest that variants within these groups lead to AD, but their impact may vary in severity. However, it is still not completely understood why we observe differences between the variants and how they lead to SORLA impairment. This research seeks to establish whether the severity of various variants can be differentiated using in vitro models overexpressing SORLA CR variants. We will investigate how the variants impact the folding and functioning of SORLA with the use of computational and cell-based methods. Furthermore, we will also examine intracellular trafficking of APP, TAU, and GLUA1, which is facilitated by SORLA and is disrupted in AD. Ultimately, we aim to connect the differences among the variant groups to the differences in age of AD onset observed in genetic data for patients carrying variants in SORLA CR domains. This research could provide crucial information for counseling patients carrying variants in the CR domains and help determine whether patients may benefit from SORL1-targeting personal medicine.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Alzheimer's Disease, SORL1, personalized medicine

Inhibition of PI4KIIIα as a Novel Potential Approach for Parkinson's Disease Treatment - **CANCELLED**

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Parkinson's Disease (PD) is a complex neurodegenerative disorder with various underlying causes, predominantly linked to α-synuclein aggregation and dopaminergic neuronal death in the substantia nigra. Phosphatidylinositols (PI) and Phosphatidylinositol kinases (PIKs), specifically PI4KIIIα, play a critical role in membrane structure and trafficking. Emerging studies suggest a potential connection between PI4KIIIα inhibition and reduction in α-synuclein aggregation. Our pilot studies indicate a possible relationship between PI4KIIIα inhibition using Phenylarsine oxide (PAO) and decreased α-synuclein aggregate levels, resulting in increased cell viability. This study aims to further investigate the impact of PAO and other PI4KIIIα inhibitors, such as GSK-A1, Quercetin and PIK93, on α-synuclein levels through various experiments, including spatial transcriptomics, mRNA sequencing and protein analysis on mouse tissue, primary neurons and SH-SY5Y cell cultures. The study's goal is to provide insights into gene and protein dysregulation in PD and identify key proteins and pathways involved in the downregulation of intracellular α-synuclein following PI4KIIIα inhibitor administration, potentially leading to novel therapeutic targets for neurodegenerative symptoms.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Parkinson's disease, PI4KIIIa, α-synuclein

Prevalence of isolated REM-sleep behavioral disorder in Idiopathic Polyneuropathy with cardiac sympathetic denervation: A Cohort Study.

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Background: The prevalence of polyneuropathy (PN) in patients with Parkinson's Disease (PD) is estimated to be 4-55% compared to 9% in the background population. PD is a Lewy body disease (LBD), which also includes Dementia with Lewy Bodies (DLB) and Pure Autonomic Failure (PAF). In LBD, non-motor symptoms include dysautonomia, hyposmia and REM-sleep behavioral disorder (RBD). Hyposmia and isolated RBD (iRBD) can occur decades before the diagnosis of LBD. Whether idiopathic PN (iPN) with dysautonomia is an early manifestation of Lewy Body Disease remains to be elucidated.

Hypothesis: iRBD is more prevalent in patients with iPN and abnormal cardiac MIBG-scintigraphy as compared with normal cardiac MIBG-scintigraphy. Patients with iPN and cardiac sympathetic denervation (assessed by 123I-MIBG scintigraphy) are hypothesized to progress to iRBD, PD or DLB. Primary outcome: iRBD. Secondary outcome: DLB, PD or MSA.

Material: Patients diagnosed with iPN confirmed by nerve conduction studies (large fiber PN) or skin biopsy (small fiber PN).

Methods: Phenotypic characterization of autonomic dysfunction: Autonomic symptom scores combined with functional autonomic testing. Cognitive screening tests (Montreal Cognitive Assessment, Trail Making Test B), depression (Beck Depression Inventory-II), olfactory testing, motor function (MDS-UPDRS-III), rating of parasomnia, daytime sleepiness, combined with video-polysomnography. Multimodal imaging including brain MRI, 18F-PE2I-PET, cardiac 123I-MIBG-Scintigraphy). Diagnosis of iRBD, DLB or PD in collaboration with specialists in dementia, PD, and sleep disorders. Visits: baseline, 5-year follow-up.

Results: Ongoing inclusion

Themes: Neurodegenerative disorders, Neuroscience
Keywords: polyneuropathy, REM sleep behavior disorder (RBD), Autonomic dysfunction

Reinnervation as prognostic mediator in patients with amyotrophic lateral sclerosis

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Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal, neurodegenerative disease characterized by progressive loss of muscle strength due to degeneration of motor neurons (MN). One motor neuron, its axon and the muscle fibres it innervates is termed a motor unit (MU). When a MN dies, the muscle fibres cannot be activated (denervation). To counteract the consequent muscle weakness, collateral sprouting of the remaining MNs occur resulting in larger MU and preservation of strength. We hypothesize that ability for reinnervation influences progression rate.

Methods

Patients will be examined at baseline (BL), 4 months and 8 months with an electrophysiological technique quantifying the number and size of MU in a muscle (MScanFit). Additionally, patients will fill out a questionnaire to determine decline of functional status. Based on this, patients will be categorized as either fast or slow progressors, and change in MU size will be compared as a measure of reinnervation.

Healthy subjects (HS) and patients with a MN disease with slow progression (pMND-SP) will be included with a BL visit for methodological comparisons.

To describe the muscular and patient-reported changes, the examination will also include questionnaires on fatigue, strength assessment with dynamometer, bioelectrical impedance analysis and muscle ultrasound.

Results

The number of included patients is not yet sufficient to allow presentation of valid results. We aim to include 60 patients with suspicion of ALS, 30 HS and 30 pMND-SP.

Discussion

The study will shed light on the process of reinnervation in ALS as well as explore the potential utility of biomarkers of reinnervation to enhance prognostic precision.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Amyotrophic lateral sclerosis, Reinnervation, Clinical neurophysiology

Diagnostic potential of monoclonal antibodies targeting cytotoxic α-synuclein oligomers

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The accumulation of alpha-synuclein (a-syn) as insoluble amyloids, but also soluble oligomers (aSOs), are causing neuronal degeneration in different cell populations in synucleinopathies, including Parkinson's Disease (PD), dementia with Lewy Body (DLB), and multiple system atrophy (MSA). Interestingly, the aSOs have been thought to be more toxic than the fibrils. As the cell populations and anatomical areas affected differ among the diseases, it has been proposed that different a-syn strains and conformers contribute to these differences. Unfortunately, the current tools for pathological detection of a-syn are limited. Furthermore, there is a lack of correlation between neurodegeneration and Lewy Body (LB) pathology in PD, as healthy aging brains also tend to harbor LBs. Moreover, prior to overt a-syn aggregation, cellular dysfunction seems to occur.

We aimed to investigate the diagnostic potential of novel monoclonal antibodies (mAbs) in post-mortem brain tissue from patients suffering from synucleinopathies. Furthermore, we wanted to examine their affinity towards monomeric a-syn in rodent brain tissue.

Five selected mAbs successfully identified a-syn-related pathologies in postmortem brain tissue from patients diagnosed with PD, DLB, and MSA. Of these five, three mAbs were specifically useful for pathological evaluation, including possible detection of early stages of PD. In addition, upon pre-incubation with monomeric a-syn prior to staining of rodent brain tissue, some mAbs were able to recognize non-monomeric rat a-syn present in the hippocampus. This underlines the need for a toolbox of mAbs for future diagnostics in synucleinopathies.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Pathology, Antibodies, alpha-synuclein

TMEM16A chloride channel in control of cerebral perfusion in health and ischemic stroke

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The brain is the most active and highly metabolic-demanding organ (1), oxygen delivery to which is carried out through strictly controlled cerebral perfusion via local redistribution of blood flow under variations in neuronal activity. There is an intimate relationship between cerebral vasculature and neuronal tissue, where changes in local perfusion may affect supplied cells and vice versa, glia and neurons influence adjacent blood flow (2). Anoctamin-1 (TMEM16A) belongs to the family of Ca2+-activated Cl- channels (3) and is suggested to act as a central regulator of neuromodulation. The mechanism of its action involves activation by intracellular Ca2+ ions, leading to Cl- influx across the cell membrane and subsequent depolarization of smooth muscle cells (3). This enables an amplification loop for voltage-dependent Ca2+ influx and cerebrovascular contraction. The aforementioned reinforces the idea of TMEM16A implication for ischemic stroke outcome, one of the leading causes of mortality and morbidity worldwide (4). Acute Ischemic Stroke is caused by a rapid loss of blood supply to a part of the brain due to thromboembolic occlusion in the cerebral circulation (5). Understanding the mechanisms contributing to the harmful action of stroke reperfusion is therefore of great importance for new treatment paradigms to improve stroke survival and outcome.

We aim to evaluate the importance of cerebrovascular TMEM16A for neuroprotection during ischemic stroke.

We used 3.5-6 months old, smooth-muscle specific conditional TMEM16A knockout (KO) male mice. These mice expressed TMEM16A gene floxed around exon 7 and Cre recombinase with estrogen receptor type 2 under the control of smooth muscle myosin heavy chain promoter. Age-matched male mice expressing Cre only were used as a control (WT). All mice were treated with tamoxifen injections for 5 constitutive days. Cerebral blood flow was assessed with Laser Speckle Contrast Imaging. Ischemic stroke was induced with occlusion of the middle cerebral artery (MCA) for 60 min in mice anesthetized with isoflurane. Stroke severity was analyzed with post-mortal 2,3,5-triphenyltetrazolium staining (TTC).

MCA occlusion comparatively reduced perfusion in the ipsilateral hemisphere both for TMEM16A KO (n=7-8) and WT (n=8; $p < 0.05$) (fig.1a). Blood flow reduction was stronger in

TMEM16A KO than in WT at the end occlusion ($p > 0.01$) (fig.1a). No difference between genotypes in brain perfusion was observed 24 hours after reperfusion ($p < 0.05$) (fig.1a). When blood flow changes during MCA occlusion were analysed in detail, a larger area of severe blood flow drop (<80%) was seen in TMEM16A KO mice over the occlusion period ($p > 0.01$) (fig.1a). TTC staining suggests the larger infarct volume in TMEM16A KO (n=7) than in control mice (n=7-8; p=0.125) (fig.2).

We found that smooth muscle specific knockout of TMEM16A worsens ischemic stroke-reperfusion outcome in mouse model. We suggested that this occurs due to diminished cerebral blood flow control in TMEM16A knockout mice and their abnormal vascular tone. This proposes that under ischemic conditions, when there is an imbalance in ion concentrations, TMEM16A is an important component for vascular tone optimization.

Themes: Neuroscience, Animal Models
Keywords: , ,

"Exploring RIC-miRNAs as novel mediators in stroke-related inflammation"

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Stroke is the second leading cause of death worldwide. Disrupted blood flow deprives cells of oxygen, triggering oxidative stress and subsequent inflammation. Specifically, inflammation can lead to the breakdown of the blood-brain barrier (BBB) allowing harmful substances into the brain.

Recanalization, the only approved treatment for ischemic stroke, must be administered within 4.5 to 6 hours. Thus, new treatments offering prolonged neuroprotection are urgently needed. Remote Ischemic Conditioning (RIC) is a promising non-invasive treatment with the potential to improve stroke outcomes. Upon RIC treatment, microRNAs (miRNAs) released into the bloodstream control protein translation, influencing cellular homeostasis.

RIC-induced miRNAs (RIC-miRNAs) are hypothesized to protect cells by regulating gene expression and preserving BBB integrity. To assess the impact of RIC-miRNAs during inflammation, human brain microvascular endothelial cells (HBMECs) are transfected with four RIC-miRNAs: miR-16-5p, miR-144-3p, miR-182-5p, and miR-451a. Following, inflammation is induced in vitro by exposing HBMECs to conditioned media from LPS-activated microglia.

RNA sequencing revealed 700 downregulated genes as potential direct targets of RIC-miRNAs under inflammatory conditions. Enrichment analysis uncovered the biological function of the genes, highlighting pathways related to cellular stress and inflammation. Lastly, in silico analysis helped to identify specific targets for miR-16-5p, miR-144-3p, miR-182-5p, and miR-451a, narrowing the focus to seven genes for further investigation.

In the future, RIC-miRNAs may offer a new stroke treatment, addressing current therapy limitations.

Themes: Neuroscience, Molecular biology
Keywords: , ,

SESSION 11 - Public health 1

Variation in answering machine messages in daytime general practice and its relation to the use of out-of-hours primary care

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Background: Variation in accessibility and availability of daytime general practices could result in differences in use of out-of-hours primary care (OOH-PC). Many daytime general practices use answering machines outside telephone slots, and the phrasing of the messages varies from practice to practice. The content of the message may introduce an increased threshold for patients to access their own general practitioner (GP), thereby increasing the use of OOH-PC.

Aim: The aim is to explore the relation between levels of restrictiveness of telephone answering machine messages in daytime general practices and OOH-PC use

Design: Registry-based observational study.

Method: We included all contacts with the OOH-PC service in the Central Denmark Region from 1st of April 2017 to 31st of August 2023. Data concerning telephone answering machine messages and practice characteristics (e.g. telephone opening hours, staff) was manually collected. The OOH-PC registration system provided data on type, time, and date of contact. Registers provided data on contact pattern with primary care (e.g. contacts with daytime general practice) and patient characteristics including socio-economic status. We categorized answering machine messages into levels of restrictiveness. Using a regression model, we investigated the relation between the restrictiveness of the answering machine message and contacts to OOH-PC.

Results: In progress.

Perspective: Give additional insights into factors in daytime general practice that influence OOH-PC use and how to sustain available and accessible healthcare for all citizens.

Themes: Public health, Public health
Keywords: Out-of-hours primary care, General practice, Telephone answering machine messages

Effect of implementing a uniform telephone answering machine messages in daytime general practices on the use of out-of-hours primary care.

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Background : Differences in the accessibility of daytime general practices seem to influence the utilization of out-of-hours primary care (OOH-PC). Most daytime general practices use answering machine messages (AMM) outside their regular telephone hours, but the wording of these messages varies significantly across practices. This variation can potentially create a barrier for patients attempting to reach their own general practitioner (GP), thereby leading to a higher number of patients contacting OOH-PC.

Aim: To assess the impact of implementing a uniform telephone AMM in the Central Denmark Region's daytime general practices on the use of OOH-PC.

Design: Registry-based observational study that included all general practices in Central Denmark Region between 1 April 2021 and 31 August 2024.

Method: Data on telephone answering machine messages (AMM) in daytime general practices and practice characteristics were manually collected from practices websites and telephone calls. Patient characteristics and contact information were gathered from national registers. We plan to conduct descriptive analyses of the included practices and patient demographics. A regression model will calculate contact rates for out-of-hours primary care (OOH-PC) before and after implementing the uniform answering message.

Results: The study is currently under conduction.

Themes: Public health, Public health
Keywords: Out-of-hours primary care, Accessibility / Availability, General Practitioner

Proton Therapy for Rectal Cancer

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Background: Colorectal cancer (CRC) is the third most common malignancy with 1.9 million new cases worldwide in 2020. The standard treatment for locally advanced rectal cancer (LARC) is preoperative radiotherapy (RT) followed by surgery. RT often cause acute and late toxicities, including sexual dysfunction. Proton therapy (PT) presents dosimetric advantages over photon therapy, allowing trials on reduced toxicity or dose-escalation to improve tumor control with less or equal toxicity. The clinical use of PT for rectal cancer has not yet been explored. We aim to prepare and initiate a randomized controlled trial (RCT) of dose-escalated proton therapy for LARC.

Methods: Three projects are planned to prepare the RCT:

Toxicity: To investigate if PT results in lower or similar toxicity compared to standard RT, we will thoroughly describe current toxicity through assessment of physician and patient reported data.

Shared decision making (SDM): We will identify barriers to trial participation through qualitative interviews and develop aids to support SDM for the RCT.

Comparative dose planning: We will compare the dosimetric outcome of standard RT versus PT planning, with and without dose escalation to determine optimal dosing for standard and new organs at risk.

Results/status: Toxicity: CTCAE and patient reported outcomes from 170 patients are ready for analysis of acute and late toxicity.

SDM: Systematic review of patient involvement and SDM aids in rectal cancer is in progress. Patient interviews and questionnaires will form basis for SDM aids for the RCT.

Comparative planning: Clinical strategy for PT for rectal cancer both with and without dose escalation will be determined.

Themes: Cancer, Public health
Keywords: Rectal cancer, Proton therapy, Toxicity

Health literacy strengths and challenges among people with gout

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Introduction

Gout, a common form of inflammatory arthritis, affects up to 4% of the population. Treatment focuses on urate-lowering medication, but poor adherence often leads to suboptimal results. A nurse-led telehealth intervention emphasizing self-management and medication adherence may improve care. Considering health literacy (HL) and eHealth literacy (eHL) skills is crucial for successful interventions.

Thus, the aim of this study is to investigate HL and eHL strengths and challenges in people with gout.

Methods

We applied Step 1 of the Optimising Health Literacy and Access (Ophelia) framework to identify HL-profiles. Gout patients (ICD-10 M10*) in the Central Denmark Region were identified through the Hospital Business Intelligence Register. The Health Literacy Questionnaire (HLQ) and the eHealth Literacy Questionnaire (eHLQ) were distributed via e-Boks, with phone or mail options available for those without e-Boks. Cluster analysis using Ward's linkage identified HL-profiles across nine HLQ and three eHLQ domains.

Results

Of 511 eligible patients, 260 participated (87.3% male, mean age 67.7). About 10% scored high in all HL and eHL domains, while 13% had notable challenges. Most challenges were observed in HLQ1: "Feeling understood and supported by healthcare providers" (scores 1.25–3.56). The greatest strength was noted in HLQ4: "Social support for health" (scores 2.07 to 3.71).

A total of fourteen HL- profiles emerged with unique strengths and challenges.

Conclusions

This study reveals HL and eHL strengths and challenges in gout patients, highlighting the need for tailored interventions. The profiles will aid in developing a tailored multi-model intervention.

Themes: Health Education, Public health
Keywords: Health literacy, Self-management, Gout

Association Between Cardiac Arrhythmia and Air Pollution

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Background

Air pollution impacts human health by increasing morbidity and mortality. Studies suggest that fine particulate matter (PM2.5) is associated with cardiovascular disease with high-risk patients experiencing acute pro-arrhythmic effects from PM2.5 exposure. Implantable cardiac defibrillator (ICD) is a treatment for the primary and secondary prevention of sudden cardiac death in high-risk patients.

Previous studies have modeled air pollution at municipality-level. To strengthen the association, we will investigate the association at an individual level.

To investigate the association between transient fluctuations in air pollution and occurrence of tachyarrhythmia detected by an ICD through four studies

Hypothesis

A high concentration of PM2.5 in the preceding days is associated with increased risk of:

1. Atrial arrhythmia compared to control days, utilizing PM2.5 modeled with a 1x1 km resolution

2. Ventricular arrhythmia compared to control days, utilizing PM2.5 modeled with a 1x1 km resolution

3. Atrial arrhythmia compared to control days, utilizing PM2.5 measured by personal sensors.

4. Ventricular arrhythmia compared to control days, utilizing PM2.5 measured by personal sensors.

Patient population

Events of tachyarrhythmia from an established consecutive cohort of 1,795 ICD patients will be correlated with ambient PM2.5 at home address.

ICD (including CRT-D) patients followed by Remote Monitoring at Aarhus University Hospital will be enrolled for studies with personal sensors to be worn for a total of four weeks.

Statistics

We will conduct case cross-over analysis where each subject serves as its own control. All time-in-variant covariates are controlled for by design.

Themes: Cardiology, Public health
Keywords: Cardiac arrhythmia, Air pollution,

A process evaluation of an RCT with cross-sectoral videoconferences between general practitioners and endocrinologists discussing patients living with type 2 diabetes

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INTRODUCTION

This article reports on a process evaluation of an RCT testing if videoconferences between general practice and endocrinologists can improve the medical management of patients living with type 2 diabetes.

AIM

To assess how cross-sectoral video conferences between general practices and endocrinologists were implemented and explore the potential mechanisms of impact.

METHOD

The process evaluation was guided by the MRC-framework focusing on implementation and the mechanisms of impact. Quantitative data were derived from registrations by the endocrinologists and analysed using descriptive statistics. Qualitative data consisted of interviews with endocrinologists, general practitioners and the trial secretary that was analysed thematically using NVivo.

RESULTS

The intervention was implemented with high fidelity and dose adherent to the planned format. Videoconferencing was feasible and acceptable in both general practice and hospital setting. However, it was challenging to schedule the meetings. The potential mechanisms of impact were learning through the case discussions, using technology to provide an overview of the patient population, and benefiting from the relational continuity of meeting the same endocrinologist.

DISCUSSION

This study gives insight into how videoconferences between hospital specialists and general practitioners can potentially improve medication management. Future similar interventions should consider the identified factors that may impact acceptability and feasibility of videoconferences in other clinical settings. Future studies could preferably

further explore mechanisms of impact and possible negative consequences of the intervention.

Themes: Public health, Public health
Keywords: Cross-sectoral videoconferences, Type 2 diabetes, Process evaluation

Management of Wilson Disease across Europe: An international physician-oriented survey by the ERN-RARE Liver group.

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BACKGROUND: Diagnosis and treatment of Wilson Disease (WD) is complex and highly specialized. We explored differences in WD diagnosis, management and patient-focused issues across European centers.

METHODS: A 37-question questionnaire was distributed among physicians involved in the management of WD patients across European WD centers. Questions related to diagnosis, treatment, and monitoring of WD.

RESULTS: 58 physicians from 20 countries responded to the survey. 91% adhered to international guidelines and 88% to Leipzig diagnostic criteria. Most had a wide range of diagnostic tools available, e.g. 24-hour urinary copper, slit-lamp examination and genetics (98%, 95% and 93% respectively). Some were less commonly available, e.g. liver biopsy for copper quantification, penicillamine challenge test and non-ceruloplasmin bound copper (74%, 53% and 43%).

21% of small centers did not offer trientine, cost was a limiting factor to some. Initial treatment of hepatic WD was uniform, whereas variability was observed for neurological presentations, neurological departments were more uniform, n=5). Recommendations for copper restricted diet varied, 48% recommended temporary low copper diet and 38% recommended it indefinitely.

CONCLUSIONS: In conclusion, this physician-oriented survey shows adherence to international WD guidelines among European centers. The survey also uncovers important differences; particularly related to the initial treatment of non-hepatological WD,

availability of trientine and recommendations for low copper diet. The survey highlights numerous areas in WD care in which evidence is lacking.

Themes: Gastroenterology and hepatology, Public health
Keywords: Rare disease, Questionnaire, Equal access

Breaking Barriers in Breast Cancer Trials: Non-Accrual Insights from DBCG NATURAL and PROTON trials

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Background and Aim: 5000 Danish patients (pts) are diagnosed with breast cancer (BC) annually. Danish Breast Cancer Group (DBCG) provides guidelines for standard adjuvant radiotherapy (RT) and develops new RT strategies through trials. Trial participation may vary due to socio-economic, geographic, and time-related barriers. This study, supported by the Danish Clinical Quality Improvement Program, Danish Comprehensive Cancer Center, and the Danish Cancer Society, examines reasons for non-inclusion in the DBCG NATURAL and PROTON trials.

Methods: From September 2021 to December 2023, a screening log recorded non-trial participation reasons across all Danish RT departments. Each pt was reviewed to determine reasons for not being included in trial.

Results: Non-inclusion rates for the NATURAL Trial varied in four recruiting departments, thus 54%-79% eligible pts were not included. The key reasons for omitting trial were patient preference (71%), eligibility not mentioned in MDT meetings (12%), ineligibility (4.4%), physician does not discuss trial with the ptatient (8%). For the PROTON Trial, the rates of not accruing eligible pts at 6 departments were 40%-79%. Primary factors: patient preference (49%), geographic barriers (25%), language barriers (8%).

Conclusion: The marked variations across centres suggest a need for standardised patient information on trial benefits. Significant disparities in inclusion highlight the importance of improved patient awareness regarding trial benefits. Enhanced information could reduce non-inclusion rates, supporting equitable BC care in Denmark.

Themes: Cancer, Public health
Keywords: Disparity, Breast cancer, Radiotheraphy

Actively engaging multi-level stakeholders in cancer related studies: a scoping review

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Background & objectives: Stakeholders are commonly utilized in studies as a way of gathering feedback or insight about study populations or interventions. However, there is no standard method of engagement and they are engaged in many different ways and to different extents. The objective of this scoping review is to explore how stakeholders have been engaged in cancer related studies.

Methods: This scoping review will follow the methodology put forth by the Joanna Briggs Institute. A search strategy will be formed by examining the keywords and MeSH terms of a sample of relevant articles then refined based on a test search. From there, a comprehensive selection of databases will be searched. In addition, unpublished articles and the references of included articles will be searched. Articles will be included if they utilize active stakeholder engagement by eliciting perspectives, are related to cancer, and this active engagement is documented. There will be no restrictions related to location nor language and non-English abstracts and articles will be translated using Deepl. Articles published at any time point will be considered with no restrictions. A pilot test of the title and abstract screening will be done to refine the inclusion and exclusion criteria. The title/abstract screening will be done using Covidence and the full text data extraction will be done using NVivo.

Results: There are currently no results available as this work is ongoing.

Conclusions: Mapping how stakeholders have been utilized in past work will allow us to better use them in future projects.

Themes: Cancer, Public health
Keywords: , ,

Femoral arterial cannulation and invasive blood pressure measurement in out-of-hospital cardiac arrest – a pilot study

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Background

Invasive blood pressure (IBP) measurement during cardiopulmonary resuscitation (CPR) could enable physiology-guided CPR, which may be superior to conventional CPR. Femoral arterial cannulation (FAC) competency is a necessary step in such a strategy, but the feasibility in out-of-hospital cardiac arrest (OHCA) is unknown. We aimed to train prehospital critical care anesthesiologists to perform FAC and set up IBP measurements during OHCA.

Methods

This was a pilot study on one physician-staffed emergency medical vehicle in the Central Denmark Region's (population ~1.3 mill.). The study period was from July 1st, 2023 to June 30th, 2024. Training consisted of 2 hours of skill- and team-training. Patient inclusion criteria were adult, non-traumatic, and prolonged OHCA, or unconscious return of spontaneous circulation (ROSC). Ultrasound-guided insertion of a 5 fr. introducer sheath in the femoral artery and IBP transduction were attempted.

Results

Ninety-two patients with OHCA were treated by 38 FAC-trained physicians. Fifty-four patients fulfilled the inclusion criteria. The median age was 68 (IQR 19) years. FAC was attempted in 33 (61%) patients. The reasons for not attempting FAC were available time and space. Twenty-six (79%) catheters were placed in the femoral artery, 3 were in the femoral vein and 3 in others tissue. Arterial IBP was successfully measured in 23 patients; 18 during CPR and 5 after ROSC.

Conclusion

Invasive blood pressure measurement via the femoral artery during OHCA is feasible but requires training. Cannulation was attempted in most eligible patients and was successful in most of the attempts. A larger feasibility study is warranted.

Themes: Cardiology, Public health
Keywords: cardiac arrest, femoral artry cannulation, invasive blood pressure

Enhanced Normal Tissue Sparing in Proton Minibeam Radiation Therapy (pMBRT): Experimental Evidence and Quantification

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Proton minibeam radiotherapy (pMBRT) has shown promise in sparing normal tissues with its spatially fractionated dose profile. This study evaluates the therapeutic gain of pMBRT over conventional proton therapy (CONVPT) for potential clinical application, focusing on reducing normal tissue damage while delivering a uniform target dose for equivalent tumor control.

Using a multislit collimator in a mouse irradiation setup, we delivered a uniform target dose with high dose contrast in the entrance region. Acute skin toxicity was assessed in 75 C3H/HeNRj mice using a seven-level scoring scheme (0.5–3.5) up to 25 days post-irradiation. To compare tumor control, CDF1 female mice with C3H mammary carcinoma in the foot were treated. Dose-response curves for skin toxicity and tumor control were obtained for both pMBRT and CONVPT as a function of PTV dose.

pMBRT demonstrated significantly enhanced normal tissue sparing compared to CONVPT at the same target dose. No high toxicity scores (2.5, 3.0, 3.5) were seen in pMBRT-treated mice, unlike the higher toxicity levels observed in CONVPT-treated mice at equivalent PTV doses. At the maximum deliverable dose, pMBRT toxicity was still too low to complete dose-response curves, underscoring its reduced toxicity. Grid factors of <0.65 (Score 1.5) and <0.7 (Score 2) suggest a substantial tissue-sparing effect. Both treatments achieved similar tumor control, with TCP50 of 46.9 Gy for CONVPT and 45 Gy for pMBRT.

Our study demonstrates pMBRT's efficacy, showing reduced acute normal tissue toxicity compared to CONVPT at the same PTV dose, while maintaining similar tumor control, suggesting a potential therapeutic gain for pMBRT.

Themes: Cancer, Cancer
Keywords: pMBRT, NTCP, TCP

SESSION 12 - Cardiovascular disease session 1

Initiation of cardioprotective glucose-lowering drugs according to sex and educational level: a Danish nationwide cohort study

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Background and aims: Cardioprotective glucose-lowering drugs (GLDs) are recommended in patients with type 2 diabetes (T2DM) and cardiovascular disease (CVD). We aimed to investigate how initiation of cardioprotective GLDs differ according to sex and educational level.

Materials and methods: Using Danish health care registries, we identified patients with a dual diagnosis of T2DM and CVD from January 1, 2012 to December 31, 2022. T2DM was defined using a validated algorithm. CVD was identified using the National Patient Register and National Surgery Codes. Cardioprotective GLDs included sodium-glucose co-transporter-2 inhibitors (SGLT-2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA). We plotted cumulative initiation proportions by sex and education level (0-10 years of education, 10-15 years of education and >15 years of education). We used Poisson regression models to account for competing risk of death to estimate initiation rates and adjusted initiation rate ratios (IRR).

Results: A total of 114,243 patients were included in the study (38.5% female and 61.5% male). Compared with women with 0-10 years of education, IRR for educational level 10-15 years and >15 years were 1.14 (95%CI: 1.07-1.20) and 1.17 (95%CI:1.08-1.28). IRR compared with men with 0-10 years of education were 1.12 (95%CI:1.08-1.17) and 1.08 (95%CI:1.02-1.14) for educational level 10-15 years and >15 years, respectively.

Conclusion: A low level of education (0-10 years) is associated with slower initiation rates of cardioprotective GLDs, affecting both men and women, with a more pronounced impact on women.

Themes: Endocrinology, Cardiology
Keywords: Diabetes and Cardiovascular disease, Treatment and prognosis, Socioeconomic and demographic factors

Heat shock protein 47: A novel biomarker of thrombosis risk

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Background: Venous thromboembolism (VTE), which includes deep vein thrombosis and pulmonary embolism, is the 3rd leading cause of vascular death. Immobilization is a strong and independent risk factor of VTE. Despite this, brown bears mitigate the risk of VTE during hibernation. This led to the identification of Heat Shock Protein 47 (HSP47) on platelets being down regulated 55-fold in hibernating bears. HSP47 is a part of collagen signalling and, thus, important for aggregation and adhesion of platelets. Therefore, by lowering platelet HSP47, clotting of blood is prevented.

Aim: To investigate whether platelet HSP47 levels can serve as a novel biomarker for thrombosis risk in patients with VTE.

Methods: We plan to include 120 patients with VTE and 120 healthy individuals. The patients will have their platelet HSP47 level measured at inclusion within 48 hours of diagnosis, and again at follow-up after 3 and 12 months. HSP47 levels will be analysed using proteomics. Further, patients will have their primary and secondary haemostasis and fibrinolysis assessed by impedance aggregometry (Multiplate(R)), thromboelastometry (ROTEM), flow cytometry, ex vivo thrombin generation and fibrin clot formation and lysis assay.

Perspective: This study will elucidate the role of HSP47 in VTE, establishing its potential as a novel biomarker for thrombosis risk. Additionally, the study could position HSP47 as a promising therapeutic target for next-generation antithrombotic drugs, leading to more effective and safer treatment.

Themes: Cardiology, Cardiology
Keywords: Thrombosis, Venous Thromboembolism, Heat Shock Protein 47

The association of weight change and incident hypertension in the Danish Blood Donor Study cohort

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Hypertension is a major risk factor for cardiovascular disease (CVD), the leading cause of mortality worldwide. Preventing hypertension can reduce the future burden of CVD but requires an understanding of its risk factors. Body composition, including muscle and fat mass, is biologically linked to factors influencing blood pressure, such as autonomic control, endothelial function, and renal function, among others. Thus, we hypothesize that weight change, regardless of starting body mass index, contributes to the risk of developing hypertension.

In this study, we aim to investigate the relationship between weight change and hypertension risk using data from the Danish Blood Donor Study (DBDS). This large cohort provides an opportunity to explore weight changes over time with up to 8 completed questionnaires, allowing for adjustment of analyses based on variables such as smoking status, sex, age, and self-reported physical and mental health. Furthermore, the DBDS is linked with the Danish National Prescription Register (DNPR), allowing identification of antihypertensive medication initiation through prescriptions for ACE inhibitors, angiotensin receptor blockers, or calcium channel antagonists.

We expect that individuals with weight gain will be more likely to initiate antihypertensive therapy, while weight loss may reduce the need for such interventions. By identifying these trends, the study aims to clarify how weight management can help prevent hypertension and provide insights for clinicians and policymakers addressing the growing burden of hypertension-related health issues.

Themes: Public health, Cardiology
Keywords: obesity, hypertension, weight change

Experimental evaluation of the Effects of Hypoxia on FLASH

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Abstract:

Radiotherapy is a vital cancer treatment, with over half of all cancer patients requiring it. Recently, FLASH-Radiotherapy (FLASH-RT) has gained attention for its potential to reduce toxicity to normal tissues while maintaining tumor control comparable to conventional (CONV) radiotherapy. However, the underlying mechanism of FLASH-RT remains unclear. A leading hypothesis suggests that radiolytic oxygen depletion (ROD) is responsible for protecting normal tissues, as hypoxic environments are known to confer increased radioresistance.

This study aims to provide experimental evidence supporting the ROD hypothesis as an explanation for the FLASH sparing effect using an established radiobiological setup for in vivo irradiation of mouse legs. The experimental design consists of four treatment groups of female C3HHeNRj mice subjected to either CONV or FLASH electron therapy under aerobic or hypoxic conditions. Hypoxia will be induced by clamping the right hind leg with tourniquets to restrict blood supply prior to irradiation. Acute biological responses will be measured through acute skin toxicity assay. Late radiation effects will also be assessed.

Initial data from clamped mouse legs exposed to CONV confirm the anticipated increase in radioresistance due to induced hypoxia. Experiments with FLASH are scheduled for mid-September 2024, with preliminary findings expected for presentation at the upcoming meeting.

If FLASH-RT's protective effects are solely attributed to ROD, we anticipate no significant differences in acute or late damage grades between FLASH and CONV under hypoxic conditions. This research will elucidate the role of ROD in FLASH-RT

Themes: Cancer, Cardiology
Keywords: Radiobiology, FLASH, Cancer treatment

Effect of Treatment with Finerenone on Cardiovascular Target Organ Damage in Patients with Type 2 Diabetes – A Randomized Trial.

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Background: Type 2 diabetes remains the leading cause of chronic kidney disease, and patients with type 2 diabetes face a more than two-fold increased risk of cardiovascular disease. The new drug finerenone lowers the risk of kidney and heart disease in patients with type 2 diabetes and chronic kidney disease and may as well reduce the risk of diabetic retinopathy. Preclinical studies suggest that finerenone might exerts its effects through anti-fibrotic pathways, but little is known about the mechanisms driving the protective effects of finerenone. Furthermore, we lack knowledge about the effect of combination therapy with an SGLT2-inhibitor.

Purpose: In this 26-week placebo-controlled double-blinded randomized clinical trial, we investigate the effects of finerenone in combination with an SGLT2-inhibitor on renal, cardiovascular and retinal target organ damage in 80 high-risk patients with type 2 diabetes and chronic kidney disease treated with an SGLT2-inhibitor. This study will mainly focus on the cardiovascular and retinal outcomes. We hypothesize that finerenone in combination with an SGLT2-inhibitor (1) Reduces left ventricular mass and the progression of cardiac fibrosis, (2) Improves arterial function measured by arterial stiffness and (3) reduces retinal thickness.

Perspectives: An understanding of the disease mechanisms reversed by finerenone in combination with an SGLT2-inhibitor will provide important information regarding the pathophysiology of late diabetic complications. This can pave the way for better and more personalized medicine and ultimately contribute to improving patient outcome.

Themes: Endocrinology, Cardiology
Keywords: Randomized controlled trial, Type 2 diabetes mellitus, Cardiovascular disease

The fibrinolytic system in venous thromboembolism recurrence: pathophysiology and risk assessment

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Background:

Venous thromboembolism (VTE) is the third most common life-threatening cardiovascular disease after myocardial infarction and stroke. Up to 30% of VTE patients will experience recurrent VTE, but currently we cannot predict who will experience a new VTE, and thus would benefit from long-term anticoagulant treatment.

The fibrinolytic system is responsible for fibrin clot breakdown in the circulation. Increasing evidence suggest that altered fibrinolysis contribute to VTE development. Platelets may play a role in modulating the fibrinolysis, since platelets have been identified as a major storage of the most important inhibitor of fibrinolysis, plasminogen activator inhibitor-1 (PAI-1).

Aims and hypotheses:

The aim of our study is to investigate fibrinolysis markers as predictors of VTE recurrence risk. Furthermore, to investigate whether platelets contribute to altered fibrinolysis in VTE.

We hypothesise that fibrinolysis markers are decreased and/or platelet function is increased in patients with VTE, and that these alterations are associated with VTE recurrence within 12 months.

Methods:

The core study is conducted on a prospective cohort of adult VTE patients referred to either The Coagulation Clinic or the Thrombosis Clinic, Aarhus University Hospital. Blood samples are taken at inclusion and 3 and 12 months after inclusion.

Perspectives:

To improve individual risk assessment which will facilitate more individually tailored recommendations on anticoagulant treatment, thus lowering the risk of VTE recurrence, major bleeding and mortality for patients with VTE.

Themes: Cardiology, Cardiology
Keywords: Venous thromboembolism, Fibrinolysis, Platelet function

Healthcare activities in general practice preceding FH diagnosis

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Introduction

Familial hypercholesterolemia (FH) affects 1 in 250 people and is characterized by elevated low-density lipoprotein cholesterol (LDL-C), increasing the risk of premature atherosclerotic cardiovascular disease (ASCVD). Despite available treatments and primary care access, FH remains underdiagnosed and undertreated in Denmark and other Western countries. General practitioners (GPs) are key to identifying FH, but barriers like low awareness and competing priorities can hinder detection.

Purpose

This study aims to assess the role of general practice in FH identification by exploring patient-GP interactions and healthcare activities leading up to FH diagnosis.

Method

This nationwide, register-based cohort study used Danish health registers to examine the diagnostic trajectory of FH patients. The analysis included GP consultations, blood tests, and cardiovascular medications before diagnosis, comparing FH patients with matched controls.

Results

The preliminary findings show that FH patients have more frequent GP visits before diagnosis. However, FH suspicion seems rare, and LDL-C measurements are inconsistently linked to FH screening. Many patients receive cardiovascular medication without comprehensive lipid testing and diagnostic follow-up.

Conclusion

General practice is pivotal in identifying FH patients, yet barriers delay diagnosis. Increased awareness and structured pathways in primary care are needed to enhance FH identification and referral processes.

Themes: Public health, Cardiology
Keywords: Epidemiology, General Practice, Familial Hypercholesterolemia

Prediction of Cardiovascular Markers and Diseases Using Retinal Fundus Images and Deep Learning: A Systematic Scoping Review

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Background: Rapid development in deep learning for image analysis inspired studies to focus on predicting cardiovascular risk using retinal fundus images. This scoping review aimed to identify and describe studies using retinal fundus images and deep learning to predict cardiovascular risk markers and diseases.

Methods: We searched MEDLINE and Embase on 17/11/2023. Abstracts and relevant full-text articles were independently screened by two reviewers. We included studies that used deep learning for the analysis of retinal fundus images to predict cardiovascular risk markers or cardiovascular diseases and excluded studies only using predefined characteristics of retinal fundus images (e.g. tortuosity) were not considered. Study characteristics were extracted by the first author, verified by the senior author, and presented using descriptive statistics.

Results: We included 24 articles published between 2018 and 2023. Among these, 21 (88%) were cross-sectional studies and eight (33%) were follow-up studies with clinical CVD outcomes. Five studies included a combination of both designs. Most studies (96%) used convolutional neural networks to process images. We found nine (38%) studies that incorporated clinical risk factors in the prediction and four (17%) that compared the results to commonly used clinical risk scores in a prospective setting. Three of these reported improved discriminative performance. External validation of models was rare (21%).

Conclusions: There is increasing interest in using retinal fundus images in cardiovascular risk assessment with some studies demonstrating small improvements in prediction. However, more prospective studies, comparisons of results to clinical risk scores, and models augmented with traditional risk factors are needed.

Themes: Diagnostics & technology, Cardiology
Keywords: cardiovascular disease, retinal fundus image, deep learning

Understanding the neuroprotective role of the novel HCO3– sensor RPTPγ during ischemic stroke

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Stroke is the leading cause of morbidity and disability. In ischemic stroke, inadequate cerebral blood flow to an area of the brain relative to the metabolic demand lowers tissue oxygenation and causes acute damage. This leads to secondary injury characterized by vasospasm, tissue acidosis, and inflammation. I explore how disturbances in acid-base balance influence stroke severity.

RPTPγ is a novel extracellular HCO3– sensor expressed by neurons, microvascular endothelial cells, and immune cells. The molecular mechanisms by which it regulates cerebral perfusion and oxidative metabolic demand remain unclear. Previous studies found that loss-of-function RPTPγ variants increase stroke risk in humans 7-fold.

Using wild-type and RPTPγ knockout mice, I induce stroke by unilateral carotid artery ligation with subsequent hypoxia. The stroke severity is quantified using post-mortem staining (stroke frequency and infarct volume) and neurological scoring.

Our ongoing studies show that stroke frequency (75% in KO vs. 25% in WT, p value = 0.0064) and neurological deficits (median value 3 in KO vs. 0 in WT) are increased in RPTPγ knockout mice compared to wild-type mice.

We conclude that lack of RPTPγ increases stroke severity and propose that HCO3—sensing via RPTPγ confers neuroprotection.

Themes: Neuroscience, Cardiology
Keywords: Cerebrovascular disease, Animal models/disease models, Laboratory Science

Inter-arm blood pressure differences and within-visit blood pressure variability in early pregnancy and the risk of pre-eclampsia

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Objectives: To investigate the association of inter-arm blood pressure differences (IAD) and the within-visit variability of blood pressure in early pregnancy with the risk of pre-eclampsia.

Methods: The study analyzed detailed blood pressure data from the Pre-eclampsia Screening in Denmark (PRESIDE) study, a prospective, non-interventional multicenter study investigating the performance of the Fetal Medicine Foundation first-trimester screening algorithm for pre-eclampsia in a Danish population. Three consecutive blood pressure (BP) measurements were performed simultaneously on both arms in participants attending the first-trimester ultrasound at 11 to 14 weeks of gestation. Data on maternal characteristics, medical history and pregnancy outcome were collected. Primary outcome was pre-eclampsia; secondary outcomes were preterm pre-eclampsia (<37 weeks of gestation) and term pre-eclampsia.

Results: The study cohort included 8,117 women of which 303 (3.7%) Objectives: To investigate the association of inter-arm blood pressure differences (IAD) and the within-visit variability of blood pressure in early pregnancy with the risk of pre-eclampsia.

Methods: The study analyzed detailed blood pressure data from the Pre-eclampsia Screening in Denmark (PRESIDE) study, a prospective, non-interventional multicenter study investigating the performance of the Fetal Medicine Foundation first-trimester screening algorithm for pre-eclampsia in a Danish population. Three consecutive blood pressure (BP) measurements were performed simultaneously on both arms in participants attending the first-trimester ultrasound at 11 to 14 weeks of gestation. Data on maternal characteristics, medical history and pregnancy outcome were collected. Primary outcome was pre-eclampsia; secondary outcome was preterm pre-eclampsia (<37 weeks of gestation).

Results: The study cohort included 8,117 women of which 303 (3.7%) developed pre-eclampsia, 55 (0.7 %) preterm pre-eclampsia. Women who developed pre-eclampsia had a higher diastolic blood pressure IAD (OR 1.05 (95 % CI: 1.00;1.11) and pulse pressure IAD (OR 1.04 (95 % CI: 1.01;1.07)). After adjusting for covariates pulse pressure IAD was associated with pre-eclampsia (adjusted OR 1.04, 95 % CI 1.01,1.07). The study found no associations between within-visit blood pressure variability and pre-eclampsia.

Conclusion: Diastolic IAD and pulse pressure IAD in early pregnancy, were higher in women developing pre-eclampsia indicating an association with pre-eclampsia. More research is needed to examine whether the addition of diastolic IAD and pulse pressure IAD improves the prediction of pre-eclampsia.

Themes: Gynecology and obstetrics, Cardiology
Keywords: Preeclampsia, Prediction, Blood pressure

Functional capacity by cardiopulmonary exercise testing is not related to health status in obstructive hypertrophic cardiomyopathy

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Background: In obstructive HCM, the primary goal of therapy is to improve patient quality of life by decreasing symptom burden. Increasingly, CPET with pVO2 is used to assess efficacy of novel therapies in clinical studies and selectively in clinical practice to determine treatments. However, the relationship of CPET variables to symptom burden in HCM is not well established. Therefore, we examined the relationship between CPET variables and health status measured by KCCQ and NYHA in a cohort of obstructive HCM patients.

Methods: Consecutive patients with HCM and resting LVOT obstruction (>50 mmHg) underwent CPET between October 2022 to January 2024. Patients with a peak RER <1.0 were excluded (n=4). To investigate distribution of patient reported health status (KCCQ) and NYHA, patients were stratified into groups for pVO2 (<14, 14-20, and >20 mL/kg/min) to reflect moderate to severe, mild to moderate, and little to no functional limitation, respectively.

Results: Of 58 patients, clinical evaluation was at 59 ±13 years of age, 55% male, with LVOT gradient of 83 ±28 mmHg at rest with 84% NYHA class II or III and 76% with KCCQ-OS <75. Both pVO2 and VE/VCO2 had significant but weak correlation with NYHA class and KCCQ scores, with the strongest correlation observed with pVO2 and KCCQ-OS (R2= 0.13, p=0.004). Notably, despite 14 patients being classified as having little to no limitations by pVO2, 29% of these patients had mild to moderate disability and 29% had moderate to severe disability by KCCQ-OS.

Conclusion: In patients with symptomatic obstructive HCM, objective measures of exercise performance correlate poorly with measurements of health status.

Themes: Cardiology, Public health
Keywords: Hypertrophic cardiomyopathy, Cardiopulmonary exercise testing, Health status

SESSION 13 - Immune mediated diseases 1

Identifying patients with polymyalgia rheumatica in primary- and secondary health care in Denmark: the positive predictive value of a register-based method.

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Aim: To assess the positive predictive value (PPV) of a register-based identification of patients with polymyalgia rheumatica (PMR) in primary and secondary health care in Denmark.

Background: Among the elderly population, PMR is the most common inflammatory rheumatic disease1. PMR is characterized by proximal extremity pain, morning stiffness and constitutional symptoms. The treatment for PMR consist of glucocorticoids (GC), often an effective treatment albeit frequently followed by diseases as diabetes, osteoporosis and infections2-5. PMR is mainly diagnosed and managed in primary care and previous studies have reported that general practitioners (GPs) initiate treatment with doses of GC above recommended levels6. In primary care, diagnostic codes are not reported to central registers.

Methods: Data for this study is retrieved from national Danish health registers. The identification in primary care will be based on exclusion of differential diagnoses treated with GC and >1 redeemed prescriptions for GC. GPs will be contacted by letter and invited to review the medical charts of identified CPR numbers associated to their clinic. The identification in secondary care will be based on ICD 10-diagnostic codes for PMR and >1 redeemed prescription for GC within the following month. The diagnosis in secondary care will be review in 250 medical records at three hospitals.

Statistics: The PPV will be presented with a 95% confidence interval, representing the proportion of verified PMR cases among the identified cases.

Perspectives: The PPV of the register-based PMR diagnosis will provide a reliable basis of future register-based studies in PMR

Themes: Epidemiology, Immune diseases
Keywords: validation study, positive predictive value, Register-based research

Targeted Interferon Beta Delivery for Multiple Sclerosis Therapy Using Programmable Immune Reactive Cells

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Multiple Sclerosis (MS) is an autoimmune disease, causing demyelination and neurodegeneration. The first approved therapy for MS was intravenous administration of pegylated-interferon beta (IFNβ), however, this therapy has low efficacy and causes severe side-effects. Thus, there is a high unmet need to develop safe and broadly effective therapies.

My project aims to develop a cell therapy using the properties of the immune cell type called plasmacytoid dendritic cells (pDCs). These cells are differentiated and genetically engineered using sources of pluripotent stem cells. We have named them "Programmable Immune Reactive Cells" (PIRC) as they are engineered to release IFNβ locally upon engaging a specific myelin antigen. This provides a targeted and local IFNβ release at the site of inflammation, overcoming the systemic challenges of using IFNβ therapy. Given the therapeutic and regulatory properties intrinsic to pDCs, we anticipate a dual effect: harnessing these attributes alongside localized IFNβ release to mitigate MS symptoms while reducing side effects.

To assess the functionality of the receptor system I have so far used lentiviral transduced cell lines expressing the receptor system and testing how these cells respond to receptor activation by antigen-coated beads, via flow cytometry and ELISA readouts.

My preliminary results confirm a functional and inducible IFNβ system and IFNβ release highly correlated with the degree of receptor expression. Based on these findings, we are proceeding to express the system in PIRCs for further validation in a co-culture with antigen-expressing cells and later move into an in vivo disease model.

Themes: Genetic engineering, Immune diseases
Keywords: Targeted Cell Therapy, Multiple Sclerosis, Cell Engineering

An in vitro system for testing human antibody responses to carbohydrate antigens

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Acinetobacter baumanii, commonly acquired by immunocompromised individuals in hospitals, causes a spectrum of symptoms including serious lung infection, with the potential to may develop untreatable with conventional antibiotics. The expanding problems with antimicrobial-resistant bacteria, underscores the need for broader vaccination options. The vaccination against A. baumanii represents an attractive option, due to identifiable people at risk. However, its cellular biology directly hinders effective Ab formation, mainly due to a dense coating with LPS. In the case of carbohydrates, the route to Ab production does not involve T cell responses. Instead, T cell-independent B cell response may still be induced if the carbohydrates are multivalent. The higher efficacy of such antigens, apparently from increasing the antigen availability in the B cell receptor-expressing membrane environment suggesting a route for increasing B cell responses by regulating the topological presentation of multiple antigens, e.g. on the surface of nanoparticles (NPs).

The study aims to establish an in vitro system for testing Ab formation to A. baumannii-derived polysaccharides while testing its immunotoxicology properties. We will incubate THP-1 cells with carbohydrate-decorated polystyrene NPs, using multiplex immunoassays to characterize the cytokine profile to investigate potential risks of overactivation of the innate immune system. Next, B cell lines and primary human B cells are incubated with NPs to investigate cell proliferation and Ab synthesis. Using flow cytometry, to analyze its ability to trigger effector mechanisms such as complement activation and phagocytosis.

Themes: Pharmacology, Immune diseases
Keywords: Acinetobacter baumannii, carbohydrate-based vaccines, nanoparticles, immune-toxicology studies

Faecal Microbiota Transplantation against chronic diarrhea in Patients with Systemic Sclerosis – a randomized, double-blinded, safety and pilot-efficacy study

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Background: Systemic Sclerosis (SSc) is an autoimmune disease which affects the skin and internal organs. The Gastrointestinal tract is the internal organ most often affected by SSc and consequences for the quality of life (qol) are severe. Chronic diarrhea is a common and debilitating symptom in patients with SSc, yet effective treatments remain limited.

Aim: This investigator-initiated, 9-week, randomized, double-blind, placebo-controlled pilot trial aims to assess the safety and preliminary efficacy of capsule faecal microbiota transplantation (FMT) as adjunctive therapy for chronic diarrhea in SSc patients.

Method: The study consists of two sequential intervention periods. A total of 20 patients will be recruited and undergo baseline assessments. Patients will then be randomly assigned in a 1:1 ratio using block randomization to receive either active FMT or placebo during the first double-blind intervention period. The active group will receive two consecutive components of FMT capsules, while the placebo group will receive two consecutive components of placebo capsules.

Four weeks after the second dose, baseline assessments will be repeated. In the second intervention period, all participants, regardless of their initial assignment, will receive a single dose of active FMT. Final assessments will be performed at the end of this 4-week period to evaluate the overall efficacy and safety of the intervention.

Conclusion: This pilot trial will provide critical insights into the safety and feasibility of capsule FMT in patients with Ssc and chronic diarrhea, while also exploring its potential mechanisms of action and effects on both gastrointestinal symptoms and quality of life.

Themes: Gastroenterology and hepatology, Immune diseases
Keywords: Faecal Microbiota Transplantation, Systemic Sclerosis, Microbiome

VZV-induced acute retinal necrosis in a patient with a splice-site variant in ZC3HAV1 suggests an important antiviral role for ZC3HAV1/ZAP in VZV infections

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Varicella zoster virus (VZV) is an α-herpesvirus that causes varicella during primary infection and remains latent in sensory ganglia until reactivated, causing zoster. In rare cases, VZV causes severe infections in the central nerves system (CNS), including acute retinal necrosis (ARN). Previous studies have reported key molecules and pathways against VZV infections. However, the exact pathogenesis remains incompletely understood. Therefore, we aim to identify novel inborn errors of immunity in patients with severe VZV CNS infections to discover new key molecules playing a role in controlling these infections. Whole exome sequencing (WES) and variant filtering on DNA from a patient with VZV ARN revealed a splice-site variant in ZC3HAV1 (Zinc Finger CCCH-Type Antiviral Protein 1) (c. 1994-2A>T), encoding the protein ZAP. This antiviral protein is shown to exhibit antiviral activity by binding viral mRNA and thereby mediating its degradation and/or inhibiting its translation. Expression levels of ZAP, measured by Western blot, were lower in patient cells compared to healthy controls. Using RT-qPCR, PBMC's of the patient, infected with VZV, showed increased expression of VZV open reading frame (ORF) genes, suggesting elevated viral replication. Similarly, ZAP KO HEK293FT cells showed increased viral ORF expression after VZV infection compared to WT HEK293FT cells. These results suggest that ZAP plays an important role in restricting VZV replication and that impaired ZAP function might have an impact on disease pathogenesis in patients with VZV CNS infection.

Themes: Infectious Diseases, Immune diseases
Keywords: , ,

Comparative Study of High-Efficacy, Disease Modifying Treatment of Relapsing Multiple Sclerosis CoSHED RMS

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Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system, typically presented in young adults. Previously, MS was considered a T-cell-mediated disorder, but evidence has accumulated that B cells have been found to play a central role. In recent years, therapeutic antibodies to CD20 have been widely used. The first-in-class of these antibodies was rituximab, and subsequently several other candidates have been introduced. These B cell-depleting therapies reduce relapse rate and disease progression. A national Danish investigator-initiated phase-III study of the effect of ocrelizumab versus rituximab in patients with active MS (DanNORMS: Danish Non-inferiority study of Ocrelizumab and Rituximab in MS NCT0488788). In parallel with this study, we have initiated a prospective clinical non-randomized open-label multi-center follow-up study CoSHED RMS (Comparative Study of High-Efficacy Disease-modifying treatment in relapsing MS) of the DanNORMS patients versus ofatumumab treated patients. Forty patients have been included in total in the three treatment groups, ocrelizumab, rituximab and ofatumumab and will be compared to an age and gender matched control group. The follow-up period is 2 years. We will register aspects of both immunological, virological, and epigenetic responses. Findings are compared with the relative efficacy of the three treatments, and the course of disease for the patients. With this study we aim to increase our understanding of the mechanism of action of the three B cell-depleting treatments, and the pathogenic mechanisms in MS. The aim is to optimize personalized medicine for MS patients.

Themes: Neuroscience, Immune diseases
Keywords: Multiple Sclerosis, B cell depleting therapy, Immunology

CRISPR/Cas base editing to genetically correct chronic granulomatous disease-causing variants in CYBA and CYBB

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Chronic granulomatous disease (CGD) is an inborn error of immunity resulting from phagocyte dysfunction. The only curative treatment for CGD is allogeneic hematopoietic stem cell (HSC) transplantation, which can result in severe adverse effects. Therefore, ex vivo gene editing of au-tologous human HSCs is being studied as an alternative. DNA double-strand break (DSB)-free gene editing technologies such as base editing have been developed to circumvent the challenges of DSB-dependent gene editing. Here, we use base editing to correct CGD-causing variants in the CYBA and CYBB genes. Peripheral blood mononuclear cells were obtained from patients or healthy carriers of the pathogenic variants CYBA c.371C>T, CYBB c.252G>A, and CYBB c.625C>T and used to test base editing efficiencies. For CYBA c.371C>T and CYBB c.625C>T on-target editing of more than 80% was observed with minimal indel formation. In addition to the PBMCs, we obtained CD34+ hematopoietic stem and progenitor cells (HSPCs) from a healthy donor heterozygous for the CYBB c.252G>A variant. Base editing of these cells resulted in 72% alleles carrying the wild type variant. Similar colony-formation potential was observed for treated and untreated cells, while xenotransplantation of immunodeficient mice showed a slight decrease in bone marrow engraftment for base edited HSPCs. The presence of long-term repopulating HSCs in these mice was validated by secondary transplantations which resulted in up to 5% humanization in the bone marrow of secondary recipients. Future studies will confirm base editing in these LT-HSCs and include functional analysis of edited cells as well as off-target analyses.

Themes: Genetic engineering, Immune diseases
Keywords: CRISPR/Cas, Base editing, Chronic granulomatous disease

Pomalidomide as an immune-enhancing agent for the control of HIV (PEACH)

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Antiretroviral therapy (ART) suppresses HIV replication and prevents the development of AIDS, but lifelong treatment is required. Persistence of HIV in latently infected CD4+ T cells remains a major barrier to a cure. Other obstacles include the dysfunctional immune responses associated with chronic HIV infection. A key component of future HIV cure strategies could therefore be the use of immune-modifying drugs to stimulate HIV specific immune responses.

Pomalidomide is an immune-enhancing drug that is licensed for the treatment of cancer. Ex vivo studies conducted on samples from people with HIV (PWH) showed that pomalidomide treatment was associated with a reduction in the frequency of dysfunctional NK cells, an expansion of HIV-specific CD8+ T cells and an increased CD8+ T cell-mediated HIV-specific lysis ex vivo. This profile supported a better killing of HIV infected cells.

PEACH is a randomised, placebo-controlled clinical trial of pomalidomide in PWH. Participants will be enrolled from Denmark and Australia and will be randomised 1:1 to receive pomalidomide 2 mg or placebo concurrent with aspirin 75 mg for three treatment cycles, each consisting of 21 days on and a minimum of 7 days off. In phase I, participants will receive cycle I while on suppressive ART. In phase II participants will receive cycle II and III in the setting of an analytical treatment interruption. Primary outcomes are safety and time to viral rebound. Targeted enrolment is 16 per arm.

In conclusion this clinical trial will investigate pomalidomide as an immune-enhancing agent that may support immunological control of HIV in the absence of ART.

Themes: Infectious Diseases, Immune diseases
Keywords: HIV, Immune-modulating therapy, Analytical treatment interruption

Multi-omics characterization of the immunological and HIV-1 landscape after treatment with broadly neutralizing antibodies

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Introduction: Treatment with broadly neutralizing antibodies (bNAbs) may induce drug-free, immune-mediated control of HIV-1 replication in a subset of people living with HIV. However, a deeper understanding of the underlying molecular mechanisms is needed to strengthen clinical evidence and improve treatment regimes. Modern multi-omics approaches can help to unravel these mechanisms.

Methods: We analyzed samples from an individual who was treated with antiretroviral therapy (ART) and a 30-day bNAbs regime upon HIV-1 diagnosis. After one year on ART, this individual underwent analytical treatment interruption. To describe the viral landscape, we performed matched integration site and proviral sequencing at three time points: during viremia, during ART, and at viral rebound. To capture the immunological landscape, we conducted single-cell RNA sequencing of CD4 T cells during viremia and integrated our data with publicly available genomic features, chromatin conformation, and chromatin immunoprecipitation sequencing databases.

Results: Our findings indicate that HIV-1 genomes retrieved at the time of viral rebound were less likely to be found near activating histones and were more frequently located in regions with lower transcriptional activity.

Conclusion: These findings support the theory that immune-mediated pressure selects for HIV-1 clones in lowly expressed genomic regions. The observation that this effect is already measurable after just one year suggests that treatment with bNAbs may accelerate this process. Further application of this multi-omics approach to additional individuals and a control group is necessary to strengthen and confirm our findings.

Themes: Omics, Infectious Diseases
Keywords: Single-cell, Multi-omics, HIV-1 cure

Atg14-Atg6 subcomplex has a central role in the organization of phagophore assembly site

Yan Hu, Department of Biomedicin, 10 min oral presentation

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Autophagy is an intracellular degradative process conserved among eukaryotes that is involved in multiple physiological functions and essential to maintain cellular homeostasis. The hallmark of autophagy is the novo formation of phagophores and their elongation and closure into autophagosomes, which is mediated by complexes formed by the autophagy-related (Atg) proteins. One of these complexes is the phosphatidylinositol 3-kinase (PI3K) complex I, in which has Vps34-Vps15 and Atg14-Atg6 subcomplexes are organized with a V-shaped architecture. The established function of the PI3K complex I in autophagosome formation is the generation of phosphatidyllnositol-3-phosphate (PtdIns3P), which is mediated by Vps34-Vps15 subcomplex, to recruit other Atg proteins. While the Atg14-Atg6 subcomplex is important to stimulate PtdIns3P biosynthesis , it remains unknown if it has additional functions in autophagy. Here we show that Atg13 and Atg9 are important to assemble the PI3K complex I in Saccharomyces cerevisiae by localizing the Atg14-Atg6 subcomplex to the phagophore assembly site (PAS). Additionally, Atg14-Atg6 subcomplex plays a crucial role in organizing the PAS formation because in its absence, Atg8-positve membranes adjacent to the vacuole do not associate with Atg9-positve membranes tethered to the endoplasmic reticulum. These results uncover a key organizational role of the Atg14-Atg6 subcomplex in the PAS autophagy and reveal that at least two distinct membrane sources contribute to formation of the PAS and phagophore nucleation.

Themes: Molecular biology, Molecular biology
Keywords: Autophagy, PI3K complex I, saccharomyces cerevisiae

SESSION 14 - Rehabilitation

Efficacy of community-based brisk walking on physical function, comorbidities, cognition, disease severity, and quality of life in people with Parkinson's disease.

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Background and aim: Walking difficulty is considered one of the most bothersome symptoms that people with Parkinson's disease wish to improve, affecting ability to work and quality of life. No study has investigated the effects of community-based brisk walking on perceived walking difficulties in people with Parkinson's disease. The primary aim is to investigate the acute and long-term effects a 24-week walking intervention (WALK) compared to a group receiving an activity tacker (HOME) and a control group (CON) on perceived walking difficulties in people with Parkinson's disease.

Material and methods: Test would be performed at baseline (0 weeks), post intervention (24 weeks), and at follow-up (48 weeks). A sample of 129 people with Parkinson's disease would be recruited. Inclusion criteria include diagnosed with Parkinson's disease, age ≥ 40 years, Hoehn & Yahr stage ≤ 3, and experience of walking difficulty (Walk-12G score ≥ 11.5). Exclusion criteria include alcohol abuse and dementia. CON receives walking advice at baseline. HOME receives an activity tracker and monthly telephone calls. WALK receives an activity tracker, monthly telephone calls, bi-weekly supervised group session and an individualized home-based walking program.

Perspectives: The project has the potential to establish brisk walking as a safe, easily accessible, sustainable, and cost-effective treatment of a frequent and disabling motor symptom, namely walking difficulty. The project can lay the ground for a yet unexplored area of research with important implications for millions of people with Parkinson's disease.

Themes: Rehabilitation, Neurodegenerative disorders
Keywords: Exercise, Neurodegenrative disorder, Gait

The WORK-IT-OUT study. Optimizing Biopsychosocial Rehabilitation for Low Back Pain: Integrating Workplace Interventions to Support Employees on Sick Leave – A Systematic Review.

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Background: Effective management of Low Back Pain (LBP) requires a biopsychosocial approach, integrating physical, psychological, social, and occupational elements. Moderate evidence supports the effectiveness of both multidisciplinary biopsychosocial rehabilitation and workplace intervention individually, but the impact of integrating these approaches for employees on sick leave due to LBP remains unexplored.

Objective: The present systematic review investigated the effectiveness of integrating workplace interventions in biopsychosocial rehabilitation for employees on sick leave due to LBP.

Methods: Systematic searches were conducted using MEDLINE, EMBASE, CINAHL, PEDro and PsycInfo. Grey literature was also researched. Two reviewers independently screened studies, extracted data, and assessed the risk of bias. The results were synthesized narratively, including a description of the included interventions using the Template for Intervention Description and Replication. The overall quality of evidence was presented using the Grading of Recommendations Assessment, Development and Evaluation.

Results: Four randomized controlled trials, representing three interventions, involving 346 workers on sick leave due to LBP were identified. The evidence quality was low to very low for pain, return to work, and sick leave, but moderate for improvement of disability after 12 months of follow-up.

Conclusion: This review suggests a potential benefit of integrating workplace intervention into multidisciplinary biopsychosocial rehabilitation for employees on sick leave due to LBP. Further research is needed and should focus on expanding biopsychosocial rehabilitation for LBP.

Themes: Rehabilitation, Public health
Keywords: Rehabilitation, Low back pain, Biopsykosocial

The IMPROVEHIP Study: Early diagnostics and treatment of acute bleeding in older patients with hip fracture to prevent delirium and improve rehabilitation

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AIMS

We aim to enhance the diagnosis and treatment of acute bleeding in older patients with hip fractures to minimize the occurrence of delirium and fatigue during hospitalization and recovery.

BACKGROUND7,000 patients over the age of 65 are hospitalized in Denmark caused by hip fractures. Often these patients are frail and have multiple health conditions. Their prognosis is poor, with a 10% mortality rate within 30 days of the fracture. Only half of the patients regain their pre-fracture physical abilities within the first year. Bleeding and subsequent acute anemia are common issues. Blood loss can lead to inadequate oxygen supply to the organs. Affection of the brain may cause delirium, which affects up to 50% of the patients with hip fractures. Delirium is linked to dementia, increased risk of institutionalization, and death. Also, bleeding can affect rehabilitation outcome caused by iron deficiency, fatigue and impeded muscle strength.

METHODS

We plan to conduct two randomized, controlled, patient-blinded studies for patients aged 75 years and above. Study 1 (n=200) aims to reduce occurrence of delirium by minimizing the duration of anemia. Study 2 (n=586) investigates if iron treatment can prevent fatigue and muscle weakness, thus improving rehabilitation. The studies will take place in Gødstrup Hospital and Aarhus University Hospital, and for Study 2, Regional Hospital Randers as well.

PERSPECTIVES

Hip fractures in older patients may result in cognitive and physical decline, impacting independent living. With these studies we can potentially gain knowledge to prevent delirium and fatigue, benefiting patients and society.

Themes: Rehabilitation, Rehabilitation
Keywords: Geriatrics, Delirium, Hip fracture

Suffering and well-being as experienced by adults with refractory epilepsy undergoing rehabilitation in a community setting and their next of kin - a qualitative study.

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Introduction: Adults with Refractory Epilepsy (RE) and their next of kin are influenced on their well-being after in-patient rehabilitation. Despite this knowledge, research on the challenges experienced by adults with RE and their next of kin is sparse, and further there is lack of knowledge on how professionals can support the well-being of both actors in the rehabilitation process in community settings.

Aim: To identify challenges faced by adults with RE and their next of kin with focus on their perceptions of suffering and wellbeing, and further to integrate this knowledge with the perspectives of rehabilitation professionals from the epilepsy field in the development of recommendations for rehabilitation care in community settings after discharge.

Methods: The project is based on a phenomenological-hermeneutic design. To gain significant insights into patients and next of kin's experiences during the rehabilitation process in a community setting the study will be based on individual in-depth research interviews with adults with RE, their next og kin and professionals.

Perspectives: The project will contribute with recommendations that promote well-being for adults with RE and their next of kin undergoing rehabilitation in community settings after discharge. The recommendations will be dedicated professionals involved in the community rehabilitation in order to bridge the in-patient rehabilitation and the community support after discharge with national and international value to both society, rehabilitation professionals, the adults with RE and their next of kin.

Themes: Rehabilitation, Qualitative research
Keywords: Phenomenology, Epilepsy Care, Hospital to home

Development and reporting of a cross-sectoral cognitive rehabilitation intervention for critically ill patients

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Introduction: Though 80-90% of patients survive admission to the Intensive Care Unit (ICU), many struggle with significant cognitive impairments years after discharge. Cognitive rehabilitation has been used in neuro rehabilitation for years, but not in the general ICU.

Objectives: We aimed to develop a cognitive rehabilitation intervention to support ICU patients' cognitive function throughout the care pathway from ICU to home.

Methods: The Medical Research Council's guideline for developing and evaluating complex interventions guided the study. The development process was based on stakeholder involvement of health professionals, researchers, former ICU patients and relatives through:

1) An initial workshop with the purpose of stakeholders openly sharing ideas for interventions that might support the patients' cognitive rehabilitation.

2) A three round Delphi process starting with the stakeholder panel sharing ideas regarding cognitive rehabilitation; then two rounds where the ideas were narrowed down, based on which interventions were rated to be most important.

3) Expert consultations with health professionals experienced in cognitive neuro-rehabilitation contributed to the final development, and the decision on which interventions to feasibility test.

Results: The process resulted in two interventions: "Mindfulness" and "Brain training", which are currently being investigated in a feasibility study.

Perspective: The results of the ongoing feasibility study will inform whether to continue with evaluating effect of the interventions in a full-scale RCT. The results have potential to improve the rehabilitation pathway of ICU survivors' worldwide.

Themes: Rehabilitation, Public health
Keywords: Cognitive rehabilitation, intervention development, intensive care

Nutritional care: A complex nurse-led intervention to address overweight in adults following their first-time stroke.

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Background: Overweight and obesity are prevalent among stroke patients, particularly in the chronic phase of recovery. Addressing the nutritional needs of individuals with stroke is fundamental in nursing practice and remains crucial across the entire rehabilitation trajectory. However, despite the existence of established nutritional guidelines, there is a lack of initiatives specifically addressing weight management, including limited emphasis on secondary prevention within the primary health sector following a stroke.

Aim: This PhD project aims to develop and evaluate the feasibility of a cross-sectoral, nurse-led intervention to address overweight among stroke survivors within the context of their everyday lives.

Methods: The project is guided by the framework for developing complex interventions and comprises four interconnected studies:

- Study I: A scoping review mapping existing knowledge on nutritional interventions for preventing overweight in stroke rehabilitation.
- Study II: A retrospective, population-based study to identify the prevalence of overweight and risk factors in first-time stroke patients in Central Denmark Region.
- Study III: A prospective cohort study examining patient-reported weight changes over one year following moderate to severe stroke.
- Study IV: A feasibility study evaluating the cross-sectoral nurse-led intervention in the post-stroke rehabilitation trajectory.

Conclusion: To prevent recurrent strokes and improve long-term outcomes, this project aims to address the critical need for effective professional interventions that enhance patients' health literacy and support weight management during stroke rehabilitation.

Themes: Rehabilitation, Qualitative research
Keywords: Nutritional nursing care., Stroke rehabilitation., Weight management.

Virtual Reality: Acceptability of an intervention for relaxation and distraction in intensive care.

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Background: Less sedation has become the standard regimen in patients admitted to an intensive care unit. Consequently, conscious patients experience discomfort and anxiety during their admission.

Virtual reality (VR) is used in other hospital settings to distract patients and reduce discomfort and anxiety; however, its acceptability in intensive care has yet to be explored.

Purpose: To identify and adapt an existing VR intervention to meet the needs of patients admitted to an intensive care unit.

Methods: Our study was guided by the Medical Research Council's framework for developing and evaluating complex interventions. We combined knowledge from the literature and VR experts in the initial phase of the identification process. We collected data through think-aloud interviews with stakeholders and analysed it using the framework method to adapt the intervention.

Findings: We interviewed seven patients and eleven nurses. Our analysis produced three themes: 1) the experience, 2) the content, and 3) the functionality related to identifying an acceptable VR intervention. Stakeholders preferred viewing known nature scenes accompanied by ambient nature sounds and calming music. An acceptable length of the film was 10 minutes. Staff should be able to follow the VR session on a tablet. Uncertainties regarding VR's effect on delirium affected nurses' acceptability of VR.

Conclusion: VR was an acceptable intervention in intensive care. The identified and adapted VR software intervention was a 10-minute 360-degree natural beach film combined with nature sounds and calming music. The identified hardware intervention was a VR headset connected to a control tablet.

Themes: Rehabilitation, Qualitative research
Keywords: Intervention Development, Intensive care, Virtual Reality

Early Remote Rehabilitation to Improve Health of the Elderly after Cardiac Surgery (RECARD) Trial

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Introduction: Older adults undergoing heart surgery often experience delayed recovery, exacerbated by sarcopenia, multiple chronic conditions, and emotional distress. Cardiac rehabilitation (CR) is vital for improving outcomes after surgery, but it is typically delayed by 6–8 weeks due to concerns over sternum healing, leaving patients vulnerable during a critical period. Emerging evidence suggests that early rehabilitation is safe and effective, and digital healthcare technologies offer early intervention opportunities. This study pioneers early remote cardiac rehabilitation, leveraging digital health technologies to offer immediate intervention following heart surgery. This approach has the potential to fill a critical gap in recovery during the vulnerable post-surgical period.

Methods: This randomized controlled trial will include 120 patients aged ≥ 65 undergoing heart surgery via sternotomy. Participants will be randomized to receive early remote CR with home-based exercises via a mobile app and physiotherapist support, or standard care. The primary outcome is change in 30-second chair stand test (30CST) at 6 weeks. Secondary outcomes include gait speed, 6-minute walk test, and HRQoL.

Results: Data collection is ongoing, with results expected to compare functional improvements and sarcopenia prevention between the intervention group and the standard care group.

Conclusion: If successful, the findings from this trial have the potential to revolutionize current cardiac rehabilitation practices, advocating for immediate post-discharge interventions through remote, digitally delivered care.

Themes: Rehabilitation, Cardiology
Keywords: Cardiac rehabilitation, Digital health technologies,

Development of the intervention Get going After concussIoN Lite (GAIN Lite) for adults with mild-to-moderate persistent post-concessional symptoms: Participants perspective on relevance, feasibility and acceptability

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Purpose: The present study describes the development of Get going After concussIoN Lite (GAIN Lite) to enable its replication, and facilitate learning on intervention development practice. The specific purpose is to describe participants' perspectives on relevance, feasibility and acceptability of the GAIN Lite intervention.

Materials and methods: The development process was informed by the framework established by the UK Medical Research Council. A qualitative methodology was employed to assess the relevance, feasibility, and acceptability of the intervention's content, format, and delivery, as experienced by both recipients and providers involved in the development process.

Results: The GAIN Lite intervention programme underwent refinement, testing, and evaluation across six iterative cycles from January 2021 to April 2023. Seventeen recipients were interviewed, while an additional four responded to three oral questions. The finalised GAIN Lite intervention programme comprised: 1) an initial remote interview, 2) self-administered e-learning videos, and 3) up to three hours of remote counselling.

Conclusion: The intervention was declared relevant, feasible, and acceptable by both recipients and providers. The thorough description offers valuable insights into the development of complex interventions. A notable limitation of the study was the lack of cost-effectiveness analysis. The effectiveness of the GAIN Lite intervention will be further evaluated through an ongoing randomised controlled trial

Trial registration: URL: ClinicalTrials.gov Identifier:NCT05233475. Registered on 10th of February 2022.

Themes: Rehabilitation, Health Education
Keywords: Persistent post-concussion symptoms, Digital health, Complex intervention

The Effect of Local Anesthetic Volume for Popliteal Plexus Block on Nerve and Muscle Function in the leg

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Background and Objectives:

The original volume of local anesthetic (LA) being used for the Popliteal Plexus Block (PPB) is 10 mL. However, the optimal volume is unknown. Cadaver studies indicate that larger volumes may spread to branches of the femoral and sciatic nerves, potentially impairing muscle function. However, this has not been tested in vivo. This study evaluates the spread of PPB with 10 mL, 20 mL, and 30 mL of LA. We hypothesized that increasing volumes of LA for PPB would impair motor function of the leg and anesthetize the saphenous nerve.

Methods:

Forty healthy volunteers were randomized to receive one active nerve block in each leg. We obtained 20 observations of each PPB with volumes 10 ml, 20 ml and 30 ml of lidocaine 1%. Control observations of femoral and sciatic nerve blocks were obtained to identify changes caused by motor branch affection. Pre-block baseline values were compared to post-block values assessed 45 minutes after block performance. The primary outcome was relative changes in maximum voluntary isometric contraction (MVIC) of ankle plantar- and dorsi flexion. Secondary outcomes included MVIC of knee extension, relative changes in compound muscle action potential of the gastrocnemius-, anterior tibial-, vastus medialis-, and vastus lateralis muscles, and frequency of saphenous anesthesia.

Results:

There were no significant differences between the PPB groups in any outcomes

Conclusion:

PPB with LA volumes of 10, 20 or 30 mL does not impair muscle function of the leg. The saphenous nerve was affected in only 40-60% of cases. Clinical trials may safely explore higher volumes of LA for PPB without risking motor impairment.

Themes: Surgery, Rehabilitation
Keywords: Popliteal Plexus Block, Regional anesthesia,

SESSION 15 – Cancer 1

Risk of preeclampsia in women with moderate cervical dysplasia

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AIM

Our study aims to determine whether women diagnosed with cervical intraepithelial neoplasia grade 2 (CIN2) are at a higher risk of developing preeclampsia and gestational hypertension if the lesion is left untreated i.e. active surveillance, compared to those who undergo surgical intervention i.e. cone biopsy.

BACKGROUND

Currently, CIN2 treatment options include active surveillance and cone biopsy, with recommendations based on women's age. Nevertheless, not much is known about potential risk associated with active surveillance. Recent research has suggested that having an HPV infection disrupts the intrauterine environment and, thus increases risk of preeclampsia. As active surveillance results in an untreated lesion, and therefore an underlying HPV infection, these women may have a higher risk of preeclampsia.

METHODS

We conducted a nationwide population-based cohort study in Denmark using data from Danish healthcare registers.

We acquired data for all women aged 18-40 years who received a first-time diagnosis of CIN2 based on cervical biopsies between January 1st 1998 and December 31st 2018 whom later had a singleton birth following their CIN2 diagnosis. The primary outcomes were preeclampsia and gestational hypertension.

RESULTS

We included 10,537 women with CIN2 and a subsequent singleton birth; 4,430 women (42%) underwent active surveillance, and 6,107 women (58%) had a cone biopsy, also known as Loop electrical excision procedure (LEEP).

Further analysis is ongoing, and the results will be finalized and prepared for presentation at the PhD Day 2025.

CONCLUSION AND PERSPECTIVES

Clinical management of CIN2 is complex due to the risk of overtreatment and potential harm, alongside unknown risks of active surveillance. This impacts the clinical care of women negatively. Hence, if our study shows increased preeclampsia risk, it will be beneficial for future clinical guidance.

Themes: Gynecology and obstetrics, Cancer
Keywords: Moderate cervical dysplasia, Preeclampsia, HPV

Towards preventing reoperations in breast cancer patients with intraoperative surgical margin assessment using spectral microCT

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Introduction:

In Denmark there are annually 550 breast cancer patients that need reoperation due to narrow margin of the cancer or ductal carcinoma in situ (DCIS). The need for reoperation is determined microscopically several days after the surgery. Ideally, the evaluation should be done perioperatively, where re-localization of the positive margin is easier, and additional tissue can be removed immediately. Spectral microCT is a novel imaging technique that may overcome the deficiencies of existing imaging technologies.

Methods:

In this study we aim to evaluate the performance of the spectral microCT scanner as a tool for surgical margin assessment. The study will include a prospective cohort of 200 patients undergoing surgery because of breast cancer or DCIS. The specimen will be scanned with the spectral microCT scanner before processing at the department of pathology. The imaging data will be correlated with histology, the current gold standard for evaluating surgical margins. This will be used to generate a tumor/DCIS model based on the spectral information that can be incorporated into an artificial intelligence (AI) tool. The performance of this tool will be further improved by adding a calcium label and DCIS probability map based on the presence and distribution of calcifications. The performance of the AI tool and its clinical feasibility will then be validated in another prospective cohort.

Results: pending

Conclusion:

This study will provide clinically relevant insight into the potential of spectral microCT imaging for intraoperative surgical margin assessment in BCS; a tool that may be extended to other cancer types with the aim of reducing reoperations.

Themes: Diagnostics & technology, Cancer
Keywords: Spectral microCT, Margin assessment, Breast cancer

Investigating the impact of T cell receptor repertoire diversity on cancer outcome

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T cells are key effector cells in the adaptive immune system, playing a central role in the defense against pathogens. However, as we age, T cells undergo functional decline due to immunosenescence, the gradual decay of the immune system with age. This decline negatively affects the function and composition of immune cells, leading to an increased susceptibility to age-related diseases, such as cancer. We hypothesized that characterization of the peripheral blood T cell receptor (TCR) repertoire has the potential to provide insights into the current state of the immune system and serve as a biomarker for cancer progression. To investigate this, we explored the peripheral blood TCR repertoire in both healthy individuals and cancer patients, utilizing sequencing data of the TCR-β chain from multiple cohorts obtained locally and from public sources. In both healthy individuals and cancer patients, we observed a contraction of the proportion of non-expanded clones and increase in the proportion of expanded clones with increasing age. Analyses of TCR-β diversity across different age groups revealed sex differences in the diversity among older individuals. Additionally, investigating the relationship between tumor stage and TCR-β diversity showed that lower diversity correlates with more advanced tumor stages. Our results suggest that low TCR diversity represents reduced immune competency and a limited ability to prevent cancer progression.

Themes: Bioinformatics, Cancer
Keywords: T cell receptors repertoire diversity, Immune system, Cancer biology

Co-creating an Advance Care Planning (ACP) model in general practice with professional end-users

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BACKGROUND: ACP allows patients with life-threatening diseases to state their values and preferences thereby ensuring patient-centred care. However, ACP has not been implemented as a routine in primary care. Little knowledge exists on the significance of general practitioner (GP)-initiated ACP, and how ACP can be facilitated in a trajectory of life-threatening disease.

AIM: To develop a model for systematic ACP in general practice for patients with newly diagnosed life-threatening diseases, while integrating the perspectives and practical needs of professional end-users.

METHODS: Four workshops with 18 GPs and three individual semi-structured interviews (GP, oncologist and community nurse) were conducted. All interviews underwent deductive and inductive analysis to identify overarching ACP themes.

RESULTS: GPs viewed ACP as an important task. They highlighted flexibility of timeframe for initiating ACP and adaption of discussed themes as key issues. Time constraints were regarded as main barrier. The oncologist stressed the need for clearly defined roles between GP and the responsible hospital physician. The nurse highlighted the importance of information sharing between involved healthcare professionals.

DISCUSSION: Professional end-users of a GP-initiated ACP model emphasised the importance of an adaptable approach to accommodate current needs throughout the patient's disease trajectory. The ACP model calls for cross-sectoral collaboration to ensure interprofessional communication. Next step involves feasibility test in general practice to refine the model for implementation.

Themes: Public health, Cancer
Keywords: Advance Care Planning, Cancer, Cross-sectoral collaboration

Protocol: Mammography Screening with Artificial Intelligence

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Background

Breast cancer is the most common cancer in women. Early detection, along with effective treatment, is considered essential in reducing breast cancer specific mortality. To achieve this, biennial mammograms are recommended for women aged 50-69 in Denmark. Two breast radiologists review each mammogram (blinded double reading), with a consensus conference held in case of discrepancies between their assessments.

Recent advancements in Artificial Intelligence (AI) decision support systems for mammogram cancer detection indicate benefits, such as a potential increase in breast cancer detection, and addressing staffing shortages.

Reliable detection accuracy and workload monitoring are crucial, as they may be influenced by differences in screening workflows and population diversities.

Method

This study evaluates the implementation of AI through a stepped wedge design in the Central Denmark Region's ongoing breast cancer screening program.

AI will assign a risk score and triage the mammograms towards single or double reading by radiologists, selecting only high-risk cases for double reading.

We anticipate that the intervention will initially comprise approximately 25% of the screening population, and gradually increase to approximately 70% of screened women. Key screening parameters, including the frequency of consensus conferences, the number of recalled women, and the number of cancers detected, will be monitored throughout the intervention.

We expect to evaluate AI-assisted screening after at least 12 months, using metrics such as positive predictive value, and false positive rates.

Themes: Diagnostics & technology, Cancer
Keywords: , ,

Predictors of late breast cancer recurrence: development and validation of an algorithm to predict late breast cancer recurrence

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Background

Breast cancer can recur more than 30 years after primary diagnosis. Studies have investigated predictors of BCR risk up to 10 years after primary diagnosis. No clinical tool exists to predict recurrence risk beyond 10 years. With a population-based case-cohort study, we aim to develop a clinic-pathologic prediction model for late BCR based on characteristics measured at primary diagnosis.

Methods

We will identify women in Denmark diagnosed with an incident, early-stage breast cancer from 1987-2011 using data from the Danish Breast Cancer Group (DBCG). Variables available at diagnosis—tumor characteristics, treatment regimens, comorbidities, and comedications—will form a candidate set of variables for use in the prediction model. From this, we will build a conventional model for late BCR by iteratively adding independent variables into a multivariable logistic regression. Further, we will apply a suite of machine learning algorithms to derive additional prediction models. These will then be combined in an ensemble tool, with individual models weighted in proportion to their predictive performance. After development, we will evaluate model performance in a validation set, using outcome-specific areas under receiver-operating characteristic curves and by calculating positive and negative predictive values.

Results

Expected by February 2025.

Conclusions

We anticipate that this study will uncover clinicopathological predictors and primary tumor biomarkers that may help identify patients with increased risk of late BCR. This may pinpoint candidates for prolonged surveillance or novel targeted therapies.

Themes: Epidemiology, Cancer
Keywords: Breast cancer, Prediction models,

Sexual Dysfunction and Gynaecological Complication in Women After Treatment for Anal Cancer

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Background: Anal cancer (AC) is rare in Denmark, with approximately 200 cases annually. Despite advancements in chemoradiotherapy (CRT), many women experience long-term sexual dysfunction due to radiation exposure to organs at risk (OARs) such as the vulva, vagina, and bulboclitoris. Although the effects of pelvic radiotherapy on sexual function are well-documented in other cancers, research specifically on female AC patients remains limited. This project addresses this gap by investigating the prevalence, risks, and interventions for sexual dysfunction post-CRT.

Objectives and Methods: This project involves four interlinked stages:

- Literature Review (Study 1): A systematic review of gynecological toxicities post-CRT to identify research gaps.
- Retrospective Data Analysis: Analysis of patient-reported outcomes and physician-reported toxicities in ~250 Danish female AC patients from the DACG-I and DACG-II studies. Study 2: Assess prevalence of sexual dysfunction, correlating dose-volume parameters for OARs with morbidity. Study 3: Conduct normal tissue complication probability (NTCP) modeling on significant parameters. Study 4: Comparative dose planning to assess feasibility of sparing sexual OARs.
- Multicenter Clinical Study: Assess post-RT vaginal changes and evaluate sexual counseling, prioritizing patient involvement to ensure counseling meets their needs and expectations.
- Guideline Implementation: Develop RT planning guidelines to spare sexual organs at risk and create patient awareness materials.

Impact: This project fulfills a critical need in survivorship care for female AC patients, aiming to support personalized RT approaches that improve sexual health outcomes.

Themes: Cancer, Cancer
Keywords: Anal cancer, Radiotherapy, Survivorship

Temporal Trends in Incidence and Mortality of Colorectal Cancer in Denmark from 2007 to 2022

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Introduction: Colorectal cancer (CRC) is the third most common cancer in the Western world and represents a significant burden on healthcare systems worldwide. We aimed to describe temporal trends in incidence, tumour characteristics, and survival for patients with CRC in a nationwide, population-based cohort in Denmark.

Methods: We used population-based Danish healthcare registries to study all patients diagnosed with CRC from 2007-2022. We present age-standardized incidence rates (ASIR) as new cases per 100,000 population standardized to the European standard population. Survival analyses were performed using the Kaplan-Meier estimator.

Results: 77,277 people in Denmark were diagnosed with CRC from 2007 to 2022. ASIRs were relatively stable from 2007 to 2013 with an ASIR of 66 per 100,000 for colon cancer and 32 per 100,000 for rectal cancer. In 2014, an increase in incidence was observed (80.0 per 100,000 for colon cancer and 37.4 per 100,000 for rectal cancer), followed by a decline in later years. Median survival times were 4.1 (IQR: 0.8 to 14.1) years for patients diagnosed between 2007 to 2010, 5.3 (IQR: 1.1 to NA) years for patients diagnosed from 2011 to 2013 and 7.6 (IQR: 1.7 to NA) years for patients diagnosed from 2014 to 2017. The assessment of mutational and molecular profiles increased consistently throughout the study period.

Conclusion: We observed an initial increase in CRC incidence in 2014, corresponding with implementation of the national screening programme, followed by a subsequent decline. In recent years, the incidence has dropped below pre-screening levels.

Themes: Epidemiology, Cancer
Keywords: Colorectal Cancer, ,

Adequacy of excisional treatment for cervical precancer in Denmark.

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Introduction:

An effective cervical cancer screening program relies on a high-quality screening test and high participation rates. However, it is also of the utmost importance that women with cervical precancer receive adequate treatment with a large loop excision of the transformation zone (LLETZ) to avoid progression to cancer. European quality indicators recommend that 80% of LLETZ patients have negative margins, and 70% have a negative test of cure (TOC) six months after treatment. TOC was implemented in the Danish clinical guideline in 2013.

Aim:

The primary outcome was to describe the proportion of women with a negative resection margin after LLETZ, and secondly to describe the proportion of women with a negative TOC.

Materials and methods:

Nationwide population-based observational study of all cases of first-time LLETZ. We included women >18 years of age with a status of resection margins from 1998 to 2020, and a TOC status from 2013 to 2020. The data source was the Danish Pathology Register.

Results:

Preliminary results include a total number of N=85,661 women with a first-time LLETZ for status of resection margins and N=22,291 for TOC status. Histology for the LLETZ was

primarily CIN3 (64.8%). Resection margins were reported as negative for 52% of the overall study population. TOC was negative in 85% of investigated cases in the given period. Further results will be presented at the PhD day 2025.

Conclusion:

Compared to the European quality indicators, Danish women do not accomplish negative margins above 80%. However, the TOC standards were well above the European quality indicators.

Themes: Gynecology and obstetrics, Cancer
Keywords: Cervical cancer and precancer, Large loop excision of the transformation zone, Test of cure

Danish National Penile Cancer database: patient and penile cancer characteristics, and management

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Introduction

To characterize Danish PC patients, we have created a comprehensive retrospective database of a nationwide cohort from 1999 to 2023. The database currently contains patient and tumor characteristics. Treatment and outcome information is under validation.

Methods & Materials

The Danish National Penile Cancer database, DaPeCa-RedCap, contains information on patients referred to a university center from 1999-2023 with invasive penile cancer. Patients with penile intraepithelial neoplasia (PeIN) are yet to be included. The set of variables was pre-defined, and data were extracted by retrospective medical chart review.

Results

The median age at the time of diagnosis was 68 years.

At diagnosis, 45% of patients presented with pT1, 33% with pT2, 16% with pT3, 2% with pT4, and 3.7% with pTx. Fourty percent presented with lymph node metastases and 3% with distant metastases.

The reporting of histopathological grade varied through the study period. For patients diagnosed in 1999-2009, 47% were reported with with G1, 38 % with G2, and 16% with G3. In 2010-2016 the fractions were 34%, 37% and 24% for G1, G2 and G3 tumors. In 2017-2023 reported percentages were 16% G1, 36% G2 and 41% G3 tumors.

Conclusions

Most patients present with pT1 tumors. Four out of 10 patients present with initial lymph node metastases, and 3% present with distant metastases at diagnosis.

Changes in reporting of grade may be due to inter-observer variation and increased attention and interest during the study period.

Themes: Urology & Nephrology, Cancer
Keywords: Penile cancer, ,

HbA1c Levels and Breast Cancer Prognosis in Women without Diabetes

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Background: Diabetes is associated with impaired breast cancer (BC) prognosis; however, the effectiveness of glycosylated hemoglobin (HbA1c) as a prognostic biomarker in BC remains uncertain, especially for patients without diabetes. We aimed to determine whether elevated HbA1c is associated with a worse prognosis in BC patients without known diabetes.

Methods: The study population comprised women with primary invasive stage I-III BC between 2010 and 2020 surgically treated at Aarhus University Hospital, Denmark, without a diabetes diagnosis at baseline. We assessed HbA1c at BC diagnosis as quartiles (HbA1c-Q1=21-33 mmol/mol, HbA1c-Q2=34-36 mmol/mol, HbA1c-Q3=37-38 mmol/mol, HbA1c-Q4=≥39 mmol/mol). We used multivariable Cox regression to estimate hazard ratios (HRs) and associated 95% confidence intervals (95% CIs) of new BC events (BC recurrence or contralateral BC) and all-cause mortality.

Results: In total, 2,514 women were included. During median 5.6 years follow-up for new BC events, 230 (9.1%) events occurred. An escalating risk of new BC events was observed with increasing HbA1c quartiles (HRadjusted [95% CI], HbA1c-Q2: 1.09 [0.75-1.60]; HbA1c-Q3: 1.35 [0.88-2.07]; HbA1c-Q4: 1.69 [1.13-2.54]) compared to HbA1c-Q1. During median 6.0 years follow-up for all-cause mortality, 267 deaths (10.6%) occurred. No apparent association was evident between increasing HbA1c quartiles and all-cause mortality.

Conclusions: For women with primary BC and no known diagnosis of diabetes, higher levels of HbA1c were associated with an increased risk of new BC events, but not all-cause mortality. HbA1c may serve as a prognostic metabolic biomarker for BC patients without diabetes.

Themes: Cancer, Epidemiology
Keywords: Breast Cancer, Diabetes, HbA1c

SESSION 16 - Epidemiology

Inflammatory Bowel Disease during Pregnancy and the Well-Being of Offspring

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic disease that frequently manifests during reproductive age. Symptoms such as diarrhea, weight loss and fatigue may impact quality of life. Additionally, active IBD is linked to an increased risk of adverse pregnancy outcome, including miscarriage, preterm birth and small for gestational age infants. Despite these concerns, research indicates normal development and overall good health in offspring. However, the well-being during school age of children born to mothers with IBD has never been investigated.

Aim: This study aims to investigate the well-being reported in public school questionnaires by children aged 10 to 15, comparing those exposed to maternal IBD during pregnancy with non-exposed children.

Methods: Since 2015, all children attending Danish public schools have participated in annual well-being assessments, covering social, academic aspects, and support experiences. This cohort study includes children born between 1999 and 2015, who participated in at least one school well-being assessment. We will compare well-being of those exposed to maternal IBD during pregnancy to their peers. Exposure will be defined as maternal IBD diagnosed before birth of the child based on ICD-8 and ICD-10 codes. Ordinal logistic regression analyses will be performed to estimate odds ratio for well-being when comparing the exposed group with the unexposed group. We will use pooled well-being data for each child, accounting for the number of completed questionnaires. Sub analyses will assess the results on each grade level as well as severity of maternal disease and other relevant factors.

Themes: Epidemiology, Gastroenterology and hepatology
Keywords: Inflammatory Bowel Disease, Epidemiology, Well-being

Real-life clinical experience of antifibrotic therapy in patients with progressive pulmonary fibrosis: Risk factors for progression and non-adherence

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Background: Interstitial lung diseases (ILD's) comprise a broad group of rare lung disorders with known or unknown underlying causes or exposures. A significant number of patients with ILD develop a progressive phenotype (progressive pulmonary fibrosis, PPF). PPF is a severe condition characterized by rapid development of scar tissue in the lungs leading to a decline in lung function, increased breathlessness, reduced quality of life, and early death. Antifibrotic therapy, recently approved in Denmark for PPF, can slow down disease progression but is often associated with severe adverse events that can reduce quality of life and lead to treatment discontinuation.

Aim: The aim of the project is to 1) Identify patients at risk of PPF, 2) Identify those at increased risk of adverse events and treatment discontinuation, 3) Predict disease progression using imaging and blood biomarkers.

Method: This is a prospective observational multicenter cohort study. We plan to include 120 patients with PPF. We will investigate clinical characteristics, frailty, biomarkers (blood), imaging (HRCT), quality of life (PROM's), adverse events, impact of concurrent immunosuppressive treatment.

Results: Pending, inclusion initiated.

Perspectives: With high mortality rates and limited treatment options, early diagnosis and continuous treatment with antifibrotic medication are crucial to improve survival and quality of life for patients with PPF. This real-life study will help tailor treatment strategies based on individual risk profiles to enhance treatment adherence for those who benefit the most while ensuring that patients unlikely to benefit are offered alternative, palliative care options.

Themes: Epidemiology, Diagnostics & technology
Keywords: Pulmonary fibrosis, Biomarkers, Antifibrotic therapy

Incidence Rate of Infective Endocarditis by Socioeconomic Position: A Danish Nationwide Cohort Study (2000–2022)

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Background: People with lower socioeconomic position (SEP) have a higher risk of cardiac and infectious diseases than those with higher SEP. However, whether a difference exists in infective endocarditis (IE) incidence across SEP is largely unknown.

Methods: Using nationwide Danish registries, we investigated the incidence rate of IE hospitalizations (2000¬–2022) among Danes ≥30 years. As SEP indicator, we used the affluence level (accounting for household-level income and wealth), dividing the population into tertiles of low, medium, and high affluence. Hazard models were used to obtain the slope index (SII) and relative index of inequality (RII) (the expected absolute and relative excess risk across the entire affluence scale). We stratified by sex and age groups.

Results: Per 100,000 person-years, IE incidence rate increased from 8.9 in 2000 to 20.1 in 2022 for those with low affluence; from 6.7 to 13.9 for those with medium affluence; and from 6.3 to 12.9 for those with high affluence. The SII increased from 4.0 additional cases (95% CI: 0.5–7.5) in 2000 to 10.9 (95% CI: 6.1–15.7) in 2022. RII increased from 1.73 (95% CI: 0.91–2.55) to 2.00 (95% CI: 1.39–2.61). Higher incidence rates with lower affluence levels were observed in all sex and age groups, except those ≥85 years of age, where no difference was observed.

Conclusion: The IE incidence rate increased in all affluence levels, with highest rates in the lowest affluence group. Absolute and relative inequality increased overall throughout the study period. Considering these socioeconomic differences when designing public health and clinical strategies may aid in making interventions more effective in preventing IE.

Themes: Epidemiology, Cardiology
Keywords: Infective endocarditis, Socioeconomic position, Incidence rate

Physical Activity and fecundability in a Danish Preconception Cohort – isotemporal substitution analysis

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Background: There is little knowledge on how the type, intensity or duration of PA may influence fertility.

Objective: To quantify associations between theoretical replacement of sitting activity (SA) with walking, moderate PA (MPA) or vigorous PA (VPA) and fecundability in Danish women trying to conceive.

Methods: This prospective cohort study was based on self-reported questionnaire data from the SnartForældre.dk study. We analyzed data from 8,962 females aged 18-49 years, residing in Denmark, and trying to conceive with a male partner without the use of fertility treatment. Information on PA was collected using the International Physical Activity Questionnaire. We used isotemporal substitution analysis to quantify associations between differences in PA and fecundability (the cycle specific probability of conception) and modeled substitution of 30 minutes of SA with 30 minutes of walking, MPA or VPA. Fecundability ratios (FRs) and 95% confidence intervals (CIs) were computed using proportional probabilities regression models adjusted for potential confounders.

Preliminary results: In the full cohort (n = 8,962), the FR (95% CI) was 1.06 (1.01-1.11), when replacing 30 minutes of SA with 30 minutes of VPA. Among participants with > 30 minutes of daily VPA (n = 1,009), the FR was 1.06 (95% CI 1.00-1.11) when replacing SA with walking, and 0.94 (0.79-1.12) replacing SA with VPA. Among participants with < 30 minutes of daily VPA (n = 7,953) the FR (95% CI) was 1.00 (0.98-1.01) replacing SA with walking and 1.08 (0.88-1.31) replacing SA with VPA.

Conclusion: We found a slightly higher fecundability when SA was replaced with 30 minutes of VPA. However, the association was weak.

Themes: Epidemiology, Gynecology and obstetrics
Keywords: Physical activity, Fertility, Substitution analysis

The Clinical Presentation of and Mortality in Patients with Stroke Using Glucocorticoids

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Background: Stroke patients using glucocorticoids (GC) have a higher mortality compared with stroke patients not using GC. The underlying mechanisms are poorly understood.

Objectives: To characterize stroke patients using GC regarding stroke severity, stroke treatment, comorbidity, co-medication, lifestyle, and socioeconomic position, and to investigate the association with all-cause mortality.

Methods: In a population-based cohort study we identified all patients with first-time stroke during 2005-2017 (N = 79,110 with ischemic stroke and N = 10,520 with intracerebral hemorrhage). The exposure was current use of systemic GC (use up to 90 days prior to stroke, N= 3,455). Patients with former GC use (use between 91 to 180 days prior to stroke, N = 1,285) and patients with non/rare use (N = 84,885) were included in comparison cohorts. Cohorts were followed from stroke diagnosis until death, emigration or up to one year following stroke. The Kaplan-Meier method was used to compute 30-day and 1-year mortality.

Results: 20% of all current GC users had severe or very severe strokes compared to 17% of former and non/rare users according to the Scandinavian Stroke Scale Score. Prevalences of comorbidities were similar among current and former users, but lower among non/rare users. The 30-day mortality was higher among current users (15% [95% CI: 14%-16%) compared with former (11% [95% CI: 9%-12%) and non/rare users (8.2% [95% CI: 8.0%-8.4%]).

Conclusion: Stroke severity, and comorbidity prevalence, differed slightly according to GC ex-posure. We found an increased mortality among current GC users compared with former and non/rare users.

Themes: Epidemiology, Endocrinology
Keywords: Glucocorticoids, Stroke, Prognosis

Risk of Urogenital Infections in Patients with Type 2 Diabetes Initiating SGLT2i Versus GLP-1RA: A Danish Cohort Study

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Background

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA) offer many beneficial effects but come with side effects. Evidence shows SGLT2i increase genital tract infections (GTI) compared with GLP-1RA, whereas evidence for urinary tract infections (UTI) is limited. This study aimed to compare the risks of UTI and GTI in new users of SGLT2i versus GLP-1RA.

Methods

In this cohort study emulating a target trial, we included all adult metformin users initiating SGLT2i or GLP-1RA in Denmark in 2016-2021 and used inverse-probability of treatment weighting to balance potential confounders. We estimated weighted risk and risk ratios of community- or hospital-treated UTI and GTI, performing both intention-to-treat and on-treatment analyses.

Results

This study included 52,414 SGLT2i initiators and 27,023 GLP-1RA initiators with a median follow-up of 2.9 to 3.9 years.

The estimated risks of UTI within the first year were nearly identical: 10.0% in SGLT2i, 10.2% in GLP-1RA in intention-to-treat analyses corresponding to a risk ratio of 0.98 (95% CI 0.94, 1.03). For GTI the 1-year risks were clearly elevated under SGLT2i therapy 2.0% versus 0.7%, risk ratio 2.95 (95% CI 2.52, 3.44). During 5-year follow-up the relative UTI risk remained almost constant (0.96 [95% CI 0.94, 0.99]) whereas the GTI risk ratio with SGLT2i decreased to 1.64 (95% CI 1.49, 1.80). Similar but more pronounced relative risks were observed in on-treatment analyses.

Conclusion

In routine clinical care, SGLT2i initiation is not associated with increased risk of UTI as compared to GLP-1RA initiation. However, early GTI risk is up-to 3-fold larger in SGLT2i users.

Themes: Epidemiology, Endocrinology
Keywords: Epidemiology, Type 2 diabetes, Urogenital infections

Are Individuals Born Small for Gestational Age at Increased Risk of Acute Kidney Injury?

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Background

Acute kidney injury (AKI) is associated with increased morbidity and mortality. Individuals born small for gestational age (SGA) may be more vulnerable to AKI due to reduced nephron development. However, the long-term risk of AKI in SGA individuals remains unclear. This study examined the risk of AKI across levels of birth weight for gestational age.

Methods

We conducted a population-based cohort study including 609,463 individuals born in Denmark between 1995 and 2022. All data were obtained from national medical databases. Birth weight for gestational age was categorized as SGA (≤10th percentile), appropriate for gestational age (AGA, 10th–90th percentile), and large for gestational age (LGA, ≥90th percentile). AKI was defined using plasma creatinine measurements according to KDIGO guidelines. The 25-year cumulative incidence of AKI was calculated for each group, and hazard ratios (HRs) were estimated using Cox regression to compare risks across groups.

Results

Over a median follow-up of 8.6 years (IQR: 5.6–16.0 years), 12,347 individuals developed AKI. The 25-year cumulative incidence of AKI was highest in the SGA group (4.3%) compared to the AGA (3.4%) and LGA (3.2%) groups. SGA individuals had a 38% higher risk of developing AKI compared to AGA individuals (HR: 1.38, 95% CI: 1.30–1.46). The risk for individuals born LGA was comparable to those born AGA (HR: 0.96, 95% CI: 0.91–1.02).

Conclusion

Individuals born SGA have an increased long-term risk of AKI compared to those born AGA and LGA, highlighting SGA as an important risk factor for AKI.

Themes: Epidemiology, Urology & Nephrology
Keywords: Acute kidney injury, Small for gestational age, Epidemiology

Perinatal hypoxia assessed by umbilical cord blood pH in combination with Apgar score and the risk of attention deficit hyperactivity disorder

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Background: Perinatal factors' role in the etiology of attention deficit hyperactivity disorder (ADHD) remains to be understood. Apgar score is a clinical assessment of the state of the newborn. Low Apgar score has been associated with an increased risk of ADHD. Hypoxia, but also other perinatal exposures can cause low Apgar score. Biochemical measures (umbilical cord blood pH) are needed to evaluate if the newborn has been exposed to hypoxia. It is sparsely investigated if hypoxia at birth assessed by combining Apgar score and umbilical cord pH is associated with ADHD.

Aim: We aim to estimate the association between hypoxia assessed by Apgar score in combination with umbilical cord blood pH and the risk of ADHD.

Methods: A population-based cohort of 817,563 singletons born in Denmark 2004-2018. Apgar scores and umbilical cord pH were retrieved from the Danish Medical Birth Registry and information on ADHD from the Danish National Patient Registry. For various combinations of reduced Apgar scores and low pH we estimated the risk of ADHD using multivariable logistic regression.

Results: Preliminary results showed increased risk of ADHD for newborns with pH 7.00-7.09 and Apgar 4-6 (OR 1.99 (1.34;2.98)), and newborns with pH 7.10-7.19 and Apgar 0-3 ((OR 2.06 1.08;3.94)) and for newborns with pH 7.10-7.19 and Apgar 4-6 (OR 1.53 (1.07;2.18)). Newborns with pH <7.00 but normal Apgar score and newborns with Apgar score 0-3 but normal pH did not have increased risk of ADHD compared to newborns with both normal pH and normal Apgar score.

Conclusion: Preliminary results suggest perinatal hypoxia is associated with ADHD.

Themes: Epidemiology, Paediatrics
Keywords: Perinatal hypoxia, Attention deficit hyperactivity disorder, Population-based cohort study

Development of the Nordic Nutrition Recommendations 2023 food-based diet score and its association with all-cause mortality in two Swedish cohorts

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Background and objective: The 2023 Nordic Nutrition Recommendations (NNR23) focus on promoting planetary health and preventing disease through food-based guidelines. However, the health impacts of adhering to NNR23 remain unexplored. This study aims to develop a diet score to assess adherence to NNR23, evaluate micronutrient intake, and examine its association with mortality.

Methods: We developed a diet score based on NNR23, comprising 15 food components. Points were assigned proportionally from 0 to 1 for each component, reflecting the level of adherence, with a maximum possible score of 15 points. We then followed men aged 45-79 from the Cohort of Swedish Men (n=48,850) and women aged 48–83 years from the Swedish Mammography Cohort (n=39,984), with extensive information collected on diet and lifestyle in 1997, 2009 and 2019. Cases were retrieved through the Swedish Patient Register and the Death Register. Participants were followed until death or administrative end of follow-up on 31st of December 2019. Multivariable Cox proportional hazards regression models were used to estimate hazard ratios (HRs) with 95 % confidence intervals (CIs) using age as the underlying timescale.

Results: Participants with the highest adherence to NNR23 (>10 points, HR 0.77, 95% CI 0.74-0.80) showed a lower risk of all-cause mortality compared to those with the lowest adherence (<8 points).

Conclusion: Our study suggests that high adherence to NNR23 may contribute to a reduction in overall mortality.

Themes: Epidemiology, Health Education
Keywords: Sustainable diet, Cohort study, Epidemiology

Prevalence, incidence, and age at diagnosis of males with hypospadias – a nationwide population-based epidemiological study

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Background: The exact cause of hypospadias remains unclear. Population-level monitoring may uncover risk factors. Our aim was to assess the prevalence, incidence, diagnostic age, and surgical outcomes of hypospadias cases in Denmark.

Methods: Males recorded with a hypospadias diagnosis or surgery code in the Danish National Patient Registry (DNPR) from 1977 to 2019 were identified (n=10,276). A medical file review in a subpopulation (n=1,710) (diagnostic validation, grade (anterior/posterior) informed a diagnostic algorithm. Prevalence (hypospadias males/100,000 newborn boys, 1901-2019) and incidence (hypospadias males/100,000 background population males, 1977-2019) were calculated. Temporal trends were analysed by linear regression. Differences in hospital contacts and age were analyzed by the Mann-Whitney test.

Findings: Hypospadias was verified in n=9,189 (89.4%) (anterior n=8,404 (91.5%); posterior n=785 (8.5%)). The prevalence rose significantly from 1977-2006 and peaked at 847 (anterior 768, posterior 79) in 2007. From 2008-2018, the prevalence stabilized at a mean of 774 (95% confidence interval (CI): 738-810). A rise in incidence was observed (p<10-4). Posterior hypospadias was diagnosed earlier (0.0 years, CI: 0.0-6.2) than anterior hypospadias (0.2 years, CI: 0.0-10.1). Males with posterior hypospadias had more hospital contacts (median=7 (95% CI 2-16)) than anterior (median=3 (95% CI 1-8)), (p<10-4). From 1977, at least one surgical admission was recorded for n=4,550 (58.4%) (anterior n=3,921 (55.3%), posterior n=629 (89.2%)). Anterior hypospadias represented 97.7% of males that never had surgery (n=3,244, 41.6%).

Interpretation: This study reports a high and increasing prevalence of hypospadias of approximately 850 per 100,000 newborn boys. From 1977, the diagnostic age decreased, posterior grades were diagnosed earlier and had more surgical admissions than anterior grades. A significant proportion were never operated.

Themes: Epidemiology, Paediatrics
Keywords: Malformations, Hypospadias,

SESSION 17 - Cancer diagnostics 1

Diagnostic Delay in Cutaneous T-cell Lymphomas

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Background: Primary cutaneous T-cell lymphomas (CTCLs) are non-Hodgkin lymphomas of the skin. Despite favorable disease-specific survival rates, patients often experience poor quality of life, comparable to end-stage renal disease. The primary focus of treatment is management of symptoms, why early diagnosis and timely treatment intervention is important to ensure specialized care for improved patient outcome. Unfortunately, the diagnosis of CTCL can be difficult, as early disease often presents similar to conditions like eczema or psoriasis. This leads to a considerable diagnostic delay which can lead to increased morbidity and decrease in quality of life for patients.

Aim: This study aims to evaluate the diagnostic delay for MF, SS, and primary cutaneous CD30+ LPDs, test the reproducibility of prior findings on diagnostic delays, and establish a REDCap database of patients with CTCL.

Methods: We will conduct a retrospective analysis of CTCL patient records from Aarhus University Hospital and Bispebjerg Hospital. Diagnostic timelines will be assessed using electronic health records and pathology databases, comparing findings to previous studies on MF.

Perspective: This research will contribute to a growing body of knowledge regarding CTCL, addressing the need for improved diagnostic protocols to enhance patient outcomes and quality of life. The REDCap database will also be used in future research projects.

Themes: Cancer, Diagnostics & technology
Keywords: Cutaneous Lymphomas, Diagnostic delay, Cancer

Overweight, obesity and the clinical course of endometrial cancer

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Introduction

Obesity is more strongly associated with the development of endometrial cancer than any other type of cancer in women. This study evaluates how overweight, and obesity influence the risk of endometrial cancer recurrence and mortality, considering synergistic effects of socioeconomic factors and comorbidities.

Methods

We will include all women in Denmark diagnosed with FIGO stage I-A to III-C endometrial cancer from 2005 to 2022. We will retrieve data on patient, tumor and treatment details, as well as self-reported comorbidities from the Danish Gynecological Cancer Database. Information on education, cohabitation, income, and employment before diagnosis will be obtained from Statistics Denmark. We will retrieve data on cancer recurrences via a validated algorithm incorporating diagnostic, pathology and procedure codes, and mortality from the Danish Registry of Causes of Death. We will begin follow-up 90 days post-surgery and continue until the first of the following events: recurrence, emigration, death, new primary cancer, 5 years of follow-up, or December 31, 2023. We will present descriptive characteristics of the study population and use Cox regression to calculate hazard ratios for recurrence and mortality related to overweight and obesity, adjusting for confounders. We will stratify on education, cohabitation, income, employment, and comorbidities.

Clinical implications

Our findings will enhance understanding of the synergistic effects of between obesity, socioeconomic factors, and comorbidities in endometrial cancer outcomes, informing the planning of individualized, differentiated follow-up strategies.

Themes: Cancer, Epidemiology
Keywords: Endometrial cancer, Cancer recurrence, Cohort study

The molecular landscape of EML4-ALK variants and their clinical importance

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Lung cancer is the most common cancer type and the leading cause of cancer-related deaths worldwide. The translocation of the anaplastic lymphoma kinase (ALK) gene is a main oncogenic driver in non-small-cell lung cancer (NSCLC). The echinoderm microtubule-associated protein-like 4 (EML4) is the most frequent ALK fusion partner, observed in 5–7% of all NSCLC cases and categorized into different variants.

Patients diagnosed with incurable EML4-ALK-positive NSCLC are treated with targeted ALK tyrosine kinase inhibitors (TKIs). While this treatment is generally well tolerated and improves survival rates, patient responses can vary, and resistance may develop over time. Therefore, it is essential to investigate and distinguish the EML4-ALK variants to evaluate their potential impacts on clinical outcomes.

The study aims to identify and characterize the EML4-ALK fusion and its various variants. It will also examine any molecular differences among the variants, including co-mutations, to assess their potential influence on treatment outcomes. This will be achieved by analyzing circulating tumor DNA (ctDNA) in plasma from blood samples collected from 70 EML4-ALK-positive patients.

The pre-treatment, post-treatment initiation, and progression disease samples will be examined to determine how the molecular landscape, including EML4-ALK fusion variants and co-mutations, influences the treatment response. Hopefully, the study can identify potential molecular mechanisms that explain the varying treatment responses and failures.

This research has the potential to enhance patient outcomes by providing more tailored and effective treatment strategies, improving prognosis and survival.

Themes: Cancer, Diagnostics & technology
Keywords: ctDNA, Liquid biopsy, Lung cancer

OPTIMIZED-FIT: Use of FIT-values to decide differentiated screening-intervals in colorectal can-cer screening – a nationwide register based cohort study

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Background: The Danish colorectal cancer(CRC) screening program based on the Fecal Immu-nochemical test (FIT) was initiated in 2014 with a four-year run-in period. Since 2018 the FIT has been offered biennially. The cut-off value for deciding the recommendation of a colonosco-py is 100 ng/mL. However, studies have shown that FIT values are associated with the risk of advanced neoplasia, even if the FIT value is negative, but the FIT is only used to identify who should be offered a colonoscopy.

Aim: We aim to investigate if the CRC screening program can be optimized by using the FIT value among participants with a value below 100 ng/mL to decide the screening-intervals for CRC screening.

Method: This nationwide register-based cohort study includes screening participants aged 50 to 70 years with a negative index FIT within the four-year run-in period. Due to the implementa-tion period it is possible to group the study-population based on their subsequent screening-interval being either 2 or 3 years. The study population will be further divided into participants with unmeasurable negative index FIT (≤35ng/mL faces) or participants with measurable nega-tive index FIT (>35 ng/mL faces and <100 ng/mL faces). The outcomes will be rate of CRC detected before the next FIT-screening test and the rate of screening-derived cancers after the next FIT.

Results: The study is in its preparation phase and data management is ongoing.

Perspectives: The study may serve as a foundation for an optimizing of the CRC screening program and holds the potential to be significant for all men and women of screening age in Denmark, as it may suggest changes in screening-interval based on FIT values.

Themes: Cancer, Epidemiology
Keywords: Colorectal cancer screening, Screening interval,

Paving the way for complete registration of Danish women with ductal carcinoma in situ in the breast from 2008-2023: A Danish Breast Cancer Group project

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Introduction:

Data on diagnosis, treatment and recurrence of early breast cancer (BC) is prospectively collected and registered in the Danish Breast Cancer Group (DBCG) database. Data on patients with precursor lesions, mainly ductal carcinoma in situ (DCIS), is registered in a similar in situ database at DBCG. However, registration is incomplete, and missing data is not collected.

The Danish Pathology Data Bank (Patobank) contains detailed nationwide records of all cyto- and histopathological diagnoses in Denmark since 1997.

Methods:

A computer-based algorithm was developed to identify all patients diagnosed with pure DCIS (i.e. no previous or simultaneous BC) from Patobank data in the period 2008-2017. To test the performance of the algorithm, all patients treated for pure DCIS at Aarhus University Hospital (AUH) in the same period were identified manually from Patobank data.

Results:

The algorithm identified a total of 13.720 patients with a DCIS diagnosis. Of those, 4.302 (31%) patients were identified with pure DCIS (8.578 (63%) patients excluded due to simultaneous invasive BC; 797 (6%) due to previous BC or DCIS).

Of the 4302 patients, 389 (10%) were not registered in the DBCG database. 559 (13%) were registered with only Central Person Register number and laterality, and for ~75% of patients, important information on histopathology and treatment was missing. The algorithm correctly identified 97% of patients in the AUH cohort.

Conclusion:

The algorithm is considered optimal for identifying DCIS patients not registered in the incomplete DBCG in situ database. It will be used to identify all DCIS patients from 2008-2023, allowing for analysis of recurrence patterns.

Themes: Cancer, Epidemiology
Keywords: Cancer precursor lesions, Ductal carcinoma in situ, Patobank

COST OF ILLNESS OF OROPHARYNGEAL CANCER: A MATCHED COHORT ANALYSIS

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Background

Squamous cell carcinoma of the oropharynx (SCCOP) has within recent years emerged as the most frequently diagnosed head and neck cancer in Denmark. This upsurge is attributed to Human Papilloma Virus (HPV). HPV-associated SCCOP differs markedly from tobacco induced SCCOP, both regarding disease survival, and demographic and socioeconomic composition. The escalation of SCCOP combined with a changing demographic profile and improved survival has socioeconomic implications, and derived societal and health economic effects. Health care costs associated with SCCOP in the HPV-era, are poorly described. In this study, we aim to delineate the health care costs associated with SCCOP.

Methods

We will conduct a retrospective matched cohort analysis on patients treated for SCCOP in Denmark during the period 01.01.2013 to 31.12.2022. Data is acquired through the RKKP database from The Danish Head and Neck Cancer Group and from national registers (Danmark Statistik, Sundhedsdatastyrelsen).

Analysis

Annual costs during a period from 2 years before diagnosis to 5 years after diagnosis will be calculated. Costs are based on primary and secondary care, medication and home care services. Differences in health care costs among HPV-SCCOP and non-HPV-SCCOP will be estimated. To estimate the incremental burden associated with SCCOP, patients will be matched on demographic characteristics.

Clinical perspectives

The results of the study will provide insights into the economic burden of oropharyngeal cancer and the evolution of healthcare inequality over time and aid policymakers and health care providers in addressing disparities and improving access to care for patients with SCCOP.

Themes: Cancer, Epidemiology
Keywords: Health economics, socio economy,

Analyzing antibodies against neo-antigens on a single cell level in melanoma patients.

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The immune system's ability to selectively recognize and target cancer cells makes it a central subject in immuno-oncological research. Neo-antigens or tumor-specific antigens (TSAs), generated by mutations and recognized as non-self, are particularly promising as a therapeutic target as they are only expressed on tumor cells. These antigens elicit potent immune responses involving both T-cells and B-cells, especially within tertiary lymphoid structures (TLS). While significant progress has been made in characterizing T-cell responses to TSAs and B-cells on a populational level, the properties and effectiveness of antibodies generated against neo-antigens on a single-antibody level remains less understood.

Here, we aim to achieve single-antibody resolution in mapping neo-antigen–antibody interactions by utilizing a microfluidic platform. We want to analyse antibody repertoires derived from melanoma patients' PBMCs. Stimulated memory B-cells will be paired with a neo-antigenic phage display library in a high-throughput, droplet-based format, using fluorescent relocation to identify potent binding pairs. This approach will allow us to isolate and characterize individual antibody-neo-antigen pairs, yielding insights into the specificity, affinity, and diversity of antibody repertoires generated in melanoma patients. Additionally, our study can be expanded to include B-cell repertoires from TLS's to further compare circulating antibodies and those arising from TLSs, offering a deeper understanding of antibody response in the tumor microenvironment.

Themes: Cancer, Diagnostics & technology
Keywords: Microfluidics, Onco-immunology, Antibody repertoire

Dosimetric Impact of Respiratory and Anatomical Variations in Patients from the International Randomized PROTECT Trial: Photon versus Proton Therapy for Locally Advanced Esophageal Cancer

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Background: Esophageal cancer (EC) is associated with poor survival and high toxicity rates. The European phase III randomized PROTECT trial compares photon (XT) and proton therapy (PT) for safer treatment in locally advanced (LA) EC.

Aim: To assess accumulated dose coverage using daily cone beam computed tomography (CBCT) scans and compare it to weekly surveillance CT (sCT) scans.

Methods: This study included the initial 24 patients enrolled in the PROTECT trial and treated at AUH, randomized between XT (n=12) and PT (n=12). Weekly sCTs were acquired to assess dose distribution, and patients with notable anatomical changes underwent adaptive re-planning based on reCT scans. Daily CBCT-based positioning allowed for daily dose calculations, relying on calibrated CBCT curves (MIM Software) for XT or synthetic CBCT models (RaySearch Laboratories) for PT. The daily delivered doses were accumulated onto the planning CT (pCT), allowing for a comparative analysis of dose coverage for the clinical target volume accounting for respiratory motion (iCTV) against the scaled dose from the weekly sCT scans.

Results: The analysis of iCTV dose coverage demonstrated consistent adherence to prescribed dose levels, with both V95% (volume receiving 95% of prescribed dose) and mean dose requirements consistently achieved. This consistency was observed across the pCT, sCTs, and accumulated doses, including cases where adaptive re-planning was required.

Conclusion: The accumulated dose analysis confirms that the initial 24 PROTECT patients consistently achieved intended dose coverage, with adaptive re-planning enhancing treatment precision, thereby supporting the efficacy of XT and PT for LA EC.

Themes: Cancer, Diagnostics & technology
Keywords: Radiotherapy, Esophageal cancer, Daily treatment CBCT

ctDNA can detect minimal residual disease in curative treated non-small cell lung cancer patients using a tumor agnostic approach

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Background

Circulating tumor DNA (ctDNA) has the potential to become a reliable biomarker for identifying minimal residual disease (MRD) and predicting recurrence in patients with non-small cell lung cancer (NSCLC) following definitive treatment. However, there is a lack of studies that investigate the clinical validity of ctDNA using a tumor-agnostic approach, which provides significant clinical benefits.

Methods

In this national multicenter study, we enrolled 45 NSCLC patients from five medical centers, all of whom had undergone definitive treatment. 38 pre-treatment plasma samples and 76 post-treatment plasma samples were analyzed using a commercially available cancer personalized profiling by deep sequencing (CAPP-seq) strategy, and a tumor-agnostic approach.

Results

The presence of detectable ctDNA post-treatment was significantly associated with higher odds of tumor recurrence and reduced recurrence-free survival (RFS). Subgroup analysis further demonstrated that in patients who received radiotherapy or chemoradiotherapy as definitive treatment, the detection of ctDNA was significantly associated with shorter RFS only when it was identified after 6.1 months of follow-up (Min.: 4.5 months, Max.: 7.5 months).

Conclusion

The findings suggest that post-treatment ctDNA, detected using a tumor-agnostic approach, is a reliable biomarker for predicting recurrence in NSCLC patients following definitive treatment. However, the optimal timing for blood sampling to detect MRD appears to depend on the type of definitive treatment received.

Themes: Cancer, Diagnostics & technology
Keywords: Circulating tumor DNA, minimal residual disease, Lung cancer

Feasibility of Weekly Cisplatin and Radiotherapy for Localized Anal Cancer – A Danish Anal Cancer Group report

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Background: Chemoradiotherapy (CRT) with fluorouracil and mitomycin is the standard treatment for squamous cell carcinomas of the anus (SCCA). The associated acute toxicity often hinders compliance, which is crucial for locoregional control. Weekly cisplatin is an established treatment for other SCCs, but it has not been evaluated in SCCA.

Purpose: To investigate if radiotherapy (RT) with weekly cisplatin is a feasible option for SCCA and to report the acute toxicity.

Material/methods: Patients treated with RT and weekly cisplatin 40mg/m2 between 1998–2020 were identified. Data were obtained from medical records and an observational study with prospectively collected physician-assessed toxicity (CTCAE 4.0) and patient-reported outcomes (PRO) (EORTC-QIQC30 + CR29) at baseline, mid, end of and 2–4 weeks after treatment. Disease-free survival (DFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Results: We included 116 patients (retrospective data n=65, prospective data n=51). T-stages were T1:4%, T2: 71%, T3: 17%, T4: 8% and 47% had N+ disease. RT doses to tumour were 54–64 Gray with a median overall treatment time of 43 days. The median cumulative cisplatin dose was 350mg. Hospitalisation occurred in 20% and treatment breaks in 7%. Hematologic toxicity was low with 17% G3+ reported. Anal pain, skin, gastrointestinal and urogenital toxicity were mild. Within 6 months after CRT 89% had complete response. The median follow-up time was 4.5 years, with a 5-year DFS and OS of 77% (95%CI 69-85%) and 86% (95%CI 78-92%), respectively.

Conclusion: RT and weekly cisplatin for SCCA is a safe treatment option in relation to outcome and acute toxicity.

Themes: Cancer, Epidemiology
Keywords: Anal Cancer, Chemoradiotherapy, Acute toxicity

Pembrolizumab as first line treatment for recurrent or metastatic head and neck squamous cell carcinoma: a multi-institutional DAHANCA cohort study

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Introduction: The aim of was to investigate phase IV efficacy of the PD-1 inhibitor pembrolizumab on an off-study multi-center cohort of patients with recurrent/metastatic Head and Neck Squamous Cell Carcinoma (rmHNSCC).

Materials & methods: Patients were included if they had histologically confirmed rmHNSCC and had received pembrolizumab as first-line palliative treatment. Data were collected from patient files at four Danish head and neck cancer centers (discovery cohort) and from The Leeds Teaching Hospitals NHS Trust (validation cohort). The iRECIST criteria were used for evaluation of treatment efficacy. Endpoints were overall survival (OS), progression-free survival (PFS), overall response rate (ORR) and disease control rate (DCR). Survival was estimated using the KM method and co-factors were investigated using univariate and multivariate analysis.

Results: A total of 228 patients were identified for the discovery cohort. Here, a median OS of 10 mos. [95% CI: 10-12], median PFS of 4 mos. [95% CI: 4-6], ORR of 19% [95% CI: 14-24] and DCR of 56% [95% CI: 49-62] were found.

For the validation cohort 101 patients were identified, and the only significant difference was in terms of DCR (30% [95% CI: 21-41]).

Baseline WHO performance status (PS) and neutrophilia (NP) were identified as co-factors with a seemingly negative impact on progression-free survival (HRPS: 1.4 [95% CI: 1.0-2.0] and HRNP: 1.8 [95% CI: 1.2-2.5]).

Conclusion: In this real-world multi-center rmHNSCC pembrolizumab cohort, efficacy equivalent to that of the registration studies were established. These results from Danish patients were successfully validated using an English cohort.

Themes: Cancer, Epidemiology
Keywords: rmHNSCC, Pembrolizumab, Validation

SESSION 18 - Drug risks and benefits

Is there an effect of local vaginal estrogen treatment on the hemostatic parame-ters and contact activation in women? - A research year project

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Background: Vaginal estrogen products are widely used and considered safe for treating for vaginal atrophy symptoms. However, limited clinical trials prevent a definitive conclusion on its risk-benefit profile, especially in relation to the effect on the coagulation system.

This study aims to evaluate the hemostatic balance in postmenopausal women receiving standard vaginal estrogen treatment by applying specific assays for coagulation, fibrinolysis and contact activation parameters.

Methods: This prospective cohort study (Sep. 2024-Aug. 2025) includes 90 postmenopausal women with vaginal atrophy symptoms at the Dept. of Gynecology, Aarhus University Hospital. Participants include a control group without prior VTE (n=45) and an intervention group with prior VTE (n=45). All participants receive vaginal estrogen 10 µg at least three times a week for three months. Blood samples are collected at baseline and three months later to assess parameters of coagulation (thrombin generation parameters, factor VIII, antithrombin, protein S and protein C, D-dimer, CRP) and fibrinolysis (Tis-sue plasminogen activator and Plasminogen activator inhibitor-1). Moreover, contact activation pa-rameters (factor XII, prekallikrein, high molecular weight kininogen (HK), cleaved HK, C1-esterase inhibitor, and the kallikrein generation capacity) will be analysed.

Results: The study is ongoing.

Conclusion: This study addresses a crucial gap in the current knowledge regarding the effect of vaginal estrogen on coagulation markers, fibrinolysis, and the contact activation system. This is essential for developing more accurate and evidence-based guidance for individualized patients counselling on vaginal estrogen.

Themes: Gynecology and obstetrics, Pharmacology
Keywords: Vaginal estrogen treatment, Hemostasis, Postmenopausal women

Sodium-Glucose Cotransporter-2-Inhibition Prevents Development of Left Ventricular Hypertrophy

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Background: Clinical studies demonstrated beneficial effects of sodium-glucose cotransporter-2 inhibitors (SGLT2i) in heart failure (HF). It has been proposed that improved metabolic communication in the kidney plays an important role in this SGLT2i effect. Whether this mediates changes in the heart is yet not investigated, but cardiac metabolism is associated with HF development, including left ventricular hypertrophy (LVH).

Hypothesis: SGLT2i prevent cardiac remodeling due to an improved cardiometabolic state, thus reducing the severity of HF.

Methods: 5 groups of C57Bl/6jRj male mice received; I) normal diet, II) vehicle-treatment with Western Diet (WD); III) vehicle-treatment with WD and N-nitro-1-arginine methyl ester (L-NAME, 600 mg/kg/day) in drinking water; IV) SGLT2i-treatment (dapagliflozin; 10 mg/kg diet (DAPA)) with WD; and V) SGLT2i-treatment with WD and L-NAME for 6-8 weeks. A combination of WD and L-NAME is known to induce HF with preserved ejection fraction.

Blood pressure and echocardiography were assessed prior to and every 2nd week during the intervention period. Data is presented as means ± SEM. $P<0.05$ is considered statistically significant.

Results: L-NAME increased mean arterial pressure (MAP) in both groups WD- and WD+DAPA groups. Six weeks after intervention, MAP was 90±3, 115±4, 88±4 and 118±4 mmHg (n=6-8, P=0.0001) in WD, WD+L-NAME, WD+DAPA and WD+DAPA+L-NAME, respectively. Furthermore, LVH was observed in the WD- and WD+L-NAME-groups but was prevented in the groups receiving DAPA (P=0.0581).

Conclusion: Prevention of LVH, a known part in the pathogenesis of HF, may be an underlying cardioprotective mechanism of SGLT2i.

Themes: Cardiology, Pharmacology
Keywords: Heart failure, SGLT2 inhibitors, Metabolites

64Cu-Methanobactin (ARBM-101) biodistribution and excretion examined in pigs by whole-body PET/CT – pharmacokinetics of a potential new treatment for Wilson disease

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Background: Wilson disease (WD) is caused by malfunction of the copper-transporting protein ATP7B, essential for hepatic copper clearance. Methanobactin (MB) is a promising new treatment for WD. MB's high copper affinity makes it suitable for characterizing the pharmacokinetics of 64Cu-labeled MB (64Cu-MB). We investigated the biodistribution and excretion of 64Cu-MB in pigs.

Methods: Eight pigs received 50 MBq i.v. 64Cu-MB (10 mg MB-ARBM-101) and five pigs received 50 MBq 64CuCl2. A 90-minute whole-body PET/CT was conducted post-injection. Time activity curves (TAC) were obtained by placing volumes of interest in the liver. Three of the 64Cu-MB pigs had surgically implanted flow probes on the hepatic artery and portal vein and catheters placed in the portal and liver vein.

Results: 64Cu-MB PET scans demonstrated rapid hepatic excretion into the gallbladder and intestines, with liver TAC showing a rapid increase to a standardized uptake value (SUV) of 11.34±1.61 within 10 minutes, followed by a 73% reduction in SUV. The 64CuCl2 PET scans showed hepatic accumulation of 64CuCl2 with minor excretion, with liver TAC showing a gradual rise, reaching a plateau with a mean SUV of 9.52±1.13 after 90 minutes. 64Cu-MB was also excreted by the kidneys into the bladder, whereas the 64CuCl2 accumulated in the renal parenchyma. There was no notable biodistribution of 64Cu-MB in other organs. MB's hepatic extraction fraction was ~34%.

Conclusion: 64Cu-MB is excreted rapidly through the liver and kidneys, exhibiting a faster elimination rate than 64CuCl2. This suggests an alternate hepatic elimination pathway distinct from the ATP7B-mediated mechanism.

Themes: Gastroenterology and hepatology, Pharmacology
Keywords: Wilson disease, Copper, Pharmacokinetics

Haemodynamic Effects of Dobutamine in Patients with Wild-type Transthyretin Amyloid Cardiomyopathy (ATTRwt)

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Background: Wild-type transthyretin amyloid cardiomyopathy (ATTRwt) is a restrictive cardiomyopathy with poor prognosis and frequent heart failure (HF) hospitalizations. Some of these patients may require advanced HF treatment including inotropic support.

Dobutamine is a commonly used inotropic agent for systolic HF, but its efficacy and safety have not been studied in ATTRwt. Additionally, dobutamine is often used as a stressor during echocardiography to determine the severity of aortic stenosis with low-flow, low-gradient, which coexists frequently with ATTRwt.

Aims: To evaluate the effects of dobutamine infusion on cardiac output and invasive filling pressures, and safety assessment in ATTRwt.

Methods: This prospective, single-arm clinical study will enroll symptomatic ATTRwt patients (NYHA II-IV) on loop diuretics with reduced ejection fraction (EF) and/or stroke volume index (SVI). Exclusion criteria: Significant valvular disease, coronary artery disease, recent myocardial infarction, end-stage renal disease, and established dobutamine contraindications. Participants will attend a single visit to receive titrated dobutamine infusions every 5 minutes from 2 to 20 (up to 40) mcg/kg/min, with hemodynamic responses evaluated using simultaneous echocardiography and right heart catheterization.

Discussion: The primary endpoint is a 10% increase in cardiac output. Secondary endpoints include an increase in SVI, a reduction in pulmonary capillary wedge pressure, an increase in EF and a safety endpoint.

Perspectives: Demonstrating dobutamine's efficacy and safety in ATTRwt may support its use in managing worsening HF and diagnosing low-flow, low-gradient aortic stenosis in ATTRwt.

Themes: Cardiology, Pharmacology
Keywords: transthyretin amyloidosis, Dobutamine, restrictive cardiomyopathy

Untangling the Postmortem Metabolome: A Machine Learning Approach for Accurate PMI Estimation

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Accurately estimating the post-mortem interval (PMI) is essential in medico-legal investigations, as it provides critical timelines for criminal cases. Existing PMI estimation methods often lack the required precision, limiting their forensic reliability. In this study, we developed models for precise PMI estimation across various tissues within the first four days post-mortem. Using untargeted UHPLC-qTOF-MS, we analysed thousands of molecules in rat tissues with different PMIs. We employed machine learning on stable and highly reproducible molecules in each tissue to select candidate biomarkers and then built a second model using only the top 15 molecules. Both Lasso and Random Forest approaches achieved high cross-validation accuracy across all tissues, with Random Forest showing a slight performance advantage. Validation was conducted using an independently collected rat dataset. The metabolites identified—including amino acids, derivatives, nucleosides, and other markers—are common to both humans and mammals, highlighting their potential applicability in human forensic contexts. Our findings emphasize the tissue-specific predictive potential and variable accuracy across different tissues in this rodent model.

Themes: Omics, Bioinformatics
Keywords: Metabolomics, Postmortem Interval, Forensics

A Systematic Review of Pharmacogenomic Markers Associated with Drug-Induced QT Prolongation

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Background: QT prolongation is a major risk factor for malignant arrhythmias and sudden cardiac death. Common drugs, e.g. antibiotics, antidepressants, and antipsychotics, can cause drug-induced QT prolongation (diQTP). While several pharmacogenetic markers have been identified, a comprehensive review of pharmacogenetic associations across drug classes is lacking.

Methods: This systematic review with a pre-registered protocol followed PRISMA-P guidelines. We identified and assessed peer-reviewed reports on pharmacogenomic markers of diQTP using standardized data extraction and risk of bias tools. Studies were categorized by design, and gene associations were classified as pharmacokinetic or -dynamic. Identified genes were subjected to pathway enrichment analyses. Descriptive statistics for variations were computed by study category and drug classes.

Results: Out of 4,493 records, 84 studies were included. While 210 unique variations across 42 drug classes were identified, only a small portion (9%) of findings were replicated, with KCNE1-Asp85Asn as the most robust association. 82% of diQTP-associated genes came from candidate gene studies, suggesting bias towards known markers. Genes were mainly linked to “cardiac conduction” and “muscle contraction” pathways (FDR = 4.71e-14). We also found overlap between diQTP-associated genes and congenital long QT syndrome genes.

Conclusion: Key diQTP-associated genes, drugs, and pathways were identified, but no strong pharmacogenomic markers emerged due to low replication rates. The

overrepresentation of candidate genes limits novel discoveries. Further research using unbiased designs, like genome-wide association studies, is needed.

Themes: Omics, Pharmacology
Keywords: pharmacogenomics, drug-induced long QT syndrome, adverse events

Aspirin versus Aspirin and Fondaparinux Prior to Early Invasive Strategy in Patients with NSTEMI - FOXY Trial

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Current guidelines for the management of Non-ST-Elevation Myocardial Infarction (NSTEMI) recommend the use of anticoagulants in combination with aspirin. In Denmark, fondaparinux is the first of choice anticoagulant. However, these guidelines are based on older studies conducted before the widespread adoption of early invasive strategies. This must raise questions about the validity of studies as a foundation for the guidelines recommending anticoagulants in these patients. The FOXY trial aims to evaluate whether aspirin alone is non-inferior to aspirin combined with fondaparinux in preventing death and refractory ischemia within 30 days in NSTEMI patients undergoing early coronary angiography (CAG).

This nationwide, multicenter, open-label, randomized controlled trial will include about 5,000 NSTEMI patients, who will be randomized in a 1:1 ratio to receive either aspirin alone or aspirin with fondaparinux prior to CAG. The primary outcome is a composite of 30-day mortality and refractory ischemia, while secondary outcomes include bleeding complications and long-term major adverse cardiovascular events.

The trial seeks to assess whether aspirin alone can reduce bleeding risks without compromising efficacy, potentially simplifying treatment protocols and improving patient safety. Results will contribute to future guideline updates and clinical practice for NSTEMI management.

Themes: Cardiology, Pharmacology
Keywords: NSTEMI, AMI, Fondaparinux

Can fremanezumab (a monoclonal antibody targeting calcitonin gene-related peptide) reduce pain intensity in patients with complex regional pain syndrome?

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BACKGROUND AND AIM: Complex regional pain syndrome (CRPS) is an uncommon pain condition in the limbs which may cause lifelong pain and disability. Evidence-based treatments are unavailable. Exaggerated neurogenic inflammation induced by release of neuropeptides such as calcitonin gene-related peptide (CGRP) is thought to play an important role in the pathophysiology of CRPS. Recently, drugs targeting CGRP have proven efficacy and tolerability in migraine.

The aim of this study is to assess the efficacy of the anti-CGRP antibody fremanezumab on pain in patients with CRPS.

METHODS: In this randomized, double-blind, placebo-controlled, proof-of-concept study, 60 adult patients with CRPS with a disease duration of 3-18 months are randomized to treatment for eight weeks with fremanezumab 225 mg or placebo at a 1:1 rate. Study procedures include pain diary, questionnaires, physical examination, a restricted version of quantitative sensory testing, CRPS severity score, blood samples (inflammatory markers), skin biopsies and measurement of cutaneous blood flow at different time points. Adverse effects and blinding will also be assessed.

RESULTS: Enrollment of patients is ongoing. As of October 2024, 12 patients have been included in the study, ten of whom have been randomized.

PERSPECTIVES: If found effective, fremanezumab and other anti-CGRP antibodies may emerge as a treatment option for patients with CRPS which could hopefully improve the overall care of patients with this devastating disease.

Themes: Neuroscience, Pharmacology
Keywords: Complex regional pain syndrome, Pain, Drug therapy

Impact of maternal antibiotic use during pregnancy on ABC family transporters in human, term placenta

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The prevalence of medicine use during pregnancy is increasing and today more than 60% of Danish women use at least one prescription drug during pregnancy. Use of medication can be vital for pregnancy health, but it also increases the risk of unwanted fetal exposure through trans-placental transfer. The human placenta is essential in supporting the healthy growth and development of the unborn child. The placental transport system ensures the transfer of nutrients, growth factors, and hormones from maternal to fetal circulation. Moreover, placental transporters function as a protective barrier with efflux transporters reducing fetal exposure to medication. Various medication can affect the expression of placental transporters within the ABC family, hereby potentially increasing the vulnerability of the unborn child - especially in cases of polypharmacy where there is a risk of drug-drug interactions. Even short-term exposures to some types of medicine, e.g. antibiotics, can increase the risk of congenital malformations.

With this study, we are characterizing the potential effect of antibiotics on the expressional level of five placental transporters (ABCB1, ABCG2, ABCC1, ABCC4, and ABCB4) in term placenta. Additionally, the effect of maternal body weight is analyzed, as we know that increased maternal body weight affects placental ABCB1 expression in early pregnancy. With informed consent, term placental samples are being collected shortly after delivery (<5 hours) (permit no.: 1-10-72-180-22) and analyzed using qPCR. In total, 11.2% has been exposed to maternal antibiotic intake during pregnancy. Study is ongoing, preliminary results will be presented at the PhD day.

Themes: Gynecology and obstetrics, Pharmacology
Keywords: Medication in pregnancy, Placental transporters,

Lactate is a positive inotropic agent with vasorelaxant and venocontractile properties

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H+ facilitates metabolic blood flow regulation while negatively impacting cardiac contractility. We know less about cardiovascular effects of conjugate bases accumulating alongside H+ during acidosis. Here, we screen metabolic and microbial carboxylates and evaluate lactate for actions on isolated arteries and veins, isolated perfused hearts, and cardiovascular function in vivo. The tested carboxylates generally relax arteries and veins. Lactate relaxes human and rat arteries up to 70% (EC50=10.1 mM) and rat brachial and mesenteric veins up to 30% of thromboxane-induced pre-contractions, but stands out by augmenting thromboxane-induced contractions of rat femoral, saphenous, and lateral marginal veins and human internal thoracic and great saphenous veins up to 50%. In isolated perfused hearts, lactate increases coronary flow (17.1±7.7%) and left ventricular developed pressure (10.1±3.0%) without affecting heart rate. Lactate infusion in rats increases left ventricular end-diastolic volume (11.3±2.8%), stroke volume (22.6±3.0%), cardiac output (23.4±3.5%), and ejection fraction (10.6±2.0%), and lowers systemic vascular resistance (34.1±3.7%) without substantially influencing blood pressure or heart rate. In conclusion, carboxylates generally relax arteries and veins. Lactate causes arterial relaxation to lower systemic vascular resistance, preferential venocontraction with increased ventricular diastolic filling, and elevated cardiac contractility and cardiac output. We propose that Lactate-induced hemodynamic adaptations benefit cardiovascularly-compromised individuals during metabolic disturbances.

Themes: Cardiology, Animal Models
Keywords: Hemodynamics, Metabolism, Cardiovascular

Second ROUND OF SESSIONS

SESSION 19 - Basic medical research 2

Quantitative investigation of reversible binding of Na+

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In physiology, 24-hour studies indicate a steady state of sodium, where an increase in sodium intake correlates with a corresponding increase in urinary sodium excretion. However, long-term studies reveal oscillatory patterns of excretion that are independent of sodium intake. Glycosaminoglycans (GAGs) may contribute to explain this phenomenon by acting as a sodium storage mechanism. Expectedly, their high negative charge content causes electrostatic interactions with positive cations like sodium. However, quantitatively the binding capacity of GAGs and sodium saturation at physiological conditions is relatively undescribed. I therefore investigate the dissociation constant (KD) for the highly negatively charged chondroitin sulfate A (CSA). This is conducted by dialyzing chondroitin sulfate against different known sodium concentrations, and thereafter measuring total sodium concentration with nuclear magnetic resonance. The initial results indicate that CSA will be fully saturated at the physiological extracellular sodium concentration of 140 millimolar. However, the results also showed that dialyzing at a sodium free solution a substantial amount of sodium remained bound to GAGs. This indicates that two populations of sodium are bound to CSA: releasable and non-releasable. I aim to investigate two possible mechanistic explanations for these observations:

- GAGs undergo conformational changes depending of the amount of bound Na+ and thereby shield further release
- there are marked differences in affinity for Na+ between the negatively charged carboxylic acid and sulfate groups in the GAGs.

Themes: Diagnostics & technology, Molecular biology
Keywords: Glycosaminoglycans, Sodium homeostasis, Physiology

The Role of Extracellular Vesicles in Ischemic Preconditioning

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Mortality associated with ischemic heart disease has been reduced through timely surgical and/or pharmacological reperfusion. However, reperfusion can also provoke ischemia/reperfusion injury (IRI), potentially contributing to post-infarction heart failure. Despite advances in myocardial infarction treatments, heart failure rates continue to rise. Remote ischemic conditioning (RIC), involving cycles of brief ischemia-reperfusion to a limb, and blood-flow-restricted resistance exercise (BFRRE), which may mimic the effects of occlusion-reperfusion through muscle contraction and relaxation, show promise in inducing ischemic tolerance and protecting against IRI.

Extracellular vesicles (EVs) are considered key mediators of RIC and BFRRE effects, potentially by delivering specific microRNAs (miRNAs), but the mechanisms remain poorly understood. Our previous work has shown that EVs from healthy individuals subjected to RIC, +/- exercise, may improve the viability of brain-derived endothelial cells in vitro and protect the brain against stroke in vivo. Additionally, unique miRNAs from these interventions were identified.

Building on these findings, a randomized controlled trial was conducted with heart failure patients exposed to RIC, BFRRE, or control conditions, with plasma EVs collected for analysis.

This project investigates whether conditioned EVs from heart failure patients are cardioprotective and if specific EV-carried miRNAs contribute, using in vitro cell cultures, in vivo rat heart infarction models, and miRNA profiling. Upregulated miRNAs will be identified as therapeutic candidates, loaded into EVs, and tested in the aforementioned models.

Themes: Cardiology, Molecular biology
Keywords: Remote ischemic conditioning, Ischemia/reperfusion injury, Extracellular vesicles

Phagocytosis of neurons by brain macrophages (microglia) and its role in neurodegenerative disease

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Background: Microglial cells, the brain's resident phagocytic immune cells, have been implicated as key players in neurodegeneration through excessive phagocytosis of healthy neurons and synapses.

The microglial phagocytosis is normally balanced by "eat me" signals and "don't eat me" molecular signals. Particularly noteworthy is the "don't eat me" signaling pathway SIRPα-CD47, which stands out as the most important factor in protecting neurons from phagocytosis.

Over the next three years, this PhD project will investigate the influence of SIRPα on neurodegeneration, aiming to evaluate its potential as both a therapeutic target and a biomarker for neurodegenerative diseases.

Aim: This project will focus on two primary objectives:

1) To show that it is possible to downregulate microglia-mediated phagocytosis of neurons using SIRPα-mRNA containing lipid nanoparticles (LNP's). Proof of principle for this concept will be performed using in vitro co-culture models.

2) To evaluate the use of SIRPα and other phagocytosis checkpoint molecules as biomarkers for diagnosing and monitoring progress of neurodegenerative disease (Alzheimer's, Parkinson's, Multiple Sclerosis).

Results: The study began on August 1, 2024, and results are not yet available. We hope to provide insight into the efficacy of SIRPα-mRNA nanoparticles in reducing neuronal phagocytosis in vitro and explore the potential of SIRPα as a biomarker.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: Microglia, Phagocytosis, Biomarker

Packaging CRISPR/Cas9 toolkits in virus-derived nanoparticles for precise DNA editing

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The CRISPR/Cas9 genome editing tool has quickly become a popular technique in laboratories worldwide, driving significant advancements in modern biomedical research. However, CRISPR/Cas9-based gene therapies face significant limitations, particularly in terms of delivery mechanisms. Recently, the CRISPR/Cas9 toolkit has expanded to include techniques such as prime editing, twin prime and PASSIGE, methods that enable genome modifications without creating double-stranded breaks, and therefore reduce the risk of harmful side effects. Despite this progress, the primary challenge remains the development of a safe and efficient delivery system for large-scale therapeutic use. Here, I introduce the functional packaging and delivery of genome editing ribonucleoprotein (RNP) complexes using lentivirus-derived nanoparticles (LVNPs) for a transient 'hit-and-run' delivery strategy. The LVNP delivery vehicle has been optimized to overcome molecular bottlenecks in RNP packaging, release, and localization, improving particle efficacy. The versatility of this approach is further highlighted through the delivery of the prime editor as an RNP complex in LVNPs (referred to as prime editing LVNPs, PE-LVNPs). This approach supports robust correction of a C>T variant in the Rpe65 gene, which is linked to Leber congenital amaurosis in humans. Future progress within this project will lead to in vivo studies utilizing PE-LVNPs as delivery vehicle and include the development of LVNPs for insertion of DNA using PASSIGE, a new technique that combines prime editing with recombinase-directed DNA insertion.

Themes: Genetic engineering, Molecular biology
Keywords: Lentivirus-derived Nanoparticles, CRISPR/Cas9,

Understanding cellular response and transport mechanisms affecting nuclear uptake of genome editing tool kits delivered in virus-derived nanoparticles

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CRISPR/Cas-based gene editing is based on delivery of a tool kit consisting of the Cas9 nuclease complexed with a single guide RNA (sgRNA), leading to formation of a double-strand DNA break in a targeted genomic locus. In our research group, we have pioneered the engineering of lentivirus-derived nanoparticles (LVNPs) for delivery of Cas9/sgRNA ribonucleoprotein (RNP) complexes for efficient, safe, and cell-targeted gene editing. We believe that LVNP-directed RNP delivery benefits from effective intracellular transport, including nuclear uptake through the nuclear pores, but the existence of cellular factors supporting or restricting LVNP function remains unclear. In this project, we exploit genome-wide CRISPR screening technology to identify genes that are essential for RNP delivery using LVNPs. To perform a screen based on the CRISPR/Cas12a system, we produced a model cell line with stable expression of a fluorescence reporter (d2eGFP) and enAsCas12a endonuclease. In this cell line, we demonstrated 100% knockout of d2eGFP after exposure to LVNPs packaged with Cas9 and sgRNAs targeting the d2eGFP gene. Using this cell line, we can sort for d2eGFP-positive cells carrying Cas12a library sgRNAs mediate knockout of genes supporting LVNP-directed d2eGFP knockout. In additional library screens using interferon- reporter cell lines (IBER), we can study the immunogenicity of LVNPs and unveil cellular factors sensing and restricting LVNP-directed RNP delivery.

Themes: Genetic engineering, Molecular biology
Keywords: CRISPR/Cas-based editing tools, Nanoparticles, Cellular transport mechanisms and immunity

Unravelling the molecular roles of Ankrd1 and its associated signaling pathway in DCM etiology

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Dilated Cardiomyopathy (DCM), the most common form of heart failure, is a condition where the heart's ability to pump blood is impaired. The disease etiology is still unclear, and the heterogeneous nature of the disease limits the treatment options with only 50% of patients surviving 5 years post-diagnosis.

A mouse model, used to investigate disease development, exhibits many of the pathological hallmarks found in human DCM patients is MLP-knockouts (MLPko). This model is characterized by aberrant protein kinase Cα (PKCα) signaling, disrupted cardiac calcium handling and upregulation of CARP1.

The Lange laboratory was able to show that CARP1 is differentially phosphorylated and displays an altered subcellular localization to the intercalated disc in MLPko hearts, compared to healthy control. This relocation seems to activate PKC pathway and start a vicious circles of changings leading to the development of DCM. Specifically, I study, which proteins are deregulated in DCM, and if the changes are primarily responsible for disease development. This project delineates the crucial roles that Ankrd1 (the gene encoding CARP1) plays in DCM development; reveals the function of pathological posttranslational modifications in PKC substrates; and seeks to find small molecules that prevent or revert the progression of the disease.

Themes: Cardiology, Molecular biology
Keywords: Cardiomyopathy, MLP, CARP1

Unravelling the role of Cullin3-linked protein degradation in the development of neuromuscular disorders

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Many neuromuscular disorders are caused by the deficient degradation of proteins. Skeletal muscles depend on the ubiquitin-proteasome system (UPS) to degrade most of their old/unwanted proteins. The UPS relies on the activity of enzymes, such as E3-ubiquitin ligases, to mark cellular targets for degradation, by the addition of a polyubiquitin tag. Cullin3 (Cul3), one of these ligases, and its accessory adaptor proteins are essential for muscle development and function. Studies conducted in mice showed that the loss of Cul3 in skeletal muscle results in postnatal lethality characterized by a severe myopathy. Cul3 uses around 180 adaptor proteins for its specificity to different cellular targets. In humans, mutations in several Cul3 adaptor proteins, such as Klhl9 or Kbtb13, are linked to various neuromuscular disorders. To further explore the molecular role of Cul3 and its adaptor proteins in muscle development, we silenced all its 180 adaptor proteins by using siRNAs in C2C12 skeletal muscle myotube cultures, and analyzed morphological parameters related to myotube development and maturation. The main morphological parameter analyzed was the fusion index, a measure of muscle cell maturity. Our results indicate that silencing of different Cul3 adaptor proteins previously not linked to muscle differentiation, such as Ankfy1 or Kctd9, affect muscle cells development and maturation, as reflected by changes in the fusion index. Currently, characterization and validation experiments are performed to better profile the newly identified adaptor proteins.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: Neuromuscular disorders, E3-ubiquitin ligases, Muscle development

IMPAIRED DIMERIZATION PROPERTIES AS A COMMON MECHANISM OF PATHOGENECITY FOR A SUBSET OF ALZHEIMER'S DISEASE-ASSOCATED SORL1 VARIANTS IN 3FN-DOMAINS

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The gene SORL1, encoding the endosomal sorting receptor SORLA, is now recognized as a causal gene for Alzheimer's Disease (AD). A SORL1 missense variant, p.W1862C, located at a strictly conserved sequence position in the 3Fn-domains of SORLA was identified in case-control studies to be associated with AD. Therefore, we set out for a functional characterization of the p.W1862C variant to establish its functional consequences on receptor function and how it might cause AD. We performed an in-silico analysis to identify homologous pathogenic mutations in 3Fn-domains of other proteins at the same sequence position. We identified 7 homologous disease-causing mutations in other 3Fn-domains supporting that this SORL1 variant is pathogenic. It was suggested previously to use receptor maturation, shedding and trafficking as measures for evaluating the pathogenicity of SORL1 mutants. Using cell-based assays we showed that p.W1862C significantly decreased receptor maturation and shedding as demonstrated previously for this and other SORL1 variants. We found that trafficking of the mutant to the cell surface was reduced, but it was still able to sort correctly to endosomal compartments. Importantly, we found that the mutation impairs the physiologically relevant homodimerization of SORLA in endosomes. We have recently described a SORL1 mutation in the third 3Fn-domain that is causal of AD (p.Y1816C) and displays similar functional defects as the p.W1862C variant located in the fourth domain. This indicates a common mechanism of pathogenicity associated with impaired dimerization for mutations located at critical positions in several 3Fn-domains of SORLA.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: Alzheimer's disease, Mutations, SORL1

Liver Sinusoidal Endothelial Cell Junctions in Metabolic Dysfunction-Associated Steatotic Liver Disease - **CANCELLED**

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is an accumulation of fat in the liver (steatosis) in individuals who consume little or no alcohol. MASLD can progress to MASH (steatohepatitis), which includes inflammation, increasing risks of fibrosis, cirrhosis, and liver cancer. There is currently no approved treatment for MASLD.

Liver sinusoidal endothelial cells (LSECs) line the hepatic sinusoids and are involved in e.g. the exchange of nutrients and metabolites between the blood and hepatocytes. Junctional proteins (JPs) are crucial for LSECs permeability, determining the solute exchange. Unlike typical endothelial cells, LSECs have a sparse junctional network, contributing to their leaky, fenestrated structure and rapid substance exchange. During MASLD and MASH development, LSECs lose fenestrations and form a basement membrane, resembling large-vessel endothelium. Aquaporins (AQPs) facilitate water transport across cell membranes; some AQPs modulate epithelial cell JPs and cellular signaling pathways.

This project aims to determine the localization and levels of JPs and AQPs in LSECs from different stages of MASLD and MASH, alongside liver resection samples without steatosis for comparison. Preliminary results indicate changes of adherens and tight JPs in rat liver tissue. Subsequent studies will examine the regulatory mechanisms and physiological impact of these changes, as JP dysregulation may reduce solute exchange, disrupting liver homeostasis. The goal is to improve the understanding of MASLD and MASH pathophysiology and potentially inspire new diagnostic methods and targeted treatments.

Themes: Gastroenterology and hepatology, Molecular biology
Keywords: Metabolic dysfunction-associated steatotic liver disease (MASLD), Liver sinusoidal endothelial cells (LSEC), Junctional proteins

Post-traumatic headache: Phenotyping, exploring pathophysiological insights and novel treatment strategies

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Background: Headache associated with head injury, post-traumatic headache (PTH), is one of the most common symptoms after mild traumatic brain injury (mTBI). Between 30-90% of mTBI patients may develop some form of headache, of which 18-22% develop persistent (> 3months) PTH. PTH is highly disabling with no adequate treatment options. Unfortunately, PTH presents a challenge due to the limited knowledge on disease characteristics and disease mechanisms.

Aim: To advance the knowledge on the characterization and pathophysiology of PTH. The aim is also to evaluate the effect of repetitive transcranial magnetic stimulation (rTMS), a novel intervention on PTH.

Methods: A randomized, placebo-controlled clinical trial on patients with moderate to severe PTH has been performed. Patients received 5 sessions of either active rTMS (n=30) or sham rTMS (n=32) 4-6 months post-mTBI. Follow-up was made 1- and 3 months post-treatment. Primary outcome was defined as a change in the proportion of headache days of moderate-severe intensity from baseline to 1-month post intervention. Blood samples were taken before and after intervention, and at 1 month follow-up. Blood samples will be examined for the associations between biomarkers such as calcitonin gene-related peptide and symptom severity of PTH. PTH phenotyping will be made based on self-reported headache questionnaires. Data-analysis are currently ongoing.

Perspectives: This study will result in a better understanding of PTH and can potentially contribute to the development of a clinical prognostic model. Additionally, the study may help to clarify if rTMS treatment can reduce the long-term disability in patients with PTH.

Themes: Neuroscience, Rehabilitation
Keywords: concussion, Mild traumatic brain injury, rTMS

SESSION 20 - Reproductive health

Investigating mosaicism for monosomy X in the placenta and fetus: A registry-based study of cases from Denmark 1983 - 2021

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Background: Invasive prenatal diagnostic procedures such as chorionic villus sampling (CVS) are essential when diagnosing chromosomal disease, which affects up to 15 % of unborn children. In 4% of CVS, a mix of both chromosomally normal and abnormal cells is detected – a condition defined as mosaicism. In some cases, mosaicism is generalized to the fetus (true fetal mosaicism, TFM), which can cause fetal disorders. In other cases, it is confined to the placenta (confined placental mosaicism, CPM) and may cause placental dysfunction.

We investigate the potential outcomes after mosaicism for monosomy X in CVS, the risk of TFM and the risk of adverse outcomes such as preterm birth and small for gestational age (SGA) in case of CPM.

Methods: Data on all Danish singleton pregnancies with mosaicism detected in CVS from 1983-2021 was collected from the two nationwide registries: Danish Cytogenetic Central Registry and Danish Fetal Medicine Database.

Results:

The risk of TFM is 51.8 % (40.6 ; 62.9) in individuals with 45,X/46,XY mosaicism (N = 83) and 45.4 % (36.6 ; 54.3) in individuals with 45,X/46,XX mosaicism (N = 130).

The risk of CPM and SGA is 9.7 % (2.0 ; 25.8) for 45,X/46,XY (N = 31) and 5.7 % (1.2 ; 15.7) for 45,X/46,XX (N = 53).

The risk of CPM and preterm birth is 6.5 % (0.8 ; 21.4) for 45,X/46,XY (N = 31) and 11.3 % (0.4; 23.0) for 45,X/46,XX (N = 53).

Conclusion: When detecting mosaicism for monosomy X in CVS the risk of TFM is high. If confined to the placenta (CPM) the risk of SGA and/or preterm birth is only slightly increased compared to the general obstetric population.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Genetic mosaicism, Sex chromosome aberrations, Prenatal diagnostics

Correlation Between Expert Clinical Diagnoses and Invasive Urodynamic Findings

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Background: In Denmark, approximately 500.000 individuals suffer from urinary incontinence, and three out of four patients are women. The condition has a negative impact on qualitive of life and accounts for 2% of national healthcare costs. Diagnostic work-up and treatment of urinary incontinence are time consuming. Evaluation often includes invasive urodynamic (IUD) investigations, conducted by specialized continence nurses. However, there is a shortage of these professionals, limiting the number of centers and consequently long waiting lists for the patients. With the aging population it is necessary to optimize evaluation strategy.

Purpose: This study aims to explore the correlation between urinary incontinence diagnosis provided by an expert urogynecologist and the findings from IUD investigations.

Method: This retrospective study will include women who underwent IUD investigations for urinary incontinence in 2022 at the Pelvic Floor Unit, Aarhus University Hospital. Relevant clinical data from each patient's initial clinical visit will be collected from medical records, including information from standardized questionnaires, voiding diaries, physical examination, cough test, transvaginal ultrasound, non-invasive uroflow exams and IUD investigations results.

Conclusion: The study will contribute with new knowledge that will improve the future diagnostic of urinary incontinence essential for developing timely and tailored treatment plans for patients. Additionally, some of the IUD investigations may be omitted in selected patient populations, potentially reducing waiting lists and lowering healthcare costs on these patient groups.

Themes: Gynecology and obstetrics, Urology & Nephrology
Keywords: Urinary incontinence, Urodynamics, Diagnostics

Prenatal exposure to parental smoking and infertility in sons and daughters: a cohort study

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Background: Infertility affects between 15–20% of couples worldwide. In Denmark, it is the most prevalent chronic condition among men and women of reproductive age. Despite advances in reproductive health, approximately one-third of infertility cases remain unexplained, underscoring the pressing need for research into modifiable risk factors that may contribute to curb the alarming development and safeguard reproduction in future generations. Emerging research highlights the prenatal period as a particularly sensitive phase, where harmful exposures may predispose individuals to diseases like infertility later in life.

Objective: To estimate the potential causal association between prenatal exposure to parental smoking and infertility in adult sons and daughters.

Methods: This study leverages a large, well-characterized cohort of 11,144 offspring from the Healthy Habits for Two (HH42) birth cohort, with detailed data on prenatal exposures collected during pregnancy and infertility outcomes obtained from national registers. Associations will be examined using Cox regression models, accounting for competing risks for infertility. Including the partners of the offspring will reduce misclassification of female and male infertility, ensuring robust and comprehensive analyses.

Results: Preliminary findings will be presented at the PhD Day.

Perspectives: These findings will not only enhance our understanding of early life determinants of infertility but could also contribute to clinical guidelines aimed at reducing infertility risk through early intervention, thus contributing to preventive strategies for future generations.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Infertility, Reproductive health, Prenatal exposures

A case-control study of the clinical utility of DNA-methylation markers for endometrial cancer detection in patient-collected urine and vaginal samples

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BACKGROUND :

Endometrial cancer (EC) is the most common gynaecological cancer in developed countries including Denmark. Current diagnostics, transvaginal ultrasound, has a good sensitivity (94.8%) but a low specificity (51%), resulting in unnecessary amounts of invasive and time-consuming endometrial biopsies in women without EC. Thus, there is a clinical need for a simpler, non-invasive and more specific test to aid EC diagnostics.

DNA-methylation analysis of cancer-specific genes has proven their potential for detection of various cancers. Therefore, this study will determine and compare the diagnostic accuracy of DNA methylation testing in patient-collected urine and vaginal samples to differentiate EC cases from healthy controls.

METHODS:

We expect to start study inclusion for this multisite case-control study in the spring of 2025. We will include 60 women with EC at Aarhus and Odense University Hospital and 60 healthy age-matched controls. Participants will be asked to self-collect paired full-void urine and vaginal samples at the hospital. Samples will be analysed for six DNA-methylation markers: GHSR, CDH13, and SST (urine) and CDO1, GHSR and ZIC1 (vaginal). Test performance from women with EC will be compared to results from the controls and presented as ROC-curves and quantified by AUC with 95% CI's.

PERSPECTIVES:

If DNA methylation analysis in patient-collected samples effectively can distinguish EC cases from controls, the test has the potential to be used in the diagnostic assessment for women with postmenopausal bleeding suspected of EC. This will hopefully spare women for invasive procedures and reduce costs in the health-care system in the future.

Themes: Gynecology and obstetrics, Diagnostics & technology
Keywords: Endometrial cancer, DNA-methylation, Liquid biopsy

Pharmacological activation of CPS1 increases activation of ovarian dormant follicles, through elevated arginine levels and mTORC1 signaling

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Globally, 15% of couples experience infertility, with female infertility accounting for approximately 54%. Current female infertility treatments are hormone-based, yet early folliculogenesis stages, including primordial follicle activation, are hormone-independent. Primordial follicle activation is regulated by signaling pathways, such as mTORC1. In this study, we investigated if a pharmacological activator (NCG) of the urea cycle protein CPS1 increases primordial follicle activation. Here, in vitro-cultured mouse ovaries, ex-vivo-cultured human ovarian tissue, and cultured human granulosa tumor-like cells (KGN) were treated with 30 µM NCG. Histological analysis of mouse ovaries and human tissue treated with NCG revealed an increase in primordial follicle activation. Mechanistic investigations using Western blotting revealed a significant rise in mTORC1's down-stream factor pS6K in mouse ovaries and KGN cells when treated with NCG. Furthermore, arginine starvation of KGN cells revealed a significant downregulation of pS6K. However, the pS6K expression in arginine-starved cells were rescued and increased significantly after 2 hours of NCG treatment. Additionally, CO-immunoprecipitation showed less binding between the arginine censor CASTOR1 and the inhibitor GATOR2 upstream from mTORC1 activation when NCG treatment was performed. Previous studies have reported increased primordial follicle activation upon NCG treatment. However, the underlying mechanisms were unclear. Our findings align with previous studies and suggest that activation of CPS1 by NCG increases the arginine level in the ovaries, resulting in mTORC1 activation and increased primordial follicle activation.

Themes: Gynecology and obstetrics, Molecular biology
Keywords: Primordial follicle activation, Arginine, mTORC1

The essential role of calcium signalling in lactation: An analysis of calcium signalling mechanisms in murine models

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Through the production of nutrient-rich milk, the mammary gland performs an indispensable role in neonatal survival and development. Despite the gland's critical role, the regulatory mechanisms governing its function during lactation remain poorly understood. One signalling pathway that has proven essential for maintaining lactational function in the mammary epithelium is calcium. During lactation, the expression of calcium channels increases, facilitating the transport of large amounts of calcium from the maternal bloodstream into milk. In particular, the mammary epithelium upregulates the calcium influx channel Orai1. This channel has been shown in transgenic mouse models to be necessary, not only for calcium enrichment of milk, but also efficient milk ejection, and ultimately, pup survival. However, the upstream regulators of Orai1 during lactation are yet to be identified. Canonically, Orai1 is activated following the depletion of internal calcium stores by Stromal Interaction Molecule 1 (Stim1), a calcium sensor that monitors the calcium levels within these stores. This project aims to investigate the interaction between Orai1 and Stim1 in milk-producing and milk-ejecting mammary epithelial cells, using transgenic mouse models and advanced 4D ex vivo live imaging. Findings will help advance our understanding of the role of calcium signalling in the lactating mammary gland, ultimately shedding light on a neglected area of research with significant implications for maternal and neonatal health.

Themes: Animal Models, Molecular biology
Keywords: Calcium signalling, Lactation, Mammary gland

Transvaginal cervical cerclage – how well do surgeons assess their own procedures?

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Introduction: To prevent preterm birth, a supportive stitch can be applied to the pregnant cervix, known as a transvaginal cerclage. Quality assessment of the procedure relies on the surgeon's self-assessment and pregnancy outcomes rather than objective criteria and feedback. To address this issue, we aimed to quantitatively assess surgical performance and compare it to the self-assessed performance on a transvaginal cerclage simulator.

Materials and methods: Experienced cerclage surgeons performed a transvaginal cerclage on a simulator. We obtained from the simulator measurements on the cerclage height, number of bites, suture bite depth, and reduction of the cervix surface area. The measurements were compared to the same outcomes self-assessed by each participant after the cerclage procedure. We visualized the continuous paired data in a Bland-Altman plot and compared these data with a paired t-test. Paired binary data was analyzed using McNemars test.

Results: Twenty-nine participants performed on a transvaginal cerclage in the simulator. They demonstrated an overall good agreement between observed and their self-assessed measurements of their procedures. However, height of their cerclage was significantly underestimated with a mean difference of 6.0 mm (95% CI 2.1 – 9.9), (p 0.002) between the observed and the self -assessed measurements.

Conclusions: Overall, the experienced cerclage surgeons demonstrated a genuine understanding of their surgical performance in transvaginal cerclage. This knowledge lays the base for a randomised controlled trial in my PhD, where transvaginal cerclage serves as the control arm.

Themes: Gynecology and obstetrics, Health Education
Keywords: Preterm birth, Transvaginal cerclage, Self-assessment

Maternal drug exposure and the risk of congenital and early-onset hearing loss in children: a systematic review

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BACKGROUND: Congenital hearing loss affects 1 - 2 of 1000 children and has a big impact on language development and social well-being. The aetiology is unknown in 40% of the children. Several drugs are known to cause hearing loss in adults. METHODS: This systematic review explored the evidence on whether drug exposure in pregnancy can increase the risk of congenital hearing loss. A litterature search was conducted on 25th January 2023 using PRISMA guidelines. RESULTS: A database search on Embase, PubMed, and Web of Science yielded 951 unique records, of which 16 studies were included: four RCTs, ten cohort studies and two case-control studies. The main studied drugs were magnesium sulfate, systemic corticosteroids, ASA and other NSAIDs and antibiotics. Magnesium sulfate alone or combined with betamethasone yielded an overall point estimate of OR 0.35 (95% CI: 0.23 - 0.55). Betamethasone and other systemic corticosteroids yielded an overall point estimate of OR 0.82 (95% CI: 0.50 – 1.37). ASA and NSAIDs yielded an overall point estimate of OR 1.21 (95% CI: 0.87 – 1.68), and in one study an additional subgroup analysis yielded a higher OR of 1.53 (95% CI: 1.12 – 2.11) for ASA at low doses (<300 mg) compared to a lower OR of 1.00 (95% CI: 0.81 – 1.12) for ASA > 300 mg and other NSAIDs. A meta-analysis of all antibiotics together yielded an overall point estimate of OR 1.43 (95% CI: 1.00 - 2.02). CONCLUSION: This study revealed several drugs that may be related to congenital hearing loss, but most studies were limited in terms of design and size and larger studies are necessary to draw clinically relevant conclusions.

Themes: Gynecology and obstetrics, Paediatrics
Keywords: Intrauterine drug exposure, Congenital hearing loss in children, Systematic review

Diseases during pregnancy – is gut the answer? - **CANCELLED**

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Pregnancy complications increase morbidity and mortality for both mother and child. Even though several maternal factors affect the risk of developing these pregnancy-associated complications, many unknowns still exist. Therefore, it is now postulated that maternal gut impacts the risk of these complications. However, due to a high variation in methods and focuses, the research on this subject is conflicting.

Therefore, our aim was to compare all research regarding pregnancy and intestinal flora, thereby addressing the relationship between maternal gut microbiome, maternal factors and pregnancy complications.

Using a systematical search approach in PubMed including only primary human research in Scandinavian or English, 526 articles were achieved. After screening and quality assessment performed by two independent researchers, 94 studies were included in the review.

Further description and comparison of the studies will be presented.

Perspectives: With these results, we will determine the correlation between maternal gut microbiome, maternal factors and pregnancy-associated diseases. This is crucial for understanding mechanisms behind these diseases and might even be used for a non-invasive disease prediction in the clinics during prenatal visits.

Themes: Gynecology and obstetrics, Gastroenterology and hepatology
Keywords: Pregnancy, Intestinal microbiome, Systematical review

Siblings' Experiences of Transitions Between Hospital and Home in Pediatric Oncology: A Qualitative Study

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Background: Frequent transitions between paediatric oncology treatment centres and home disrupt family cohesion and intensify uncertainty, especially affecting siblings. Understanding siblings' experiences of these transitions is important for informing care practices and developing tailored support interventions.

Aim: To explore how siblings of children or adolescents with cancer experience transitions between a paediatric oncology treatment centre and home.

Methods: A phenomenological hermeneutic approach was employed to capture the lived experiences of eight siblings, aged six to 16 years, of children undergoing active cancer treatment. Semi-structured interviews, supported by photo-elicitation methods, were conducted in the siblings' homes. Interviews were audio-recorded, transcribed verbatim, and analysed using Nvivo software.

Findings: Three overarching themes emerged: 'Grappling to find a new family position situated on the periphery', 'Living with the risk of sudden family separation', and 'Adapting to a changing siblingship'.

Conclusion: Siblings are deeply affected by the instability of pediatric oncology regimens, experiencing pervasive worry, uncertainty, emotional insecurity, and a limited sense of inclusion within the family.

Implications: We call for family-based interventions recognizing siblings as active agents, fostering family cohesion. Future research should investigate if frequency of hospitalisations and distance from home to treatment centres is associated with lower quality of life among siblings. Longitudinal qualitative studies tracking siblings' experiences over time could explain how childhood cancer change and affect siblings' bonds and life choices.

Themes: Qualitative research, Paediatrics
Keywords: Qualitative, Pediatric oncology, Siblings

SESSION 21 - Neuroscience 3

The combined impact of migraine and smoking on risk of premature stroke and myocardial infarction: A Danish population-based cohort study

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Background: Migraine is a common headache disorder, particularly prevalent among women aged 35-39 years, and is associated with an increased risk of stroke and myocardial infarction (MI) in the general population. Alongside migraine, another risk factor for stroke and MI is smoking. However, the potential interaction between migraine and smoking on risk of stroke and MI is poorly understood.

Aim: To examine the separate and combined impact of migraine and smoking on risk of premature stroke and MI, and to examine the potential biological interaction between the two exposures.

Methods: We will conduct a population-based cohort study in Denmark. The study population will include all women aged 15 years or older who gave birth to a child from 1996 to 2022. The women will be divided into four cohorts based on exposure to migraine and smoking, i.e., women with migraine, women who smoked, women with migraine who smoked, and a comparison cohort of women without migraine who did not smoke. For each cohort, we will use the Aalen Johansen estimator to calculate the absolute risk of ischemic stroke, haemorrhagic stroke, and MI, treating death as a competing risk. We will compute adjusted absolute risk differences (RD) of stroke and MI comparing the exposed cohorts to the comparison cohort. Using adjusted RD, we will calculate the proportion of the risk of stroke and MI in women with migraine who smoked that was due to biological interaction between migraine and smoking.

Results: Pending.

Perspectives: Understanding the potential interaction between migraine and smoking may improve patient counseling and targeted prevention of stroke and MI among people with migraine.

Themes: Epidemiology, Neuroscience
Keywords: Migraine, Smoking, Cardiovascular disease

How to Reduce Overuse of CT in Patients with Minor Head Trauma: Study Protocol for a Multicenter Cluster-Randomized Trial (HEADWISE)

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Background: Excessive use of computed tomography (CT) is common in patients with minor head trauma (MHT). In Denmark, an estimated 12,150 emergency CTs are performed annually for MHT, yet less than 1% of these scans affect treatment. This overuse is largely due to current guidelines lacking precision in identifying high-risk patients.

Aim: To test new Choosing Wisely guidelines for managing MHT patients against current Scandinavian Neurotrauma Committee (SNC) guidelines. The new guidelines are expected to reduce CT usage by 25% without compromising patient safety.

Methods: In a stepped-wedge design, 10 Danish emergency departments (EDs) will sequentially transition from the SNC guidelines to the Choosing Wisely guidelines at randomized time points. Eligible patients are adults presenting to ED with MHT. Data will be retrieved from national registries. Preliminary sample size analysis indicate 1,600 patients per group, necessitating an estimated 120 days to complete patient inclusion.

The primary outcome includes two safety targets; non-inferiority in failure to detect hemorrhage and no more than 5% of missed hemorrhages resulting in death or neurosurgery, and one efficacy target; reduction of head CTs by at least 15%. Secondary outcomes include overall mortality, readmission-free survival time, and total number of head CTs conducted.

Data will be adjusted for sex, age, and cluster effects.

Conclusion: The HEADWISE trial may provide scientific validation of a new, cost-effective, and safe approach to managing MHT patients. Given the global challenge of excessive CT usage following MHT, the results could impact future clinical practices both nationally and internationally.

Themes: Diagnostics & technology, Neuroscience
Keywords: Minor head trauma, Computed tomography, Choosing Wisely

Isoflurane anesthesia alters 31P Magnetic Resonance Spectroscopy markers in mouse Brain: A comparative in vivo study

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The brain's high energy demand is used in numerous functions, including maintenance and signal processing. Thus, a continuous energy supply is essential for its proper functioning and health. Phosphorous Magnetic Resonance Spectroscopy (31P MRS) is a noninvasive technique that measures crucial markers of brain energy metabolism, such as adenosine triphosphate (ATP), inorganic phosphate (Pi), and phosphocreatine (PCr), as well as indicators of cell membrane phospholipid turnover, including phosphomonoester (PME) and phosphodiester (PDE). Historically, preclinical rodent 31P MRS has been performed exclusively under anesthesia, despite evidence indicating that anesthesia can alter neuronal activity and brain energy metabolism. Isoflurane, a widely used anesthetic in rodent imaging studies, is known to cause respiratory depression, hypothermia, and lactate accumulation in a dose-dependent manner, disrupting brain physiology. In this study, we demonstrate the feasibility of conducting brain 31P MRS on awake, MR-habituated mice for the first time. Our results show that 31P metabolite levels differ between awake and anesthetized states in mice. Specifically, we observe that low-dose isoflurane anesthesia reduces PCr levels in the anesthetized mouse brain, along with decreases in intracellular pH and PME levels.

Themes: Neuroscience, Imaging techniques
Keywords: Awake Phosphorous Magnetic Resonance Spectroscopy, brain energy metabolism, preclinical rodent MRS

Associated Autoimmunity in Myasthenia Gravis in Denmark:

A Nationwide Case-Control Study

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Background and objectives

Myasthenia gravis (MG) is an autoantibody-mediated disease of unknown etiology often co-occurring with other autoimmune diseases (AIDs). In this study, we aimed to determine the association between incident AID and the subsequent development of MG.

Methods

In this nationwide population-based case-control study, each patient was matched in a 1:10 ratio to the general population based on age, sex, and diagnostic index date. Data was obtained from Danish health registers through individual-level data linkage across health registers from 1985 to 2020. Conditional logistic regression was applied to calculate odds ratios (ORs) with 95% confidence intervals (CI). Analyses were stratified by sex and age group (<= 50 and >50). Moreover, analyses were adjusted for baseline comorbidity level identified via the Charlson Comorbidity Index (CCI).

Results

Our study population included 2,110 MG patients (1,061 females) and 21,100 matched individuals from the general population, with 27.4% <= 50 years. Prior to diagnostic index date, 4.7 % of MG patients and 2.7 % of the general population were diagnosed with another AID, resulting in an OR of 1.8 (95% CI 1.5-2.3). Notably, the highest OR was observed for patients 50 years, with an OR of 3.3 (95% CI 2.1-5.4). Adjusting for comorbidity did not significantly alter the associations.

Discussion

MG patients have a 1.8-fold higher risk of having another AID at time of diagnosis, suggesting a common pathophysiological mechanism that may predispose to poly-autoimmunity. Understanding the predisposing immunological pathways is indispensable for prevention and treatment strategies.

Themes: Epidemiology, Neuroscience
Keywords: myasthenia gravis, autoimmune disorders, neuroepidemiology

Search for Cortical Magnetic Resonance Imaging biomarker for Amyotrophic Lateral Sclerosis

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Introduction:

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder with no known cause or cure. Diagnosis relies on neurological examinations and evidence of motor neuron dysfunction. While Magnetic Resonance Imaging (MRI) is essential for early diagnosis, no specific biomarker reliably distinguishes ALS from mimicking conditions. Our study aims to apply advanced microstructural imaging techniques sensitive to tissue properties to address this gap. ALS pathophysiology involves degeneration of motor neurons in the cerebral cortex, brainstem, and spinal cord. Advances in genetic models has significantly enhanced our understanding of ALS. Here, we utilize two mouse models, SOD1 and CAS-ZX, to investigate cortical changes.

Methods:

Conventional structural MRI produces weighted images with millimeter resolution but lacks biological specificity. By leveraging “Biophysical Modeling” at the micrometer scale, “Virtual MR Microscopy” can link MRI signals to tissue microstructure. Diffusion MRI is used to map axonal density and water diffusivities along with other cellular properties. While white matter modeling is well-established, our recently developed gray matter diffusion model estimates neuron soma density, size, and permeability – key metrics in ALS. As validation, light microscopy is employed to refine their biological interpretation.

Results:

This study provides histologically validated MRI methods for mapping neuronal properties. These findings will enable the identification of cortical biomarkers for ALS and provide insights into their cellular underpinnings.

Themes: Imaging techniques, Neuroscience
Keywords: Cortical MRI Biomarker, Amyotrophic lateral sclerosis, Biophysical modeling

KetoBrain: Effects of exogenous ketone ester supplementation in human cerebrospinal fluid

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Introduction: Over the last decade, there has been a growing interest in the use of ketone supplements to explore various aspects of human metabolism. These ketone supplements transiently elevate the concentrations of the ketone bodies 3-hydroxybutyrate (3-OHB) and acetoacetate in the circulation. Ketones serve as an alternative fuel source for the brain. Exogenous ketones have been shown to increase cerebral blood flow, and maintain mental alertness while raising plasma concentrations of dopamine post-exercise, also improving sleep efficiency and quality after high-intensity exercise. Furthermore, ketones may promote brain energetics in neurological diseases where glucose metabolization is impaired, including Alzheimer's disease and Parkinson's disease. The cerebrospinal fluid (CSF) carries nutrients to and around the brain, and the cerebral metabolism of ketone bodies depends on the passage across the blood-brain barrier. No study has measured 3-OHB concentrations in blood and cerebrospinal fluid after the ingestion or infusion of ketones.

Purpose: This study aims to investigate:

1) The 3-OHB CSF/blood ratio after oral ingestion of 30 g ketone ester

2) The window of effect: Ketone supplementation 1h or 2h before CSF sampling

3) If concentration measurements by point-of-care testing are non-inferior to mass spectrometry

4) If acute 3-OHB ingestion increases CSF and plasma dopamine and BDNF-levels

Methods: Patients referred to elective lumbar puncture (n = 24) ingest 30 g of ketones 1h (n = 8), 2 h (n = 8) or placebo (n = 8) before lumbar puncture procedure.

Preliminary results: Exogenous ketones elevate CSF ketone levels in the 2h group.

Themes: Endocrinology, Neuroscience
Keywords: Ketones, ,

Course of neurocognitive development from 7 to 15 in children at familial high risk of schizophrenia or bipolar disorder. The Danish High Risk and Resilience Study – VIA 15

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Background

Schizophrenia (SZ) and bipolar disorder (BP) are highly heritable with offspring having not only an increased risk of the parental disorder, but other severe mental disorders as well. SZ and BP are recognized as neurodevelopmental disorders and first-degree relatives show patterns of neurocognitive impairments similar to patients, however to a lesser degree. Investigating the course of neurocognitive development in offspring at familial high risk (FHR) of SZ and BP offers insights into both shared and disorder-specific neurocognitive endophenotypes and developmental trajectories.

The previous assessments of the presented cohort at age 7 and 11 showed stable neurocognitive deficits in children at FHR-SZ compared to population-based controls (PBC) and neurocognitive functioning in children at FHR-BP comparable to PBC.

The present study aims to study the neurocognitive development in children at FHR-SZ and FHR-BP compared with PBC from age 7 to 15.

Methods

The Danish High Risk and Resilience Study (VIA) is a population-based cohort of 522 children (202 FHR-SZ, 120 FHR-BP, and 200 PBC). They were assessed at baseline at age 7 (VIA 7) and at first follow-up at age 11 (VIA 11). VIA 15 is the second follow-up at age 15 where data collection is completed with a retention rate of 82% of the original cohort.

Neurocognitive functioning was assessed with the same comprehensive neurocognitive test battery of validated tasks.

Results

Preliminary results will be presented.

Perspectives

Examining the development of neurocognitive deficits in children at FHR-SZ and FHR-BP will elucidate shared and distinct endophenotypes and help differentiate the pathophysiology of SZ and BP.

Themes: Epidemiology, Neuroscience
Keywords: Schizophrenia and Bipolar disorder, Neurocognitive development, Familial high risk

Are neuromuscular Long-term COVID-19 complications chronic? A quantitative and single fiber electromyography follow-up study

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Background: Fatigue and myalgia are among the most common Long Covid symptoms. Long Covid or Post Covid myopathy has been shown on electromyography (EMG) and muscle biopsy. The prognosis of having Long Covid neuromuscular manifestations remains unknown.

This study aims at re-assessing the changes in quantitative EMG (qEMG) and single-fiber EMG (sfEMG) in patients with Long Covid at 12-24 month follow-up.

Method: 50 Long Covid patients with myopathic qEMG and/or abnormal sfEMG were re-examined. qEMG of biceps brachii (BB), vastus medialis (VM) and tibialis anterior (TA) and sfEMG of TA were performed. Mean MUP duration, amplitude, percentage of polyphasic potentials, and mean jitter were compared between 1st and 2nd examinations using the Wilcoxon test.

Results: In BB, MUP amplitude(median:266µV vs 316 µV, p=0.0001), and MUP duration (median:9.70ms vs 11.35ms, p=0.0001) were increased and MUP polyphasia (p=0.4248) was unchanged.

In TA, MUP amplitude (median:391µV vs 531µV, p=0,0001), and MUP duration (median:11.15ms vs 12.90ms, p=0,0001) were increased, and MUP polyphasia (p=0,6499) was unchanged

In VM, MUP amplitude (median: 312µV vs 402µV, p=0,0001), MUP duration (median: 10.20ms vs 12.50ms, p=0,0001) were increased, and MUP polyphasia (p=0,1262) was unchanged.

sfEMG in TA (p=0,0536) and EDC (p=0,2171) was unchanged.

At baseline examination, 78% had myopathy and 54% had abnormal sfEMG. At follow-up, 20% had myopathy, 52% had abnormal sfEMG, and 20% were normal on EMG.

Conclusion: Patients with Post Covid myopathy still have electrophysiological abnormalities at an 18-month follow-up. qEMG changes indicate chronicity of myopathic changes and sfEMG values did not improve.

Themes: Infectious Diseases, Neuroscience
Keywords: Post Covid Myopathy, Long Covid, Myopathy

Brain Dynamics of Music Improvisation: Insights from MEG and fMRI

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Musical improvisation is the real-time creation of original musical ideas, often in interaction with fellow musicians. This process requires the synthesis of cognitive functions, including sensory perception, motor control, real-time performance monitoring, and memory retrieval. Although neuroscience has examined brain activity during improvisation, less is known about the preparatory processes that set the stage for it.

Here, we adopt a multi-methods approach to examine such preparatory mechanisms. By using functional Magnetic Resonance Imaging (fMRI) and Magnetoencephalography (MEG), we aim to capture the brain dynamics during the listening, preparation, and performance stages of musical improvisation. Participants were asked to either imitate (control condition) or improvise (target condition) in response to hearing short music sequences. Our focus is the preparation phase, wherein we hypothesize that the processes associated with preparing to improvise and preparing to imitate will differ, reflecting the condition-specific mental effort required for each performance goal. Although working memory recruitment is essential to both tasks, additional cognitive integrations during planning likely support the flexibility unique to improvisation. Leveraging the temporal precision of MEG, we aim to capture the timing of regional activity during the anticipatory phase, shedding light on how the brain prepares itself for creative improvisation versus stipulated imitation.

Ultimately, this research not only advances understanding of creative cognition but may have broader clinical implications, such as interventions for neurological disorders and music therapy.

Themes: Neuroscience, Imaging techniques
Keywords: Cognitive neuroscience, Music improvisation,

SESSION 22 - Infectious disease biology

Investigating MAVS' role in a Novel Human Airway Epithelial Model

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The respiratory epithelium is the first line of defense against important human pathogens, such as the influenza A virus (IAV). The respiratory epithelium is a complex structure composed of various cell types, with mucociliary clearance of airborne particles and a cellular defense consisting of the innate immune system. This complexity poses a challenge for experimental investigation of the innate immunity within the airways.

The Mitochondrial Antiviral-Signalling adaptor protein (MAVS) is a key component of the innate immune response following the recognition of cytosolic viral RNA. Without MAVS, an important step in the signaling cascade that leads to the production of interferons and cytokines during RNA virus infections is missing. However, despite extensive examination, it remains unclear whether MAVS has a non-redundant protective role in the respiratory epithelium.

To address the complexity of the respiratory epithelium, our lab has developed a physiologically relevant model using primary human airway epithelium cells (HAE) in an air-liquid interface (ALI) culture. This model can be genetically modified by knocking out the MAVS gene at the basal cell stage, followed by differentiation into respiratory epithelium with reduced MAVS expression. The HAE-ALI-culture allows direct examination of MAVS's importance in fully differentiated human primary cells during viral infections. We hypothesize that the lack of MAVS activation will lead to decreased interferon production, which is expected to influence viral replication of IAV and the level of host cell apoptosis.

Themes: Infectious Diseases, Genetic engineering
Keywords: Air-liquid interface (ALI) culture, Innate immunity, Influenza A virus

Detecting FcγR activation by anti-HIV bNAb immune complexes

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Experimental treatment with anti-HIV broadly neutralizing antibodies (bNAbs), has exhibited promising results, with a greater than expected proportion of patients achieving post-treatment control. Fc-FcγR-mediated effector functions are believed to be responsible for the induction of enhanced humoral and cellular protective immune responses.

Fc-FcγR interactions form a complex system, as FcγR-expressing cells include most innate immune effector cells, each with specific interactions. Additionally, in human biology, three groups of FcγRs have been described: CD64, CD32 and CD16 which can be activating or inhibitory. A deeper understanding of HIV-specific Fc-FcγR interactions along with identifying the main FcγRs involved in the induction of protective immunity, is essential for optimizing the therapeutic potential of anti-HIV bNAbs.

The aim of this study is to detect FcγR activation upon stimulation with HIV-specific immune complexes (IC), using a cell based in vitro reporter assay. Transfected BW5147 mouse thymoma cells expressing FcγR-ζ chimeras (with human CD64, CD32 and CD16 extracellular domains) will be used, including seven different FcγR subtypes and a wild-type BW5147 cell.

FcγR activation will be tested using anti-HIV bNAbs 3BNC117 and 10-1074 forming ICs with pseudo-HIV particles or Raji cells expressing HIV envelope proteins. Activation results in a TCR-like signal and will be measured by surface CD69 expression using flow cytometry and mouse IL-2 secretion, quantified by ELISA.

Themes: Infectious Diseases, Molecular biology
Keywords: HIV, Immunotherapy,

Effects of T cell function and specificity on time to viral rebound during analytical antiretroviral treatment interruption in people with HIV

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An estimated 39 million people are living with HIV globally. Antiretroviral therapy (ART) can efficiently suppress replication of HIV and thereby prevent the progression of HIV infection. However, ART has no effect on transcriptionally silent, latent provirus, creating a HIV reservoir in resting CD4+ T cells. When ART is interrupted, this reservoir is reactivated, resulting in viral rebound and progression of the infection. The time to viral rebound following ART interruption varies between people living with HIV (PLWH), however, the underlying mechanisms explaining the difference in time to viral rebound are not well understood.

To investigate this mechanism, this project will examine samples from the CLEAR study, an investigator initiated single group, non-randomized phase 1/2 clinical trial. In the CLEAR study 15 PLWH receiving suppressive ART were treated with panobinostat, a histone deacetylase inhibitor working as a latency reversing agent, for 8 weeks followed by an optional analytical treatment interruption (ATI), in which 9 individuals chose to participate. Seven of the participants had viral rebound (>1000 copies per mL) within 3 weeks, one after 4 weeks and one after 8 weeks of ATI. Upon viral rebound participants were restarted with ART. Weekly ATI samples from all participants will be analyzed using both the ELISpot and lymphocyte proliferation assay.

The aim of this project is therefore to examine the effects of HIV-specific T cell responses and proliferative capacity on time to viral rebound during an ATI in PLWH receiving suppressive ART, creating a better understanding of the immunological mechanisms underlying viral rebound.

Themes: Infectious Diseases, Molecular biology
Keywords: HIV, Treatment interruption, T-cells

HIV Reservoir Size & Neutralization Efficacy of Broadly-Neutralizing Antibodies (bNAbs) in HIV-2 Infected Individuals in Guinea-Bissau.

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Introduction

While HIV-1 is the most prevalent strain worldwide, HIV-2, primarily found in West Africa, progresses more slowly and has a lower transmission rate. Its unique immune profile, including a higher natural production of broadly neutralizing antibodies (bNAbs), suggests that HIV-2 could offer insights for HIV-1 cure strategies. However, research on HIV-2 reservoirs and bNAbs efficacy is limited. Moreover, although bNAb-based passive immunization has shown promise in clinical trials for HIV-1, its potential in HIV-2 remains unexplored. This study, set in Guinea-Bissau, where HIV-2 prevalence is highest, aims to fill these gaps.

Objectives

The primary aims of this study are to:

1. Compare HIV-1 and HIV-2 reservoir sizes in HIV-1, HIV-2, and dually infected individuals.

2. Assess the efficacy of bNAbs in HIV-2 infected individuals, focusing on differences between those on antiretroviral therapy (ART) and ART-naïve patients.

Methods

Approximately 200 participants, primarily HIV-2 and dually infected individuals (HIV-1/2), will be enrolled. Blood samples will be collected for PBMC-isolation in Guinea-Bissau, followed by subsequent analysis in Denmark. HIV-reservoir quantification will be performed using digital droplet PCR (ddPCR). To evaluate bNAb efficacy, an EGFP-labeled pseudovirus assay will measure neutralization through flow cytometry.

Conclusion

The findings could enhance our understanding of HIV-2's distinct immunology and help establish HIV-2 as a potential model for passive immunization strategies. Effective bNAb-based treatments could reduce ART dependency in resource-limited settings, offering a promising step toward functional cures for both HIV-1 and HIV-2.

Themes: Infectious Diseases, Molecular biology
Keywords: HIV, ,

Development of a self-amplifying circular RNA vector based on the hepatitis delta virus

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The safety and effectiveness of mRNA vaccines during the COVID-19 pandemic has sparked a growing interest in RNA-based therapies. Despite this success, the short in vivo half-life of mRNA limits the duration of gene expression, necessitating repeated doses. This challenge has led to the exploration of new RNA technologies that can provide stable and prolonged gene expression.

We aim to exploit unique properties of hepatitis delta virus (HDV) – a small, circular, single-stranded RNA with viroid-like characteristics – to develop a self-amplifying circular RNA vector. We propose that the distinctive traits of HDV RNA – including rapid self-replication via its circular, highly self-complementary structure – provide an ideal platform for achieving long-term expression. The project focuses on three main goals: 1) to design and optimize HDV RNA vectors for sustained expression in vitro; 2) to achieve efficient delivery using lipid nanoparticles in vitro and in vivo; and 3) to explore vector mobilization and its capacity to encode therapeutic proteins.

Preliminary experiments have demonstrated stable HDV RNA replication and robust transgene expression in an artificial system using transient transfections with HDV cDNA constructs, validating HDV RNA's potential as a gene delivery vector. The next phase is to establish this concept in a DNA-free system, ultimately aiming to apply an HDV RNA vector for the delivery of therapeutic antibodies. This research could significantly advance RNA-based therapies by providing a stable, self-amplifying circular RNA system capable of prolonged gene expression, offering a more durable alternative to current mRNA technologies.

Themes: Infectious Diseases, Molecular biology
Keywords: Hepatitis delta virus, RNA-based therapeutics, Gene delivery technologies

Longitudinal changes in the nasal microbiome in patients with long COVID-19 compared to healthy controls

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Background: Inflammatory conditions such as SARS-CoV-2 play a major role in olfactory dysfunction and may connect to the nasal microbiome as it has been found to play an essential role in modulating the passage and removal of odorants to and from their respective receptors in the nasal cavity. Our own preliminary results of a pilot study of ten controls and ten COVID-19 patients indicated a difference in microbiome between the two groups. Supported by this, our theory is that the composition of the microbiome changes during different stages of COVID-19 disease.

Methods: Nasal and pharyngeal swabs were collected from

1) 30 patients presenting with long COVID in the outpatient clinic for at least two visits

2) 30 controls with a normal sense of smell

3) 15 COVID-19 positive patients in the acute phase

The swabs were analyzed using next-generation sequencing targeting 16S and 18S ribosomal RNA. Characterization of the microbiome was performed by 16S/18S amplicon-based metagenomics. Group 1 and 2 were furthermore tested with Burghart Messtechnik Sniffin' Sticks to evaluate olfactory function.

Results: We hope to present results on a possible link between the change in microbiome composition and the change in olfactory score or status. Furthermore, we hope to present any changes in microbiome composition in patients with long COVID from the first to the second and third visits. Lastly, we hope to compare the microbiome of the long COVID patients' first visit to the long COVID clinic to the microbiome of patients in the acute stage of COVID-19 and healthy controls. We will do the same for the microbiome of the last visit.

Themes: Infectious Diseases, Bioinformatics
Keywords: Microbiome, Long COVID-19, Olfactory dysfunction

Identification of novel antiviral targets against measles virus infection

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Measles is a very contagious airborne disease caused by the measles virus, which in severe cases can lead to meningitis or encephalitis. Globally, measles cases have risen substantially in recent years due to declining vaccination coverage. Consequently, measles infection remains a critical cause of illness and death worldwide. An antiviral treatment against measles would therefore be beneficial in fighting the virus. Monocytes in the lungs are among the first cells to be infected when the measles virus is transmitted to a person. Human cells have host factors that naturally restrict viruses, and we have discovered a network of NRF2-dependent genes with strong antiviral potential against SARS-CoV-2, HSV-1, and VACV.

With this project, we aim to identify potential antiviral NRF2-regulated host genes that inhibit replication of measles viruses in monocytes. Using CRISPR activation, we will overexpress a panel of selected NRF2-regulated genes in monocytes and subsequently infect the cells with measles virus. We will then use qPCR, immunoblotting and TCID50 assays to analyze viral replication to determine the antiviral properties of the CRISPR-induced genes. Moreover, we will aim to determine the underlying mechanism for the antiviral effects. Through this project, we hope to enhance our understanding of the human host response to viral infections, enabling us to exploit this knowledge for potential antiviral therapies in the future.

Themes: Infectious Diseases, Molecular biology
Keywords: Measles infection, Innate immunology, Antiviral genes

HIV-resistant anti-HIV CAR T cells to effectively control HIV in vivo

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HIV remains a serious global health issue. Current treatment, antiretroviral therapy, can effectively control HIV replication but fails to eliminate the virus. Therefore, treatment must be maintained for life, emphasizing the urgent need for novel treatment strategies. We propose a chimeric antigen receptor (CAR) T cell-based immunotherapy. Anti-HIV CAR T cells face obstacles that limit their therapeutic effect, such as inefficient HIV tar-geting and HIV susceptibility of the infused CAR T cell product.

Here, we present ongoing work to establish a HIV-resistant anti-HIV CAR T cell therapy that we believe can achieve durable HIV control in vivo. We aim to ensure efficient HIV targeting utilizing single-chain variable fragments from clinically potent, broadly neutral-izing antibodies (bNAb). We have engineered HIV-resistant CAR T cells using CRISPR/Cas9-mediated integration of a CAR cassette into the CCR5 locus, a co-receptor essential for HIV entry into target cells. Integrating at this site enables simultaneous CAR expression and CCR5 disruption, protecting the cell from infection. We have success-fully engineered CAR T cells based on the anti-HIV bNAb 10-1074 and validated antiviral efficacy in vitro and ex vivo. To achieve a combinatorial CAR T cell therapy, we will identify additional bNAbs with different HIV targeting. Furthermore, we have established a xenograft mouse model that we will use to evaluate CAR T cell efficacy in vivo. CAR T cells are promising as an HIV cure strategy; however, the field still faces obstacles. We hope to further advance CAR T cell technology and ultimately develop a CAR T cell therapy with a potential to functionally cure HIV.

Themes: Infectious Diseases, Genetic engineering
Keywords: HIV, Gene editing, CAR T cells

Safety of the monoclonal anti-HBsAg antibody HepB mAb19 in chronic Hepatitis B infection: A first-in-human trial

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Background

Chronic infection with hepatitis B virus (HBV) remains treatable but not curable. Persistent production of hepatitis B surface antigen (HBsAg) drives immune exhaustion, a key barrier to achieving a cure. This study is the first to investigate HepB mAb19, a novel monoclonal antibody targeting HBsAg, in humans.

Methods

A two-step, single-dose, dose-escalation clinical trial. In Part A, participants will receive a single escalating dose of 3, 10, and 30 mg/kg HepB mAb19 or a placebo (n=4 per group, randomization 3:1) to establish safety and determine the maximal tolerated dose (MTD). Part B will assess MTD in an open-label expansion group (n=18). All participants will be monitored for 48 weeks post-infusion, with each participant undergoing 13 visits. The study will enroll 30 people with chronic hepatitis B, who are: Aged 18 to 70, hepatitis e-antigen negative, on antiviral treatment for HBV with low levels of HBV DNA in plasma, and without advanced liver fibrosis or HIV, hepatitis C, or hepatitis D co-infections.

Results

The first four patients have been enrolled and have received either placebo or HepB mAb19 at a dose of 3 mg/kg. Reported adverse events (AEs) have generally been mild (grades 1-2) and included fever, flu-like symptoms, and transient elevations in liver enzymes. Grade 3 lymphopenia was observed in n=1 but resolved within 24 hours

Conclusion

In the first four study participants, HepB mAb19 was well-tolerated at the 3 mg/kg dose, with mainly mild adverse events and manageable lymphopenia. Results support further dose escalation to assess its potential in reducing HBsAg levels.

Themes: Infectious Diseases, Gastroenterology and hepatology
Keywords: Hepatitis B immunotherapy, Monoclonal antibody, First-in-human trial

Studies of the clinical features and host-immune response in vascular graft and endograft infections

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Infections in medical implants are a growing global issue, driven by expanding surgical indications and an aging population. These infections may occur during surgery itself or later via hematogenous seeding. Many bacteria involved can form biofilms, three-dimensional bacterial structures encased within an extracellular matrix. Once attached to an implant surface, biofilms protect bacteria from immune responses and antibiotics, making these infections extremely difficult to treat without device removal.

Vascular graft and endograft infections (VGEI) are particularly serious, as grafts in the aorta are often irremovable, and antibiotics alone are rarely effective, necessitating prolonged or even life-long antibiotic regimens, with risk of antibiotic resistance and mortality exceeding 75%.

During the PhD-program, we aim to:

1. Conduct a matched case-control study on risk factors for VGEI in patients treated in the central Denmark Region 2012-2023

2. Conduct a cohort study retrospectively assessing mortality of VGEI-patients undergoing surgical or conservative treatment

3. Establish a prospective cohort of patients with VGEI

Within this cohort we seek to explore the host immune-response including flowcytometric phenotyping, and assess the utility of novel diagnostic tools such as sequencing of microbial cell-free DNA

4. Create a biobank for VGEI patients laying the foundation for future studies

These studies aim to expand our understanding of VGEI and other biofilm-associated infections, thereby enhancing diagnostic accuracy and developing improved treatment strategies, ultimately improving outcomes and quality of life for future patients.

Themes: Infectious Diseases, Infectious Diseases
Keywords: Vascular graft infection, Biofilm, VGEI

Increased water intake dilutes protective uromodulin levels in urine and increases rates of ascending UTI in a murine model

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Urinary tract infections (UTIs) rank among the most prevalent infections in humans, carrying substantial implications for public health. UTIs are most frequently caused by uropathogenic Escherichia coli, against which the urinary tract has an innate defence via antimicrobial peptides and uromodulin. Alongside antibiotics, patients with UTIs are encouraged to increase fluid intake to flush out bacteria. We tested whether augmented fluid intake increases bacterial clearance in a mouse model of ascending UTI.

UTI was surgically induced in 8–10-week-old female BALB/cJ mice by injecting E. coli directly into the bladder, whereafter mice were randomised to gel food (GF) or regular chow. Immune response and infection severity were determined 24 hours post-infection.

Gel feeding increased urine output (1.40±0.77µl min−1, $p<0.01$) and diluted the urine (668.7±177 mOsmol kg−1, $p<0.0001$) compared to mice on regular chow (urine output: 0.34±0.27µl min−1, osmolality: 1439±473.5 mOsmol kg−1). Surprisingly, GF mice had a higher risk of pyelonephritis (87.5%) and more severe infections (26.22±9.88 CFU mg-1) compared to chow-fed mice (43.75%; 3.87±3.56 CFU mg-1, $p<0.01$). Correspondingly, GF mice had lower urine levels of uromodulin (13.70±1.89 µg ml−1, $p < 0.01$) compared to controls (24.65 ± 2.70 µg ml−1), whereas the E. coli growth rates in both mouse and human urine were unaffected by dilution in the physiological range.

In conclusion, increasing fluid intake does not increase bacterial clearance from the urinary tract in mice; rather, it worsens the infection, most likely by reducing the urinary tract's innate bacterial defence. This effect ought to be investigated in patients with UTIs.

Themes: Urology & Nephrology, Infectious Diseases
Keywords: Urinary tract infection, Increased fluid intake, Uromodulin

SESSION 23 - Surgery 2

Determinants of survival after pancreatic cancer surgery

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Pancreatic cancer (PC) is a highly fatal disease with a 5-year survival of less than 10%. Surgery is the only chance for long-term survival, but it is a major procedure with a substantial risk of complications and postoperative death. Around ~20% of patients undergoing curative-intent surgery experience recurrence within six months, and the surgical procedure can thus be considered futile. Improved knowledge of patient-specific expected outcomes is needed to support clinicians in better selection of patients for curative-intended surgery.

We will conduct three population-based cohort studies. We will assemble a cohort of all patients with a diagnosis of PC in the Danish Cancer Registry during 2012-2022. The three studies will examine the validity of PC diagnosis in the Danish Cancer Registry, whether routine blood tests can predict 2-year survival after PC surgery, and the interaction between age and comorbidity on mortality after PC surgery.

We expect that the projects outlined in this proposal will provide us with new knowledge that will guide us towards better selection of patients for curative-intent PC surgery.

Themes: Cancer, Surgery
Keywords: Pancreatic cancer, Cohort studies, Improve patient selection for surgery

How to measure quality of hip fracture care across healthcare sectors

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Background

Older hip fracture patients require coordinated care across healthcare sectors, but current efforts focus primarily on hospitals. Danish studies highlight inequalities in treatment and outcomes but patient and family perspectives are rarely included. Expanding quality measures to encompass the full care pathway offers substantial potential for improvement.

Objective

The project aims to address the current challenge of variability in the quality of treatment and prognosis for older hip fracture patients by establishing a foundation for new quality measures that encompass the entire patient pathway and incorporate both the patient and relative perspectives.

Project Studies

The project consists of four sub-studies, combining epidemiological, clinical, and qualitative methods based on registry and prospectively collected data.

- Study 1 (Registry Study): To examine if municipal variation in 30-day readmission rates for older hip fracture patients is a valid measure of the quality of cross-sectional healthcare efforts.

- Study 2 (Scoping Review): To investigate which patient-reported outcome measures are currently used to assess the recovery of older hip fracture patients.

- Study 3 (Interview Study): To identify key areas that older hip fracture patients consider essential for measuring their recovery.

- Study 4 (Cross-Sectional Audit): To examine current practices in cross-sectional treatment, care, and rehabilitation for older hip fracture patients.

Setting: The Ph.D. project will be conducted in the Central Denmark Region in collaboration with Aarhus University Hospital (AUH) and in the Capital Region with affiliation to Hvidovre Hospital (HVH).

Themes: Epidemiology, Surgery
Keywords: Hip Fracture, Quality of Care, Cross-sectional

Open surgical reconstruction versus sham surgery in the treatment of hip abductor tendon tears (HIPAS): A double blinded, randomized, placebo-controlled trial

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Background

Patients with hip abductor tendon tears experience debilitating lateral hip pain in their daily living, that affects their physical function and quality of life. Reconstructive surgery for ruptured hip abductor tendons is a new treatment option. However, the efficacy of the surgical reconstruction of hip abductor tendon tears has yet to be investigated. Hence, we are conducting a randomised controlled trial investigating the efficacy of an open surgical reconstruction of the hip abductor tendons compared to sham surgery in patients with clinically and magnetic resonance imaging verified hip abductor tendon tears.

Method

In this randomized controlled trial, 36 patients will be randomized to either reconstructive surgery or sham surgery. Allocation will be blinded to both patients, testers, and the post-surgical rehabilitation team. The primary outcome is between-group difference in change of hip pain measured with the subscale 'pain' on the patient-reported outcome measure the revised Copenhagen Hip And Groin Outcome Score from pre-surgery to the final follow-up at 6 months post-surgery. Secondary outcomes are changes in patient-reported outcomes, muscle strength and functional capacity. The study will be terminated in case of superiority for the intervention group at the planned interim analysis.

Ethics

The study is approved by the Committee on Health Research Ethics in the Central Denmark Region (ID: 1-10-72-188-23) and is registered at both the Central Region Denmark List of Research projects (ID: 1-16-02-128-24) and ClinicalTrials.gov (ID: NCT06398015). Informed consent will be obtained from participants before participation. Screening started on May 1st 2024.

Themes: Rehabilitation, Surgery
Keywords: Hip abductor tendon tears, Surgical reconstruction, Rehabilitation

First-linetreatment for femoroacetabular impingement syndrome and hip-related quality of life: study protocol for a multicentre randomised controlled trial comparing a 6-month supervised strength exercise intervention to usual care (the Better Hip Trial).

Frederik Nicolai Foldager, Department of Clinical Medicine, Health

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Introduction:

Femoroacetabular impingement syndrome (FAIS) is a motion- and position-related clinical condition of the hip associated with pain, reduced physical function, and hip-related quality of life (QoL). Interestingly, higher maximal muscle strength is associated with less pain, better physical function, and improved QoL in people with FAIS. Furthermore, preliminary evidence suggests that a proportion of patients with FAIS respond positively to strength exercise as first-line treatment. Nonetheless, there is little evidence supporting a specific exercise intervention offered as first-line treatment. We will conduct a randomized controlled trial investigating the clinical- and cost-effectiveness of a 6-month strength exercise intervention compared with usual care as first-line treatment in patients with FAIS.

Methods and analysis:

This is a multicenter, randomized (1:1), controlled trial that will be conducted at hospitals and physiotherapy clinics across Denmark and in Australia. A total of 120 patients with FAIS will be randomized to 6 months of supervised strength exercise or usual care. The primary outcome is the change in hip-related QoL measured using the International Hip and Outcome Tool 33 (iHOT-33) from baseline to the end of intervention. A health economic evaluation will be conducted from a societal and healthcare perspective based on the data collection over a 12-month period starting at baseline. The analysis will calculate incremental cost-effectiveness ratios (ICER) using quality-adjusted life years (QALY) and iHOT-33 scores while estimating costs using microcosting and cost questionnaires. Secondary outcomes include objectively measured physical function at

baseline and after 6 months and patient-reported outcomes measured at baseline, 3-, 6-, and 12-month follow-up.

Ethics and dissemination:

Approved by the Central Denmark Region Committee on Biomedical Research Ethics (1-10-72-45-23), La Trobe University Human Ethics Committee (HEC24042), registered at the Central Denmark Region List of Research Projects (1-16-02-115-23) and on ClinicalTrials.gov (NCT05927935).

Themes: Rehabilitation, Surgery
Keywords: Femoroacetabular impingement syndrome, Exercise,

Mental disorders increase the risk of reoperations and mortality after surgery for hip fracture: a Danish population-based cohort study

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Background: Despite the rising burden of mental disorders worldwide, the impact of mental disorders on complication risk after hip fracture surgery remains unclear. We examined the risk of reoperation and mortality after hip fracture surgery, comparing patients with and without mental disorders.

Methods: Using Danish databases, patients undergoing surgery for their first hip fracture were identified. The history of mental disorders and reoperations were added. We estimated the risk of reoperation and mortality with adjusted hazard ratios (aHR), treating death as a competing risk and with 95% confidence intervals (CI).

Results: Out of 110 625 hip fracture patients from 2004 to 2021, 15 254 (14%) had a mental disorder. The 30-day aHR for reoperations was 1.17 (CI: 1.1-1.3) for patients with any mental disorder compared to those without mental disorders, varying from 1.05 (CI: 0.9-1.2) for patients with organic mental disorders to 1.67 (CI: 1.3-2.1) for patients with disorders due to substance use. The 365-day aHR for reoperation was 1.05 (CI: 1.0-1.1) for patients with any mental disorder, compared to those without mental disorders, varying from 0.92 (CI: 0.9-1.0) for organic mental disorders to 1.37 (CI: 1.2-1.5) for neurotic related disorders. Patients with any mental disorder had 365-day mortality of 35% (CI: 34-36) compared to 25% (CI: 24-25) for patients without mental disorders.

Discussion: Both the risk of reoperation and mortality were significantly higher for patients with mental disorders at 365-day after hip fracture surgery. These findings emphasize the need for targeted prevention strategies with a focus on mental disorders to reduce reoperations and mortality.

Themes: Epidemiology, Surgery
Keywords: Hip Fracture, Reoperations, Mental Disorders

Perioperative treatment with tranexamic acid in melanoma (PRIME): protocol for a Danish multicentre randomised controlled trial

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Introduction

Perioperative inflammation may contribute to carcinogenesis, as inflammation is a hallmark of cancer (Hanahan 2011). Thus, understanding and modulating inflammation may improve treatment. Tranexamic acid (TXA) is suggested as a candidate for drug repurposing in cancer. TXA inhibits the plasminogen-plasmin pathway, modulating inflammation and possibly carcinogenesis (Godier 2013, Levi 2005, Heissig 2020, Heissig 2021). This trial aims to prevent early relapses in patients with melanoma by >10% using perioperative treatment with TXA (Kristjansen, 2024).

Methods

• Design: Parallel, two-arm, randomized, blinded, Danish multicenter superiority trial

• Intervention: Perioperative TXA or placebo

• Patients: Melanoma patients (T2b) undergoing SLNB (n=1204).

• Primary outcome: Relapse within two years

• Primary analysis: Primary analysis: risk difference between the treatment arms ($\chi 2$ test)

• Secondary outcomes: Postoperative complications and adverse events.

• Sample size calculation: A sample of 1204 allocated 1:1 is needed to show a risk difference for recurrence between groups of 11% (37–26%) with a 3% superiority margin, 85% power, and alpha 0.05.

Status

The trial complies with the Declaration of Helsinki and Good Clinical Practice. The trial is approved by the National Committee on Health Research Ethics, the Danish Medicine

Agency (CTIS: 2022-502633-26-00), and registered under the Data Protection Act. Inclusion was initiated in August 2023 and will run until complete at 1204 included patients. Registration: ClincalTrials.gov ID: NCT05899465.

Themes: Cancer, Surgery
Keywords: Clinical trial, Melanoma, Surgery

The Effect of Remote Ischemic Conditioning on Delayed Cerebral Ischemia in Aneurysmal Subarachnoid Hemorrhage - Rationale and Study methods

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Rationale: Aneurysmal subarachnoid hemorrhage (aSAH) frequently results in cerebral vasospasm and delayed cerebral ischemia (DCI), both of which significantly contribute to neurological morbidity and elevated mortality rates. There is a critical need for more efficacious preventive therapeutic strategies. Remote ischemic conditioning (RIC), following securing of the aneurysm, holds promise in modulating the hemodynamic processes associated with vasospasm and in providing neuroprotective, anti-ischemic effects.

Aims: To evaluate whether RIC initiated before vasospasm and DCI is safe and improves long-term functional outcome in aSAH.

Methods and design: This prospective, single-center, randomized, sham-controlled, and patient-assessor blinded pilot study is currently enrolling adult patients with aneurysmal subarachnoid hemorrhage (aSAH) who present within 72 hours of ictus, have a secured aneurysm, and were previously independent in their daily activities. Participants will be randomized in a 1:1 ratio to receive either Remote Ischemic Conditioning (RIC) or sham-RIC. The treatment protocol includes five cycles, each consisting of 5 minutes of cuff inflation followed by 5 minutes of cuff deflation. The cuff will be applied to the thigh, with the pressure for RIC set to ensuring the absence of a pulse in the ipsilateral dorsal pedal artery, and 50 mmHg during sham-RIC inflation. In cases where patients are unable to provide consent, informed consent will be obtained from the next of kin. Treatments will continue until post-hemorrhage day 14.

Study outcomes: The primary outcome will be mRS score measured at six-month follow-up (ordinal logistic regression).

Themes: Rehabilitation, Surgery

Keywords: Cerebral Ischemia, Ischemic conditioning, Subarachnoid hemorrhage

Intelligent Physical Exercise Training (IPET) and intraoperative ergonomic recommendations (ERGO) for preventing and rehabilitating musculoskeletal pain among abdominal and pelvic surgeons: Protocol for a multicenter randomized controlled trial

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Background: Surgeons are highly specialized professionals facing increased demand due to the aging population's need for surgery. However, musculoskeletal pain (MSP) is highly prevalent among surgeons and threatens career longevity. While improving intraoperative ergonomics is important, physical exercise training is widely used to prevent and rehabilitate MSP. This protocol investigates the combined effectiveness of Intelligent Physical Exercise Training (IPET) with ergonomic recommendations (ERGO) on reducing MSP among abdominal and pelvic surgeons.

Methods: This 20-week multicenter randomized controlled trial protocol will assign surgeons to either an IPET+ERGO (intervention) or ERGO-only (control) group in a 1:1 ratio. The IPET program includes 50-minute individualized weekly exercise sessions, tailored to each surgeon's job profile, physical capacity, and MSP levels, delivered via a mobile app. ERGO provides ergonomic recommendations for operating rooms through presentations, videos and posters. Eligible participants must perform surgery for at least four hours weekly. The primary outcome is the change in MSP in the most painful body region, from baseline to 20 weeks.

Discussion: This trial protocol addresses the lack of targeted interventions to reduce MSP in surgeons by combining ergonomic guidance with tailored exercise training. Its pragmatic design and broad eligibility enhance generalizability, though adherence and retention may affect internal validity. Results may inform future strategies to reduce surgeon MSP and mitigate potential workforce shortage.

Themes: Rehabilitation, Surgery
Keywords: Musculoskeletal pain, Surgical ergonomics, Intelligent Physical Exercise Training

An iliopsoas plane block and a subpectineal obturator nerve block reduces opioid consumption after hip arthroscopy. Results of two Triple-Blind, Randomized, Placebo-Controlled Trials

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Background: Hip arthroscopy causes severe pain the first hours postoperative. Postoperative pain control is often achieved by high doses of opioids. This may cause opioid related adverse events and prolong recovery. The nociceptors in the hip joint capsule located anteriorly are innervated by the femoral and obturator nerves. We hypothesized that both an iliopsoas plane block (IPB) and a subpectineal obturator nerve block (SOB) would reduce the postoperative opioid consumption.

Methods: Respectively fifty and forty hip arthroscopy patients were enrolled in two independently, randomized, triple-blind controlled trials. In the trials patients were allocated to an active IBP or SOB or placebo respectively. Primary outcomes were postoperative opioid consumption. Secondary outcomes were pain, nausea, and quadriceps/adductor strength.

Results: IPB trial: 49 patients were analyzed and the mean IV opioid consumption in the active IPB group was reduced by 56%, 10.4 mg versus 23.8 mg in the placebo group ($p<0.001$). SOB trial: 34 patients were analyzed and the mean intravenous morphine equivalent consumption in the active SOB group was reduced by 40%, 11.9 mg versus 19.7 mg in the placebo group ($p<0.001$). No other intergroup differences were observed regarding the secondary outcomes apart from significantly reduced hip adductor strength in the active SOB group.

Conclusion: We found a significant reduction in the opioid consumption for patients receiving an active IPB or an active SOB. The postoperative IV morphine equivalent reduction the first hours was reduced by 56% and 40% for patients receiving an IPB or SOB in the two randomized, triple-blind controlled trials.

Themes: Surgery, Pharmacology
Keywords: Regional Anesthesia, Pain, Hip Arthroscopy

SESSION 24 - Basic medical research 3

Establishing an experimental porcine marginal kidney model - CANCELLED

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BACKGROUND

Transplantation is the gold standard in treating end stage renal disease. Donor shortage has led to the use of marginal kidneys, characterized by some degree of chronic injury. Experimental research in graft reconditioning and viability assessment is however, mainly conducted in healthy kidneys exposed to warm ischemia. We aim to establish an experimental porcine model, resembling marginal donor kidneys, to act as a basis for future research and increase transferability to clinical practice.

MATERIALS AND METHODS

Bilateral renal artery stenosis will be induced by embedding a copper coil in the renal arteries of Danish landrace pigs (n=8). The diet will be changed to a high-fat high-cholesterol atherogenic diet, imitating typical comorbidities of marginal kidney donors. Renal deterioration will be monitored by blood and urine samples, biopsies and determination of glomerular filtration rate. 10 weeks post induction of renal artery stenosis, nephrectomies are performed and the kidneys are assessed ex vivo.

RESULTS

The inclusion of animals is expected to begin in January of 2024, and will still be active at the time of the congress. Preliminary results from pilots will, if available, be presented at the congress.

CONCLUSION

No conclusions will have been made, by the time of the congress.

Themes: Animal Models, Urology & Nephrology
Keywords: Animal model, Kidney transplantation, Urology and Nephrology

Bradykinesia and postural instability in a model of prodromal Synucleinopathy with α-Synuclein aggregation in the gigantocellular nuclei

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α-Synuclein (aSyn) accumulation within the extra-nigral neuronal populations in brainstem, including the gigantocellular nuclei (GRN/Gi) of reticular formation, is a recognized feature during the prodromal phase of Parkinson disease (PD). Accordingly, there is a burgeoning interest in animal model development for understanding the pathological significance of extra-nigral synucleinopathy, in relation to motor and/or non-motor symptomatology in PD. Here, we report an experimental paradigm for the induction of aSyn aggregation in brainstem, with stereotaxic delivery of pre-formed fibrillar (PFF) aSyn in the pontine GRN of transgenic mice expressing the mutant human Ala53Thr aSyn (M83 line). Our data show that PFF aSyn-induced aggregate pathology in GRN leads to progressive decline in spontaneous locomotion and an early phenotype of postural instability. This early phase of bradykinesia was followed by a moribund stage, characterized by worsening motor performance and impaired survival with substantial aSyn aggregation in several brain regions beyond the GRN. Collectively, our observations suggest an experimental framework for studying the pathological significance of aSyn aggregation in GRN in relation to features of movement disability in PD. With further refinements, we anticipate that this model holds promise as a test-bed for translational research in PD and related disorders.

Themes: Animal Models, Neurodegenerative disorders
Keywords: alpha-synuclein, Gigantocellular nuclei, Parkinson's disease

Piperine increases submaximal and maximal concentric contractility of intact fast- and slow-twitch rat muscles

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Background: The alkaloid piperine has recently been shown to increase isometric twitch force of isolated fast- and slow-twitch rat skeletal muscles. It is not known how piperine affects muscle power during dynamic contraction.

Purpose: To investigate piperine's effect on dynamic contractility of isolated fast- and slow-twitch rat muscles.

Methods: Dynamic contractility of isolated fast- (extensor digitorum longus - EDL) and slow-twitch (soleus) muscles from 4-week-old female Wistar rats was investigated by determining isotonic low- (60- and 20 Hz, respectively) and high-frequency (150- and 80 Hz, respectively) concentric force-velocity (FV) relationships. FV tests were performed on contralateral muscles, examining the effects of 50 µM piperine and controlling for vehicle (ethanol) effects.

Results: In soleus muscles, piperine (n=6) increased peak high-frequency power (Pmax) by 10 ± 2% (P=0.01) (mean diff ± SE) and high-frequency maximal shortening velocity (Vmax) by 9 ± 2% (P=0.01), compared to vehicle (n=6). In EDL muscles, piperine (n=6) increased high-velocity high-frequency power by 4 ± 1% (P=0.02) and high-frequency Vmax by 6 ± 1% (P=0.01), compared to vehicle (n=5). During low-frequency activation, Vmax and Pmax of both muscle types were enhanced by 20-25% (P≤0.01) and 36-54% (P≤0.01), respectively.

Conclusion: Piperine enhances Vmax and power during high velocity shortening contractions in EDL muscles and Vmax and Pmax in soleus muscles during maximal activation. Further, Vmax and Pmax during submaximal activation were markedly enhanced in both muscle types. Consequently, piperine can be a potential precursor for designing drugs to enhance muscle function.

Themes: Animal Models, Pharmacology
Keywords: Skeletal Muscle Contraction, Contractile Power, Myosin-activating Compound

Activation of the Innate Immune System in Brain-Dead Donors Can Be Reduced by Luminal Intestinal Preservation During Organ Procurement Surgery - A Porcine Model

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Organs obtained from brain dead donors can have suboptimal outcomes. Activation of the innate immune system and translocation of intestinal bacteria could be causative. Thirtytwo pigs were assigned to control, brain death (BD), BD + luminal intestinal polyethylene glycol (PEG), and BD + luminal intestinal University of Wisconsin solution (UW) groups. Animals were observed for 360 minutes after BD before organ retrieval. 2000ml luminal intestinal preservation solution was instilled into the duodenum at the start of organ procurement. Repeated measurements of plasma C3a, Terminal Complement Complex (TCC), IL-8, TNF, and lipopolysaccharide binding protein were analysed by immunoassays. C3a was significantly higher in the BD groups compared to controls at 480 minutes after brain death. TCC was significantly higher in BD and BD + UW, but not BD + PEG, compared to controls at 480 minutes. TNF was significantly higher in the BD group compared to all other groups at 480 minutes. LPS binding protein increased following BD in all groups except BD + PEG, which at 480 minutes was significantly lower compared with all other groups. Brain death induced innate immune system activation was decreased by luminal preservation using PEG during organ procurement, possibly due to reduced bacterial translocation.

Themes: Animal Models, Animal Models
Keywords: Transplantation, Innate Immune System, Intestinal preservation

Reducing neurological injury following cardiac arrest in a clinically relevant porcine model

Cecilie Munch Johannsen, Department of Clinical Medicine, 2.5 min pitch

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Purpose

To advance our understanding of neurological injury following cardiac arrest and identify new promising interventions.

Background

In Denmark, cardiac arrest occurs in 7,500 people per year, with mortality rates as high as 80-90%. Neurological injury is the leading cause of death following cardiac arrest. This can be reduced by improving blood flow to the brain during cardiopulmonary resuscitation (CPR) or by reducing the

degree of brain injury after the patient has been resuscitated. Epinephrine is the only recommended pharmacological intervention to improve blood flow during CPR, yet it has limited effect on long term outcomes. Glibenclamide, and the combination of Levosimendan and Angiotensin II are promising interventions to improve survival following cardiac arrest. However, confirmatory studies in a large animal model of cardiac arrest are warranted.

Methods

The dynamics of cerebral edema and perfusion, and the effects of novel interventions will be investigated in a clinically relevant porcine model of myocardial infarction and cardiac arrest. Animals will receive CPR according to international guidelines. Cerebral swelling and blood flow will be measured over time by repeated advanced magnetic resonance imaging. Interventional studies will be blinded, and animals will be randomized to receive the intervention or normal saline as placebo.

Perspectives

This project has the potential to significantly expand our understanding of neurological injury following cardiac arrest and it will provide preliminary data for two promising interventions. If interventions are proven efficacious, next step will be testing in large randomized human trials.

Themes: Animal Models, Cardiology
Keywords: Cardiac arrest, Neurological injury, Animal model

The role of secretin and its receptor in renal disease progression

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Background and aim

In recent years, gastrointestinal hormones like GLP-1 have shown remarkable effects on renal and cardiovascular disease progression. Secretin, another hormone released in the postprandial phase, has been demonstrated by our group to elicit a substantial modulatory effect on renal glomerular filtration. Congruently, we also showed that loss of its receptor leads to glomerular hyperfiltration, a pathophysiological condition which entails irreversible kidney damage over time.

The main aim of this PhD-study is to investigate whether secretin and its receptor play a role in the development of renal disease.

Methods

The project is centered around the secretin receptor (SCTR) KO mouse model. The mice will be examined under baseline conditions and after being subjected to a hypertensive and a dietary challenge.

A broad spectrum of methods will be employed. These include transcutaneous GFR measurements, blood pressure measurements, echocardiography, analysis of urine and blood along with western blotting and staining for fibrosis of kidney and heart tissue.

Preliminary results

Under baseline conditions SCTR KO mice present with marked proteinuria compared to controls. Additionally, KO mice have elevated GFR at a young age but show strongly diminished GFR when old compared to controls.

Conclusion and perspectives

So far, the SCTR KO mice have a robust phenotype indicative of renal disease. Further experiments detailing the phenotype have commenced and the above-mentioned interventions and are being planned.

The results will aid in the understanding of the interplay between secretin and renal disease and provide information concerning the SCTR as a therapeutic target.

Themes: Animal Models, Urology & Nephrology
Keywords: , ,

Tunable transcriptional modulation using CRISPR-based tools

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CRISPR-based transcriptional activation (CRISPRa) and interference (CRISPRi) have revolutionized targeted gene regulation by leveraging nuclease-deficient Cas (dCas) to recruit transcriptional modulators for transient and gene-specific transcriptional modulation. In this study, we advance the frontiers of transcriptional engineering by developing a versatile trimodal genetic engineering platform that integrates orthogonal transcriptional regulation with permanent gene knockout using AsCas12a. This trimodal strategy demonstrates remarkable efficiency in primary human T cells, achieving transient yet precise control of transcription of two genes while inducing permanent gene editing of a third, all without compromising essential T cell health or functionality. The one-step delivery protocol streamlines complex genetic manipulations, enabling simultaneous transcriptome modulation and gene editing. Additionally, we explore the tunability of CRISPRa and CRISPRi systems by deploying truncated sgRNAs for fine-tuned transcriptional control. Notably, spacer sequences as short as 12 bp exhibit broad transcriptional regulation with desired reduced activation levels. This finding opens new avenues for optimizing CRISPR-based transcriptional modulation, offering enhanced control over gene expression.

Our work underscores the potential of combining multiple CRISPR systems in a streamlined, efficient manner to engineer complex genetic outcomes. These findings position CRISPRa, CRISPRi, and Cas12a-based knockout as complementary tools, paving the way for refined approaches in cellular therapy and regenerative medicine.

Themes: Genetic engineering, Genetic engineering
Keywords: CRISPR-based transcriptional modulation, Trimodal genetic engineering, Tunable gene expression control

Lipoxins mediate restoration of lymphatic function in an experimental model of obesity

Madison Clark, Department of Biomedicin, Second year student PhD day 2025

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Background and aims: Obesity leads to lymphatic dysfunction, which can contribute to inflammation-driven cardiometabolic diseases. Lipid mediators from the lipoxin family have demonstrated the ability to reduce obesity-induced inflammation and may hold promise as novel anti-diabetic treatments. In this study, we explore whether lipoxins (LXA4 and LXB4) can improve lymphatic function in an experimental obesity model.

Materials and methods: Male and female C57BL/6J mice were fed a standard-fat (SFD, 10% fat) or high-fat diet (HFD, 60% fat) for 12 weeks. From week 5, mice received intraperitoneal injections of vehicle (0.01% ethanol), LXA4 (5ng/g), or LXB4 (5ng/g) three times per week. Blood and organs were collected for evaluation of lymphatic functions and obesity-related organ injury, with each group consisting of 10 mice per sex.

Results: The HFD regimen led to significant weight gain in male (SFD: 8.4±0.6g vs. HFD: 18.8±1.53g, $p < 0.0001$) and female (SFD: 6.07±0.45g vs. HFD: 13.1±1.03g, $p < 0.0001$) mice. Lipoxin treatment did not affect weight gain or hyperglycemia, suggesting that any protective effects of lipoxins are independent of these factors. Obesity increased dermal lymphatic vessel density ($p < 0.001$), which was prevented by LXA4 and LXB4 ($p < 0.0001$). Obesity also reduced blood vessel density ($p < 0.0257$), restored only by LXA4 treatment ($p < 0.0302$).

Conclusion: Our preliminary data show that lipoxins improve obesity-induced alterations in lymphatic vessel density. Current research is focused on uncovering the molecular mechanisms through which lipoxins offer protection against obesity-related inflammation and cardiometabolic disease.

Themes: Animal Models, Immune diseases
Keywords: Obesity, Lymphatics, Lipoxins

Megalin is Essential for the Visual Cycle and Retinal Health

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Mutations in the LRP2 gene, encoding the endocytic receptor megalin, are associated with hereditary retinal dystrophy. While the function of megalin in renal protein reabsorption is well-documented, its role in the retina remains largely unexplored. Megalin localizes to the retinal pigment epithelium (RPE), which serves an important barrier function and supports photoreceptors. This includes enzymatic conversion and recycling of retinoids necessary for phototransduction in the visual cycle. We hypothesize that megalin has a role in this conversion of retinoids.

Using an inducible megalin knockout mouse model, histological analysis with H&E staining and functional assessment via optokinetic drum tests revealed that megalin ablation leads to progressive retinal degeneration, characterized by substantial photoreceptor cell loss and consequent blindness. Immunofluorescence analysis of RPE flatmounts reveals significant disturbances in visual cycle proteins (including RPE65) as early as three weeks post-knockout. This effect of RPE65 is supported by the accumulation of retinyl ester, the RPE65 substrate, suggesting impaired synthesis of 11-cis retinol. Notably, the megalin knockout model mirrors the retinal dystrophy and visual cycle impairment observed in the commonly used RPE65 knockout model.

In conclusion, megalin deficiency disturbs the visual cycle, potentially contributing to the observed retinal degeneration. Optical coherence tomography (OCT) will be used to characterize the sequence of dystrophic changes, and the mechanistic role of megalin will be explored using co-immunoprecipitation to identify binding partners and through spatial transcriptomics.

Themes: Animal Models, Imaging techniques
Keywords: Megalin, Retinal dystrophy, Visual cycle

Methanobactin rapidly facilitates biliary copper excretion in the LPP Wilson disease rat model visualised by 64Cu PET/MRI

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Background: Methanobactins (MBs) are peptides with very high copper affinity and can potentially treat Wilson disease (WD). We used 64Cu-PET/MRI to examine how two MBs (ARBM101 and MB-OB3b) affected in-vivo copper handling in the LPP WD rat model, compared to D-penicillamine (DPA) or saline. Heterozygotes served as controls.

Methods: 64Cu was administered i.v. to 19 LPP and 4 control rats. A baseline scan was performed one hour later. Then, LPP rats received one dose of saline, DPA, MB-OB3b or ARBM101 i.p., followed by a 90-minute dynamic scan and a final static scan 24 hours later. Controls followed identical procedures without i.p. injection. 64Cu levels were evaluated as the percentage of the injected dose (%ID) in the liver, kidney, and “abdominal-pelvic region” (colon, small intestine, and other non-hepatic, non-renal organs).

Results: At baseline, before intervention, hepatic %ID was 33.9±10.0% in untreated LPP rats and 21.6±1.7% in heterozygous controls (p=0.03). Abdominal-pelvic %ID was higher in controls, with no intraintestinal activity in LPP rats, indicating a loss of biliary excretion in LPP rats. After MB but not saline or DPA injection in LPP rats 64Cu was visible in the small intestines within 10-15 minutes. Hepatic 64Cu increased over 24H in saline and DPA-injected rats but decreased in control rats. ARBM101 almost normalised 24H hepatic 64Cu content relative to controls, while MB-OB3b had an intermediary effect.

Conclusion: A single dose of i.p. MB rapidly restored biliary copper excretion in LPP rats, suggesting a therapeutic potential. The effect was more pronounced with ARBM-101 than with MB-OB3b.

Themes: Gastroenterology and hepatology, Animal Models
Keywords: Rare disease, In-vivo animal experiment, Copper handling

SESSION 25 - Cancer 2

Predicting renal cell carcinoma outcomes with spatial transcriptomics

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Renal cell carcinoma (RCC) accounts for ~3 percent of diagnosed cancers, with the number of incidences rising globally. Clinical management of RCC is challenged by >30 percent of patients experiencing relapse after surgical removal of localized tumors and less than half of patients with metastatic disease respond to first-line treatments. Risk stratification is based on tumor stage and histological parameters, without guidance from molecular makers, although the predictive ability of single biomarkers and small panels has been studied extensively.

In this project, multiple tumor samples from 110 RCC patients with >5 years of follow-up will be analyzed with the CosMx molecular imager, resulting in the quantification of 6000 transcripts at the level of single cells. By combining semisupervised clustering and spatial information, maps of cell types will be made for each tumor sample. By training a machine learning algorithm to predict recurrence and response to treatments based on these maps, we hope to deepen the understanding of the molecular mechanisms that drive clinical outcomes and establish a novel method for patient stratification.

Themes: Cancer, Omics
Keywords: Renal cell carcinoma, Biomarkers, Spatial transcriptomics

Using CRISPR Cas9 as a shredding machine to target the repetitive elements that lie in the exclusively open chromatin areas in cancer

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CRISPR-Cas9, a versatile gene-editing tool, functions by precisely cleaving DNA at specific sites; however, its activity is impacted by the accessibility of target sequences within chromatin. In chromatin regions tightly bound by histones and other structural proteins, Cas9 is impeded by nucleosomes, hindering it from reaching and cleaving these sequences. Cancer cells, such as those found in multiple myeloma (MM), frequently display unique patterns of chromatin accessibility distinct from those in healthy cells. These differences arise due to cancer-associated epigenetic modifications and chromatin remodeling, which expose genomic regions that remain inaccessible in normal cells. Leveraging this differential chromatin accessibility, we propose targeting repetitive and transposable elements—DNA sequences often enriched in cancer-specific accessible regions. By directing Cas9 to these highly repetitive elements in MM cells, our aim is to induce extensive genome fragmentation, or "shredding," thereby triggering cell death. This approach is designed to selectively exploit the vulnerability of MM cells, with minimal impact on normal cells where these repetitive sequences are shielded by closed chromatin. Our project will evaluate the precision, efficacy, and specificity of Cas9-induced genome shredding in MM, validating chromatin accessibility as a selective marker and advancing a novel therapeutic avenue for targeting malignancies with distinct epigenetic landscapes.

Themes: Cancer, Genetic engineering
Keywords: , ,

Bortezomib-induced neuropathy detected with neurofilament light chain - a biomarker for axonal damage.

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Introduction: Multiple myeloma (MM) is a chronic cancer with a steadily increasing overall survival due to novel agents including the effective proteasome inhibitor bortezomib. The first in line treatment bortezomib is unfortunately associated with the risk of sensory and autonomic neuropathy and neuropathic pain. Chemotherapy-induced neuropathy (CIPN) is often diagnosed with a significant delay resulting in the risk of chronic neuropathy. Still no effective prophylactic nor treatment strategies are available.

Neurofilament light chain (NfL), a biomarker for axonal damage, has been associated with CIPN in both solid tumors and MM.

Aim: We aim to investigate the usefulness of NfL as a biomarker for early detection of bortezomib-induced neuropathy (BIPN) in MM patients.

Primary outcome: NfL increase after two cycles of chemotherapy compared to baseline in patients with BIPN compared to patients without BIPN

Material and methods: A follow up study of 40 newly diagnosed MM patients referred to bortezomib treatment. The patients will be evaluated at baseline and after 12 weeks regarding small and large nerve fiber neuropathy and NfL concentration in blood (Single Molecule Array (Simoa™)). Neurological evaluation includes symptoms (interview and questionnaires), signs (clinical neurological examination, Neuropathy Impairment Scale_lower leg (NIS_LL), mapping of allodynia, hyperalgesia and loss of sensibility) and confirmatory tests (DPN-check, intraepidermal nerve fiber density, thermal detection thresholds, sweat test)

Perspectives: Our findings will have impact on the ability to detect and minimize long-term complications and hereby improve the quality of life in patients with MM

Themes: Cancer, Neurodegenerative disorders
Keywords: Bortezomib-induced peripheral neuropathy, Multiple myeloma, Neurofilament light chain

Investigating the role of CD47 in Cancer Cachexia

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Cancer cachexia, a multifactorial metabolic syndrome affecting up to 80% of all advanced cancer patients, contributes to 20-30% of all cancer-related deaths. It is characterized by involuntary weight loss, which cannot be reversed by dietary support, and loss of skeletal muscle mass and strength. Despite its prevalence and impact on patients, cachexia remains underdiagnosed and understudied.

Our lab previously showed that elevated expression of CD47 in muscle stem cells (MuSC) of aged mice plays a role in the regenerative decline of skeletal muscle that accompanies aging. CD47hi MuSCs produce elevated levels of thrombospondin-1 (THBS1), which inhibits the function of healthy CD47lo MuSCs. Administrating anti-THBS1 antibodies inhibited the negative effect of CD47hi MuSCs, boosting the regenerative capacity of aged skeletal muscle.

Preliminary analysis in a model of pancreatic cancer showed elevated THBS1 levels in skeletal muscle. Hence, we hypothesized that THBS1/CD47 pathway could be dysregulated in the muscles of cachectic cancer patients, playing a key role in the development of cachexia. My research plan involves establishing a novel cancer cachexia model, by inoculating cancer cells into the pancreas of a healthy mouse using ultrasound-guided injection. This method could revolutionize the field of cachexia research by minimizing confounding factors and more accurately simulating the disease. Using this model we will test our hypothesis by targeting THBS1 and CD47 signaling using blocking antibodies, and simultaneously analyzing MuSC subset distribution, signaling responses and muscle function, using single-cell analysis at the protein level and strength assays.

Themes: Cancer, Omics
Keywords: Cancer-Cachexia, pancreatic cancer, Ultrasound-guided inoculation, Minimally invasive procedure, Thrombospondin-1, CD47, SIRP-alpha, Muscle stem cells, Myoblasts., CyTOF, FACS, qRT-PCR, Functional Muscle Assays,

Gene Therapy for Childhood Cancers Driven by Fusion Oncogenes

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Childhood leukemia frequently arises from cells harboring fusion oncogenes, with the most common rearrangements involving runt-related transcription factor 1 (RUNX1), RUNX1 translocation partner 1 (RUNX1T1), and histone-lysine N-methyltransferase 2A (KMT2A). KMT2A rearrangements are particularly prevalent in children under two years of age and associated with high relapse rates and poor long-term survival depending on fusion partner. Creation of the fusion oncogene is believed to be a primary event and thus, it is present in all malignant cells. Despite the critical role of the fusion oncogenes, there is a lack of targeted treatments in childhood leukemia. As the fusion oncogenes are both drivers of disease progression and are unique to the cancer cells, they act as ideal targets for therapeutic intervention. This PhD project aims to use CRISPR-Cas9 to inactivate the fusion oncogenes using a frameshifting dual-intron targeting approach. The fusion oncogene-specific CRISPR-Cas9 genome editing components are used to induce DNA double strand breaks, which will result in disruption of the fusion gene and subsequently inactivate the leukemia driver. For CRISPR-Cas9 delivery, lipid nanoparticles (LNPs) will be used, which is translational for in vivo applications. Our preliminary studies show that disruption of the RUNX1-RUNX1T1 fusion gene in primary patient cells is possible, and that LNPs can be used as a cargo carrier to deliver gene therapy to cells in vitro. This PhD project focuses on further developing this technology into a clinically available option for children with fusion driven leukemias.

Themes: Cancer, Paediatrics
Keywords: hematology, gene therapy, CRISPR

Glutamine Metabolism Fuels Oncolytic Virotherapy in KEAP1-mutant Lung Cancer

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Lung cancer is a leading cause of cancer death worldwide and often bear mutations in the NRF2 transcription factor or its repressor KEAP1. This causes constitutive activation of NRF2 which is associated with resistance to available treatments, emphazising the need of new therapeutic strategies. NRF2 is a major regulator of oxidative stress within the cell. Preliminary data indicate that KEAP1 mutant lung cancer cells are more susceptible to the oncolytic vesicular stomatitis virus Δ51 (VSVΔ51) and that these cells rely on glutaminolysis for proliferation.

We hypothesized that NRF2-mediated glutamine dependency in KEAP1 mutant lung cancer aids oncolytic virus replication. Combined RNAseq and ChIPseq analysis revealed NRF2's regulation of glutamine metabolism enzymes in A549 KEAP1 mutant lung cancer cells. A Seahorse assay indicated increased mitochondrial respiration in KEAP1 mutant cells compared to wild-type KEAP1 cells. VSVΔ51 susceptibility decreased when glutaminolysis was inhibited by pharmacological glutaminase inhibitors or by glutamine deprivation, but the latter could be reversed by addition of glutamine or partially by addition of alfa-ketoglutarate. Overall, these findings suggest VSVΔ51 relies on glutamine metabolism for replication in KEAP1 mutant lung cancer cells, though further research is needed to fully understand the mechanism.

Themes: Cancer, Infectious Diseases
Keywords: Oncolytic Virotherapy, Cancer, Metabolism

Pentose Phosphate Pathway Implication on Prostate Cancer Progression

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Prostate cancer (PCa) is the most common cancer amongst men, often manifesting as indolent disease not needing immediate treatment but can become aggressive. Understanding the transition from slow to aggressive cancer is crucial. A hallmark of cancer cells is their elevated metabolism, which supports the increased energetic and biosynthetic demands necessary for rapid proliferation. In our study, RNA sequencing analysis revealed that PCa cells exhibit a distinct metabolic profile compared to healthy controls, characterized by the upregulation of genes involved in the pentose phosphate pathway (PPP).

This project will explore the role of the PPP in prostate cancer using specific PPP inhibitors alongside treatments that lower glucose levels and PPAR inhibitors. The study will assess human and mouse prostate cells in vitro, with further investigation using a CRISPR mouse model of PCa to evaluate tumor progression and metastasis when targeting the PPP. Various techniques will be used to analyze molecular changes in tumor tissues, including transcriptional, mass spectrometry, and radiophotography, alongside classical histology, to understand how metabolic interventions hinder tumor growth. Results will be validated in human PCa samples.

Ultimately, this project aims to clarify the role of the PPP in prostate cancer and whether targeting it can prevent the transition from indolent to aggressive disease. If successful, this approach could provide a viable treatment for newly diagnosed PCa patients with low-risk disease, leveraging the well-tolerated nature of PPP inhibitors currently in clinical trials.

Themes: Cancer, Animal Models
Keywords: Prostate Cancer, Metabolism, Animal models

Feasibility of CSF acquisition and ctDNA nanopore sequencing for pediatric patients with CNS tumors in a population-based multicenter approach

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Approximately 60 children a year in Denmark gets diagnosed with a brain tumor. Brain tumors can cause severe damage before appropriate treatment can be started. The longer time passes, the greater is the risk of developing short or life-long neurological, cognitive and/or hormonal impairments, as well as the risk of disease progression, which can compromise the effectiveness of treatment and ultimately prognosis. However, appropriate treatment requires knowledge of the precise molecular diagnosis of the tumor. Currently, tumor tissue obtained during surgery is required for diagnosis. With currently established molecular diagnostic methods, it takes 14 (or more) days after surgery to obtain a diagnostic result.

Previous studies have shown the feasibility of circulating tumor DNA (ctDNA) detection in spinal fluid (CSF) from patients with brain tumors. Detection of ctDNA withholds the potential of diagnosis and improved disease monitoring, which would be significant for clinical management. We have collected CSF from patients with CNS tumors since January 2021 and the aim of our project serves two purposes: Firstly, we aim to establish an overview of the number of patients enrolled in the project and ascertain the subset from whom cerebrospinal fluid (CSF) samples have been collected. We will evaluate the role of sampling and processing for the effectiveness of ctDNA. Secondly, we will evaluate if Nanopore sequencing of ctDNA in CSF can be used as a faster diagnostic tool in children with malignant brain tumors.

Our goal with this project is to improve diagnostic and clinical care for Danish children with brain tumors.

Themes: Cancer, Paediatrics
Keywords: , ,

Exploring Rock1 activation in invasive Nf1-deficient Glioblastoma

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Glioblastoma (GBM) is the most prevalent and aggressive brain tumor in adults, that is considered incurable. Neurofibromin (NF1) is lost in 14% of GBM cases, often associated with the mesenchymal subtype and features resembling epithelial-mesenchymal transition (EMT) and diffuse morphology.

This study investigates the mechanisms underlying the diffuse morphology in NF1-deficient GBM. Using CRISPR-induces murine models with mutations in Pten, P53, and either Rb1 or Nf1, tumors were generated, revealing that Nf1-deficient tumors exhibited a more diffuse phenotype than those deficient in Rb1.

An unbiased kinase screen showed elevated Rock1 activity in NF1-deficient tumors, hinting that Rock1's known role in migration might drive the diffuse phenotype. To investigate this, CRISPR models with Pten, P53, Nf1, and Rock1 deficiencies were created, resulting in tumors with denser cores, reduced diffuse regions, and increased survival. Single-cell RNA sequencing revealed clusters of immune, stromal, and tumor cells, with a specific tumor cluster (Tumor 2) involved in migration to be reduced in Rock1-deficient tumors. This suggests that Rock1 influences migration and the diffuse phenotype in GBM.

Ongoing work established primary cell lines with loss of Rock1 in a Nf1 deficient background. Preliminary data from in vivo engraftment confirms findings from the CRISPR model as loss of Rock1 results in a dense tumor and increase survival. Furthermore, focus on Periostin and cross-talk to the microenvironment is in focus as the single-cell data analysis reveals a possible connection.

Themes: Cancer, Animal Models
Keywords: Glioblastoma, CRISPR-induced murine models, scRNA sequencing

The Usefulness of Circulating Fibrosis Markers in Detection of Carcinoid Heart Disease in Patients with Neuroendocrine Tumors

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Background: Carcinoid heart disease (CHD) is a potential serious fibrotic complication in patients with neuroendocrine tumors (NETs), affecting the heart valves. Transthoracic echocardiography (TTE) is the gold standard for diagnosis. Early detection is crucial to avoid severe manifestations; however, no available biomarkers perform well as screening tools. We aimed to investigate circulating fibrosis markers as a screening tool in detection of CHD.

Methods: We included patients with disseminated small-intestinal NET at risk of having CHD. We performed TTE for the diagnosis of CHD, and we drew blood samples for measurement of different circulating fibrosis markers (CALC2, MIM, PRO-C3, PRO-C6, TIM, C2M, C3M, C6Ma3). The area under the receiver operating characteristic (AUROC) curve was calculated to evaluate the fibrosis markers as a screening tool for detection of CHD.

Results: Ninety-eight (98) patients were included in the study of whom 16 (16%) had CHD. Levels of the specific fibrosis marker, PRO-C3, were significantly increased in patients with CHD compared to patients without CHD (127 ng/ml (102 – 158) vs. 94 (82 – 115), p = 0.002). The AUROC for PRO-C3 for detection of CHD was 0.77 (95% CI: 0.64 – 0.90).

Conclusion: PRO-C3 demonstrated good performance in detection of CHD, outperforming the currently recommended screening biomarker, NT-proBNP. However, as an initial screening tool to determine whether patients should undergo TTE, PRO-C3 cannot stand alone.

Themes: Gastroenterology and hepatology, Cancer
Keywords: Neuroendocrine tumors, Fibrosis, Biomarkers

SESSION 26 - Public health 2

Accelerometer-Measured Physical Activity in the First Year Postpartum: A systematic review

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Background: Physical activity (PA) plays a significant role in women's health. However, there is limited knowledge on the levels of PA among women during the postpartum period. Therefore, the aim of this systematic review was to describe women's moderate to vigorous physical activity (MVPA), measured in minutes per day or minutes per week, using accelerometers, from delivery to one year postpartum.

Methods: A systematic search of Embase and PubMed was conducted on the 16th of Marts 2023. Title, abstract and full texts articles were screened by the author. MVPA from all included studies was extracted, and studies defining MVPA by counts per minute (cpm) were presented separately from those using other definitions.

Results: After screening 1126 studies, 11 studies were included. Six studies reported MVPA defined by cpm, measured at different time points within a postpartum timeframe from 1.5 to 12 months. The cpm-defined-MVPA ranged from 6.9 to 44.7 minutes per day. Five studies reported MVPA that was not defined by cpm, measured at different time points from 0 to 7 months postpartum. Non-cpm-defined MVPA ranged from 8.4 to 87.1 minutes per day.

Conclusion: Preliminary findings suggest a slight tendency for MVPA to increase from early to late postpartum period, but further studies are necessary to explore and validate this trend. The comparability of outcomes across studies is challenging due to the lack of consensus, mainly on definitions and cut-off points for MVPA. More studies investigating objectively measured PA postpartum are needed to expand our knowledge in this subgroup of the population.

Themes: Public health, Gynecology and obstetrics
Keywords: Postpartum, Physical activity, Accelerometry

Pre-Pregnancy Weight Loss and Reducing Childhood Overweight

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Introduction:

The prevalence of overweight in women of childbearing age has risen significantly. Children born to overweight mothers are at higher risk of obesity, perpetuating an intergenerational cycle. Breaking this cycle is crucial for preventing obesity and related health issues in future generations.

Methods:

The PREPARE CHILD AUH study is a randomized controlled trial at Steno Diabetes Center Aarhus, recruiting 140 healthy overweight couples (BMI 27-45 kg/m²) planning another child within three years. Couples are followed from the current pregnancy to the birth of their next child and randomized into intervention and control groups. The intervention group receives dietary counseling and participates in physical activity, aiming for a 10% weight loss between pregnancies.

Primary outcomes include neonatal fat mass (PEA POD) and epigenetic changes in cord blood. Secondary parental outcomes include glucose metabolism, body composition (DEXA), VO2 max, and energy expenditure. For offspring, secondary outcomes are glucose metabolism, skinfold thickness, and cardiac function (echocardiography).

Results:

Recruitment began on June 9th, 2023, with 31 couples enrolled until now. No results are available yet, but the study design and methodology will be presented.

Conclusion:

The PREPARE CHILD study seeks to demonstrate the impact of a healthy lifestyle on maternal, paternal, and fetal health, aiming to prevent childhood obesity and improve long-term health outcomes across generations.

Themes: Public health, Gynecology and obstetrics
Keywords: Pregnancy, Lifestyle, Obesity

Parental or child neurological conditions as predictors or risk factors for physical child abuse

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Background: In Denmark, child abuse is prevalent among 22% of the child population, yet only 1% are formally diagnosed. Identifying risk factors for child abuse is crucial for improving our ability to identify and predict it. Few studies have explored the correlation between neurological conditions and physical child abuse. A recent study indicates epilepsy in parents as a possible risk factor, but there is a need for further knowledge. This study aims to predict physical child abuse among parents and children with neurological conditions, to facilitate the provision of preventive measures and early intervention.

Method: The project comprises three individual studies, initially conducting a systematic review to evaluate the association between paediatric traumatic brain injury, including abusive head trauma, and neurological conditions or sequelae, both pre-existing and those arising subsequently. The following studies will analyse diagnostic codes for neurological conditions and abuse, sourced from registers and the Police Victim Register. Additionally, self-reported physical abuse will be assessed through questionnaires distributed to 280.000 young adults aged eighteen to twenty-one.

Conclusion: This project will comprehensively assess a diverse range of data, significantly contributing to understanding parents and children with neurological disorders and identifying their risk of physical child abuse. This will enable proactive prevention and early intervention measures.

Themes: Public health, Paediatrics
Keywords: Child Abuse Risk Factors (Forensic Medicine), Social and Neuropediatrics, Neurological conditions

The impact of infection status on reported symptoms, post-acute sequelae, and long-term sick leave

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Background: Data comparing long-term sick leave and other key sequelae of COIVD-19 to other infections is limited. One study found higher rates of returning to work after hospitalization with influenza than COVID-19. There are no similar studies of non-hospitalized populations and therefore those with less severe acute infections who comprise the majority of those with chronic post-acute sequelae, often referred to as Long COVID, are not found.

Aim: Investigating the association between infection status on long-term sick leave and the occurrence of symptoms.

Method: The study will use data from the BiCoVac cohort, a Danish population-based cohort that collected information with four questionnaires between May 2021-July 2022 including self-reported information on COVID-19, other infections, and symptoms using the 25-item Bodily Distress Syndrome checklist. Linkage to national registers will be used to gather additional information on COVID-19, sick leave, and covariates.

The association between infection status and symptoms will be assessed in each follow-up questionnaire using a cross-sectional design, while the investigation of sick leave will be conducted as a prospective cohort design.

We will use multiple logistics and linear regression to compare the exposure groups according to reported symptoms. Sick leave will be handled as time-to-event data. All models will be adjusted for confounders for each exposure-outcome relationship. Inverse probability weights will be employed to address potential selection bias.

Results: Pending

Perspective: Using data from the COVID-19 epidemic is important as previous knowledge on long-term effects of infections is scarce.

Themes: Public health, Epidemiology
Keywords: COVID-19, Post-acute sequelae, Sick leave

Navigating Relief: A Comprehensive Scoping Review of Mechanisms of Change in Interventions for Low Back Pain in Primary Care

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Introduction: LBP is the most frequent reason for Danes to seek healthcare in general practice. International guidelines recommend optimized treatment strategies focusing on early identification and adequate patient education of people with LBP. High workload and little available time challenge the delivery of guideline-concordant treatment in general practice. Trained physiotherapists (PT) could assist General Practitioners (GP) in early application of guideline-concordant bio-psycho-social approaches in primary care. This scoping review aims to elucidate the proposed mechanisms of change underlying various interventions for low back pain provided by physiotherapists or similar healthcare professionals in general practice and in other primary care settings.

Methods: A scoping review will be performed, including a systematic literature search in Embase, PEDro, Medline, CINAHL, Academic search premier, PsycINFO, and SPORT Discus. The following inclusion criteria will be used: Adults with LBP, interventions in any primary care setting. Studies describing LBP secondary to cancer, infections, fracture, trauma, back surgery or inflammatory diseases will be excluded. The data extraction form includes study characteristics (author(s), source of origin, aims, population, intervention, and method), descriptions of proposed mechanisms of change and information on how an article contributes with knowledge.

Interpretation: Findings will identify how individuals or systems interact with intervention activities to produce intended or unintended outcomes varying depending on the context. The findings will be used to inform a co-creation study aiming to develop an early intervention.

Themes: Public health, Health Education
Keywords: Low Back Pain, Complex intervention, General practice

Long COVID – sick leave, predictors for return to work and societal costs

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Background: The COVID-19 pandemic has led to a new group of patients with post-viral syndrome; patients with long COVID. While most COVID-19 patients fully recover, some experience prolonged symptoms affecting daily functioning and work participation, with personal and societal impact. Identifying predictors for non-return to work is essential for effective rehabilitation and preventing labour market marginalisation.

This project aims to explore how long COVID impact patients work life, identifying factors associated with non-return to work and evaluate the societal costs of long COVID.

Methods: The project includes three register-based studies:

1) A nationwide prospective cohort study of ~ 8000 individuals (age 18-60) with long COVID will investigate associations between socio-demographics, sick leave and return to work, and analyse the duration of sick leave.

2) A prediction study using a retrospective cohort of 750 patients examined at the Long COVID Clinic, Aarhus University Hospital will explore the degree to which socio-demographics, sick leave, and patient-reported-outcomes (PRO) contribute to the prediction of return to work.

3) A nationwide cost-of-illness study will evaluate direct and indirect costs of long COVID compared to the general population.

Perspectives: The results will provide important insight for managing post-infectious conditions across patient groups and will assist clinicians identify patients at risk for non-return to work, supporting tailored rehabilitation, and reducing labor market exclusion. The evaluation of the economic burden is of major importance in the policy decision making when allocating resources.

Themes: Public health, Infectious Diseases
Keywords: Long COVID, Return to work, Rehabilitation

Communication as a contributing factor to adverse events after tele-triage in out-of-hours primary care in Denmark: a register-based case-control study

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Background: The triage process in out-of-hours primary care is challenging and vulnerable as both measures of safety (i.e. identifying patients in need of acute care) and efficiency (i.e. giving patients the lowest effective level of care) must be sufficient despite limited knowledge of the patient. Additionally, the health professional has no or limited visual cues. Thus, the most important diagnostic tool in tele-triage is medical history-taking, which relies mostly on verbal communication with the patient. Consequently, inefficient or faulty communication may result in adverse events (AEs) if critical conditions are overlooked and undertriaged.

Aim: The study aims to investigate what goes wrong in the dialogue in calls that are followed by adverse events.

Methods: The study will be conducted as a case-control study investigating the quality of communication in recorded audio files from out-of-hours tele-triage contacts ending in adverse events, i.e. safe vs. unsafe tele-triage contacts.

Perspectives: The findings provide new insight into communication failure in tele-triage and thus better training of triage professionals, reducing mortality and long-term sequelae.

Themes: Public health, Health Education
Keywords: Out-of-hours primary care, Doctor-patient communication, Triage

A realist process evaluation of a rehabilitation intervention for patients with long COVID in a Danish setting

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Background: Following the COVID-19 pandemic, a new group of patients with post-viral syndromes have emerged: those with long-term symptoms after COVID-19 (long COVID). They may experience impaired daily functioning, leaving them with a distinct rehabilitation need. Knowledge on how the rehabilitation works, for whom and under which circumstances is scarce. Thus, the aim of the study was to evaluate the processes of a long COVID rehabilitation intervention in Denmark by exploring its implementation, and explore the interactions between the mechanism of impact, the context and outcomes of the intervention to confirm or refine the initial programme theory.

Methods: This mixed-methods study using quantitative and qualitative data followed the Medical Research Council's framework for conducting process evaluations. This framework led the evaluation of the implementation components. Using a realist perspective, Context-Mechanism-Outcome configurations explored the interactions between impact mechanisms, context and outcomes to validate or refine the programme theory.

Quantitative data included patient records detailing rehabilitation services received and questionnaires covering demographics, mental fatigue and functioning at enrollment. Qualitative data comprised interviews with healthcare professionals and 12 participating patients.

Results: The study is ongoing, and results will be presented on the PhD Day.

Perspectives: By exploring how the rehabilitation intervention works, for whom and under which circumstances, the study offers an opportunity to provide a foundation for optimising rehabilitation strategies for patients with post-viral syndrome.

Themes: Public health, Rehabilitation
Keywords: Long COVID, Complex interventions, Process evaluation

Does short-term exposure to PM2.5 concentration effect the transient risk of Myocardial Infarction?

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Research on the association between short-term ambient PM2.5 (particulate matter less than 2.5 µm in aerodynamic diameter) exposure and myocardial infarction (MI) has yielded inconsistent results. These findings are often limited by a common issue: low-resolution exposure measurement. Recent studies suggest that stratifying by MI type—ST-elevation myocardial infarction (STEMI) versus non-ST-elevation myocardial infarction (NSTEMI)—is essential, as findings indicate a positive association between STEMI risk and ambient PM2.5 concentrations, while no such association is found for NSTEMI. However, much of the existing literature does not examine the effect of this stratification.

The Danish health registries, combined with high-resolution air pollution metrics, provide a state-of-the-art framework for examining the association between short-term ambient PM2.5 exposure and MI risk. Specifically, the Western Denmark Heart Registry allows for clinical stratification between STEMI and NSTEMI patients, while the Urban Background Model provides exposure estimates on a 1 x 1 km grid with daily averages. For this study we will use a case-crossover design, which matches MI cases with control days from the same individual's recent history.

This study intends to investigate whether ambient PM2.5 concentrations in the four days preceding an MI event are associated with an increased risk of MI.

A sensitivity analysis will explore whether other pollutants, including NO2, NOx, CO, PM10, O3, EC, OC, SO2, NH3, SOA (secondary organic aerosol), SIA (secondary inorganic aerosol), and sea salt, confound or interact with the association between PM2.5 and MI.

Themes: Public health, Epidemiology
Keywords: Air Pollution, Myocardial Infarction, Case-Crossover

"Catastrophic Health Expenditures: Evaluating the Effectiveness of Nepal's National Health Insurance Program Using Propensity Score Matching and Doubly Robust Methodology"

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Introduction: Catastrophic health expenditure (CHE) is a critical issue in low- and middle-income countries like Nepal, exacerbating financial hardship among vulnerable households. This study assesses the effectiveness of Nepal's National Health Insurance Program (NHIP), launched in 2016 to reduce out-of-pocket (OOP) healthcare costs and mitigate CHE.

Methods: Conducted in Pokhara Metropolitan City, the study used an analytical cross-sectional design, sampling 1276 households through a two-stage random sampling method. Data was collected via face-to-face interviews between May and October 2023. The analysis used SPSS version 29, incorporating propensity score matching (PSM) to minimize biases and create comparable groups of enrolled and non-enrolled households in the NHIP. A 1:1 matching process resulted in a sample of 1,068 households, with 534 from each group. Additionally, a doubly robust methodology was employed, combining propensity score adjustment with regression modeling to enhance the reliability of the results.

Results: Among the 1276 samples, 534 households (41.8%) were enrolled in NHIP. Of them, 84.3% of households renewed their insurance card, though some cited long waiting times, lack of medications, and complex procedures as barriers to renewal. Approximately 57.3% of households reported known diseases before enrollment. The data indicates that 12.5% of enrolled households experienced CHE versus 9.2% among non-enrolled. Enrolled households incur higher mean out-of-pocket expenditures (OOPE) across all categories, especially for non-communicable diseases (NCDs) (NRS 2639.5 vs. NRS 1399.2), with a median lower than the mean, indicating that a small number of households face exceptionally high costs. Enrollment into NHIP does not contribute to lower CHE (AOR: 1.22, 95% CI: 0.79-1.87). Key factors associated with increased CHE risk were the presence of NCDs (AOR: 3.27, 95% CI: 1.62-6.59), the presence of diabetes (AOR: 1.87, 95% CI: 1.15-3.03), heart disease (AOR: 3.80, 95% CI: 2.19-6.60), acute illnesses/injuries (AOR: 4.90, 95% CI: 3.08-7.82), presence of elderly members (AOR: 1.84, 95% CI: 1.12-3.02), and households below the poverty line (AOR: 2.36, 95% CI: 1.19-4.68). Other factors such as gender, education level of household head, caste/ethnicity of family, household size, and under-five children were statistically insignificant. If the NHI benefits package threshold

were increased from the current NRS 100,000 to NRS 200,000, 5.4% of enrolled households and 3.4% of non-enrolled households could have avoided CHE.

Discussion and conclusion: The study concludes that enrollment in the NHIP does not significantly reduce the risk of CHE. This could be because of inadequate coverage, where high-cost medicines, treatments, and transportation costs are not fully included in the insurance package, leading to significant out-of-pocket expenses. We also considered the long waiting time, lack of medicines, and complex procedures for utilizing NHIP benefits, which might result in underusing covered services. Finally, gaps in enrollment and retention might leave certain households vulnerable to CHE. It is recommended that NHIP benefits and coverage be expanded to better protect against high healthcare costs. Policymakers should focus on expanding coverage, streamlining administrative procedures, and removing barriers to healthcare access, especially for costly treatments and NCDs.

Themes: Public health, Public health
Keywords: Catastrophic Health Expenditure, National Health Insurance Program, Nepal

SESSION 27 - Health statistics

Strategies for defibrillation during out-of-hospital cardiac arrest (STRAT-DEFI)

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Out-of-hospital cardiac arrest affects 5000 people annually in Denmark. Patients with shockable rhythms have better outcomes, but 75% do not respond to initial defibrillation, with only 1 in 5 surviving after 30 days. Despite these poor outcomes, defibrillation methods have remained largely unchanged for 50 years, highlighting the need for new approaches.

Current guidelines recommend placing defibrillation pads in an anterior-lateral position. Alternative strategies can be considered for patients with refractory shockable rhythms. One method involves repositioning the pads to an anterior-posterior placement. Another approach, double sequential defibrillation, uses two separate defibrillators to deliver two shocks in quick succession. A recent trial suggested improved survival rates with these methods, but limitations have sparked skepticism.

Conducted nationwide in Denmark with international collaboration, this investigator-initiated, randomized trial will involve adults in non-traumatic cardiac arrest after one defibrillation attempt, when two defibrillators are available. Randomization will occur on-site.

This trial aims to compare anterior-posterior defibrillation and double sequential defibrillation against standard anterior-lateral defibrillation in patients with refractory shockable rhythms during out-of-hospital cardiac arrest. The primary outcome is 30-day survival, with secondary outcomes of 90-day survival and neurological status at 30 and 90-days.

The trial will include 909 patients and is set to begin in early 2025, with a three-year inclusion period. This trial could significantly influence future international cardiac arrest guidelines.

Themes: Cardiology, Statistics
Keywords: Out-of-Hospital Cardiac Arrest, Randomized Clinical Trial, Defibrillation

Colorectal Cancer ctDNA Detection Using a Statistical Model of Nucleotide Variant and Indel Error Rates

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Background: Circulating tumor DNA (ctDNA) is a promising biomarker for monitoring tumor burden in cancer patients, but its low abundance—especially in early-stage cancers—poses significant detection challenges. This study evaluates ctDNA detection methods using deep targeted panel sequencing data, comparing the performance of two algorithms: DREAMS and Shearwater. Both methods assess nucleotide mismatches using error models. DREAMS employs a neural network to predict mismatches based on an extensive set of features and has been extended to detect insertions and deletions (indels). Shearwater, originally designed for detecting low-frequency cancer variants, utilizes error frequencies derived from a panel of normal samples. We adapted Shearwater for ctDNA detection by integrating evidence across multiple variants and including indels.

Methods: Performance was assessed using synthetic data and deep targeted sequencing data from pre-operative plasma samples of colorectal cancer (CRC) patients. The training cohort included stage I–IV CRC patients (n=126) and controls (n=37), while the validation cohort comprised stage I–III CRC patients (n=255) and controls (n=24).

Results: Initial results on synthetic data at six different allele frequency ranges shows that DREAMS and Shearwater both achieve an Area Under the Curve (AUC) exceeding 0.95 in the Receiver Operator Characteristics (ROC) curve down to an allele frequency of 0.05%. At all allele frequency ranges DREAMS obtains higher AUC values for the ROC curve compared to Shearwater.

In the training cohort, both DREAMS and Shearwater currently achieve an AUC of 0.90 and a sensitivity of 80% at 95% specificity in ctDNA detection. Ongoing optimization of DREAMS—including enhancements to its neural network architecture and the incorporation of additional features—is expected to further improve its performance.

Conclusion: Both DREAMS and Shearwater demonstrate strong performance in distinguishing cancer patients from controls using deep targeted sequencing data. While their current performances are comparable, the continued optimization of DREAMS, particularly through enhancements to its neural network architecture, is likely to yield further improvements.

Themes: Cancer, Statistics
Keywords: ctDNA detection, Cancer genomics, Deep Learning

Compensation claim patterns in out-of-hours primary care services

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Background: The out-of-hours primary care (OOH-PC) services in Denmark handle approximately 1.9 million telephone contacts annually. Tele-triage is one of the most challenging parts of OOH-PC. It holds a high risk of adverse events (AEs) with detrimental effects. Patients experiencing suboptimal care in the Danish healthcare system have the option to file a compensation claim. These claims often stem from AEs were patients believe the harm could have been prevented. However, studies indicate that only a small fraction of eligible patients actually file a claim, with socially deprived patients being particularly underrepresented among claimants.

Aim: We aim to analyse compensation claims to categorise the types of issues identified in patient claims related to AEs following contact with OOH-PC services.

Methods: We will conduct a retrospective cohort study of 1,164 patients who filed a claim for compensation following a tele-triage contact with OOH-PC during 2019-2024. Compensation claims will be categorized using the Healthcare Complaints Analysis Tool: domains, problem categories and sub-categories.

Results: We will use descriptive statistics to describe compensation claims. Accepted and denied cases will be compared to estimate changes in severity and compensation claim patterns.

Perspectives: Insights from this study will provide new knowledge on compensation claim patterns in OOH-PC.

Themes: Public health, Statistics
Keywords: , ,

Advancing Forensic Analysis: A Machine Learning Approach to Estimating Blood Sample Time-of-Deposition

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Violent crime scenes frequently contain blood evidence crucial for investigative processes. Identifying the individual source of a blood sample is a standard procedure in forensics; however, determining the exact time the blood was deposited (time-of-deposition, or TOD) can be equally important for accurately contextualizing the evidence. Currently, no routine forensic methods exist for reliably determining TOD in blood samples.

The TraceAge project addresses this gap by developing a predictive method for TOD estimation using chemical analysis of blood, enhanced by machine learning (ML) models. The method relies on liquid chromatography-mass spectrometry (LC-MS), an analytical technique that separates and quantifies the compounds within samples with high precision and sensitivity. As blood is exposed to the atmosphere it undergoes changes in its chemical composition – this change can be profiled by LC-MS and the temporal profile of the blood can be correlated to the elapsed time.

The chemical data was used to develop both a LASSO regression model, that relies on simple linear regression principles, along with a more flexible Random Forest algorithm model. The LASSO model ultimately had the highest prediction accuracy, achieving an impressive RMSE of 13.11 hours and an R2 of 0.87. Additionally, the LASSO is much more interpretable than the Random Forest model, which makes the LASSO model much more suitable for use in legal courts. Further refinement of these models could in the future equip forensic investigators with a valuable tool for a currently unresolved aspect of criminal investigation.

Themes: Omics, Statistics
Keywords: , ,

Principled normative modelling of brain functional connectivity predicts the future development of brain pathology

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Many brain diseases and disorders lack objective measures of brain

function as indicators of pathology. The search for biomarkers is complicated by the fact that it is the interplay between multiple brain regions rather than properties of individual regions that is often affected. Furthermore, the conditions are often described as a spectrum from normal to abnormal rather than a sick-healthy dichotomy. Recently, normative modelling has emerged to characterize the normal variation of brain measurements given sex and age. Abnormalities are then identified as deviations from the distribution of normal brain measures. In fMRI studies, brain function is often assessed as functional connectivity (FC), which is calculated as the correlation matrix of activity between brain regions or networks. Normative modelling of FC requires a large, healthy population and a method to predict FC from sex and age. However, predicting FC is challenging because of its mathematical structure and high dimensionality. Current normative modelling studies have mainly focused on predicting the individual elements of the FC rather than as a whole. Here, using resting fMRI data from the UK Biobank, we adapt a newly developed method from statistics literature to find projections of FC that depend on sex and age. Using this approach, we identify two sex- and age-dependent projections, which successfully characterize the normal range of FC. Subjects with Parkinson's disease or bipolar disorder were significantly more likely than healthy subjects to be deemed abnormal even on scans up to 5 years before being diagnosed, which shows the potential of the method as a brain function biomarker.

Themes: Neuroscience, Statistics
Keywords: fMRI, Normative modelling, Machine learning

time-resolved in-vivo dosimetry during electron beam FLASH with a fibre-coupled inorganic scintillator-based detector system - **CANCELLED**

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Aims: An inorganic scintillator-based detector system was previously developed for time-resolved in-vivo dosimetry in murine proton FLASH studies, this has been adapted for similar studies using pulsed electron beam FLASH. The system can handle the high instantaneous dose rates of e FLASH and perform dose-per-pulse (DPP) measurements. This study presents the first in-vivo results with this adapted detector system.

Methods: The detector had two probes, each with a 1mm3 ZnSe:O crystal and a 0.5mm diameter optical fibre. The light was recorded by a Si-photomultiplier and read out at 40MHz, ensuring >100 samples per pulse.

Detector response was characterised with UHDR beams with DPP ranging from 0.02–1.16Gy/pulse and 2.5–4μs/pulse. The detectors were validated against a calibrated current transformer.

In the murine studies, the detectors were placed on the target, which was irradiated in water with 1.16Gy/pulse beams. For 124 mice receiving 10.5–22 Gy, integrated detector signals were compared with doses derived from the current transformer.

Results: Afterglow in the ZnSe:O crystal (τ=6μs) resulted in a distinct tail in the detector signal not present in the actual beam pulse shape . Despite this shape distortion, the integrated DPP signal was linear up to 0.4Gy/pulse with saturation starting above.

The in-vivo measured integral signals had a good linear correlation with the doses derived from the current transformer.

Conclusion: The adapted system was used for in-vivo dosimetry in murine experiments, providing in-vivo monitoring of both DPP and total dose for each mouse.

Themes: Cancer, Statistics
Keywords: Dosimetry, FLASH radiotherapy, in-vivo study

Navigating Transitions of Care: Construct Validity of PACT-M and CTM-15 in a Danish healthcare setting

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Background: Transition of care from hospital to home is a complex process involving significant patient safety risks. Comprehensive measures that incorporate patient perspectives are needed to better identify patients at high risk of facing suboptimal transitions. Patient-reported experience measures (PREMs) are questionnaires that offer insights into how patients experience healthcare service. This study aimed to assess the construct validity of the two PREMs: Partners at Care Transitions Measure (PACT-M) and Care Transitions Measure 15 (CTM-15) in a Danish healthcare context.

Methods: Patients hospitalised in two Danish regional hospitals due to an acute, medical condition were included in a cohort study. Baseline data, including age, gender, cohabitation status, health literacy, health-related quality of life and frailty, were collected at the hospital. Following discharge, the patients completed the two PREMs. Construct validity were assessed by confirmatory factor analyses, and factor loadings were evaluated. Furthermore, a priori hypotheses about the scores of the PREMs and selected baseline measures were tested. Internal consistency was assessed by calculating Cronbach's alpha.

Results: Data collection is ongoing and is expected to end by November 2024. Preliminary results will be presented at PHD Day 2025.

Perspectives: The validated PREMs are expected to improve transitions of care by being integrated into the monitoring of transitions, serving as indicators in research projects and improvement initiatives, and enabling cross-national comparisons. Additionally, they are anticipated to help identify patient groups at risk of adverse events thereby enhancing patient safety.

Themes: Epidemiology, Statistics
Keywords: Patient-reported experience measures, Validation, Sector transitions

Inducing Self-Related Emotion Evaluation by Modulation the Speaking voice (SEEMS)

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Recent behavioral studies using real-time acoustic feedback manipulation reveal that subtle shifts in the emotional tone of one's own voice can influence the speaker's mood, but only when the speaker remains unaware of the manipulation. This suggests that these effects rely on self-referential cognitive processes. We aim to study the brain mechanisms involved in this cognitive process with a fMRI study.

We collected fMRI data from 70 participants reading passages designed to be neutral in valence but varying in arousal. Participants wore active noise-cancelling microphones and headphones, with their voice manipulated through software (DAVID) to create three conditions: (1) unchanged voice, (2) a tone resembling smiling, or (3) a tone resembling sadness. After each passage, participants rated their emotional state on a valence-arousal scale to identify emotional responders. Explicit detectors, aware of the manipulation, were identified via an interview post-experiment, while implicit detectors were identified through compensatory pitch responses without conscious awareness.

Preliminary results reveal both responders and detectors in our data. Interestingly, responders exhibited overlapping emotional effects across different manipulations. Initial fMRI data suggest involvement of brain areas related to self-processing, acoustic perception, and emotion, mediating the emotional feedback effect. Final analysis will consider order effects and classifications of responders and detectors, leading to recommendations for optimizing design and stimulus presentation, including improved scanner noise cancellation.

Themes: Neuroscience, Statistics
Keywords: emotion, vocal feedback, self-perception

Cancer Risk in Individuals with Neurofibromatosis 1 – A Danish Nationwide Cohort Study with Long-term Follow-up

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Background: A limited number of population-based studies with long follow-up periods have assessed cancer risk in neurofibromatosis 1 (NF1). This study aimed to evaluate the cancer risk including overall cancer risk, risk of specific cancer types, and subsequent cancers.

Methods: The NF1 cohort included 2053 individuals identified in the Danish National Patient Registry and a clinical database matched to population comparisons without NF1 in a 1:10 ratio on the date of NF1 diagnosis. Study participants were linked to the Danish Cancer Registry to obtain cancer information. We calculated cumulative incidences of first and second cancer in the cohort born from 1971-2020 and for adult-onset cancer types in individuals born 1951-2020. We used multistate models to estimate the probabilities of being in different health stages (cancer-free, one cancer, ≥two cancers, dead) at age 50 years.

Findings: The study population was followed up to 71 years from birth. The 50-year cumulative incidence of any first cancer was 27.2% (95% CI 23.1–31.4) for individuals with NF1 and 5·0% (4.0–6.0) for population comparisons, with 21.2% (14.5-27.9) of those with NF1 and 6.4% (0.0-15.0) of the comparisons diagnosed with a second cancer 20 years after the first. The breast cancer risk was not significantly different. A person born with NF1 had a 69.8% (65.6-74.2) probability of being alive and cancer-free at age 50 compared to 93.5% (92.4-94.6) for a person without NF1.

Interpretation: This study illustrates the elevated cancer risk in NF1 and presents novel findings with potential implications for clinical management. Further research on post-cancer survival is essential to guide screening decisions.

Themes: Cancer, Epidemiology
Keywords: Neurofibromatosis 1 (NF1), Cancer risk, Cohort study

SESSION 28 - Diagnostics and technology

A study in healthy volunteers to help victims of nitrous oxide related crimes

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Nitrous oxide (N2O), colloquially known as laughing gas can cause analgesia, sedation and euphoria when inhaled. It is used for medical purposes, particularly in obstetrics, but it is also used recreationally. However, its role in criminal contexts remains poorly understood due to challenges associated with detecting N2O in biological samples, which include an apparent lack of metabolites and short half-life. Currently, prosecution of N2O related traffic crimes is not feasible in a judicial setting. This randomized, participant-blinded, placebo controlled clinical trial aims to address these challenges. Participants will be exposed to either placebo or N2O. Blood, exhaled air, oral fluid and urine will be collected and analyzed using Headspace-gas chromatography/mass spectrometry. A proprietary handheld nondispersive infrared N2O sensor will be tested, akin to law enforcement's well known alcohol breathalyzer. A reference interval for N2O exposed and non-exposed individuals will be established. N2O induced vitamin B12 associated metabolic changes will be explored as a potential diagnostic marker for N2O exposure. Additional exploratory metabolomics analysis on blood and urine will be performed using ultra-performance liquid chromatography high-resolution time-of-flight mass spectrometry. Improved understanding of N2O pharmacokinetics and exploration of non-conventional forensic biological matrices, such as exhaled air, for the detection of N2O are necessary to enable law enforcement to improve traffic safety in society.

Themes: Pharmacology, Diagnostics & technology
Keywords: Forensic toxicology, ,

Validation of a Reversible Kinetic Model for 20-min Dynamic Whole-Body PET Imaging of the Total Distribution Volume

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Purpose: Dynamic whole-body(D-WB) PET/CT allows for parametric imaging with the irreversible Patlak model, but many organs require a reversible model for physiologically meaningful parametric imaging. The current reversible Logan Model(LM) requires complete dynamic blood- and tissue data to estimate the total distribution volume(Vt), which restricts Vt imaging to the scanner's axial field-of-view(FOV) and necessitates a 70-min dynamic PET scan. This study validates a novel reversible Delayed Logan Model(DLM), only requiring data from 50-70 min post injection(p.i.) and a scaled population-based input function(sPBIF).

Methods: The DLM was validated using 50 patients examined with 18F-FDG using a D-WB 70-min protocol on a PET/CT scanner (26.3cm FOV, 214ps TOF). A deep learning model was used for organ segmentation. Aorta image-derived input function(IDIF) was used to calculate a sPBIF. Region-based kinetic analysis and voxel-based Vt imaging were conducted with LM (0-70 min p.i.) and DLM (50-70 min p.i.). The region-based LM kinetic analysis served as gold standard.

Results: We found excellent agreement between Vt estimations in parametric images generated by DLM and the gold standard with biases between [3%;13%]. The LM generated Vt images with biases between [-40%;-1%]. The Vt images generated by LM and DLM showed similar characteristics, but DLM images had fewer artifacts and generated WB parametric Vt images. Only minor biases of [1.6%;1.9%] were observed using the PBIF confirming the feasibility of a 20-min D-WB PET examination.

Conclusion: The new DLM model allows WB Vt imaging based on a clinically feasible 20-min D-WB PET examination on a conventional PET/CT scanner.

Themes: Imaging techniques, Diagnostics & technology
Keywords: Parametric Imaging, Dynamic whole-body PET, Logan

The Ventilation during In-hospital Cardiac Arrest (VENT-IHCA) Study Protocol

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Background: During cardiopulmonary resuscitation (CPR), patients are treated with chest compressions and ventilations. However, guidelines on how to ventilate during CPR are based on very-low certainty evidence and expert opinion due to an absence of direct measurements of intra-arrest ventilation. The recent development of portable devices allows the measurement of tidal volumes and ventilation rates during CPR. The aim of this study is to identify the tidal volumes and ventilation rates associated with the highest chance of survival following in-hospital cardiac arrest (IHCA).

Methods: We will conduct a prospective, observational, multicenter study to investigate intra-arrest ventilation by measuring tidal volumes and ventilation rates produced with a bag-resuscitator during CPR using a novel flow measurement device (EOlife®, Archeon, France). We will collect data from the IHCA registry (DANARREST) as well as electronic patient journals on patient and cardiac arrest characteristics, survival outcomes, post-arrest care and complications. We will use restricted cubic spline curve analysis to investigate the associations of tidal volumes and ventilation rates with survival outcomes. The primary outcome will be return of spontaneous circulation.

Results: We will start data collection in 2024 and results are pending.

Conclusion: This will be the first study to investigate the associations between tidal volume and survival outcomes following cardiac arrest. Therefore, the study may impact international resuscitation guidelines and clinical practice worldwide. Furthermore, the study may lay the foundation for randomized clinical trials on intra-arrest ventilation interventions.

Themes: Cardiology, Diagnostics & technology
Keywords: cardiopulmonary resuscitation, manual ventilation, in-hospital cardiac arrest

Connectome analysis of dynamic whole-body PET for detection of disease-specific metabolic patterns

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Introduction: Humans maintain steady physiological conditions through dynamic, self-regulating multi-organ interactions with energy-consuming systemic feedback loops that orchestrate organs to respond to perturbations. This is known as homeostasis. Dynamic whole-body PET/CT imaging has the potential to detect deviations in the balanced metabolic state using the radioactive glucose analogue 18F-FDG.

Aim: This study aims to explore variations in the inter-organ glucometabolic correlation in diabetes and lymphoma patients in comparison to a healthy control group. Applying correlation analyses and metabolic connectivity frameworks, metabolic alterations caused by diabetes and lymphoma can be quantified, making it possible to evaluate if the alterations can be indicative of the diseases and if the effects can be separated on a group-level and individual level.

Method: Dynamic whole-body 18F-FDG images will be acquired from a control group of healthy participants (N=40), and three groups (N=20) of diabetes patients, lymphoma patients and patients with both diabetes and lymphoma. Static and dynamic image features will undergo inter-organ correlation analyses within patient groups and will be compared with the healthy control group to explore disease-specific deviations in inter-organ glucometabolic correlations.

Perspective: Imaging of patient glucose metabolism may give valuable information on patient health, and deviations from homeostasis might reveal disease-specific characteristics, with possible consequences to patient treatment outcomes.

Themes: Imaging techniques, Diagnostics & technology
Keywords: Dynamic whole-body PET, Metabolic Connectivity, Multi-organ Interactions

Development and Evaluation of a Lipid Nanoparticle (LNP) Library for Enhanced Bi-functional Cargo Delivery

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Lipid nanoparticles (LNPs) are emerging as versatile carriers for nucleic acid delivery in gene therapy, offering a non-viral alternative for effective nucleic acid therapeutics. Despite advances, optimising LNP formulation remains challenging due to the complexity of lipid composition and the diverse requirements across cell types and tissues. This study focuses on systematically developing an LNP library to identify optimal settings for efficient delivery using Design of Experiments (DoE).

In our initial library, we generate a 36X LNP library by varying the ratios of SM-102, DSPC, cholesterol, and DMG-PEG 2000 with DoE to identify optimal formulations. We optimised a strategy to generate bi-functional LNPs containing a CY5-labelled fluorescent oligonucleotide and mRNA encoding the green fluorescent protein, enabling quantitative monitoring of LNP uptake and gene expression. We assess each formulation by determining encapsulation efficiency, particle size and distribution, and zeta potential, followed by cellular uptake and expression efficiency assessments via flow cytometry. Initial results demonstrate promising variability in delivery efficiency across cell lines, including HEK293T, Kasumi, and HUVECs suggesting that lipid ratio modifications could enhance delivery profiles.

Future work will explore in vivo LNP screening using barcoded cargos and single-cell sequencing to further optimise formulations for efficient, specific cell and tissue targeting. Our findings highlight the potential for tailored LNP compositions to improve targeted gene delivery, advancing the field toward more effective, cell-specific therapies.

This project is supported by the Lundbeck Foundation

Themes: Genetic engineering, Diagnostics & technology
Keywords: Lipid nanoparticles, Non-viral delivery, Library development

Racial differences in continuous glucose monitoring-based 60-min glucose predictions among people with type 1 diabetes

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Background: Non-Hispanic white (White) populations are overrepresented in medical studies. Machine learning models reflect the data they are trained on, which can potentially lead to racial disparities in healthcare. We aimed to evaluate algorithmic fairness in glucose predictions and how transfer learning might improve this. We hypothesized a divergence in performance by race i.e. increasing the proportion of white participants in the training data would improve predictive performance for whites but impair the performance for non-Hispanic black (Black) participants.

Method: This study utilized continuous glucose monitoring (CGM) data, measured at 15-minute intervals, from 101 White and 104 Black participants with type 1 diabetes. The dataset was split into 60-minute observation windows, including four measurements as predictors of blood glucose 60 minutes ahead. Deep learning models were trained on ten datasets made up of different ratios of White and Black participants (100% White - 0%Black, ..., 0% White - 100% Black), for each participant, . These models were then tailored to each individual using transfer learning. Root mean squared errors (RMSE) were calculated on each participant's last two weeks of data, which was held out for evaluation. Linear mixed-effect models were used to investigate the association between RMSE and racial ratio, including the interaction between ratio and race while accounting for age, sex, and size of training data.

Results: A median of 9 weeks (IQR: 7, 10) of CGM data was available per participant. The RMSE for White and Black participants when the model was trained on zero percent whites were 2.04 [95%CI: 1.95, 2.13] and 2.05 [1.96, 2.14] mmol/L, respectively. When models were trained on 100% white participants, the RMSE was 2.01 [1.92, 2.10] mmol/L for white participants and 2.06 [1.97, 2.15] mmol/L for black participants. This divergence in performance was in line with our hypothesis, although it was not statistically significant for either group individually. Still, the difference between groups (by ratio slope (0 to 100%)) was statistically significant: -0.041 mmol/L [95% CI: -0.075, -0.008], p = 0.016. This difference attenuated in the model using transfer learning (-0.021 [-0.054, 0.011], p = 0.195).

Conclusion: The racial composition of training data created a small statistically significant difference in the performance of the models in this study, which was not present after fine-tuning. This demonstrates the potential value of transfer learning for developing more personalized and fair prediction models.

Themes: Public health, Diagnostics & technology
Keywords: Clinical Prediction, Algorithmic Fairness, Diabetes

Phenotyping and characterization of a Danish Wild-type Transthyretin Amyloidosis Cardiomyopathy cohort: A cross-sectional study

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Background: Wild-type transthyretin cardiac amyloidosis (ATTRwt-CM) is a progressive cardiomyopathy leading to heart failure, reduced quality of life (QoL) and poor prognosis in elderly patients. ATTRwt-CM is caused by amyloid fibril deposition in the myocardium, amyloid fibrils form due to misfolding and aggregation of transthyretin (TTR).

Hypothesis: We hypothesize 1) that more severe ATTRwt-CM stages lead to poorer QoL and 2) that misfolded (misTTR) and fragmented (fragTTR) TTR are detectable and correlated to disease severity based on clinical, biochemical, and diagnostic imaging parameters in patients with ATTRwt-CM.

Aims: 1° To examine QoL measures in a contemporary ATTRwt-CM cohort and its relation with disease severity according to clinical characteristics and prognostic disease stage markers. 2° To assess the feasibility of measuring misTTR and fragTTR in patients with ATTRwt-CM and their correlation with ATTRwt-CM severity.

Design: Prospective cross-sectional study

Setting: From the outpatient amyloidosis clinic at Aarhus University Hospital we will include 100 consecutive ATTRwt-CM patients representing all disease stages according to the National Amyloid Center system. A control cohort of 30 heart-healthy patients will also be included for comparison of mis-/fragTTR values.

Perspectives: This study will provide comprehensive insights into ATTRwt-CM and its impact on QoL. MisTTR and/or fragTTR show promise as a simple and harmless method for evaluating the clinical disease progression of ATTRwt-CM. Overall, the study may provide novel insights to guide future personalized treatment strategies and contribute to improving the prognosis of patients with ATTRwt-CM.

Themes: Cardiology, Diagnostics & technology
Keywords: Cardiac amyloidosis, Quality of life, Biomakers

RESPECT: preliminary results on intra-subject test-retest repeatability and reproducibility of diffusion measurements

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Chronic kidney disease (CKD) is a progressive renal condition, affecting more than 10% of the world's population. The RESPECT project aims at advancing multi-parametric renal MRI as a promising, contrast-free technique to improve the understanding and characterization of renal pathophysiology thus fostering early diagnosis and patient specific treatment. For this study 80 healthy volunteers and 60 CKD patients from 4 sites are being enrolled and scanned on 3T MRI systems from 2 different vendors. Each healthy volunteer underwent three MRI scans, two scans in the same day to evaluate intra-subject test-retest repeatibility and a third one after 7-14 days to assess reproducibility. As part of the multiparametric MRI protocol, diffusion-weighted imaging (DWI) was acquired to assess kidney diffusivity and microstructure. DWI scans from the first 22 subjects were analysed using both monoexponential and intravoxel incoherent motion (IVIM) models; the former providing the apparent diffusion coefficient ADC and the latter yielding the diffusion coefficient D, pseudodiffusion D* and perfusion fraction F. Cortico-medullary ADC and D parameters, as well as their difference (ΔD and ΔADC) were also quantified. Repeatibility and reproducibility were measured using within-subjects coefficient of variations (CV%) and with Bland-Altman statistics. Our study shows that both for repeatibility and reproducibility, all diffusion parameters have a zero bias and CV<5% for both ADC and D. Repeatibility and reproducibility was lower for F with CV>10% and D* with CV<7%. Overall these preliminary results are in line with previous findings and support the reliability of DWI parameters.

Themes: Imaging techniques, Diagnostics & technology
Keywords: MRI, Diffusion weighted imaging, Repeatability

Optimizing mitochondrial and kidney function during the process of kidney donation, preservation and ultimately transplantation

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Ischemia reperfusion injury (IRI) is inevitable during the process of kidney donation, preservation and transplantation and has a major impact on graft viability and post transplantation outcome. It is associated with delayed graft function, rejection and chronic graft dysfunction. Injury and dysfunction of the mitochondria play an important and early role in the pathogenesis of IRI and therefore could be an attractive target to reduce IRI. During the process of IRI, the transient shortage of oxygen and nutrients leads to formation of reactive oxygen species (ROS), a critical factor in IRI, responsible for activation of various downstream injurious pathways.

MitoQ, a mitochondrial therapy, acts as an ROS scavenger. Previous studies demonstrated efficacy, safety and stability up to 24 hours in various kidney transplant models and demonstrated decreased oxidative stress, decreased expression of pro-inflammatory and immune-related genes and improved perfusion parameters.

Machine perfusion is increasingly adopted as the golden standard for organ preservation prior to transplantation, with superior post transplantation outcome. In addition, machine perfusion provides a dynamic platform for therapeutic organ reconditioning and repair prior to transplantation.

Our aim is to improve mitochondrial (dys)function and thus decrease IRI during the process of donation and transplantation by administration of MitoQ to the preservation solution in the preservation period with in the end improve graft function. We hypothesize that MitoQ improves (mitochondrial) preservation, reduces IRI and improves kidney function.

Themes: Urology & Nephrology, Diagnostics & technology
Keywords: kidney transplantation, mitochondria, machine perfusion

SESSION 29 - Mental health 2

The alterations of brain dynamics in schizophrenia are mainly from the association cortex

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Schizophrenia (SCZ) is a mental disorder of altered brain connectivity, which is conceptualized as “dysconnectivity” and can relate to either a hypo- or hyper-integrative/connective condition between different brain areas. Astride the development of neuroimaging, the “dysconnectivity” hypothesis of SCZ has been gathering progressive support. Studies have so far demonstrated the extensive and repeatable deficiencies in integrative and connective competence of SCZ. What remains unclear, however, is how the hypothesized decisive role of such intrinsic dynamical alteration in SCZ with biophysical changes within and between brain regions. Substantial evidence demonstrated that computational models have provided a novel perspective for studying brain diseases through the relationship between brain structure, function, and dynamics. Therefore, the purpose of this study was to utilize computational models (parametric mean field model) to explore how brain dynamics varied in SCZ. Global coupling increases significantly in SCZ ($t = -4.59$, $p < .0001$), and both altered recurrent connection and altered subcortical input were significantly distributed in association cortex. The two altered biophysical maps are inversely correlated ($r = -0.58$, $p < .0001$), and these alterations have a significant spatial correlation ($p < 0.05$, spin test) with the maps of MOR, 5-HT2a, mGluR5, VAChT, D2, NET. This finding shed light on the regional biophysical alterations of brain activity in SCZ and provide a new perspective for understanding the brain dynamical changes in SCZ.

Themes: Mental health, Neuroscience
Keywords: Neurodynamic, Schizophrenia, Biophysical model

Coercion in child and adolescent psychiatry. Who are at risk? (CoCAP)

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Background: Each year children and adolescents are exposed to coercion in Danish child and adolescent psychiatry (CAP) to protect them from harming themselves or others. Many initiatives have been taken to try to reduce the use of coercion, but still, the percentage of young people exposed to coercion is high.

Aim: The overall aim of the study is to provide new knowledge on the characteristics of children and adolescents exposed to coercion, identify high-risk groups, and describe long-term outcomes.

Study 1. Describe and analyse characteristics of children and adolescents exposed to coercion in CAP with regard to e.g. age, sex, family background, psychiatric diagnoses, number and length of admissions and types of coercion.

Study 2. Identify characteristics of groups at particular high risk for frequent episodes of coercion in CAP.

Study 3. 5-10 years follow-up of children and adolescents exposed to coercion in CAP with regard to education, labour market status, somatic and psychiatric health.

Methods: The studies will be based on data from Danish health, social, and educational registries at The Danish Health Data authority and Statistics Denmark. All patients under the age of 18 admitted to CAP in the study period 2015 to 2023 will be included, approx. 14.000 patients. Cases are those exposed to coercion corresponding to approx. 300 patients yearly.

Perspectives: This research project addresses a critical gap in the existing literature, aiming to provide a nuanced understanding of risk factors for coercion for children and adolescents admitted to CAP. This information is highly needed to support the development and implementation of preventive strategies and interventions.

Themes: Mental health, Mental health
Keywords: Child and adolescents psychiatry, Coercion,

Internet-based versus synchronous cognitive behavioural therapy for patients with Gambling Disorder: A non-inferiority randomized controlled trial

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Background: Gambling disorder (GD) involves persistent and harmful gambling behaviors that can lead to significant negative effects on individuals and their families. While Cognitive Behavioral Therapy (CBT) is the most evidence-based treatment for GD, traditional face-to-face CBT often encounters barriers such as geographical distance, scheduling conflicts, and stigma. Internet-based interventions allow patients to access treatment from home at their own pace, potentially overcoming these challenges. However, the effectiveness of internet-based programs compared to synchronous CBT (sCBT) delivered in real time remains unclear.

Objective: This non-inferiority randomized controlled trial aims to compare the effects of the internet-based program "SpilleFri" with sCBT for patients with GD. The primary goal is to assess whether SpilleFri is not clinically inferior to sCBT in reducing gambling severity.

Methods: A total of 150 patients with GD will be randomized to either SpilleFri or sCBT. The trial will evaluate gambling severity, symptoms of anxiety and depression, and relationship quality at baseline, at the end of treatment, and three months post-treatment. Key moderators, such as patient subtype and readiness to change, will also be explored.

Hypotheses: We hypothesize that SpilleFri will demonstrate non-inferiority to sCBT in reducing gambling severity, with no significant differences in secondary outcomes. Moderators are expected to influence treatment outcomes.

Conclusion: If SpilleFri proves as effective as sCBT, it could provide a more accessible and flexible treatment option, particularly for those facing barriers to traditional CBT.

Themes: Mental health, Qualitative research
Keywords: Gambling Disorder, Internet-based psychotherapy, Randomized controlled non-inferiority trial

Well-being in schoolchildren with neurodevelopmental disorders: A nationwide study

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Background: Neurodevelopmental disorders (NDDs) significantly impact behavior, memory, or learning abilities in school-aged children. Studies comparing well-being across the spectrum of NDDs are limited.

Objective: To examine well-being in children with NDDs in Danish public schools using the Danish National Well-being Surveys (2015-2022).

Methods: In a register-based cohort study, we analyzed well-being data from grades 0-9 for children born in Denmark between 2000 and 2014. Children with NDDs (e.g. autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD)) were matched to 10 reference children without NDDs by age and sex, using exposure density sampling. Analyses were limited to children with ≤1 survey answer, using logistic regression models to estimate odds ratios (ORs) for reporting poor well-being.

Selected results: From a population of 918,320 children, 771,340 (85%) responded to ≤1 survey, including 16,520 (2.1%) children with ASD matched to 165,200 reference children, and 22,180 (2.9%) with ADHD matched to 221,800. In total, 141,580 children (24% girls) with ASD and their peers completed 570,560 well-being surveys, and 187,350 children (27% girls) with ADHD and their peers completed 804,370 surveys (grades 4-9, 2015–2022). Children with ASD and ADHD had higher odds of reporting poor overall well-being (ASD: aOR 2.32; ADHD: aOR 2.25), poor social (ASD: aOR 2.49; ADHD: aOR 2.24), and poor academic (ASD: aOR 2.12; ADHD: aOR 2.22) well-being compared to reference children.

Conclusion: Children with ASD and ADHD report significantly poorer well-being compared to peers, highlighting the need for targeted support in educational settings.

Themes: Mental health, Epidemiology
Keywords: Neurodevelopmental disorders, Well-being, Epidemiology

Stop for Stress - comparing an online and a group intervention for work-related stress

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Aim Many afflicted with work-related stress will not receive specialised treatment due to limited availability, distance, and stigma. Online interventions can overcome these barriers. We aim to compare a new therapist-guided online intervention for work-related stress, Stop for Stress, based on the evidence-based group intervention, MARS, and to identify markers of enhanced outcomes in either format.

Methods The two interventions will be compared in a two-armed single-blinded randomized controlled equivalence trial. 220 patients with work-related stress will be randomized to Stop for Stress or MARS. Participants will answer questionnaires on mental health, perceived work-environment, and workability at baseline and at 3, 6, and 12 months. Objective cognitive functioning will be assessed using a computer-based program. Register data will provide information on return-to-work.

Results The effects of the interventions will be evaluated on questionnaire data, objective cognitive functioning, and return-to-work. If the interventions show no difference in effect size, the online format will be considered sufficiently effective. A prognostic model will evaluate if specific patient characteristics predict enhanced treatment outcomes.

Discussion Stop for Stress is a more accessible format of an evidence-based intervention, and this trial will inform whether it can be offered to patients on equal terms as the group-based format. The prognostic model will support recommendations of intervention format to future patients.

Conclusion This trial will provide knowledge on online stress management and its effects on symptoms and return-to-work among patients with work-related stress.

Themes: Mental health, Rehabilitation
Keywords: Work-related stress, Online intervention, Group intervention

Efficacy and acceptability of pharmacological interventions for insomnia in patients with severe mental illness:

A systematic review and meta-analysis of randomised trials

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Background: Medication for insomnia is frequently used by individuals with severe mental illness (SMI), but no review has gathered all evidence on illness-specific or transdiagnostic outcomes. We aimed to perform a systematic review and meta-analysis of randomized controlled trials (RCTs) studying the efficacy and acceptability of pharmacological interventions for insomnia among individuals with SMI, i.e., schizophrenia, bipolar disorder (BD), or major depressive disorder (MDD).

Methods: Embase, Medline, PsycINFO, Cochrane Library and clinicaltrials.gov were searched for RCTs of pharmacological interventions for insomnia that used either placebo or another medication as inactive control or active comparator. Two independent reviewers performed the literature screening, data extraction, and risk of bias assessment (RoB2). We performed random effects meta-analyses on the co-primary outcomes total sleep time (TST), sleep quality and acceptability.

Results: The search identified 3331 hits, of which 25 RCTs (n=2476) were included, with 18 RCTs (n=2199) in MDD, 4 RCTs (n=162) in BD, and 3 RCTs (n=115) in schizophrenia. Of 25 RCTs, 22 had high risk of bias. Compared to placebo, medication for insomnia was associated with improved sleep quality (RCTs=8, g=0.23, 95%CI=0.05-0.42) and TST (RCTs=10, MD=23.77 minutes, 95%CI=8.28-39.05), with similar acceptability (RCTs=10, RR=1.06, 95%CI=0.90-1.25).

Conclusions: Medication for insomnia in patients with SMI showed better efficacy with similar acceptability compared to placebo. However, surprisingly few RCTs have studied this clinically important aspect, although insomnia is highly prevalent in SMI.

Themes: Mental health, Pharmacology
Keywords: Insomnia, Sleeping pills, Severe mental illness

End-of-life quality-measures for Patients with Pre-Existing Severe Mental Disorders

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Background: Studies show mixed results on end-of-life (EOL) care quality for patients with Severe Mental Disorders (SMDs).

Aim: To assess EOL quality indicators among Danish patients with SMDs in specialized palliative care.

Methods: Data from the Danish Palliative Database was analyzed for patients who died in 2023 in Central Region Denmark. Hospital records identified patients with SMDs—schizophrenia, other psychotic disorders, moderate to severe depression, and bipolar disorder—listed in the National Patient Register. EOL quality measures included: place of death, time from referral to death, waiting time, symptom assessment, and multidisciplinary conference discussions. Analyses used t-tests and chi-squared tests.

Results: Among 1,869 patients, 80 (4.3%) had pre-existing SMDs. These patients died younger than those without SMDs (mean age: 66.9 years, 95% CI: 64.2–69.6, vs. 71.0 years, 95% CI: 70.4–71.5) and were more likely to die from organ failure than cancer (30.0% vs. 14.2%, $p < 0.001$). There was no significant difference in place of death. Patients with SMDs were less likely to have systematic symptom assessments (64.5% vs. 75.9%, $p = 0.012$) and had a non-significantly longer time from referral to death (mean: 162.9 days, 95% CI: 77.7–248.1, vs. 114.9 days, 95% CI: 100.5–129.2). Waiting time and multidisciplinary discussions showed no significant differences.

Conclusions: Results suggest generally good EOL care quality for patients with SMDs, who still tend to die younger and more often from organ failure. Findings indicate a high degree of equality on most EOL quality-measures, but emphasize the need for better systematic symptom assessments for SMD patients.

Themes: Mental health, Public health
Keywords: Palliative Care, Severe Mental Disorders, Quality-measures

Detection of Bias in Prediction Models for Clinical Psychiatry based on Data from Electronic Health Records

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Machine learning (ML) can uncover patterns in health data to enable early detection and intervention. However, ML models may inherit biases present in the data, thereby risking automation and amplification of these imbalances in clinical practice. Thus, without recognising and addressing bias in ML models, we might, inadvertently, perpetuate disparity in healthcare. This project aims to investigate whether ML models predicting clinical outcomes among patients receiving hospital treatment for mental illness are biased across protected attributes, including age, sex, and ethnicity.

The project will use electronic health record (EHR) data from the PSYchiatric Clinical Outcome Prediction (PSYCOP) cohort, which includes almost 120,000 patients from Central Denmark. The exhaustive EHR data enable development of large-scale ML prediction models as well as investigation of multifaceted biases in model predictions and in the dataset. The PSYCOP cohort has been used for developing a series of ML models predicting clinical outcomes, including coercive measures, diagnostic progression, and development of cardiovascular disease. Multiple fairness metrics will be used to quantify discrepancies in model performance across protected attributes, with each metric revealing different aspects of bias. For instance, some metrics assign greater weight to false negatives compared to false positives – a crucial distinction in clinical settings, where the impact of different error types is highly context-specific. This approach allows us to optimise for the most relevant bias measures for each clinical application.

The analyses are being finalised and the results will be presented at PhD Day 2025.

Themes: Mental health, Statistics
Keywords: psychiatry, fairness, machine learning

Five-factor Personality Traits and Functional Somatic Disorder: A Systematic Review and Meta-Analysis

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Introduction: Functional Somatic Disorders (FSD) is an umbrella term for various conditions characterized by persistent and troublesome physical symptoms, that are not better explained by other psychiatric or somatic conditions. Personality traits may play a crucial role in FSD, but the link is not fully understood. This study presents a systematic review and meta-analysis examines the relationship between the Five-Factor Model (FFM) of personality traits and FSD.

Methods: The review was based on the PRISMA statement, and drew data from systematic searches in PsycInfo, PubMed, and Embase. To be eligible for inclusion, studies had to include eligible FSD groups and control groups and to assess FFM traits. Data were analyzed using random effects models.

Results: In total 6,841 records were screened and 52 included. FSD cases scored higher on neuroticism (k=46, Hedge's g=0.72, [95% CI, 0.61:0.83]) and lower on extraversion (k=31, g= -0.41, [-0.55:-0.28]) and agreeableness (k=15, g= -0.22, [-0.36:-0.09]) than healthy/unspecified controls. FSD cases scored higher on neuroticism (k=9, g= 0.26 [0.08:0.44]) and agreeableness (k=4, g=0.43 [0.28:0.59]) than somatic controls, but did not differ on extraversion (k=6, g= -0.17 [-0.45:0.11]). No significant differences were found for conscientiousness and openness. For psychiatric controls, meta-analysis was only possible for neuroticism (k=3,= -0.61, [-1.98:0.77]).

Conclusions: This review reveals significant associations between FFM traits and FSD, providing insight into the etiology, classification, and management

Themes: Mental health, Rehabilitation
Keywords: Functional Somatic Disorder, Five-factor model, Personality

SESSION 30 - Qualitative research and mental health

Navigating the Unknown: A Qualitative Study of Parental Responses to a Prenatal Genetic Mosaicism Result

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Background: Sometimes prenatal genetic testing raises more questions than it answers, for example when mosaicism is found in a placental biopsy. It can affect the fetus or lead to growth restriction and preterm birth, while some pregnancies remain unaffected. This uncertainty complicates genetic counseling, leaving expectant parents to navigate difficult choices, consider further invasive testing, and endure long waits for diagnostic results. The aim of this study is to explore the experiences and counseling needs of expectant parents diagnosed prenatally with confined placental mosaicism (CPM).

Methods: An exploratory, qualitative study design was used based on participant observation and semi-structured interviews. Participants were recruited from two Departments of Clinical Genetics, including women (and their partners) who received a prenatal diagnosis of CPM and continued the pregnancy. A total of 14 interviews were conducted, all of which were audio-recorded, transcribed verbatim, and pseudo-anonymized. Data will be analyzed using reflexive thematic analysis.

Preliminary results: Receiving results (by phone) was stressful for parents, as the healthcare professional could not provide sufficient information about mosaicism, leading them to imagine 'the worst'. Following genetic counseling, many struggled with the lack of clear answers and risk estimates, yet most found the consultation reassuring and felt supported. Waiting for diagnostic results was difficult, and strategies to manage worry were discussed. These findings will be further explored.

Conclusion: A diagnosis of CPM generates uncertainty among parents, highlighting the need for specialized genetic counseling.

Themes: Qualitative research, Gynecology and obstetrics
Keywords: Prenatal Diagnosis, Genetic counseling, Qualitative

Unveiling the Musical Features of EDM Subgenres: A Music Information Retrieval Approach

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This paper presents the first study of a PhD project focused on music-induced altered states of consciousness (ASC). In the context of raves, Electronic Dance Music (EDM) goes beyond creative expression; it serves as a powerful tool for inducing transformative spiritual experiences that can lead to profound and lasting changes in self-perception and life outlook. The rhythmic pulses and bass vibrations of EDM, combined with multimedia technologies, deeply engage listeners, immersing them in the music and dance experience. Despite the general effects of EDM in these settings, little is known about how specific musical features contribute to the induction of ASC.

This study presents ongoing research utilizing Music Information Retrieval (MIR) techniques to identify musical features that differentiate four EDM subgenres: psytrance, minimal techno, progressive house, and dubstep. We analyzed 4,676 30-second demo tracks tagged by Spotify, extracting 30 features related to melody, harmony, rhythm, tone color, and dynamics using the Essentia library. To identify the features that best distinguish these subgenres, we applied statistical and machine learning methods, including linear discriminant analysis, logistic regression, and decision trees. Additionally, we curated a subset of 200 songs from the dataset based on expert ratings to further validate our results and create a refined dataset for future research.

Our findings will contribute to the development of EDM-like stimuli for investigating the phenomenology and neural correlates of EDM-induced altered states of consciousness in future studies.

Themes: Qualitative research, Neuroscience
Keywords: Music Information Retrieval, Electronic Dance Music, Altered States of Consciousness

Facilitators and barriers to collaboration between general practice and sickness benefits office in return to work processes

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Background: Effective collaboration among stakeholders is essential in supporting return to work (RTW) processes for individuals on sick leave. However, collaboration between the sickness benefits office and general practice is poorly functioning.

In this scoping review, we map the existing literature on collaboration between the sickness benefits office and general practice in RTW processes and identify facilitators and barriers to collaboration.

Methods: Following Joanna Briggs' guidelines, a systematic search was conducted across five databases in March 2023. Two independent researchers conducted screening and data extraction.

Extracted data was mapped, and facilitators and barriers were analyzed using descriptive thematic analysis. Tentative results were discussed with a reference group.

Results: Among the 7,471 papers screened, 21 met the inclusion criteria.

Most used qualitative methods and Scandinavia composed the most significant geographical cluster. Written communication emerged as the prevalent collaborative activity. A significantly greater number of barriers than facilitators were identified. Barriers included stereotyping, differing priorities, and relying on written communication. Facilitators comprised face-to-face meetings and high-quality written communication.

Conclusion: This review reveals ongoing challenges over the past twenty years. While literature primarily focused on barriers, some facilitators were identified, highlighting their interconnection—facilitators can address barriers. A lack of consensus in the literature on key concepts like collaboration also prompted a call for more explicit theoretical definitions in future research.

Themes: Qualitative research, Rehabilitation
Keywords: Collaboration, Return to work, Review

Parental Decision-Making After Receiving a Prenatal Diagnosis of Turner Syndrome: A Qualitative Interview Study

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Background: Turner syndrome (TS) is characterised by a partial or complete absence of the second X chromosome, resulting in a 45,X karyotype or variants thereof. In Denmark, approximately 42% of TS cases are prenatally detected; of these, 69% lead to pregnancy termination.

Prior studies have identified an array of factors influencing the parental decision to terminate or continue a pregnancy after a prenatal TS diagnosis, including specific karyotype, foetal anomalies, and the provision of nuanced counselling. However, few qualitative studies have examined parents' experiences of the diagnostic process, from initial diagnosis through counselling to their final decision. Understanding these experiences is essential to providing patient-centred care to prospective parents in this complex situation.

Objectives and Methods: Fifteen women/couples who continued their pregnancies after receiving a prenatal TS diagnosis are interviewed using a semi-structured format. All interviews are audio-recorded, transcribed verbatim, and analysed using reflexive thematic analysis. The study aims to explore:

a. The women's/couples' experiences and management of the diagnostic process, including obstetric and genetic counselling,

b. Which factors influenced the women's/couples' decision to continue the pregnancy, and

c. How the TS diagnosis affected the women's/couples' experience of the remainder of the pregnancy.

Results: Preliminary results will be presented at PhD Day 2025.

Perspectives: By enhancing our understanding of parental decision-making following a prenatal diagnosis of TS, we can improve genetic and obstetric counselling to ensure parents feel supported in making informed choices.

Themes: Qualitative research, Endocrinology
Keywords: Turner Syndrome, Prenatal Diagnostics, Parental Decision-Making

A two-year transition program shows impact on newly graduated nurses' job satisfaction and intention to stay.

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Background: Transitioning from student to registered nurse can be overwhelming for newly graduated nurses. They express a lack of knowledge and experience, underscoring the need for structured support during the transition process. Transition programs are widely recognized as effective in aiding this process, and job satisfaction is a critical factor for nurse retention. The aim was to explore the impact of a two-year transition program on newly graduated nurses' job satisfaction and intention to stay within three medical wards in a teaching hospital.

Method: The study was qualitative with a hermeneutic approach. In total, 13 nurses were invited to participate. Seven nurses in their final year of the program and six nurses who had completed the program within the past year. One of the nurses in the program rejected participation. Data were collected through qualitative semi-structured interviews and analyzed using qualitative content analysis.

Results: Preliminary findings suggest that participation in the two-year transition program enhances newly graduated nurses' job satisfaction and strengthens the nurses' intentions to stay in their profession. The opportunity for a clear career path appears to be a significant factor in their decision to stay.

Conclusion and implication: The study is expected to provide valuable insights for healthcare managers and policymakers to better support the transition of newly graduated nurses into clinical practice in hospital medical wards.

Themes: Qualitative research, Public health
Keywords: Transition program, Newly graduated nurses, Job satisfaction

Epistemic Structures and Their Influence on Illness Understanding of Functional Somatic Disorder

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Background

Functional somatic disorders (FSD) are characterized by bodily symptoms without an exclusively biomedical explanation. The aetiological and nosological uncertainty of such disorders is central to the illness experience as patients navigate an explanatory vacuum in an unsuitable epistemic paradigm of post-positivistic biomedicine. This influences the epistemic credibility of the patients in the health care system, in social relations, and within the private sense-making and meaning making processes of the individual. Offering a framework for illness understanding is considered key to the treatment, yet the underlying epistemic structures and their impact on the patient's ability to understand their illness is less well understood. This study explores epistemic structures of relevance to the illness understanding of patients with FSD.

Methods

8 patients were followed through assessment and patient education at the Clinic for FSD, Aarhus University Hospital. Consultations were observed and audio recorded, using this data to inform qualitative patient interviews. Analysis is conducted using thematic analysis.

Results

Existential themes have been identified based on an enactive framework of Sanneke de Haan. Coding and analysis has been done drawing on e.g. Miranda Fricker's concept of epistemic injustice. Analysis is ongoing and results will be presented on the PhD day.

Discussion

Negotiating a nuanced illness understanding is a central yet sometimes challenging clinical endeavor. This study will provide insights to how epistemic structures influence the patients perspectives on their disorder, posing epistemological questions to the modern health care system.

Themes: Qualitative research, Mental health
Keywords: Illness understanding, Epistemology, Patient centered care

Evaluating User Perspectives in Cross-Sectoral Care for Functional Somatic Disorders - A Qualitative Process Evaluation

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Aims: This study investigates user perspectives of a healthcare intervention for patients with moderate-to-severe functional somatic disorders (FSD). The intervention provides coordinated diagnostic and treatment services across primary and secondary healthcare sectors.

Background: FSD, a group of complex multi-factorial disorders, involve an interplay of biological, psychological, and social factors. Affecting 8–10% of the population, FSD is associated with high healthcare utilization across sectors. Patients often experience delayed diagnoses, repeated referrals, and inefficient use of resources, increasing the risk of iatrogenic harm, incl overtreatment, chronic illness, dissatisfaction, and psychological distress. Comprehensive diagnostic evaluations at Silkeborg Regional Hospital's Diagnostic Clinic for Functional Disorders are coordinated with primary care, focusing on only necessary investigations and developing personalized treatment and self-management strategies across sectors.

Methodology: Through semi-structured interviews and observations with patients, GPs, and hospital clinicians, this study explores user experiences and examines critical mechanisms and contextual factors impacting its effectiveness. This complements the ongoing DISTRESS randomized controlled trial, which assesses the intervention's effectiveness and cost-efficiency.

Expected Results: The study will provide insights into patient, GP, and clinician experiences within the cross-sectoral structure. It will explore how the intervention improves coherence and collaboration, explaining outcome variations and supporting the development of tailored care strategies.

Themes: Qualitative research, Public health
Keywords: Functional Somatic Disorders, Process evaluation, Health services

Development and Feasibility Testing of a Clinical Trial Patient Decision Aid

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Introduction

Clinical research is the cornerstone of developing novel therapies to improve cancer treatment by enhancing tumor control and reducing long-term side effects. However, only 5-8% of cancer patients participate in clinical trials. Proton therapy for head and neck cancer is available only through participation in an RCT, which is conducted at Aarhus University Hospital. The decision-making process for clinical trial participation is complex due to structural, systemic, physician, and patient-related barriers. This study aimed to develop and test the feasibility of integrating a patient decision aid when informing patients about an RCT.

Methods

The current PhD project is conducted within the Medical Research Council (MRC) framework for complex intervention development and evaluation. First, the core elements related to trial participation were explored in two qualitative studies using interpretive description, a qualitative, inductive approach to examine health-related phenomena. Based on these findings, a patient decision aid tailored to an RCT involving proton therapy for patients with head and neck cancer was developed according to the International Patient Decision Aid Standards (IPDAS). Finally, the intervention is being tested for feasibility and acceptability through qualitative interviews with patients and healthcare professionals to assess its potential for integration into the clinical workflow when informing patients about the RCT, and to gain insights into their experiences with the PDA and its potential to improve informed decision-making regarding participation.

Results

Results can be presented at the PhD day.

Themes: Qualitative research, Cancer
Keywords: Clinical trial decision-making, Complex intervention development, Feasibility of introducing a patient decision aid in clinical trial communication

SESSION 31 - Public health 3

Occupational mechanical exposures and upper body osteoarthritis

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Introduction:

Osteoarthritis (OA) is a chronic disease causing erosion in the articular cartilage and alterations in the subchondral bone, capsule, and ligaments. It is considered a complex chronic condition affecting millions of people globally. In the work environment, occupational mechanical exposures pose a risk of developing OA, exposing workers to prolonged strain and forceful exertions. Therefore, we hypothesise that workers exposed to occupational mechanical exposures have an increased risk of developing upper body OA compared to non-exposed workers.

Methods:

This Ph.D.-project is a register-based cohort study utilising information from a unique cohort (DOC*X), which is a nationwide Danish occupational cohort. The cohort includes all persons gainfully employed and living in Denmark from 1976 until now (approx. 7 million people). Upper-body OA is identified in the Danish National Patient Registry, while mechanical exposures stem from two specific Job-Exposure Matrices (JEMs). Exposures are then assigned for each year by linking the JEMs to yearly job codes from the DOC*X.

Using the target trial framework, G-methods will be used to explore the association to account for healthy worker survivor bias and estimate exposure-response relations, including the inverse probability of treatment weighting for the adjustment of confounding variables in observational studies.

Descriptive statistics and trajectory analysis will be used to investigate prognosis and identify sub-populations in the dataset based on, e.g., long-term sickness absenteeism, public benefits, and early retirement.

Themes: Epidemiology, Public health
Keywords: Musculoskeletal diseases, Work,

Exposome-wide association study (ExWAS) investigating dietary, physiological, and medical factors in relation to BMI z-score and BMI in children and adolescents

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Introduction: The prevalence of overweight and obesity among children and young adults has plateaued at a high level. Despite various interventions to reverse the trend, there is lack of substantial positive results. This may be related to the complexity of obesity. It may also be related to unknown risk factors that have yet to be addressed. Up until now research has focused strongly on certain elements, such as diet and physical activity, while neglecting other elements.

Aim: To identify examined and less examined putative determinants of BMI z-score and BMI in children and adolescents.

Methods: The study uses data from the National Health and Nutrition Examination Survey (NHANES) III (1988-1994) and NHANES Continuous (1999-2018). The analysis includes individuals aged 2 to 25 years. Four survey cycles are put aside for the subsequent validation analysis. Associations between putative determinates from the NHANES dataset and BMI z-score in childhood and young adulthood are being investigated systematically. The study population is stratified by age and gender. All analyzes are adjusted for ethnicity. The false discovery rate (FDR) is used to control for type 1 error ascribable to multiple testing. The factors associated with childhood obesity, that remain after controlling for the FDR are validated by rerunning analyses with the participants from the validation group. Due to the cross-sectional nature of the data determining temporal relationships are not possible. The associations found in this study will be carried forward to longitudinal analysis and evaluated in physiological models before eventual being assessed as possible causes of the obesity epidemic.

Themes: Epidemiology, Public health
Keywords: BMI, child, Adolescent

Pubertal timing and tempo and risk of depression in adolescence

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Background: Depression is a common psychiatric disorder affecting adolescents globally, and early pubertal timing as well as rapid pubertal tempo may increase the risk of developing a depressive disorder.

Aim: This study investigates the associations between pubertal timing (early, average, late) and tempo (rapid, average, slow), and risk of depression in boys and girls.

Methods: A cohort study, including 7,739 adolescents will be conducted using data from the Puberty Cohort in the Danish National Birth Cohort, the 18-Year Follow-Up, and linked with the Danish National Patient Registry (LPR). Participants reported several pubertal milestones, including Tanner stages, age at menarche in girls and age at first ejaculation and voice break in boys every six months from ages 11 to 18 years. Depression was evaluated using the Major Depression Inventory (MDI) from the 18-Year Follow-Up and F32-diagnoses from the LPR.

We will investigate the associations between pubertal timing, the tempo of Tanner stages, and key puberty milestones (age at menarche, voice break, and first ejaculation) with MDI scores. To do this, we will use ordinal logistic and multiple linear regression models. Additionally, we will investigate the risk of receiving a depression diagnosis using standard logistic regression. All analyses will be stratified by sex.

Results: Key results will be presented at the Ph.D. Day.

Conclusion: If associations are confirmed, adolescents at higher risk of depression due to altered pubertal development may benefit from regular screening.

Themes: Epidemiology, Public health
Keywords: Pubertal development, Depression,

The interplay between genetic liability and psychosocial working conditions in the aetiology of major depressive disorder

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Background and Aim: Major depressive disorder (MDD) is one of the most prevalent mental disorders worldwide, including in the Nordic countries. The aetiology is complex, involving multiple risk factors, and is only partly understood. In this research project, we will examine whether (i) exposure to adverse working conditions is associated with onset of MDD; (ii) genetic liability modifies the association between working conditions and MDD; and (iii) working conditions affect labour market participation after diagnosis with MDD. We will further (iv) estimate the economic effects of reducing MDD risk due to improved working conditions.

Methods: The study population is derived from the iPSYCH2015 case-cohort sample that includes 24,213 individuals with MDD diagnosed in young adulthood. Genetic liability for MDD is estimated by polygenic scores using genome-wide single nucleotide polymorphisms derived from frozen blood spots. We measure exposure to working conditions by linking job exposure matrices to the sample, estimating e.g. emotional demands. Information on covariates (e.g., sex, age, education, parental psychiatric history) and labour market participation is retrieved from registers. Economic costs of MDD are calculated based on recently published estimates from Danish register studies. We will conduct Cox proportional hazard analyses, calculate additive and multiplicative interactions, and estimate simulated interventions for the hypothetical effects of improving working conditions.

Results and Conclusion: We expect first results by the end of 2024. Results will be published in peer-reviewed journal articles and summarized in a PhD thesis to be submitted in 2027.

Themes: Epidemiology, Public health
Keywords: Occupational Health, Psychiatric Epidemiology, Gene-environment interaction

Discontinuation of semaglutide (Wegovy®) therapy for weight loss: Population-based study of the first 83,193 users in Denmark

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Introduction

A concern has recently emerged that many people may stop using new anti-obesity medications not long after starting. We examined the likelihood of early discontinuation and associated factors among adults who initiated semaglutide for weight loss (SEMA-WL) in Denmark.

Methods

Using data from nationwide health registries, we created a cohort of all adult first-time SEMA-WL users without diabetes between 01-12-2022 and 31-10-2023. We estimated the likelihood of stopping SEMA-WL use within the first 6 months (early discontinuation) and examined pre-treatment predictors of early discontinuation.

Results

We identified 83,193 SEMA-WL initiators (median age 50 years, 71% women). Over the first 6 months 23,028 (28%) individuals stopped treatment, when defined as no new prescription filled within 30 days after the previous ended. When extending this period to 60 or 90 days, fewer (18% and 12%, respectively) were assigned discontinuers. There was an increased risk of discontinuation in young users (age/sex- adjusted risk ratios (RR) 1.74, 95% CI 1.69-1.80 for 18-30 years vs. 45-60 years old), in people with previous gastrointestinal (RR 1.22, 95% CI 1.19-1.25) or psychiatric medication use (RR 1.25, 95% CI 1.22-1.28), cardiovascular disease (RR 1.21, 95% CI 1.16-1.26), or high Charlson index score 3+ (RR 1.32, 95% CI 1.23-1.41), and in users living in a low- versus high-income municipality (RR 1.11, 95% CI 1.05-1.16).

Conclusion

Three of ten SEMA-WL initiators discontinue therapy early. Factors associated with discontinuation include young age, socioeconomic deprivation, higher comorbidity rates and a history of gastrointestinal or psychiatric medication use at baseline.

Themes: Epidemiology, Public health
Keywords: , ,

Post-acute non-specific symptoms following COVID-19 vaccination: A Danish population-based study

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Background: Common adverse events after COVID-19 vaccination include muscular pain, headache, and fatigue. While these non-specific symptoms are recognized as acute responses, post-acute progression remains unclear. This study investigates differences in post-acute non-specific symptom reporting between COVID-19 vaccinated and unvaccinated individuals, stratified by COVID-19 vaccine hesitancy.

Method: This longitudinal study uses repeated measurements from the BiCoVac cohort, a random population-based sample of Danish citizens aged 16-65. We included 132,776 observations from 61,316 vaccine-unconcerned individuals, 52,325 observations from 25,272 vaccine-sceptical individuals, and 10,242 observations from 5064 vaccine-concerned individuals. Data were collected via national registers and questionnaires (May 2021–June 2022). Non-specific symptoms were assessed using the 25-item Bodily Distress Syndrome checklist and analysed using logistic and linear regression models with robust standard errors.

Result: Among vaccine-unconcerned individuals, those vaccinated had lower odds of most non-specific symptoms >4 weeks post-vaccination compared to unvaccinated. Similar tends were observed for sceptical individuals. Conversely, among vaccine-concerned individuals, those vaccinated had higher odds of reporting symptoms >4 weeks post-vaccination compared to unvaccinated.

Interpretation: For >90% of the population aged 16-65, we found no evidence of post-acute non-specific symptoms after COVID-19 vaccination. However, vaccinated vaccine-concerned individuals were more susceptible to report symptoms compared to those unvaccinated, potentially due to reporting bias or nocebo effects.

Themes: Epidemiology, Public health
Keywords: COVID-19 vaccination, Adverse events, Vaccine hesitancy

Associations between multimorbidity patterns and patient-perceived treatment burden: A population-based cross-sectional study of Danish survey and register data

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Background: Multimorbidity poses significant challenges to patients and healthcare systems, increasing treatment burden – patients' perceived effort in managing healthcare – which can lead to poor compliance and low health-related quality of life. While specific conditions have been linked to high treatment burden, research on distinct multimorbidity patterns and their associations with treatment burden remains limited.

Aim: This study investigates associations between multimorbidity patterns and patient-perceived treatment burden in a Danish population undergoing treatment.

Methods: We apply Latent Class Analysis to identify statistically distinct and clinically relevant disease patterns from 39 conditions listed in the Danish Multimorbidity Index. Treatment burden is measured using the Multimorbidity Treatment Burden Questionnaire. We use data from the 2021 Danish National Health Survey, linked to healthcare and demographic registers. Analyses include: 1) identifying multimorbidity classes, 2) characterising socio-demographic profiles of the classes, and 3) evaluating associations between class membership and high treatment burden using the latent class three-step BCH approach, calculating class-conditional probabilities of high treatment burden with 95% confidence intervals and testing differences in probabilities between each pair of classes.

Expected Results: Findings will identify multimorbidity patterns associated with high treatment burden.

Conclusions: This study enhances understanding of treatment burden across multimorbidity patterns, informing tailored healthcare planning and patient-centered care strategies, ultimately supporting improved quality of care.

Themes: Epidemiology, Public health
Keywords: Multimorbidity, Treatment burden,

Physical Activity Patterns and Spontaneous Abortion

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Background: Spontaneous abortion (SAB) is one of the most common pregnancy complications and affects up to 30% of all pregnancies. Evidence on whether and how physical activity (PA) influences the risk of SAB is inconsistent.

We will examine PA patterns and their association with the rate of SAB.

Methods: Nearly 5,000 participants who conceived after entry into the SnartForældre.dk-cohort from 2011 to 2024 will be included. We collected data from baseline and bi-monthly follow-up questionnaires to Danish health registries. PA before conception was measured using the International Physical Activity Questionnaire. Pregnancy outcomes were identified through follow-up questionnaires and Danish registries.

We will use latent class analysis and hierarchical clustering to identify PA patterns based on combinations of frequency, duration, and intensity of PA, and then compare the patterns from each approach.

To examine the association between PA patterns and SAB rate we will use Cox proportional hazards regression models to compute hazard ratios (HRs) and 95% confidence intervals (CIs) with gestational weeks as the underlying time scale.

Expectations: Around 18% of the participants had an SAB. We expect that regular PA (e.g., 5 days/week) will be associated with a lower SAB rate compared to infrequent PA (e.g., 1 day/week) despite similar weekly duration and intensity. Further, we expect that the data-driven methods will identify novel PA patterns, providing deeper insight into existing behaviors.

Perspectives: This study will contribute to a better understanding of how different PA patterns influence the risk of SAB, offering insights for public health recommendations.

Themes: Epidemiology, Public health
Keywords: physical activity, spontaneous abortion, cohort study

Effectiveness of a kindergarten-based obesity prevention intervention to reduce risk of overweight at school entry

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Background: Accelerated weight gain between the ages of two to six is known to be associated with overweight and obesity in adolescence. However, the long-term effects of obesity prevention programs targeting physical activity and diet in preschool children remain unknown.

Aim: To examine the effectiveness of a kindergarten-based obesity prevention intervention on Body-Mass-Index z-score (BMIz) and risk of overweight at school entry.

Methods: A kindergarten-based obesity prevention intervention group (n=1,755) was compared to a no-intervention group (n=750). The intervention consisted of two workshops focusing on developing activities to promote healthy behaviors, targeting pedagogues and parents of children in the kindergartens. The children's weight and height were measured during school health examination at age five to seven years. Socioeconomic data including family type, country of origin, parental education and income was obtained from national registers. Group differences in BMIz and risk of overweight/obesity were analyzed, adjusted for socioeconomic data.

Results: Overall, no significant differences were found in BMIz (0.03, 95% (CI): -0.06, 0.12) or risk of overweight (risk ratio 0.96, 95% CI: 0.78, 1.19) between the groups. However, the subgroup with lower parental education had a trend toward lower BMIz in the intervention group compared to the no-intervention group, although not statistically significant.

Conclusion: While the kindergarten-based obesity prevention intervention showed no overall effect on BMIz or overweight risk at the population level, children from families with lower parental education levels may have more benefit of the intervention.

Themes: Public health, Paediatrics
Keywords: Obesity prevention, Health promotion, Childhood

SESSION 32 - Immune mediated diseases

Anti-PM/Scl-75 and 100 autoantibodies increase IL-8 cytokine production in PM/SSc overlap syndrome patients.

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Background: Anti-PM/Scl antibodies, targeting PM/Scl-75 and PM/Scl-100 proteins, are significant biomarkers in patients with polymyositis (PM), systemic sclerosis (SSc), and overlap syndromes. These antibodies are present in a considerable subset of patients with these diseases. Understanding the cellular function of the two autoantibodies may provide insights into novel treatment approaches, addressing underlying pathogenic mechanisms and improving patient outcomes in these complex autoimmune disorders.

IL-8 is a key pro-inflammatory chemokine in the pathophysiology of chronic inflammation associated with autoimmune diseases. It mediates the recruitment and activation of neutrophils and other leukocytes to inflamed tissues, promoting a sustained inflammatory response.

Material and Methods: IL-8 production was measured in wild-type and knockout (KO) THP-1 cells, pre-stimulated with the two autoantibodies of interest using IgG from PM/Scl-positive patients (n=6) compared with PM/Scl-negative individuals. Subsequently, the concentration of the cytokine was determined via ELISA.

Results: The impact of anti-PM/Scl on the THP-1s revealed a significant increase in IL-8 production; meanwhile, the effect decreased to the level of non-stimulated controls when stimulating the STING KO cell-line. In contrast, IgG from a healthy individual showed no impact on IL-8 production.

Conclusion: Taken together, these data support that PM/Scl antibodies, promote the recruitment of neutrophils and T cells. This recruitment amplifies the inflammatory response by increasing immune cell infiltration, cytokine production, and the release of enzymes and reactive oxygen species, all of which contribute to tissue damage and the perpetuation of chronic inflammation.

Themes: Immune diseases, Molecular biology
Keywords: Autoantibodies, Chronic inflammation, Il-8

Prevalence and heritability of autoantibodies neutralizing type I interferons in centenarians and mono- versus dizygotic twins

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Introduction: Neutralizing autoantibodies (auto-Abs) against type I interferons (IFNs) have been shown to increase the risk of life-threatening viral diseases, including COVID-19. The prevalence of these auto-Abs is low in the general population below 65 years but increases sharply with age hereafter.

We hypothesize 1) that centenarians have lower prevalence of auto-Abs neutralizing type I IFNs than expected based on age, because carriers of auto-Abs died of infectious disease earlier in life and 2) production of these auto-Abs is genetically driven, even in the elderly.

Methods: Plasma/serum samples from Danish (n=258) and Colombian (n=99) centenarians as well as 1319 Danish twin pairs aged > 65 years were analysed. Samples were stimulated with IFN-α2, IFN-β and IFN-ω in high (10 ng/ml), intermediate (1 ng/ml) or low (100 pg/ml) concentrations, and the neutralizing activity of type I IFNs was assessed by measuring luciferase reporter activity in a transfected HEK293T cell system. Concordance rates between mono- and dizygotic twins were calculated.

Results: In Danish centenarians, 4.7% had auto-Abs neutralizing 10 ng/ml IFN-α2 and/or IFN-ω and 1.9% only neutralized 100 pg/ml IFN-α2 and/or IFN-ω compared with 3.0% and 6.1%, respectively in Colombian centenarians. In the twins 1.1% had auto-Abs neutralizing any of the type I IFNs tested.

Conclusion: We do not observe lower nor higher prevalence of auto-Abs against type I IFNs in the centenarians than expected based on age. Type and level of the auto-Abs between the two cohorts varied slightly, and we plan to study this further in additional centenarian cohorts. In the twins, no substantial genetic component could be detected.

Themes: Immune diseases, Immune diseases
Keywords: Autoantibodies, Type I interferons, Immunology

Measurement of the bioactivity for anti-topoisomerase 1 antibody in plasma from Systemic Sclerosis Patients

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Systemic sclerosis (SSc) is a chronic autoimmune disease with ~35% of the patients having anti-topoisomerase 1 autoantibodies (ATA). Understanding the cellular effects of ATA is crucial for improving treatment and predicting patient medical outcomes.

The bioactivity of ATA was assessed by investigating its impact on the enzymatic activity of topoisomerase 1 (TOP1). TOP1 activity is easily measured with a rolling circle enhanced enzyme activity detection (REEAD) assay, which allows for quantitative measurements of TOP1 activity in a simple, fast, and gel-free manner in crude extracts of clinical samples.

Material and Methods: The influence of ATA in plasma on TOP1 function was evaluated using plasma samples from SSc ATA-positive individuals (n=33), SSc ATA-negative individuals (n=9), and a group of healthy controls (n=26).

Results: The impact of plasma with ATA on TOP1 activity revealed considerable differences among patients, with reductions in TOP1 activity spanning from 0% to 85%. Plasma from SSc ATA-negative patients and healthy controls had a minor influence on TOP1 activity.

Conclusion: The REEAD setup measured TOP1 activity, which can benefit the evaluation of patients suffering from SSc by assessing the degree of inhibition of TOP1 by ATA in plasma. As such, REEAD presents a valuable tool for understanding SSc, enabling the establishment of an association between the bioactivity of ATA and the progression of the SSc.

Themes: Immune diseases, Molecular biology
Keywords: Autoantibodies, Systemic sclerosis, Topoisomerase 1

Repurposing disease-modifying antirheumatic drugs in low-grade inflammation

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Introduction: There is a clear association between arthritis, diabetes, obesity and cardiovascular diseases, largely through inflammation, genetic predispositions, and common risk factors such as obesity and physical inactivity. We know the proinflammatory cytokines are elevated in these conditions, and disease modifying antirheumatic drugs used to treat patients with rheumatoid arthritis (RA) can lower the risk of diabetes, even when adjusted for disease activity and body mass index (BMI). Given the established link between RA and cardiovascular disease, understanding the interaction between RA, diabetes, cardiovascular risk and obesity could provide new insights into disease mechanisms and potentially new treatment options through repurposing of existing drugs

Method: Retrospective cohort studies: using a stratified approach with six distinctive phenotypic groups based on BMI (Lean, Overweight, Obese) and metabolic health (Healthy, Unhealthy), we will investigate the prevalence of patients with autoinflammatory conditions in the six different groups, and describe their patterns of biomarkers in relation to the groups and conditions

Data, including biomarker analyses and genetic analyses, will be obtained from diabetes cohorts, nationwide registries and biobanks.

Status: in the process of identifying the number of patients with autoimmune and cardiometabolic diseases in different cohorts and accessing the data

Perspective: This research aims to bridge the knowledge gap regarding low-grade inflammation and autoinflammation and to explore opportunities for novel treatment options using drug repurposing of anti-inflammatory agents

Themes: Immune diseases, Endocrinology
Keywords: Low grade inflammation, Repurposing drugs, Biomarkers

Risk factors for cardiovascular disease in Systemic Lupus Erythematosus: Examining DNA-protein nanoparticles.

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Systemic lupus erythematosus (SLE) is an autoimmune disease that may affect multiple tissues and organs. The leading cause of mortality among these patients is cardiovascular disease (CVD). SLE patients face a 2- to 6-fold higher risk of cardiovascular events compared to the general population, with these events constituting 30% of mortality within 5 years of diagnosis. Classical risk factors for CVD in these patients cannot fully explain the increased risk. Other factors contributing to this elevated risk include inflammation, disease activity, and lupus nephritis (LN).

The complement system can be initiated by mannan-binding lectin (MBL) through the lectin pathway. Studies of recombinant human (rh)MBL have indicated a possible oligomerization of MBL, forming large superoligomeric (sp) MBLs. Studies have shown an increase in spMBLs in SLE compared to healthy controls, correlating with the patient's disease activity. spMBLs can be increased by cell-free (cf) DNA and increased levels of cfDNA is well-documented in SLE.

This project aims to find a possible connection between inflammation and plaque formation in the blood vessels of SLE patients and the size and concentration of spMBL/DNA complexes. We want to include 100 patients with SLE, examining blood samples at baseline for spMBL complexes and performing coronary computed tomography angiography. Clinical data on CVD will be compared with data on spMBL/DNA complexes with the hypotheses i) high spMBL/DNA concentration distinguishes patients with LN from patients without LN, and ii) the spMBL/DNA concentration is correlated with coronary artery plaque surface size and possibly the composition of the plaque.

Themes: Immune diseases, Molecular biology
Keywords: Systemic lupus erythematosus, Cardiovascular disease, Complement system

Towards an advanced understanding of microglia as pharmacological targets in disease: A molecular exploration of microglia dynamics at the single-cell level in models of multiple sclerosis

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Multiple sclerosis (MS) is a disabling disease of the central nervous system (CNS) with a high female predilection (69 % of patients are women). MS is characterized by chronic neuroinflammation and exacerbated activity of specific populations of microglia, innate immune cells of the brain, which are hypothesized to be key drivers of disease progression. Investigating changes in microglia populations during disease progression, considering sex-specific influences, and understanding their spatial relationship to pathological lesions is expected to provide novel insights into microglia dynamics in MS and inform strategies for pharmacological modulation of microglia activity to enhance future MS treatments. Hence, the objectives of this PhD project are to: I) Apply human induced pluripotent stem cells (iPSC)-derived male and female microglia to profile, compare, and rank the therapeutic potential of selected compounds, each affecting microglia functions by different mechanisms, II) investigate whether there is a sex bias in the microglia response to autoimmunity in animal models of MS using single cell transcriptomics analysis, and elucidate how these microglia-targeting compounds affect microglia functions and heterogeneity, and III) Identify the microglia subpopulations that associate with demyelinating lesions in MS and investigate if microglia-targeting compounds alter the spatial distribution of microglia subsets.

Themes: Neurodegenerative disorders, Bioinformatics
Keywords: Microglia, Multiple Sclerosis, Single cell and spatial transcriptomics

Diagnostic accuracy of a clinical polymyalgia rheumatica diagnosis: Impact of prednisolone initiation and a short-term discontinuation

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Aim: The impact of prednisolone initiation on the ability to make a polymyalgia rheumatica (PMR) diagnosis is unknown. This study aimed to investigate the diagnostic accuracy of clinically diagnosing PMR before and after prednisolone initiation as well as after a short-term prednisolone discontinuation.

Methods: 198 case report forms (CRFs) were constructed using data from a prospectively collected cohort of treatment-naïve PMR and non-PMR patients assessed at baseline (n=66/27), as well as PMR patients assessed 8 weeks after prednisolone initiation (n=57) and after a short-term prednisolone discontinuation (n=48). CRFs contained patient demographics, symptoms, physical examination and laboratory test results. Six rheumatologists assessed all CRFs, blinded for diagnosis, prednisolone treatment and visit. The probability of a PMR diagnosis was rated from 0-10, and each CRF was classified as either PMR or non-PMR.

Results: For patients assessed at baseline, assessors distinguished well between PMR and non-PMR demonstrating a sensitivity/specificity of 85.9%/82.7% and median PMR probability scores of 7.8 and 2.8 respectively. The sensitivity decreased to 3.5% after prednisolone initiation and increased to 25.0% after a short-term prednisolone discontinuation. Likewise, the median PMR probability score decreased to 1.0 after prednisolone initiation and increased to 2.3 after a short-term prednisolone discontinuation.

Conclusion: This study emphasizes that establishing a diagnosis of PMR becomes highly challenging after prednisolone is commenced and that short-term prednisolone discontinuation does not increase the diagnostic accuracy to pre-treatment level.

Themes: Immune diseases, Diagnostics & technology
Keywords: Polymyalgia Rheumatica, Prednisolone, Diagnostic accuracy

Genome-wide association study of allergen-specific Immunoglobulin E sensitization towards common respiratory sensitizers

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Allergic rhino-conjunctivitis and asthma are complex, heterogeneous diseases influenced by the interplay between genetic predisposition and environmental factors. Immunoglobulin E (IgE), a primary mediator of allergic inflammation, is commonly associated with atopic conditions due to the presence of allergen-specific IgE (sIgE) antibodies against common respiratory sensitizers. Genome-wide association (GWA) studies have previously identified several genetic loci linked to atopy; however, most have focused on total IgE levels in serum, with limited research on sIgE responses to specific allergens causing hay fever.

In this study, sIgE levels were quantified in more than 25,000 participants from the Danish Blood Donor Study using an enzyme-linked immunosorbent assay (ImmunoCAP Phadiatop) at Thermo Fisher Scientific. Genotyping was performed with the Illumina Global Screening Array at deCODE Genetics, Iceland. This dataset enables an extensive analysis linking sIgE levels with genetic profiles, other laboratory data, registry data, and responses from allergy and asthma questionnaires.

The objective of this study is to identify genetic variants associated with sIgE sensitization to common respiratory sensitizers, as well as to investigate distinct endotypes of asthma and allergic rhino-conjunctivitis. As the largest GWA study on sIgE sensitization to date, this research will contribute to a deeper understanding of the genetic underpinnings of IgE-mediated allergy and the overlap with hay fever symptoms.

Themes: Immune diseases, Epidemiology
Keywords: IgE sensitization, Allergic rhino-conjunctivitis, Genome-wide association study

Effectiveness of SARS-CoV-2 vaccination in immunocompromised patients

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Background: Immunocompromised patients are at risk for severe COVID-19 infections and reduced responses to vaccines.

Methods: From ENFORCE, we included immunocompromised patients prior to their first vaccination with scheduled visits at day 0, 21, 90, 180, 365 and 730, and before and after each booster. Vaccine responses were evaluated by quantifying antibodies against the Spike protein and compared with 679 immunocompetent matched controls.

Results: We included 383 patients: 233 hematological patients, 40 with HIV (PLWH), 78 solid organ transplant recipients (SOTRs), 26 with primary immunodeficiency, and 7 with more than one disease. Nearly 60% of the participants were aged 65 or older, and 61.2% were male.

After the 2nd vaccine dose (day 90), 79% of patients were IgG positive in contrast to 100% in controls. PLWH had the highest seropositivity rate (100%), while 84.8% of hematological patients, 68.0% with primary immunodeficiencies and 58.4% of SOTRs were seropositive. After the first booster, seroconversion rate increased to 91.6%.

In all groups, Spike Ig levels increased after each booster vaccination. However, between doses, antibody levels substantially declined in patients who did not experience break-through infections. Compared to controls, the measured levels of Spike Ig were significantly lower at visit 3 and 4, as well as after the first booster, in all groups of immunocompromised patients except in PLWH.

Conclusion: Serological responses to SARS-CoV-2 vaccines are reduced in immunocompromised patients. IgG levels increase after each booster but decline between doses. Therefore, the timing of booster vaccinations is critical for maintaining adequate immunity.

Themes: Infectious Diseases, Immune diseases
Keywords: Vaccine, COVID19, Immunocompromised

SESSION 33 - Paediatrics

Fibroblasts and Inflammation in the Paediatric Stroma (FIPS)

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The "Fibroblasts and Inflammation in the Paediatric Stroma (FIPS)" project explores immune-mediated connective tissue diseases in pediatric patients, with a focus on Juvenile Idiopathic Arthritis (JIA). In Denmark, approximately 1,200 JIA cases were reported in 2017, and current treatments still rely on a trial-and-error approach, lacking detailed insights into the immunological activity in affected tissues.

Taking inspiration from personalized treatment in pediatric oncology, where targeted treatments are guided by extensive diagnostic evaluations, our project aims to deepen the understanding of JIA and support the development of more personalized treatment.

Central to the project are fibroblasts—cells typically involved in maintaining connective tissue but also actively participating in inflammation. In JIA, synovial fibroblasts produce inflammatory factors and interact with immune cells, contributing to tissue damage. Moreover, immune cells such as T and B cells contribute to inflammation, forming lymph node-like structures within the synovium. Our aim is to investigate fibroblasts, their interactions with immune cells, and their role in JIA.

To explore these interactions, we are developing three-dimensional joint organoids from biopsies obtained from pediatric JIA patients. These organoids replicate the microenvironment of the diseased joint, enabling research into disease mechanisms and potential therapeutic targets.

Themes: Paediatrics, Paediatrics
Keywords: Rheumatology, 3D organoids, juvenile idiopathic arthritis

AID-early onboarding: Automated Insulin Delivery at Diabetes onset in children – Sleep, Metabolic regulation, cognitive function and family burden: Study protocol

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Steno Diabetes Center Aarhus (SDCA)

Background and aims: The incidence of Type 1 Diabetes Mellitus (T1DM) is increasing in children and adolescents. Complications are linked to poor metabolic control. Continuous insulin delivery with insulin pumps and sensor-based glucose measuring, termed Automated Insulin Delivery (AID) systems, has improved glycemic regulation in patients with T1DM. AID treatment has also revealed better sleep in both children and parents, along with an increased quality of life (QoL) as evaluated by questionnaires. It is still unknown whether AID treatment, initiated at diabetes onset (referred to as early onboarding), improves architecture of sleep, cognitive function, psychological burden, or metabolic control compared to standard treatment. We hypothesize that early onboarding has positive effects on sleep architecture, metabolic control, cognitive function, and diminish family burden.

Methods: The study is a randomized controlled clinical trial involving 40 children and adolescents diagnosed with diabetes onset. Participants are randomly assigned to receive either Multiple Daily Injections (MDI) treatment using insulin pens or AID utilizing the Tandem Control IQ Algorithm. After a period of 6 months all patients initially assigned to MDI will transition to AID treatment, and all participants will be monitored for an additional 6 months. The follow-up period for the study is 12 months in total, during which sleep investigations, questionnaires, cognitive testing, and metabolic evaluations will be conducted at 6 and 12 months. The inclusion period is 18 months at Aarhus University Hospital.

Expected results: The study is currently pending, awaiting the commencement of recruitment. The full protocol will be presented at the upcoming meeting.

Conclusions: We anticipate early onboarding will lead to a significantly improve quality of sleep for bothchildren/adolescents and parents of newly diagnosed children with type 1 diabetes. This improvement is expected to result in better metabolic control and a reduction in psychological burden for both children and parents, ultimately enhancing the cognitive function and overall Quality of Life.

Themes: Paediatrics, Endocrinology
Keywords: Type 1 Diabetes, ,

Blood pressure and cardiovascular risk factors in Danish children and their parents

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Introduction: The prevalence of high blood pressure in childhood increases globally and the condition in highly underdiagnosed. The patients are at an increased risk of hypertension, cardiovascular disease(CVD) and chronic kidney disease(CKD) in adulthood. In children and adolescents high blood pressure is often asymptomatic and therefor they do not seek medical attention. Currently, blood pressure measurement is not included in the Danish child health examination program, which is inconsistent with international guidelines.

Aim: To characterize a Danish pediatric cohort by their blood pressure levels, associated cardiovascular and metabolic risk factors, and parents' cardiometabolic status and risk factors. And to determine the prevalence of hypertension according to international guidelines after standardized oscillometric measurement of blood pressure during a single examination in the Danish pediatric population.

Method: This study utilize data from the Lolland-Falster Health Study, LOFUS: a Danish cohort study which enrolled randomly selected households. The data includes questionnaires, clinical examination, oscillometric blood pressure measurements, and urine and blood samples. We included data from 2270 individuals (4-17 years of age) and their parents(N=4713, total).

Results: Statistical analyses were initiated in October 2024, and preliminary results will be presented at the 2025 PhD-Day.

Discussion: End organ damage can be reversible and development of CVD and CKD is preventable by timely treatment of childhood hypertension. Knowledge on how to best identify Danish children at risk is essential for planning of future national screening and diagnostic strategies.

Themes: Paediatrics, Cardiology
Keywords: Pediatric hypertension, Cross sectional, Prevention

Efficacy of solifenacin, mirabegron and combination therapy in children with daytime urinary incontinence (BeDry): A randomized single-blinded controlled trial

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Background: According to International Children's Continence Society (ICCS), first-line treatment of children with daytime urinary incontinence is standard urotherapy, eventually followed by pharmacotherapy of anticholinergics. The effect of medical treatment is sparsely investigated and primarily in non-randomized trials.

Objectives: The primary objective is to evaluate if (1) combination therapy of solifenacin and mirabegron in low doses is superior to monotherapy of solifenacin in high dose and if (2) combination therapy of mirabegron and solifenacin in low doses is superior to monotherapy of mirabegron in high dose in treatment of daytime urinary incontinence among children aged 5 to 14 years who are none complete responders to respectively monotherapy of solifenacin in low dose or monotherapy of mirabegron in low dose.

The secondary objective is to evaluate the treatment response of combination therapy of solifenacin and mirabegron in low doses, monotherapy in high dose and monotherapy in low doses as supplementary comparisons. Additionally, the secondary objective is to evaluate side effects, safety, and tolerability of the medical treatment as well as the effect of treatment on well-being and quality of life.

Methods: Children aged 5-14 years diagnosed with daytime urinary incontinence refractory to standard urotherapy will be randomized to four treatment groups, randomization 1:1:1:1. Initially two groups will receive solifenacin 5 mg and two groups will receive mirabegron 25 mg. After 6 weeks, non-complete respondsers will receive add-on treatment according to their primary randomization group; group 1A will reviece solifenacin 5 mg and add-on solifenacin 5 mg, group 1B will receive solifenacin 5 mg and add-on mirabegron 25 mg, group 2A will receive mirabegron 25 mg and add-on mirabegron 25 mg, group 2B will receive mirabegron 25 mg and add-on solifenacin 5 mg. Total treatment period will be 18 weeks.

The primary endpoint measure is treatment response assessed by change from visit 2 to end of study, according to number of wet days pr. 7 days by DryPie.

Results: Participants will be included from June 2024 to December 2027.

Perspectives: The trial has the potential to optimize medical treatment of children with daytime urinary incontinence, to shorten the treatment period, diminish side effects and minimized unnecessary medical expenses.

Themes: Paediatrics, Urology & Nephrology
Keywords: daytime urinary incontinence, children, pharmacological treatment

Improvements in Daily Physical Activity and Exercise in School Children: The ActChild Study Protocol

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Introduction: An increasing number of Danish children are not meeting the national guidelines for daily physical activity. This physical inactivity is linked to obesity and a decline in overall quality of life (QoL). Physical inactivity in childhood often leads to continuous inactivity in adulthood, increasing the risk of lifestyle-related diseases.

Aim: This study aims to investigate the health promoting effects of a school-based exercise intervention on Danish school children over a 5-year follow-up period.

Method/Participants: We will conduct a quasi-experimental school-based trial involving 600 school children from Aarhus municipality, who will be pragmatically assigned to either an exercise group or a control group. The primary outcomes include changes in sleep, eating behavior, and quality of life over a 5-year follow-up period. Secondary outcomes include physical activity levels and weight.

The added value of this study: To our knowledge, this is the first school-based trial with 5-year follow-up effects of school-based exercise interventions on eating behavior. Additionally, the study aims to enhance our understanding of the long-term impacts on sleep, physical activity, quality of life, and weight management.

Themes: Paediatrics, Endocrinology
Keywords: Exercise, Eating behavior, Sleep

Study protocol: The CI-CAP Youth Project on Cognitive Bias and Interoception in chronic abdominal pain in youth

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BACKGROUND: Functional abdominal pain disorders (FAPD) and inflammatory bowel disease (IBD) present with rising incidences in pediatric populations. Despite different pathologies, the disorders show similar symptoms, incl. impairing chronic abdominal pain. Based on the theory of predictive processing, it may be that the perception of symptoms, rather than the symptoms themselves, is at fault. Thus, the main hypothesis is that cognitive biases (abnormalities in attention, interpretation and memory of specific stimuli) and altered interoception (the physiological perception of internal bodily signals) are important common underlying mechanisms for the experience of chronic abdominal pain in youth across disorders.

STUDY DESIGN: A total of 180 children and adolescents (8-17 years) will be included in the study, i.e., 60 with FAPD, 60 with IBD and 60 healthy controls. Cognitive bias will be assed using the BY-GIS task (Bias in Youth toward GastroIntestinal-related Stimuli). Interoceptive accuracy will be assessed using the heart rate discrimination task (HRDT), the respiratory resistance sensitivity task (RRST) and the water load symptom provocation task (WLSPT). All participants will perform the BY-GIS task and the HRDT, while only a subset (15 from each group, 45 in total) will perform the WLSPT and the RRST. Participants will fill out questionnaires on gastrointestinal symptoms, overall somatic symptom load and emotional distress incl. health anxiety symptoms.

PERSPECTIVES: The results of this study could be groundbreaking with regard to identifying new treatment strategies and thereby pave the way for improved interventions for chronic abdominal pain in young patients.

Themes: Neuroscience, Paediatrics
Keywords: interoception, chronic pain, predictive processing

Early-onset neonatal infection and school performance

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Background

Long-term consequences following neonatal invasive bacterial infection remain understudied. We aimed to study the association between early-onset infection and results from mandatory school tests in reading and mathematics from 9 to 15 years of age.

Methods

We conducted a nationwide register-based cohort study including all Danish near-term and term singletons born from 1997 to 2009. Early-onset infection was defined as an invasive bacterial infection during the first week of life. Infections were categorized into clinical infections defined by diagnoses, and culture-positive infections verified by bacteria cultured from blood or cerebrospinal fluid. Multivariable mixed model linear regression was used to estimate mean differences in test scores, expressed as standard deviation scores (SDS).

Results

Among 638,402 children, 2,362,046 test scores were available. A total of 5,347 and 73 children had clinical sepsis and meningitis, while 135 and 20 had culture-positive sepsis and meningitis, respectively. Clinical sepsis was associated with lower test scores with mean differences in both reading and mathematics of -0.08 SDS (95% CI: -0.10, -0.05). Clinical meningitis was associated with even lower test scores with mean differences in reading of -0.22 SDS (95% CI: -0.43, 0.00) and mathematics of -0.31 SDS (95% CI: -0.55, -0.07). Similar results were found when only culture-positive infections were considered.

Conclusion

Early-onset sepsis was associated with modest reductions in test scores, which may be important on a public health level. Early-onset meningitis was associated with more substantial reductions, emphasizing the severity of this rare condition.

Themes: Paediatrics, Infectious Diseases
Keywords: Neonatal infection, School performance,

New aspects on alarm treatment of nocturnal enuresis.

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Aim

Despite numerous studies investigating enuresis alarm therapy, the precise mechanism of the alarm's efficacy remains uncertain.

The aim of this study was to investigate if the alarm activates progressively later in the night during the treatment period, to explore whether alarm therapy causes a transition from enuresis episodes to nocturia, and to examine the feasibility of predicting the treatment duration.

Methods

Since 2016, caregivers at Aalborg University Hospital have tracked alarm times and nocturia in all children undergoing treatment. Data from completed forms, along with bladder diaries and family history, were retrospectively analyzed for children who had full effect of alarm treatment.

Results

In total, 141 children were included. Median treatment duration was 44 days (30.5; 58.5). 50 % of the children achieved complete dryness within 6 weeks of treatment. Time to first alarm increased by 37.4 minutes (95 % CI 10.8; 64.08) during the first 6 weeks of treatment. The proportion of children experiencing nocturia reduced from 40% in the first week of treatment to 28% in the final week. An inverse relationship between daytime bladder capacity prior to treatment and treatment duration was observed.

Conclusion

Among children with nocturnal enuresis and full response to alarm therapy, 50% achieved complete success within six weeks of treatment. Enuresis episodes gradually occurred later in the night. Alarm therapy did not induce a shift from enuresis to nocturia. These findings support the hypothesis that the mechanism of action for alarm therapy involves an increase in nighttime functional bladder capacity.

Themes: Paediatrics, Urology & Nephrology
Keywords: Nocturnal enuresis, Alarm therapy, Children

Impact of a simulation-based team training program for healthcare professionals in pediatric departments: A non-randomized controlled trial

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Background: Healthcare systems face ongoing challenges in patient safety, quality care, and interprofessional collaboration. Simulation-based team training (SBTT) offers a solution by allowing healthcare professionals to practice teamwork and communication in realistic clinical scenarios that mimic real-life situations. In this PhD project, we implemented a simulation intervention in pediatric departments.

Methods: In a parallel-group, non-randomized controlled trial, we introduced an SBTT intervention in four pediatric departments across the Central Denmark Region, with four others in the Region of Southern Denmark serving as controls. From April 2023 to April 2024, healthcare professionals in the intervention group participated in frequent, structured simulations, all of which were logged. We analyzed the impact on 1) sick leave, 2) patient safety culture, and 3) management of critically ill newborns (Apgar score). Parametric and non-parametric tests were applied.

Results: Over 12 months, the intervention group completed 244 simulations (1,988 hours) compared to 84 (534 hours) in the control group. Significant improvements in patient safety culture dimensions ($p < 0.05$) and reduced sick leave were observed, suggesting potential benefits for staff well-being. The management of critically ill newborns also improved more in the intervention group.

Conclusion: The SBTT intervention led to notable improvements in staff well-being and patient safety culture, with additional benefits observed in managing critically ill newborns. The positive impact on staff and targeted clinical areas highlights the value of structured, frequent simulation for enhancing healthcare environments.

Themes: Health Education, Paediatrics
Keywords: Simulation-based team training, Patient safety improvement, Healthcare staff well-being

SESSION 34 - Cardiovascular disease 2

Pulmonary Perfusion Changes of Oxygen in Acute Pulmonary Embolism: A [15O]-H2O PET exploration in a porcine model

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BACKGROUND: Acute pulmonary embolism (PE) is the third-most common cause of cardiovascular death worldwide. A recent study has shown promising effects of oxygen administration in acute PE. However, understanding the pulmonary vasodilating mechanisms of oxygen in acute PE remains unclear. Positron emission tomography (PET) using radioactive [15O]-H2O offers a unique opportunity to explore perfusion dynamics though its application in lung perfusion studies, particularly in PE, is underexplored. We hypothesize that oxygen augments pulmonary perfusion globally rather than locally at the site of the emboli.

MATERIALS AND METHODS: Five pigs will receive large, autologous PE in this experimental, controlled study of repeated measurements. Evaluation is conducted at three consecutive time points: Baseline, after induction of acute PE (FiO221%), and after increase of FiO2 to 60%. Evaluation consists of invasive measurements including right heart catheterization, blood gasses, and pulmonary perfusion assessed through O-15-labeled-water PET scans.

RESULTS: Experiments will be performed throughout December 2024. Preliminary data and results will be presented at the congress.

PERSPECTIVES: Current guidelines by the European Society of Cardiology solely recommend administration of supplemental oxygen when saturation levels fall below 90%, albeit without accompanying references validating the merits of oxygen administration. The study will provide valuable insights into changes in lung perfusion during acute PE and the effects of supplemental oxygen treatment.

ACKNOWLEDGEMENTS: The study is funded by the National Institutes of Health. The authors have no conflict of interests to declare.

Themes: Cardiology, Animal Models
Keywords: Acute pulmonary embolism, Heart-lung-interaction, O-15[H2O] PET

Visualization of Coronary Artery Disease for Modification of Risk Factors (VICAD-RISK study)

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Background: With the increasing use of coronary computed tomography angiography (CTA) in patients with chest pain, the prevalence of patients with non-obstructive coronary artery disease is growing. The presence of angina with non-obstructive coronary arteries (ANOCA) is associated with an increased risk of an unfavorable clinical outcome. Therefore, guideline-directed preventive strategies such as initiation and maintaining lipid lowering with statins are important in patients with ANOCA. This study aims to assess whether visualization of CTA images, combined with a short specialized consultation in patients with a new diagnosis of ANOCA can improve the lowering of low-density lipoprotein (LDL) cholesterol, statin adherence, influence the perception of statin-associated side effects, and the coronary plaque burden.

Methods: This study is a Danish multicenter randomized controlled trial including patients referred to coronary CTA on a suspicion of stable angina with LDL cholesterol > 2.0 mmol/L, and no history of coronary revascularization. A total of 390 patients will be randomized into three groups of each 130 patients; (1) usual care group, representing current clinical practice; (2) low-intensity intervention, where patients will receive a specialized nurse consultation, or (3) high-intensity intervention, where patients will have their CTA-images presented along with the specialized nurse consultation.

Conclusion: The VICAD-RISK study will evaluate whether the combination of CTA image visualization and specialized consultation improves initiation and adherence to statin therapy and has the potential to improve the management of ANOCA patients.

Themes: Cardiology, Rehabilitation
Keywords: Non-obstructive coronary artery disease, Coronary computed tomography angiography, Statins

24 hours of donor heart machine perfusion before heart transplantation - is that possible?

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Background: Static cold storage remains the gold standard for preserving donor hearts before transplantation but is associated with ischemia, anaerobic metabolism and unacceptable organ injury if the cold ischemic time exceeds 4-5 hours. Hypothermic oxygenated machine perfusion (HOPE) has been shown to be feasible for longer preservation times and reduced post-transplant complications in relation to donation after brain dead (DBD). Donation from circulatory dead donors (DCD) has emerged as an option to expand the donor pool.

Aim: The aim of this study was to examine whether it is possible to transplant both DCD and DBD hearts and regain good contractile graft function after 24 hours of preservation with HOPE in a porcine model.

Methods: Sixteen heart transplantations were included. The study was conducted as a prospective randomized intervention study and included the following groups: 1) DCD versus 2) DBD both followed by direct procurement and 24 hours of HOPE before implantation, reperfusion and in vivo evaluation in the recipient.

Results: All the 8 DCD hearts and the 8 DBD hearts were explanted and completed 24-hour HOPE. After weaning 1 recipient in each group were excluded due to pulmonary hypertension and pulmonary artery bleeding, respectively. All the included transplantations in both the DCD and the DBD group were successful with a cardiac output above 4 L/min 2 hours post-CPB and a mean arterial pressure above 60.

Conclusion: Both DCD and DBD hearts can be directly procured and regain good contractile graft function after 24 hours of preservation with HOPE in a large animal model. Our results encourage the future clinical use of machine perfusion.

Themes: Cardiology, Animal Models
Keywords: Heart Transplantation, Hypothermic oxygenated machine perfusion (HOPE), World record

Use of Antianginal Medication at Referral to Myocardial Perfusion Imaging in Patients with Established Chronic Coronary Syndrome

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Aims: The importance of initiating and optimising medical therapy in patients with symptomatic chronic coronary syndrome (CCS) is increasingly recognised. However, clinical inertia may delay timely implementation. This study examined the prevalence of antianginal medication use at the time of referral to myocardial perfusion imaging (MPI) in patients with symptomatic CCS.

Methods and Results: A multicentre cohort study was performed using MPI procedures from all hospitals in Western Denmark. Patients with established CCS referred for MPI due to new-onset angina or angina equivalent symptoms were eligible. Prevalent use was defined as 1 prescription redemption from the Danish National Prescription Registry for antianginal medication within 180 days before referral.

During 2018–2021, 8837 patients were referred to MPI. Here, 23% of patients did not use any, 41% used only one type, 27% used two types, and 9.9% used three or more types of long-acting antianginal medication. Between 2018 and 2021, no clinically significant difference in the proportion of patients using one or more types of long-acting antianginal medications was observed (79% users during 2018–2019 versus 76% users during 2020–2021 (difference in proportions -2.7%, 95% confidence interval -4.4 to -0.9)).

Conclusion: More than half of symptomatic patients with established CCS used no or only one type of antianginal medications before referral to MPI, with no clinically significant time changes in the overall use during 2018–2021. These findings suggest clinical inertia and an untapped potential for optimisation of antianginal therapy before referral to MPI.

Themes: Cardiology, Epidemiology
Keywords: Chronic coronary syndrome, Myocardial perfusion imaging, Myocardial ischemia

Mortality related to left ventricular ejection fraction and coronary artery disease in non-ST-segment elevation myocardial infarction

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Background: Both reduced left ventricular ejection fraction (LVEF) and coronary artery disease (CAD) confer poor prognosis after non-ST-segment elevation myocardial infarction (NSTEMI). However, the contemporary risk of all-cause death associated with the extent of obstructive CAD over a range of LVEF remains unclear.

Purpose: To assess the impact of LVEF and CAD on all-cause death following a first-time NSTEMI.

Methods: We included first-time NSTEMI patients undergoing coronary angiography (CAG) from 2010 to 2021 and stratified them by LVEF (≥51%, 41-50%, or 10-40%) and extent of vessel disease (VD; 1, 2, or 3VD). The primary outcome was all-cause death. We calculated 5-year cumulative incidence proportions (CIP) and adjusted hazard ratios (HR).

Results: A total of 8,770 patients with first-time NSTEMI and obstructive CAD were examined with CAG. The increase in mortality associated with decreasing LVEF was greater than observed by extent of CAD: The 5-year mortality increased stepwise by CAD from 14% for 1VD to 31% for 3VD, but from 12% for LVEF ≥50% to 40% for LVEF 10-40%. When combining LVEF and extent of CAD, the 5-year mortality increased from 9% for 1VD and LVEF ≥51% to 46% for 3VD and LVEF 10-40%, corresponding to a risk difference of 37%. Using patients with LVEF >50% and 1VD as reference group, the 5-year risk of mortality were three times higher in those with LVEF 10-40% and 3VD.

Conclusion: In a contemporary all-comers cohort of first-time NSTEMI patients, declining LVEF and increasing extent of CAD were both associated with a gradual increase in 5-year mortality. This study highlights the importance of considering both for prognostication among patients with NSTEMI.

Themes: Cardiology, Epidemiology
Keywords: , ,

The differences in measurement of adherence in secondary prevention of atherosclerotic cardiovascular disease – A scoping Review

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Background: Adherence is an ongoing issue in secondary prevention of atherosclerotic cardiovascular disease (ASCVD). However, the tools used to measure adherence varies in secondary prevention of ASCVD is still discussed. This study aims to explore the literature for a possible aligned measurement of adherence for patients with ASCVD.

Method: We performed a comprehensive search strategy in PubMed, CINAHL, Web of Science and EMBASE, limited to publication after year 2000. The primary search was conducted May 2023 and a repeated search was performed November 2024. Search terms were produced under the supervision of a professional librarian. The PRISMA-ScR checklist were followed. Retrieved studies was exported and independently evaluated in an online reference manager software Covidence® 2023 by two reviewers. Evaluation of the title and abstract of the search results was performed and eligible studies went through to full text screening. All conflicts were resolved through discussion by a third reviewer.

Preliminary results: 1739 studies were retrieved, and 87 studies were eligible for inclusion. 205 studies were duplicates and 1393 were excluded on abstracts. Hereafter, 54 studies were excluded due to either population group, study design, outcome measures, data before year 2000 as well as used language. 95,4 % studies included data from patients with coronary artery disease, 62,1 % studies with Stroke and 56,3 % studies with peripheral artery disease. The studies included data from both patients reported outcome and medical records. Different measurements of adherence were found in the studies.

Conclusion: There is a need for a more aligned measurement of adherence.

Themes: Cardiology, Rehabilitation
Keywords: Atherosclerotic cardiovascular disease, Adherence, Patient-Reported Outcome

Low-Density Lipoprotein Cholesterol, Coronary Plaque burden, and Cardiovascular Risk in individuals beyond 75 years of age: The Western Denmark Heart Registry

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Background: The need for preventive strategies to manage low-density lipoprotein cholesterol (LDL-C) in older individuals remains controversial.

Purpose: To assess if LDL-C is associated with plaque on coronary computed tomography angiography (CCTA) and future cardiovascular risk in statin-naïve individuals across different ages.

Methods: This cohort study included individuals undergoing CCTA from 2008-2021 from the Western Denmark Heart Registry. Outcomes and measures included coronary heart disease (CHD), any plaque, and early revascularization.

Results: The study included 37,910 statin-naïve individuals. Median age was 57 years, and 52% were women. The prevalence of any plaque was 19,962 (53%) and 2,194 (6%) experienced early revascularization. The overall adjusted risk ratio (aRR) for any plaque and early revascularization in individuals with high vs. low LDL-C (>4.4 vs. <2.7 mmol/L) was 1.34 (95% CI 1.30-1.39) and 2.65 (2.28-3.07), respectively. The absolute risk for early revascularization was highest among individuals aged >75 years with LDL-C >4.4 mmol/L (90-day risk 20% [95% CI 13-29%]).

During the 5.1-year follow-up, 944 (2%) experienced CHD. The overall adjusted hazard ratio (aHR) for CHD in individuals with high vs. low LDL-C was 2.74 (95% CI 2.15-3.48). The absolute risk of CHD was highest in individuals aged >75 years with LDL-C>4.4 mmol/L (5-year risk 9% [95% CI 3-18%]).

Conclusion: LDL-C was associated with coronary plaque burden and future cardiovascular risk across all ages, with the absolute risk being highest in individuals aged >75 years. These findings indicate that LDL-C management remains important throughout life.

Themes: Cardiology, Epidemiology
Keywords: Atherosclerosis, Coronary artery disease, Coronary computed tomography angiography

Labor market participation among working-age heart failure patients with a cardiac resynchronization therapy device

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Purpose. Labor market participation is an important rehabilitation goal for working-age patients living with heart failure (HF). Cardiac resynchronization therapy (CRT) reduces mortality and HF hospitalizations and improves quality of life, but no studies have investigated labor market participation following CRT. We therefore aimed to describe labor market participation in patients with HF before and after CRT implantation.

Methods. This region-wide register-based cohort study comprised HF patients aged 40-63 years, with ejection fraction 35% and QRS duration >130 milliseconds, who received a CRT system from 2000-2017 in the Central Denmark Region. Using individual-level linkage in Danish medical and administrative registries, we assessed weekly employment status from one year prior to CRT implantation until two to five years of follow-up and conducted stratified analyses by sociodemographic and disease-related risk factors.

Results. We identified 546 patients, of whom 42% were in early retirement one year prior to implantation. Active employment decreased from 45% to 19% from one year before until implantation, declining primarily the last eight weeks before implantation. The proportion of patients in active employment increased in the first eight weeks after CRT implantation and then stabilized, reaching 31% at one-year follow-up. We observed lower labor market participation in patients with older age, multimorbidity, lower educational level and upgrade procedures, but higher in later calendar years.

Conclusions. In working-age patients with HF, labor market participation increased after CRT implantation, despite many patients being retired prior to implantation.

Themes: Cardiology, Epidemiology
Keywords: Cardiac Resynchronization Therapy, Heart Failure, Labor market participation

SESSION 35 – Cancer 3

Tumor-specific circulating cell-free DNA (ctDNA) and its clinical value in predicting response to palliative systemic treatment or survival in patients with pancreatic cancer: a systematic review and meta-analysis

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Background: We investigate the clinical utility of ctDNA response evaluation criteria and examine the value of ctDNA in predicting disease outcomes in patients with pancreatic ductal adenocarcinoma (PDAC).

Methods: The protocol was registered in PROSPERO (CRD42023438774). Searches in PubMed, MEDLINE, Embase, and Cochrane were managed in Covidence. Studies examining ctDNA dynamics related to treatment response, progression-free survival (PFS), or overall survival (OS) in PDAC patients receiving palliative treatment, were eligible. Studies providing hazard ratios (HR) based on univariate analysis with 95% confidence intervals were included in the meta-analysis.

Results: 1682 studies were screened for eligibility. CtDNA dynamics were reported in 903 of 2340 patients across 31 studies. Common ctDNA methods included Next Generation Sequencing (NGS) and digital droplet PCR targeting KRAS. Detection rates ranged 26-100%, with higher rates for multi-target NGS. Cut-offs for ctDNA dynamics comprised ctDNA detection, concentration, and change as proportions, ratios, or slopes. CtDNA change was linked to clinical outcomes in 26 studies; 19 used diverse statistical approaches; five studies were eligible for meta-analysis, showing ctDNA increase/persistence correlated with poor PFS, HR 5.9 (1.4-24.5; n=151), and OS, HR 2.2 (1.1-4.3; n=143).

Conclusion: CtDNA response shows promise for predicting clinical outcomes in PDAC. However, data is heterogeneous, and clear definitions of ctDNA response and progression

vary. Ongoing prospective studies must seek to validate ctDNA response criteria (ctDNA RECIST) and compare it with imaging evaluation in randomized trials.

Themes: Cancer, Molecular biology
Keywords: tumor-specific circulating cell-free DNA (ctDNA), pancreatic ductal adenocarcinoma (PDAC), systematic review

Allogeneic Bone Marrow Transplantation in CTCL: Potential Pathway to Cure

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Introduction: Cutaneous T-cell lymphoma (CTCL) is a rare, challenging malignancy with limited treatment options, particularly in advanced stages. Allogeneic bone marrow transplantation (allo-BMT) has shown potential in achieving durable remissions, though the molecular mechanisms underlying its efficacy are not fully understood. This translational study investigates the molecular changes occurring in CTCL patients before and after allo-BMT to identify biomarkers associated with response, changes in the tumor microenvironment and compare these findings to the clinical effects such as impact on disease progression and quality of life.

Materials and methods: We aim to include patients with advanced-stage CTCL eligible for allo-BMT. We collect medical photographs, skin biopsies, blood samples and questionaries. We will perform digital spatial profiling (DSP) on skin biopsies collected pre-transplant and at multiple intervals post-transplant to monitor shifts in T-cell phenotypes, tumor microenvironment alterations, and graft-versus-tumor-related immune responses. The molecular findings will be compared to clinical findings to apply a translational approach.

Results and conclusion: Other studies suggest that allo-BMT may offer prolonged molecular and clinical remission in selected patients. This study aims to reveal the dynamic molecular landscape in CTCL, particularly in those treated with allo-BMT, potentially identifying targetable pathways to enhance treatment outcomes. Our findings will provide a basis for future investigations focused on optimizing allo-BMT protocols and tailoring post-transplant therapies to sustain remission and improve patient survival.

Themes: Cancer, Molecular biology
Keywords: Translational research, Rare malignancy, Clinical research

Circulating tumor DNA for assessing neoadjuvant treatment response and recurrence risk in rectal cancer patients

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Introduction: Disease recurrence after surgery is the main factor affecting survival in rectal cancer patients. Hence, identifying high-risk patients is important to optimize postsurgical treatment. In recent years, effective use of neoadjuvant therapy (NAT) has led to increased focus on non-operative strategies. However, clinical modalities for assessing complete response following NAT are not sufficiently accurate for patient selection. Circulating tumor DNA (ctDNA) offers great potential for predicting NAT response and identifying high-risk patients.

Materials and Methods: We recruited 114 patients with locally advanced rectal cancer treated with NAT and surgery. Plasma samples (n=319) were collected before therapy, after NAT, and postoperatively. Analysis of ctDNA was performed using a tumor-agnostic droplet digital PCR test targeting three methylation markers.

Results: The pre-treatment ctDNA detection rate was 86.8%. Post-NAT ctDNA status was significantly associated with pathologic complete response (pCR; p=0.03, Fisher's exact). None of the 11 patients with pCR had ctDNA detected following NAT and the sensitivity for detecting residual disease was 32%. Detectable ctDNA was associated with worse recurrence-free survival (RFS) and overall survival (OS), both after NAT (RFS HR 3.2, 95%CI 1.5-6.8, p=0.004; OS HR 3.0, 95%CI 1.1-8.4, p=0.03) and after surgery (RFS HR 8.3, 95%CI 3.7-18.9, p<0.001; OS HR 10.6, 95%CI 3.4-33.4, p<0.001).

Conclusions: In conclusion, we showed that ctDNA status after NAT was significantly associated with pCR. Moreover, our study demonstrated the prognostic value of ctDNA analysis in predicting recurrence and survival outcomes in rectal cancer patients.

Themes: Cancer, Molecular biology
Keywords: Circulating tumor DNA, Rectal cancer,

Therapeutic modulation of the KEAP1/NRF2 axis improves efficacy of onco-virotherapy in hard-to-treat high-grade cancers.

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Cancer remains a leading cause of death globally, with pancreatic and brain cancers showing poor survival rates despite advancements in therapies like CAR-T cells and immune checkpoint inhibitors. Onco-virotherapy, utilizing viral vectors to target cancer cells, has emerged as a promising treatment, particularly for cancers resistant to conventional therapies. A key factor influencing cancer cell susceptibility to oncolytic viruses is the redox mediator NRF2, regulated by the KEAP1 protein. NRF2 activation, while conferring resistance to chemotherapy, also downregulates antiviral genes, potentially enhancing the effectiveness of onco-virotherapy. This study explores the role of the KEAP1-NRF2 axis in enhancing susceptibility to oncolytic viruses in pancreatic and brain cancers. We hypothesize that overexpression of NRF2 in these cancers creates a therapeutic window, and manipulating NRF2 activity through KEAP1 inhibitors may enhance the efficacy of onco-virotherapy, offering a novel treatment approach for these incurable cancers.

Themes: Cancer, Molecular biology
Keywords: Onco-virotherapy, Cancer, Precision medicine

A phagocytosis checkpoint receptor with cancer biomarker potential: Soluble Leucocyte Immunoglobulin-like Receptor subfamily B member 1 (sLILRB1)

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Background

The phagocytosis checkpoint receptor LILRB1 is expressed on macrophages and regulates phagocytosis and immune activation. A splice variant produces a soluble form of LILRB1 (sLILRB1), which may correlate with LILRB1 in the membrane and hold biomarker potential in cancer. We studied the regulation of sLILRB1 expression in human macrophages in vitro and in human serum and urine.

Methods

The expression of LILRB1 and sLILRB1 were studied in human monocyte-derived macrophages (MDMs) polarized with either LPS and IFN-γ, IL-4 and IL-13, IL-10 or left untreated. RT-qPCR was used to measure mRNA levels, while protein levels were quantified using flow cytometry and ELISA. To assess biomarker potential, sLILRB1 reference intervals (RI) were determined in serum (n=124) and urine (n = 253). In a pilot study, serum (n = 9) and urine (n=10) samples from the Bladder Cancer biobank at MOMA, AUH were compared to healthy.

Results

The sLILRB1 levels varied after different stimulations of MDMs and sLILRB1 correlated with changes in LILRB1. Soluble LILRB1 was detected in serum from all healthy donors (95% RI: 6.2-18.8 µg/L) and in 80% of urine samples (upper reference limit: 2.42 µg/L). The stability of sLILRB1 was high during long-term storage. In the pilot study, serum sLILRB1 in bladder cancer samples were not different from healthy, however urine sLILRB1/creatinine ratios were increased.

Conclusion

The sLILRB1 expression changes in response to different immune stimuli and sLILRB1 varies in parallel to LILRB1. Further, sLILRB1 is measurable in human serum and urine and shows high stability. These biomarker features form the basis for further studies of sLILRB1's biomarker potential.

Themes: Cancer, Molecular biology
Keywords: Macrophages, Bladder cancer, Biomarker

Long non-coding RNAs in childhood ependymoma: key mediators of cellular differentiation?

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Ependymoma (EPN) is one of the most common types of pediatric brain tumors and is often associated with poor outcome. Current treatment strategies consist of surgical resection and non-specific therapies partly because only few somatic driver mutations are known, and the underlying pathobiology is poorly described. Long noncoding RNAs (lncRNAs) are a class of non-coding RNAs emerging as important oncogenic drivers and tumor suppressors in many cancers. However, they remain mostly unexplored in pediatric brain tumors. Using Next Generation Sequencing, we profiled the expression landscape of lncRNAs in ten EPN and three control samples. We identified a total number of 9145 lncRNAs expressed in the samples, including many upregulated lncRNAs of which many were found to be neighbors to sense genes related to brain development. When comparing EPN samples from deceased patients to survivors, many lncRNAs were also found to be differentially expressed, revealing some of the most high-risk EPN associated lncRNAs to be DELEC1, CD44-AS1 and H19. Moreover, three candidate lncRNAs, HOTAIRM1, HOXB-AS1 and IGF2-AS were studied in vitro, using two EPN cell lines, to elucidate their functional role in EPN pathogenesis. Knock down of the candidate lncRNAs resulted in genes defining specific neoplastic subpopulations to be differentially expressed. Using in situ hybridization, we found the expression of the candidate lncRNAs to be limited to cancer cells and specific tissue regions. Together our data suggests that lncRNAs are important in the development of EPN tumors and that HOTAIRM1, HOXB-AS1 and IGF2-AS may play a role in maintaining EPN cells in specific neoplastic cellular states.

Themes: Cancer, Molecular biology
Keywords: Pediatric brain cancer, Non-coding RNA, Ependymoma

The role of long non-coding RNAs and the tumor microenvironment in the treatment response to bendamustine-rituximab therapy in mantle cell lymphoma

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Mantle cell lymphoma (MCL) is an aggressive and mostly incurable B-cell malignancy. Bendamustine and rituximab (BR) combination therapy has emerged as an effective treatment option for MCL, particularly in elderly patients who may not be eligible for intensive therapies. Despite high response rates to BR, many patients experience relapse after treatment due to various resistance mechanisms. Increasing evidence shows that the tumor microenvironment (TME) is key in developing drug resistance, making it a valuable target for studying acquired resistance in MCL. Long non-coding RNAs (lncRNAs) constitute a large group of RNAs that are non-protein coding but play diverse roles in gene regulation. We profiled lncRNA expressions in MCL using RNA sequencing data from primary samples and healthy controls. We identified 661 significantly upregulated lncRNAs in MCL patients, with some showing increased expression in higher-risk groups. Further in vitro studies in MCL cell lines revealed one lncRNA that executes target-directed microRNA degradation (TDMD) of a microRNA with known tumor suppressor properties. This lncRNA's potential impact on MCL progression needs further investigation into its potential carcinogenic properties and role in the disease. In the future, we will investigate spatial expression of sixty immuno-oncology proteins in MCL tumors and their microenvironment, using single-cell spatial analyses to examine samples from BR-treated patients. Spatially mapping cell types with the addition of in-depth protein characterization of the TME, could potentially identify drivers of TME-mediated drug resistance, leading to a better understanding of treatment responses in MCL.

Themes: Cancer, Molecular biology
Keywords: Non-Coding RNA, Lymphoma, Tumor Microenvironment

Low T cell diversity is associated with poor outcome in bladder cancer: a comprehensive longitudinal analysis of the T cell receptor repertoire

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T cells are one of the primary effector cells in the endogenous defense against cancer, yet the clinical impact of their quantity, diversity, and dynamics remains underexplored. Here we investigated the clinical relevance of the T cell receptor (TCR) repertoire in patients with bladder cancer. In advanced-stage bladder cancer, low pre-treatment peripheral TCR diversity was associated with worse overall survival ($p = 0.024$), particularly when it coincided with a low fraction of circulating T cells ($p = 0.00049$). The low-diversity TCR repertoires were dominated by hyper-expanded clones that persisted throughout treatment and disproportionately targeted latent viral infections. Longitudinal analysis revealed a reduction in TCR diversity after treatment indicating an adverse effect on the immune system. In early-stage bladder cancer, we showed that immunotherapy had a stimulatory effect on TCR diversity in patients with good outcomes. Single-cell sequencing identified most hyper-expanded clones as cytotoxic T cells, while non-expanded clones were predominantly naive T cells. Overall, our findings suggest that TCR diversity is a promising new biomarker that may offer new avenues for tailored oncological treatment to enhance clinical outcomes for bladder cancer patients.

Themes: Cancer, Bioinformatics
Keywords: T Cell Receptor sequencing, Bladder cancer, immunoinformatics

SESSION 36 – Dentistry

Factors affecting long-term prognosis of root-canal treated teeth

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Objective: To assess the overall survival, identify and analyze prognostic factors related to the long-term prognosis of root-filled teeth performed by dental students.

Materials and methods: This study involves a follow-up of patients who received root canal treatment at the Department of Dentistry and Oral Health, Aarhus University, between January 1st, 2014, and December 31st, 2019. The patients will undergo clinical examinations of the coronal restoration and surrounding tissues, as well as radiographic assessments of periapical conditions. The primary outcome measures include tooth survival, defined as the tooth being present at the examination, and the success of treatment, evaluated through a standardized set of outcome measures for root canal therapy based on clinical and radiographic findings and the type of coronal restoration including measures for quality of root-filling and coronal seal.

Results: A statistical analysis of tooth-level data will be conducted to identify the factors influencing the success and survival of root canal-treated teeth with statistical significance set at 5%. The prognostic factors affecting the survival and success of root canal treatment related to the timing and type of coronal restoration will be further analyzed. The analysis will be adjusted for patient-level confounding factors, such as smoking and age.

Themes: Dentistry, Public health
Keywords: Endodontically treated teeth, Tooth Survival, Prognostic factors

Oral Hygiene Habits in Caries-Prone Individuals after Radiotherapy for Head and Neck Cancer – an Exploratory Clinical Study

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Background: Reduced salivary flow or hyposalivation is a frequent side effect after curative-intended radiotherapy of the head and neck area. As a result these patients are most often at high risk of rampant dental caries. Today, we know little about these patients' oral hygiene habits and use of high-dosage fluoride toothpaste.

Objective: To explore caries status, salivary flow rate, oral fluoride levels, oral hygiene habits and high-dosage fluoride toothpaste-use in individuals after curative-intended head and neck radiotherapy.

Materials and methods: This observational study is an interdisciplinary collaboration between Arhus University and Aarhus University Hospital planned to recruit approx. 50 individuals at their 6-months follow-up to curative-intended head and neck radiotherapy. Unstimulated and stimulated saliva (sialometries) and dental biofilm will be sampled for fluoride determination using a modified fluoride ion-selective electrode, dental caries status registered, and a questionnaire-based interview regarding oral hygiene habits will be conducted.

Expected outcomes: The study is anticipated to shed light on the dental care habits of individuals suffering from varying levels of reduced salivary flow after head and neck radiotherapy, as well as generate knowledge about their caries status and oral fluoride levels.

Significance: The project could contribute to establish future best-practice recommendations for the oral hygiene regimen including fluoride treatment of individuals with reduced salivary flow/hyposalivation after curative-intended head and neck radiotherapy aiding them to maintain their teeth and uphold their quality of life.

Themes: Dentistry, Cancer
Keywords: Hyposalivation, High-Dosage Fluoride Toothpaste, Oral Hygiene Habits

Empowering Tomorrow's Dentists: Tackling Social Inequality in Dental Health through Practice-Oriented Initiatives

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The occurrence of social inequality in dental health is a recognized fact and an area where health inequality is evident. Population groups that are socioeconomically underprivileged and disadvantaged populations with greater healthcare needs often receive less care than advantaged populations with lower needs. These individuals experience significant challenges in maintaining adequate dental care, and some citizens do not go to the dentist at all, which can have long-lasting individual and socio-economic consequences. The aim of this pilot project is to help prepare future dental students to engage in practice-near efforts of addressing social inequality in dental health. The overall purpose of the project is to formulate equality-promoting didactic concepts and learning activities to improve the social justice education in dentistry and furthermore provide guidelines for the general dental community. To this end, the project pursues two empirical avenues: First, it investigates how social engagement impacts the education of current dental and medical students. Secondly, it seeks to identify common obstacles to achieving greater equality in dental healthcare that characterize the clinical reality in which future dentists will practice. This empirical work is based on a mixed-methods approach that supplements a predominantly qualitative design (interviews, participant observation) with statistical material (surveys, data collected from bridge-building to dental visits). The project is a collaboration between the Department of Dentistry and Oral Health, Aarhus University, The Department of Philosophy and History of Ideas, Aarhus University and the NGO Social Health.

Themes: Dentistry, Health Education
Keywords: Inequality in Dental Health, Dental Education, Student Motivation

Leveraging Deep Learning to Improve Cone Beam Computed Tomography Image Quality, Reduce Patient Radiation Exposure and Enhance Diagnostic Capabilities

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Cone-beam computed tomography (CBCT) is extensively utilized in dentistry to visualize anatomy in three dimensions. However, CBCT images frequently suffer from limitations including low spatial resolution and noise that can hamper diagnostic efficacy. Moreover, CBCT has limitations in detecting vertical root fractures (VRFs), which can lead to tooth loss. Increasing the resolution of CBCT may enhance its capacity for VRF diagnosis. Our project aims to develop a deep learning (DL) approach to enhance the quality of CBCT images.

The project has three objectives to address these challenges:

1. Develop a DL framework to enhance the overall quality of CBCT images. It will be trained on CBCT volumes generated by systematically degrading high-resolution CBCT scans to simulate clinical image quality loss from factors like low radiation dose and motion.

2. Assess an optimized DL framework to convert ('translate') standard low-dose, low-resolution CBCT acquisitions into realistic high-resolution CBCT images comparable to normal clinical protocols. This could enable major reductions in patient radiation exposure from dental CBCT exams without sacrificing diagnostic image quality. The models will be applied to anonymized standard low-dose CBCT volumes acquired clinically.

3. Validate the DL-based enhancement's effectiveness in improving detection of subtle VRFs from CBCT volumes of extracted teeth. The study will comprise inspecting extracted teeth with confirmed VRFs and normal roots.

Potential impacts include reducing CBCT patient radiation exposure by enabling low-dose imaging while simultaneously improving diagnostic yield and accuracy for subtle findings like VRFs.

Themes: Dentistry, Imaging techniques
Keywords: cone-beam computed tomography, artificial intelligence, deep learning

Synthetic Dental Radiography using Generative Artificial Intelligence

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Synthetic data generation using AI has tapped different scientific domains, with dental imaging being no exception. The use of generative AI addresses a limitation of AI research in terms of generalization and adaptability, because of the low quantity and quality of available real-life data as well as privacy concerns. Generative models such as Conditional Generative Adversarial Networks (GANs) and Diffusion Models have shown promise in generating high-quality images. Furthermore, models like Contrastive Language-Image Pre-training (CLIP) have introduced efficient cross-modal text-image encodings, significantly enhancing the generation. In this work we aim to use different Generative AI methods along with an ambition of Auto Segmentation techniques at later stages. Specific project goals we envision are – (1) Public and private data exploration, (2) object detection and segmentation, (3) conditional generation of panoramic radiographs with models like GANs and diffusion, (4) data augmentation using the generated images and building more performant prediction models, (5) making the proposed models robust with reinforcement learning and human-in the-loop methods with the goal of clinical implementation. Specifically – (1) Research question: Can deep learning be used to generate realistic dental panoramic radiographs; (2) Objectives: (a) To develop deep learning-based generators of dental panoramic radiographs. (b) To allow for customization of the generated radiographs based on user-defined prompts. (3) Hypotheses: (a) Image quality metrics do not differ between synthetic and actual radiographs. (b) Dental professionals are unable to distinguish synthetic from actual radiographs. Figure 1 illustrates some images from a public dataset which are processed to have two data inputs for the learning algorithm. One being condition, for example, “Q3 T6 Caries” meaning third quadrant, sixth tooth with Caries disease, and another being the cropped image itself. After learning (training) is done, similar conditions can be fed to the model as a query to generate corresponding (synthetically) high quality images.

Themes: Dentistry, Imaging techniques
Keywords: Generative AI, Panoramic Radiographs,

A Feasibility Study on the reliability of Dental Dedicated MRI in two-dimensional Orthodontic Diagnosis and Treatment Planning

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Introduction: Magnetic resonance imaging (MRI) is widely used for imaging diverse tissues. Recently, dental-dedicated MRI (ddMRI) has emerged as a promising radiation-free tool in dentistry, offering multiplanar imaging without known adverse effects. In orthodontics, ddMRI could be feasible for visualizing dentofacial structures, the temporomandibular joint, jaw muscles, and facial morphology. While lateral cephalograms are standard for cephalometric analysis of teeth and jaws, they expose patients to radiation. A high-quality two-dimensional (2D) ddMRI could provide a safe, radiation-free diagnostic alternative for orthodontic treatment planning in the 25% of the Danish youth who undergo orthodontic treatment. .

Aim: This study examines the reliability of 2D ddMRI in orthodontic diagnosis, focusing on its accuracy in morphological landmark identification and treatment planning.

Materials and Methods: Thirteen volunteers underwent ddMRI scanning to generate 2D images for orthodontic landmark identification. Three independent observers identified standard orthodontic landmarks including Sella, Nasion, Gonion, and Gnathion. Inter- and intra-examiner reliability were evaluated to assess diagnostic precision.

Results: The study will analyze ddMRI's reliability for 2D orthodontic diagnosis, with a focus on inter- and intra-observer agreement. Inter-examiner reliability is expected to demonstrate clinically acceptable agreement on landmarks, while intra-examiner reliability should confirm consistent individual assessments.

Conclusions: This study may support ddMRI as a reliable, radiation-free imaging tool in orthodontics. Based on reliability outcomes, ddMRI could be a viable alternative for orthodontic diagnosis and treatment planning, providing a safer, radiation-free diagnostic pathway.

Themes: Dentistry, Imaging techniques

Keywords: Magnetic-resonance-imaging, orthodontics, diagnosis and treatment planning

Unravelling the mechanisms of TMD pain disorders

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The term nociplastic pain is characterized by altered pain processing in the absence of ongoing tissue damage, meaning its identification currently relies on patient history and the exclusion of other pain mechanisms. Temporomandibular disorders (TMD) include several conditions concerning the temporomandibular joint and masticatory muscles. They are the major cause of nondental pain in the orofacial area and their pathogenesis is not clear.

With this study we aim to develop a multidimensional tool to aid in the identification of TMD pain patients with a nociplastic pain mechanism that can be used in clinical practice and research. The participants will undergo several assessments, including somatosensory evaluation, brainstem and spinal reflexes, imaging, inflammatory markers, clinical examination and questionnaires. The collected data will be sent to experts in the field of orofacial pain, who will classify patients into nociceptive, neuropathic, or nociplastic pain mechanisms. The agreement between examiners will be calculated to determine the diagnostic accuracy of the tool. At the same time, a support vector machine (SVM) for multi-class classification will be used to stratify patients into the three different clusters. The performance of the SVM model will be compared with the experts´ classification.

Our hypothesis is that we will be able to distinguish between nociceptive, neuropathic, and nociplastic pain in painful TMD patients, allowing more targeted and effective treatment strategies. We believe this will allow us to develop a new chair-side protocol to identify pain mechanisms, improving clinical accessibility.

Themes: Neuroscience, Dentistry
Keywords: Nociplastic Pain, Temporomandibular Disorders, Diagnostic tool

3D Cephalometric evaluation in Orthognathic Patients: Outcomes from a Total Digital Workflow

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Background: For years, dental casts, articulators, and 2D lateral cephalometric radiographs have been the cornerstone for surgical planning for orthognathic patients, relying heavily on traditional 2D cephalometric measurements. However, recent advancements in software tools have enabled a fully digital workflow, incorporating 3D cephalometric measurements. We hypothesize that 3D cephalometric measures offer improved precision in the surgical planning of the orthognathic patient.

Materials and Methods: Patients were divided into two groups based on the surgical procedure they underwent: bimaxillary surgery or the Le Fort I procedure. Prior to surgery, cone beam computed tomography (CBCT) scans were performed, followed by the creation of virtual surgical plans (VSP). Surgical splints were then directly 3D printed from the VSP. Postoperatively, the patients were rescanned using CBCT. Nineteen anatomical landmarks were identified on both the VSP and post-surgical scans. Measurements were conducted twice to assess consistency and accuracy.

Preliminary Results: The placement of some anatomical landmarks demonstrated high precision, while others exhibited greater variability in positioning. The use of 3D cephalometry allowed for a more detailed assessment of these variations.

Conclusion: This study shows the potential of 3D cephalometry in assessment of outcome and improvement of the precision of orthognathic surgical planning. The total digital workflow demonstrates enhanced precision in orthognathic surgical outcomes. Certain landmarks require further refinement in placement accuracy and further research is needed to optimize consistency of landmark identification.

Themes: Dentistry, Surgery
Keywords: 3D Cephalometry, Virtual Surgical Plan, Digital Workflow

Advancing Forensic Odontology: A 3D Pipeline for Disaster Victim Identification

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The field of forensic odontology is advancing with the integration of intraoral 3D photo scans, offering new possibilities for identifying disaster victims. As 3D dental records become part of clinical dentistry, it is essential for forensic identification to incorporate this till now unexploited data, particularly in cases where traditional methods covering 2D data struggle. To address this need, we have developed a novel comparative dental analysis pipeline specifically for 3D data.

This pipeline involves four key steps: data preprocessing, data description, comparison, and scoring. In the preprocessing stage, we created a technique to computationally remove soft tissue. For data representation, we identified Difference of Curvature (DoC) keypoint detection and Signature of Histograms of OrienTations (SHOT) encoding as the most effective approach. The comparison step evaluates the similarity between keypoints from different dental scans based on encoding distances. By using the median distance of the 10% most similar keypoints as the final matching score, we achieved 100% accuracy in distinguishing between dental scans from the same individual and those from different individuals in our mock disaster dataset. These findings demonstrate the strong potential of our pipeline for future applications in disaster victim identification, especially in cases where conventional methods fall short.

Themes: Bioinformatics, Dentistry
Keywords: Disaster Victim Identification, Automation, Software

SESSION 37 – Cancer diagnostics 2

Selecting the right patient for enteral feeding tube and optimizing the trans-sectoral support - The S.E.O.S. Head and Neck Cancer Project

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Patients (pts) treated with curative (chemo)radiotherapy for head and neck cancer (HNC) experience risk of malnutrition. The treatment can lead to side effects that can cause dysphagia and difficulties eating. Many pts requires enteral feeding tubes (EFT) during and after treatment. The need and duration for EFT vary. Understanding the impact of clinical/treatment related factors and the radiotherapy dose and volume on oral and swallowing structures is crucial for timely treatment with EFT. Furthermore, transitioning from hospital to primary care is challenging and a structured approach like an online multidisciplinary team conference (MDT) could improve coordinated care.

Aim: Enhance nutritional treatment and rehabilitation for HNC pts undergoing curative intended (chemo-)radiotherapy.

Data from 1,200 pts treated between 2014-2023, from the DAHANCA database, will be explored for possible clinical and treatment predictors. Using the same cohort, statistical analysis will be performed to correlate dosimetric parameters with the onset and duration of EFT use. Combining the results, models will be built for early identification of pts in risk of long-term EFT dependency in the clinic.

Secondly, a case-control study will investigate if pts faster become independent of EFT if exposed to a better coordinated clinical handover to the primary health care system. For this, we will use an online MDT with pts present. Controls will receive standard of care.

Present status: Data from >750 pts are now updated and we have established a patient panel and together with a workgroup from Aarhus Health Care, we have developed the frame and workflow for the online MDT and inclusion has begun.

Themes: Cancer, Rehabilitation
Keywords: Cancer, Enteral Feeding Tubes, Clinical pathway

Unravelling the molecular heterogeneity of grade group 1 prostate cancer

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Background: Prostate cancer (PC) is the most common cancer among Danish men. Diagnostic biopsies are assessed for PC and assigned an ISUP grade group (GG) of 1-5, with a higher GG indicating a worse prognosis. Patients with GG1 PC are often offered active surveillance (AS) instead of surgery to reduce the risk of overtreating this patient group, yet 30% of the patients transition to surgery within four years, suggesting that not all GG1 tumours are or remain indolent.

Aim: This project aims to explore the molecular heterogeneity in GG1 PC, to develop a gene signature for risk assessment, through mRNA sequencing of biopsy tissue samples from a cohort of newly diagnosed PC patients.

Methods: We performed mRNA sequencing (QuantSeq) of 246 formalin-fixed and paraffin-embedded biopsy tissue samples (adjacent normal (AN) = 54, GG1 = 68, GG2 = 39, GG3 = 16, GG4 = 34, GG5 = 35) from the primary tumour of 166 PC patients. Using the mRNA sequencing data, we will develop a gene signature that can subdivide GG1 tumours into a molecular low-risk and high-risk subgroup, wherein one subgroup shows similarity to AN and the other resembles more aggressive PC (GG ≥ 2).

Results: Samples with fewer than 1.5 million total reads or fewer than 10,000 genes with read count above 10 were excluded (GG1 = 6, GG2 = 1). Genes with less than 10 read counts in over 23% of the samples were filtered out. This left 239 samples with a median of 3.5 million reads and 16,096 genes for downstream analysis.

Perspectives: This project is the first step towards more personalised, molecular-guided treatment decisions for patients with GG1 PC using routinely collected patient material.

Themes: Cancer, Urology & Nephrology
Keywords: Prostate Cancer, RNA sequencing, Molecular heterogeneity

Dysphagia and quality of life in patients with oral squamous cell carcinoma before and after treatment

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Background: Swallowing problems (dysphagia) is common in patients with oral cavity cancer (OCC), both due to the tumour itself and because of the treatment, which is primarily surgery. In a pilot study we found that 45% of patients reported difficulties swallowing two years after their treatment. Dysphagia is associated with malnutrition, reduced quality of life (QoL), aspiration pneumonia, prolonged hospitalization, and death.

Aim: The overall goal is to reduce post-treatment dysphagia in patients with OCC through improved risk stratification methods and individualized rehabilitation efforts.

Methods: The study is prospective and observational. All patients diagnosed with OCC and treated with curative intent are invited to participate. We plan to include 100 patients during a two-year period.

Questionnaires addressing QoL and instrumental swallowing evaluation (Modified Barium Swallow Study) will be performed at baseline (before surgery), and two and 12 months post-treatment. The following data will be collected: type and location of tumour, treatment modality, tobacco and alcohol consumption, body weight, diet, complications, and hospital admissions within the first year after treatment. Information concerning the extent and type of completed exercise program will be obtained from the municipal occupational therapist patient six months post-treatment. Furthermore, the quality and effects of the rehabilitation program will be obtained from the patients.

Themes: Cancer, Rehabilitation
Keywords: Oral cavity cancer, Dysphagia, Quality of life

Overdiagnosis in the Danish breast cancer screening program

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Background: Breast cancer screening have been implemented gradually in Denmark since 1991 in order to detect breast cancer at an earlier stage and thereby reduce morbidity and mortality. However, this also leads to overdiagnosis – the detection of cancers that would never progress to be symptomatic within a person's remaining lifetime. Overdiagnosis can lead to unnecessary treatments, psychological stress for patients and increased healthcare costs, emphasizing the need to quantify and minimize the frequency of overdiagnosis. With the increasing moves towards individualized breast cancer screening it is more and more important to be able to estimate overdiagnosis both overall and in subgroups of women.

Method: To estimate the frequency of overdiagnosis, we use the g-formula, a statistical model designed to account for time-varying treatment and time-varying covariates. As we have 30 years of follow-up, these are two important factors in accurately estimating overdiagnosis. By using the g-formula, the study aims to account for dynamic changes in health behaviours, treatments, and patient characteristics over time, to remove the health user bias, that are effecting observational studies comparing women participating in screening to non-participants.

Aim: We aim to develop and validate the use of g-formula method to estimate the frequency of overdiagnosis in the general population as well as in different subgroups, within the Danish breast cancer screening program. By producing more robust estimates, this research will contribute to the ongoing efforts to tailor screening recommendation, and thereby support more personalised and effective screening protocols.

Themes: Statistics, Epidemiology
Keywords: Screening, Breast cancer, Machine learning

Detection of plasma circulating tumor DNA is not affected by kidney and liver function in patients with muscle-invasive bladder cancer.

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Background: The utilization of plasma circulating tumor DNA (ctDNA) has shown promising results in early detection of relapse and therapeutic monitoring in patients with muscle-invasive bladder cancer (MIBC). To enhance its clinical implementation, it is essential to investigate the factors that may influence plasma ctDNA detection.

Primary objective: To assess the relationship between plasma ctDNA detection and biochemical parameters indicative of kidney and liver function in patients with MIBC.

Patient cohorts, data collection and statistical analyses: Tumor-informed plasma ctDNA analysis was conducted on plasma samples from 174 patients with MIBC who received neoadjuvant chemotherapy (NAC) before undergoing radical cystectomy, and 102 NAC-naïve patients treated solely with radical cystectomy. Standard laboratory measurements of biochemical parameters and clinical data were retrieved from the patients' electronic health records. Biochemical measurements were included if collected within 10 days of an available ctDNA test. Analyses were conducted using the Wilcoxon rank-sum test and Spearman's correlation in R.

Results: Our primary finding revealed that kidney and liver function did not correlate with plasma ctDNA detection. In contrast, immune parameters, including leukocytes (p=0. 00098), neutrophils (p=0. 0004), neutrophil-to-lymphocyte ratio (p=0.00016) and C-reactive protein (p=0.04), exhibited a positive correlation with plasma ctDNA detection. Biochemical parameters alone showed no prognostic value.

Conclusion: Clinical application of ctDNA can be implemented with minimal risk of detection being influenced by fluctuations in the patients' kidney and liver function.

Themes: Cancer, Urology & Nephrology
Keywords: Circulating tumor DNA, Kidney and liver function, Muscle-invasive bladder cancer

HPV sublineages in Danish cervical cancer screening samples

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Background: Improved risk-stratification of HPV-positive women is essential to avoid over-management and unnecessary referrals to gynecologists. The cancer risk associated with different HPV sublineages varies. With growing insights into HPV sublineage carcinogenicity, this information could enhance risk stratification for HPV-positive women. However, research characterizing these sublineages, particularly beyond HPV16, remains limited. We aim to design a targeted next-generation sequencing (NGS) panel for analysis of HPV sublineages for all IARC high-risk HPV types.

Methods: Our NGS panel targets 12 high-risk, 13 probably/possibly high-risk, and 2 low-risk HPV types. HPV sublineages were analyzed using a custom bioinformatic pipeline with references retrieved via PaVE. The method's accuracy was tested using purified HPV plasmids in a human DNA background. In addition, 119 cervical cancer screening samples from Danish women were analyzed, whereof six had a negative HPV screening result (BD Onclarity HPV test).

Results: The six HPV-negative samples remained negative with our NGS assay. For HPV-positive samples, our NGS assay agreed with the BD Onclarity assay in 96.5% (109/113) of cases. Sublineage analysis revealed type A lineages as most common for HPV16, HPV18, HPV33, HPV35, HPV39, HPV51, HPV52, HPV58, and HPV68. The most prevalent sublineage was B1 in HPV45 and HPV56, and B2 in HPV66. HPV31 and HPV59 exhibited more diverse sublineage distributions.

Conclusion: This method enables identification of HPV sublineages in cervical cancer screening samples. The study continues, aiming at sequencing 1000 individual cervical cancer screening samples.

Themes: Cancer, Gynecology and obstetrics
Keywords: screening, HPV, next-generation sequencing

Allelic imbalance for early detection of breast cancer in high depth ultima genomics whole genome sequencing

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Current breast cancer screening methods, such as mammograms and MRIs, suffer from poor sensitivity and specificity in early-stage lesions. Circulating tumor DNA (ctDNA) offers a promising alternative biomarker for early cancer detection. Plasma whole genome sequencing (WGS) enables inference of tumor-derived copy number variation (CNV) events, including amplifications, deletions, and loss of heterozygosity (cnLOH), through allelic imbalance in single nucleotide polymorphisms (SNPs). Current tumor-agnostic ctDNA detection methods rely on sparse cancer mutations, methylation patterns, or coverage analysis, all suffering from high false positive rates. In this study, we present a novel de novo classifier leveraging B-allele frequency (BAF) for the detection of early-stage breast cancer.

Plasma samples from 9 BRCA mutant breast cancer patients with early-stage lesions underwent deep (~200x) WGS with low-cost Ultima Genomics technology. Long-read sequencing of normal samples was conducted to phase parental haplotypes in phase blocks. The BAF was then defined as the frequency of the observed major allele. In each phase block, a paired t-test was used to test if the B-allele frequency is greater than the A-allele frequency. A sample-level BAF score was calculated from the sum of t-statistics across all phase blocks. BAF score analysis demonstrated strong predictive performance, separating pre-operative patients from post-operative patients with an AUC of 0.86.

In conclusion, we have developed a novel de novo BAF classifier for sensitive detection of early-stage breast cancer. This approach holds significant promise as a non-invasive screening tool for early-stage lesions.

Themes: Bioinformatics, Cancer
Keywords: Early cancer detection, Liquid biopsies, Allelic imbalance

CO-CHAIRS'S ABSTRACTS

Engaging the PD-1 Pathway in systemic sclerosis attenuates inflammation-mediated fibrosis.

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Background: The molecular mechanisms driving fibrosis in diffuse cutaneous systemic sclerosis (dcSSc) remain to be elucidated. The immune regulatory programmed cell death protein 1 (PD-1) pathway is upregulated in inflammation and has been connected to fibrosis. In this study, we elucidate the impact of the PD-1 pathway in diffuse cutaneous systemic sclerosis (dcSSc), with a particular emphasis on both immune activation and fibrosis progression.

Methods: We obtained plasma samples from 35 dcSSc patients and 20 healthy controls. We also analyzed PBMCs and dermal fibroblasts from dcSSc patients and healthy controls. Furthermore, we used recombinant PD-1 protein (PD-1:Fc), isotype controls, and anti-PD-1 antibodies to stimulate PBMCs, dermal fibroblast cultures, and co-cultures. Additionally, we sorted, bulk sequenced, and analyzed the PD-1hi and PD-1lo populations of dcSSc PBMCs. Finally, we used a murine bleomycin model for lung fibrosis to study the effect of PD-1:Fc on lung fibrosis in mice.

Results: PD-1 was elevated in dcSSc at both the soluble and cellular levels. Soluble PD-1 correlated with key clinical parameters such as CRP, FVC, and mRSS. Fibroblasts from dcSSc expressed high levels of PD-L1 and exhibited increased activation levels based on surface markers such as ICAM and VCAM. We identified a distinct myofibroblast population in dcSSc fibroblasts, displaying differential clustering compared to HCs fibroblasts. DcSSc fibroblasts produced increased amounts of extracellular matrix proteins (ECM) such as Type 1 Procollagen and fibronectin when compared to HCs. This secretion was downregulated by PD-1:Fc. Monocultures of dcSSc PBMCs and autologous dcSSc PBMCs and fibroblasts co-cultures were treated with PD-1:Fc, and we observed a significant decrease in inflammatory cytokines and ECM protein production compared to NT samples. Additionally, dcSSc PBMCs could activate fibroblasts in healthy dermal and lung fibroblasts, and the addition of PD-1:Fc to these cultures reduced ECM production (fig 1A). We next sorted PD-1hi and PD-1lo T cells from dcSSc PBMCs. Evaluated by bulkRNA

seq, the PD-1hI T cells clustered very differently, and had a different and more regulatory transcriptional profile compared with the PD-1lo T cell population(Fig 2).

Our in vitro findings were finally supported by animal studies in the bleomycin model of lung fibrosis. We demonstrated that early treatment with PD-1:Fc could inhibit the development of lung fibrosis and decrease the levels of total insoluble collagen in the lungs (fig 3). This effect was mediated through the downregulation of inflammatory and profibrotic cytokines.

Conclusion: Our study's findings underscore the significant role of the PD-1 pathway in dcSSc. Targeting the PD-1 pathway by PD-1:Fc attenuates fibrosis resulting from inflammation. These data suggest the PD-1 pathway as a potential treatment target to decrease the development of fibrosis in dcSSc.

Themes: Immune diseases, Animal Models
Keywords: Systemic Sclerosis, Fibrosis, PD-1

All-cause mortality and serious adverse events after shoulder arthroplasty: A population-based matched cohort study

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Background and purpose: As mortality and serious adverse events rates after shoulder arthroplasty are variable in the existing literature, we aimed to determine the 30- and 90 day incidence in a population-based cohort study with a matched cohort.

Patients and methods: We identified patients who underwent shoulder arthroplasty from 2006-2021 in the Danish Shoulder Arthroplasty Registry . Data from the Danish Shoulder Arthroplasty Registry were linked to data from the Danish National Patient Register and the Danish Civil Registration System and Statistics Denmark . Patients identified in the Danish Shoulder Arthroplasty Registry were matched (1:10) on age, sex, and year of birth to the Danish background population. Data on first serious adverse events and mortality were estimated at 30 and 90 days after discharge.

Results: 14186 patients with a shoulder arthroplasty procedure were identified. This resulted in 141860 controls from the background population. The 30-day incidence of mortality for shoulder patients was 20.28 versus 9.43 in the matched cohort, corresponding to an incidence rate ratio (IRR) of 2.15 (95% CI; 1.70-2.71). Patients with fracture as the surgical indication had the highest mortality risk. The 30-day incidence of serious adverse events for shoulder patients was 73.47 versus 14.83 in the matched cohort, corresponding to an IRR of 4.95 (95% CI; 4.32-5.68). For serious adverse events the risk was higher across all surgical indications, when compared to the matched cohort.

Conclusion: Patients treated with shoulder arthroplasty had an overall 30-day all-cause mortality of 2.15, which is higher than the rates in the matched cohort. Serious adverse events were higher across all surgical indications. Our results may be used to inform the shared decision-making process and develop a treatment plan.

Themes: Surgery, Epidemiology
Keywords: Shoulder replacement, Mortality, Serious adverse events

Is Chronic inflammation a crucial part of Turner syndrome?

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Background: Turner syndrome (TS) is characterized by short stature, hypogonadism, autoimmune diseases, and metabolic conditions, along with genome-wide transcriptome and methylome changes. Although studies often focus on the 45,X karyotype, most TS patients have other karyotypes.

Methods: We analyzed TS patients with various karyotypes and controls. DNA methylation and gene expression profiles were examined. Leukocyte profiles were studied via flow cytometry, and biochemical and epidemiological data were collected.

Results: TS patients showed similar transcriptome and methylome profiles regardless of karyotype, particularly involving PAR1 and X/Y homologues. We observed higher neutrophil counts ($p < 0.01$), increased activation, and elevated markers (myeloperoxidase, elastase, S100A8/9), indicating pathological activation. TBLX1 upregulation correlated with neutrophil fraction ($p < 0.0001$). Elevated neutrophil counts were seen from childhood. Epidemiological analysis showed increased autoimmune and metabolic risks but lower infection risk in TS vs. Klinefelter syndrome.

Conclusions: The X chromosome p-arm, especially PAR1, drives genome-wide transcriptome and methylome changes in TS. Our findings highlight neutrophil-driven chronic inflammation in TS, offering insights into its pathophysiology. Chronic inflammation may precede metabolic syndrome, type 2 diabetes, and hypertension, contributing to the elevated risk of autoimmune conditions in TS.

Themes: Endocrinology, Gastroenterology and hepatology
Keywords: Sex-Chromosome disease, Liver, Inflammation

Using sequence context and genomic features to predict site specific mutation rate

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The human mutation rate is not uniformly distributed, and the genome exhibits a heterogeneous mutational landscape. At a site-specific level, it has previously been shown that the mutation rate varies significantly depending on the context of the nucleotide sequence. A loss-of-function (LoF) mutation in a critical gene can have a detrimental effect on individual fitness and development. Here, we present a model that predicts the mutation probability of every site in the genome, given the adjacent sequence context and a set of informative genomic features. Furthermore, we show how this model can be used to identify genes that are important for maintaining genomic integrity.

We use de novo mutations from parent-offspring trios as training data. To prevent sparsity and overfitting, we use KmerPaPa to partition the sequence context into the most informative IUPAC-based k-mers. Additionally, we annotate each position with genomic features, such as methylation, recombination rate, and replication timing.

Using our model as a null model, we calculate the expected mutational burden of LoF mutations for all known genes. Combined with observed LoF mutations from the Genome Aggregation Database (gnomAD), we generate a ratio of observed to expected (OE) LoF mutations. Genes with a low OE ratio are expected to play an active role in maintaining genomic integrity, as LoF mutations are being purged from the population. A low ratio is expected to correlate with essential and haploinsufficient genes, as losing a copy of these genes would have a detrimental effect on an individual's fitness. Preliminary results suggest that the OE ratio performs well in ranking haploinsufficient genes.

Themes: Bioinformatics, Statistics
Keywords: De novo mutations, Modelling, Genes

Acetylsalicylic acid in pregnancy and fetal growth

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Background: Acetylsalicylic acid (ASA) is recommended to pregnant women at high risk of developing preeclampsia or with a history of fetal growth restriction (FGR). We investigated differences in fetal growth patterns, birthweight (BW) and uterine arterial flow (UtA) according to maternal use of ASA in pregnancy by subgroups.

Methods: Information on pregnancies between 2013 and 2023 with routine ultrasound scans were obtained from the Central Denmark Region and linked to the Danish national health registries. Measures of fetal size were internally standardized. The weekly impact of ASA treatment were estimated in adjusted models. UtA was reported as the median in the subgruops through pregnancy.

Results: A total of 136,346 singleton pregnancies were identified. Overall, ASA use was not associated with fetal growth. ASA use in interaction with history of FGR or history of preeclampsia was not associated with fetal growth, whereas history of FGR alone was associated with reduced growth in BPD, AC, FL, and BW, the fetuses had a reduced AC/BDP ratio but an unaltered UtA. ASA use in interaction with pre-pregnancy diabetes was associated with increased fetal growth assessed by AC and BW, but not BPD or FL, pre-pregnancy diabetes alone was also associated with increased fetal growth in AC and BW. The median UtA tended to be reduced among ASA exposed pregnancies with pre-pregnancy diabetes.

Conclusion: ASA treatment was not associated with fetal growth. In women with pre-pregnancy diabetes, ASA appeared to be associated with faster fetal growth measured by AC and an increased BW, possibly explained by a reduction in UtA, increasing the placental perfusion.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Obstetrics, Fetal growth, Acetylsalicylic acid

Curbing Autoimmunity: Development of an Anti-CD40L Fab Fragment for Inhibition of the CD40-CD40L Axis - **CANCELLED**

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Purpose: Autoimmunity is a global problem, and recent numbers estimate that around 10% of the population suffers from an autoimmune disease. A hallmark of many autoimmune diseases is the production of tissue-damaging autoantibodies by B cells where the CD40-CD40L axis provides a pivotal T cell-mediated co-stimulatory signal for B cell activation. Notably, in many autoimmune diseases, the CD40-CD40L axis is dysregulated.

We aimed to inhibit the CD40-CD40L interaction to mitigate disease-causing reactions and symptoms in autoimmunity. Previous therapeutic strategies with anti-CD40L antibodies caused severe Fc-mediated side effects. Thus, our aim was to develop antibody fragments, known as Fab fragments, to take advantage of their significantly smaller size and lower immunogenicity.

Methods: We developed 30 different monoclonal antibodies targeting CD40L. Antibodies were screened by immunoassays and flow cytometry to select the most potent inhibitory candidate before we engineered it into a Fab fragment. The Fab fragment was tested in a complex in vitro assay for its ability to inhibit B cell proliferation, differentiation and antibody production.

Results: We successfully developed an inhibitory anti-CD40L Fab fragment that blocks CD40 from binding to CD40L on T cells, effectively inhibiting B cell proliferation, differentiation and antibody production.

Conclusion: This anti-CD40L Fab fragment offers a promising new treatment approach with clear advantages over antibodies. The Fab fragment will be tested for its ability to ameliorate autoreactive symptoms in vivo. We believe this represents a new treatment strategy, expanding opportunities for patients with autoimmune diseases.

Themes: Immune diseases, Molecular biology
Keywords: Autoimmunity, CD40-CD40L, Fab fragments

High-Protein diet for Metabolic-dysfunction associated steatotic liver-disease

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Background: Metabolic-dysfunction associated steatotic liver disease (MASLD) is a highly prevalent condition characterized by accumulation of intrahepatic fat and accompanied by inflammation and fibrosis. Patients with MASLD have an increased risk of type 2 diabetes and an overall increased mortality, mainly driven by cardiovascular disease.

The primary treatment is weight management, but optimal lifestyle approaches are warranted. Clinical and animal studies have shown promising effects of high protein diets (HPD) in ameliorating other aspects of the metabolic syndrome and observational studies showed that high intake of dairy products was inversely associated with MASLD and insulin resistance (IR).

Aim: To investigate if a high protein diet supplemented with dairy proteins can ameliorate MASLD in overweight patients with MASLD.

Method: This randomized, controlled trial was conducted at two centers. 46 overweight patients with MASLD were randomized to HPD (25/35% protein) or to a normal, control diet (15/25%). The intervention consisted of two phases: 4 weeks isocaloric feeding followed by 20 weeks of hypocaloric feeding. The primary endpoint was changes in steatosis assessed by MR-spectroscopy. Secondary endpoints were changes in liver enzymes and markers of inflammation and fibrosis.

Results: 34 of 46 participants completed both intervention phases. At baseline, median age was 41years, median BMI was 33.2 kg/m2, and median hepatic fat-fraction was 27.6%. Weight stability was achieved in the first intervention phase in both diet groups. Groups achieved similar weight loss in the 2nd intervention phase with a median change of -3.6% (2.17% - 5.27%).

Themes: Gastroenterology and hepatology, Endocrinology
Keywords: Steatotic liver-disease, Lifestyle intervention,

Quantifying human body mass and buoyancy for optimizing search and recover operations through post-mortem computed tomography.

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Each year, multiple individuals tragically disappear in the inner Danish waters, resulting in search and recovery efforts to recover the bodies in a timely manner. A significant challenge to these operations arises from the unpredictable movement of local currents. Various water currents, often moving in different or even opposite directions at different depths, severely increase the difficulty of predicting the direction and speed at which a body may drift. A body's vertical position in the water, and therefore its exposure to these currents, is dictated by its buoyancy, which is determined by the relative mass of its tissues compared to the water.

Buoyancy can be calculated using known principles of fluid dynamics, where the lift or sink potential of a body depends on the volume and density of different tissue types. Post-mortem computed tomography (PMCT) provides a non-invasive method to measure the volume of various tissues, and combining these measurements with known density values allows for precise buoyancy estimations. Currently, there is a lack of reliable data on the buoyancy characteristics of different human body types, hindering effective predictive modeling for search and recovery.

This study seeks to develop a workflow to acquire buoyancy data of various body types using PMCT volume measurements with long term goals of enabling more accurate predictions of body movement in water, ultimately improving the efficiency of search and recovery operations in Danish waters.

Themes: Imaging techniques, Imaging techniques
Keywords: Post-mortem CT (PMCT), Buoyancy Estimation, Search and Recovery Optimization

First clinical online real-time motion-including prostate and bladder dose reconstruction during prostate SBRT delivery

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Background and Aim

Organ motion causes dose errors during prostate radiotherapy. This study aims to implement real-time monitoring of the motion-impact on the delivered dose during treatment to increase treatment accuracy and reduce side effects.

Methods

The prostate position was monitored during treatment using implanted prostate markers and MV-kV images acquired every 3.5s. Upon prostate misalignments exceeding 1.5mm the treatment was interrupted and the patient realigned. The in-house developed software DoseTracker was integrated into the prostate radiotherapy workflow and used for fast motion-including dose reconstruction based on the available prostate motion.

During treatment of 20 prostate cancer patients receiving 35Gy or 40Gy in 5 fractions the motion-including prostate and bladder doses were monitored. The motion-induced difference in the dose volume parameters D95% for the prostate Clinical Target Volume (CTV) and V36Gy for the bladder were extracted. For comparison, the hypothetical dose without patient realignment was reconstructed retrospectively. The DoseTracker real-time doses were validated against a commercial Treatment Planning System (TPS).

Results

The mean (±SD) motion-induced dose error was -0.6±1.1% (CTV D95%) and +0.1%±0.5% (bladder V36Gy) with patient realignment and increased to -2.0±6.6% (CTV D95%) and +4.1±2.0% (bladder V36Gy) without realignment. The real-time doses by DoseTracker agreed with the TPS ground truth doses within 1%.

Conclusion

The world's first real-time motion-including prostate and bladder dose reconstruction was performed successfully during prostate radiotherapy. MV-kV guidance reliably prevented severe motion-induced dose errors.

Themes: Cancer, Imaging techniques
Keywords: Radiotherapy, Dose reconstruction, Prostate cancer

Temporal trends and determinants of geographic variation in oral anticoagulant treatment of atrial fibrillation 2013-2022: a Danish nationwide cohort study

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Background: Geographic variation in anticoagulant treatment (OAC) for patients with atrial fibrillation (AF) has been demonstrated both between and within countries, yet the underlying drivers of this variation have been sparsely investigated.

Aim: To explore temporal trends in geographic variation in OAC for patients with AF in Denmark, and to assess the extent to which this variation is explained by differences in patient populations.

Design and setting: A register-based cohort study including Danish patients with AF and CHA2DS2-VASc score ≥2 was conducted from 1 January 2013 to 31 December 2022.

Methods: The outcome was OAC adherence operationalised as the proportion of days covered (PDC). Descriptive statistics was used to describe 1) the temporal development in OAC adherence nationwide and in the individual administrative regions, and 2) the temporal trends in the use of OAC subgroups. Poisson regression models were employed to assess the contribution of patient-level determinants to geographic variations in OAC adherence.

Results: A continuous rise in overall adherence (PDC) from 53% to 78% was observed during the study period. Concurrently, the treatment pattern shifted from vitamin K antagonists to predominantly direct oral anticoagulants with preference for rivaroxaban and apixaban. The difference in PDC between the top and bottom regions decreased from 9,9% in 2013 to 7,3% in 2022. The difference in PDC in 2022 was reduced to 6,9% when adjusting for patient demographics, socioeconomics and comorbidities.

Conclusion: Geographic variation in OAC adherence decreased as overall adherence improved; however, substantial unexplained variation remained.

Themes: Epidemiology, Cardiology
Keywords: Atrial fibrillation, Anticoagulants, Variation

Inequity in Old Age: The Role of Social Determinants in Health, Well-being, and Homecare Nursing

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Background: Health disparities are rising globally, driven by various factors. Social determinants of health (SDoH) refer to the conditions in which people are born, grow, live, work, and age, and significantly contribute to health inequities. While SDoH are well-studied in working-age populations, their impact on retirees is less understood. Studies indicate that health inequities persist into old age, along with significant disparities between older and working-age patients. SDoH also affects healthcare access and delivery. Homecare nurses, who provide and coordinate care for older patients, play a critical role. This study explores how SDoH influences older patients' health and the provision of homecare nursing to them.

Methods: An interpretive phenomenological approach was employed, involving participant observations, situational interviews, and small group interviews with twelve home care nurses from two municipalities. Data analysis included paradigm cases, exemplars, thematic analysis, and collaborative analysis with older individuals receiving home care nursing and civil society stakeholders.

Results: Key SDoH impacting older patients' health, and the provision of homecare nursing to them include transport, housing, gender roles, income, digitalization, and social networks. The complexity of the healthcare system and the increasing demands it puts on patients exacerbate these issues, especially as the population ages.

Conclusion: Health inequity among older patients is a critical social justice issue. Healthcare services must become more considerate of SDoH as well as more caring to meet the needs of an aging population with complex health needs.

Themes: Public health, Qualitative research
Keywords: Social Determinants of Health, Health Inequity, Old age

The Great Sheath Debate: Can Smaller Size Beat the Clock on Hemostasis and RAO? - Randomized comparison of sheath size for coronary intervention: time to hemostasis and risk of radial artery occlusion.

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Background: Trans-radial access is recommended for coronary artery interventions. This study aimed to assess whether sheath size impacts time to hemostasis or the risk of radial artery occlusion (RAO).

Aims: To compare the effects of 5F and 6F sheaths on hemostasis time and RAO risk during radial coronary intervention.

Methods: A total of 3,600 patients were included, randomized to either 5F or 6F sheaths unless the operator preferred the 6F. Time to TR-band deflation and removal was recorded, and radial artery patency was assessed using the reverse Barbeau test at discharge.

Results: Of the patients, 942 were randomized to 5F and 945 to 6F, while 1,713 received the 6F sheath based on operator preference. Intention-to-treat analyses showed no differences between 5F and 6F groups in time to TR-band deflation (80 vs. 81 minutes), TR-band removal (101 vs. 105 minutes), or RAO rates (1.6% vs. 2.1%, P=0.44). In per-protocol analyses, time to full deflation and TR-band removal differed between groups: 77, 82, and 87 minutes, and 98.5, 105, and 111 minutes, respectively (P<0.01), with no difference in RAO risk (1.8%, 1.9%, and 1.2%, P=0.34).

Conclusion: Routine use of the 6F sheath is safe for radial coronary interventions, with no increased RAO risk. The 5F sheath showed a significant crossover to 6F without a difference in RAO risk.

Themes: Cardiology, Diagnostics & technology
Keywords: Randomization, Radial intervention, Complications

Dissecting vascular smooth muscle cell subpopulations regulated by mechanical forces and pro-inflammatory stimulation.

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Vascular smooth muscle cells (SMCs) exhibit high plasticity, enabling them to adapt to environmental changes through phenotypic modulation. Unfortunately, many of the resulting alternative phenotypes contribute to the progression of atherosclerosis. Atheroprone sites, such as arterial curvatures and bifurcations, are characterized by altered mechanical forces due to blood flow dynamics and increased inflammation driven by lipid retention.

To study how SMCs respond to such environmental changes, we employed an in vitro setup where human aortic SMCs were cultured on flexible membranes and subjected to physiological stretch, pathological stretch, or static conditions. We studied the transcriptomic response using RNA-sequencing and utilized an NF-kB reporter system to evaluate SMC inflammatory signaling in response to stretch or TNF-induced inflammation.

Our RNA-sequencing results revealed that physiological stretch induced an anti-inflammatory phenotype in SMCs and attenuated TNF-induced inflammation. In contrast, static or pathological stretch promoted a pro-inflammatory phenotype. Interestingly, while the NF-κB reporter did not show a marked increase in inflammatory SMCs in response to stretch, TNF treatment only modestly increased the number of NF-κB-positive cells, suggesting that only a subset of SMCs is responsible for the increased inflammation initially observed.

To further elucidate the heterogeneity of SMCs, we plan to employ single-cell RNA-sequencing to dissect the SMC phenotypes under these conditions. This approach can provide valuable insights into SMC phenotypic modulation, which is crucial for understanding atherosclerosis progression.

Themes: Omics, Immune diseases
Keywords: Atherosclerosis, Vascular smooth muscle cells, Mechanical forces

Predicting radiotherapy photon dose plans using deep learning

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Introduction

Accurate dose planning is essential for delivering high-quality radiotherapy to patients with brain cancer. Ensuring the quality of patient treatment plans is critical, Detecting potential low-quality dose plans could be performed using a reference dose plan for comparison. By predicting individualized dose plans using deep learning we aim to automatically generate photon radiotherapy dose plans which can be used for quality assurance of manually created plans. This study evaluates the accuracy of the GAN-based model

Method

A GAN is a type of generative model type which uses two models who each contribute to generating new images such as dose plans. The proposed GAN model employs a UNet architecture in the Generator and a simple encoder-like architecture in the discriminator. Model training involved 77 photon dose plans, with 70 used for training and 7 in the test set. Evaluation was performed using gamma analysis with a 3%/3mm threshold.

Results

Results showed a mean gamma pass rate of 84.57%, with the lowest gamma pass rate being 76 % and the highest being 91%, indicating resemblance between the clinical dose plans and the predicted dose plans.

Themes: Cancer, Cancer
Keywords: Deep learning, AI, Radiotherapy

Three years after elexacaftor/tezacaftor/ivacaftor: impact on pulmonary pathogens in a Danish cystic fibrosis cohort

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Background: Introduction of elexacaftor/tezacaftor/ivacaftor (ETI) has revolutionized the treatment of cystic fibrosis (CF) and improved clinical outcomes. Prevalence rates of CF pathogens in airway samples have generally been reported as decreasing after ETI, but whether persistent infection also declines over time remains an important clinical question. ETI-mediated mucus reduction and change in airway sample representativeness may complicate monitoring of airway infections in people with CF (pwCF).

Methods: We conducted a national cohort study of airway secretion pathogens from 5 years before to 3 years after ETI initiation in Danish pwCF above 12 years of age (N=282). We investigated microbial changes in the airway samples and change in infection status in pwCF in clinically relevant subgroups of sex, age, lung function and mutation type during follow-up years.

Results: We observed a statistically significant reduction in the average percentage of airway cultures with growth of Pseudomonas aeruginosa, Staphylococcus aureus, Aspergillus species, and Stenotrophomonas maltophilia in the years after ETI initiation ($p<0.001$). Despite of this, 18% of the cohort had growth of P. aeruginosa in more than 50% of their samples in the third year after ETI. Sampling of airway secretion decreased from 10.5 to 7.3 samples per person per year during follow up.

Conclusion: Our work underscores the positive effect of ETI on CF airway microbiology as a significant and sustained reduction of key CF airway pathogens on a population level and across relevant subgroups during 3 years of follow-up. However, the majority of pwCF remained culture positive in the 3 years after ETI. We emphasize the importance of continued close microbial monitoring.

Themes: Infectious Diseases, Infectious Diseases

Keywords: Cystic fibrosis, Pulmonary infection, Elexacaftor/tezacaftor/ivacaftor

Diabetes and changes in bone mineral density following anti-osteoporotic treatment

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Aim: This epidemiological study investigates how type 1 (T1D) and type 2 (T2D) diabetes affect the response in bone mineral density (BMD) following anti-osteoporotic treatment (AOT) and what role surrogate measures of insulin resistance (IR), accumulation of advanced glycation end products (AGEs) in bone and impaired bone vascularization play in patients with T2D.

Background: Diabetes increases the risk of fracture. Hip fracture risk is increased 6.94 (3.25–14.78) and 1.38 (1.25–1.53) fold in individuals with T1D and T2D, respectively. With Z-scores in the hip of −0.37±0.16 and 0.41±0.01 the risk is higher than would be expected from BMD alone. The mechanism is not understood.

However, diabetes decreases bone turnover, which may lead to accumulation of microcracks and bone weakening. Bisphosphonates, the cornerstone in AOT, consolidate BMD by decreasing bone turnover. Thus, diabetes may affect the response in BMD following AOT.

Bone disorders develop over many years and bone tissue is not easily accessible. Therefore, we seek to investigate bone pathophysiology through epidemiology.

Material and methods: A database containing 47.000 patients with DXA scans performed in the Northern Denmark Region from 2001 to 2023 will be used. Patients with scans just before and 2-3 years after initiation of AOT will be included. Exposure is diabetes status. The primary outcome is changes in hip T-score. The number of concomitant antidiabetics, accumulated HbA1c exposure and diabetic microvascular disease will be used as surrogate measures for IR, AGEs in bone and affection of bone vascularization. DAGs are used to assess how to adjust for confounders and mediators.

Themes: Endocrinology, Epidemiology
Keywords: Bone mineral density, Diabetes, Osteoporosis

Optimizing Elective Nodal Irradiation in Head and Neck Cancer: A TCP Dose Optimization Algorithm Balancing Tumour Control and Normal Tissue Complications

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Introduction: Elective irradiation of lymph node levels (LNLs) enhances tumour control but simultaneously increases risks of normal tissue complication (NTCP). This study proposes an optimization algorithm based on tumour control probability (TCP) for elective irradiation of lymph node levels, aiming to balance tumour control and NTCP.

Materials & Methods: A lymphatic spread model was used to identify the LNLs at risk of harbouring occult metastases. This model guides the implementation of risk-based target volumes by assigning specific probabilities for the presence of occult metastases to each voxel, facilitating probabilistic radiotherapy treatment planning. These probabilities are integrated into a TCP model for elective irradiation of LNL II and III, which is used as objective function in the optimization. By adjusting the weight assigned to the TCP objective, it aims to maximize tumour control while simultaneously minimizing the irradiation to organs-at-risk.

Results: Three oropharyngeal SCC patients were retrospectively included in our analysis. Adjustments to the TCP objective weights resulted in significant NTCP reductions for xerostomia (from 60.5% to 52.6%) with only minimal impacts on TCP (99.4% to 97.8%). Likewise, we observed a reduction for dysphagia (from 53.1% to 50.1%), however, with a small compromise in TCP (99.0% to 97.6%).

Conclusion: We have demonstrated that balancing TCP and NTCP to deliver inhomogeneous doses, guided by a voxel-wise TCP model, optimizes therapeutic outcomes and minimizes side effects. This approach has theoretically proven effective in controlling tumours while simultaneously sparing sensitive organs for unnecessary irradiation.

Themes: Cancer, Statistics
Keywords: Tumour Control Probability, Radiotherapy, Normal Tissue Complication

Atopic dermatitis in childhood and biomarkers of male reproductive health: A study in the Danish National Birth Cohort

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Background: Atopic dermatitis (AD) may be associated with reproductive health. However, epidemiological studies are yet to explore this hypothesis.

Objective: To investigate whether AD in childhood is associated with poorer reproductive health in young men from the general population.

Methods: This study is based on the Danish National Birth Cohort (DNBC) and its sub-cohort, the Fetal Programming of Semen Quality Cohort (FEPOS), which consists of young men born between 1998 and 2000 and whose mothers were included in the DNBC. In total, 5,697 young men were invited during the recruitment period from 2017 to 2019, where 1,058 were enrolled and completed a comprehensive questionnaire regarding health and lifestyle, provided semen and blood samples, and self-measured their testicular volume. Information on maternal-reported doctor-diagnosed AD was obtained from the DNBC during childhood. The associations of semen characteristics, testicular volume, and reproductive hormone levels with the occurrence of AD were analyzed using negative binomial and linear regression models.

Results: In total, 220 (21%) young men had childhood AD. Men with childhood AD had slightly higher sperm concentration compared to those without (17%, 95% confidence intervals (CI): 3% to 33%), and lower FSH (-9%, 95% CI: -17% to 0%) and LH (- 8%, 95% CI: -14% to -1%). Testosterone and estradiol levels and the remaining reproductive health outcomes were comparable between men with and without childhood AD.

Conclusion: This study indicates that childhood AD might not have a clinically significant negative association with semen quality or reproductive hormone levels in young adulthood.

Themes: Epidemiology, Gynecology and obstetrics
Keywords: Atopic dermatitis, Semen quality, Reproductive hormones

Dose-dependent distribution of methotrexate in the juvenile pig brain following intravenous high-dose methotrexate infusion

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Background

High-dose methotrexate (HD-MTX) is an essential chemotherapeutic drug in the treatment of paediatric leukaemia with central nervous system (CNS) involvement and malignant brain tumours. However, our understanding of MTX distribution and elimination in the brain is incomplete. While HD-MTX is effective, it is also known to cause kidney damage and CNS toxicity in some patients. The mechanism behind the latter is unknown but assumed to be linked to MTX-mediated changes in brain metabolism. This calls for further investigation into alternative MTX treatment strategies and associated changes in the metabolomic profile of the CNS.

Methods

Healthy, anaesthetised juvenile pigs, fitted with a frontal lobe microdialysis probe and a catheter in the lateral ventricle, were treated with a four-hour intravenous infusion of standard 5 g/m2 HD-MTX or an increased dose of 20 g/m2 very high-dose MTX (VHD-MTX). MTX concentrations in frontal lobe extracellular microdialysate, spinal fluid, blood plasma, and urine, along with markers of renal toxicity and drug-induced metabolomic changes of the CNS, will be analysed using highly sensitive liquid chromatography-mass spectrometry (LC-MS).

Preliminary results

Median MTX exposure, expressed as the area under the drug concentration curve (AUC), is increased by three to fourfold in plasma and microdialysate after VHD-MTX infusion compared to HD-MTX. The relative increase is sustained after an additional four hours after infusion.

Conclusion: The results indicate a dose-dependent increase in MTX exposure in CNS. Further studies using this model will investigate the effects of combining VHD-MTX with strategies to manage systemic toxicity.

Themes: Animal Models, Omics
Keywords: Preclinical neuro-oncology, Pharmacokinetics, Metabolomics

Exploring pre-diagnosis hospital contacts in women with endometriosis using ICD-10: A Danish case-control study

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Background: Endometriosis is a benign gynecological disease that can cause severe pelvic pain and infertility. It is underdiagnosed and associated with a diagnostic delay that has been reported as long as 10 years from onset of symptoms until diagnosis. Women with endometriosis have a higher healthcare utilization before diagnosis. To our knowledge, no study has investigated the type of contact related to the higher utilization using the ICD-10 diagnoses registered to the hospital contact.

Methods: This study was conducted as a national Danish registry-based case-control study of 129,696 women. Cases were women with a first-time hospital-based diagnosis of endometriosis between 1 January 2000 and 31 December 2017.

Preliminary results: Using density sampling, we identified 21,616 cases, that were matched 1:5 to women without hospital-diagnosed endometriosis at the time of matching. The probability of having a high number of hospital contacts (six or more) was more common among women with endometriosis (68.6 %) compared to women without endometriosis (55.7 %). Women with endometriosis were more likely to have a diagnosis in nearly all of the included ICD-10 chapters for the entire period compared to controls, with the only exception being in the chapter related to pregnancy.

Conclusion: Women with hospital-diagnosed endometriosis had more frequent hospital contacts in the 10 years leading up to the diagnosis compared to women without a diagnosis of endometriosis. The contacts were related to registered diagnoses in nearly all of the included ICD-10 chapters for the entire period, except in the chapter related to pregnancy.

Themes: Epidemiology, Gynecology and obstetrics
Keywords: Endometriosis, Health care utilization, case-control study

Mechanical and Geometric Characterization of a Novel 2-Ply Vacuum-Pressed Biological Scaffold Patch Design for Posterior Mitral Valve Reconstruction

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Purpose

To assess the mechanical properties of small intestinal submucosal extracellular matrix (SIS-ECM) iterations and choose the optimal version for evaluating functional geometrics after posterior mitral valve reconstruction.

Methods

Four SIS-ECM versions (2- and 4-ply vacuum-pressed and lyophilized) underwent uniaxial tensile testing. A posterior mitral valve reconstruction patch was developed based on MRI scans (n = 5). Posterior mitral valve reconstruction using 2-ply vacuum-pressed SIS-ECM was performed (n = 7), and geometrics were evaluated using a modified left heart simulator.

Results

The vacuum-pressed iterations displayed superior maximum stress values compared to lyophilized (2-ply: median [IQR], 15.8 [15.2-19.0] vs 7.9 [7.3-8.3] MPa, $p<0.001$; 4-ply: median (IQR), 15.8 –[14.6-22.0] vs 7.9 [7.6-8.4] MPa). All reconstructed valves were competent with preserved total leaflet area, but individual leaflet segment areas were redistributed.

Conclusion

Posterior mitral valve reconstruction with our 2-ply vacuum-pressed SIS-ECM patch design was feasible in vitro. Further in vivo evaluation is warranted.

Themes: Surgery, Animal Models
Keywords: Mitral Valve, Bioscaffold,

LONG-TERM RISK OF NEURODEVELOPMENTAL DISORDERS FOLLOWING NEONATAL, INVASIVE GROUP B STREPTOCOCCUS DISEASE - A POPULATIONS-BASED COHORT STUDY FROM DENMARK

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Background/ hypothesis: Invasive group B Streptococcus disease (iGBS) affects approximately 500,000 newborns yearly. iGBS has a high mortality rate and risk of neurodevelopmental impairments. The long-term consequences following iGBS are sparsely investigated. We examined the association between infant iGBS (sepsis or meningitis) and the risk of epilepsy and psychiatric disorders until adolescence.

Methods: We conducted a population-based cohort study using administrative and medical registries (1997-2018) in Denmark. Exposed children had hospital-diagnosed iGBS during the first 89 days of life. A general population comparison cohort was randomly sampled and matched 10:1 to the exposed iGBS cohort by sex, year of birth, and gestational age.

Epilepsy and psychiatric disorders were defined by the International Classification of Diseases, Tenth Revision codes (ICD-10-codes). Cumulative risk (CR) was calculated treating death as a competing event. Cox proportional hazards regression was used to compute hazard ratios (HRs) and associated 95% confidence intervals (CIs).

Results: The overall CR (0-22 years) of epilepsy following iGBS was 3.6% (95% CI, 2.6-5.0%), compared with 2.3% (95% CI, 1.9-2.7%) in the comparison cohort. The overall CR for any psychiatric disorder following iGBS was 22.6% (95% CI 19.4–25.9%) compared with 19.4% in the comparison cohort (95% CI 18–20.8%). The adjusted HR for epilepsy was 2.04 (95% CI, 1.46-2.85) and 1.42 (95% CI 1.22–1.66) for psychiatric disorders. We found the incidence rates to be affected by sex, gestational age, and maternal socioeconomic position.

Conclusion: Our study showed an increased long-term risk of epilepsy and psychiatric disorders following neonatal iGBS.

Themes: Epidemiology, Infectious Diseases
Keywords: Neurodevelopmental disorders, ,

Inter-fraction motion robustness in dose-escalated proton reirradiation for locally recurrent rectal cancer: initial results from the prospective phase II trial, ReRad II

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Introduction: Pelvic Intensity Modulated Proton Therapy (IMPT) robustness is challenged by inter-fraction motion caused by constant anatomical variations. In this study, the dosimetric impact of inter-fraction motion on target coverage and dose to organ at risk (OAR) was quantified in a prospective phase II study on dose-escalated proton reirradiation for locally recurrent rectal cancer (LRRC).

Materials and methods: The inter-fraction motion robustness was assessed for the initial twelve patients enrolled in the study. Patients with resectable LRRC were assessed for neoadjuvant IMPT (55 Gy(RBE)/44Fx) and unresectable recurrences for definitive IMPT (57.5-65 Gy(RBE)/ 46-52Fx). Target coverage and dose to OAR were assessed for robustly optimised three-field IMPT, on 12 plan CT scans (pCT) - and 47 repetitive control CT scans (cCTs) during the treatment. The target coverage and doses to OAR were re-calculated on each cCT and the mean dose ratio (pCT/cCT-ratio) and target coverage (V95%) was evaluated.

Results: The target coverage was robust with a mean dose pCT/cCT-ratio of 1.00 (+/-1%). In the robust evaluation the V95% target coverage for every cCT were above the accepted worst-case scenario. Considerable variation in bladder-, bowel bag-, and bowel loop volume was observed, with the largest variation noted for the bladder (pCT/cCT-ratio: 1.3 (range: 0.5-4.7).

Conclusions: Target coverage was anatomically robust in IMPT for dose-escalated reirradiation of LRRC despite OAR variability. Inter-fraction motion resulted in varying dose to OAR within a clinically acceptable range.

Themes: Cancer, Cancer
Keywords: Locally advanced rectal cancer, Intensity Modulated Proton Therapy, Inter-fraction motion robustness

Evaluation of glenohumeral joint kinematics following the Latarjet and Eden-Hybinette procedures. A dynamic radiostereometric cadaver study.

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Anterior shoulder instability with glenoid bone lesion can be treated with the Eden-Hybinette procedure utilizing a tricortical iliac crest bone graft or the Latarjet procedure. This study aimed to evaluate the glenohumeral joint (GHJ) kinematics throughout an external shoulder rotation following the Eden-Hybinette and Latarjet procedures. Eight human specimens were examined with dynamic radiostereometry during a GHJ external rotation with anteriorly directed loads from 0-30 N. In 30- and 60-degree GHJ abduction, the kinematics (measured as the humeral head center and contact point) was sequentially recorded for a 15% anterior glenoid bone lesion, the Eden-Hybinette, and the Latarjet procedure. The Latarjet and Eden-Hybinette procedures resulted in up to 9.7 mm (95%CI 0.5;18.8) more posterior and a 7.4 mm (95%CI 0.3;14.4) superior humeral head center location compared to the glenoid bone lesion. With 0-20 N anterior directed loads, the Latarjet procedure resulted in a more posterior humeral head center and contact point of up to 7.6 mm (95%CI 3.6;11.5), especially in 60 degrees of GHJ abduction, compared to the Eden-Hybinette procedure. Opposite, at 30 N anterior-directed load, the Eden-Hybinette procedure resulted in a more posterior humeral head center of up to 7.6 mm (95%CI 0.3;14.9) in 30 degrees GHJ abduction compared to the Latarjet procedure. The results support considering the Latarjet procedures in patients who need the stabilizing effect with the arm in the abducted and externally rotated position (e.g. throwers) and the Eden-Hybinette procedure in patients exposed to high anterior-directed loads with the arm at lower abduction angles (e.g. epilepsia).

Themes: Surgery, Imaging techniques
Keywords: Glenohumeral joint kinematics, Anterior shoulder instability,

Impact of Splenic Endothelial Cells on Lung Tumor Immunology

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The spleen interacts with blood-borne tumor antigens and limits productive immune response towards cancer by enabling myeloid cell expansion and displaying distinct characteristics. The interaction of these tumor antigens with spleen-resident immune cells (ICs) can be mediated by endothelial cells (ECs) that act as a selective barrier between blood and the underlying tissue. ECs in various tissues are known to exhibit unique immunological features beyond their role in IC recruitment. Identification of such immune-EC subsets in health and during cancer warrants further exploration of such ECs in other parts of the body, especially in crucial immune hubs like spleen. However, the intricate density and complexity of the tissue have posed challenges in understanding the tissue's discrete function.

Here, we aim to elucidate the complexity of splenic EC functions and understand the molecular mechanisms governing IC-EC interactions that determine the tumor response using single-cell RNA sequencing technology. We isolated CD45+ and CD45- splenic cells from a mouse orthotopic lung tumor model and healthy controls and characterized the composition, functions and interaction of splenic ICs and ECs. We obtained high-quality single-cell transcriptome data from 191594 splenic cells. We observe an increase in the expression of inflammation related genes and gene ontologies in capillary artery and veins during tumor, and an increase in the interaction between ECs and ICs like DCs, Neutrophils, and Monocytes, indicating an increase of immumodulatory functions of tumor splenic ECs. These findings will be further validated using immunoflourescence staining and cell-based functional assays.

Themes: Cancer, Omics
Keywords: Endothelial cells, Cancer, Omics

Linear energy transfer constrained equivalent uniform dose in proton therapy of prostate cancer

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Introduction

Proton therapy (PT) is a modality of radiotherapy currently being explored for use in several treatment sites, including prostate. PT relies on the use of the relative biological effectiveness (RBE) which commonly assumes protons to be 10% more effective compared to photons. However RBE has been shown to vary with several factors including linear energy transfer (LET). Therefore the aim of this study was to investigate if LET values in PT of prostate cancer are associated with patient morbidity.

Materials and methods

884 PT treated prostate cancer patients were analysed in this study. We compared the equivalent uniform dose (EUD) in the rectum and bladder for patients with/without gastrointestinal (GI) morbidity and genitourinary (GU) morbidity, respectively. The EUD was calculated for all dose above an LET threshold, with LET thresholds ranging from 0 to 6 keV/um. The groups were compared by the mean and 95% confidence interval (CI). Furthermore we conducted a relative risk analysis for exceeding the upper 95% percentile of the patient population without morbidity.

Results

For the late GI morbidity, the rectum EUD 95% CIs were separated for LET threshold below 2.1 keV/um. The relative risk measure was highest for a LET threshold of 1.9 keV/um at 2.6 with 95% CI [1.8; 3.7]. For late GU morbidity the bladder EUD 95% CIs were separated for LET thresholds above 2.3 keV/um. The relative risk in this case was highest for a LET threshold of 5.2 keV/um at 4.4 [2.2; 8.7].

Discussion

Rectal and bladder EUDs were found to be associated with GI and GU morbidity, for LET values below 1.9 keV/um in the rectum and LET values above 5.2 keV/um in the bladder, respectively.

Themes: Cancer, Statistics
Keywords: Proton therapy, linear energy transfer, prostate cancer

Fractionated FLASH sparing in a murine model

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Background: FLASH protects normal tissue from damage while effectively maintaining tumour control. Up to 55% higher doses are required for FLASH to cause the same acute skin toxicity in mice as for conventional low-dose rates. Despite a decade of research, few have explored clinically relevant irradiation settings like fractionation, and no studies have enabled a quantitative evaluation. This study quantified the FLASH effect on acute skin toxicity using fractionated electron irradiation in a murine model.

Method: The right hind leg of unanaesthetised female CDF1 mice was irradiated with a 16 MeV electron beam. The mice were randomised into groups of conventional (CONV, 0.188 Gy/s) or FLASH (228 Gy/s) dose rates. The dose was delivered in four fractions with one daily dose on four consecutive days (4 x 8.4-21.5 Gy). The radiation-induced skin toxicity on the foot was assessed daily, and the maximally reached score was used to generate dose-response curves. The protection ratio was calculated as the ratio between TD50 (dose giving 50% toxicity risk) for FLASH relative to CONV.

Results: Fractionated electron FLASH irradiation required a 20% higher dose to cause the same skin toxicity as conventional low dose rates. The data included 4-8 mice per dose group.

Conclusion: The study quantified the effect of electron FLASH, with a protection ratio of 20% for four-fraction irradiation. Compared to 46% protection with single-fraction electron FLASH, the fractionated FLASH protection is more than halved. Therefore, introducing FLASH irradiation to a fractionated scheme will aid in tissue protection for acute skin damage, but more fractions might reduce the tissue-sparing effect.

Themes: Cancer, Animal Models
Keywords: Radiobiology, acute toxicity, murine model

Patient and public involvement in neonatal research – experiences and insights from parents and researchers

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Background

Involving parents in decisions about their infant's care is a common practice in - neonatal intensive care units worldwide. However, parental involvement is less frequent in neonatal research. As a part of a PhD project, previously admitted parents were involved as active contributors in a study about couplet care. The aim of this study was to explore the experiences of parents and researchers regarding their involvement in the research process.

Methods

A qualitative approach was used, involving two focus group interviews, one dyadic interview, and four individual interviews with parents and researchers. Two semi-structured interview guides structured the interviews. Data were analyzed through inductive content analysis.

Results

Nine parents and four researchers participated in the study. Seven themes emerged from the analyses, and these were consolidated into three core concepts: 'Embracing the ethos and pathos of patient and public involvement', 'Finding the path to maximize meaningful involvement', and 'Building expertise in patient and public involvement.' These concepts highlighted both similarities and differences, as well as the challenges and facilitators of patient and public involvement in research.

Conclusion

The involvement process was mutually beneficial, fostering learning and reflection for parents and researchers. However, challenges emerged, emphasizing the importance of building rapport between parents and researchers, appreciating each person's unique perspectives and expertise, and ensuring clear communication with well-defined roles and goals. These insights offer valuable guidance for future patient and public involvement in health research.

Themes: Paediatrics, Qualitative research
Keywords: Patient and public involvement, Neonatal intensive care unit, Qualitative research

School absence legislation governing in Norway, Sweden and Denmark for children with chronic illness in compulsory education—A comparative study

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Background: Health and education are interrelated and influence social, economic, and health perspectives. Children with chronic illnesses experience barriers in the educational system regarding school attendance and social isolation.

Methods: The study uses a comparative approach to explore the support of children with chronic illnesses in compulsory education across Norway, Sweden, and Denmark. The documents included are 3 education acts and 15 secondary documents, which are notes and guidelines for the education acts. The data were analysed using manifest content analysis.

Findings: We found four categories and six subcategories: (1) school obligation and rights; (2) chronic illness; (3) school absence: (a) categorisation of absence; (b) registration of absence; and (c) sanction; and (4) education support: (a) Hospital school support; (b) Home instruction support; and (c) technological support.

Conclusion: This study's findings demonstrate the similarities and differences in the Scandinavian compulsory education legislation and guidelines regarding chronic illness and school absence. We found similarities across the countries regarding chronic illness and school absence. Still, the findings showed differences in the systematic registration of school absence and requirements for attendance with compulsory education in Norway and Denmark compared with compulsory schooling in Sweden. This knowledge will inform and enlighten future discussions and decisions in education and public health. Future research focusing on the experience of children with chronic illness and educational support is needed.

Themes: Public health, Rehabilitation
Keywords: Chronis illness, School absence, Educational support

Risk of venous thromboembolism after surgery for lung cancer according to the surgical approach: Video-assisted thoracoscopic surgery vs. thoracotomy - CANCELLED

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Objectives: We conducted a nationwide cohort study to investigate the risk and timing of venous thromboembolism (VTE) after surgery for non-small cell lung cancer (NSCLC) according to the surgical approach: video-assisted thoracoscopic surgery (VATS) vs. thoracotomy.

Methods: Through the Danish Lung Cancer Registry, we identified all patients operated for NSCLC between 2003 and 2021, and assessed the risk of VTE events at 1-year follow-up by time-to-event analyses. Incidence rates were calculated within strata of surgical approach and year, and cumulative incidence functions within strata of surgical approach.

Results: We included 13,197 patients (mean age 67.6 years, 52.4% female) of which 53.3% of patients underwent a VATS procedure. At 1-year follow-up, 151 VTE events had occurred in the VATS group (rate: 2.40 events/100 person-years) compared to 184 events in the thoracotomy group (rate: 3.41 events/100 person-years). The cumulative incidence of VTE at 1-year was 2.2% (95% confidence interval (CI): 1.9-2.6) in the VATS group, compared to 3.0 % (95% CI: 2.6-3.5) in the thoracotomy group. In both groups, the hazard was highest within the first three months. The lower risk of VTE among patients undergoing VATS was observed throughout the study period.

Conclusions: Surgery by VATS suggests a lower risk of VTE compared to those undergoing thoracotomy, with 1-year cumulative incidence rates of 2.2% and 3.0%, respectively. Despite substantial changes in both indications and performance of VATS over time, the risk of VTE seems lower with VATS.

Themes: Surgery, Cancer
Keywords: Lung cancer surgery, Venous thromboembolism, Epidemiology

The effect of infection on mortality in Periprosthetic Joint Infections after Total Knee Arthroplasty

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Background: Periprosthetic Joint Infection (PJI) after total knee arthroplasty (TKA) is a serious complication that may increase mortality. This study aimed to assess mortality following PJI revisions compared to major aseptic revisions in a nationwide, microbiologically verified cohort.

Methods: Data from the Danish Knee Arthroplasty Register and Danish Microbiology Database were used to identify patients who underwent PJI revisions between January 2010 and November 2023. These patients were compared to those undergoing major aseptic revisions in the same period, with follow-up until April 2024. Mortality rate was calculated using the Kaplan-Meier method, and adjusted hazard ratios were estimated using Inverse Probability of Treatment Weighting (IPTW) to balance confounders, including age, sex, weight, Charlson Comorbidity Index, and marital status.

Results: We identified 916 PJI revisions and 4,129 major aseptic revisions after primary TKA. The mean follow-up was 7.0 years for PJI and 7.3 years for aseptic revisions. PJI patients were generally older, had a higher proportion of men, greater obesity, and more comorbidities than aseptic patients. Crude mortality was 4.6 deaths/100 person-years for PJI revisions and 1.6 deaths/100 person-years for aseptic revisions. The IPTW-adjusted hazard ratio for PJI-associated mortality was 1.62 (95% CI: 1.35–1.95, $p<0.001$).

Conclusion: PJI following TKA is linked to significantly higher mortality compared to major aseptic revisions.

Themes: Epidemiology, Surgery
Keywords: Periprosthetic Joint Infection, Complication, Arthroplasty

Temporally resolved single-cell RNA sequencing reveals protective and pathological responses during herpes simplex virus 1 CNS infection

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Herpes Simplex Virus 1 (HSV-1) is a common human neurotropic virus with the majority of adults harboring latent-recurrent infections. In rare cases, HSV-1 infection can access the central nervous system through the neuronal route and develop into life-threatening encephalitis. Here, we used a mouse model for HSV-1 infection to describe the transcriptomic profile of the infected brain stem at the single-cell level and with temporal resolution. Among resident brain cells, microglia increased in proportion during the course of infection, while astrocytes, pericytes, and endothelial cell levels decrease. At the levels of peripheral immune cells, we found notably monocytes to strongly influx the infected brain. Large dynamic changes were found in the abundance of subpopulations of the different cell types following virus infection. For instance, we identify one subpopulation of microglia exhibiting very high type I interferon and chemokine expression early during infection. This population was also enriched for viral transcripts, suggesting localization at foci of infection, and orchestrating recruitment of other immune cells. In contrast, for the infiltrating monocytes, we identified a larger panel of unique subpopulations with antiviral and inflammatory phenotypes, and found not all of these being highly positive for viral transcripts, thus indicating monocyte activities beyond the infected brain areas. Finally, investigation of endothelial cell cross-talk with other cell types revealed that cytokines derived from microglia and monocyte, but also T cells, contribute to disturbance of the blood brain barrier. Our work thus reveals for the first time the complex nature of the cellular response in the virus-infected brain, which seeks to eliminate infection but can also prime for pathological changes.

Themes: Infectious Diseases, Omics
Keywords: , ,

Quantification of late-gadolinium enhancement magnetic resonance imaging to predict ventricular arrythmias and sudden cardiac death: A systematic review

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Introduction: Late gadolinium enhancement (LGE) on cardiac magnetic resonance imaging (CMR) is a recognized tool for identifying heart muscle fibrosis in non-ischemic cardiomyopathy (NICM). However, definitions lack consensus, and even smaller amounts of LGE can be associated with adverse outcomes depending on location and underlying pathology, complicating interpretation. This review summarizes knowledge on current LGE quantification methods and their ability to predict ventricular arrhythmias (VA) in NICM.

Methods and Results: We included 35 studies with 12,286 NICM patients. Two main methods were used to quantify LGE: Thresholding based on standard deviation (SD) above signal intensity in unaffected heart muscle (20 studies) and the Full Width Half Maximum (FWHM) method (15 studies). Summary statistics were pooled, and figures were constructed to show LGE variability and its link to VA risk. LGE amounts varied by method: Lower thresholds (e.g., 2 SD) identified larger LGE volumes, while higher thresholds (5-6 SD) reported smaller amounts. The risk of VA increased with LGE, with hazard ratios ranging from 1.31 to 1.47 per 10 grams of LGE. Septal and midwall LGE, especially when both were present, was linked to higher risks of VA.

Conclusion: This review highlights the variability in LGE quantification methods and their impact on VA risk prediction in NICM. Standardizing LGE quantification is crucial for improving the reliability of risk assessment. The presence, amount, and specific locations of LGE are key predictors of VA. Future research should aim to standardize these methods to improve risk prediction accuracy.

Themes: Cardiology, Statistics
Keywords: Systematic review, Arrhythmia, Cardiomyopathy

The Prognostic Potential of circRNAs in Multiple Myeloma: Insights from Whole Bone Marrow and Purified Plasma Cells

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Multiple myeloma (MM) is a hematological malignancy with abnormal proliferation of plasma cells in the bone marrow (BM). MM patients with highly proliferative plasma cells have reduced overall survival. Circular RNAs (circRNAs) are endogenous, non-coding molecules that are promising biomarkers in cancer. Here, we present the largest study of circRNAs in MM to date, and explore the prognostic potential of circRNAs and the link between proliferation and circRNA expression in MM. We performed deep total RNA sequencing (RNA-seq) on two cohorts: one cohort consisting of 45 whole BM MM patient samples and 13 healthy controls (HCs), and another cohort consisting of 43 CD138-purified plasma cell MM patient samples. We found that circRNAs are globally upregulated in whole BM of MM patients compared to HCs. In whole BM, low proliferation and high circRNA levels were associated with a poor prognosis, while in purified plasma cells, low proliferation and high circRNA levels were associated with a favorable prognosis. Individual circRNAs from purified plasma cells were found to be significantly associated with MM patient outcomes and provide additional prognostic value to the proliferative indexes. Together, our findings emphasize the potential of circRNAs as prognostic biomarkers in MM.

Themes: Molecular biology, Cancer
Keywords: , ,

Brain Network Imbalances in Patients with MCS

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Aims: Functional somatic disorders (FSDs) are characterized by persistent physical symptoms that other somatic or psychiatric conditions cannot explain. MCS is a non-allergic FSD characterized by odor intolerance and attributed to the influence of toxic environmental chemicals in low, usually harmless doses. In recent decades, a number of different types of FSDs have been defined, but so far there is no clear explanation of their pathophysiology. The latest evidence of the long-covid diagnosis and strong overlaps with FSDs suggests the potential presence of new forms of somatoform disorders in the human population. Surprisingly, smell complaints were also one of the negotiable symptoms during the covid epidemic.

Methods: This study included a test battery of questionnaires and paraclinical tests, including the Sniffin' Stick olfactory test, minimal mental state examination, Sino-nasal outcome test 22, pain measurement thresholds tests, and heart rate variability test. Accordingly, whole-brain computational modeling based on MRI-derived functional and structural connectomes has been employed using the 3T MR scanner. We have deliberately initiated the project with 16 MCS patients compared to 15 healthy subjects. Results: MCS group showed obvious brain structural differences in terms of significant connectivity differences. Notably, for MCS, the olfactory cortex, especially the right hemisphere, had decreased connectivity with the limbic system. Conclusion: Given the nature of these data, a study of the cerebral events immediately after olfactory stimulation combined with a test battery for potential biomarkers will be the next step in studying the olfactory response in MCS, FSDs, and long-covid in relation to normal olfaction. We hope that brain computational mobe is used as a "fingerprint" in diagnosis and "treatment monitoring" by machine learning in FSDs and new diagnoses such as long-covid patients.

Themes: Neuroscience, Imaging techniques

Neighbourhood matters too: the association between mental disorders and mortality according to neighbourhood socioeconomic deprivation and the interaction with individual socioeconomic position

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Aims

This study aims to investigate the role of neighbourhood socioeconomic deprivation in mortality in mental disorders and its interaction with individual socioeconomic position (SEP).

Methods

Using Danish nationwide registers, we identified people who was first diagnosed with mental disorders between January 1, 2000, and December 31, 2020, exact matched with up to five counterparts on age and sex, at the date of first contact. Individual SEP was measured by household income. Neighbourhood deprivation was defined using a composite measure of aggregated information on income, education, employment status, manual workers, and household crowding and was ranked into percentiles. Mortality rate ratios and rate differences were estimated using Bayesian multilevel Poisson regression models, through the 'brms' package in R.

Results

In preliminary analyses, we found that individuals with mental disorders had elevated mortality rates compared with individuals undiagnosed regardless of neighbourhood deprivation levels. For natural causes of death, mortality rate ratios between people with and without mental disorders were similar across deprivation levels, whilst mortality rate differences were larger in the most deprived rather than the least deprived groups. For external causes of death, we observed similar mortality rate differences across deprivation levels.

Conclusion

This study provides a comprehensive analysis of the role of SEP at multiple levels in the associations between specific types of mental disorders and cause-specific mortality. The identified socioeconomic gradients should be prioritized for mortality prevention for people with mental disorders.

Themes: Mental health, Public health
Keywords: Psychiatric epidemiology, Neighborhood deprivation, Mortality

Herpesvirus CNS infections in autosomal dominant IRF7 deficiency

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Inborn errors of immunity (IEI) impairing brain-intrinsic immune defences can underlie recurrent lymphoid meningitis (RLM, Mollaret's meningitis) caused by HSV-2 and have also been reported in patients with acute retinal necrosis (ARN) driven by HSV-1 or other alpha herpesviruses. By whole exome sequencing of cohorts of RLM and ARN patients we identified two heterozygous variants in interferon (IFN) regulatory factor 7 (IRF7). Single gene IEI in IRF7 were previously reported in patients suffering from severe influenza, COVID-19 and other respiratory virus infections. Both, the IRF7 Q185X and A86Rfs23X variants resulted in truncated proteins and were found to be loss-of-function variants. PBMCs from the RLM patient showed greatly reduced type I IFN responses and -amplification to HSV-2 infection, dsDNA and TLR9 ligands. Heterozygous knock-in of the IRF7 Q185X variant in THP-1 cells recapitulated the impaired IFN-I production and -amplification by monocytes and demonstrated a dominant phenotype of the variant allele. Moreover, a non-redundant role of the TLR9-IRF7 pathway in HSV-2 sensing by plasmacytoid dendritic cells (pDCs) was shown by CRISPR/Cas9 knock-out in in-vitro differentiated pDCs. Finally, we established efficient CRISPR repair of the patient variant to rescue the phenotype in hematopoietic stem cell-derived patient pDCs. This study highlights the role of IRF7 in controlling recurrent HSV infections of the CNS and identifies AD IRF7 deficiency as an IEI predisposing to RLM and ARN. The results suggest a previously underappreciated role of peripheral immune cells in innate antiviral responses to herpesviruses in the CNS.

Themes: Immune diseases, Infectious Diseases
Keywords: IEI, Innate immunity,

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