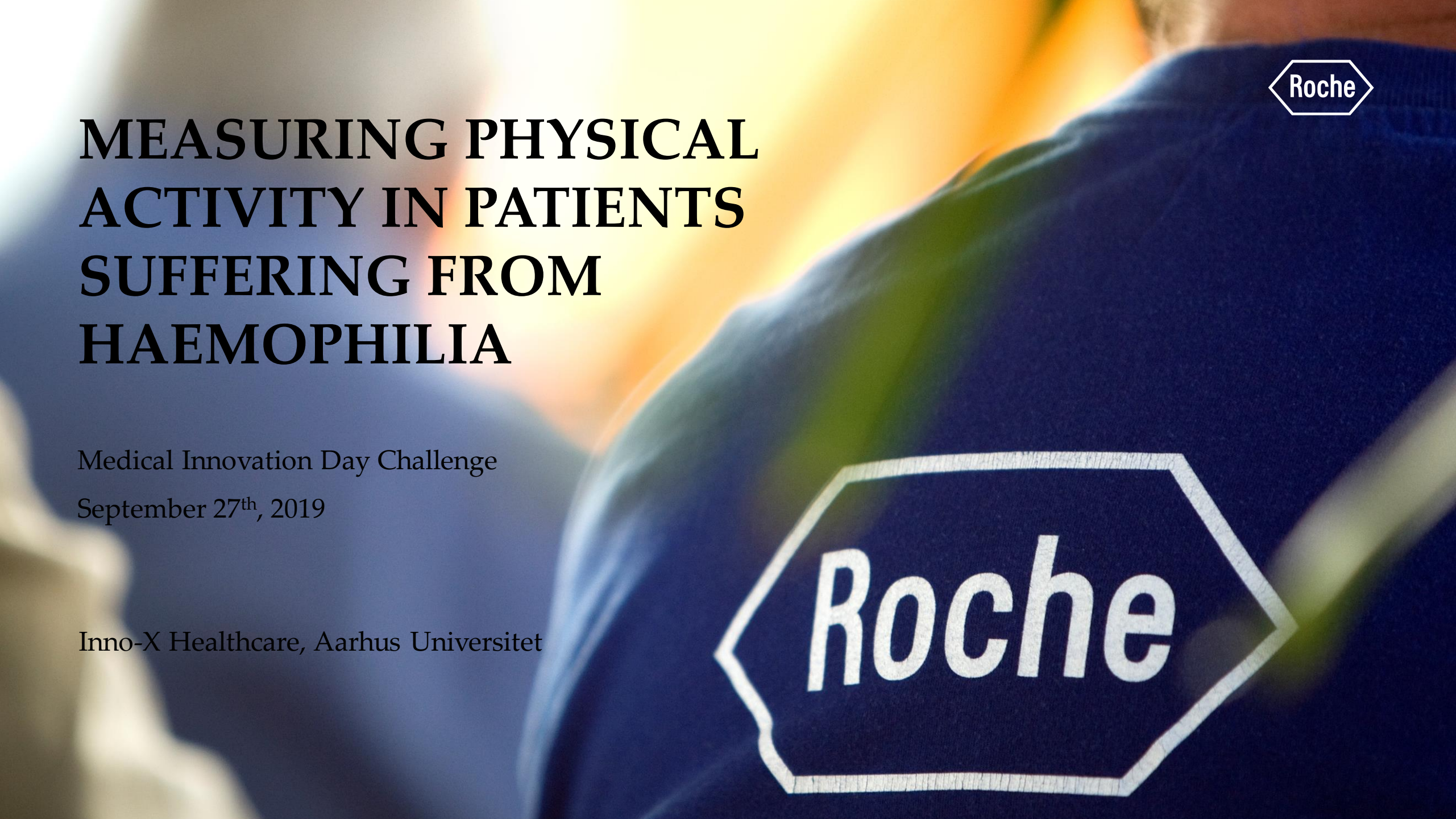
MEASURING PHYSICAL ACTIVITY IN PATIENTS SUFFERING FROM HAEMOPHILIA

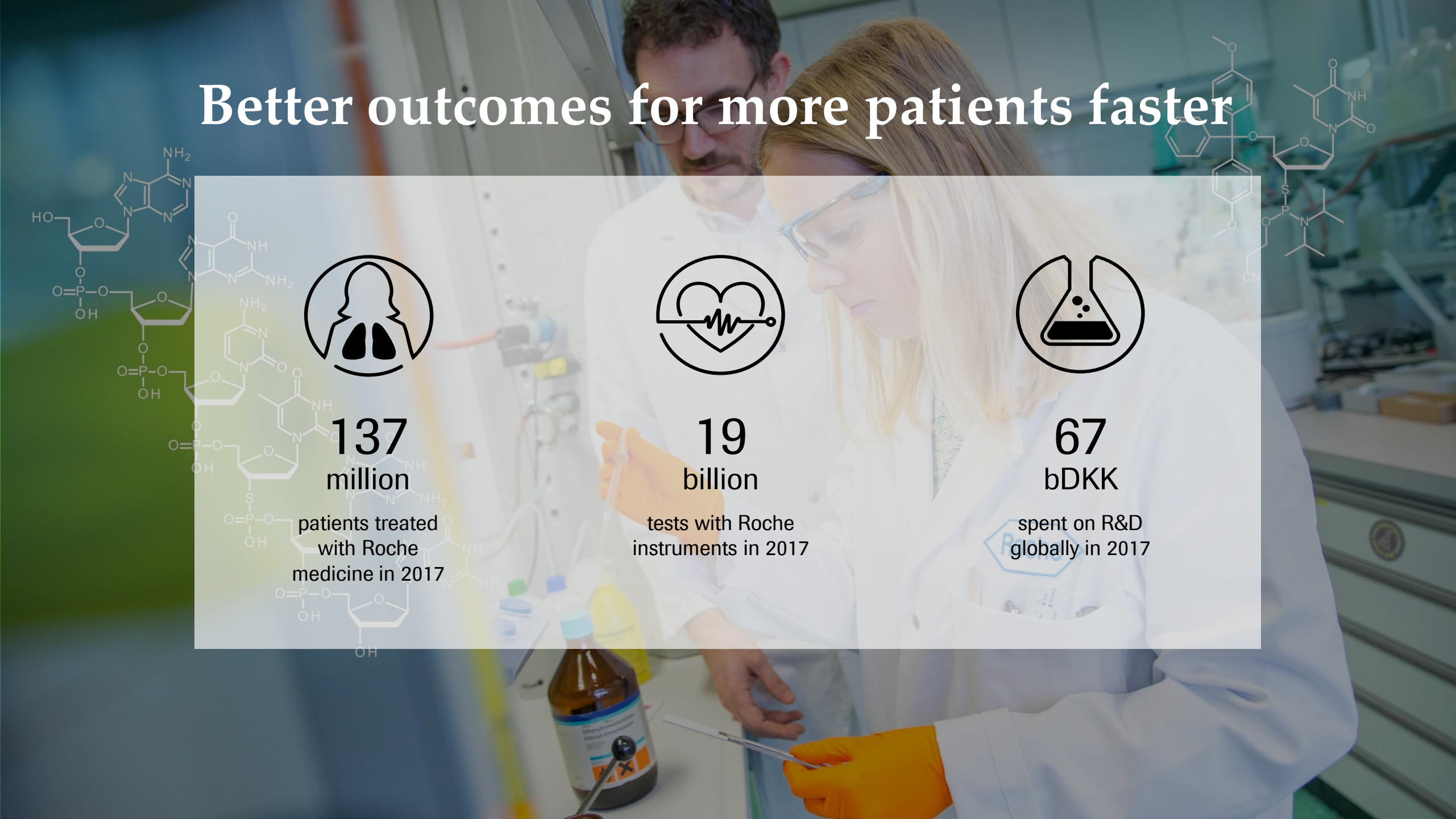
Medical Innovation Day Challenge

September 27th, 2019

Inno-X Healthcare, Aarhus Universitet



Better outcomes for more patients faster



137
million

patients treated with Roche medicine in 2017

19
billion

tests with Roche instruments in 2017

67
bDKK

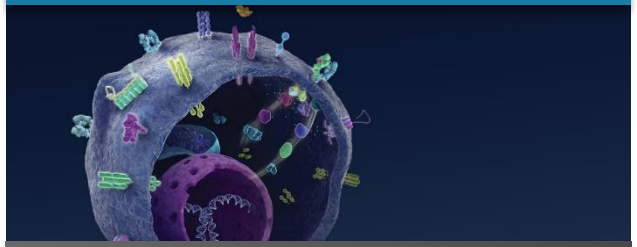
spent on R&D globally in 2017

Our presence in Denmark

Roche Denmark

Frontrunner within Personalized Healthcare
#2 most clinical trials in Denmark
For each DKK spent on a Roche Treatment, we add back 1,2 DKK

Roche Pharmaceuticals



- 125 employees
- Development of medicine

Roche Diagnostics & Diabetes Care

- 90 employees
- In-vitro diagnostics

Roche Innovation Center Copenhagen (RICC)

- 75 employees
- RNA molecule research

Background for the Challenge

What is Hemophilia?

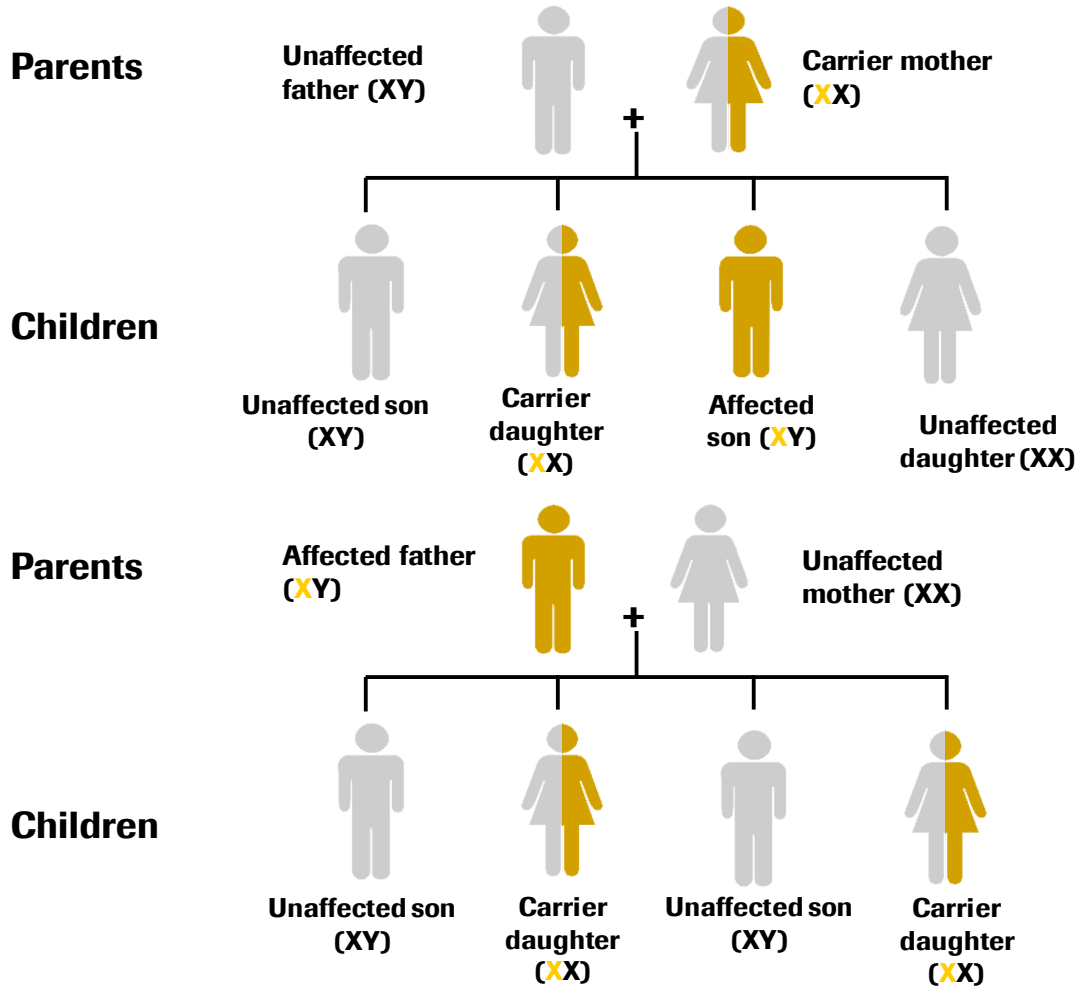
Hemophilia is a bleeding disorder. People with hemophilia do not bleed any faster than normal, but they can bleed for a longer time. Their blood does not have enough clotting factor. Clotting factor is a protein in blood that controls bleeding. The most common type of hemophilia is called hemophilia A. This means the person does not have enough clotting factor VIII (factor eight). Hemophilia B is less common. A person with hemophilia B does not have enough factor IX (factor nine). The result is the same for people with hemophilia A and B; that is, they bleed for a longer time than normal.

Worldwide, there are approximately **400,000** patients with hemophilia[1]

Hemophilia is quite rare. About 1 in 10,000 people are born with it.

Hemophilia A represents **80–85%** of the total hemophilia population.

Although the number of patients diagnosed with hemophilia is increasing, it is suspected that many patients remain undiagnosed



Background for the Challenge

Severity of hemophilia and prevalence in Denmark

- The severity describes how serious the bleeding disorder is. The level of severity depends on the amount of clotting factor that is missing from a person's blood.
- People with severe hemophilia usually bleed frequently into their muscles or joints. They may bleed one to two times per week. Bleeding is often spontaneous, which means it happens for no obvious reason.
- People with moderate hemophilia bleed less frequently, about once a month. They may bleed for a long time after surgery, a bad injury, or dental work. A person with moderate hemophilia will rarely experience spontaneous bleeding.
- People with mild hemophilia usually bleed as a result of surgery or major injury. They do not bleed often and, in fact, some may never have a bleeding problem.
- The prevalence, which is the current number of patients diagnosed with hemophilia, in Denmark is 508. The incidence, which is the number of new patients diagnosed every year, in Denmark is Y.

Level	Percentage of normal factor activity in blood	Number of international units (IU) per millilitre (ml) of whole blood
normal range	50%-150%	0.50–1.5 IU
mild hemophilia	5%-40%	0.05–0.40 IU
moderate hemophilia	1%-5%	0.01–0.05 IU
severe hemophilia	less than 1%	less than 0.01 IU

	Center	Severe A/B	Moderate A/B	Mild A/B	Total A/B	Approximate referral population size	Country population size (census)
DENMARK		152/30	45/9	209/63	406/102	5,585,509	5,580,000
	Aarhus	83/9	33/5	131/33	247/47	3,048,020	
	Copenhagen	69/21	12/4	78/30	159/65	2,537,489	

Source: Nordic Hemophilia Guidelines

Authors Nordic Hemophilia Council guideline working group 2015

Background for the Challenge

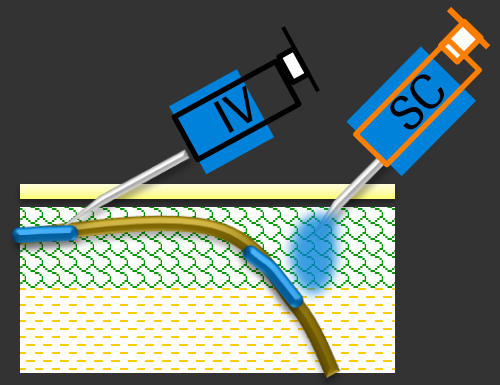
Guidelines for management of hemophilia and treatment procedure

Recommendations for patients with haemophilia A

The recommendations for hemophilia A are divided into prophylactic (preventive) treatment and on-demand treatment (treatment if needed).

Prophylactic treatment

In severe haemophilia A, spontaneous joint and muscle bleeding is seen, which in the long term leads to severe joint changes, disability and chronic pain. The goal of prophylactic treatment is to avoid joint bleeding, joint damage and life-threatening bleeding. Patients with severe haemophilia A and some patients with moderate haemophilia A are offered prophylactic home treatment with a FVIII preparation. In practice, this is done by the patient or his parents even administer intravenous infusion of a FVIII preparation several times a week.

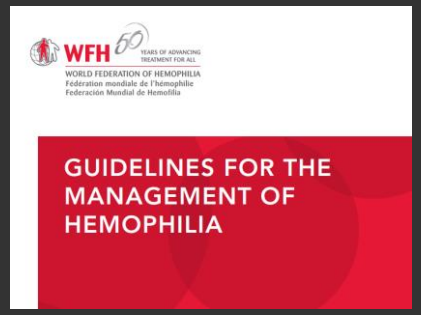


Standard FVIIIs, extended half-lives (EHLs) and a medicinal product, which mimic the function of FVIII and are administered subcutaneously 1-4 times a month, are distinguished.

Guidelines for management of hemophilia

"Physical activity should be encouraged to promote physical fitness and normal neuromuscular development, with attention paid to muscle strengthening, coordination, general fitness, physical functioning, healthy body weight, and self-esteem."

Source: https://www.wfh.org/en/resources/wfh-treatment-guidelines



Background for the Challenge

Adherence

Adherence to (or compliance with) a treatment plan is generally defined as the extent to which patients take medications as prescribed by their healthcare providers. According to the World Health Organization, rates of non-adherence with any medication treatment may vary from 15% to 93%, with an average estimated rate of 50%. Adherence to a prophylaxis protocol is critical to its success. Prophylaxis is most effective if factor levels are continuously maintained above the target level. Missing or skipping a dose can cause clotting factor levels to fall below this target, which increases the risk of bleeding. Bleeding that occurs while a patient is on prophylaxis is called 'breakthrough bleeding'. Patients and healthcare providers must work together to ensure that the protocol is manageable for the person with hemophilia and their family. A patient's adherence to the protocol should be assessed regularly during clinic visits and strategies to improve adherence, including changes to the protocol, should be explored wherever possible.

Venous access – Prophylaxis requires frequent injections and it can be difficult to find suitable veins in very young children with hemophilia. An implanted venous access device (e.g. Port-A-Cath) can make injections much easier and may be required for administering prophylaxis in young children. However, there are risks involved with the use of these devices, including the risk of local infection and the formation of blood clots that may cause blockage. These risks need to be weighed against the advantages of starting intensive prophylaxis early. In 70% of children early prophylaxis is possible without venous access devices. An important option is starting prophylaxis once a week as it does not require the implantation of a Port-A-Cath which makes the treatment easier for patients and families to accept.

Source: https://www.wfh.org/en/abd/prophylaxis/prophylaxis-barriers-and-challenges?

Challenge Statement

Area of Focus

- Patients with Hemophilia A as it is the most common type of hemophilia
- Patients with **Severe** hemophlia A as it has the greatest impact on peoples life's –patient and caregivers
- Who are getting **Prophylatic treatment** as it is the recommended treatment for patients with severe hemophilia A and it requires intravenous infusion of a FVIII preparation several times a week.
- Adherence as it is critically important for living a life without bleedings
- Fitness or physical activity as it is one important aspect of life, also living with hemophilia

Challenges

OVERALL CHALLENGE:

How can it be measured whether patients with hemophilia A live a life with the same level of physical activity as a matched control without hemophilia?

ADDITIONAL CHALLENGES:

What role does patient adherence play in the wellbeing and physical activity level of the patient?

Are any patient groups more prone to adherence issues and should the treatment reflect this?

Does the bleeding pattern impact the patients physical activity level and/or the desire to be physical active?

How might we over time build evidence to support that the user experience and reported user value of a treatment is an important factor for patients, doctors and payers that should be evaluated equally to documented efficacy and safety data?

Explainatory Videos

- Hemophilia Infusion: https://www.youtube.com/watch?v=kvJbqTkiuZM
- Hemophilia Infusion through Port: https://www.youtube.com/watch?v=hgK-hzci_KQ
- Hemophilia Treatment: https://www.youtube.com/watch?v=xTiJ2qonFIE
- Hemophilia Treatment: https://www.youtube.com/watch?v=lZVwGf-8qRQ
- Hemophilia – causes, symptoms, diagnosis, treatment and patology: https://www.youtube.com/watch?v=nkC1vZaUpxs

Additional Ressources

- What is Hemophilia: https://www.wfh.org/en/page.aspx?pid=646
- Learn more about the disease here: https://www.wfh.org/en/page.aspx?pid=1297
- Severity of hemophilia: https://www.wfh.org/en/page.aspx?pid=643
- Physical activity and hemophilia (Danish): https://www.bloderforeningen.dk/livet-med-blodersygdom/sport/hvorfor-er-det-vigtigt-dyrke-sport-som-bloeder
- WFH guidelines for the management of hemophilia: https://www.wfh.org/en/resources/wfh-treatment-guidelines
- Adherence: https://www.wfh.org/en/abd/prophylaxis/prophylaxis-barriers-and-challenges?