Goal Attainment Scaling: pinpointing elusive differences in haemophilia therapy effectiveness

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Asterix Patient Think Tank

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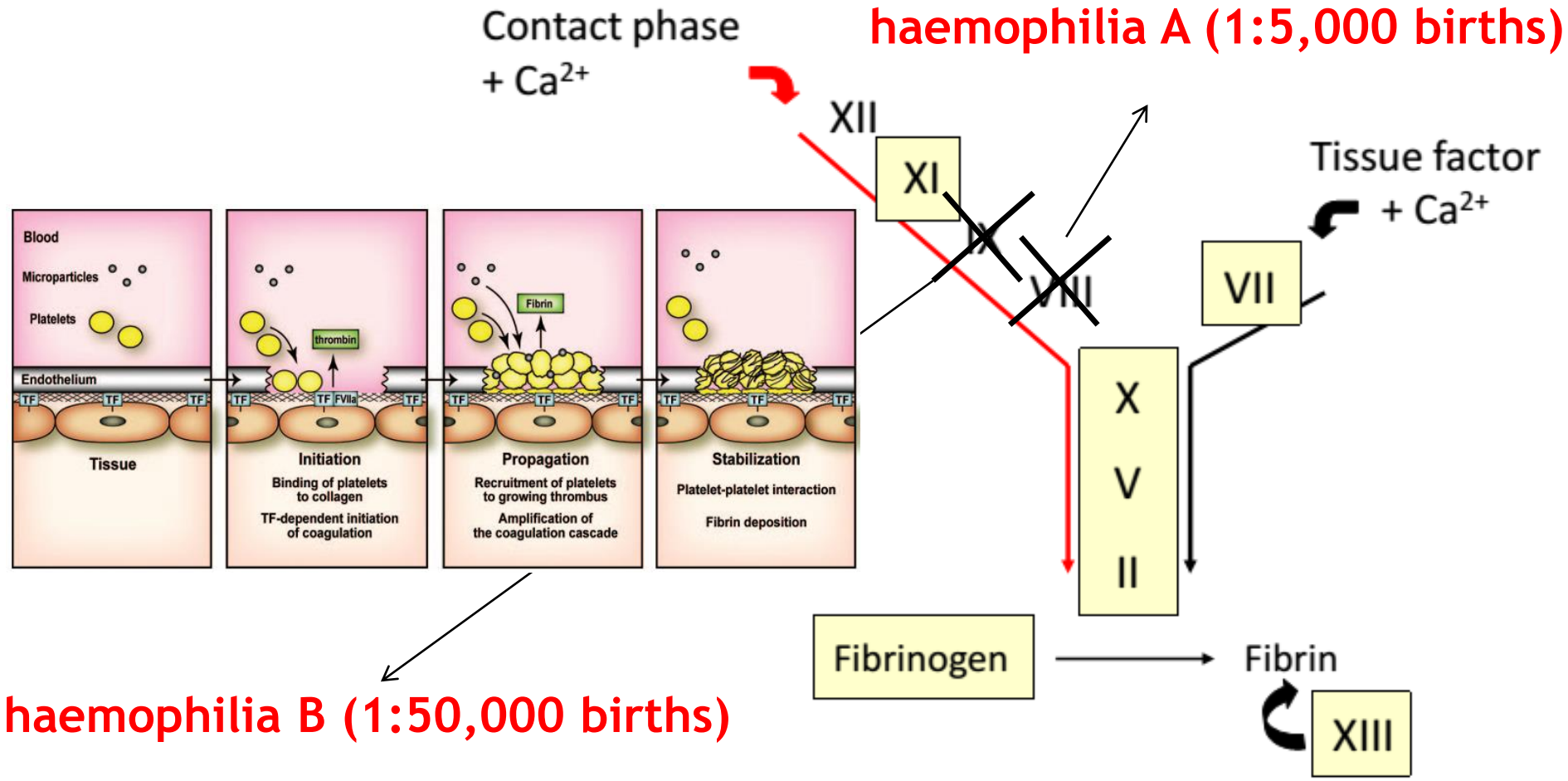
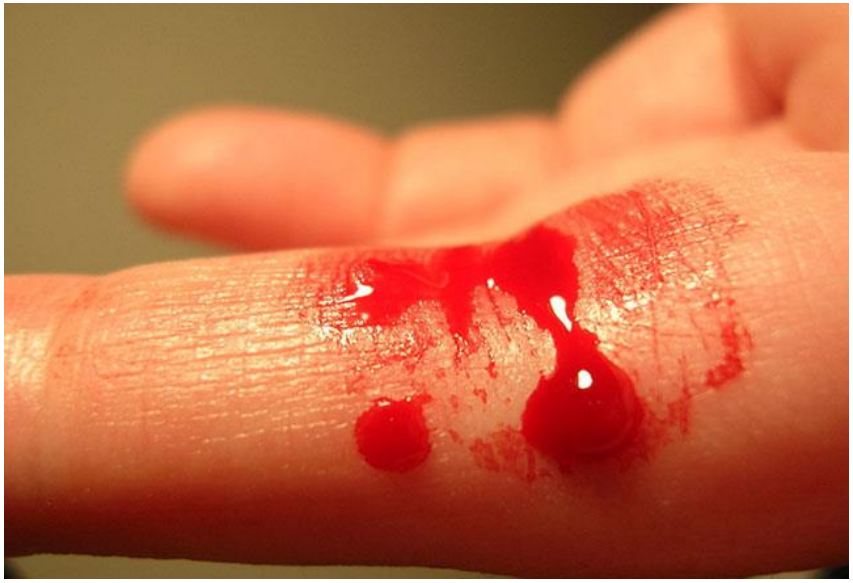
Haemophilia is a rare disease, but a common inheritable bleeding disorder resulting from defects in secondary haemostasis.

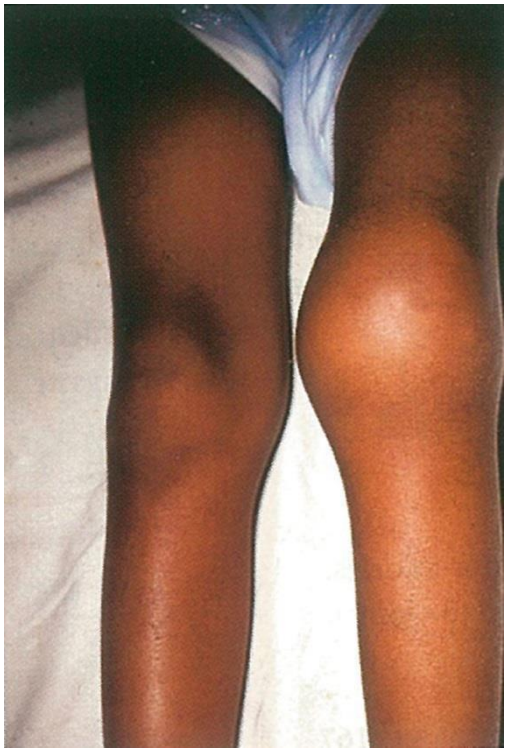


Mackman et al. Arterioscler Thromb Vasc Biol. 2007;27:1687-1693

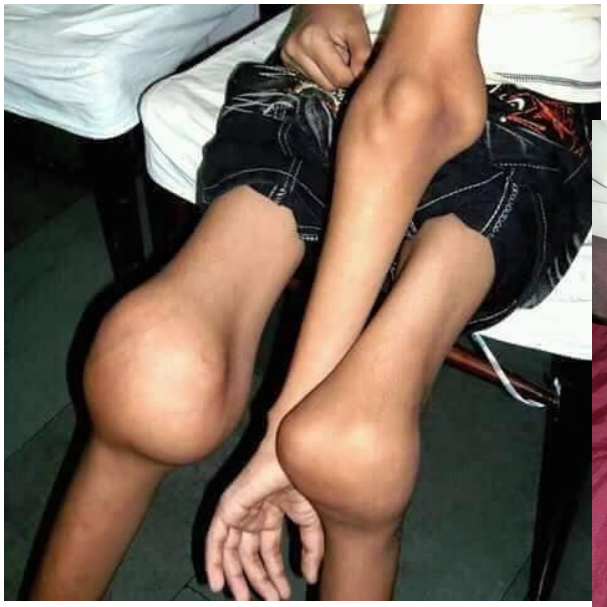
The main symptom of severe haemophilia A and B (<1% FVIII or FIX level; normal levels: 50-150%) is bleeding into the joints and muscles.

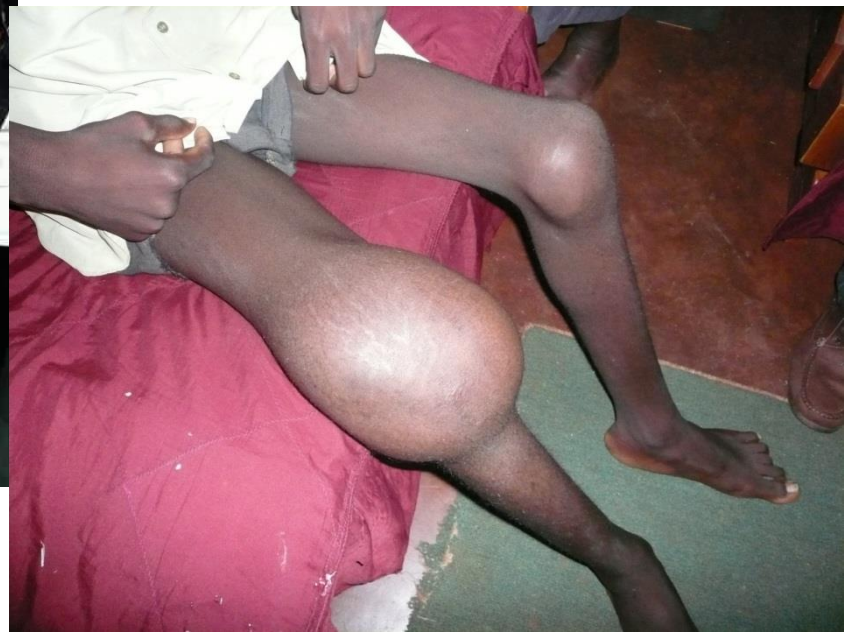
Contrary to a popular belief, external bleeding is usually easy to control.





Recurrent spontaneous bleeds lead to chronic synovitis, joint damage and muscle atrophy.

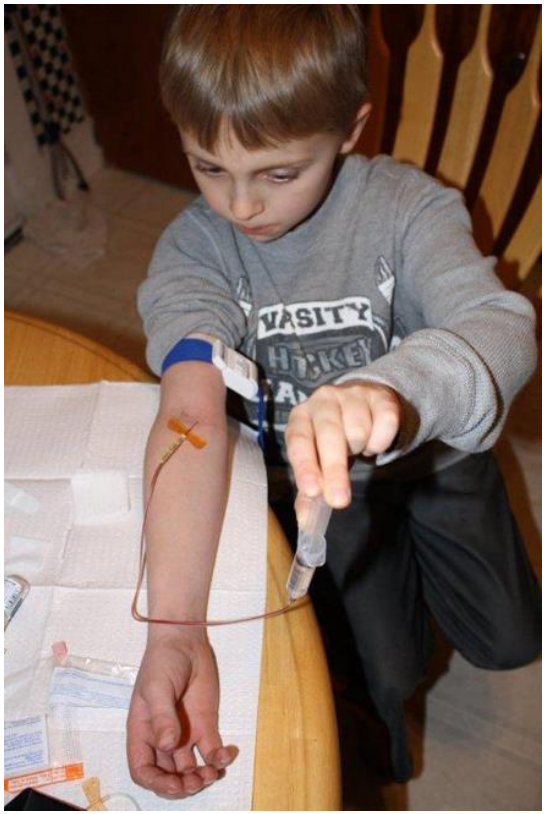




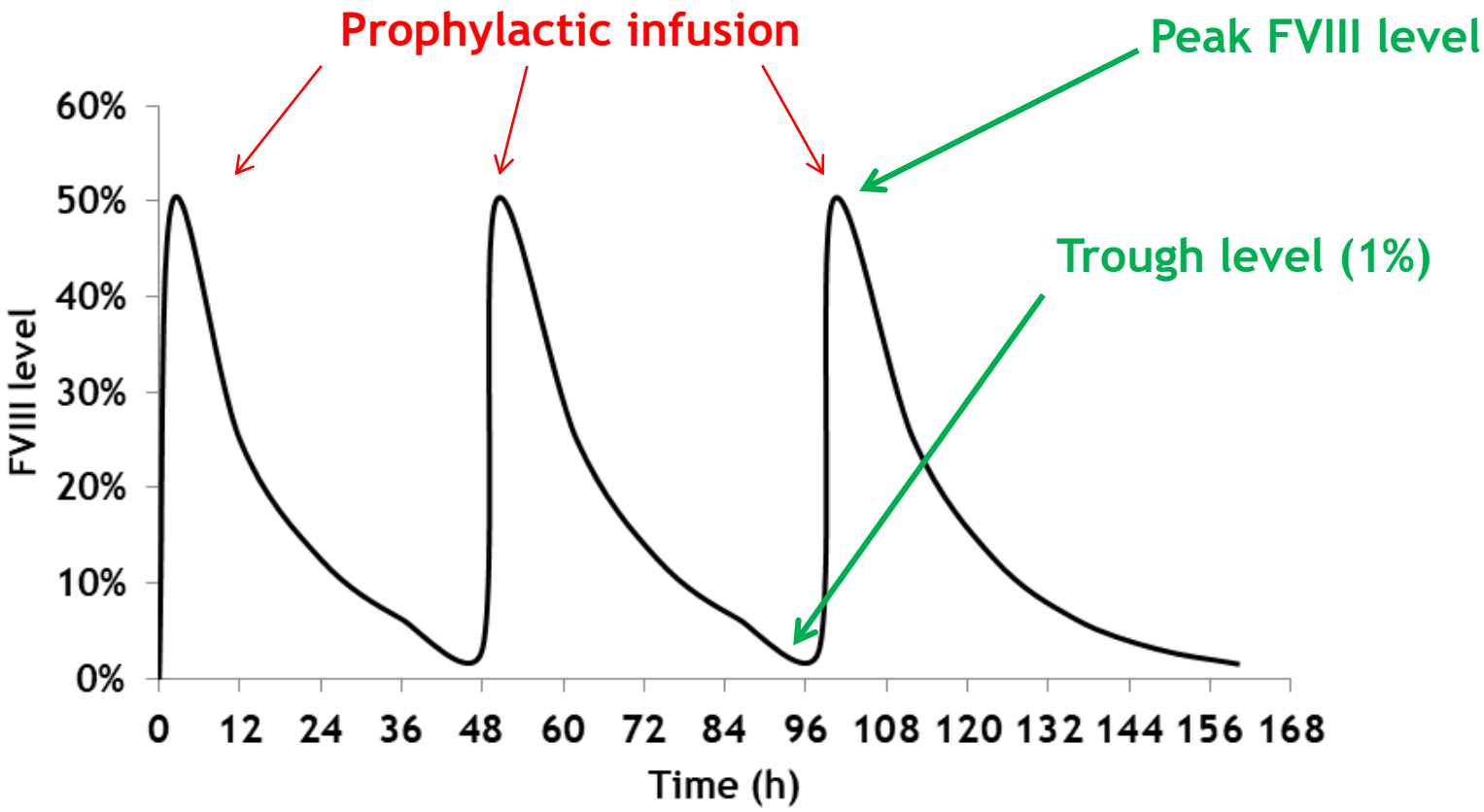
Treatment or prevention of bleeds requires intravenous infusions of the deficient coagulation factor concentrate (factor replacement).

Home treatment and prophylaxis have been the standard of care for over 20 years.

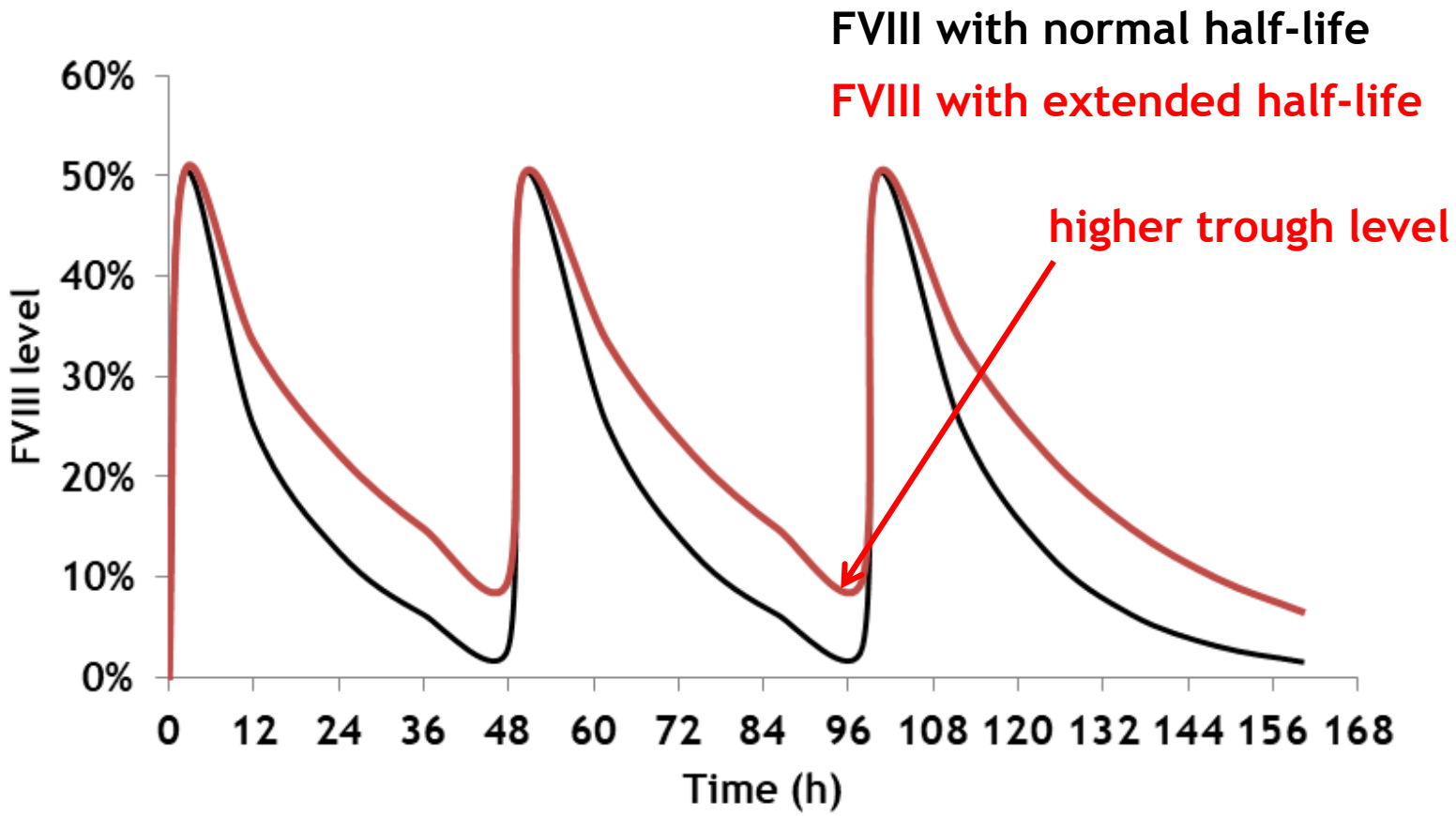
The aim is to reduce the bleeding rate, which, without adequate treatment, can go as high as several dozen acute bleeds.



Keeping the deficient factor level all the time over 1% dramatically reduces the ABR and so the joint damage.

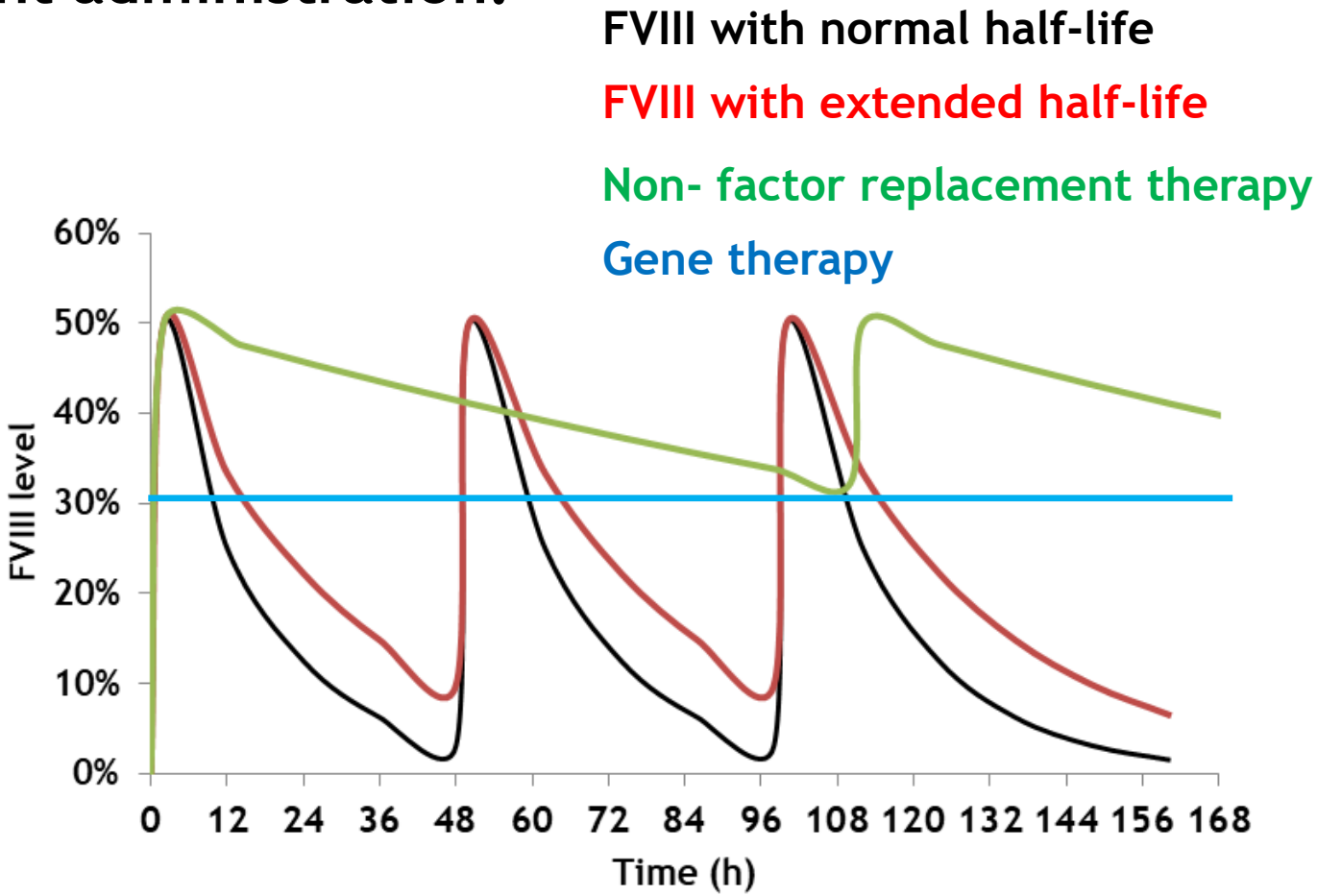


New generations of clotting factor concentrates show extended half-lives and may offer better protection from bleeds.



Annual bleeding rate may be reduced from ~3 to ~0.

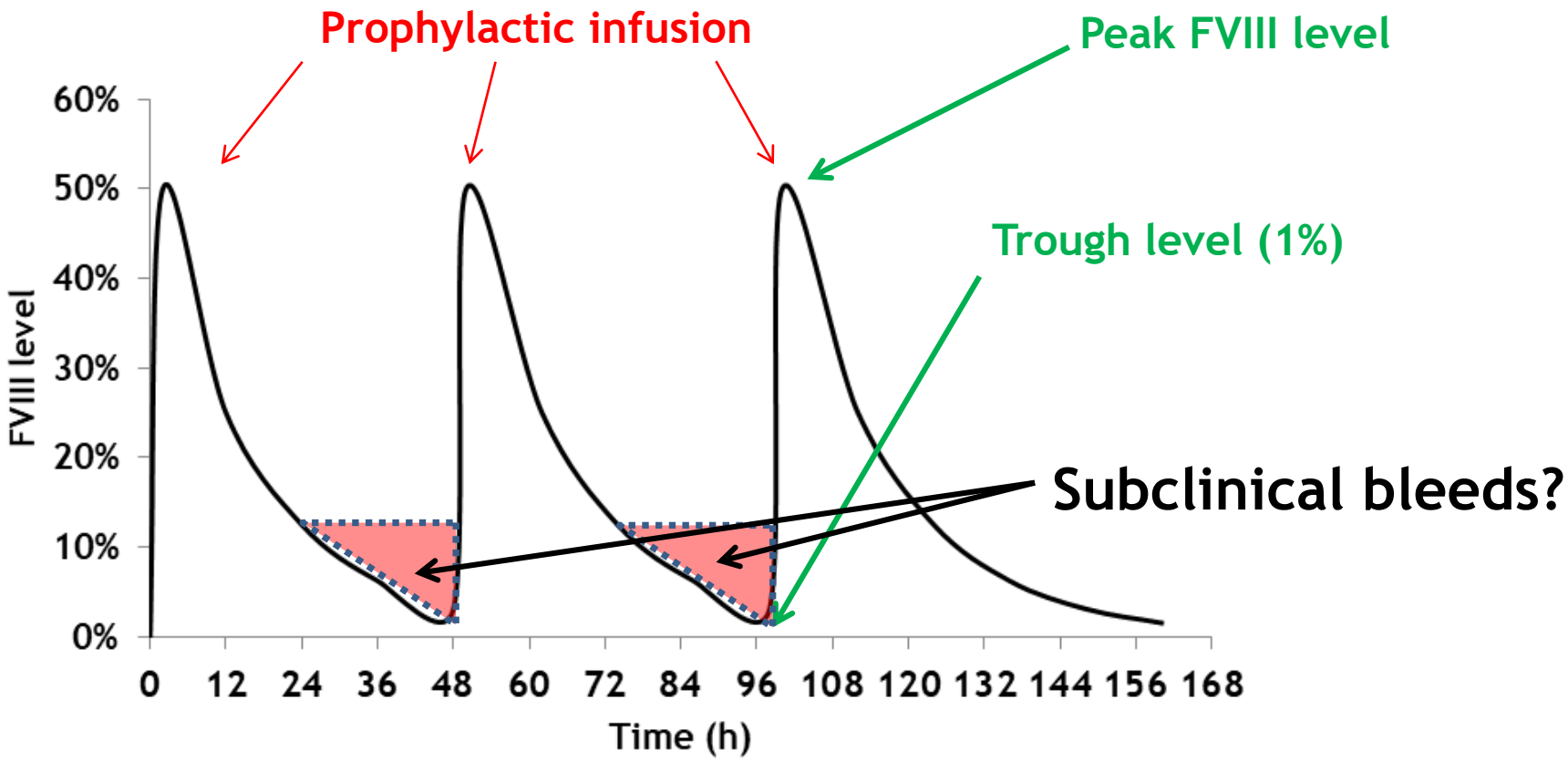
More innovative therapies (non-factor replacement therapies) may offer still better protection and less frequent administration.



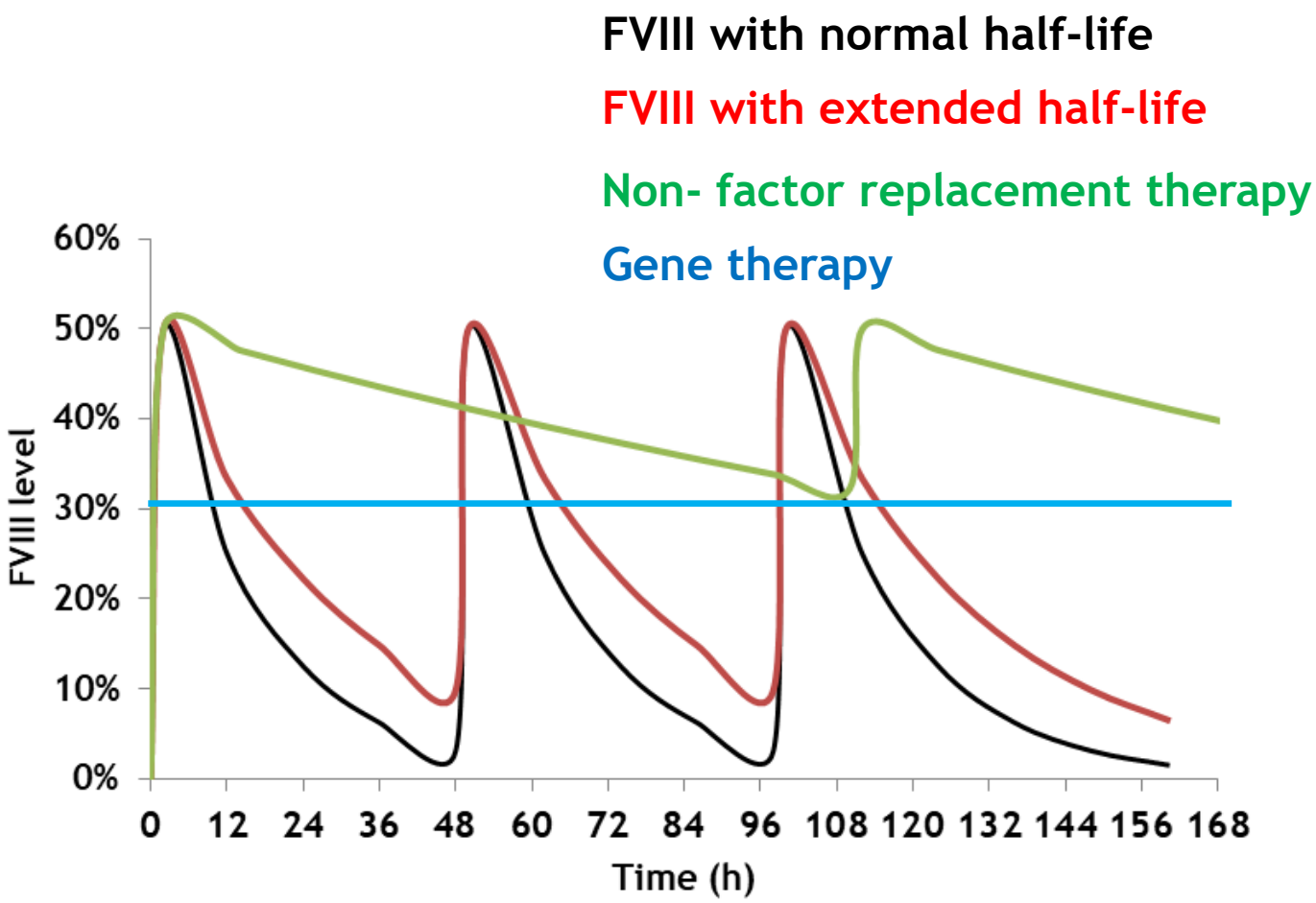
How to capture the differences if no difference in ABR? Or does that just mean no difference?

Some patients develop joint damage despite prophylaxis.

Subclinical bleeds may go unreported or misinterpreted, obfuscating the „true" ABR.



ABR difference between these therapies may be small or zero, but higher trough level may still have a dramatic impact on QoL.



Example:

A severe haemophilia A patient in his 50s, „cured” from haemophilia as a side effect of liver transplant (his FVIII level corrected from 0% to stable 57%).

Before the surgery, he had been on a high-dose prophylaxis for many years.

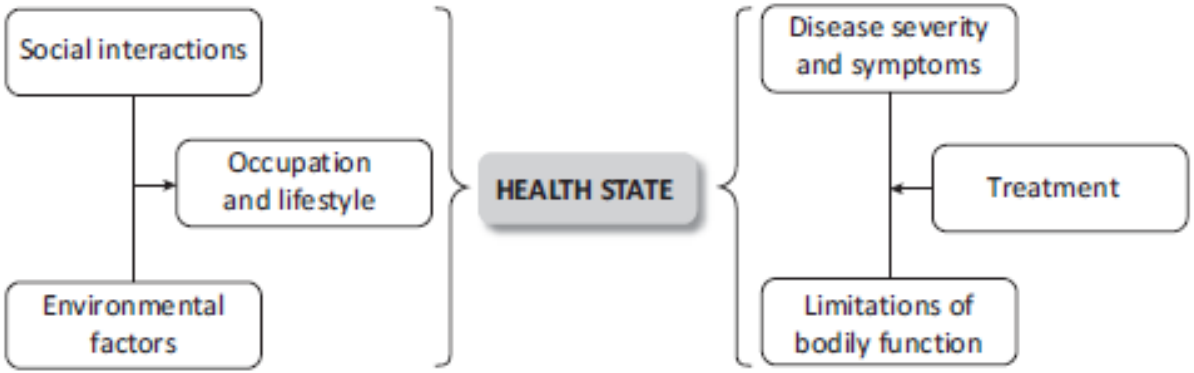
Yet, he had been limiting his physical activity due to joint pain and stiffness flares, which he attributed to artropathy developed in childhood.

After the transplant these flares largely resolved, he signed up to a gym and resumed his physiotherapy exercise program.

While ABR with standard and new therapies approach zero, we may be missing the full picture of impact of therapy on QoL.

Sensitive outcome measure tools are needed to capture and quantify elusive benefits.

There is a growing trend toward individualisation of therapy.



Recht et al. Haemophilia. 22, 825-832, 2016

Goal attainment scaling (GAS) may overcome limitations of classical PROs and clinical outcome measures.

While not yet validated, it was shown to offer a good overall responsiveness, a key advantage in quantifying small, idiosyncratic benefits.

Gaasterland et al. BMC Med Res Method. 16, 2016

GAS may also take into account individual differences in lifestyles, careers and physical activity.

Table 2. Selected goal areas in haemophilia.

General category	Goal area
Managing haemophilia	Being able to administer factor
	Weight, exercise and nutrition
Haemophilia complications	Joint problems
	Pain
Impact of haemophilia on life	Work attendance
	Self-esteem
	Attending school
	Relationships with friends
	Relationships with family
	Narcotic use
	Career planning
	Leisure activities

Recht et al. Haemophilia. 22, 825-832, 2016

For a teenager, a set of goals may include adherence to exercise program and treatment regimen, school attendance, ability to participate in leisure activities

For an active adult, a set of goals may include work attendance and commitment, relationships with friends and family (e.g. ability to play with a child), use of painkillers, weight control, ability to perform specific physical tasks e.g. resistance and aerobic exercises, ascending and descending stairs

Physically active and sedentary individuals will have different goals and needs.

Thank you