

# Exploring haemophilia prophylaxis

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One of the most memorable sessions at WFH 2024 World Congress focused on the optimal dosage of prophylaxis treatment for individuals with haemophilia, highlighting the importance of this treatment in preventing bleeding episodes and joint damage. Discussions included varying dosages and frequency of prophylaxis, emphasizing the need for tailored approaches based on individual needs.

## **How much prophylaxis is enough?**

**Chairs** ~ *Manuela Carvalho, Portugal;*  
*Emna Guider, Tunisia*

**Adequacy of prophylaxis - What should be the target?** ~ *Jan Blatny, Czech Republic*

**The role of prophylaxis in personalized medicine**  
~ *Manuel Carcao, Canada*

**Low-dose emicizumab** ~ *Veena Selvaratnam, Malaysia*

In the session, the speakers mentioned that prophylaxis treatment dosages for individuals with haemophilia vary across different countries, with more economically developed countries often offering higher doses and more frequent treatments due to better access to resources and healthcare infrastructure. In contrast, lower-income countries may struggle to provide adequate dosages, resulting in less effective management of haemophilia and increased risk of complications. This disparity underscores the importance of addressing healthcare inequities to ensure all individuals have access to optimal prophylaxis treatments regardless of their economic situation.

Dr Jan Blatny, a consultant haematologist from Czech Republic, summarised the history of the goal and focus of haemophilia treatment to the present day.

The initial haemophilia treatment goal was to respond to acute bleeds, often with episodic treatment. Then prophylaxis with a target of a factor level greater than 1% was introduced

to reduce bleeding for patients with a severe phenotype, and later an increased target of a factor level above 3-5% was introduced to prevent bleeds and preserve joint health. He saw the evolution of treatments as moving from reducing bleeds towards eliminating bleeds.

I see this evolution of haemophilia treatment as being correlated to prevention as the core of health care. This is a crucial component of promoting overall well-being and reducing the burden of disease. It involves strategies aimed at preventing the occurrence or progression of illnesses through actions such as screenings, healthy lifestyle behaviours, and early interventions. By focusing on prevention, healthcare systems can help individuals maintain good health, reduce healthcare costs, and improve the quality of life for populations. Emphasizing prevention can lead to long-term benefits for both individuals and society.

In the WFH 2023 Comprehensive Care Summit, Dr Maria Elisa Mancuso, a haematologist from Italy, suggested - based on her research findings - that prophylaxis treatment should maintain a high factor VIII (8) trough level at 40% or above to achieve zero bleeds and that prophylaxis treatment should also be available for mild haemophilia patients. However, more intravenous infusions would be required to achieve high dose prophylaxis, which would also mean higher cost.

Dr Blatny questioned how much prophylaxis is enough, and are we able to achieve zero bleeds?

He presented his concept of the balancing act, showing that health care providers need to maintain a balance between the burden of bleeds and the burden of treatment on quality of life. He proposed a concept shift in treatment to hopefully achieve zero bleeds and better quality of life by offering treatment sustaining a high factor level, looking to further advances in non-factor therapy, rebalancing agents and gene therapy. >

## The balancing act

- Bleeds
- Fear of bleeds
- Reduced HRQoL



- Time taken for treatment
- Treatment-imposed lifestyle restrictions

New therapies altering the balance



HRQoL, Health-related quality of life

Dr Manuel Carcao, a paediatric haematologist and Clinician Investigator from Canada, supported the idea of commencing prophylaxis treatment as early as possible to preserve joint health and to minimise bleeds. However, how should we achieve that with minimal treatment burden in order to have a better quality of life?

Before the year 2000, the practice was to put patients on 'one size fits all' regimens, with prophylaxis doses varying across different countries, depending on their economic status.

## Pre-2000: "One size fits all" regimens

### CFC Prophylaxis Regimens

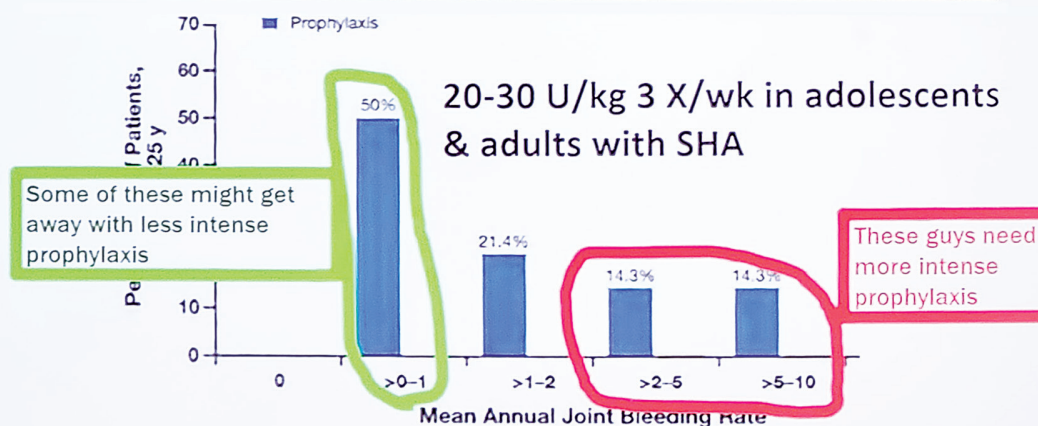
Low dose	Intermediate dose	High dose
10 U/kg 1-2/wk	20-30 U/kg 2X/wk	25-40 U/kg q2days

*"We tend to put our patients on ..."*

- Sweden – High dose
- Italy – intermediate dose
- Tunisia – Low dose
- Most of the world – None; On demand



## Some pts on same prophylaxis regimen do well & some not so well



*Thromb Haemost*. 2015 Jul;114(1):35-45. doi: 10.1160/TH14-05-0407. Epub 2015 Apr 9.

Benefits of prophylaxis versus on-demand treatment in adolescents and adults with severe haemophilia A: the POTTER study.

Tagliaferri A<sup>1</sup>, Feola G, Molinari AC, Sartorio C, Rivolta GF, Cutrera DB, Gagliardi F, Zanoni E, Mancuso ME, Valdrè L, Mamelli L, Amoresano S, Mathew P, Coppola A. POTTER Study Group.

Dr Carcao pointed out this regimen did not always work as well due to the individual patients' factor levels, genetic and mutation types, plus the status of their joint health and levels of activity. He presented a study by Feola G, et al. 2015, *Benefits of prophylaxis versus on-demand treatment in adolescents and adults with severe haemophilia A: the POTTER study* which showed that patients had different bleeding rates and responses even when on same prophylaxis regimen. As a result, personalised prophylaxis treatment is now seen as the key to achieve patient centred care. That is reflected in our clinic, where treatment options and regimens are discussed in the yearly review with the specialist due to lifestyle variations, social economic status changes and bleeding episodes since the last clinic review.

Dr Carcao suggested that prophylaxis treatment should be started as early as possible to achieve joint health preservation and minimise bleeds.

However, he noted that prophylaxis treatment in haemophilia is expensive and around 80% of the world has very little or zero access to the products. Consequently, although low dose prophylaxis

tailored to individual needs and affordability are not enough, they are much better than no prophylaxis. This approach still allows patients with haemophilia to reduce bleeding and slow the deterioration of joint health, leading to better lives.

Non-factor treatment is an option for personalised prophylaxis treatment, but raises questions such as the risk of thrombosis, cost and how individuals will handle the variety of medications when experiencing a bleed. Is low dose non-factor treatment an option for low to middle income countries?

Dr Veena Selvaratnam, a haematologist from Malaysia, presented the results on her low dose emicizumab studies, showing that low dose emicizumab resulted in zero bleeds in 9 out of 10 patients over 37- 293 weeks, and their QoL (quality of life) score improved significantly. Some other countries also showed positive outcomes with low dose emicizumab. Finland set a low maintenance dose and had zero bleeds in 10 out of 11 patients during 8-80 weeks. India also had zero bleeds in 8 patients who participated in low maintenance dose emicizumab, with an average trough factor level of 12.9% after 7 days.

