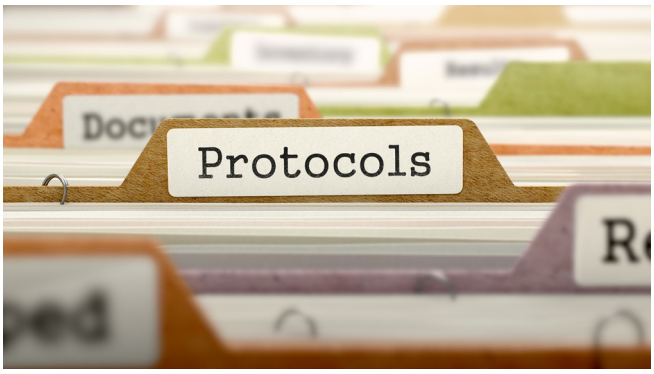
sciendo

CLINICAL PRACTICE

Do nurses have the switch factor?

Greta Mulders, Nanda Uitslager, Sharon Alavian, Anne Wareing, Kathi Stein Oldenburg; on behalf of the Haemnet Horizons Research Group

Introduction: Switching between clotting factor products is becoming increasingly common as product choice increases and financial pressure grows to choose the most cost-effective options. Guidance on carrying out the switch recommends a complex and long process that may benefit from being defined in a protocol. Haemophilia nurses may be responsible for managing product switches; anecdotal evidence suggests that clinical practice is variable. **Aim:** To explore the role of specialist nurses in switching between clotting factor products and their use of a protocol. **Method:** Nurses attending the 2018 World Federation of Hemophilia Congress were surveyed about clinical practice at their treatment centre and use of a protocol for switching clotting factor products. **Results:** Of 192 nurses attending the conference, 49 nurses returned completed questionnaires, 45 of which were included in the study after exclusions. Responses were exclusively from economically developed countries. Almost all respondents (96%) had direct experience of switching. Half of those who responded to a question about protocol-based switching reported that switches were based on a protocol. When authorship was reported, the protocol was written by haemophilia nurses in about half of cases. Practice about blood testing to determine individual pharmacokinetic parameters prior to the switch was variable, but most nurses (86%) reported screening for inhibitors prior to switching. Respondents agreed to share their protocols among their peers, although only four were received by the research team. **Conclusions:** Clinical practice in switching between clotting factor products is variable. Some nurses are switching treatments for patients without the supported of a written protocol, whereas others are involved in writing and implementing protocols. Sharing protocols is a first step in helping to establish best practice.



© Shutterstock

An international survey of haemophilia nurses finds that, while opportunities exist to establish protocol-based best practice, their experience of switching patients' treatment products is varied.

GRETA MULDERS
Advanced Nurse Practitioner, Haemophilia Treatment Center, Erasmus University Medical Centre, Rotterdam, The Netherlands. Email: g.mulders@erasmusmc.nl

NANDA UITSLAGER
Advanced Nurse Practitioner, Van Creveldkliniek, University Medical Center Utrecht, Utrecht, The Netherlands

SHARON ALAVIAN
Former Clinical Nurse Specialist, Hammersmith Hospital Haemophilia Centre, Imperial Healthcare NHS Trust, London, UK

ANNE WAREING
Clinical Nurse Specialist, Department of Haemostasis, St George's University Hospital NHS Foundation Trust, London, UK

KATHI STEIN OLDENBURG
Department of Paediatrics, Division of Oncology and Haematology, Charité Universitätsmedizin Berlin, Germany

Keywords: *nurse experience, switching treatment, haemophilia*

Haemophilia, a disorder of coagulation attributed to reduced levels of Factor VIII (haemophilia A) or Factor IX (haemophilia B) is treated by replacement of the missing factor in affected people either after a bleed (on-demand) or as prophylaxis to minimise bleeding events. The discovery of 'antihaemophilic globulin' in the twentieth century enabled the development of plasma-derived and later recombinant factor concentrates, facilitating home treatment, prophylaxis and self-infusion [1]. More recently, there have been significant changes in haemophilia management as new molecules have been developed, giving clinicians more choice in which treatments to use [2]. This growth in the choice of treatment products means that switching patients from one treatment product to another has become an increasingly important task for haemophilia nurses all over the world. As new treatments continue to be developed, so too the need to switch patients' treatment products will continue. However, it is likely that the process will become more complex as a result of the differences between, for example, standard and extended half-life factor products, as well as various non-factor treatments.

Many countries around the world have national or regional tenders for factor concentrates, which are encouraged to ensure adequate supply and effective pricing [3]. Tendering is a formal procedure to purchase medications using competitive bidding, and although useful for cost containment, can lead to decreased competition in a given market and drug shortages can occur. In all cases, this can result in changes to treatment.

The literature on switching clotting factor products in people with haemophilia recommends that patients should be informed about their choices and the possible benefits and risks of switching; their management should be reviewed; the presence of inhibitors should be excluded; and patients should be followed up periodically after switching to assess individual pharmacokinetics [4-7]. However, the complexity and duration of the switching process suggests that a protocol would be a useful tool to ensure that patients' needs are met.

Haemnet Horizons is a nursing research group within Haemnet (*www.haemnet.com*) that fosters and develops research by haemophilia nurses across Europe. The group discussed procedures for switching clotting factor products in their own centres and noted variable practice and a lack of information about the role of haemophilia nurses in switching. This experience

Pictured: Visual minutes by WovenInk from the Haemnet Horizons Meeting, London, 2018. The study reported here evolved from the recognition that, while good protocols are available in some HTCs, switching patients to another factor treatment product can be a complex process and there is a need for haemophilia nurses to support each other.

has been further highlighted in a recent study of haemophilia nurses in the UK following the introduction of a new treatment product and the withdrawal of others after a tendering process [8].

Nurses, working as part of the wider multidisciplinary team, play a critical role in providing continuous high-quality care and excellent outcomes for patients. Informal conversations among the research group and with other specialist nurses suggest that activities related to switching patients' treatment products require a significant amount of their time, and that nurses may not have sufficient time to fulfil responsibilities additional to the switching procedure when this is required.

The current study sought to explore nurses' role in treatment switching procedures, including whether or not protocols are used to guide the switching process, among a cross section of haemophilia nurses from different countries

METHOD

A non-validated questionnaire was devised by nurses attending the Haemnet Horizons meeting in London, UK, on 21 April 2018. The questionnaire comprised ten questions requiring short answers about how the process of switching treatment products was carried out, including the nurse's role in decision-making,

Table 1. Summary of questionnaire responses

QUESTION	NUMBER OF RESPONSES (TOTAL=45)			
Number of unique nurse responses (from individual centres)	45	UK USA Netherlands Canada New Zealand Ireland Sweden Australia, Croatia, Denmark, Finland, Germany, Romania, Switzerland	10 9 6 5 4 2 2 1 each	
			NUMBER OF RESPONSES	% OF RESPONSES
Ever switched clotting factor product?	45	Yes No	43 2	95% 5%
Reason(s) for switch (more than one answer possible)	33*	Clinical need Funder/purchaser changed product Patient request/preference	34 30 21	
Was switch protocol-based?	40*	Yes No	20 20	50% 50%
If so, who wrote the protocol?	24*	Haemophilia team Nurse/nurse specialist Doctors	15 4 5	62.5% 16.5% 21%
Frequency of blood tests for pharmacokinetics before switch	26*	Don't know No prior testing Blood testing at least once Depends on product	1 6 18 1	4% 23% 69% 4%
Frequency of blood tests for pharmacokinetics after switch**	25*	None Depends on product Depends on clinical need No/inappropriate response	4 4 1 16	16% 16% 4% 64%
Screen for inhibitors before switch?	43*	Yes No	37 6	86% 14%
Was patient association involved?	43*	Yes No Not sure	11 27 5	26% 63% 11%

* Missing data

** Question was interpreted differently by respondents; see text for discussion

informing/supporting patients, and the clinical process of switching and follow-up (see Appendix).

The questionnaire was distributed by a member of the Haemnet research team and the authors at the end of pre-congress nurses' day at the World Federation of Hemophilia (WFH) Congress in Glasgow, Scotland, on 19 May 2018 and after sessions in the nursing track during the congress itself, from 20–24 May 2018. Nurses who agreed to complete the questionnaire either did so and returned it straight away, or returned their completed questionnaire to the research team via the 'treatment room' set up for the duration of the congress. In addition to completing the questionnaire, nurses provided basic information including hospital/HTC names, and had the option to submit any local switching protocols to the authors via email, if these were available and able to be shared.

The completed questionnaire data was entered into an excel spreadsheet and analysed for basic demographics (country, HTC, experience of switching), common themes and concepts.

Of 91 nurses registered at the WFH Congress who were approached, 49 filled in and returned questionnaires. Four questionnaires (were excluded from the analysis: these included questionnaires completed by nurses from same HTC and containing the same information, and questionnaires where the responses were not legible. The remaining 45 questionnaires were unique returns. All respondents were from economically developed countries. The majority (27; 60%) were from Europe (Croatia, Denmark, Finland, Germany, Romania, Switzerland, the Netherlands, Ireland, Sweden, UK), and the remainder from Australia (1), Canada (5), New Zealand (4) and the US (9). The results are summarised in Table 1.

All respondents had been actively involved in the switching process in their respective countries, and most (43; 95.5%) had personal experience of switching individual patients' clotting factor treatment. Thirty-three respondents provided reasons for switching, with the most common – reported by all – being clinical need. This was followed by national contracts or tender agreements (30; 91%), and patient request/choice (21; 64%).

Twenty respondents (50%) stated that their centre had a protocol to guide switching. Where a local protocol existed, the majority were co-written by the haemophilia clinical team and the remainder equally either by the haemophilia nurse or the medical team.

Twenty-six (58%) respondents provided information about blood testing for pharmacokinetics before switching, of whom most reported that at least one measurement was carried out. Around one quarter stated that testing was not performed. Forty-three respondents provided information about screening for inhibitors pre-switch, of whom six (14%) reported that inhibitor screening was not undertaken. Approaches to inhibitor testing after the switch were mostly unclear, although some stated this would depend on the product being switched from and to, as well as individual clinical need.

Twelve respondents stated they would share their local protocol/standard operating procedure with the Haemnet Horizons team, of whom six subsequently did (UK 2, Netherlands 2, Sweden 1, US 1). Of these, one was a practical guide to switching based on a tender; three dealt with switching from standard to extended half-life (EHL) products only; and two covered switching from plasma-derived factor to a recombinant product. One protocol provided comprehensive information in a step-by-step guide, detailing what to do when, and who should undertake various aspects of the switching process. Two protocols included patient questionnaires for nurses to assess their patients' perspective on the procedure. Of the 43 respondents who provided information about the involvement of patient organisations, about one quarter stated that patient organisations were involved in the switching process in some way. One respondent stated that the patients' association involvement was via a newsletter which explained to patients why their clotting factor product was being switched.

DISCUSSION

This study demonstrates remarkably similar experiences among 45 haemophilia nurses from different countries who have participated in switching patients from one haemophilia treatment product to another, most often due to clinical need, but also due to changes in funding/purchasing agreements and to facilitate patient choice. Patient choice was reported by nearly two thirds of those who gave reasons for switching products, although patients' ability to choose their treatment may sometimes be impacted by other factors – for example, in countries with national tendering programmes that can demand frequent product switches at national (rather than individual patient) level [8]. Tendering programmes were initially undertaken with significant patient counselling, consenting and testing; however, more recently clinicians have been less concerned about inhibitor development and are therefore more relaxed about the process [9].

From our results, half of the respondents suggested that they had a centre-based protocol that was followed when switching products; however, very few protocols were made available for review. Importantly, half of respondents reported that they did not have a centre-based protocol for the switching process. The protocols that were provided were similar in that they recognised switching where there was choice (e.g. a new product to the market which enhanced patient care including choice) and those where there was no choice (such as a product no longer being commercially available), identification of which patients could switch and how the switch would take place (routine follow-up or more urgently), and the necessary follow-up to ensure safe and effective care. Key elements that should form the basis of any switching protocol include:

- Providing information to the patient about the switch and receiving patient consent
- Undertaking blood testing and assessing quality of life and joint health prior to the switch
- Ensuring that the patient is supervised when administering the new product for the first time
- Undertaking blood testing and assessing quality of life and joint health post-switch.

There appeared to be no consensus on the testing for pharmacokinetics and/or inhibitor screening post-switching products. It is also unclear whether the inhibitor testing was part of routine practice or specifically associated with the switch. Twenty participants either did not answer this question or stated that no testing was done. This may be due to less clinician anxiety about inhibitor development post switching due to previous experience [8-10]. The recent WFH treatment guidelines suggest that there is no increased risk of inhibitor development following product switch, therefore inhibitor screening may be of a more academic than clinical interest [11].

During the most recent large-scale switching of factor products in the UK, prompted by a national tender (2018), template letters were used to inform people with haemophilia about the upcoming tender/switch and was reported as "enabling an easier process by nurses" [8].These were developed following a meeting of experienced haemophilia nurse specialists and shared with nurses at HTCs around the UK. In a study of views of people with haemophilia and/or their caregivers about product switching, most reported that switching discussions happened with doctors and with their haemophilia multidisciplinary team [12]. Despite these discussions, however, most reported feeling that they had little influence on the decision to switch product.

Increasingly patients' views should be included in shared decision-making around individual treatment choices [13], not least because their views and expectations may differ significantly from healthcare professionals [14-16]. Patients' views bring added value to policymaking around tendering/switching experiences when expressed collectively through non-governmental organisations such as national or regional patient organisations [17]. Respondents in the current study reported that patient associations were generally not involved in the switching process, but as advocates they perhaps have a greater role to play in ensuring that the patient voice is heard. Nurses also play a role in advocating for patients during the switching process, representing their views, the practicalities (dose/vial/infusion volumes, packaging, storage, etc.) and ensuring appropriate follow-up occurs.

Limitations

Although the questionnaire was intended to capture data in a simple way, the responses we received raised further questions, many of which remain unanswered. The sharing of local protocols around switching may have helped to answer some of these questions, as well as helping to establish variations in the practice of switching in different countries; however, very few protocols were received by the research team. The combination of these factors is therefore a limitation of this research project.

The questions around pharmacokinetic sampling were interpreted differently by different respondents, indicating that they were perhaps not clear enough. This meant that it was not possible to consider variance in pharmacokinetic assessment at switch, and how this might relate to a general variance in practice across different countries.

CONCLUSION

As new and different products for the treatment of haemophilia become available, the need to guide patients through the switching process – whether as a results of clinical need, choice, or national tender – will continue to be a significant part of their care in which specialist haemophilia nurses play a key role. Almost all nurses who responded to this survey had direct experience of switching clotting factor products, but clinical practice in switching was variable and nurses reported different indications for switching, often driven by a tender process rather than by clinical need. Many nurses are switching treatments for patients without the support of a written protocol, whereas others are involved in writing and implementing protocols. Sharing protocols is a first step in helping to establish best practice and could be used, in the future, as a service evaluation or benchmark of centre/local/national or international care delivery and outcomes.

ACKNOWLEDGEMENTS

We thank all the nurses who contributed to the data by completing the questionnaire. Haemnet received an unrestricted educational grant from Sobi and CSL Behring to undertake the Horizons meetings.

All authors developed the questionnaire and analysed data. GM, NU and SA wrote the first draft of the paper; all authors agreed the final version.

The authors have advised no interests that might be perceived as posing a conflict or bias.

This paper reports on a survey of health care professionals and did not require research board approval. The paper reports on a survey to which participants responded knowing that any comments may be reported.

ORCID

Greta Mulders https://orcid.org/0000-0003-2278-3459
Nanda Uitslager https://orcid.org/0000-0001-8102-1118
Kathi Stein Oldenburg https://orcid.org/0000-0001-9056-0316

REFERENCES

1. Franchini M, Mannucci PM. The history of hemophilia. *Semin Thromb Hemost* 2014; 40(5): 571-76. doi: 10.1055/s-0034-1381232.
2. Mannucci PM. Miracle of haemophilia drugs: personal views about a few main players. *Haemophilia* 2018; 24(4): 557-62. doi: 10.1111/hae.13519.
3. Giangrande PLF, Peyvandi F, O'Mahony B, et al. Kreuth IV: European consensus proposals for treatment of haemophilia with coagulation factor concentrates. *Haemophilia* 2017; 23(3): 370-75. doi: 10.1111/hae.13211.
4. Collins PW, Chalmers E, Hart DP, et al. Diagnosis and treatment of factor VIII and IX inhibitors in congenital haemophilia: (4th edition). UK Haemophilia Centre Doctors Organization. *Br J Haematol* 2013; 160(2): 153-70. doi: 10.1111/bjh.12091.
5. Carcao M. Switching from current factor VIII (FVIII) to longer acting FVIII concentrates – what is the real potential benefit? *Haemophilia* 2015; 21(3): 297-9. doi: 10.1111/hae.12671.
6. Croteau SE, Neufeld EJ. Transition considerations for extended half-life factor products. *Haemophilia* 2015; 21(3): 285-8. doi: 10.1111/hae.12683.
7. Collins P, Chalmers E, Chowdary P, et al. The use of enhanced half-life coagulation factor concentrates in routine clinical practice: guidance from UKHCDO. *Haemophilia* 2016; 22(4): 487-98. doi: 10.1111/hae.13013.
8. Pollard D, Khair K, Holland M. Switching factor products: nurses' experience with NovoEight. *J Haem Pract* 2020; 7(1): 59-69. doi: 10.17225/jhp00156.
9. Santagostino E, Auerswald G, Benson G, et al. Switching treatments in haemophilia: is there a risk of inhibitor development? *Eur J Haematol* 2015; 94(4): 284-89. doi: 10.1111/ejh.12433.
10. Hay CR, Palmer BP, Chalmers EA, et al. The incidence of factor VIII inhibitors in severe haemophilia A following a major switch from full-length to B-domain-deleted factor VIII: a prospective cohort comparison. *Haemophilia* 2015; 21(2): 219-26. doi: 10.1111/hae.12563.
11. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia* 2020 Aug 3. doi: 10.1111/hae.14046. Epub ahead of print.
12. Pollard D, Khair K, Holland M. Experience of switching to NovoEight: views of people with haemophilia. *J Haem Pract* 2020; 7(1): 70-77. doi: 10.17225/jhp00157.
13. Shay LA, Lafata JE. Where is the evidence? A systematic review of shared decision making and patient outcomes. *Med Decis Making* 2015; 35(1): 114-31. doi: 10.1177/0272989x14551638.
14. Mantovani LG, Monzini MS, Mannucci PM, et al; Conan Study Group. Differences between patients', physicians' and pharmacists' preferences for treatment products in haemophilia: a discrete choice experiment. *Haemophilia* 2005; 11(6): 589-97. doi: 10.1111/j.1365-2516.2005.01159.x.
15. von Mackensen S, Kalnins W, Krucker J, et al. Haemophilia patients' unmet needs and their expectations of the new extended half-life factor concentrates. *Haemophilia* 2017; 23(4): 566-74. doi: 10.1111/hae.13221.
16. Khair K, Pollard D, Harrison C, Hook S, O'Driscoll M, Holland M. HOw Patients view Extended half-life products: impressions from real-world experience (The HOPE study). *Haemophilia* 2019; 25(5): 814-20. doi: 10.1111/hae.13803.
17. Smit C. Personal reflections of a patient representative in an appraisal committee. *Patient* 2015; 8(1): 5-10. doi: 10.1007/s40271-014-0086-8.

HOW TO CITE THIS ARTICLE:
Mulders G, Uitslager N, Alavian N, Wareing A, Stein Oldenburg K; Haemnet Horizons Research Group. Do nurses have the switch factor? *J Haem Pract 2020*; 7(1): 129-135. *https://doi.org/10.17225/jhp00162*

APPENDIX A

Questionnaire used to seek responses on product switching

1. Would you please tell us your name and country where you come from?
   - ◯ Name:
   - ◯ Country:

2. Did you ever switch patients to another factor product?
   - ◯ Yes
   - ◯ No

3. What was the reason for this switch?
   - ◯ Patient request/preference
   - ◯ The providers/buyers of haemophilia treatment bought a different clotting factor
   - ◯ Clinical need
   - ◯ Other: _____

4. Is this switch based on a protocol?
   - ◯ Yes
   - ◯ No

5. Who is this protocol written by?
   - ◯ A nurse/nurse specialist
   - ◯ The haemophilia team
   - ◯ The doctor

6. Would you share this protocol/SOP with us?
   - ◯ Yes, I will upload it on www.haemnet.uk
   - ◯ No, I am not allowed
   - ◯ No, it is too much work, I have no time

7. How frequently are blood tests performed for pharmacokinetic testing BEFORE switching? (Please provide time intervals if possible)

8. How frequently are blood tests performed for pharmacokinetic and/or inhibitor testing AFTER switching? (Please provide time intervals if possible)

9. Do you obtain an inhibitor screen prior to switching?
   - ◯ Yes
   - ◯ No

10. Was the haemophilia patient association involved during the switch to another clotting factor product?
    - ◯ Yes
    - ◯ No

J Haem Pract 2020; 7(1). doi: 10.17225/jhp00162