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Monitoring to improve quality of life in women with bleeding disorders

Declan Noone, Roseline d'Oiron

Systematic structures to understand the incidence and prevalence of bleeding disorders in women and girls are in place in some countries and becoming more robust, though there is still room for improvement. More co-ordinated data gathering is providing new insights into the diagnosis and treatment of girls with bleeding disorders and demonstrating clear deficits in care compared with boys that can have important implications around puberty. Recognition and recording of female symptoms such as heavy menstrual bleeding (HMB) may lag behind that of symptoms with a greater perception bias, such as joint bleeds, and affect quality of life and wellbeing. Addressing inequity of symptom recognition and recording is needed to drive appropriate and timely treatment interventions. New symptom tools can empower patients to differentiate normal from abnormal bleeding so they can seek and receive help. Greater awareness among health care professionals (HCPs) of women's bleeding disorders and the establishment of referral networks for diagnosis and treatment, with multidisciplinary assessment and follow-up, are still needed.

Keywords: *Women with bleeding disorders, Data collection, Registries, Prevalence, Delayed diagnosis, Inequity of care*

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REPORTS FROM THE SECOND EUROPEAN CONFERENCE ON WOMEN AND BLEEDING DISORDERS

WHERE ARE THE WOMEN AND GIRLS WITH BLEEDING DISORDERS?

The inclusion of women and girls with bleeding disorders in national and other databases is improving, but recent experience suggests there is still some way to go. Gender reporting from centres participating in the World Federation of Hemophilia Global Survey in 2019 was significantly improved [1] compared to the 2009 Survey [2] (Figure 1). Women with factor VIII (FVIII) and factor IX (FIX) levels less than 40IU/ml are starting to be identified in databases as more than carriers, and other rare bleeding disorders are being recorded more systematically. Having a population of mild haemophilia that is approximately 50% female is an indicator of a mature and robust registry. Unfortunately, we still have a long way to go in many countries for this to become a reality, as this is still rarely the case.

New and expanding registries are including gender review early, though there may still be unintended exclusions, e.g. failure to provide the option to record pelvic bleeding, inability to provide information on bruising or untreated bleeding symptoms in patient reporting apps, or inability to add period tracking data to health records. Recoding exercises are needed for older registries to ensure gender review is included.

The EHC's Women and Bleeding Disorders Survey 2017 [3] also shows that progress is being made, with

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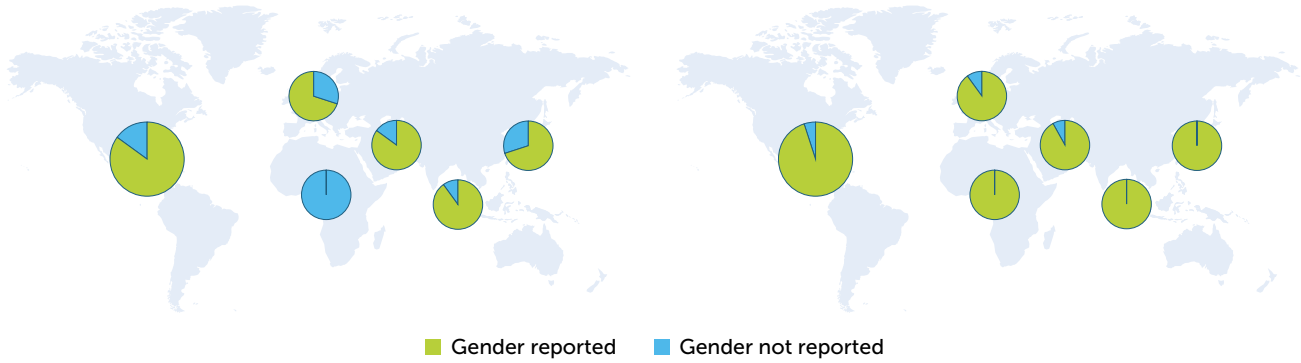
Figure 1. WFH Annual Global Survey gender reporting, 2009 (left) vs. 2019 (right)



14/27 national member organisations (NMOs) able to provide a full breakdown. However, eight out of 27 were unable to differentiate between haemophilia A/B carriers. There was also wide variation in female membership of NMOs, with a mean of 22% (range 3-51%). These suggest the need to update and improve patient organisation registries.

Diagnostic delays in women and girls

As a result of what should be historical rhetoric (i.e. women/girls do not bleed), women and girls are typically diagnosed with bleeding disorders at a later age than men and boys. There is therefore a considerable need to raise awareness among health care professionals (HCPs) in both treatment centres and other disciplines, and among the general public. Results of a retrospective US study showed that, although female patients with haemophilia A and B had their first bleed at a similar age to male patients, those with severe disease were diagnosed a median 6.5 months after their male contemporaries and those with moderate disease a median 39 months afterwards [4]. A similar trend is reported in the FranceCoag database; boys were diagnosed with mild haemophilia at just under 11 years old, compared to girls at nearly 17 years [5]. This six-year delay has important implications as it means that girls would not have been diagnosed before menarche and would therefore have been unable to anticipate and prepare for the effects their haemophilia may have on their periods.

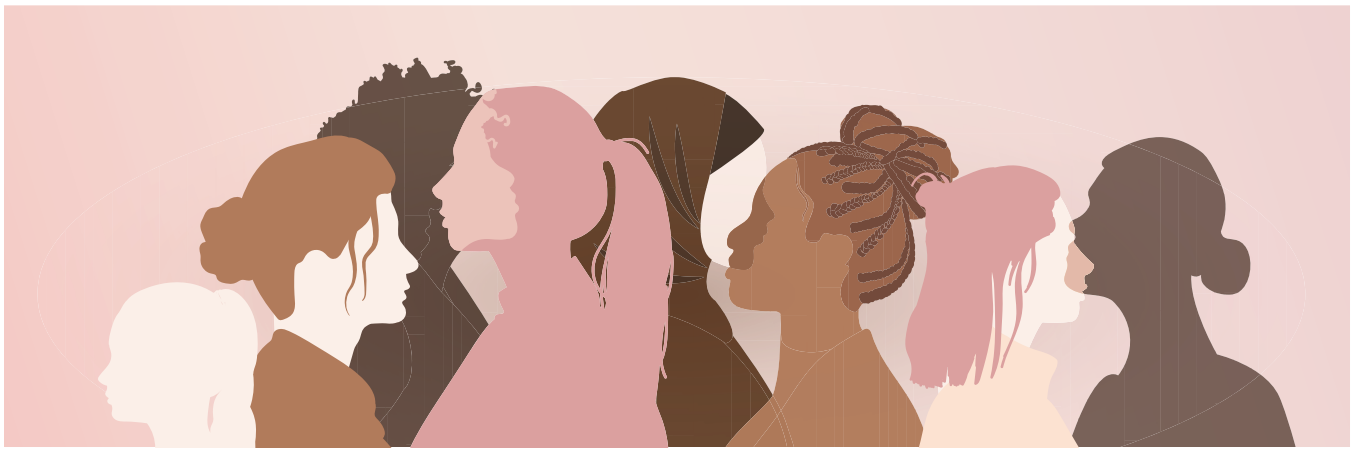
Towards better symptom recording

Recognition and recording of female symptoms such as heavy menstrual bleeding (HMB) lag significantly behind that of symptoms perceived as being more common or having greater impact, such as joint bleeds. The impact on quality of life (QoL) of someone experiencing a joint bleed is easily measurable through clinical records of reporting, physical attendance at a clinic or emergency room and/or clotting factor concentrates or other treatment through pharmacies. Women who experience HMB or other QoL-impairing symptoms (e.g. nose and mouth bleeds and bruising) may be less likely to seek help below a certain threshold, resulting in more frequent day-to-day management of their symptoms and the related reduction in QoL going mostly unrecorded. Consequently, female and/or 'minor' bleeds may not be taken seriously [6]. Barriers to care for women with bleeding disorders (WBD) include lack of healthcare provider awareness of inherited bleeding disorders, healthcare provider dismissal of symptoms, limited access to specialised care and treatment plans, and a need for self-education and advocacy [6].

The cumulative effects of HMB and all other symptoms affecting QoL of WBD need to be better captured (e.g. by recording frequency, severity, duration), and this requires education and awareness-raising. With the growing use of telemedicine and AI-driven care algorithms, it is particularly important to address inequity of symptom recognition and recording so that these can drive appropriate treatment interventions [7].

Moving beyond registry inclusion

There are four main sources of data: national registries, external public data/reports, combined bleeding disorder and general health registries, and enhanced registries with direct patient reporting input. National registries are adequate for recording diagnosis but provide limited information on treatment use and have limited connections to care providers, such as general practice, maternity and fertility services. External registries give non-bleeding disorder 'controls' and comparative information about the broader impact of bleeding disorders on care. The Period Poverty in Ireland report [8], for example, provides 'baseline' pad/towel use



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and costs against which the needs of women with bleeding disorders can be compared, and a large commercial database has been used to compare bone health in haemophilia carriers and those with von Willebrand disease with the general population [9]. However, it can be difficult to link bleeding disorders to specific concepts and there is a need to search for indicator variables. Combining registries also provides non-bleeding disorder 'controls' and comparative information about the broader impact of bleeding disorders on care, and offers easier links to the bleeding disorder community. It is possible to interrogate data quite precisely, but data on bleeding symptoms remain limited. Enhanced registries draw on data from patient-reported information via apps (e.g. the Canadian Haemophilia Society app, MyCBDR [10]) to provide individuals with indicators about how their experiences compare with others with bleeding disorders. Algorithms can then be created to identify 'red flags' and inform treatment centre staff, thereby improving the efficiency of delivering care for the clinic and payers, and creating awareness for individual levels on how to improve their care going forward at the same time.

Although progress is still needed to optimise data presentation and access for people with bleeding disorders and HCPs, opportunities for connectivity are greater than ever before. This means that organisations can piggy-back on the work of others to build evidence for better understanding of the burden of bleeding disorders for women and how best to address them.

WHAT DO WE DO WHEN WE LOSE CONTACT WITH WOMEN AND GIRLS WITH BLEEDING DISORDERS?

It is not enough to include women and girls with bleeding disorders in databases; it is also important to follow them up and consider what actions need to be implemented to ensure they receive appropriate care. Priorities need to be set for data points that it is realistic to collect over many years of follow-up. It may be possible to collect more detailed information on a limited number of WBD during a precise time period, but it is important that these are based on specific objectives for answering scientific questions, following discussions with the local bleeding disorder community.

Information from the FranceCoag database highlights follow-up issues in bleeding disorders affecting women. While only 10.8% of patients people with severe haemophilia A and 13.1% of those with severe haemophilia B did not have a follow-up visit in the previous three years, 37.6% of those with von Willebrand disease, 41.3% of those with mild haemophilia B, 43.1% of those with mild haemophilia A and 44.5% of those with rare factor deficiencies had not been followed up for three years [11]. Although these findings reflect, in part, disease severity, they also mean that data on symptoms and their effects on quality of life are missing for many patients.

Follow-up failure may occur for a number of reasons but previous negative experience of medical care may play a role. This is shown in a study of emotional and behavioural responses in Canadian haemophilia carriers, in which only 21% of respondents expressed positive emotion to previous medical experiences [12].

Patient-centred initiatives at all levels – patient, HCP, and community – are needed to help break down barriers and address inequity of care [6]. From the perspective of WBD, it may be difficult to recognise symptoms and their severity. A woman with a child with severe haemophilia may downplay her own symptoms and not seek the care she needs, or she may have had poor healthcare experiences in the past. New tools (quantitative and qualitative) are needed to facilitate symptom recognition and empower WBD to differentiate normal from abnormal bleeding so they can seek and receive help, together with detailed information about treatment options including

reporting and addressing side effects. From the HCP perspective, greater awareness of the prevalence of bleeding disorders in women and girls and the establishment of referral networks for diagnosis and treatment are needed, together with multidisciplinary assessment and follow-up. Unfortunately, only half of haemophilia treatment centres have multidisciplinary team (MDT) clinics [3].

DISCUSSION

There is a substantial list of data about WBD that could potentially be collected by registries, so it is important to consider the reality of collecting data on multiple variables on a regular basis, and to decide on priorities. If information is being collected from a large population over a long period, it may be realistic only to collect a minimum data set. However, for a smaller population being followed for perhaps two to three years, it may be realistic to collect more extensive information. The key is to agree the objectives of the registry and the scientific questions it aims to answer and to discuss these with the community who will be involved. The development of registries depends on the goodwill and commitment of clinicians and women and girls with bleeding disorders, and there appears to be a greater willingness among both groups to contribute and record information on sensitive subjects such as menstrual bleeding. Guidance to help facilitate these conversations would be helpful both within and beyond the healthcare setting – many fathers still find it difficult to talk with their daughters about menstrual bleeding.

Experience during the Covid pandemic has shown that it is realistic for patients to contribute data through apps (e.g. the ZOE app in the UK). This approach may be especially useful for reporting HMB, which some women may find difficult to talk about. General Data Protection Regulation (GDPR) and medical device issues still need to be addressed but there are more opportunities for collecting and learning from patient-reported information than ever before. For example, through the Lighthouse Projects in Ireland, patients, including people with haemophilia [13], will be able to upload information from wearable devices into registries. The next step is to work out the best way of breaking down this type of raw data and making appropriate use of it, for example, in giving people with bleeding disorders rapid feedback to inform behavioural change.

At the same time, it will be important to address gender imbalance in the perception and interpretation of symptoms reported by people with bleeding disorders through apps, and their impact on quality of life. For example, data from the PROBE study on women and men with non-severe haemophilia and healthy individuals showed that women with mild or moderate haemophilia had more bleeds and needed more pain medication than their male counterparts, but they reported less pain and better quality of life [14]. This implies a greater level of acceptance by women, with the risk that those making decisions about healthcare provision may underestimate problems experienced by some sections of the bleeding disorder community, resulting in inadequate access to multidisciplinary teams and other services. Assessment tools are needed that better differentiate quality of life effects related to equivalent symptoms.

TOP THREE TAKE-AWAYS

- Gender reporting in bleeding disorders registries is improving, but female-specific symptoms are still under-reported
- Gender imbalance in the perception and recognition of bleeding symptoms impacts diagnosis and access to treatment interventions
- New tools for patient-reported data need to take account of symptoms such as HMB and its impact on quality of life

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