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Public health assistance for people with haemophilia in Brazil (PATCH study): a cross-sectional study protocol

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ABSTRACT

Introduction Haemophilia is a rare inherited bleeding disorder with complex support and costly treatment. Comprehensive care for people with haemophilia (PwH) must take place in structured and continuously evaluated treatment centres. The aim of the *Public Assistance for People with Haemophilia in Brazil* Project (PATCH Project) is to assess the infrastructure, human resources and healthcare delivery processes of Brazilian Blood Centres (BC) involved in the provision of haemophilia care.

Methods and analysis This is a nationwide cross-sectional study involving 98 BC across Brazil's 26 states and the Federal District, focusing on the care provided to PwH. A self-administered structured questionnaire was prepared, based on national and international recommendations for management, treatment and outcomes assessment in PwH. The criteria of the World Federation of Haemophilia and the European Association for Haemophilia and Allied Disorders will be used to define standards of quality.

Ethics and dissemination Ethical approval for this study was granted by the Human Research Ethics Committee of the Federal University of Goiás, the coordinating centre (protocol CAAE 53863221.8.0000.5078), and subsequently by all participating institutions. Written informed consent is obtained from all participants prior to enrolment. Study findings will be disseminated through publication in peer-reviewed journals and presentation at international scientific conferences. Research data will be managed in accordance with ethical and legal standards and will be made available on reasonable request to support future investigations.

Protocol registration Not applicable

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The in-depth analysis of the Brazilian Blood Centres will provide unprecedented data on physical infrastructure, human resources and work processes, while underscoring the regional diversity in haemophilia care provision.
⇒ The insights generated by this study may inform public policies aimed at enhancing equity and efficiency within the Brazilian haemophilia care model.
⇒ By encompassing multiple centres across the national territory, this study ensures representation from all Brazilian macro-regions, thereby enabling a robust and comprehensive assessment of the systems and processes underpinning haemophilia management.
⇒ Difficulty in accessing haemophilia treatment centres in remote areas can be a limitation of this project, which may limit the comprehensiveness of understanding the challenges and facilitators of care in these settings.
⇒ As an observational study, the establishment of causal inferences is limited by the potential influence of confounding factors and selection bias.

BACKGROUND

Haemophilia is a rare, X-linked inherited bleeding disorder caused by pathogenic variants in the genes encoding factor VIII (in haemophilia A, HA) and factor IX (in haemophilia B, HB). Both conditions are clinically indistinguishable, with bleeding as the most common manifestation.[1 2] Depending on the severity of the disease, bleeding can begin in childhood, mainly affecting joints and soft tissues, either spontaneously or after trauma.[3 4] Haemarthrosis is the most emblematic manifestation of the disease, as it leads to progressive impairment of physical capacity and negatively impacts the quality of life.[5–8] Bleeds are also related to high mortality.[3]

Data from the World Federation of Haemophilia (WFH) estimates a population of 836 000 people with haemophilia (PwH) worldwide, 67% of whom live in low- and middle-income countries.[9] In Brazil, according to the data published in 2023 by the Ministry of Health (MH), there were 11 618 and 2277 PwH-A and PwH-B, respectively, making the country the third largest haemophilia population in the world.[10] Commonly, 74% of PwH experienced pain or discomfort, 59% mobility challenges, 46% anxiety or depression, 44% difficulties with daily activities and 19% challenges with self-care. PwH

with mobility difficulties, pain or discomfort are less likely to be employed.[11 12]

Currently, the cornerstone of treatment for PwH is intravenous replacement therapy with plasma-derived or recombinant coagulation factor concentrates (CFC), factor VIII (FVIII) for HA and factor IX (FIX) for HB. These concentrates are administered either prophylactically to prevent bleeding episodes or episodically to treat active bleeds.[13–17] However, approximately 20%–30% of severe PwH develop neutralising autoantibodies (inhibitors) against exogenous FVIII, compromising the treatment efficacy.[1] In such cases, immune tolerance induction (ITI) is indicated with bypassing agents until inhibitor eradication.[18] Recently, two non-factor replacement therapies have been approved worldwide as prophylactic alternatives: emicizumab, a bispecific antibody that mimics factor VIII, and concizumab, an antitissue factor pathway inhibitor.[19 20]

The increasing complexity and advances in haemophilia treatment have significant implications for global healthcare systems and services.[21–23] CFC infusions account for 90%–95% of total expenditure in PwH care.[23 24] In the USA, the annual cost per patient receiving CFC replacement therapy is approximately $250 000, while prophylactic treatment is estimated to cost between $407 752 and $551 645.[24 25] ITI may increase these costs by two- to fivefold, exceeding $697 000 annually.[25] Furthermore, disease severity, bleeding frequency and joint involvement further escalate treatment expenses, both direct (CFC replacement requirements) and indirect (social costs and productivity losses).[26 27]

Haemophilia care needs to be held in centres with the capacity to offer comprehensive, integral and safe treatment through preventive, curative, rehabilitative and palliative care carried out by specialist doctors and multidisciplinary teams. The centres may be structured with clinical, laboratory and rehabilitation services, providing quality care focused on the needs of the PwH.[16 28] The final purpose of the haemophilia support might be reducing the number of bleeds and their complications, resulting in improved quality of life and increased life expectancy.[29–31]

According to the WFH and the European Association for Haemophilia and Allied Disorders, comprehensive healthcare for PwH should be based on two types of care centres: Comprehensive Haemophilia Care Centres (CCHC) and Haemophilia Treatment Centres (HTC).[32] The CCHC is expected to provide 24-hour clinical and laboratory services, ensure the availability of safe and effective CFC and other haemostatic agents, in addition to offering comprehensive management of inhibitors, including diagnosis, treatment and ITI.[16 33] They should ensure access to a multidisciplinary care team, genetic testing and counselling, home-based treatment and comprehensive care for coinfections such as HIV and hepatitis C virus.[34] The HTC should cooperate with their CCHC of reference in most of the functions performed by the latter but from a regionalised perspective. Depending on the extent and geographical distribution of the country, smaller treatment centres may be necessary. It is also recommended that countries have a national patient registry, with regular data collection in addition to health education, training and research programmes.[14 16]

In Brazil, haemophilia care is fully funded and delivered at no cost to patients through the public Unified Health System (Sistema Único de Saúde—SUS, in Portuguese).[35] The system is structured around blood centres (BC) located across all states and the Federal District. The national equivalents of CCHCs and HTCs are known as coordinating blood centres (CBC) and regional blood centres (RBC), respectively. Both are integrated into the Brazilian Hemotherapy Network (Hemorrede), which is coordinated by the MH.[36–38]

In a country of continental dimensions and with a wide network of healthcare services, such as Brazil, there are several challenges to guaranteeing the right to health, especially regarding the variability that can occur in the provision of care and treatment, which also includes haemophilia as a rare disease.[37 39 40] Within the hierarchical and regionalised structure of Brazil's support network, there is a lack of detailed information on the infrastructure, human resources and care delivery processes at BC, particularly concerning the care provided to PwH.[41] Thus, the aim of the PATCH Project is therefore to systematically evaluate Brazilian BC profiles in the provision of healthcare for PwH.

METHODS

The PATCH Project is a cross-sectional, nationwide study that will involve all Brazilian BC responsible for caring for PwH. The study was approved by the Human Research Ethics Committee of the Universidade Federal de Goiás (CAAE 53863221.8.0000.5078). Subsequently, approval was obtained from local Human Research Ethics Committees in sequence.

The model of care for people with haemophilia in Brazil

In Brazil, healthcare for PwH is publicly funded, provided at no additional cost and guaranteed by the SUS through a universal, comprehensive and hierarchical care network.[35 42 43] PwH are initially attended in primary care or emergency services and subsequently referred to the nearest BC, where they can undergo diagnostic testing at a reference laboratory and receive multidisciplinary healthcare support.[38 44] The MH establishes recommendations for the comprehensive healthcare support offered at BC, but Brazilian states and the Federal District locally determine the delivery of care. Each Brazilian state and the Federal District have at least one CBC, usually located in the capital, and some have RBC distributed throughout their territory. In rare cases, a state may encompass several CBCs.[36 37] In total, there are 97 BCs in Brazil, of which 34 are CBCs and 64 are RBCs (figure 1 and online supplemental file 1). CBC and RBC constitute a network primarily based on haemotherapy. The number of BC in

Figure 1 Spatial distribution of Brazilian blood centres: coordinating blood centres (red dots); regional blood centres (black dots), Brazil, 2025.

each federal unit is related to the population size and the territorial extension.

This hierarchical network of CBC and RBC organises haemotherapy services and practices nationwide, promoting the integration of public and private health institutions responsible for the collection, storage and distribution of blood and blood products. This network structure was used to implement national support for inherited bleeding disorders, including haemophilia. The CBC provides technical support for the blood and blood products policy and is responsible for diagnosing, treating and monitoring PwH. They also offer educational and research services, technical support and quality control in collaboration with other institutions. The RBCs are macroregional units that can carry out these same roles but on a regionalised basis. [36–38]Individuals diagnosed with an inherited bleeding disorder, including haemophilia, are registered in the online electronic system called Hemovida WebCoagulopatias.[36] This is an online system created by the MH to register patients and document their treatment to obtain information to support federal planning strategies to allocate resources in healthcare promotion, surveillance and distribution of treatment products for people with inherited bleeding disorders.[9 16 45]

Participating centres and local researchers

A multistage method will be used to include all Brazilian BC. Initially, information on the BC classification (CBC or RBC), location and contacts (telephone and email) will be obtained from official websites. All BCs officially registered by the MH providing healthcare support to PwH will be invited by contacting one local researcher at each CBC. The local researcher will be a healthcare professional responsible for haemophilia support. Following formal approval (service coordinators and ethical approvals), the local researcher will fill in a questionnaire to describe each BC infrastructure, human resources and work process. BCs that do not provide support to PwH, only offer urgency/emergency treatment, or only dispense procoagulant products will be excluded. In addition, BC for which data was not provided after a 3-month periodic request will be excluded. The unit of analysis of the PATCH Project will be the BC.

Development of the study questionnaire

A wide-ranging national and international literature review was carried out on best management and comprehensive care practices and proposals about physical structure, human resources and work process for BC providing care for PwH.[6 16 18 33 34 46–50] The construction of the questionnaire prioritised clear and objective questions, with alternatives to be checked or descriptions to be made by the respondent. Alternatives such as 'I don't know', 'I couldn't find the data', and 'not applicable' were inserted to avoid unanswered questions. Once the questionnaire had been drawn up, the objective and content of the questions and the answer options were independently reviewed by the central researchers and discussed in groups until the final format was defined. The full utilised questionnaire is in online supplemental file 2.

Variables

The variables to be studied in the PATCH Project will be related to the physical structure, human resources and work process of the participating BC (table 1). Each participating BC will report the number of PwH under their care, including inhibitor status, and their protocols for registry updates to Hemovida WebCoagulopatias.

The 'infrastructure' dimension will assess the centre's location, accessibility via public transportation, compliance with disability access standards, operational hours, telemedicine capacity and available physical resources. The number of haematologists, paediatricians, orthopaedists, physiatrists, infectologists, rheumatologists, gynaecologists, geriatricians, geneticists, immunologists and radiologists will be identified, as well as the number of nurses, psychologists, dentists, social workers, physical educators, pedagogues, pharmacists, physiotherapists and nutritionists working in the service. The 'healthcare delivery processes' dimension will assess clinical services capabilities: emergency care provisions, inpatient capacity for hospitalisation, access to elective surgical procedures, rehabilitation services and clinical management offered to PwH such as prophylactic treatment, ITI protocols and home treatment programmes will be requested. To comprehensively evaluate care quality, participating BC will report their standardised outcome tools measures including

Table 1 Variables related to the physical structure, human resources and work process of Brazilian blood centres

Topic	Description
Identification of the blood centre	General information regarding the type of the centre and its relationship with formal professional education
Access and accessibility	Public transport and facilities adaptation for people with mobility restrictions
Physical structure and human resources	Number and roles of professionals, number of rooms assigned for each professional and number of appointments
Provided services	Elective and emergency appointments, hospitalisation and surgery
Registration	Number of registered people with haemophilia A and B with and without inhibitor, registration system type, professionals in charge of registration and update frequency
Outcome tools*	Tools to evaluate musculoskeletal health, life activities, psychosocial characteristics and adherence, and bleed
Patient association	Partnership with patient associations and number of meetings
Patient education	Patient and their peers meeting to discuss haemophilia management
Continuing education of professionals	Education and training in haemophilia management for professionals
Treatment	CFC management, prophylaxis, immune tolerance induction, home treatment and inhibitor monitoring
Elderly	Team preparedness to deal with the particularities of elderly care
Women	Team preparedness to deal with the particularities of women care and provision of genetic counselling
Complementary exams	Radiology and laboratory service, and participation in quality programmes
Research	Participation in haemophilia research (local research, including quality of life and other health outcomes or Clinical Trials of Investigational Medicinal Products (CTIMPs)†), publication of articles regarding haemophilia and number of PhD professionals.

*Detailed in table 2.
†Clinical Trials of Investigational Medicinal Products.
CFC, coagulation factor concentrates.

Table 2 Outcomes recommended for evaluation of people with haemophilia

Evaluation field	Indicators
Musculoskeletal health	HJHS*, joint image, chronic joint pain, joint range of motion
Life activities	HAL† /pedHAL‡, FISH§
Psychosocial characteristics and adherence	Quality of life, well-being, absenteeism, product consumption, visits to the emergency room, hospitalisations, infusion diary
Bleed	Site and severity, time-related rate

*HJHS: Hemophilia Joint Health Score; .
†HAL: Hemophilia Activities List; .
‡pedHAL: Pediatric Hemophilia Activities List; .
§FISH: Function Independence Score in Haemophilia.

those related to the assessment of musculoskeletal function, activities of daily living, psychological well-being, treatment adherence patterns and bleeding frequency (table 2). Laboratory services capabilities on diagnostic and monitoring assays, testing for inhibitors, supply chain management practices and quality control will be evaluated. Additional data will include patient and caregiver education programmes and frequency of training provision for healthcare professionals involved in haemophilia care. Finally, the study will document collaborative partnerships with patient advocacy organisations and collect data on centre-specific research activities to provide a complete assessment of both educational outcomes and academic contributions with the haemophilia care network.

Guidance on filling in the questionnaire and data management

Local researchers will receive instructions on how to properly fill in the questionnaire. The questions must be answered on the printed or digital form itself and sent to the researchers electronically (e-mail). The deadline for completion will be set at 3 months after providing the questionnaire and the instructions. After data collection, the information obtained from each participating BC will be transferred to a Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA), with appropriate coding assigned to each BC to ensure confidentiality.

Statistical analysis

Continuous variables will be evaluated for normal distribution (Kolmogorov-Smirnov with Lilliefors correction, for samples >30, or Shapiro-Wilk, for samples ≤30). For parametric distributions, data will be presented as mean and SD. For non-parametric distributions, data will be presented as median and IQR. For both distributions, minimum and maximum values will be shown. For categorical variables, data will be demonstrated as percentages of the relation between the observed and the total cases.

Study status

Data collection for the PATCH study began in December 2024 and is expected to be completed by December 2025. Although recruitment and data collection are currently underway, this protocol was developed and finalised

before any data analysis was performed. Data analysis and preparation of manuscripts presenting the study results are planned for the first semester of 2026. Publishing this protocol seeks to promote methodological transparency, allow for peer input and support reproducibility of the planned analyses.

DISCUSSION

The PATCH Project is designed to comprehensively characterise the supply and provision of services for PwH within Brazil's specialised treatment centres. The quality of care begins with accurate diagnosis, which remains a significant challenge in less developed countries where haemophilia is frequently underdiagnosed.[51 52]

Both the WFH and the Kreuth Initiative advocate universal access to coagulation factor concentrates and, when indicated, ITI.[13 16 47 53] In Brazil, the MH provides free and equitable haemophilia treatment to all patients. However, despite universal access, the per capita consumption of FVIII and FIX concentrates varies widely across Brazilian regions, potentially reflecting disparities in the organisation and capacity of regional health services to care for PwH.[10 21 35 45 54]

By evaluating the infrastructure and work processes of each participating BC, this study will assess the degree of alignment with national and international standards of excellence in haemophilia care, highlighting regional similarities and differences.[55] This unprecedented, detailed information on the determinants of haemophilia care in Brazil is invaluable for informing public health policies aimed at enhancing equity and efficiency within SUS. Moreover, the data will be collected according to international clinical excellence standards, enabling meaningful comparisons with haemophilia care in other countries. The study's strengths lie in its broad representativeness, seeking to individually assess all Brazilian BC, and the comprehensiveness of data collected, including structural aspects and quality of care metrics. Existing literature on Brazilian BC management lacks this level of granularity, making our study a pivotal resource to understand current haemophilia care practices nationwide.[10 41] Furthermore, the ability to explore emerging issues, such as ageing PwH populations and care considerations for women with haemophilia, will yield critical insights for healthcare managers.[28 48 51]

In addition, having forms completed by staff directly involved in PwH care at each centre will provide nuanced, locally grounded data that faithfully reflect the realities of service structure and care delivery processes. This detailed dataset surpasses the aggregate annual reports currently available through Hemovida WebCoagulopatias.

Given Brazil's continental scale and its marked geographical, socio-economic and cultural heterogeneity, we anticipate substantial variation in service provision across regions. Potentially, data will be gathered from public institutions in all five Brazilian regions, situated in medium to large municipalities, ensuring robust representation of regional diversity in medical and multidisciplinary care. While this is not a comparative study per se, it will allow identification of patterns, commonalities and disparities. These findings may inform the MH's future decisions aimed at standardising service delivery models and promoting greater uniformity in haemophilia care across states.

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Contributors MRFR, YRAG, IAM, PPI and SRRB formulated the conception and design of the study. MRFR, PPI, RMC, TFC and SRRB contributed to the methodologic aspects; all the authors wrote the protocol. MRFR, PPI, TFC and SRRB carried out a final review of the protocol. MRFR is our guarantor. During the preparation of this work, the authors used ChatGPT 4o (Open AI) in order to review text fluency and language, spelling and grammar errors. This tool was not used to generate content. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the published article.

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REFERENCES

1 Sarmiento Doncel S, Díaz Mosquera GA, Cortes JM, *et al*. Haemophilia A: A Review of Clinical Manifestations, Treatment, Mutations, and the Development of Inhibitors. *Hematol Rep* 2023;15:130–50.
2 Berntorp E, Fischer K, Hart DP, *et al*. Haemophilia. *Nat Rev Dis Primers* 2021;7:45.
3 Castaman G, Matino D. Hemophilia A and B: molecular and clinical similarities and differences. *Haematologica* 2019;104:1702–9.
4 Blanchette VS, Key NS, Ljung LR, *et al*. Definitions in hemophilia: communication from the SSC of the ISTH. *J Thromb Haemost* 2014;12:1935–9.
5 Gualtierotti R, Solimeno LP, Peyvandi F. Hemophilic arthropathy: Current knowledge and future perspectives. *J Thromb Haemost* 2021;19:2112–21.
6 van Vulpen LFD, Holstein K, Martinoli C. Joint disease in haemophilia: Pathophysiology, pain and imaging. *Haemophilia* 2018;24 Suppl 6:44–9.
7 Escobar M, Sallah S. Hemophilia A and hemophilia B: focus on arthropathy and variables affecting bleeding severity and prophylaxis. *J Thromb Haemost* 2013;11:1449–53.
8 Manco-Johnson MJ, Abshire TC, Shapiro AD, *et al*. Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. *N Engl J Med* 2007;357:535–44.
9 World Federation of Hemophilia. Report on the annual global survey 2023. Available from; 2024. Available: www.wfh.org [Accessed 5 Aug 2025].
10 Ministério da Saúde. Secretaria de atenção especializada à saúde. departamento de atenção especializada em temática. In: *Coordenação-Geral de Sangue e Hemoderivados. Sistematização: Dados coagulopatias hereditárias 2023*. Brasília: Ministério da Saúde, 2023.
11 Young L, Chen Y, Alvir J, *et al*. The impact of bleeding event frequency on health-related quality of life and work productivity outcomes in a European cohort of adults with haemophilia A: insights from the CHESS II study. *Orphanet J Rare Dis* 2023;18:227.
12 Fornari A, Antonazzo IC, Rocino A, *et al*. The psychosocial impact of haemophilia from patients' and caregivers' point of view: The results of an Italian survey. *Haemophilia* 2024;30:449–62.
13 Iorio A, Königs C, Reding MT, *et al*. Prophylaxis use of clotting factor replacement products in people with non-severe haemophilia: A review of the literature. *Haemophilia* 2023;29:33–44.
14 Pierce GF, O'Mahony B, Kaczmarek R, *et al*. Risk of harm to people with haemophilia from the 2023 WHO Essential Medicines List. *Lancet Haematol* 2024;11:e638–40.
15 Mannucci PM. Hemophilia treatment innovation: 50 years of progress and more to come. *J Thromb Haemost* 2023;21:403–12.
16 Srivastava A, Santagostino E, Dougall A, *et al*. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia* 2020;26 Suppl 6:1–158.
17 Chhabra A, Spurden D, Fogarty PF, *et al*. Real-world outcomes associated with standard half-life and extended half-life factor replacement products for treatment of haemophilia A and B. *Blood Coagul Fibrinolysis* 2020;31:186–92.
18 Hermans C, Giangrande PLF, O'Mahony B, *et al*. European principles of inhibitor management in patients with haemophilia: implications of new treatment options. *Orphanet J Rare Dis* 2020;15:219.
19 Español MG, Mistretta JN, Tarantino MD, *et al*. The Evolution of Hemophilia Therapeutics: An Illustrated Review. *Res Pract Thromb Haemost* 2024;8:102308.
20 Mahlangu J. Emicizumab and unmet needs of patients with hemophilia a who are managed with replacement therapies. *Expert Rev Hematol* 2024;17:741–8.
21 The Lancet Haematology. Haemophilia-unparalleled progress but inadequate access. *Lancet Haematol* 2023;10:S2352-3026(23)00067-4.
22 Soto I, Mateo J, García-Diego D-A, *et al*. The impact of improving haemophilia A management within the Spanish National Healthcare System: a social return on investment analysis. *BMC Health Serv Res* 2022;22:115.
23 Rodriguez-Merchan EC. The cost of hemophilia treatment: the importance of minimizing it without detriment to its quality. *Expert Rev Hematol* 2020;13:269–74.
24 Croteau SE, Cook K, Sheikh L, *et al*. Health care resource utilization and costs among adult patients with hemophilia A on factor VIII prophylaxis: an administrative claims analysis. *J Manag Care Spec Pharm* 2021;27:316–26.
25 Dalton DR. Hemophilia in the managed care setting. *Am J Manag Care* 2015;21:S123–30.
26 Woollacott I, Chhabra A, Burke T, *et al*. Distribution and predictors of haemophilia-related costs in the United Kingdom: analysis of the CHESS I and CHESS II burden of illness studies. *BMC Health Serv Res* 2024;24:1437.
27 Chandrasekaran R, Dávoli M, Muda Z, *et al*. Estimating the impact of improved management of haemophilia a on clinical outcomes and healthcare utilisation and costs. *BMC Res Notes* 2023;16:327.
28 Mingot Castellano ME. General concepts on hemophilia A and on women carrying the disease. *Blood Coagul Fibrinolysis* 2020;31:S1–3.
29 Hakimi Z, Ghelani R, Bystrická L, *et al*. Patient Experience of Living With Hemophilia A: A Conceptual Model of Humanistic and Symptomatic Experience in Adolescents, Adults, and Children. *JHEOR* 2024;95–102.
30 Berrueco R, Caballero N, López-Tierling M, *et al*. Mapping the Patient Experience in a Pediatric Hemophilia Unit: Our Patient Journey. *J Clin Med* 2024;13:6235.
31 Yeung CHT, Santesso N, Pai M, *et al*. Care models in the management of haemophilia: a systematic review. *Haemophilia* 2016;22 Suppl 3:31–40.
32 Colvin BT, Astermark J, Fischer K, *et al*. European principles of haemophilia care. *Haemophilia* 2008;14:361–74.
33 Pai M, Key NS, Skinner M, *et al*. NHF-McMaster Guideline on Care Models for Haemophilia Management. *Haemophilia* 2016;22:6–16.
34 Yeung CHT, Santesso N, Zeraatkar D, *et al*. Integrated multidisciplinary care for the management of chronic conditions in adults: an overview of reviews and an example of using indirect evidence to inform clinical practice recommendations in the field of rare diseases. *Haemophilia* 2016;22 Suppl 3:41–50.
35 Castro MC, Massuda A, Almeida G, *et al*. Brazil's unified health system: the first 30 years and prospects for the future. *The Lancet* 2019;394:345–56.
36 Rezende SM, Jardim LL, Lúcia Magalhães V, *et al*. Building the National Program of Inherited Bleeding Disorders in Brazil. *Blood Adv* 2019;3:48–50.
37 Souza M, ed. *Planejamento e gestão em saúde: caminhos para o fortalecimento das hemorredes*. In: *EDUFBA*. 2018. Available: http://books.scielo.org/id/c8vkc
38 Agência nacional de vigilância sanitária. In: *Resolução RDC n° 151, de 21 de agosto de 2001. Aprova o Regulamento Técnico sobre Níveis de Complexidade dos Serviços de Hemoterapia. Diário Oficial da União, Seção 1*. Brasília (DF), 2001.
39 Schneider NB, de Araujo CLP, Godoy dos Santos HW, *et al*. Epidemiology, patient journey and unmet needs related to hemophilia in Brazil: a scoping review with evidence map. *Hematology, Transfusion and Cell Therapy* 2024;46:533–41.
40 Pepe C, Fagundes G, Goode B, *et al*. Custo-efetividade do fator VII ativado recombinante (rFVIIa) e complexo protrombínico parcialmente ativado (CCPa) no tratamento sob demanda do sangramento leve/moderado de pacientes com hemofilia congênita complicada por inibidores sob a perspectiva. *JBES* 2017;9:249–59.
41 Prezotti AN, Rocha DM, Galvão EL, *et al*. Annualized bleeding rate in hemophilia A patients in Brazil: a systematic review. *Hematol Transfus Cell Ther* 2025;47:103736.
42 Mattos RA de. Princípios do Sistema Único de Saúde (SUS) e a humanização das práticas de saúde. *Interface (Botucatu)* 2009;13:771–80.
43 Antunes SV. Haemophilia in the developing world: the Brazilian experience. *Haemophilia* 2002;8:199–204.
44 Ferreira AA, Leite ICG, Bustamante-Teixeira MT, *et al*. Hemophilia A in Brazil - epidemiology and treatment developments. *J Blood Med* 2014;5:175–84.
45 da Silva Etges APB, Schneider NB, Roos EC, *et al*. Cost of hemophilia A in Brazil: a microcosting study. *Health Econ Rev* 2024;14:62.
46 Ozelo MC, Yamaguti-Hayakawa GG. Impact of novel hemophilia therapies around the world. *Res Pract Thromb Haemost* 2022;6:e12695.
47 Peyvandi F, Berger K, Seitz R, *et al*. Kreuth V initiative: European consensus proposals for treatment of hemophilia using standard products, extended half-life coagulation factor concentrates and non-replacement therapies. *Haematologica* 2020;105:2038–43.

48 van Galen K, Lavin M, Skouw-Rasmussen N, *et al*. European principles of care for women and girls with inherited bleeding disorders. *Haemophilia* 2021;27:837–47.
49 van Balen EC, Krawczyk M, Gue D, *et al*. Patient-centred care in haemophilia: Patient perspectives on visualization and participation in decision-making. *Haemophilia* 2019;25:938–45.
50 Secretaria de Atenção à Saúde. Ministério da Saúde, Brasília; Departamento de Atenção Especializada e Temática. Manual de hemofilia, 2015. Available: https://bvsms.saude.gov.br/bvs/publicacoes/manual_hemofilia_2ed.pdf [Accessed 5 Aug 2025].
51 Srivastava A. The case for equitable haemophilia care. *Lancet Haematol* 2021;8:S2352-3026(21)00132-0.
52 Boadas A, Ozelo MC, Solano M, *et al*. Haemophilia care in Latin America: Assessment and perspectives. *Haemophilia* 2018;24:e395–401.
53 Berger K, Klein HG, Seitz R, *et al*. The Wildbad Kreuth initiative: European current practices and recommendations for optimal use of blood components. *Biologicals* 2011;39:189–93.
54 Lopez K, Norris K, Hardy M, *et al*. Defining the Impact of Social Drivers on Health Outcomes for People with Inherited Bleeding Disorders. *J Clin Med* 2022;11:4443.
55 Srivastava A. Haemophilia care - beyond the treatment guidelines. *Haemophilia* 2014;20 Suppl 4:4–10.