

ORIGINAL ARTICLE

Clinical haemophilia

Building the blueprint: Formulating a community-generated national plan for future research in inherited bleeding disorders

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Funding information

National Heart, Lung, and Blood Institute, Grant/Award Number: R13HL158209; National Hemophilia Foundation

Abstract

Introduction: Decades of inherited bleeding disorders (BD) research transformed severe haemophilia from a childhood killer to a disorder managed across a full lifespan for many in economically developed countries. Health equity, a life unimpaired by disease complications, however, remains unimaginable for most people with an inherited BD (PWIBD).

Aim: The National Hemophilia Foundation (NHF) and American Thrombosis and Hemostasis Network (ATHN) undertook the development of a community-driven United States (US) National Blueprint for Inherited Bleeding Disorders Research to transform the experience of all PWIBD and those who care for them.

Methods: Extensive community consultations were conducted to identify the issues most important to PWIBD and those who love and care for them. Expert multidisciplinary teams distilled these key areas of need into prioritised research questions, and identified the resources and infrastructure required to pursue them. A summit was held to gather feedback and inform the detailed blueprint.

Results: Community-prioritised research areas fell into three broad categories: issues common across inherited BDs, those specific to individual disorders, and issues of infrastructure and capacity. NHF State of the Science Research Summit discussions of the research questions derived from the community priorities by six working groups provided important input for the drafting of the research blueprint for the coming decades.

Conclusion: The inherited BD community came together to develop the US National Blueprint for Inherited Bleeding Disorders Research dedicated to transforming the lives of all PWIBD including innovating solutions for the rarest disorders and under-represented populations.

KEYWORDS

advocacy, blueprint, community, health equity, inherited bleeding disorders, research

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1 | INTRODUCTION

Historically, inherited bleeding disorders (BD) research priorities have been defined by researchers and industry. Thirty years ago, focused almost exclusively on men with haemophilia A (clotting factor [F] VIII deficiency) and B (FIX deficiency), inherited BD research sought a safe source of replacement factor to control bleeding and provide a comparable life expectancy to that of people without an inherited BD.¹⁻³ Today, these goals have been attained. In economically developed countries, people with haemophilia (PWH) who achieve haemostatic control through prophylactic factor replacement and multidisciplinary team-based care enjoy a life expectancy similar to the average male population and a very low annualised bleeding rate (ABR),⁴⁻⁶ accompanied by better joint outcomes for children^{7,8} and adults.⁹ As gene therapy appears close to offering a 'functional cure' for these two factor deficiencies,^{3,10} we must ask if the needs of all people with an inherited BD (PWIBD) are being met.

For decades, narrowly focused clinical trial designs missed opportunities to generate robust data supporting some of the most effective treatment/diagnostic practices and the outcomes most important to PWIBD. For example, despite numerous haemophilia prophylaxis clinical trials, in 2015 the German Institute for Quality and Efficiency in Health Care (IQWiG) reported that, due to the overall inadequate quality of data for the comparison one could only conclude that prophylaxis versus on-demand treatment of children with FVIII offered a hint of an added benefit with regard to severe bleeding but no hint of an added benefit with regard to state of health and pain, all-cause mortality and life-threatening bleeding, and joint function and health-related quality of life (QoL).¹¹ Healthcare budget constraints mean an increased focus on optimising resource allocation, therefore robust data demonstrating the value of interventions that affect outcomes of importance to PWH are critical to ensuring (continued) access.¹² Such data are also required to inform clinical practice guidelines that support education, advocacy, and decision-making related to treatment and the delivery of care.¹³ Those designing and conducting clinical trials have a responsibility to optimise the collection and sharing of data on outcomes that matter most to people with the disorder, especially in rare disorders with their inherent scarcity of potential trial participants.^{14,15}

Equity, defined by the World Health Organization (WHO) as the 'absence of avoidable or remediable differences among groups of people,'¹⁶ remains out of reach for all but the most fortunate PWIBD. Simply surviving or not bleeding is far from attaining a life unimpacted by disease complications.¹ Progress towards equity is measured through patient-important, often patient-centred, impacts which include clinical/medical outcomes but also how a disease and/or its treatments may impact the life of a patient or their family (e.g. caregiver/family stresses, economic burden, etc).^{12,17,18} Significant strides remain to be made in fundamental areas such as eliminating morbidity, disability, and pain. The ability to participate fully in normal family, career, and social activities, and to live an unrestricted lifestyle are key milestones on the path to optimal wellness, just as freedom from spontaneous bleeding events and the need for additional intervention in the

context of minor trauma or surgery characterise a clinical progression towards normal haemostasis.¹

Recent and ongoing developments in haemophilia therapeutics present great promise, however, the vast majority of PWIBD cannot currently achieve health equity. Von Willebrand disease (VWD), the most common inherited BD, inherited equally by men and women, is clinically complex and technically challenging to diagnose,¹⁹ yet far fewer resources have been devoted to it than to haemophilia. Rare and ultra-rare inherited BDs which cause significant morbidity remain difficult to diagnose, and are largely underdiagnosed globally despite technical advances.^{20,21} Evidence-based guidelines for the treatment of most inherited BDs are largely absent, due to the lack of supporting aggregate data.²² Sexism has been an issue in BD for centuries. Women and girls with bleeding disorders (WGBD) experience lengthy delays in diagnosis and frequently encounter ignorance, stigmatisation, and dismissal of their symptoms by healthcare professionals (HCP) and society.²³ Health equity is also limited by greater socio-historical constraints. It cannot be achieved through health-specific projects alone, particularly for individuals who embody the cumulative effects of historic and current marginalisation, if the mechanisms generating inequalities are not addressed.²⁴

It is an exciting time in inherited BD research. New technologies and analytical tools, infusions of research funding, and blossoming international interest present an opportunity to dramatically improve the experiences of PWIBD. So, how should the research priorities for the next several decades be set? The National Hemophilia Foundation (NHF) and the American Thrombosis and Hemostasis Network (ATHN) propose a radically novel approach: people who live with inherited BDs every day of their lives are subject matter experts (SME) possessing unique and important expertise about their disorders and they should set the research agenda, aligned with what is important to them. Priorities must be driven by the community, the individuals and family members, specialists, and allied HCPs most invested in minimising the burden of inherited BDs and innovating solutions for the rarest disorders and under-represented populations.

In 2020, NHF launched a transformative community initiative to shape research priorities seeking to ensure every PWIBD has access to safe, effective, convenient therapeutics, diagnostics, and digital technologies to deliver optimal health outcomes at the lowest total cost of care (Figure 1). Extensive inclusive community consultations identified the issues most important to PWIBD and those who love and care for them. Multidisciplinary teams of HCPs, researchers, and SMEs distilled these key areas of need into prioritised research questions, and identified the resources and infrastructure required to pursue them. Their findings were reviewed by the community at a State of the Science Research Summit (SOSRS), reports of which are currently in preparation for publication as components of a research agenda. Herein, the authors detail the process of building a community-driven United States (US) National Blueprint for Inherited Bleeding Disorders Research. The resulting blueprint will embrace people-centric principles and holistically address the priorities of the inherited BD community, especially its under-represented populations. This report offers

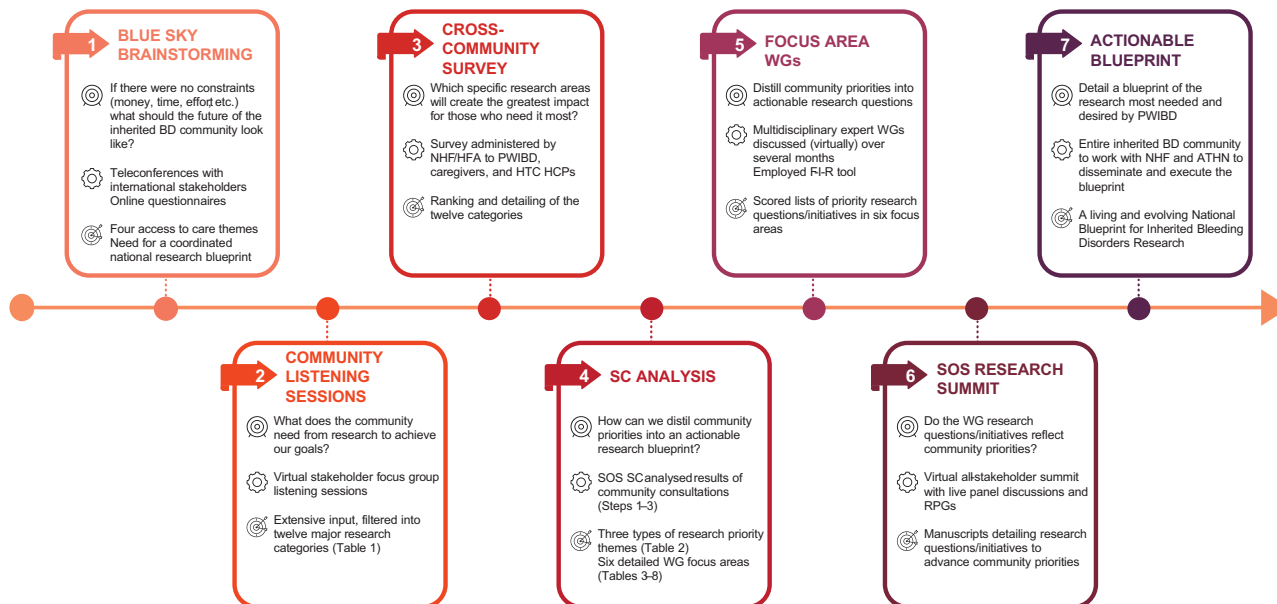


FIGURE 1 Objective, working, and output of the seven steps in the process of building a community-generated national research blueprint. Abbreviations: ATHN, American Thrombosis and Hemostasis Network; BD, bleeding disorders; F-I-R, feasibility-impact-risk; HCP, healthcare professional; HFA, Hemophilia Federation of America; HTC, haemophilia treatment centre; NHF, National Hemophilia Foundation; PWIBD, people with inherited bleeding disorders; RPG, remote participation group; SC, steering committee; SOS, State of the Science; WG, working group

insights relevant to the international inherited BD community, and the approach can be applied to any area of health research, anywhere.

2 | COMMUNITY CONSULTATIONS

2.1 | 'Blue Sky' brainstorming

In June and July 2020, NHF conducted a series of 'blue sky' teleconferences asking what the future of the inherited BD community should look like, if neither money, time, nor effort were limiting. The responses of the 101 participants from across the international inherited BD community, including physicians, nurses, other HCPs, SMEs, patient organisation leaders (national and regional), and NHF staff and board members, coalesced into four themes, all centred-on access to care:

- Sustaining and expanding the comprehensive care model to strive towards health equity.
- Harnessing/leveraging technology to expand access to care.
- Ensuring sustainability of the comprehensive care model thereby promoting access to care.
- Envisioning the NHF in 2030.

An overarching conclusion of these discussions, and the 130 responses to a follow-up online community questionnaire, was the need for a coordinated national research plan. Research will be key in transforming the future of the inherited BD community, and SMEs must be central in defining the agenda for the coming decades.

The details of the Blue Sky project will be reported separately.

2.2 | Virtual community listening sessions

Having established the primacy of access to care and the need to develop a coordinated national research blueprint, NHF, in collaboration with the Centre for Information and Study on Clinical Research Participation (CISCRP) and Tufts University Centre of Study of Drug Development, conducted a series of focus group listening sessions from June to November 2020. They asked the inherited BD community what they need from research to achieve their life goals. Due to pandemic restrictions, all listening sessions were conducted virtually. Input was solicited from diverse stakeholders including PWIBD, parents and caregivers, patient organisation representatives, local chapter and member organisation directors, HCPs, and industry representatives (Table S1). Participants included representation of the following inherited BDs: haemophilia A, haemophilia B, VWD, platelet dysfunction, Glanzmann thrombasthenia, and deficiencies of FVII, FX, FXI, and FXIII. Their expressed needs fell into twelve major research categories (Table 1).

2.3 | Cross-community survey

In order to better understand which specific research areas offer the greatest potential to transform the lives of PWIBD, especially those who need it the most, NHF created a survey to invite a wider community to rank and comment on the twelve major research categories identified above (Table 1). The survey was administered through NHF's Chapters and Haemophilia Federation of America (HFA) member organisations to the PWIBD and caregiver community,

TABLE 1 Major categories of community-prioritised research

Access to specialised care
Access to research and mechanisms (ways) to conduct research
Continuation of the HTC model of care (training future HCPs and their financial sustainability)
Health care differences in various communities (based on race, ethnicity, gender, education, income, etc.)
Joint disease and management
Mental health (depression, anxiety, emotional impact, substance misuse, etc.)
Pain management
Treatment for all BD (gene therapy, non-factor replacements, etc.)
Treatment for, specifically, other RBDs (non-haemophilia, non-VWD)
Treatment of other chronic diseases and issues affecting those with BDs – such as heart disease or diabetes, etc.
Treatment of the ageing population with BD
Women's health and care

Abbreviations: BD, bleeding disorder; HCP, healthcare provider; HTC, haemophilia treatment centre; RBD, rare bleeding disorder; VWD, von Willebrand disease.

and by NHF to haemophilia treatment centre (HTC) HCPs, in January 2021.

The 335 survey participants included 125 PWIBD and 112 HCPs. The top-ranked focus was sustaining the HTC care model, including ensuring training of future HCPs with expertise in inherited BDs and the financial stability of the centres. Many respondents emphasised the need for more research into new therapies for all inherited BDs, not just severe haemophilia. Access to care, across diverse communities and including specialised care (e.g. ultra-rare disorders), were priorities shared across stakeholder groups. Mental health, joint disease, ageing with inherited BDs, and pain management were the top daily living concerns.

3 | DISTILLING COMMUNITY PRIORITIES INTO ACTIONABLE RESEARCH QUESTIONS

Early in the blueprint development, NHF engaged independent consultant, Donna DiMichele, MD, for guidance patterning the process on her previous work with the National Heart, Lung, and Blood Institute (NHLBI) State of the Science on FVIII inhibitors in 2018.^{25,26} NHF and ATHN completed the SOSRS Executive Committee (EC), co-chaired by the NHF President and Chief Executive Officer and ATHN's Chief Science Officer. Together they recruited inherited BD community experts to the Steering Committee (SC) with partner federal agency representatives in an advisory role (Table S2).

3.1 | Focus area working groups

The SC studied all of the input gathered through community consultations. They formulated a number of research themes that they cat-

egorised into three types: those pertaining to all inherited BDs, those specific to individual inherited BDs, and infrastructure and capacity opportunities (Table 2).

The SC then organised the community-identified priorities into six focus areas and recruited expert Working Groups (WG) (Table S3) to distil each into research questions (Tables 3–8). WGs featured diverse voices from across the inherited BD community including those of under-represented groups (e.g. WGBD, the lesbian, gay bisexual, transgender, and queer [LGBTQ] community, minority ethnic populations), at least one SME, an NHF Board member, an NHF staff member, HCPs from multiple disciplines (nursing, social work, physiotherapy, haematology, obstetrics, gynaecology, dentistry, etc. as appropriate), and industry professionals. SMEs were actively encouraged by WG co-chairs to contribute to all discussions and their input frequently solicited. An NHF support person met with them periodically, individually and in small groups, throughout the process to accompany and empower them to contribute confidently. Members were recruited primarily from the US with a few international invitees. Expertise external to the inherited BD community was also sought where necessary to address the full breadth of community-identified priorities.

Under the guidance of the SC, and led by their co-chairs, the WGs met (virtually) frequently throughout the first half of 2021 to study their community-prioritised themes. They consulted the literature and existing resources, convened expert speakers, debated internally, and engaged in inter-group cross-talk. They asked whether enough data exist to determine the most important hypothesis-based research questions in their focus area. If so, the WG defined specific actionable research questions to drive meaningful and lasting change in the evidence-based care of PWIBD. If not, they were challenged to identify how a better dataset could be established through, for example, observational data collection, pilot clinical studies, or mechanistic or point of care (POC) research.

3.2 | Feasibility, impact, and risk

The WG deliberations yielded many more excellent research questions than can realistically be immediately pursued, therefore, one of the authors (DDM) devised a prioritisation matrix (Figure 2). This framework of scored questions guided WGs 1–5 in evaluating the feasibility, impact, and risk associated with each question (Table S4). *Feasibility* assessed the difficulty in answering the proposed question, including required expertise, infrastructure, and resources. *Impact* estimated the change to be affected (e.g. to standards of care or access to care), whether it might change a therapeutic paradigm or be applicable to other areas. *Risk*, scored with increasingly negative values, assessed the challenges facing each question, such as the risk/benefit ratio for novel therapies or ethical considerations. WG 6 scored on the same three dimensions, using pre-specified criteria to evaluate infrastructure, resources/funding, and future workforce development models rather than research questions. Summing across the three dimensions permitted relative prioritisation of very different initiatives in very different contexts. While an 'easy' question might

TABLE 2 Three types of community-prioritised inherited BD research themes

Category	Prioritised themes
Themes applicable across inherited BDs	<ul style="list-style-type: none"> • Research that is feasible, prioritised for impact on patient outcomes • Research to benefit future generations addressing the most pressing needs of the inherited BD community • Impact of inherited BD symptoms/manifestations across the lifespan • Therapies for non-haemophilia inherited BDs that are safe/effective/easy to use/affordable/covered by insurance; and for RBDs, disease-specific; POC management • Pain management in PWIBD • Mental health in PWIBD • Health disparities across under-represented populations (ethnic, racial, gender [including LGBTQ], and geographic) • Future workforce development and evolution of the HTC model to ensure/optimize future care of PWIBD
Priorities specific to individual inherited BDs	<ul style="list-style-type: none"> • Rare and ultra-rare inherited BDs: <ul style="list-style-type: none"> ◦ Disease-specific diagnostics and therapeutics, including recombinant replacement concentrates ◦ Impact of inherited BD symptoms/manifestations across the lifespan • Women with inherited BDs: <ul style="list-style-type: none"> ◦ Novel therapeutics for VWD ◦ Impact of inherited BD symptoms/manifestations across the lifespan ◦ Joint disease in women ◦ Haemophilia carriers • Haemophilia: <ul style="list-style-type: none"> ◦ Continuing therapeutic advance (efficacy/safety/ease of administration) toward normal QoL ◦ Defining 'cure' expectations with gene therapy ◦ Moderate/mild haemophilia research (non-severe)
Infrastructure and capacity opportunities	<ul style="list-style-type: none"> • Elements of national research infrastructure/capacitation/acclimation facilitating and optimising work on a prioritised research blueprint through: <ul style="list-style-type: none"> ◦ National patient-centred data collection ◦ Hypothesis-driven and feasible basic research/observational studies/clinical and implementation trials ◦ Future workforce nourishing an expansive national research enterprise through: <ul style="list-style-type: none"> ◦ Inclusion of an entire, well-trained inherited BD provider and patient community ◦ Regional, national, and international collaborations ◦ Multidisciplinary team science drawing expertise from within and outside the inherited BD scientific community ◦ Strategic partnerships leveraging existing infrastructure and common goals • NHF role in realising the National Blueprint for Inherited Bleeding Disorders Research

Abbreviations: BD, bleeding disorder; HTC, haemophilia treatment centre; LGBTQ, lesbian, gay, bisexual, transgender, queer; NHF, National Hemophilia Foundation; POC, point of care; PWIBD, people with an inherited bleeding disorder; QoL, quality of life; RBD, rare bleeding disorder; VWD, von Willebrand disease.

TABLE 3 WG 1: research priorities for haemophilia A and B

Co-chairs	Duc Quang Tran, Jr., MD, MSc Annette von Drygalski, MD, PharmD, RMSK
Key question	How can we use new technologies to discover therapies to improve life with haemophilia while working to deliver a safe and meaningful cure?
Community-identified priorities	<ul style="list-style-type: none"> • Therapeutics and drug delivery • Goals for gene therapy • Evolution of precision medicine-informed care • Sex/gender biology pain/comorbidities • Enhanced lifespan data collection • Ageing • Redefining non-severe phenotypes

Abbreviation: WG, working group.

TABLE 4 WG 2: research priorities for VWD, platelet dysfunction and other mucocutaneous inherited BDs

Co-chairs	Veronica H. Flood, MD Robert F. Sidonio, Jr., MD, MSc
Key question	What is needed to engender more targeted and accessible diagnostics and therapies for all people with these disorders?
Community-identified priorities	<ul style="list-style-type: none"> • Targeted/accessible diagnostics and therapy <ul style="list-style-type: none"> ◦ For all mucocutaneous BDs ◦ Across all phenotypes • Gene therapy • Biology of mucocutaneous bleeding • Enhanced lifespan data collection • Ageing • PRO measures

Abbreviations: BD, bleeding disorder; PRO, patient-reported outcome; VWD, von Willebrand disease; WG, working group.

TABLE 5 WG 3: research priorities for ultra-rare inherited BDs

Co-chairs	Suchitra S. Acharya, MD Diane Nugent, MD Amy D. Shapiro, MD
Key questions	How can we better understand the biology of these rare disorders? How can we stimulate research and optimise the regulatory process to vastly improve diagnosis and targeted treatment?
Community-identified priorities	<ul style="list-style-type: none"> Targeted/accessible diagnostics and therapy <ul style="list-style-type: none"> For all ultra-rare bleeding disorders Across all phenotypes Gene therapy Biology of rare and ultra-rare factor deficiencies Enhanced lifespan data collection Ageing

Abbreviations: BD, bleeding disorder; WG, working group.

TABLE 6 WG 4: research priorities for the health of women, girls, and people with the potential to menstruate

Co-chairs	Maureen K. Baldwin, MD, MPH Angela C. Weyand, MD
Key questions	How can we improve care for this group of PWIBD through a better understanding of the sex and gender biology of bleeding, as well as through new tools like non-invasive prenatal testing or therapies for reproductive system bleeding?
Community-identified priorities	<ul style="list-style-type: none"> Novel therapies for reproductive bleeding Gene therapy risks in women and girls Non-invasive prenatal diagnosis Sex/gender biology across inherited BDs/phenotypes Hemarthrosis/comorbidities in women and girls Inclusion in data collection/clinical trials

Abbreviations: BD, bleeding disorder; PWIBD, person with an inherited bleeding disorder; WG, working group.

score well on feasibility criteria, a more challenging question with greater potential impact could yield an equally high sum result.

3.3 | Roles for NHF and ATHN

WGs were tasked with identifying how NHF might support or facilitate their research priorities. As the largest inherited BD patient organisation, NHF is committed to a world without inherited BDs, a vision that starts with research.²⁷ Applying a people-centred approach to all initiatives, it has the capacity and expertise to support research in myriad ways including advocacy, education, policy change, liaising with regulators, and funding.

The WGs were also charged with identifying opportunities to leverage existing infrastructure and resources to pursue research priorities. ATHN constitutes one such opportunity. ATHN partners with 146 US HTCs to build a safe, secure national database—the ATHNdataset.^{28,29}

TABLE 7 WG 5: diversity, equity and inclusion, health services research, and implementation science

Co-chairs	Judith R. Baker, DrPH, MHSA Tyler Buckner, MD, MSc Vanessa R. Byams, DrPH, MPH
Key questions	How can we make the greatest impact on equal access to care and more inclusive coverage? What digital tools could be implemented to reach this goal?
Community-identified priorities	<ul style="list-style-type: none"> Diversity, equity and inclusion/Access to care Health services research Implementation science Public health Digital health Healthcare delivery networks Access to and research in mental health/pain Research/health communications PRO measures across inherited BDs

Abbreviations: BD, bleeding disorder; PRO, patient-reported outcome; WG, working group.

[Correction added on 15 July 2022, after first online publication: The PhD degree was changed to DrPH for “Judith R. Baker” and “Vanessa R. Byams”.]

TABLE 8 WG 6: facilitating priority research in the inherited BD community

Co-chairs	Margaret V. Ragni, MD, MPH (Resources and Funding) Jordan Shavit, MD, PhD (Workforce) Guy Young, MD (Infrastructure)
Key questions	How can we build and fund a research network that is centred on care delivery and designed to reduce the burden of participation? How can we encourage more trainees to join our professional community so that PWIBD are assured of having care providers well into the future?
Community-identified research priorities	<ul style="list-style-type: none"> Research infrastructure optimisation Resource/Funding procurement and development Strategies for future workforce development

Abbreviations: BD, bleeding disorder; PWIBD, person with an inherited bleeding disorder; WG, working group.

The network’s goal is to secure data, advance knowledge, transform care and ultimately improve the lives of people with bleeding and clotting disorders. Their standardised integrated systems, data, and processes offer a unique opportunity to efficiently initiate novel collaborative inclusive research within an established network, decreasing the time and cost involved.

4 | STATE OF THE SCIENCE RESEARCH SUMMIT

12–15 September 2021, NHF hosted the State of the Science (virtual) Research Summit (SOSRS), an opportunity for all community members to weigh in on the research questions and infrastructure initiatives prioritised by the WGs. The Summit, supported entirely by NHF, with no

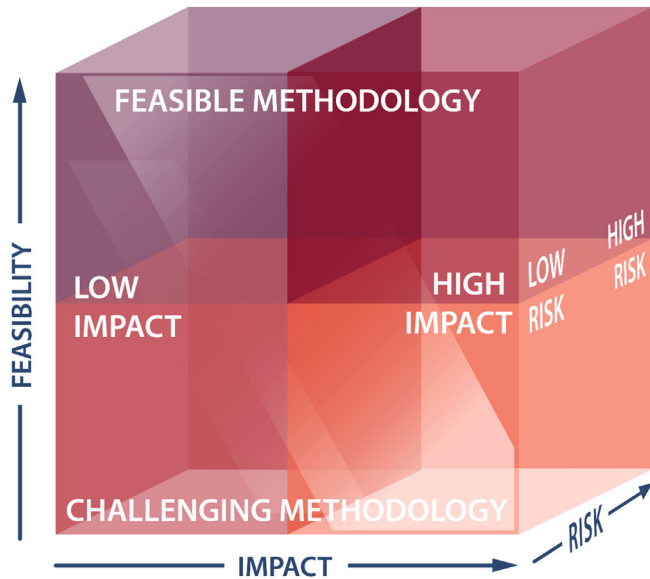


FIGURE 2 Ranking research questions on three dimensions: feasibility, impact, and risk.

funding from industry or commercial partners, was open to all without charge. NHF, ATHN, and partner social media and email campaigns featured SME and HCP testimonials emphasising the opportunity to direct inherited BD research towards PWIBD priorities (Figure S1). The NHF SOSRS was well attended with 441 unique attendees from all stakeholder groups (Table S5).

The co-chairs presented the research questions derived by each WG in response to the community-identified priorities, in the context of expert plenary presentations and SME vignettes illustrating current unmet needs (Table S6). A live 90-min panel discussion engaged co-chairs, several WG members including SMEs, and the plenary speaker with real-time input from attendees, to validate whether the WG conclusions reflected their goals. A final 2-h panel discussion between the SC, WG co-chairs, and SMEs, with live community input, synthesised the learnings from the entire Summit. Recordings of all SOSRS sessions are available on NHF's YouTube channel: <https://www.youtube.com/user/NHFvideo>.

4.1 | Remote participation

The development of a research blueprint advancing equity for all PWIBD must recognise that the broader social milieu of inequity, that has been inscribed on the very bodies of those facing disparity, also erects barriers to their participation in consultative initiatives.²⁴ NHF obtained an NHLBI R13 grant (R13HL158209) to increase outreach to, and reduce the burden of participation on, under-represented populations through the organisation and facilitation of Remote Participation Groups (RPG). This option was offered to groups of Black/African Americans, LatinX Americans, Asian Americans, Indigenous Americans, the LGBTQ+ community, the ageing community, and those living rurally or geographically challenged. Five RPGs with 3–15 participants each,

for a total of 40, amplified input from: Black/African Americans, ageing men, the LGBTQ+ community, women, and Hispanic women (RPG conducted in Spanish). RPGs met virtually or gathered locally, per preferences and pandemic restrictions, once, to view their choice of SOSRS sessions (live or recorded) with one or two facilitators. Facilitators offered explanations to empower RPG members' understanding of the content and confidence in responding to it. Participants shared real-time perspectives and comments to which the SOSRS panels were invited to respond (see also below).³⁰ Facilitator reports summarising RPG discussions, particularly whether the research priorities presented resonated with participants, whether any important priorities had been omitted, what their hopes for Summit outcomes were, and how NHF can engage the SME community to continue to advance the research priorities, were shared with WG co-chairs and informed blueprint component manuscripts (currently in preparation).

4.2 | Building the blueprint

With the conclusion of the NHF SOSRS the next phase in the formulation of a community-generated national research plan began. Each WG, lead by their co-chairs, will now refine their conclusions with the insights from the Summit panel discussions and RPGs into individual manuscripts. Their compiled final reports will be offered back to the community, published as the National Blueprint for Inherited Bleeding Disorders Research.

5 | EXECUTING THE BLUEPRINT

NHF and ATHN undertook a transformative community-driven initiative to shape the inherited BD research priorities of the future, to build upon the exciting progress made in recent years and to dramatically accelerate initiatives making the greatest difference to the individuals and families living with these disorders. They started with wide-open community consultation, enlisted the expertise of SMEs, HCPs and researchers from within and beyond the inherited BD community, and brought the conclusions full circle for community scrutiny. The culmination of this extensive inclusive process, the publication of the National Blueprint for Inherited Bleeding Disorders Research, will mark the beginning of the most important work. This Blueprint must not become yet another report relegated to gather dust on a shelf. As a blueprint it must be executed to serve its function: to build the research most needed and desired by PWIBD.

NHF and ATHN commit to actively and transparently ensuring the execution of the Blueprint through communications, education, and implementation volets. They will map out how the Blueprint will move the whole community towards transformational change, defining stakeholder roles and identifying resources required, where and how best to deploy those resources, action timelines, and mechanisms for follow-up, evaluation, and evolution.

NHF and ATHN call upon the entire inherited BD community to engage with them in ensuring the execution of the Blueprint.

Academic and industry investigators and management should look to the Blueprint for guidance as they design their research. Funding agencies have a responsibility to accelerate research progress in the areas of greatest need for affected individuals and their families. Advocates, policy makers, and regulators must bring about the changes that will facilitate a more efficient and affordable research to care pipeline delivering safe, effective, and convenient diagnostics, therapeutics, and digital technologies for all inherited BDs. Everyone must address health disparities, access barriers, and gaps in care and proactively advance equity for all PWIBD. And SMEs, and those who care for them, must continue to provide input and insights, to engage with and participate in research, and to hold all of the preceding stakeholders accountable to bring the National Blueprint for Inherited Bleeding Disorders Research to life.

ACKNOWLEDGEMENTS

Research reported in this publication was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Number R13HL158209. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Fiona Robinson, PhD provided professional medical writing support during manuscript development. The entire State of the Science Research Summit initiative and this manuscript were funded by National Hemophilia Foundation.

CONFLICT OF INTEREST

LAV, MES, and MLW state that they have no interests which might be perceived as posing a conflict or bias. The opinions expressed in this manuscript by LAV are his own and not necessarily reflective of those of the National Hemophilia Foundation or its Board of Directors. DDM acted as a paid consultant to the National Hemophilia Foundation in the design, organisation, and execution of the State of the Science Research Summit on Inherited Bleeding Disorders. MR's employers have received research support from Bayer, BioMarin, CSL Behring, Genentech, Grifols, Hema Biologics, LFB, Novo Nordisk, Octapharma, Pfizer, Sanofi, Spark, Takeda, and uniQure. MR has acted as a paid consultant to Catalyst Biosciences, CSL Behring, Genentech, Hema Biologics, Kedrion, Novo Nordisk, Octapharma, Pfizer, Sanofi, Takeda, and uniQure. He is on the Board of Directors of the Foundation for Women and Girls with Blood Disorders and Partners in Bleeding Disorders.

AUTHOR CONTRIBUTIONS

Leonard A. Valentino conceived of the development of the national research blueprint, contributed to the development and organisation of the SOSRS, and had input into all aspects of writing of this manuscript. Michelle L. Witkop and Maria E. Santaella contributed to SOSRS development and organisation, data collection and analysis, and had input into all aspects of writing and editing this manuscript. Donna DiMichele contributed to the development and organisation of the SOSRS, data collection and analysis, and manuscript editing. Michael Recht contributed to the development and organisation of the SOSRS and had input into all aspects of writing this manuscript.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

[Correction added on 15 July 2022, after first online publication: Table S3 was replaced with a revised version.]

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

[Correction added on 15 July 2022, after first online publication: Table S3 was replaced with a revised version.]

How to cite this article: Valentino LA, Witkop ML, Santaella ME, DiMichele D, Recht M. Building the blueprint: Formulating a community-generated national plan for future research in inherited bleeding disorders. *Haemophilia*. 2022;28:760–768. <https://doi.org/10.1111/hae.14588>