Received: 4 March 2024 | Accepted: 28 March 2024

https://doi.org/10.1016/j.rpth.2024.102401

ORIGINAL ARTICLE

Improved outcomes and cost savings for patients with bleeding disorders: a quality improvement project

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Handling Editor: Dr Bethany Samuelson Bannow

Abstract

Background: Providing optimal care for patients with bleeding disorders according to national standards remains a challenge at designated Hemophilia Treatment Centers (HTCs). Improved care may reduce bleeds and costs.

Objectives: To improve care and demonstrate cost savings by 1) reducing preventable hospitalizations and emergency room visits (PHER) for bleeding, 2) increasing use of prophylaxis in severe hemophilia, and 3) improving patient-HTC communication and primary care engagement.

Methods: Prospective quality improvement project using the Define, Measure, Analyze, Improve, and Control methodology to implement uniform guideline-based bleeding disorder care at a rural HTC (N = 88). Intervention used a standardized physician checklist, improved communication, and reserved physician time for urgent management. Outcomes were determined by retrospective chart review; urgent management was tracked prospectively.

Results: Intervention significantly reduced PHER by 85.4%. Use of prophylaxis in persons with severe hemophilia increased from 58.8% to 100%; attainment of a primary care physician and electronic portal enrollment met outcomes for intervention success. HTC clinic visit attendance was low at 55.2%. The majority of patients (71.6%) had at least 1 outpatient urgent episode (mean, 0.72 episode per year), and 93% had nonurgent management (mean, 9.3 episodes per year) occurring outside of a clinic visit. Hospital PHER factor cost in the group was reduced by 94.5%, from $11,800 to $640 per patient per year—a cost savings of $982,088 yearly.

Conclusion: This collaborative study shows that implementation of a carefully designed quality improvement project, such as uniform guidelines with focus on strengthening ambulatory management, led to improved outcomes and cost savings.

KEYWORDS
ambulatory care, cost savings, hemophilia, prospective studies

Essentials

- Barriers to healthcare access result in preventable hospitalizations for bleeding.
- This is a prospective cohort study at a rural Hemophilia Treatment Center with a best practices quality improvement intervention.
- Implementing best practices substantially reduced preventable bleeds and costs.
- Supporting quality improvement produces a "win-win" for patients and healthcare systems.

1 | INTRODUCTION

Persons with hemophilia and other congenital bleeding disorders (CBDs) experience morbidity and mortality from bleeding, and bleeds result in high healthcare utilization and costs [1–4]. Hemophilia Treatment Centers (HTCs) were established to deliver specialized bleeding disorder care. The HTC has an important role in coordinating care across medical specialties. Comprehensive care provided at the HTC has been shown to reduce hospitalizations and reduce mortality in persons with hemophilia [5,6]. Guideline-based care strives to prevent bleeding episodes and resultant tissue damage, along with addressing other aspects of bleeding disorder care [7,8].

We observed that patient-level and systems-level factors contribute to bleeding episodes in persons with hemophilia and other CBDs. Hospitalizations and emergency room (ER) visits were noted to occur when persons with hemophilia and other CBDs were nonadherent to therapy, ran out of therapy, had delays in obtaining care, or had barriers to disorder management. We surmised that changes to routine practices of ambulatory assessment and management could improve care quality and reduce such preventable visits. After review of then current hemophilia guidelines, recommendations from the National Bleeding Disorders Foundation (NBDF), as well as discussions with hemophilia care providers, patients, and the local chapter of the NBDF, we implemented an ambulatory quality improvement (QI) project termed "Goal 100—Goal 0" in December 2019.

The goal of this prospective QI program was to improve ambulatory HTC care and potentially provide institutional cost savings with such improved care. Herein, we report the results of this QI effort compared with baseline outcomes from our HTC population.

2 | METHODS

This single-center prospective QI project with planned retrospective observational cohort review was modeled on prior endeavors [9,10]. This project used the Define, Measure, Analyze, Improve, and Control methodology of Six Sigma, and methods are presented here as noted in the study by Improta et al [11–13]. West Virginia University (WVU) Medicine is a hospital system providing care to patients in rural Appalachia within West Virginia, Maryland, Ohio, and Pennsylvania. The WVU Hospitals HTC is the federally funded HTC within WVU Medicine, which utilizes distinct care teams for adult and pediatric patients.

The HTC comprehensive visits included the hematologist, specialty care nurse, and social worker; physical therapy was available on request. Telemedicine via telephone call or video was available before the project but was rarely used due to billing limitations (both formats) and limited site availability (video). During the COVID-19 pandemic, billing requirements for telemedicine were relaxed. The hemophilia physician (S.A.M.) used a personal iPad (Apple) with the Epic Haiku application (Epic Systems Corporation) to conduct video visits before video systems were available on faculty computers. Video capabilities were not available in the HTC clinic space. The QI project had no role in changing regulation of telemedicine visits. Telemedicine was not intended to replace usual HTC comprehensive visits because telemedicine did not include specialty care nurses, social workers, physical examination, or laboratory testing. WVU Medicine used Epic, and the Epic electronic patient portal allowed for written message communication between patient and care team, as well as video telemedicine capability. Full details of the project are available in Supplementary Methods.

2.1 | Define

The aim of the study was to improve ambulatory care based on guideline recommendations and subjective patient needs. The final Critical to Quality characteristic (primary outcome or measure) was defined as preventable hospitalizations and ER visits (PHER) for bleeding. The target was ambulatory care processes affecting PHER. Team members were the authors, and the team leader was the HTC director (S.A.M.). The intervention was planned for a 3-year period.

Inclusion criteria included age ≥18 years, treated at the HTC by adult hematologists, with care between 2016 and 2023 in the baseline and/or intervention periods (described below), and with a diagnosis of an inherited bleeding or connective tissue disorder associated with bleeding. Exclusion criteria included acquired bleeding disorders, age <18 years, and patients not receiving care through the WVU adult HTC. Persons with congenital hemophilia with acquired inhibitor were included.

Nonpreventable bleeding was defined as bleeding caused by high-risk trauma, bleeding despite home therapy, bleeding from malignancy, unexplained unusual bleeding, postprocedural bleeding (despite implementation of procedure plan), high-risk gastrointestinal bleeding (hematemesis, known cirrhosis, or varices), or bleeding with pregnancy (clinical concern for miscarriage, placental pathology, or need for obstetric intervention). Other bleeding events were categorized as preventable

and further classified as follows: 1) from nonadherence/nonuse of factor in those with severe hemophilia; 2) bleeding in persons with severe hemophilia who had factor but needed guidance with therapy; 3) bleeding in other persons (without severe hemophilia) unable to self-treat either without home treatment available or who needed guidance on therapy; and 4) related to intravenous access difficulty.

Patients were planned for inclusion when they began care with a WVU HTC–affiliated hematologist or after discharge from their index hospitalization if not previously active with the WVU HTC. An ER visit resulting in hospitalization was considered 1 hospitalization event. Hospitalizations or ER visits occurring before HTC care were not included for analysis. Patients were censored when they established care with another HTC or died. Patients who were nonadherent to therapy or follow-up were included in all analyses to minimize bias. Classification of care episodes as preventable or nonpreventable was done blinded to episode date in the final analysis to minimize bias.

2.2 | Measure

Patient care experiences and needs were explored from the 2014 and 2017 National HTC Patient Satisfaction Surveys for our center, direct patient engagement in HTC clinic on October 17 and November 21, 2019 (routine medical history with review of therapy), and a town-hall type discussion at the 2019 West Virginia NBDF chapter meeting (November 16, 2019, Bridgeport, West Virginia). Needs assessment identified the following domains: timely appointments, improved communication with the HTC, improved control of bleeds, coordinating surgical and obstetric care, obtaining dental care, and inconvenience of clotting factor concentrate (CFC) prophylaxis. An initial 3-year retrospective analysis was done of hospitalizations and ER visits occurring in persons with hemophilia A, hemophilia B, and von Willebrand disease treated at the HTC to determine reasons for care. Causes of preventable visits were assessed with a Pareto chart to prioritize areas for intervention (Supplementary Methods) [12].

2.3 | Analyze

Reasons for PHER were analyzed with an event and causal factor analysis using an Ishikawa diagram, and the individual goals of the "Goal 100—Goal 0" framework (Supplementary Table S1) were derived [12]. Secondary outcomes (secondary measures) were CFC cost due to PHER, number of urgent management requests, proportion of persons with severe hemophilia A and B using prophylaxis, proportion of patients enrolled in the electronic patient portal, and proportion of patients with a primary care provider. Prespecified outcome success (tests of change) was defined as a 50% reduction in PHER and a statistically significant reduction in the proportion of patients with a preventable bleeding visit. Prespecified secondary outcome success was defined as 75% of patients enrolled for use of the electronic patient portal, 75% of patients having a primary care provider, and 90% of persons with severe hemophilia using prophylaxis.

2.4 | Improve

The medical intervention (change) was the implementation of a physician-administered checklist (Supplementary Methods), timely return of patient inquiries, and dedicated reserved physician time for acute management. Details are listed in Supplementary Methods, but these changes impacted routine patient care, communication, and clinical operation priorities. The checklist not only included the specific goals of "Goal 100—Goal 0" developed in the analysis phase but also included other guideline-recommended care. Patient messages were evaluated within 1 hour and assessed to be urgent or nonurgent at the discretion of the hemophilia clinician. Urgent matters were addressed in real time, and regularly scheduled clinical duties were interrupted for this to occur. Nonurgent matters were addressed as soon as able without workflow interruption. If patient assessment was needed, the next available opportunity was used, such as the reserved available time on Thursdays when no regular patient care duties were scheduled.

2.5 | Control

PHER was assessed by retrospective analysis every 6 months or when staff learned of a new PHER event. At the end of the intervention, the full retrospective analysis was conducted as planned.

2.6 | Final retrospective analysis

A separate retrospective chart review was conducted of patients treated at the WVU HTC to assess outcomes after QI intervention. The inclusion criteria and exclusion criteria are listed above under Define. The prespecified time periods for analysis were December 15, 2016, to December 15, 2019, for baseline cohort and December 16, 2019, to January 1, 2023, for intervention cohort; the program was terminated early due to resource limitations, and the period of active intervention ended July 22, 2022, the time of last follow-up reported. The project was approved by the WVU Institutional Review Board. This study is presented following Strengthening the Reporting of Observational Studies in Epidemiology guidelines [14]. Detailed statistical methods are found in Supplementary Methods.

Facility CFC cost and healthcare charges were determined from administrative billing data in the baseline and intervention cohorts for Cost of Quality (COQ) analysis. CFC cost was computed from the 2022 institutional acquisition costs for factor (F)VIII CFC (Kogenate, Bayer Corp and Humate-P, CSL Behring LLC), FIX CFC (Benefix, Wyeth Pharmaceuticals LLC), von Willebrand CFC (Humate-P and Vonvendi, Baxalta Inc), and FVIII with inhibitor CFC (Novo7, Novo Nordisk Inc). Annualized care episodes, charges, and costs were computed. COQ metrics were computed based on differential costs or charges between the baseline and intervention cohorts; cost savings for CFC and healthcare charges were computed and reported as per patient per year values. The proportion of patients with PHER was the planned outcome a priori; however, the analysis of hospitalization

alone and ER visits alone was a post hoc modification of this outcome. Other outcomes added post hoc were telemedicine utilization, visit cancellation or no-show, adherence to regular follow-up (reported as 2 HTC visits in 3 years), care management outside of visit, patient-reported reasons for nonadherence to CFC, and patient-reported satisfaction with emicizumab.

3 | RESULTS

Of the 115 patients assessed for eligibility, 88 patients were included. Twenty-seven patients were excluded for acquired bleeding disorder diagnosis (acquired hemophilia or acquired von Willebrand disease, *n* = 4) or under the care of pediatrics (*n* = 23). All 62 patients in the baseline cohort were included in the intervention cohort (Table 1). During the intervention period, 8 patients were censored, 5 due to death and 3 due to establishing care at other HTCs. Causes of death were cancer (*n* = 1), ischemic stroke with hemorrhage (*n* = 1), sepsis with advanced cirrhosis (*n* = 1), dementia (*n* = 1), and myocardial infarction (*n* = 1). Medical comorbidities complicating bleeding disorder management were common, such as obesity, cirrhosis, dementia, and active cancer.

Of all HTC patients, 96.5% (85/88) had follow-up visits scheduled during the intervention period (Supplementary Table S2). Of the 3 patients who did not, 2 were nonadherent to visits immediately before the intervention, and 1 additional patient died before a visit was scheduled. HTC patients had high rates of patient-driven visit cancellations or no-show visits: of 330 visits scheduled, only 182 were attended (55.2% attendance). Telemedicine visits were utilized in 15.3% of patients who identified physical impairment, financial barriers, or logistical barriers to attending in person. Telemedicine used 11 phone visits and 8 video visits; 1 video visit encounter was done via the Doximity Dialer application (Doximitry Inc) due to Epic technical difficulties. Nonexclusive reasons for use of telemedicine services in 12/86 patients were: geographic distance/travel (*n* = 8), newborn care and travel burden (n = 2), medical comorbidity (*n* = 3), limited time off work independent of travel (*n* = 3). It was standard procedure to offer travel, meal, and hotel assistance to patients to minimize costs of attaining HTC visits before and during the intervention.

During the intervention period, 135 urgent management events occurred, and 71.6% of patients had at least 1 urgent management event (median, 2; mean, 2.1; range, 1-10) (Supplementary Table S2). Procedures (43.2%) and bleeding (28.4%) were the 2 most common reasons for urgent management. Of the urgent procedures, dental extraction was the most common class. The majority of patients (93.2%) utilized at least 1 management episode outside of a clinic visit (median, 17; range, 1-88). With 68,556 patient-days of follow-up, the 1739 management episodes yielded an annualized average of 9.3 non–visit-based management episodes per patient per year. The annualized average number of urgent management episodes per patient per year was 0.72.

Nonpreventable hospitalizations and ER visits for bleeding were similar between baseline and intervention periods (Table 2). High-risk traumas included motor vehicle accidents, falls (with or without orthopedic fractures), chainsaw trauma, and physical assault. Two nonpreventable hospitalizations for bleeding during the intervention were due to COVID-19 infection resulting in bleeding (pulmonary hemorrhage in a person with severe hemophilia and metastatic cancer; and muscle hematoma from muscle strain in a person with moderate hemophilia and impaired mobility). The proportion of patients with nonpreventable bleeding was unchanged between the intervention and baseline periods (95% CI, −0.145 to 0.105) (Table 3).

There were 16 preventable hospitalizations and 22 preventable ER visits in the baseline period (Table 2). The majority of bleeding visits were in persons with severe hemophilia unable to self-treat from nonadherence to factor or who had run out of factor (*n* = 23), followed by persons with severe hemophilia who had factor but needed guidance on therapy (*n* = 6) and persons with nonsevere hemophilia who were unable to self-treat (*n* = 5). Preventable bleeding charges were $2,689,278 in the baseline period, and the average annualized charge for preventable bleeding was $15,510 per patient per year. Preventable bleeding episodes were treated with 893,000 mcg of Novo7, 114,478 units of Kogenate, 2217 units of Vonvendi, and 14,273 units of Benefix. Total CFC cost to treat preventable bleeding episodes was $2,046,047.38, with an annualized CFC cost of $11,800.33 per patient per year.

During the intervention, there were 2 preventable hospitalizations and 4 preventable ER visits.

Hospitalizations occurred in persons with severe hemophilia unable to self-treat from nonadherence to factor or who had run out of factor (*n* = 2). ER visits occurred in persons with severe hemophilia unable to treat due to running out of factor (*n* = 2) and others unable to self-treat (*n* = 2). Preventable bleeding charges were $341,812.98 in the intervention period, and the average annualized charge was $1819.85 per patient per year. Preventable bleeding episodes were treated with 84,724 units of Kogenate and 20,709 units of Benefix. CFC cost to treat preventable bleeding episodes was $120,250.26. The annualized CFC cost of preventable bleeding was $640.23 per patient per year, a 94.5% reduction from the baseline period.

From the annualized charges before and during intervention, the intervention was associated with a $1.2 million yearly savings in healthcare charges for preventable bleeds and a health system CFC acquisition cost savings of $982,088 yearly (Table 2). The proportion of patients with PHER was significantly reduced during the intervention (Table 3), from 0.24 to 0.05 (95% CI, 0.074-0.306). Both hospitalization (95% CI, 0.021-0.199) and ER visit (95% CI, 0.056-0.264) were each significantly reduced. The relative risk reduction for PHER was 85.4% during the intervention, with an 88.4% reduction for hospitalization and 83.2% reduction for ER visit components, and all met the prespecified outcome criteria for intervention success.

The primary outcome of PHER was significantly reduced during the intervention at the patient level (Kaplan–Meier log-rank *P* = .0082; Figure). Since the largest patient group was persons with hemophilia A, a post hoc subgroup analysis of persons with hemophilia A was conducted, and the reductions in PHER were significant in this group (*P* = .0254).

Patient attainment of an active primary care physician increased from the baseline 69.4% to 86.4% during intervention (95% CI,

TABLE 1 Demographic characteristics.

Demographic characteristics	Baseline (December 15, 2016, to December 15, 2019)		Intervention (December 16, 2019, to July 22, 2022)	
	n/N (%)	Median (range)	*n/N* (%)	Median (range)
Age (y)	62/62 (100)	39.5 (18-80)	88/88 (100)	42.5 (21-81)
Sex, male	47/62 (75.8)	-	60/88 (68.2)	-
Follow-up (d)	63,287	1095 (53-1095)	68,556	950 (16-950)
Race				
White	59/62 (95.2)	-	85/88 (96.6)	-
Black	1/62 (1.6)	-	1/88 (1.1)	-
Hispanic	2/62 (3.2)	-	2/88 (2.3)	-
	n/N	%	*n/N*	%
Active cancer	2/62	3.2%	5/88	5.7%
Dementia	3/62	4.8%	4/88	4.5%
Cirrhosis	4/62	6.5%	5/88	5.7%
BMI >30	33/62	53.2%	46/88	52.3%
Hemophilia A	33/62	53.2%	42/88	47.7%
Congenital hemophilia A with inhibitor	2/62	3.2%	3/88	3.4%
Hemophilia B	12/62	19.4%	15/88	17.0%
VWD	8/62	12.9%	13/88	14.8%
Platelet disorders	3/62	4.8%	3/88	3.4%
Ehlers–Danlos syndrome	1/62	1.6%	5/88	5.7%
BDUC	2/62	3.2%	5/88	5.7%
Factor XI	1/62	1.6%	3/88	3.4%
Factor X	1/62	1.6%	1/88	1.1%
Niemann–Pick disease[a]	1/62	1.6%	1/88	1.1%

BDUC, bleeding disorder unknown cause; BMI, body mass index; VWD, von Willebrand disease.
[a]Niemann–Pick disease is a congenital hematologic disorder that can cause bleeding, and this patient required Hemophilia Treatment Center care for bleeding.

0.0348-0.305; Table 4). Similarly, patient enrollment in the electronic patient portal increased from 53.2% to 83% (95% CI, 0.151-0.445). Both met the prespecified criteria for intervention success. During the intervention, 62.5% of patients had a change of outpatient therapy (Table 4; Supplementary Table S3). Of note, shortly after the intervention period started, nasal desmopressin (DDAVP; Stimate [CSL Behring LLC]) was recalled on July 21, 2020, and was not available for the remainder of the intervention; use of intravenous DDAVP due to unavailability of nasal DDAVP was not considered a change of therapy.

All persons with severe hemophilia A or B were prescribed prophylaxis and were using prophylaxis at the end of the intervention (58.8% vs 100%; 95% CI, 0.178-0.646; Table 4), meeting the prespecified criteria for intervention success. Although Table 2 shows preventable bleeding in this patient group, the timing of prophylaxis initiation or therapy changes usually occurred at ambulatory clinic visits, which was not the same as the intervention start date. The most frequent changes to the existing therapeutic paradigms were the use of on-demand antifibrinolytics and the adoption of emicizumab prophylaxis in persons with hemophilia A (Table 4, Supplementary Table S3). None of the patients who changed to emicizumab therapy desired to change back to CFC prophylaxis. All 19 patients who used emicizumab reported improved ease of use compared with CFC, and 18 of 19 reported subjective improved bleeding frequency, with 1 of 19 reporting no change in subjective bleed frequency. Using 2 HTC visits over 3 years as a metric of clinical visit adherence, before the intervention, 71% of patients were adherent, and after intervention, 73.9% were adherent (Table 4).

Of the 7 of 17 persons with severe hemophilia who were not using prophylaxis in the baseline cohort, nonexclusive reasons/barriers were incarceration (n = 2), substance abuse (n = 2), nonadherence to HTC visits (n = 4), burden of infusion (n = 3), identification of severe hemophilia by chromogenic assay (n = 2), cost (n = 1). Two of the 17 patients characterized as adherent to prophylaxis in the baseline

TABLE 2 Visits, costs, and savings.

Outcome measure	Baseline cohort	Intervention cohort	
Patients, *n*	62	88	
Follow-up (patient-days)	63,287	68,556	
Nonpreventable ER and hospitalization[a]	17	26	
High-risk trauma	10	11	
Bleeding despite home therapy	3	3	
Malignancy and bleeding	1	2	
Unexplained hematuria	1	1	
Postprocedural bleeding	1	1	
High-risk GI bleed (hematemesis and cirrhosis)	1	5	
Early pregnancy bleeding	0	3	
Preventable ER visits[a]	22	4	
Bleeding, SH without factor	13	2	
Bleeding, had factor	4	0	
Bleeding, without factor	4	2	
Infusion difficulty	1	0	
ER charges	$232,181.37	$29,538.25	
ER factor costs	$92,884.72	$11,712.60	
Preventable hospitalizations[a]	16	2	
Bleeding, SH without factor	10	2	
Bleeding, had factor	3	0	
Bleeding, without factor	3	0	
Inpatient charges	$2,457,097.42	$312,274.73	
Inpatient factor costs	$1,953,162.66	$108,537.66	
Total preventable charges	$2,689,278.79	$341,812.98	
Annualized charge (per patient per year)	$15,510.09	$1819.85	
Total preventable factor cost	$2,046,047.38	$120,250.26	
Annualized cost (per patient per year)	$11,800.33	$640.23	
	Projected	**Observed**	**Reduction**
Preventable yearly charges, *n* = 88	$1,364,887.49	$160,146.93	$1,204,740.56
Preventable yearly factor cost, *n* = 88	$1,038,428.77	$56,339.90	$982,088.87

ER, emergency room; RRR, relative risk reduction.ER, emergency room; GI, gastrointestinal; SH, severe hemophilia.
[a]Number of visits.

cohort were partially adherent; reasons for partial adherence were nonadherence to visits (*n* = 1), burden of infusions (*n* = 1), cost (*n* = 1), and insurance problems (*n* = 1).

4 | DISCUSSION

Bleeding in persons with hemophilia and other CBDs can be frequent and can increase care utilization, morbidity, and mortality [15,16]. Although some bleeding episodes require hospitalization or ER care for management, many bleeds can be managed in the ambulatory setting or prevented by use of prophylaxis. Here, we report our prospective ambulatory QI strategy for patients with bleeding disorders that successfully reduced hospitalizations and ER visits for preventable bleeding and produced substantial cost savings for CFC across the health system.

Patient satisfaction and communication with the care team are important for adherence [17,18]. The use of prophylaxis has been shown to reduce bleeding events while improving quality of life in persons with severe hemophilia [15,19–21]. However, therapy is

TABLE 3 Preventable and nonpreventable visits.

Outcome measure	Baseline cohort	Intervention cohort	95% CI	*P* value
Proportion of patients with nonpreventable visit	0.19	0.17	−0.145 to 0.105	.753
Proportion of patients with preventable				
ER visit or hospitalization	0.24	0.05	0.074 to 0.306	.0006
ER visit	0.19	0.03	0.056 to 0.264	.0011
Hospitalization	0.13	0.02	0.021 to 0.199	.0075
Annualized preventable visit/patient			**RRR**	
ER or hospitalization	0.219	0.032	85.4%	
ER	0.127	0.021	83.2%	
Hospitalization	0.092	0.011	88.5%	

ER, emergency room; RRR, relative risk reduction.ER, emergency room; GI, gastrointestinal; SH, severe hemophilia.

expensive, burdensome, and many barriers exist to prophylaxis use or on-demand therapy adherence [22,23]. We found that the majority of preventable visits for bleeding in our population occurred in persons with severe hemophilia who were nonadherent to prophylaxis. We improved use of prophylaxis by identifying and addressing individual barriers to use, mostly not having access to prophylaxis, and the improved convenience of subcutaneous emicizumab. Hospital CFC acquisition costs were dramatically reduced by targeting PHER. Patient attendance at routine visits was low, and the intervention required frequent physician management outside of scheduled clinical visits. Even during the intervention, nonadherence to HTC visits was high. This required multiple reschedules, HTC nurse calls, and reminder letters per usual standard practice, and some patients would only follow up when insurance denied medication refills due to lack of medical documentation. The effectiveness and ease of use of emicizumab appeared to motivate return visits for patients previously not regularly using prophylaxis. Physician management was frequent, time-consuming, and not supported in a relative-value unit ambulatory clinical environment.

Discussions with patients, advocacy groups, and staff were vital to the QI effort. The project did encounter obstacles beyond time utilization. Some patients were unable to communicate via the electronic portal due to medical comorbidity, poverty, or technological limitations. Although we obtained a direct phone line for patients to access our hemophilia specialty care nurse and improve communication (as strongly desired by patients and caregivers), this occurred the month the intervention closed and, as a result, would not have influenced the outcomes reported here. Our project addressed many contributors to bleeds simultaneously (prophylaxis, communication, and adherence barriers), and it was not possible to objectively determine the efficacy of each component. However, in our opinion, the primary driver of reduced preventable bleeds was the expanded use of emicizumab prophylaxis. The subcutaneous route of administration was strongly preferred by patients, and patients previously adherent to CFC prophylaxis reported improved bleed control and greater satisfaction with emicizumab.

In the United States, revenue to support the HTC mission can come from the 340b mechanism, wherein a fraction of CFC or medication (emicizumab) sales to HTC patients through a contract pharmacy, minus fees and operational costs, is available to the HTC.

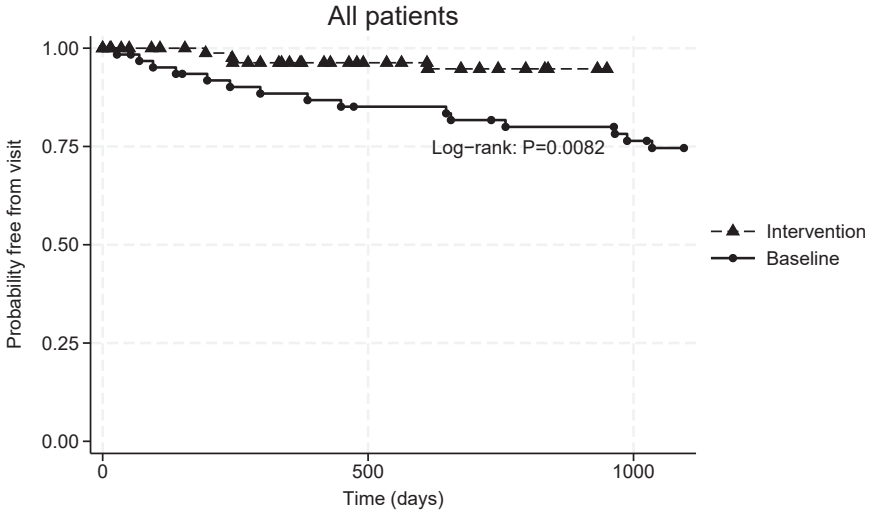

FIGURE Preventable hospitalizations and emergency room visits for bleeding for all patients with congenital bleeding disorders.

TABLE 4 Patient care changes from intervention.

	Baseline cohort		Intervention cohort			
Outcome measure	***n/N***	**%**	***n/N***	**%**	**95% CI**	***P* value**
Primary care provider (active)	43/62	69.4	76/88	86.4	0.0348 to 0.305	.012
Enrollment in patient portal	33/62	53.2	73/88	83.0	0.151 to 0.445	.001
Change in hemostatic therapy	Not assessed		55/88	62.5	N/A	N/A
Prophylaxis for severe hemophilia	10/17	58.8	18/18	100.0	0.178 to 0.646	.0027
Emicizumab in hemophilia A	1/33	3.0	19/42	45.2	0.260 to 0.583	<.0001
Clinical follow-up adherence (2 visit in 3 y)	44/62	71.0	65/88	73.9	−0.117 to 0.175	.696

N/A, not applicable.

Local state Medicare/Medicaid programs (West Virginia, Ohio, Pennsylvania, and Maryland) do not participate in our 340b program. Because of administrative reasons, our 340b program was revenue-negative before the QI project started and its ability to support patient care was limited. The increased use of emicizumab expected in the project would have exacerbated this situation. In order for the intervention to achieve its goal of improving care while being cost-saving to the institution, other administrative changes were required that are outside the scope of this work, but these are relevant for other centers contemplating or undergoing similar changes of therapy. After these measures, 340b program patient utilization, revenue, and net income increased and surpassed prior metrics. QI can have an additional cost (COQ), where changes to improve quality incur increased costs before the savings become realized [13]. This project did not increase cost or reduce revenue. However, it would have if our contract pharmacy was more widely used by patients in the early periods of the program before the administrative changes. With minimal resources, we were able to improve care quality, save costs on COQ analysis, and improve viability of the ambulatory HTC program to support patient care.

Our study has important limitations. First, we were not able to quantify annualized bleed rates at the individual level due to the nature of the study [24]. Second, the best practices and systems we implemented could already be standard practices at some centers or not be possible at other centers in low-resource settings. Third, we prevented hospitalizations and ER visits by changing outpatient therapy; a concern was that this would reduce hospital revenue or 340b program income, particularly from the expanded use of emicizumab. Although 42% of our patients had Medicaid or Medicare in the baseline group, this increased to 60% of those with preventable bleeding (data not shown). The majority of our observed healthcare costs were from CFC, as noted elsewhere [1], but reimbursement was often well below the CFC acquisition cost, especially for Medicaid or Medicare patients. For example, in 1 hospitalization, institutional CFC cost was $96,716.88 and payment was $9214.75. As such, preventable bleeding episodes were markedly revenue-negative for the institution, and preventing them was cost-saving. In addition to cost savings from prevented bleeds, the HTC 340b program yearly revenues from the intervention demonstrated persistent and marked increases from these and other HTC administrative process improvements, from $1.69 million before intervention to $3.93 million in the last year of the intervention. However, maintaining positive net revenue required contracting changes, and this is noteworthy for other centers. Finally, and most applicably, the physician effort and frequent engagement required for the intervention were not supported in a relative-value unit clinical environment, and thus, the project terminated early. An ultimately revenue positive solution at the institutional level would be to utilize the 340b revenues from the HTC factor replacement program to offset staff effort required for the quality program.

5 | CONCLUSIONS

Improving patient outcomes and reducing institutional costs for patients with bleeding disorders can be attained with goal-directed best practices based outpatient management. Importantly, such therapy changes did not reduce HTC revenue from the 340b program, but this required other administrative changes to ensure viability. Using a QI approach to address barriers to care can improve bleeding outcomes at other centers. However, the resources and collaboration necessary to undertake and continue such endeavors are crucial and require continual support.

ACKNOWLEDGMENTS

The authors wish to thank Hemophilia Treatment Center patients and families for valuable input and specifically Fernando Andrzejevski and Chelsea Hilti of the West Virginia chapter of the National Bleeding Disorders Foundation for helpful collaborations and insight. We thank Christine Troy of West Virginia University (WVU) perioperative services for perioperative process improvement collaborations and Megan Varvoutis from WVU Maternal Fetal Medicine for women's health collaborations. We thank Jim Francher, Senior Financial Analyst of the WVU Cancer Center, for assistance in 340b program financial reporting and analysis.

FUNDING

This project was accomplished without public grant or private industry support.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of West Virginia University (2209646932). University data safety and security policies were adhered to during the work. Informed consent was waived by the Institutional Review Board of West Virginia University as patient data are reported in aggregate and anonymized.

AUTHOR CONTRIBUTIONS

S.A.M., S.E.W., L.J.M., and A.D.S. contributed to study conceptualization, design, and implementation. S.A.M. and S.E.W. were involved in data acquisition. S.A.M. conducted data analysis. S.A.M., L.J.M., and A.D.S. conducted data interpretation. All authors were involved in writing, critical review, and approving the final version of the manuscript.

RELATIONSHIP DISCLOSURE

S.A.M. reports previous consultancy for Genentech, Sanofi, and the American Society of Hematology. S.E.W., L.J.M., and A.D.S. report no relevant financial conflicts of interest.

DATA AVAILABILITY

The data that support the findings of this study are available in the main figures and in the supplementary material of this article.

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SUPPLEMENTARY MATERIAL

The online version contains supplementary material available at https://doi.org/10.1016/j.rpth.2024.102401