#### ORIGINAL ARTICLE

The Practice of Emergency Medicine

# Rapid recognition and optimal management of hemophilia in the emergency department: A quality improvement project

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Funding information Genentech, Grant/Award Number: G-73527

#### Abstract

**Objectives:** This study aimed to assess the effectiveness of a continuous quality improvement initiative at the University of Florida Health Physicians practice in reducing the time to administer factor replacement therapy (FRT) for hemophilia patients presenting with bleeding in the emergency department (ED).

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**Methods:** The study, a quasi-experimental, interventional design, was conducted between January 2020 and January 2023. The intervention, implemented in September 2021, involved training ED physicians, creating a specialized medication order set within the electronic health record (EHR), and a rapid triage system. The effectiveness was measured by comparing the time from ED arrival to factor administration before and after the intervention and benchmarking it against the National Bleeding Disorders Foundation's Medical and Scientific Advisory Council (MASAC)-recommended 1-hour timeline for factor administration. An interrupted time series (ITS) analysis with a generalized least squares model assessed the intervention's impact.

**Results:** A total of 43 ED visits (22 pre-intervention and 21 post-intervention) were recorded. Post-intervention, the average time from ED arrival to factor administration decreased from 5.63 to 3.15 hours. There was no significant increase (27% vs. 29%) in the patients receiving factor within 1-hour of ED arrival. The ITS analysis predicted a 20-hour reduction in the average quarterly time to administer factor by the end of the study, an 84% decrease.

**Conclusions:** The quality improvement program decreased the time to administer FRT for patients with hemophilia in the ED. However, the majority of patients did not achieve the 1-hour MASAC-recommended timeline for factor administration after ED arrival.

#### KEYWORDS

bleeding, emergency department, factor replacement therapy, hemophilia, quality improvement

Supervising Editor: Marna Rayl Greenberg, DO, MPH

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#### 1 | INTRODUCTION

#### 1.1 | Background

Hemophilia is a rare inherited bleeding disorder characterized by a deficiency in coagulation factor VIII (hemophilia A) or factor IX (hemophilia B). In the United States, between 2012 and 2018, the estimated prevalence of hemophilia A and B was 12 and 3.7 per 100,000 males, respectively.<sup>1</sup> Beyond its clinical implications, hemophilia imposes a significant economic burden on healthcare systems, as well as on patients and caregivers.<sup>2,3</sup> The cost of treating severe hemophilia, the most prevalent form, can vary widely, ranging from an average of \$300,000 annually to over \$1 million for those who develop resistance to clotting factors.<sup>3–6</sup>

Patients diagnosed with hemophilia are at higher risk of bleeding, which can be spontaneous or result from injury, or both, primarily in joints and soft tissues, some of which may be life threatening. Over recent decades, clotting factor replacement therapies have been the cornerstone of bleeding prevention and treatment.<sup>7,8</sup> Although most bleeding episodes can be managed at-home or in an outpatient setting, some require urgent medical attention, including emergency department (ED) visits. These patients commonly present at the ED with acute bleeding episodes, and in many cases, a new diagnosis of a bleeding disorder may be made during the ED visit.<sup>9,10</sup> However, ED providers may face challenges in providing optimal care for hemophilia patients, such as lack of familiarity with the disease, limited access to specialized resources, and time pressure.<sup>9</sup>

#### 1.2 | Importance

Effective management of patients with hemophilia in the ED requires a multidisciplinary approach involving healthcare professionals trained in the management of bleeding disorders.<sup>11</sup> It is crucial that ED staff be aware of the patient's medical history, including their hemophilia diagnosis, the severity of their condition, and their current treatment regimen. Prompt administration of replacement factors is critical to prevent morbidity and mortality.<sup>12-17</sup> In line with this, the National Bleeding Disorders Foundation's Medical and Scientific Advisory Council (MASAC) recommends that hemophilia patients receive replacement therapy within 1 h of arrival at the ED.<sup>18</sup> Additionally, MASAC recommends that ED staff use factor assays to determine the patient's current factor levels and adjust the replacement therapy dosage accordingly.<sup>18</sup>

#### **1.3** Goals of this investigation

To improve the health outcomes of hemophilia patients presenting to the ED, a system-wide quality improvement (QI) initiative was launched in September 2021 to streamline the ordering and administration of replacement therapy. The goal of this initiative was to reduce the time between a patient's arrival at the ED and the ordering and

#### **The Bottom Line**

Emergency departments (EDs) face challenges in promptly administering factor replacement therapy to patients with hemophilia presenting with bleeding. Through a multifaceted quality improvement initiative at an academic institution, the time from patient ED arrival to administration of factor decreased from 5.63 to 3.15 hours. Despite the reduction, the percentage of patients treated within 1 hour remained almost unchanged (27%–29%).

administration of replacement factor. The QI initiative included several strategies, including the implementation of protocols and guidelines for the management of hemophilia patients in the ED. The initiative also involved education and training for ED staff on the recognition of bleeding episodes and the appropriate administration of replacement factors. This training was provided to all ED staff, including physicians, nurses, and other healthcare professionals involved in their care.

This paper aims to present evidence from the QI initiative relating to strategies to reduce the time from patients' ED arrival to when factor is ordered and administered.

#### 2 | METHODS

#### 2.1 Study design

This study is a quasi-experimental interventional (O-X-O) design using the electronic health records (EHRs) of ED visits between January 2020 and January 2023. We used the Standards for Quality Improvement Reporting Excellence (SQUIRE) 2.0 guidelines to guide the planning, evaluation, and reporting of this QI initiative.<sup>19</sup>

#### 2.2 Setting

The Study was conducted in 4 ED sites (three adult and one pediatric) at the University of Florida Health Physicians (UFHP) practice, an academic public institution located in Gainesville, Florida. The protocol received an Exempt Status from the IRB.

#### 2.3 | Selection of subjects

The study population included all patients with hemophilia A and B who presented with bleeding in the ED at UFHP and received the first dose of factor replacement therapy while in the ED. This included four ED sites. Specifically, we included patients who had a visit at any of the four sites between January 2020 and January 2023. However, we excluded patients with hemophilia who were encountered in the ED but did not receive any factor replacement therapy while there. This was because they were admitted to the ED for other medical conditions that were unrelated to bleeding, and therefore were not relevant to our study population.

#### 2.4 | Interventions

In September 2021, all physicians in the ED at UFHP committed to a system-wide process improvement project. The project focused on three areas: professional training, process redesign, and technology enhancement. It involved training ED physicians and staff at the four sites and creating a medication order set within the EHR.

#### 2.4.1 | Physician training

The training sessions for managing hemophilia patients in the ED were led by two hematologists (T.W. and A.R.) and targeted ED physicians and staff who may encounter hemophilia patients in the course of their work. These sessions were mandatory for all ED staff. The sessions can be broadly grouped into three components: didactic lectures, case-based discussions, and hands-on exercises.

- Didactic lectures: The didactic lectures provided an overview of hemophilia, its types, its clinical manifestations, as well as the MASAC guidelines for ED management of hemophilia patients. These guidelines cover indications for factor replacement therapy, assessment, diagnostic studies, and treatment.
- 2. Case-based discussions: The case studies illustrated common scenarios and challenges encountered in managing both pediatric and adult hemophilia patients. The case-based discussions were sessions where participants would discuss hypothetical or actual cases of hemophilia patients presenting to the ED. The discussions focused on differential diagnosis, identifying sources of bleeding, making treatment decisions, and effective communication with patients, families, and hematologists. These sessions were facilitated by experts and supported by a structured set of case scenarios and discussion questions (Supporting Information Appendix II).
- 3. Hands-on exercises: The exercises provided participants with practical experience on utilizing the factor concentrate order set and administering factor replacement therapy. These were one-time sessions at each of the ED sites, led by the hematologists, and lasting 1–2 h. These simulation exercises used visual aid examples from the EHR platform to demonstrate how to calculate factor dose and order factor concentrate, as well as providing guidance on additional treatment decisions, such as when to request a hematology consult.

#### 2.4.2 | EHR order sets

The second major intervention was the development of an antihemophilic factor replacement order set within the EHR. Order sets allow

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for the grouping of orders often placed for a similar purpose. After the implementation of the order set, it was not possible to use any alternative methods for factor replacement orders other than the new EHR order set. In this particular intervention, the order set included the following:

- 1. Order sets were triggered within the EHR if hemophilia factor was ordered during an ED or inpatient encounter.
- 2. Four order sets were created. Two were for the initial or emergent treatment of bleeding of hemophilia A and hemophilia B. The others were for the continuation of treatment of bleeding.
- A table for the target of dosing based upon bleeding severity categories of minor, moderate, and major with an example calculation was included in each set of orders.
- 4. Categorical orders for hospital formulary supply, patient supply, or special exemption products.
- Optional laboratory testing was allowed with a reminder that this did not delay treatment of suspected bleeding.
- 6. A prompt for referral to a hematology service was also included.

#### 2.5 | Measures/outcomes

The effectiveness of the intervention was measured using time-based outcomes by comparing pre- and postintervention time intervals. The preintervention phase extended from January 2020 to September 2021. After the intervention was implemented in September 2021, the postintervention phase was initiated and extended through to January 2023. The primary goal was to reduce the time required to administer factor replacement therapy after a patient's arrival at the ED. In addition, to assess the impact of different components of the intervention, the total time from patient arrival at the ED to factor administration was split into two parts: the time from ED arrival to placing the factor order and the time from placing the order to when it is actually administered. Hence, the project targeted three areas for improvement:

- The total time between a patient's ED arrival and when factor replacement therapy is administered.
- The time between a patient's ED arrival and when a factor replacement therapy order is placed.
- The time between when a factor replacement therapy is ordered and when it is actually administered.

In addition, the total time was compared against a recommended 1hour benchmark set by MASAC.

#### 2.6 | Data analysis

Patients' demographic variables within the study period were summarized using descriptive statistics. We conducted preintervention and postintervention analyses to assess the impact of the intervention. First, we compared patient demographic variables using the chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. Second, we created a raincloud plot and a boxplot to visualize and compare the postintervention distribution and the median (interquartile range) time between ED arrival to factor order, the time between ED arrival to factor administration, and the time between factor ordering and administration against the 1-hour benchmark recommended by MASAC. Third, we conducted an interrupted time series (ITS) analysis, a quasi-experimental study design. For this analysis, the quarterly mean of (1) time from ED arrival to factor replacement therapy administration, (2) time from ED arrival to factor replacement therapy order, and (3) time from order to administration was used. This analysis allowed us to measure the immediate impact (levels) and the rate of change over time (trends) in the timing of factor replacement therapy, utilizing multiple observations before and after the intervention.<sup>20-22</sup> We fit a generalized least squares model with a maximum likelihood estimation method to estimate changes in level and trend and to predict the impact of the intervention at the end of the study.23

#### 3 | RESULTS

Between January 2020 and January 2023, the four ED sites recorded 398,248 visits by 340,925 patients, with a mean of 1.17 ED visits per person. During this period, 192 visits were by 68 patients with hemophilia, with a mean of 2.82 ED visits per person. The prevalence of hemophilia among the ED visiting population was approximately 0.02%.

Of the 192 visits by patients with hemophilia. 67 received factor treatment. Of these 67 visits, 43 were patients with hemophilia receiving their first factor dose in the ED. The other 24 visits were by patients with hemophilia who came to the ED for various reasons and received their prophylactic factor doses, brought from home, while admitted as inpatients (Figure 1). Of the 43 visits by patients with hemophilia receiving their first factor dose during the ED visits, 22 occurred in the preintervention period and 21 occurred in the postintervention period, which began after September 2021. In the preintervention period (Table 1), the majority of patients were male (95.5%), White (72.7%), and not Hispanic (81.8%). Most (81.8%) had a Charlson Comorbidity Index less than two and have commercial health insurance (45.5%). The mean age was  $23.0 \pm 24.3$  years. Similarly, in the postintervention period (Table 1), the most common bleeding events included hemarthrosis, hematuria and hematemesis. However, there were more hemarthrosis postintervention compared to preintervention (Table 1).

After the intervention, the mean time from ED arrival to factor administration was reduced to 3.15 h (median: 2.62 h) from 5.63 h (median: 3.38 h). The average time from ED arrival to factor order was reduced to 2.05 h (median: 1.95 h) from a preintervention average of 3.77 h (median: 2.06 h) and the time from factor order to administration was reduced to an average of 1.10 h (median: 0.95 h) from 1.87 h (median: 1.15 h) (Table 2).

At the end of January 2023, the ITS analysis showed an immediate average reduction of 10.26 h in the time from ED arrival to factor administration and a quarterly decrease of 1.2 h. This resulted in a projected 20-h reduction (84% decrease) from what would have been expected without the intervention (Table 3; Supporting Information Appendices I and II).

## 3.1 Time between ED arrival and factor order and administration benchmarked against 1-h recommended by MASAC

When compared against the 1-h guideline recommended by MASAC, before the intervention, only 27% of patients received a factor within 1 h of arriving at the ED. After the intervention, this increased to 29%. Comparing the other time intervals against 1-h benchmark, preintervention, 32% of patients were ordered a factor within 1 hour of ED arrival, and 41% received it once it was ordered. However, after the intervention, the percentage of patients who were ordered factor within 1 hour of ED arrival increased to 43%, and the percentage of those who received factor within an hour after it was ordered increased to 67%. None of these increases in proportion are statistically significant (Figure 2a,b; Supporting Information Appendices III–V).

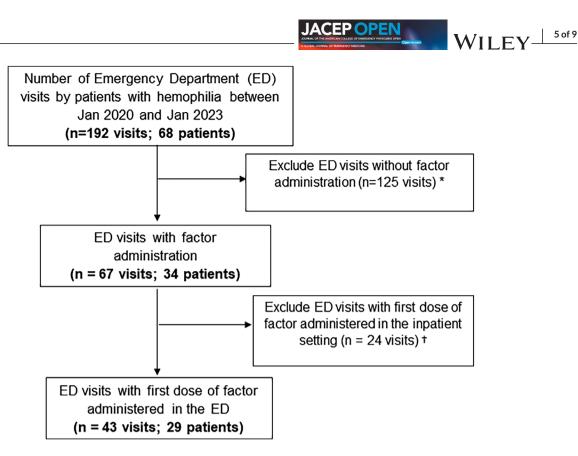
#### 4 | LIMITATIONS

A major limitation of this study was its small sample size (n = 43 visits) for hemophilia patients admitted to the ED with a bleed over a 3-year period. This is a common challenge in rare disease research and makes the estimates more susceptible to outliers and insufficiently powered to detect significant statistical differences. The absence of a control series in the ITS model, due to the lack of a suitable control, was another limitation. Although hemophilia is predominantly managed in outpatient settings and is a rare condition, replicating this study in other institutions would enhance its generalizability.

#### 5 | DISCUSSION

In this study involving all the emergency rooms at an academic institution, we evaluated the effectiveness of a multicomponent intervention targeted to reduce the time between ED arrival for bleeding and factor administration for patients with hemophilia and benchmarking on 1-h MASAC recommendation. The study analyzed (1) the total time from ED arrival to factor administration, (2) ED arrival to factor order, and (3) factor order to factor administration. Several other studies of QI in EDs deployed similar interventions and outcome measures used in this study.<sup>24-31</sup>

Each time interval improved from the preintervention baseline to the postintervention period. The total mean time from ED arrival to administration decreased by 2.48 h, mean time from ED arrival to fac-



**FIGURE 1** Study population flowchart. \*Emergency department (ED) visits for various reasons unrelated to bleeding and did not receive a factor in the ED or in the inpatient setting (for patients subsequently admitted). †ED visits by known patients with hemophilia who visited the ED for various reasons unrelated to immediate hemophilia crises and received their prophylactic factor doses, brought from home, while admitted as inpatients.

tor order decreased by 1.72 h, and from factor order to administration by 0.77 h. The ITS analysis showed an immediate drop and sustained downward trends in (1) time from ED arrival to factor replacement therapy administration, (2) time from ED arrival to factor replacement therapy ordering, and (3) time from order to administration from preto postintervention. While all intervals showed both immediate reduction and downward trend, only the total time (ED arrival to factor administration) was statistically significant. The time from ordering to administration showed marginal statistical significance, and the time from ED arrival to factor order showed no statistical difference between pre- and postintervention period.

The model predictions supported these findings. By the end of the study, the mean quarterly time from ED arrival to factor administration was expected to reduce by 18 h (84% reduction) compared to the scenario without the intervention. Additionally, the mean quarterly time from ED arrival to factor order was predicted to reduce by 9 h (80% reduction), and the time from factor order to administration by 10 h (88% reduction). These predictions illustrate the intervention's impact on reducing the time between patient's arrival in the ED and when factor replacement therapy is administered.

Although the intervention reduced the time to administer a factor after patient arrival, there was only a small increase (27% to 29%) in the proportion of patients receiving factor administration within 1 h of arrival, as recommended by MASAC. A similar study in the UK, examining the time to factor administration in the ED, found that out of 75 ED visits by hemophilia patients, only seven needed factor replacement therapy. Of these, only one case had a recorded administration time, with the factor being administered 17.25 h after arrival. None of these cases met the United Kingdom Hemophilia Centre Doctors Organization's recommendation of administering factor within 30 min of arrival at the ED.<sup>32</sup>

The total time from ED arrival to factor replacement was divided into two (ED arrival to factor order and order to administration) to help determine the most impactful component of the intervention and identify areas for improvement. The training of ED providers and process redesigns through the rapid triage was aimed at reducing the time from arrival to factor ordering. This approach centered on provider education, which included hematologist-led didactic lectures, case-based discussions, and hands-on exercises. The goal of this education was to increase awareness among ED physicians as well as improve their confidence and understanding of managing these patients. The other component of the intervention was EHR enhancement targeting the pharmacy and clinical staff, aimed at reducing the time from ordering to administration. A specialized order set for hemophilia factor products was integrated into the EHR, activated during ED or inpatient encounters. This set included dosing tables based on bleeding severity and options for hospital formulary supply or patient supply. It also allowed for optional laboratory tests, with a caution against treatment delays, and included a prompt for hematology service referral. The integration of provider education, EHR enhancements, and rapid triage proto**TABLE 1** Characteristics of patients with hemophilia that were administered factor in the emergency department.

| Patient characteristics                   | Level                         | Overall,<br>N = 43 | Preintervention,<br>N = 22 | Postintervention, $N = 21$ | p-Value |
|---|-------------------------------|--------------------|----------------------------|----------------------------|---------|
| Sex, n (%)                                | Female                        | 2 (4.7%)           | 1 (4.5%)                   | 1 (4.8%)                   | 1.000   |
|   | Male                          | 41 (95.3%)         | 21 (95.5%)                 | 20 (95.2%)                 |         |
| Age, mean (SD)                            |                               | 24.4 (22.0)        | 23.0 (24.3)                | 25.9 (19.8)                | 0.257   |
| Age group, n (%)                          | <18 years old                 | 15 (34.9%)         | 9 (40.9%)                  | 6 (28.6%)                  | 0.396   |
|   | ≥18 years old                 | 28 (65.1%)         | 13 (59.1%)                 | 15 (71.4%)                 |         |
| Race, n (%)                               | Black                         | 5 (11.6%)          | 2 (9.1%)                   | 3 (14.3%)                  | 0.569   |
|   | Undisclosed <sup>a</sup>      | 5 (11.6%)          | 4 (18.2%)                  | 1 (4.8%)                   |         |
|   | White                         | 33 (76.7%)         | 16 (72.7%)                 | 17 (81.0%)                 |         |
| Ethnicity, n (%)                          | Hispanic                      | 9 (20.9%)          | 4 (18.2%)                  | 5 (23.8%)                  | 0.721   |
|   | Not Hispanic                  | 34 (79.1%)         | 18 (81.8%)                 | 16 (76.2%)                 |         |
| Health insurance, n (%)                   | Commercial                    | 19 (44.2%)         | 10 (45.5%)                 | 9 (42.9%)                  | 0.182   |
|   | Medicaid                      | 9 (20.9%)          | 2 (9.1%)                   | 7 (33.3%)                  |         |
|   | Medicare                      | 5 (11.6%)          | 4 (18.2%)                  | 1 (4.8%)                   |         |
|   | Other                         | 5 (11.6%)          | 2 (9.1%)                   | 3 (14.3%)                  |         |
|   | Self-pay                      | 5 (11.6%)          | 4 (18.2%)                  | 1 (4.8%)                   |         |
| Bleeding event flag, n (%)                | 0                             | 28 (65.1%)         | 14 (63.6%)                 | 14 (66.7%)                 | 0.796   |
|   | 1-2                           | 12 (27.9%)         | 7 (31.8%)                  | 5 (23.8%)                  |         |
|   | 3-4                           | 3 (7.0%)           | 1 (4.6%)                   | 2 (9.5%)                   |         |
| Bleeding events description               | Abnormal vaginal bleeding     | 1 (5.9%)           | 1 (12.5%)                  | 0 (0.0%)                   | 0.672   |
|   | Cerebral hemorrhage           | 2 (11.8%)          | 2 (25.0%)                  | 0 (0.0%)                   |         |
|   | Epistaxis                     | 1 (5.9%)           | 0 (0.0%)                   | 1 (11.1%)                  |         |
|   | Hematemesis                   | 1 (5.9%)           | 1 (12.5%)                  | 0 (0.0%)                   |         |
|   | Hematuria                     | 3 (17.6%)          | 2 (25.0%)                  | 1 (11.1%)                  |         |
|   | Hemoperitoneum                | 1 (5.9%)           | 1 (12.5%)                  | 0 (0.0%)                   |         |
|   | Hemarthrosis                  | 5 (29.4%)          | 0 (0.0%)                   | 5 (55.6%)                  |         |
|   | Hemorrhage of anus and rectum | 1 (5.9)            | 0 (0.0%)                   | 1 (11.1%)                  |         |
|   | Hematoma of soft tissue       | 2 (11.8%)          | 1 (12.5%)                  | 1 (11.1%)                  |         |
| Resulted in hospitalization, <i>n</i> (%) | Yes                           | 25 (58.1%)         | 13 (59.1%)                 | 12 (57.1%)                 | 1.000   |
| Type of hemophilia, n (%)                 | Hemophilia A                  | 25 (58.1%)         | 12 (54.5%)                 | 13 (61.9%)                 | 0.625   |
|   | Hemophilia B                  | 18 (41.9%)         | 10 (45.5%)                 | 8 (38.1%)                  |         |
| Body mass index, n (%)                    | Below 18.5                    | 17 (39.5%)         | 9 (40.9%)                  | 8 (38.1%)                  | 0.252   |
|   | 18.5-24.9                     | 17 (39.5%          | 9 (40.9%)                  | 8 (38.1%)                  |         |
|   | 25.0-29.9                     | 5 (11.6%)          | 1 (4.5%)                   | 4 (19.0%)                  |         |
|   | 30.0-34.9                     | 2 (4.7%)           | 1 (4.5%)                   | 1 (4.8%)                   |         |
|   | 35.0-39.9                     | 2 (4.7%)           | 2 (9.1%)                   | 0 (0.00%)                  |         |
| Charlson comorbidity index,               | Mild (0-2)                    | 37 (86.0%)         | 18 (81.8%)                 | 19 (90.5%)                 | 0.798   |
| n (%)                                     | Moderate (3-4)                | 2 (4.7%)           | 1 (4.5%)                   | 1 (4.8%)                   |         |
|   | Severe (≥5)                   | 4 (9.3%)           | 3 (13.6%)                  | 1 (4.8%)                   |         |
| Type of factor administered,              | Hemophilic factor             | 40 (2.3%)          | 20 (4.5%)                  | 20 (0.00%)                 | 0.646   |
| n (%)                                     | Factor VIIa                   | 3 (46.5%)          | 2 (40.9%)                  | 1 (52.4%)                  |         |
| Hematology consult, n (%)                 | Yes                           | 17 (39.5%)         | 7 (31.8%)                  | 10 (47.6%)                 | 0.289   |
| Hematology note                           | Yes                           | 30 (69.8%)         | 14 (63.6%)                 | 16 (76.2%)                 | 0.370   |

<sup>a</sup>Undisclosed: patients refused to disclose their racial identity.

#### TABLE 2 Summary of time between emergency department arrival and factor order and administration pre- and post-intervention.

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|   | Preintervention  | Postintervention | <i>p</i> -Value |
|---|------------------|------------------|-----------------|
| ED arrival to factor administration (h)   |                  |                  |                 |
| Mean (SD)                                 | 5.63 (6.41)      | 3.15 (2.53)      | 0.1046          |
| Median (interquartile range (IQR))        | 3.38 (1.13-5.54) | 2.62 (0.90-4.52) |                 |
| Min-max                                   | 0.47-23.25       | 0.00-9.20        |                 |
| 95% Confidence interval                   | (2.79, 8.47)     | (2.00, 4.30)     |                 |
| ED arrival to factor order (h)            |                  |                  |                 |
| Mean (SD)                                 | 3.77 (5.21)      | 2.05 (2.04)      | 0.1765          |
| Median (IQR)                              | 2.06 (0.62-4.03) | 1.95 (0.22-3.30) |                 |
| Min-max                                   | 0.14-20.88       | 0.00-7.00        |                 |
| 95% Confidence interval                   | (1.46, 6.08)     | (1.16, 3.02)     |                 |
| Factor order to factor administration (h) |                  |                  |                 |
| Mean (SD)                                 | 1.87 (3.38)      | 1.10 (0.61)      | 0.3310          |
| Median (IQR)                              | 1.15 (0.75–1.69) | 0.95 (0.67–1.40) |                 |
| Min-max                                   | 0.25-16.77       | 0.28-2.43        |                 |
| 95% Confidence interval                   | (0.37, 3.37)     | (0.85, 1.41)     |                 |

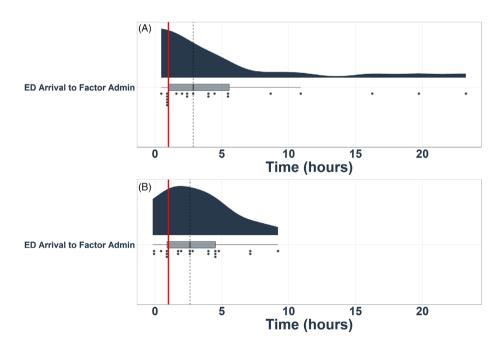
#### **TABLE 3** Summary of interrupted time series analysis.

| Timing                                | Level change <sup>a</sup> (SE) | p-Value | Trend change <sup>b</sup> (SE) | p-Value |
|---------------------------------------|--------------------------------|---------|--------------------------------|---------|
| ED arrival to factor administration   | -10.26 (2.90)                  | 0.0095  | -1.20 (0.90)                   | 0.0626  |
| ED arrival to factor order            | -5.20 (3.67)                   | 0.1997  | -0.85 (1.14)                   | 0.4805  |
| Factor order to factor administration | -5.05 (2.36)                   | 0.0699  | -1.13 (1.54)                   | 0.1682  |

Abbreviation: SE, standard error.

<sup>a</sup>The immediate effect of an intervention.

<sup>b</sup>The ongoing rate of change over time after the intervention.



**FIGURE 2** A raincloud plot and a boxplot showing the (a) preintervention and (b) postintervention distribution of the time between emergency department (ED) arrival to factor administration against the 1-h benchmark recommended by Medical and Scientific Advisory Council (MASAC) (red line). The raincloud plot combines the advantages of boxplots and kernel density plots. It displays the distribution of data using a boxplot and also overlays a kernel density plot to showcase the shape of the distribution more effectively. The dots in the plot represent each patient with hemophilia's visit to the ED, while the boxplot displays the median, interquartile range, and outliers of the distribution.

cols represents an innovative approach to emergency hemophilia care. Prior studies have demonstrated that EHR enhancements and process redesign can significantly improve ED efficiency.<sup>33–35</sup> While both time intervals decreased, there remains potential for further reduction in time to factor order and administration. We have observed a sustained improvement in time to factor administration 1 year later following a one-time education session. Given this is an academic setting with a high turnover of ED physicians and the rarity of the event, a routine refresher training should be provided to sustain the improvement recorded. In addition, future research is needed to evaluate how these reductions in time to factor administration translate into improved patient health outcomes.

There were several strengths of this study to note. First, a QI initiative targeting time to administration of factor within the ED for patients with hemophilia is relatively unreported, making this insight timely and impactful. Another strength was the use of ITS analysis design allowed for the observation of postintervention changes and adjustment for secular trends. Additionally, categorizing time measurements by steps in the medication use process provided further insights in identifying the most impactful areas and those needing more improvement.

Overall, this QI, aimed at reducing the time to administration of factor for patients with hemophilia presenting to the ED with bleeding, was a novel and successful initiative. The intervention, which was developed by hematologists in order to improve clinical knowledge and awareness for ED physicians, as well as the order set aimed at reducing barriers to ordering this medication, ultimately reduced time to administration. Other emergency rooms may benefit from adapting a similar intervention in order to improve appropriate and timely care of these patients.

#### AUTHOR CONTRIBUTIONS

Asinamai M. Ndai, Rachel Reise, and Scott M. Vouri designed the data collection methodology and measurement framework, guided the analyses, and contributed to the writing of the manuscript. Asinamai M. Ndai also did the statistical analyses and created the data figures. Brandon R. Allen provided administrative support, supervised the chart review process, provided constant feedback on the intervention, and contributed to the writing of the manuscript. Tung T. Wynn and Anita Rajasekhar developed and delivered the intervention, provided subject matter expertise, and contributed to the writing of the manuscript. Ziad Saqr and Ina Sandeli did the chart review. All authors contributed to critical revisions of the article.

#### ACKNOWLEDGMENTS

We thank PeerView Institute for Medical Education, Inc for medical education, initiatives, and support of this project. This work was supported by an educational grant from Genentech.

#### CONFLICT OF INTEREST STATEMENT

Scott Martin Vouri is a current employee at Pfizer, Inc., but was previously employed by the UF College of Pharmacy for the duration of this project. Tung T. Wynn is conducting research with Sanofi, Genentech, Takeda, AMAG, and Sobi. Tung T. Wynn's wife was employed by Takeda from June 2023 to October 2023. The remaining authors declare no conflicts of interest.

#### DATA AVAILABILITY STATEMENT

De-identified data set may be made available upon request to interested readers by contacting the corresponding author.

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#### SUPPORTING INFORMATION

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

How to cite this article: Ndai AM, Allen BR, Wynn TT, et al. Rapid recognition and optimal management of hemophilia in the emergency department: A quality improvement project. *JACEP Open*. 2024;5:e13168.

https://doi.org/10.1002/emp2.13168

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