

Methods of Estimating Annualized Bleed Rates from Medical Records Among Patients with Hemophilia A

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Background + Purpose

Background

- Medical records are an important source of retrospective bleed data in hemophilia studies.
- Within records, bleeds are captured as individual bleed events (e.g. “patient admitted for right knee bleed”) and bleed rates (e.g. “currently experiencing 1 bleed every 6 months”) in narrative text.
- Studies without access to medical record narrative text are restricted to individual ICD-coded bleed events.¹
- Given the real-world variability in how patients report and providers document bleeds in medical records, a methodology to calculate annualized bleed rate (ABR) by incorporating bleed rates from narrative text is needed to more accurately capture ABR in real-world studies.

Purpose

Among a cohort of hemophilia A patients, this study aims to:

- Calculate ABR by two methods: a) from individual bleed events only and b) from individual bleed events plus bleed rates
- Quantify differences in ABR calculated from the two methods
- Compare quantified differences across hemophilia A severity groups and during time on prophylaxis (PPX) treatment

Table 1: Characteristics of the Hemophilia A cohort at baseline

Characteristic	Hemophilia A Cohort (N=367) N (%)
Age, years*	
Median (Q1, Q3)	26 (16, 36)
Sex	
Male	339 (92)
Female	28 (8)
Race and Ethnicity**	
White	251 (68)
Black or African American	39 (11)
Other	22 (6)
Hispanic or Latino	58 (16)
Not Hispanic or Latino	239 (65)
Hemophilia A Severity	
Severe	266 (73)
Moderate	50 (14)
Mild	51 (14)

*Median age at the start of the first observation period

**Unknown race and ethnicity N (%): 55 (15) and 70 (19), respectively

Table 2: Comparison of ABR calculated with and without bleed rates

Subgroup	Bleed events only Median (Q1, Q3)	Bleed events + rates Median (Q1, Q3)	Difference in medians (95% CI)
Hem A	0.7 (0.0, 1.5)	0.9 (0.0, 1.9)	0.1 (-0.1-0.4)
During PPX	0.6 (0.0, 1.5)	0.8 (0.0, 1.8)	0.2 (-0.1-0.5)
Severe	0.7 (0.0, 1.6)	0.9 (0.0, 1.9)	0.2 (-0.2-0.5)
During PPX	0.5 (0.0, 1.5)	0.7 (0.0, 1.9)	0.2 (-0.1-0.5)
Moderate	0.9 (0.4, 1.4)	1.1 (0.4 , 2.0)	0.2 (-0.3-0.7)
During PPX	0.9 (0.0, 1.5)	1.4 (0.4, 1.9)	0.4 (-0.4-1.2)
Mild	0.5 (0.0, 1.4)	0.5 (0.0, 1.7)	0.1 (-0.6-0.8)
During PPX	0.6 (0.2, 0.8)	0.8 (0.3, 1.4)	0.1 (-0.5-1.1)

Abbreviations: PPX: Prophylaxis; Hem: Hemophilia

Results

- This study included 367 individuals with hemophilia A. Mean age was 27 years and 73% of patients had severe hemophilia A at baseline (**Table 1**). The average follow-up time was 2.7 years per person and median (Q1, Q3) number of U.S. care sites was 5 (3, 8).
- **Figure 1** presents a patient’s medical journey of documented bleeds during the study period. Three reported bleeds were added to the patient’s history when including bleed rates from narrative text.
- Among all patients, median (Q1, Q3) ABR increased when calculated with bleed rates [0.88 (0.00, 1.90)] versus without [0.72 (0.00, 1.53)] [Difference in medians (95% CI) = 0.14 (-0.09-0.38)]. During time on prophylactic medication, the difference in medians was higher [0.23 (-0.09-0.48)] (**Table 2, Figure 2**).
- Among all severity subgroups, median (Q1, Q3) ABR persistently increased when incorporating bleed rates, with the greatest increase among severe patients with bleed rates [0.86 (0.00, 1.90)] versus without [0.66 (0.00-1.58)] [Difference in medians (95% CI) = 0.18 (-0.15-0.46)]. During time on prophylactic medication, the difference in medians was only slightly higher among severe patients [0.20 (-0.13-0.49)] (**Table 2, Figure 2**).

Methods

Data Source

- PicnicHealth is a data platform that collects and structures medical records across all sites of care while providing access to the records back to patients in a streamlined digital timeline.

Study Design

- Retrospective cohort study includes individuals with hemophilia A in the United States followed from January 1, 2018 to December 31, 2022.

Analysis

- ABRs were calculated within periods of time when patients had ≥1 hematology visit every 18 months. Patients with <90 days of total observation time were excluded to prevent extrapolation of bleeds occurring during small time windows.
- Mutually exclusive windows of observed time were created by prioritizing bleed rate time windows and supplementing with individual bleed events using a lookback period from hematology visits to the nearest bleed rate end date or 18 months, whichever is sooner. For overlapping bleed rate time windows, the later window was truncated and a new bleed count was imputed and reduced in proportion to the amount of truncated time.
- To calculate ABR for each patient, total bleed count was divided by the sum of all observed time windows in years.
- 95% confidence intervals (CI) for the *median* difference in median ABR calculated with and without bleed rates were computed using a non-parametric bootstrap.^{2,3}
- Analyses were stratified by baseline factor VIII (categorized as severe <1%, moderate 1-5%, and mild 6-50%) and restricted to time on prophylactic medication.

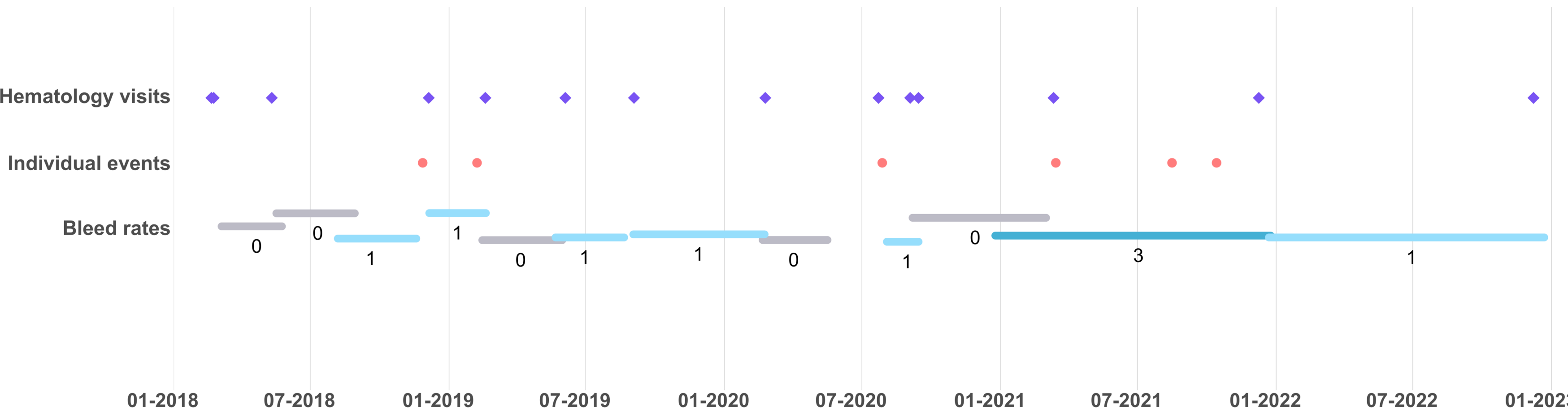


Figure 1: One patient medical journey of individual bleed events and reported bleed rates during study period. Number of reported bleeds within a bleed rate time window are displayed below each bleed rate.

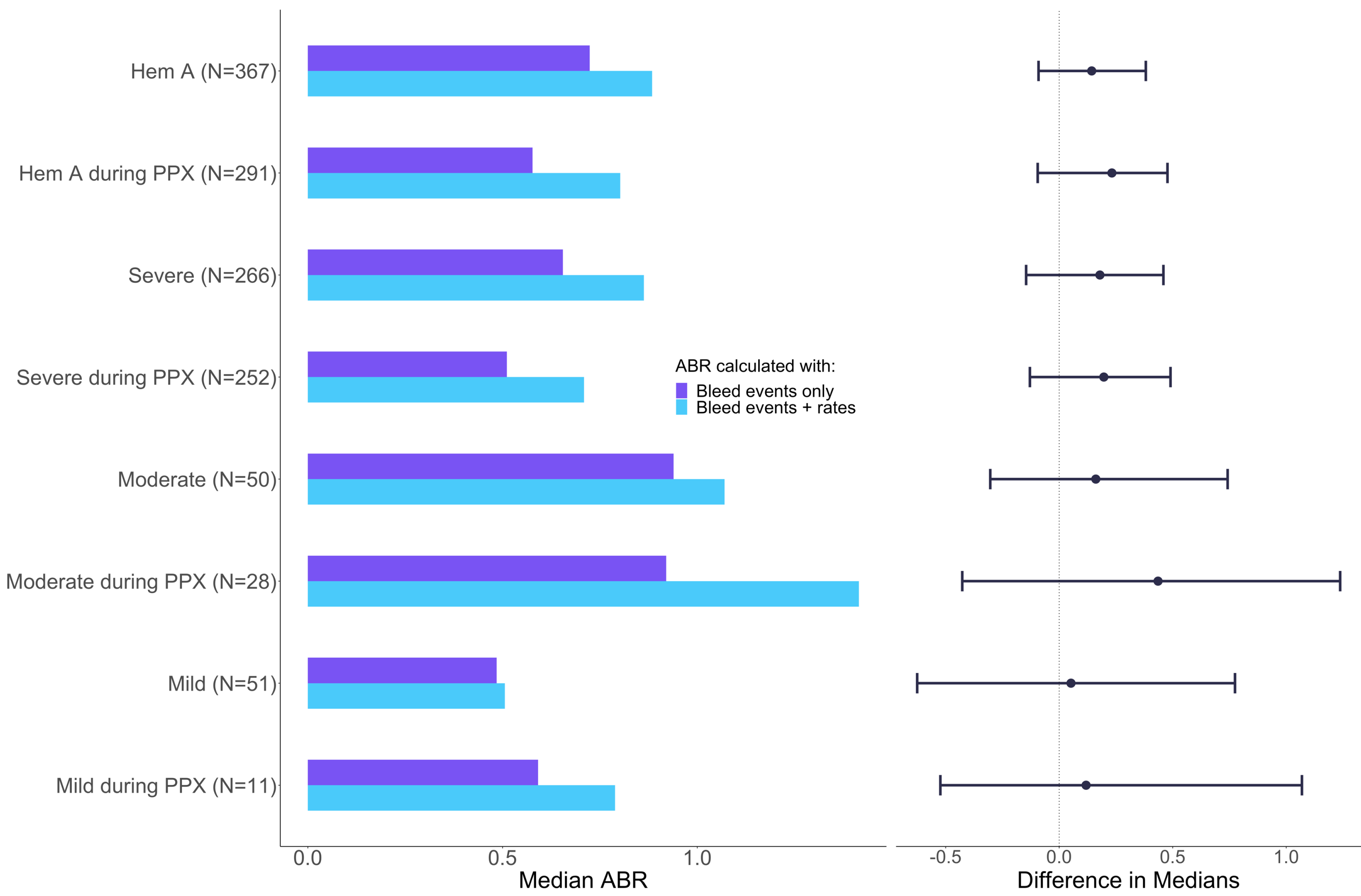


Figure 2: Median ABR calculated with and without bleed rates and difference in medians with bootstrap 95% confidence intervals

Abbreviations: PPX: Prophylaxis; Hem: Hemophilia

Conclusion

- Access to comprehensive bleed data in medical records is important for quantifying the burden of bleeding in the hemophilia community.
- This study found that incorporating bleed rates from medical record narrative text moderately increased estimated ABRs among hemophilia A patients.
- While bootstrap confidence intervals included the null, there was a consistent trend of increased ABR across all subgroups after including bleed rates. This suggests that access to medical record narrative text may be important to prevent underestimation of ABR in hemophilia A studies.
- More research may be warranted among a larger sample of mild and moderate patients.
- Real-world hemophilia studies should consider leveraging medical record narrative text in ABR estimations.

References

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Disclosures

Authors are employees and stockholders of PicnicHealth

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