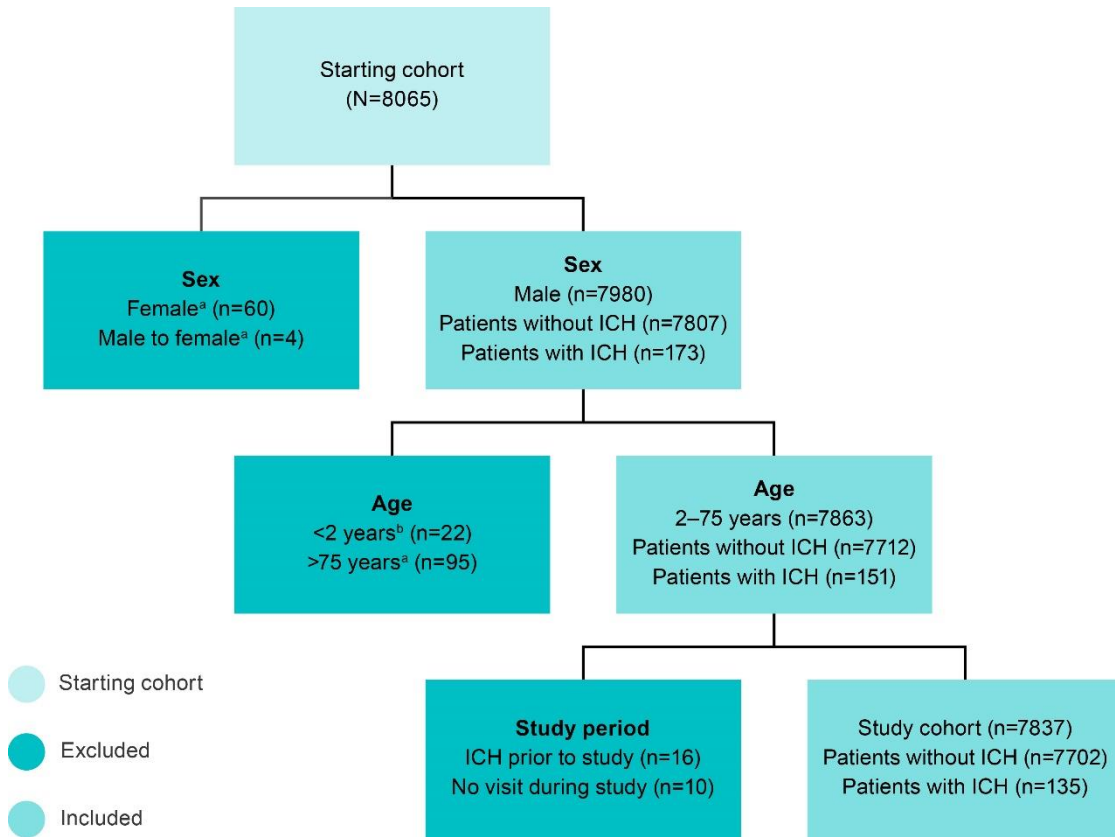


# Supplementary Figures

Supplementary Figure 1 Study design.

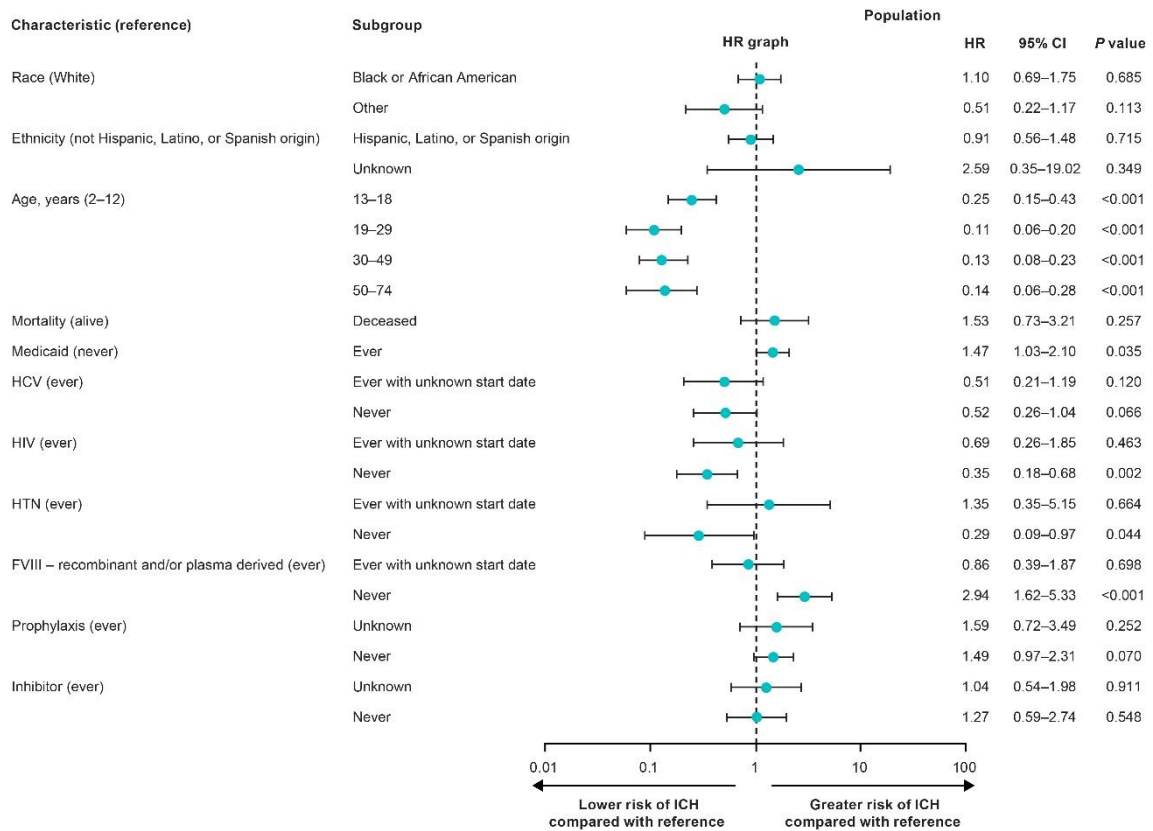


**Abbreviations:** ICH, intracranial hemorrhage.

<sup>a</sup>No individuals experienced an ICH.

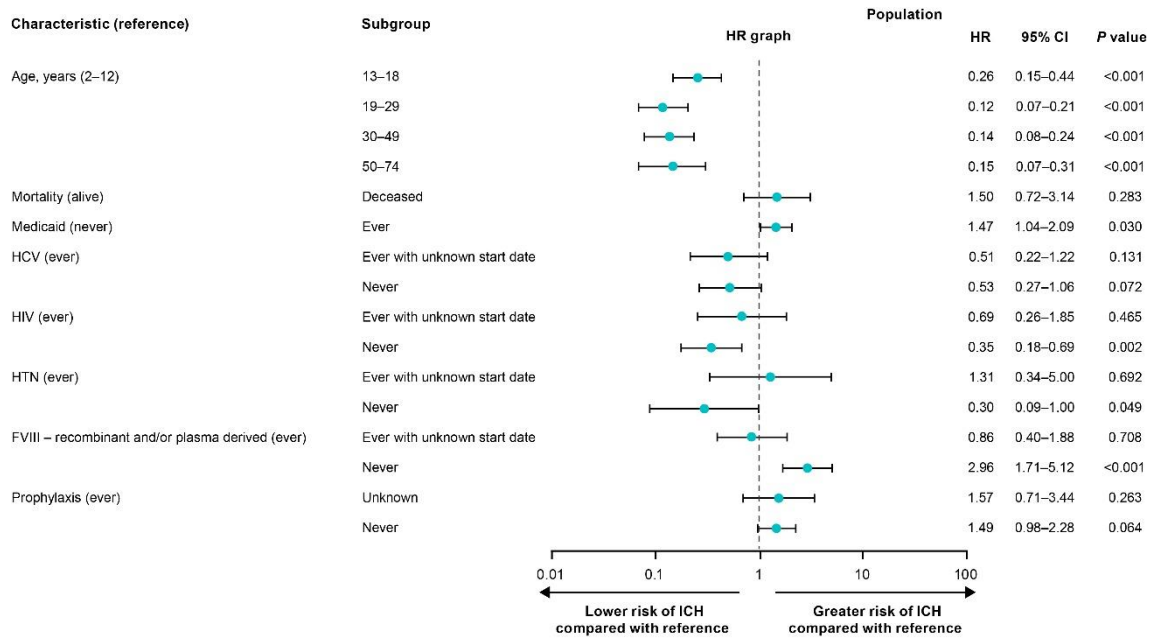
<sup>b</sup>All individuals experienced an ICH.

**Supplementary Figure 2** Risk of ICH in multivariable analysis with all covariates.



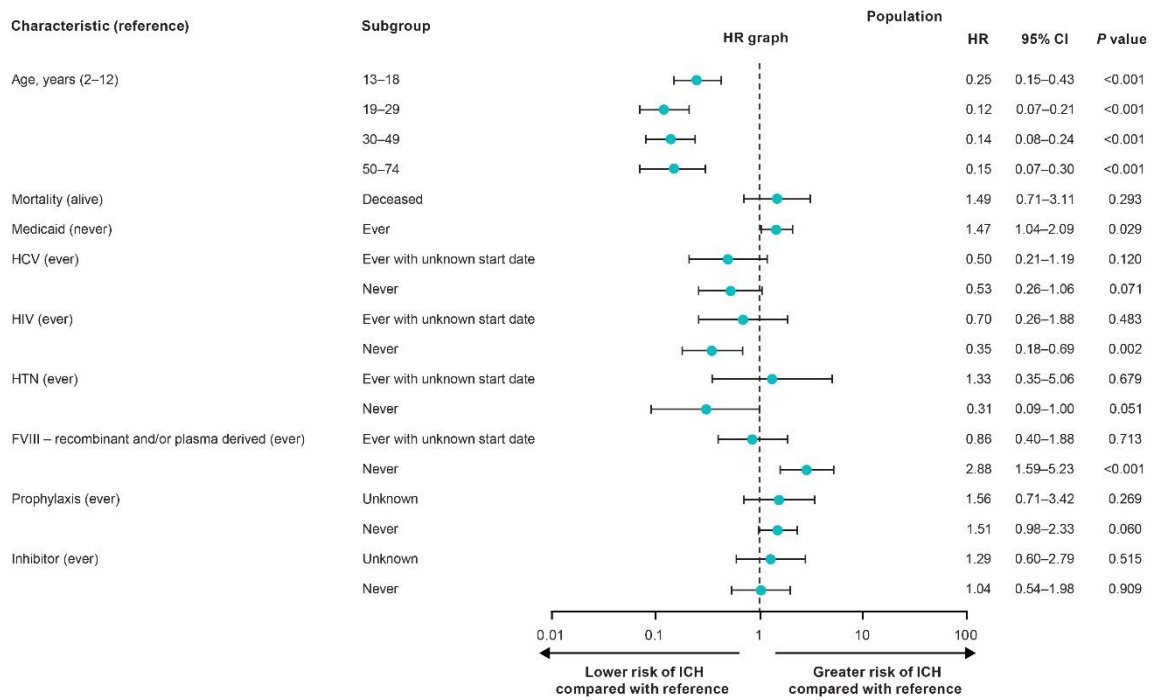
**Abbreviations:** CI, confidence interval; FVIII, factor VIII; HCV, hepatitis C virus; HR, hazard ratio; HTN, hypertension; ICH, intracranial hemorrhage.

**Supplementary Figure 3** Risk of ICH in multivariable analysis with statistically significant covariates (univariate analysis).



**Abbreviations:** CI, confidence interval; FVIII, factor VIII; HCV, hepatitis C virus; HR, hazard ratio; HTN, hypertension; ICH, intracranial hemorrhage.

**Supplementary Figure 4** Risk of ICH in multivariable analysis with statistically significant covariates (univariate analysis) and inhibitor status.



**Abbreviations:** CI, confidence interval; FVIII, factor VIII; HCV, hepatitis C virus; HR, hazard ratio; HTN, hypertension; ICH, intracranial hemorrhage.

## Supplementary Tables

**Supplementary Table 1** ICH incidence in age groups stratified by prophylaxis status

Age, years	No ICH, n (%)	ICH, n (%)	P-value
<b>2–12</b>	n=956	n=47	0.400
Yes	729 (76.3)	32 (68.1)	
No	151 (15.8)	10 (21.3)	
Yes with unknown start date	76 (7.9)	5 (10.6)	
<b>13–18</b>	n=1317	n=19	0.500
Yes	1104 (83.8)	15 (78.9)	
No	142 (10.8)	2 (10.5)	
Yes with unknown start date	71 (5.4)	2 (10.5)	
<b>19–29</b>	n=2205	n=16	0.800
Yes	1679 (76.1)	14 (87.5)	
No	349 (15.8)	1 (6.2)	
Yes with unknown start date	177 (8.0)	1 (6.3)	
<b>30–49</b>	n=2293	n=29	0.300
Yes	1544 (67.3)	16 (55.2)	
No	518 (22.6)	10 (34.5)	
Yes with unknown start date	231 (10.1)	3 (10.3)	
<b>50–74</b>	n=931	n=24	0.400
Yes	503 (54.0)	11 (45.8)	
No	354 (38.0)	13 (54.2)	
Yes with unknown start date	74 (7.9)	0 (0)	

**Abbreviation:** ICH, intracranial hemorrhage.

**Supplementary Table 2** Bootstrap sensitivity analysis of univariate CoxPH model

Characteristic	Population		Bootstrap Sensitivity	
	HR	95% CI	HR	95% CI
Race (reference: White)				
Black or African American	1.18	0.76–1.84	1.24	0.88–1.65
Other	0.60	0.26–1.36	0.93	0.37–1.27
Ethnicity (reference: not Hispanic, Latinx, Spanish)				
Hispanic, Latinx, Spanish	1.01	0.64–1.60	0.87	0.76–1.48
Unknown	1.73	0.24–12.3	1.54	8.15e-7–2.86
Age, years (reference: 2–12)				
13–18	0.25	0.14–0.42	0.37	0.24–0.51
19–29	0.12	0.07–0.22	0.23	0.13–0.27
30–49	0.21	0.13–0.34	0.40	0.22–0.41
50–74	0.43	0.26–0.71	0.56	0.35–0.69
Mortality (reference: alive)				
Deceased	2.34	1.23–4.44	2.52	1.17–3.10
Current or prior Medicaid (reference: no)				
Yes	1.51	1.08–2.12	1.27	1.04–1.65
Current or prior HCV (reference: Yes)				
Yes with unknown start date	0.42	0.20–0.91	0.37	0.31–0.86
No	0.50	0.30–0.85	0.48	0.46–0.96
Current or prior HIV (reference: yes)				
Yes with unknown start date	0.50	0.21–1.21	0.42	0.32–1.05
No	0.37	0.22–0.62	0.39	0.36–0.77
Current or prior HTN (reference: yes)				
Yes with unknown start date	1.08	0.29–4.10	1.45	0.43–2.80
No	0.36	0.10–1.00	0.66	0.23–1.19
Current or prior FVIII (rFVIII and/or pdFVIII; reference: yes)				

Characteristic	Population		Bootstrap Sensitivity	
	HR	95% CI	HR	95% CI
Yes with unknown start date	1.01	0.54–1.90	1.39	0.73–1.86
No	2.79	1.67–4.66	2.34	1.40–2.86
Current or prior prophylaxis (reference: yes)				
Yes with unknown start date	1.24	0.66–2.32	1.07	0.79–1.95
No	1.56	1.06–2.29	1.67	1.09–1.88
Current or prior inhibitor (reference: yes)				
Yes with unknown start date	0.72	0.34–1.54	0.68	0.47–1.30
No	0.57	0.32–1.04	0.59	0.44–1.03

**Abbreviations:** CI, confidence interval; CoxPH, Cox proportional hazards; FVIII, factor VIII; HCV, hepatitis C virus; HR, hazard ratio; HTN, hypertension; pdFVIII, plasma-derived FVIII; rFVIII, recombinant FVIII.