

**SUPPLEMENTARY MATERIALS**

**TABLE S1.** Treatment duration and annualized FIX concentrate dosage by age

Parameter	SHL FIX concentrates			EHL FIX concentrates		
	Nonacog alfa	Nonacog gamma	Freeze-dried Concentrated Human Blood Coagulation FIX	Albutrepenonacog alfa	Eftrenonacog alfa	Nonacog beta pegol
<b>Age 0–11 years</b>	<b>n=21</b>	<b>n=0</b>	<b>n=4</b>	<b>n=14</b>	<b>n=14</b>	<b>n=0</b>
Annualized FIX dosage (IU/kg), median (Q1, Q3)	5419.9 (3312.7, 7230.1)	—	873.6 (362.1, 5169.7)	2590.6 (1698.7, 3171.0)	2701.0 (1712.6, 3008.3)	—
Observed treatment duration by age group, n (%)						
<6 months	4 (16.0)	0 (0)	2 (50.0)	5 (27.8)	7 (46.7)	0 (0)
6 to <12 months	1 (4.0)	0 (0)	0 (0)	2 (11.1)	0 (0)	0 (0)
1 to <2 years	5 (20.0)	0 (0)	1 (25.0)	5 (27.8)	2 (13.3)	0 (0)
2 to <3 years	7 (28.0)	0 (0)	1 (25.0)	6 (33.3)	2 (13.3)	0 (0)
≥3 years	8 (32.0)	0 (0)	0 (0)	0	4 (26.7)	0 (0)
<b>Age 12–19 years</b>	<b>n=21</b>	<b>n=1</b>	<b>n=10</b>	<b>n=21</b>	<b>n=13</b>	<b>n=2</b>
Annualized FIX dosage, median (Q1, Q3), IU/kg	4422.9 (2399.9, 5766.6)	3181.4 (3181.4, 3181.4)	1922.5 (1266.7, 3180.6)	2599.6 (1729.1, 3187.2)	2070.7 (669.8, 2657.5)	2195.1 (2148.0, 2242.2)
Observed treatment duration by age group, n (%)						
<6 months	6 (21.4)	0 (0)	2 (20.0)	7 (26.9)	4 (26.7)	1 (50.0)
6 to <12 months	4 (14.3)	0 (0)	0 (0)	4 (15.4)	2 (13.3)	1 (50.0)
1 to <2 years	3 (10.7)	0 (0)	3 (30.0)	13 (50.0)	4 (26.7)	0 (0)
2 to <3 years	8 (28.6)	0 (0)	2 (20.0)	2 (7.7)	5 (33.3)	0 (0)
≥3 years	7 (25.0)	1 (100.0)	3 (30.0)	0 (0)	0 (0)	0 (0)

<b>Age 20–64 years</b>	<b>n=37</b>	<b>n=0</b>	<b>n=34</b>	<b>n=19</b>	<b>n=52</b>	<b>n=3</b>
Annualized FIX dosage, median (Q1, Q3), IU/kg	1895.3 (762.1, 3120.8)	–	2925.3 (1319.7, 4077.0)	1885.0 (1457.4, 2258.9)	2459.0 (1914.8, 3883.3)	1437.2 (1368.5, 1505.9)
Observed treatment duration by age group, n (%)						
<6 months	9 (21.4)	0 (0)	26 (43.3)	9 (37.5)	27 (33.3)	2 (66.7)
6 to <12 months	5 (11.9)	0 (0.0)	10 (16.7)	4 (16.7)	10 (12.4)	1 (33.3)
1 to <2 years	5 (11.9)	0 (0.0)	6 (10.0)	8 (33.3)	14 (17.3)	0 (0)
2 to <3 years	10 (23.8)	0 (0.0)	6 (10.0)	3 (12.5)	19 (23.5)	0 (0)
≥3 years	13 (31.0)	0 (0.0)	12 (20.0)	0 (0)	11 (13.6)	0 (0)
<b>Age ≥65 years</b>	<b>n=9</b>	<b>n=0</b>	<b>n=3</b>	<b>n=3</b>	<b>n=8</b>	<b>n=2</b>
Annualized FIX dosage, median (Q1, Q3), IU/kg	1976.5 (536.0, 4222.3)	–	707.9 (436.6, 1671.0)	2026.5 (640.0, 3412.9)	2285.2 (1726.9, 2539.2)	1165.4 (822.0, 1508.8)
Observed treatment duration by age group, n (%)						
<6 months	3 (33.3)	0 (0)	2 (66.7)	2 (66.7)	1 (12.5)	0 (0)
6 to <12 months	2 (22.2)	0 (0)	1 (33.3)	0 (0)	1 (12.5)	2 (100.0)
1 to <2 years	0 (0)	0 (0)	0 (0)	1 (33.3)	1 (12.5)	0 (0)
2 to <3 years	3 (33.3)	0 (0)	0 (0)	0 (0)	2 (25.0)	0 (0)
≥3 years	1 (11.1)	0 (0)	0 (0)	0 (0)	3 (37.5)	0 (0)

**Abbreviations:** EHL, extended half-life; FIX, factor IX; IU, international units; Q, quarter; SHL, standard half-life

**TABLE S2.** Prevalence of joint damage and hospitalization with or because of bleeding events among the study population, by age group

<b>Parameter</b>	<b>Age 0–11 y (n=36)</b>	<b>Age 12–9 y (n=38)</b>	<b>Age 20–64 y (n=106)</b>	<b>Age ≥65 y (n=17)</b>				
Patients with joint damage, n (%)	18 (50.0)	29 (76.3)	62 (58.5)	7 (41.2)				
Prevalence rate of joint damage per 100 patient-years, rate (95% CI)	15.0 (8.0–21.0)	21.0 (14.0–28.0)	18.0 (14.0–22.0)	17.0 (6.0–29.0)				
	<b>Hospitalization With Bleeding, by age</b>				<b>Hospitalization Because of a Bleeding Event, by age</b>			
<b>Parameter</b>	<b>0–11 y (n=36)</b>	<b>12–19 y (n=38)</b>	<b>20–64 y (n=106)</b>	<b>≥65 y (n=17)</b>	<b>0–11 y (n=36)</b>	<b>12–19 y (n=38)</b>	<b>20–64 y (n=106)</b>	<b>≥65 y (n=17)</b>
Patients with hospitalization, n (%)	5 (13.9)	9 (23.7)	12 (11.3)	4 (23.5)	0 (0)	1 (2.6)	5 (4.7)	0 (0)
Incidence of hospitalization per 100 patient-years (95% CI), rate	1.0 (0.0–2.0)	1.0 (0.0–3.0)	1.0 (0.0–2.0)	5.0 (0.0–10.0)	0 (0–0)	0 (0–0)	1.0 (0.0–1.0)	0.0 (0.0–0.0)
Length of hospitalization, median (Q1, Q3), days	8.0 (3.0, 11.0)	5.0 (3.0, 10.0)	20.0 (11.0, 21.0)	44.0 (21.0, 62.5)	–	16.0 (10.0, 27.0)	13.0 (11.0, 13.0)	–

**Abbreviations:** CI, confidence interval; Q, quarter

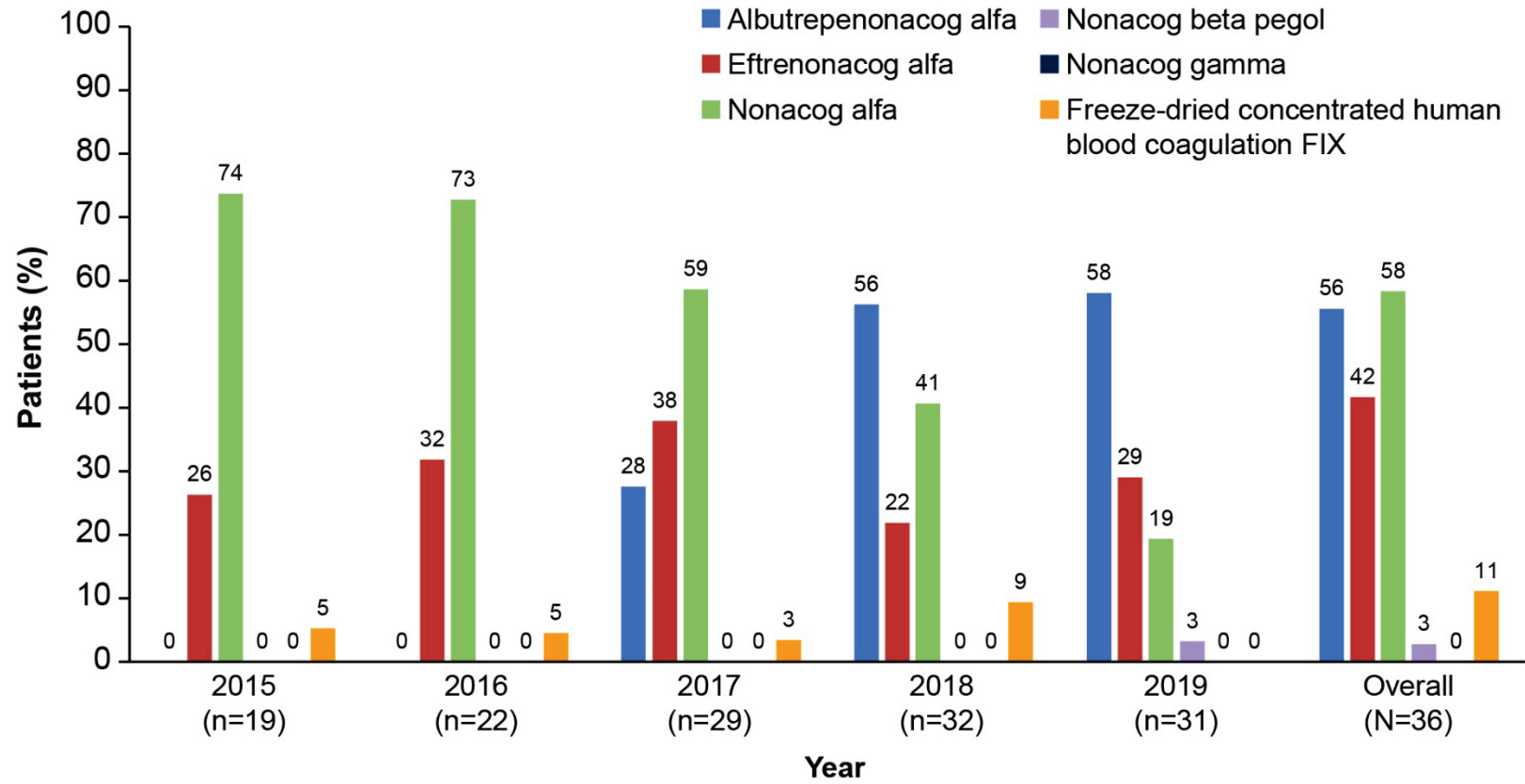
**Table S3.** Expenditure type per year, by age group

<b>Expenditure Type</b>	<b>Overall</b>	<b>2015</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>
<b>Age 0–11 years</b>	<b>n=34</b>	<b>n=19</b>	<b>n=21</b>	<b>n=28</b>	<b>n=30</b>	<b>n=29</b>
Annual total health care expenditures, median (Q1, Q3), yen	¥11,752,467 (¥4,349,971, ¥19,170,710)	¥11,069,298 (¥6,942,856, ¥18,752,942)	¥10,846,122 (¥6,019,086, ¥22,139,836)	¥12,819,837 (¥5,419,794, ¥18,820,610)	¥13,810,393 (¥4,332,760, ¥30,449,500)	¥12,971,832 (¥5,685,549, ¥32,931,592)
Annual expenditures for FIX concentrate treatment, median (Q1, Q3), yen	¥11,147,226 (¥4,307,505, ¥19,082,340)	¥11,012,658 (¥6,777,070, ¥18,124,400)	¥10,804,872 (¥5,581,830, ¥22,025,316)	¥12,603,537 (¥5,084,323, ¥18,617,662)	¥12,060,687 (¥4,047,060, ¥29,293,928)	¥12,903,816 (¥5,580,449, ¥32,809,447)
<b>Age 12–19 years</b>	<b>n=33</b>	<b>n=23</b>	<b>n=22</b>	<b>n=28</b>	<b>n=27</b>	<b>n=22</b>
Annual total health care expenditures, median (Q1, Q3), yen	¥21,542,459 (¥12,206,800, ¥27,407,632)	¥12,603,928 (¥4,529,996, ¥18,307,496)	¥12,260,776 (¥6,357,880, ¥21,519,296)	¥19,080,629 (¥9,889,142, ¥26,245,859)	¥23,289,255 (¥11,395,844, ¥31,687,928)	¥33,312,034 (¥25,508,300, ¥42,130,413)
Annual expenditures for FIX concentrate treatment, median (Q1, Q3), yen	¥20,937,317 (¥12,151,993, ¥27,291,264)	¥12,320,525 (¥3,383,580, ¥18,254,432)	¥12,165,878 (¥6,321,700, ¥21,414,626)	¥17,003,519 (¥9,812,640, ¥25,969,636)	¥23,068,524 (¥11,298,801, ¥31,608,500)	¥30,493,321 (¥25,394,767, ¥42,039,368)
<b>Age 20–64 years</b>	<b>n=91</b>	<b>n=41</b>	<b>n=43</b>	<b>n=81</b>	<b>n=82</b>	<b>n=70</b>
Annual total health care expenditures, median (Q1, Q3), yen	¥23,233,733 (¥7,285,670, ¥36,007,472)	¥9,057,510 (¥4,676,570, ¥14,778,748)	¥19,411,212 (¥5,112,075, ¥34,533,108)	¥22,389,024 (¥8,453,780, ¥32,493,080)	¥25,511,540 (¥8,809,688, ¥39,974,307)	¥31,898,870 (¥9,998,964, ¥45,963,061)
Annual expenditures for FIX concentrate treatment, median (Q1, Q3), yen	¥21,757,598 (¥7,175,597, ¥33,310,288)	¥8,673,434 (¥2,908,890, ¥11,784,850)	¥16,962,080 (¥4,511,990, ¥32,872,840)	¥21,809,865 (¥8,218,210, ¥30,752,328)	¥22,960,827 (¥8,653,205, ¥37,107,495)	¥30,718,086 (¥9,242,460, ¥41,939,394)
<b>Age ≥65 years</b>	<b>n=10</b>	<b>n=3</b>	<b>n=4</b>	<b>n=9</b>	<b>n=10</b>	<b>n=9</b>

Annual total health care expenditures, median (Q1, Q3), yen	¥19,431,739 (¥13,610,516, ¥32,651,034)	¥13,044,661 (¥4,430,256, ¥13,529,333)	¥21,232,633 (¥15,215,042, ¥26,624,829)	¥15,804,015 (¥9,732,685, ¥31,669,251)	¥20,016,821 (¥9,890,315, ¥32,225,380)	¥26,708,968 (¥20,209,360, ¥35,609,973)
Annual expenditures for FIX concentrate treatment, median (Q1, Q3), yen	¥19,185,104 (¥11,628,447, ¥31,126,798)	¥12,721,560 (¥4,374,634, ¥13,301,040)	¥21,064,054 (¥15,034,214, ¥26,330,068)	¥15,689,924 (¥9,541,170, ¥28,498,426)	¥18,661,468 (¥9,541,170, ¥32,145,730)	¥26,629,468 (¥18,708,705, ¥35,326,236)

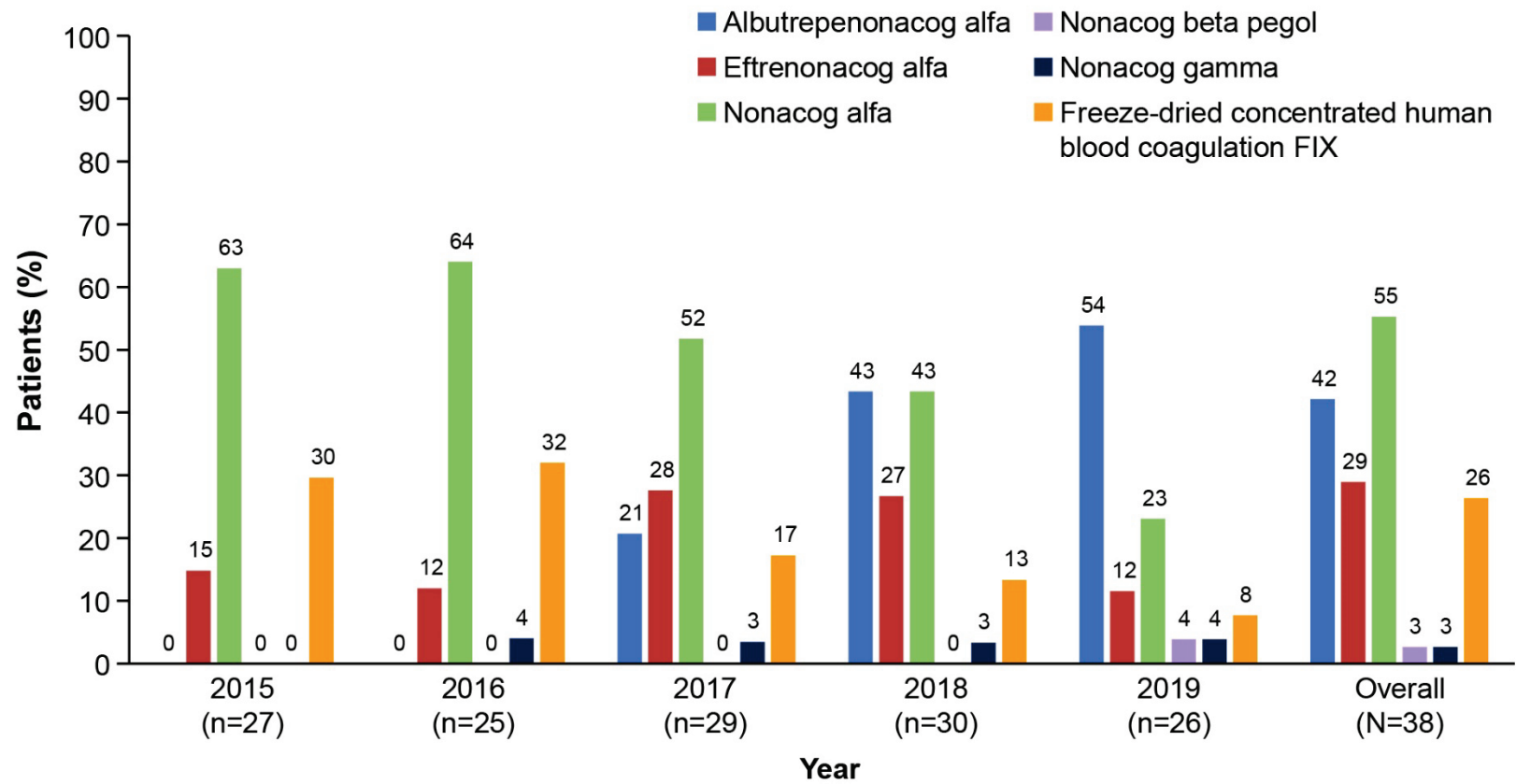
**Abbreviations:** FIX, factor IX; Q, quarter

**Supplementary Figure S1. Outpatient use of FIX concentrates, ages 0–11 years**



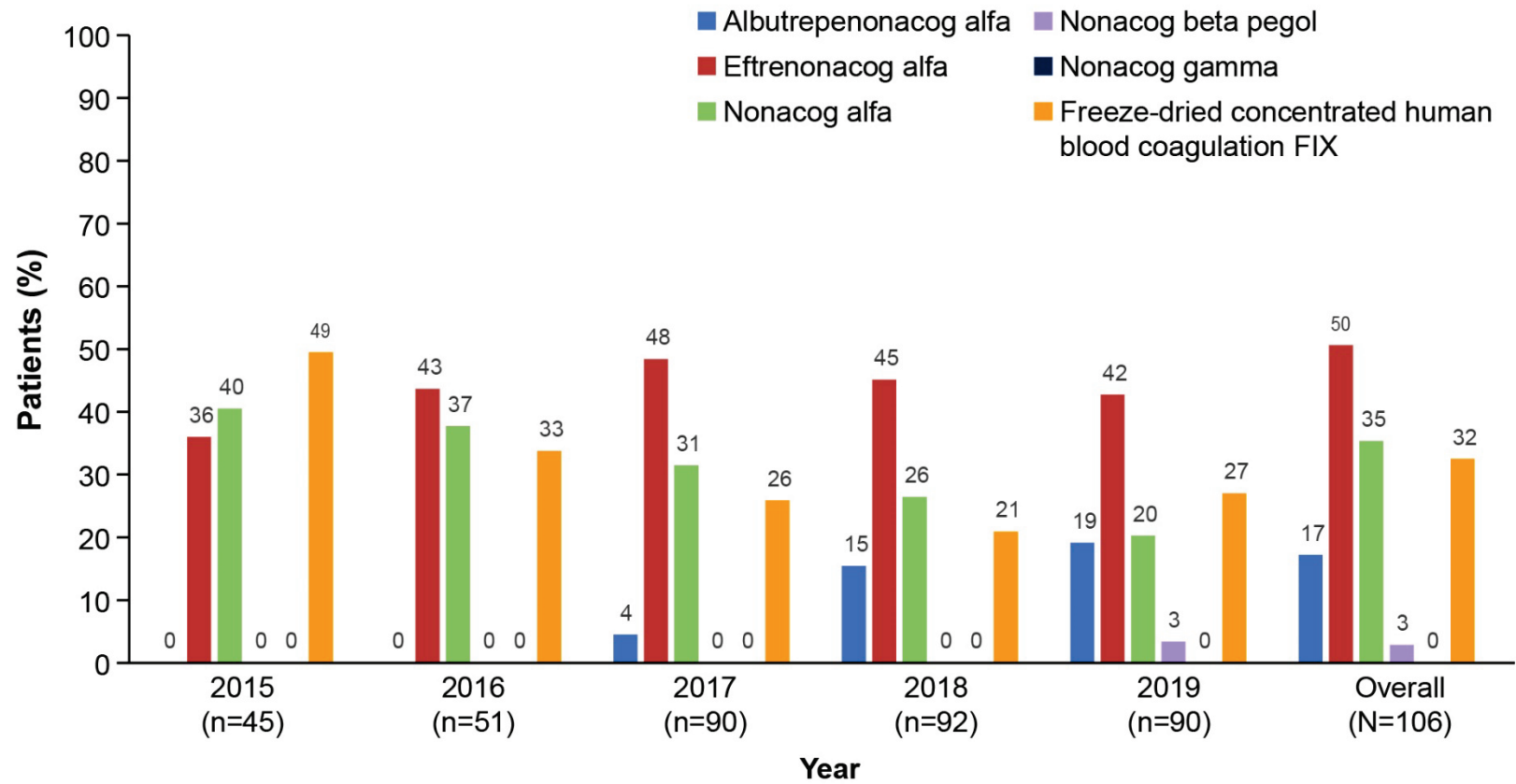
FIX, factor IX.

**Supplementary Figure S2. Outpatient use of FIX concentrates, ages 12–19 years**



FIX, factor IX.

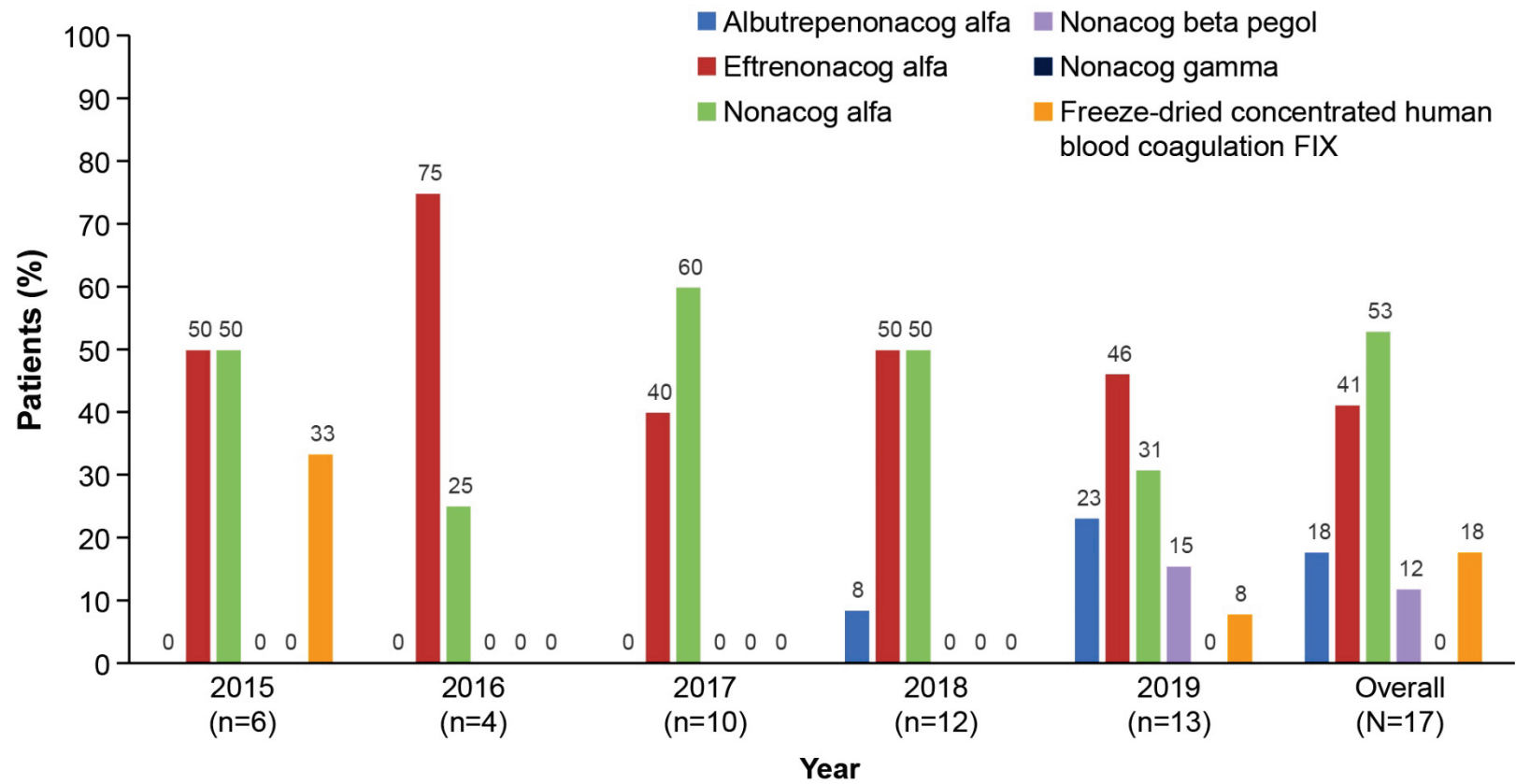
**Supplementary Figure S3. Outpatient use of FIX concentrates, ages 20–64 years**



FIX, factor IX.



**Supplementary Figure S4. Outpatient use of FIX concentrates, ages 65+ years**



FIX, factor IX.