

SUPPLEMENTARY MATERIAL

Patient Experience with Treatment of HAE Attacks: Results from a Real-World Survey of Physicians and their Patients

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Table S1 Patient demographic and clinical characteristics (matched analysis)

Characteristic	Physician reported	Patient reported
Age	<i>n</i> = 279	<i>n</i> = 279
Mean (SD) [min, max], years	33.7 (13.1) [18, 80]	33.8 (13.1) [18, 80]
Sex, <i>n</i> (%)	<i>n</i> = 279	<i>n</i> = 279
Male	134 (48)	134 (48)
Female	145 (52)	145 (52)
Current employment status, <i>n</i> (%)	<i>n</i> = 279	<i>n</i> = 278
Working full time	155 (56)	156 (56)
Working part time	27 (10)	28 (10)
On long-term sick leave	2 (1)	1 (< 1)
Homemaker	19 (7)	18 (6)
Student	64 (23)	66 (24)
Not working due to retirement	8 (3)	5 (2)
Unemployed	4 (1)	5 (2)
Number of attacks in the 12 months prior to the survey	<i>n</i> = 279	<i>n</i> = 255
Mean (SD) [min, max]	2.4 (2.3) [0, 12]	2.5 (3.0) [0, 24]
0 attacks, <i>n</i> (%)	43 (15)	38 (15)
1 attack, <i>n</i> (%)	89 (32)	74 (29)
≥ 2 attacks, <i>n</i> (%)	147 (53)	143 (56)
Number of attacks in the last month prior to the survey, of those that had ≥1 attack in the 12 months prior	<i>n</i> = 236	<i>n</i> = 181
Mean (SD) [min, max]	0.3 (0.6) [0, 2]	0.6 (1.0) [0, 7]
0 attacks, <i>n</i> (%)	177 (75)	104 (57)
1 attack, <i>n</i> (%)	47 (20)	60 (33)
≥ 2 attacks, <i>n</i> (%)	12 (5)	17 (9)
Severity of the most recent attack, <i>n</i> (%)	<i>n</i> = 275	<i>n</i> = 273
Mild	78 (28)	113 (41)
Moderate	161 (59)	128 (47)
Severe	36 (13)	31 (11)
Very severe	0	1 (< 1)
Number of individual doses of rescue medication used to treat the most recent attack	<i>n</i> = 192	<i>n</i> = 219
Mean (SD) [min, max]	1.3 (0.6) [1, 4]	1.2 (0.5) [1, 4]
Time to symptom improvement after treating the most recent attack	<i>n</i> = 188	<i>n</i> = 210
Mean (SD) [min, max], minutes	46.6 (45.2) [2, 360]	94.3 (323.2) [1, 2800]

Table S2 Overview of HAE attack locations and attack counts by time since diagnosis

Attack location	Time since HAE diagnosis				
	All patients	< 1 year	1–2 years	2–3 years	> 3 years
Hands, arms, feet, legs, fingers, toes	<i>n</i> = 753	<i>n</i> = 99	<i>n</i> = 108	<i>n</i> = 88	<i>n</i> = 457
Minimum	0	0	0	0	0
Median	1	1	1	1	1
Maximum	20	10	20	8	20
0 attacks, <i>n</i> (%)	226 (30)	40 (40)	39 (36)	29 (33)	118 (26)
1 attack, <i>n</i> (%)	206 (27)	30 (30)	27 (25)	27 (31)	122 (27)
≥ 2 attacks, <i>n</i> (%)	321 (43)	29 (29)	42 (39)	32 (36)	217 (47)
Face, lips, eyes/eyelids, nose, neck	<i>n</i> = 749	<i>n</i> = 98	<i>n</i> = 111	<i>n</i> = 87	<i>n</i> = 452
Minimum	0	0	0	0	0
Median	1	1	1	1	1
Maximum	23	10	23	7	15
0 attacks, <i>n</i> (%)	249 (33)	31 (32)	40 (36)	30 (34)	147 (33)
1 attack, <i>n</i> (%)	244 (33)	43 (44)	38 (34)	27 (31)	136 (30)
≥ 2 attacks, <i>n</i> (%)	256 (34)	24 (24)	33 (30)	30 (34)	169 (37)
Abdominal angioedema	<i>n</i> = 726	<i>n</i> = 99	<i>n</i> = 105	<i>n</i> = 85	<i>n</i> = 436
Minimum	0	0	0	0	0
Median	0	0	0	0	1
Maximum	30	30	8	8	15
0 attacks, <i>n</i> (%)	401 (55)	63 (64)	69 (66)	51 (60)	217 (50)
1 attack, <i>n</i> (%)	169 (23)	21 (21)	18 (17)	17 (20)	113 (26)
≥ 2 attacks, <i>n</i> (%)	156 (21)	15 (15)	18 (17)	17 (20)	106 (24)
Laryngeal angioedema	<i>n</i> = 701	<i>n</i> = 94	<i>n</i> = 102	<i>n</i> = 79	<i>n</i> = 425
Minimum	0	0	0	0	0
Median	0	0	0	0	0
Maximum	4	3	2	2	4
0 attacks, <i>n</i> (%)	536 (76)	69 (73)	83 (81)	61 (77)	322 (76)
1 attack, <i>n</i> (%)	115 (16)	20 (21)	16 (16)	13 (16)	66 (16)
≥ 2 attacks, <i>n</i> (%)	50 (7)	5 (5)	3 (3)	5 (6)	37 (9)
Chest/torso	<i>n</i> = 695	<i>n</i> = 91	<i>n</i> = 101	<i>n</i> = 79	<i>n</i> = 423
Minimum	0	0	0	0	0
Median	0	0	0	0	0
Maximum	6	3	6	2	6
0 attacks, <i>n</i> (%)	557 (80)	80 (88)	84 (83)	71 (90)	321 (76)
1 attack, <i>n</i> (%)	82 (12)	7 (8)	9 (9)	6 (8)	60 (14)
≥ 2 attacks, <i>n</i> (%)	56 (8)	4 (4)	8 (8)	2 (3)	42 (10)

Attack location	Time since HAE diagnosis				
	All patients	< 1 year	1–2 years	2–3 years	> 3 years
Genitals	<i>n</i> = 695	<i>n</i> = 91	<i>n</i> = 101	<i>n</i> = 80	<i>n</i> = 422
Minimum	0	0	0	0	0
Median	0	0	0	0	0
Maximum	8	3	5	2	8
0 attacks, <i>n</i> (%)	591 (85)	83 (91)	93 (92)	73 (91)	341 (81)
1 attack, <i>n</i> (%)	63 (9)	6 (7)	5 (5)	5 (6)	47 (11)
≥ 2 attacks, <i>n</i> (%)	41 (6)	2 (2)	3 (3)	2 (2)	34 (8)
Other	<i>n</i> = 28	<i>n</i> = 5	<i>n</i> = 6	<i>n</i> = 1	<i>n</i> = 16
Minimum	0	0	0	1	0
Median	0	0	0	1	0
Maximum	22	0	0	1	22
0 attacks, <i>n</i> (%)	25 (89)	5 (100)	6 (100)	0	14 (88)
1 attack, <i>n</i> (%)	1 (4)	0	0	1 (100)	0
≥ 2 attacks, <i>n</i> (%)	2 (7)	0	0	0	2 (12)

HAE hereditary angioedema

Table S3 Duration for improvement of most recent attack following treatment and number of attacks in the 12 months prior to data collection

Characteristic	Physician reported	Patient reported
Mean (SD) duration for improvement of most recent attack after treatment, minutes		
All patients	95.3 (280.4) (<i>n</i> = 627)	-
LTP-only subset	67.6 (100.4) (<i>n</i> = 80)	-
ODT-only subset	89.2 (295.5) (<i>n</i> = 247)	-
Mean (SD) number of attacks in the 12 months prior to the survey [min, max]		
All patients	2.2 (3.4) [0, 36] (<i>n</i> = 1131)	2.5 (2.9) [0, 24] (<i>n</i> = 255)
LTP-only subset	1.4 (2.1) [0, 20] (<i>n</i> = 274)	1.5 (1.5) [0, 7] (<i>n</i> = 56)
ODT-only subset	2.4 (2.9) [0, 26] (<i>n</i> = 382)	2.8 (2.1) [0, 10] (<i>n</i> = 90)

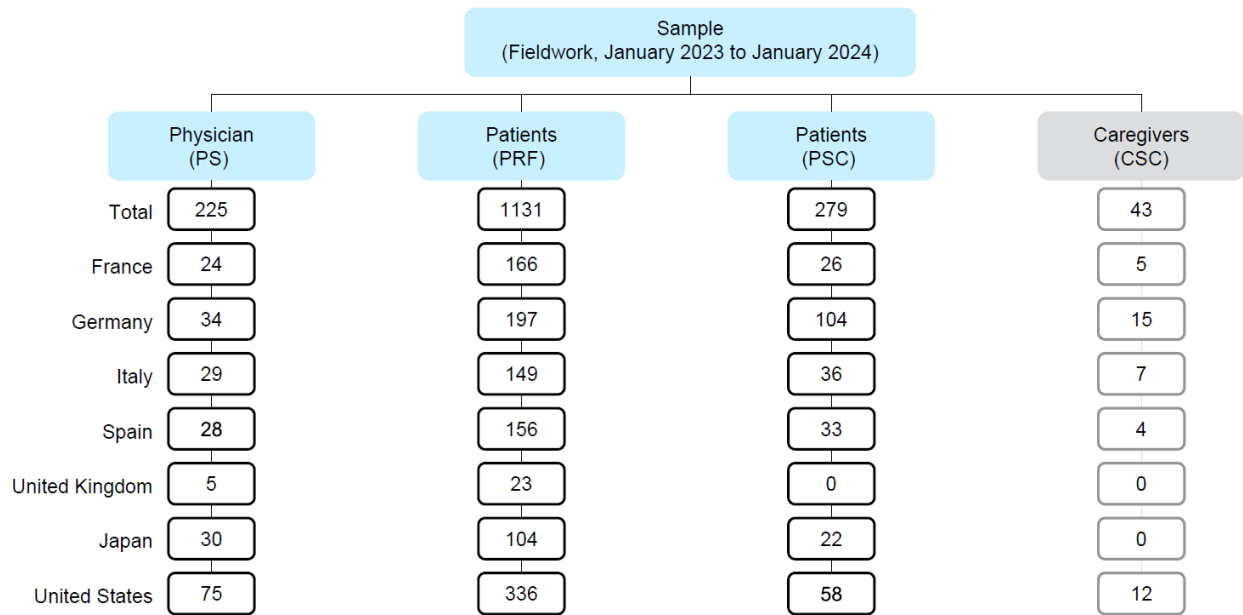
LTP long-term prophylaxis, *ODT* on-demand treatment

Table S4 LTP dose and frequency of administration

Medication	Frequency of administration at the time of data collection	Mean (SD) dose at the time of data collection [min, max]
Lanadelumab (<i>n</i> = 205)	- Once every 2 weeks: 53% - Once every 3 weeks: 4% - Once every 4 weeks: 42%	290.7 (40.9) mg [10, 300]
Plasma-derived C1INH, subcutaneous injection (<i>n</i> = 101)	- Once a week: 27% - Twice a week: 70% - Other: 3%	48.0 (18.2) IU/kg [10, 60]
Plasma-derived C1INH, intravenous injection (<i>n</i> = 84)	- Once a week: 38% - Twice a week: 62%	29.1 (30.0) IU/kg [1, 100]
Berotrastat (<i>n</i> = 102)	Once daily: 100%	147.1 (13.2) mg [100, 200]
Tranexamic acid (<i>n</i> = 140)	- Once daily: 18% - Twice daily: 40% - Three times daily: 37% - Other: 5%	866.1 (397.2) mg [100, 3000]
Danazol (<i>n</i> = 81)	- Once daily: 31% - Twice daily: 54% - Three times daily: 4% - Other: 11%	220.9 (118.8) mg [100, 600]

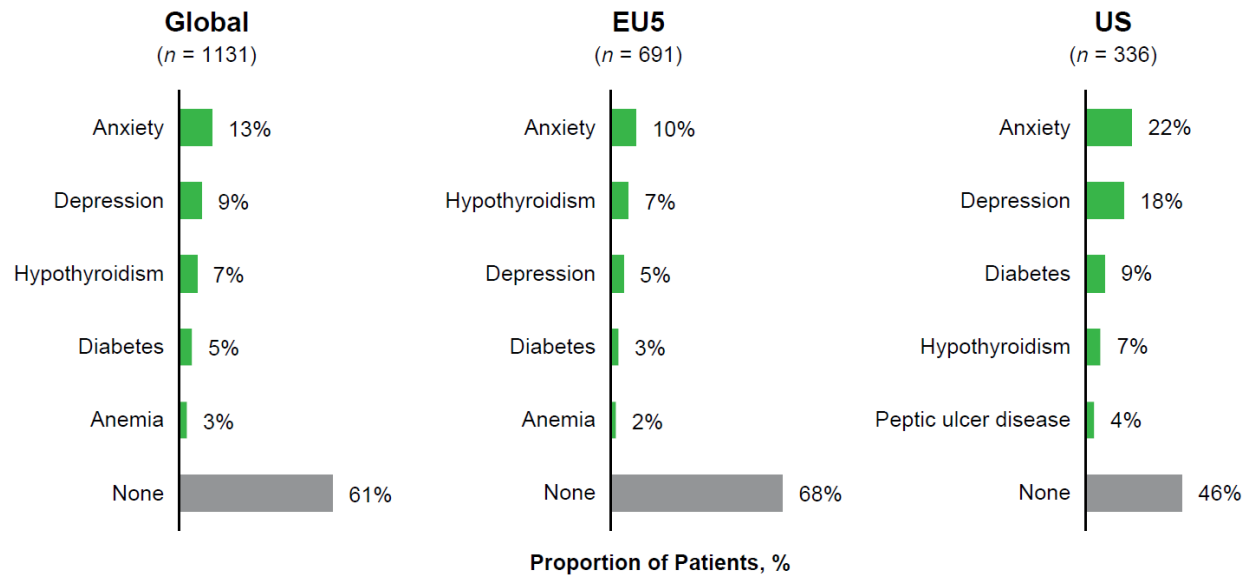
C1INH C1 inhibitor, *IU* International units, *LTP* long-term prophylaxis

Fig. S1 Physician and patient samples used in the analysis



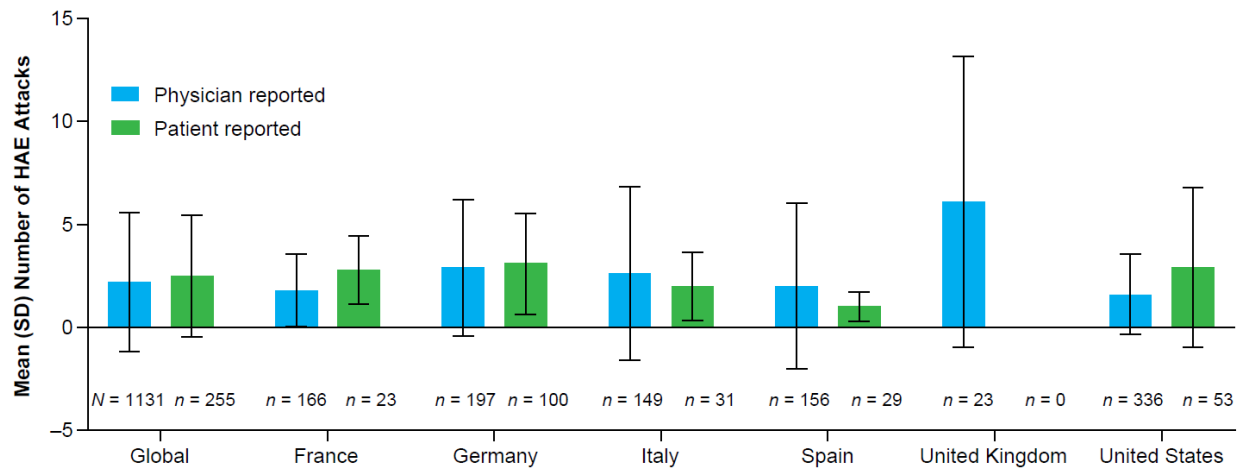
CSC Caregiver Self-Completion form, *HAE* hereditary angioedema, *PRF* Patient Record Form, *PS* physician survey, *PSC* Patient Self-Completion form. The global sample represents data collected across all geographic locations in the dataset (including Japan). Japan-specific results are not shown because of limitations in data collection among survey participants in Japan. In addition, the survey's physician screener may have enrolled respondents in Japan who were not HAE experts, which could explain deviations from established HAE management and treatment guidelines. Data from CSCs are not reported in the present analysis.

Fig. S2 Summary of concomitant conditions (physician reported)



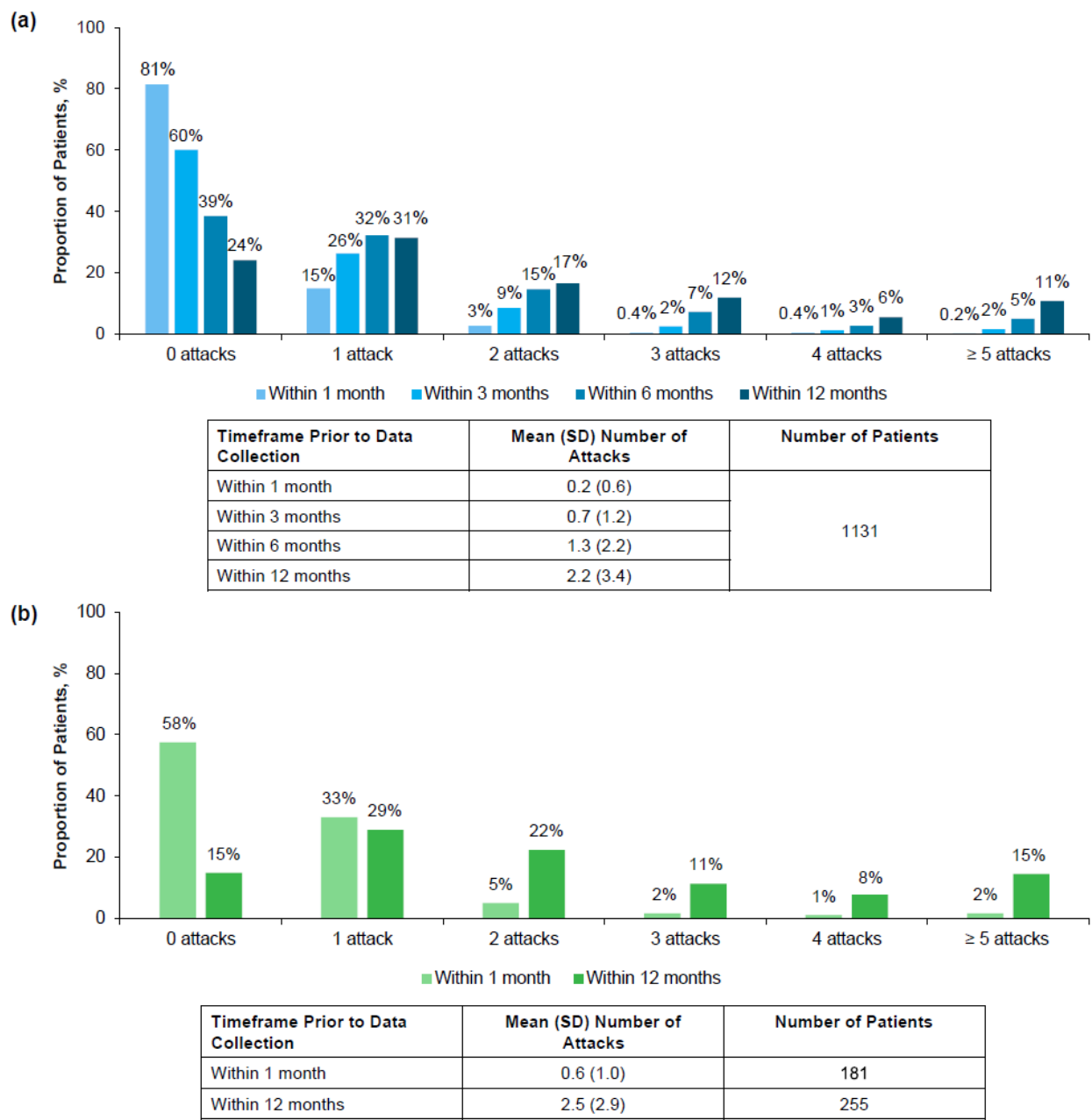
HAE hereditary angioedema. EU5 includes France ($n = 166$), Germany ($n = 197$), Italy ($n = 149$), Spain ($n = 156$), and the United Kingdom ($n = 23$). Japan-specific results are not shown because of limitations in data collection among survey participants in Japan. In addition, the survey's physician screener may have enrolled respondents in Japan who were not HAE experts, which could explain deviations from established HAE management and treatment guidelines.

Fig. S3 Number of HAE attacks reported in the previous 12 months prior to data collection by geographic location^a



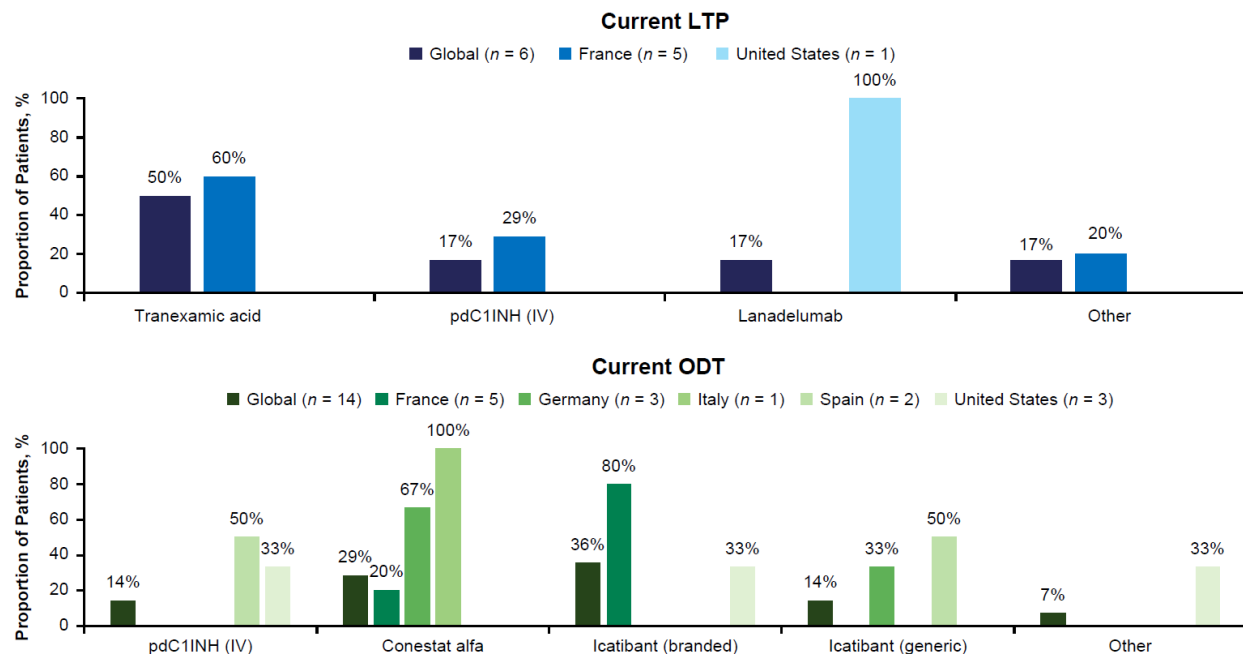
HAE hereditary angioedema, *PRF* Patient Record Form, *PSC* Patient Self-Completion form. ^aThe global sample represents data collected across all geographic locations included in the dataset. However, Japan-specific results are not shown because of limitations in data collection among survey participants in Japan (104 PRFs completed by treating physicians and 19 voluntary PSCs). In addition, the survey's physician screener may have enrolled respondents in Japan who were not HAE experts, which could explain deviations from established HAE management and treatment guidelines. There were no PSC data for the United Kingdom.

Fig. S4 HAE attacks in the 1–12 months before data collection. **a** Physician reported.
b Patient reported.



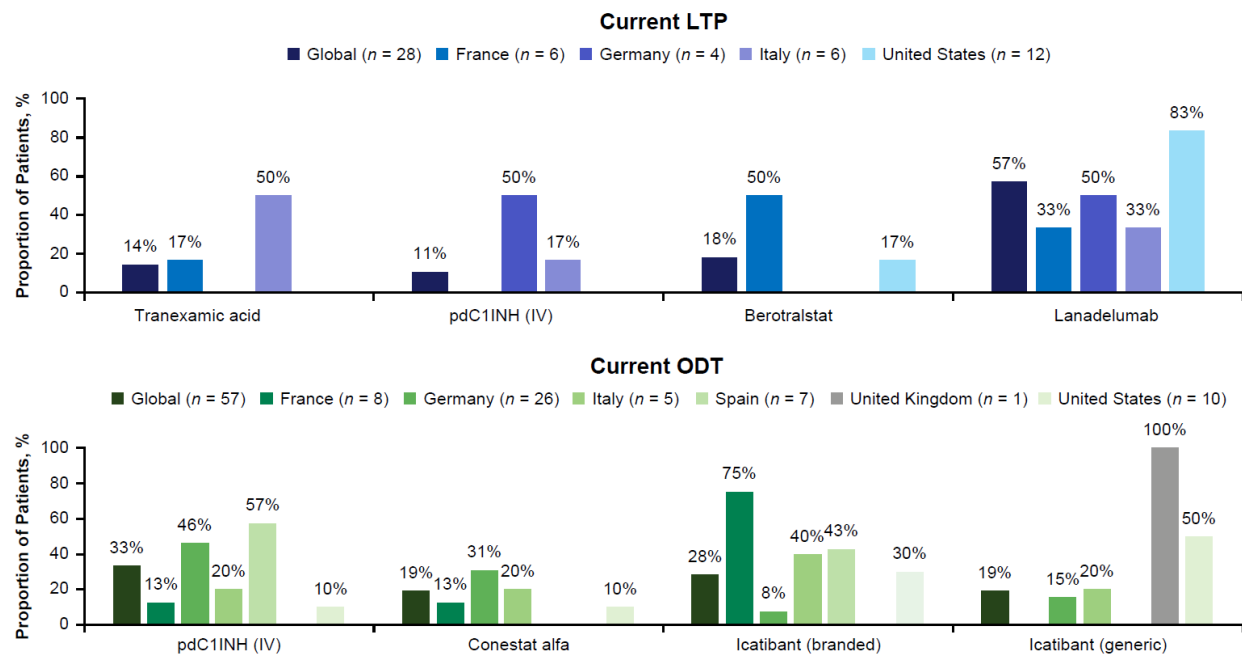
HAE hereditary angioedema

Fig. S5 Overview of medication prescribed to patients aged <12 years at the time of the survey (physician reported). LTP medication being used, top panel; on-demand medication being used, lower panel.



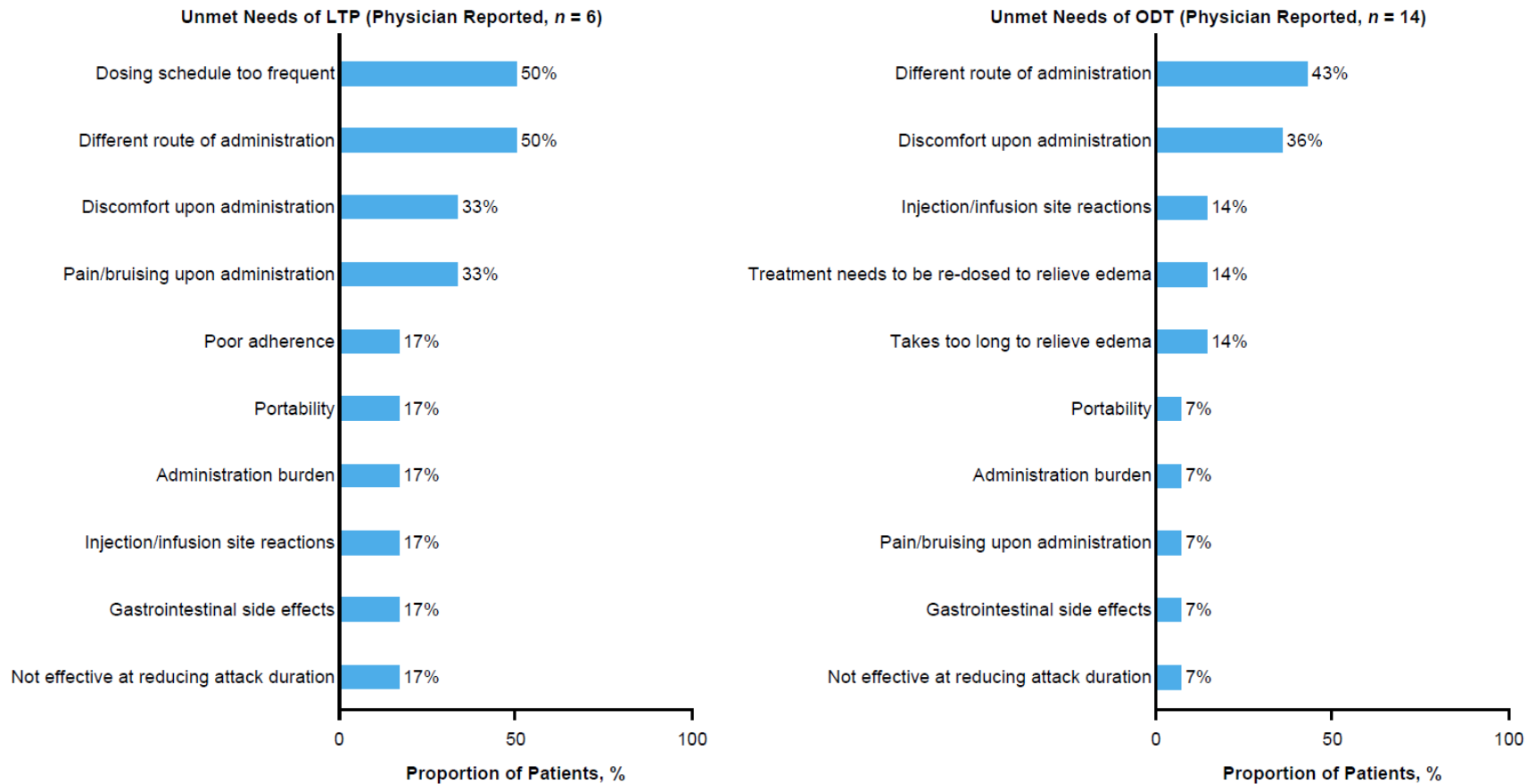
HAE hereditary angioedema, *pdC1INH* plasma-derived C1 inhibitor, *IV* intravenous injection, *LTP* long-term prophylaxis, *ODT* on-demand treatment. Information shown for the countries with available data. With the exception of the US, where icatibant was not indicated for individuals aged <18 years and conestat alfa was not indicated for those aged <12 years, the reported medications were approved for pediatric use in the countries in which they were reported [1]. Although tranexamic acid is not recommended for HAE treatment, it is often used as second-line treatment when first-line options are not available, or use of androgens is not recommended [1-3].

Fig. S6 Overview of medication prescribed to patients aged 12–17 years at the time of the survey (physician reported). LTP medication being used, top panel; on-demand medication being used, lower panel.



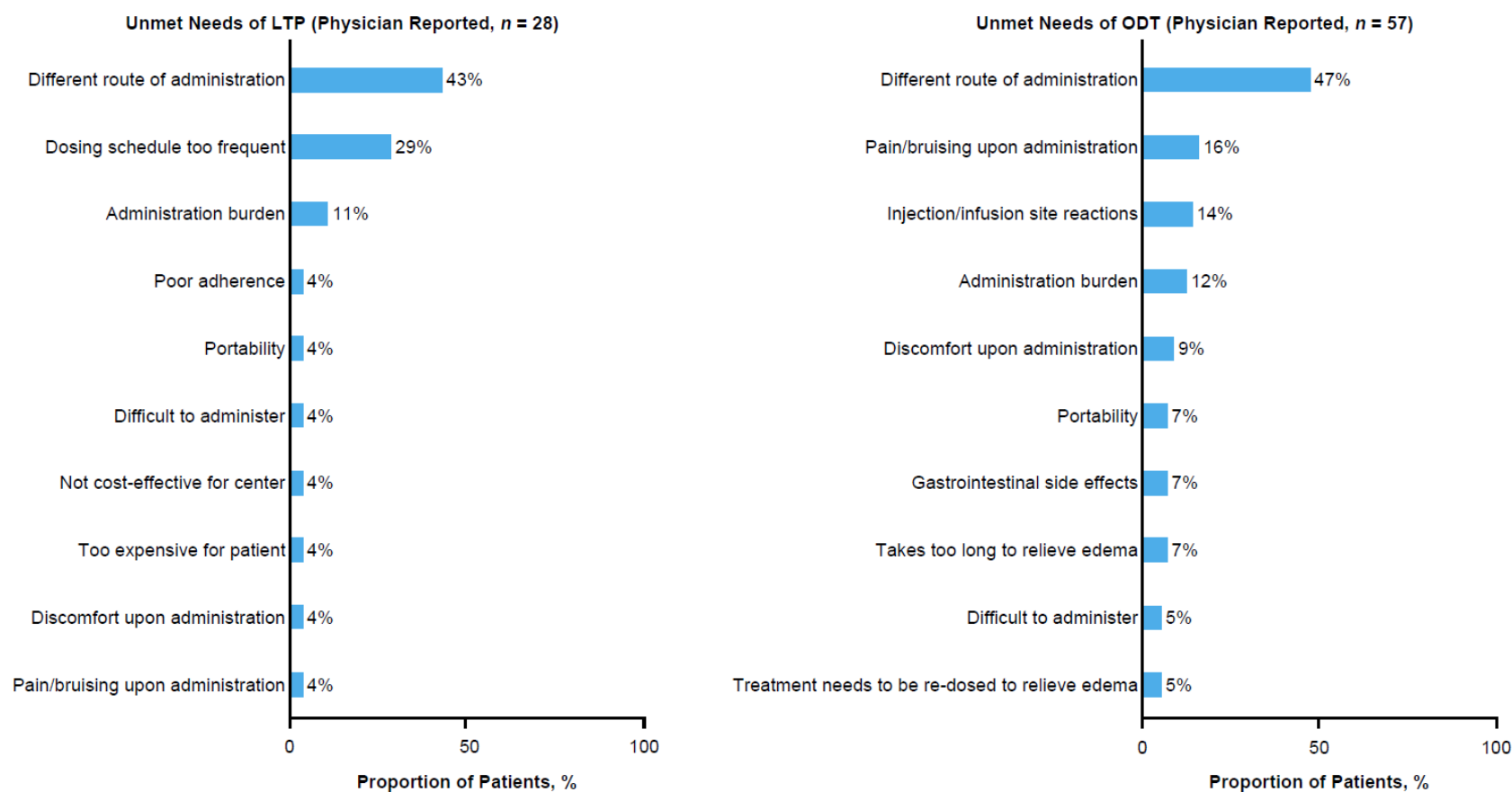
HAE hereditary angioedema, *pdC1INH* plasma-derived C1 inhibitor, *IV* intravenous injection, *LTP* long-term prophylaxis, *ODT* on-demand treatment. Information shown for the countries with available data. With the exception of the US, where icatibant was not indicated for individuals aged <18 years and conestat alfa was not indicated for those aged <12 years, the reported medications were approved for pediatric use in the countries in which they were reported [1]. Although tranexamic acid is not recommended for HAE treatment, it is often used as second-line treatment when first-line options are not available, or use of androgens is not recommended [1-3].

Fig. S7 Physician-reported unmet needs of current HAE treatment for patients aged <12 years. Top 10 unmet needs for LTP, *left panel*; top 10 unmet needs for ODT, *right panel*.



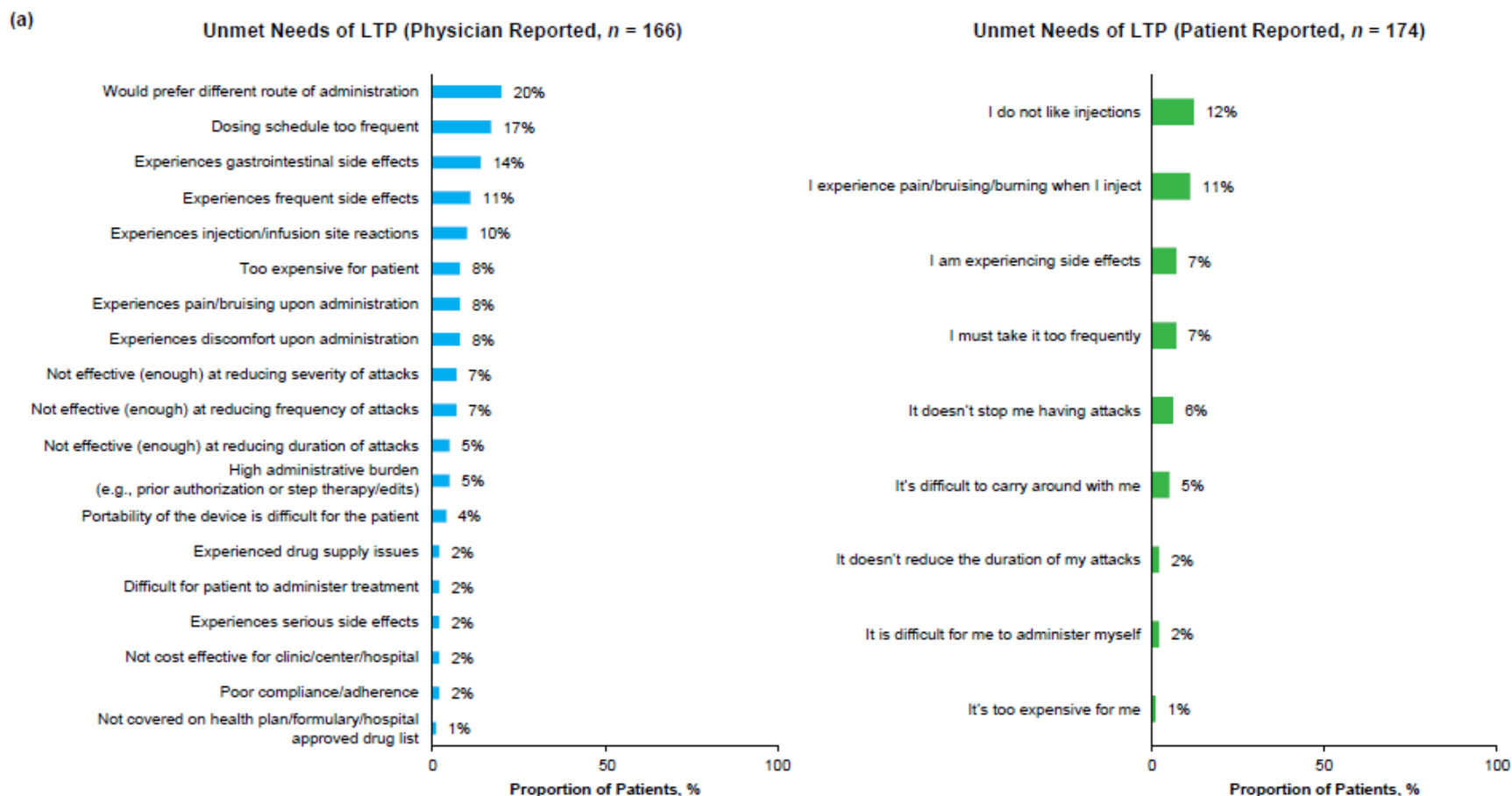
HAE hereditary angioedema, LTP long-term prophylaxis, ODT on-demand treatment

Fig. S8 Physician-reported unmet needs of current HAE treatment for patients aged 12–17 years. Top 10 unmet needs for LTP, *left panel*; top 10 unmet needs for ODT, *right panel*.

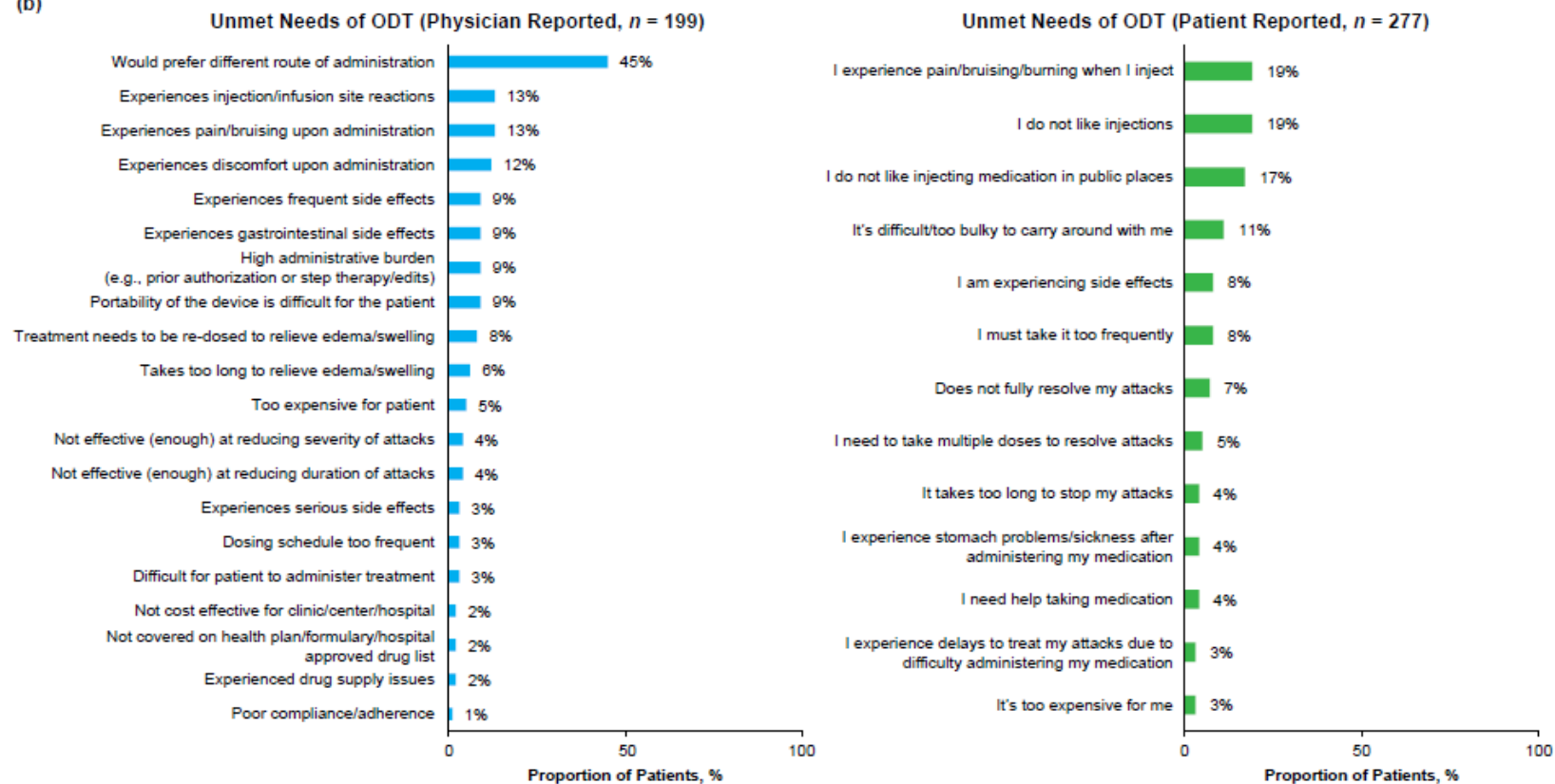


HAE hereditary angioedema, *LTP* long-term prophylaxis, *ODT* on-demand treatment. “Not effective at reducing frequency of attacks,” “gastrointestinal side effects,” “injection/infusion site reactions,” “pain/bruising upon administration,” and “frequent side effects” were also reported as unmet needs for LTP for 4% of patients each.

Fig. S9 Matched analysis **a** Unmet needs for LTP. Physician reported, *left panel*; patient reported, *right panel*. **b** Unmet needs for ODT. Physician reported, *left panel*; patient reported, *right panel*.

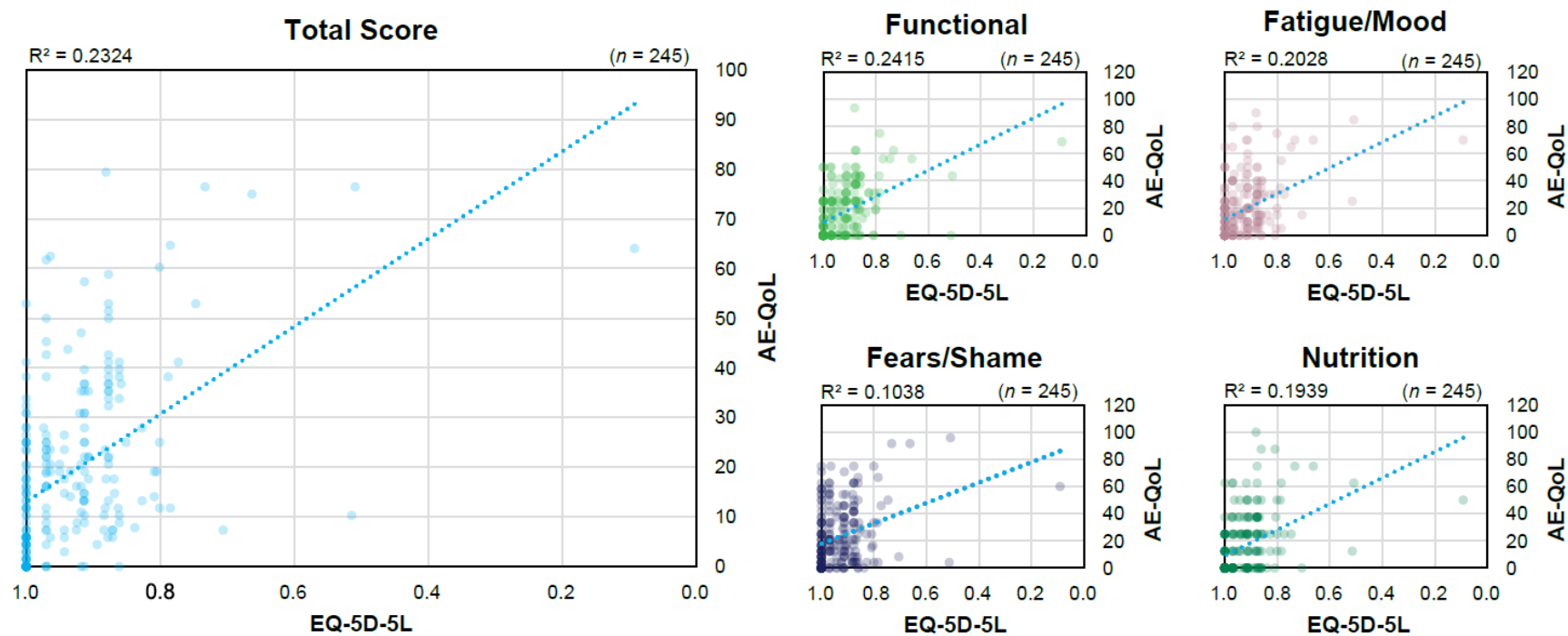


(b)



LTP long-term prophylaxis, *ODT* on-demand treatment, *PRF* Patient Record Form, *PSC* Patient Self-Completion form. The matched subset includes all PRF data for patients who also completed a PSC. Differing numbers of patients between physician- and patient-reported data are due to some physicians answering “don’t know” when completing the online PRF, some patients choosing not to answer some questions on the pen-and-paper PSC, and instances where physicians and patients were prompted not to answer certain questions based on responses to preceding questions. While such question routing occurred automatically online for physicians, patients may still have chosen to answer a question on the pen-and-paper form despite the suggested routing.

Fig. S10 Correlation between EQ-5D-5L and AE-QoL



AE-QoL Angioedema Quality of Life questionnaire, EQ-5D-5L EuroQol 5 Dimensions 5 Levels questionnaire

References

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2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. *J Allergy Clin Immunol Pract*. 2021; 9:132–50.e3.
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