

## **Supplementary information**

AU = Australia

AT = Austria

CA = Canada

FR = France

DE = Germany

ES = Spain

CH = Switzerland

UK = United Kingdom

**Table S1. Delay in diagnosis by country**

<b>Age, years</b>	<b>Total</b>	<b>AU</b>	<b>AT</b>	<b>CA</b>	<b>FR</b>	<b>DE</b>	<b>ES</b>	<b>CH</b>	<b>UK</b>
	<b>(N = 242)</b>	<b>(n = 28)</b>	<b>(n = 13)</b>	<b>(n = 32)</b>	<b>(n = 58)</b>	<b>(n = 7)</b>	<b>(n = 39)</b>	<b>(n = 8)</b>	<b>(n = 57)</b>
<b>At onset</b>									
Mean (SD)	11.54 (8.90)	9.68 (9.20)	11.92 (6.41)	13.72 (13.66)	12.81 (9.79)	8.57 (5.59)	11.90 (6.94)	10.88 (7.53)	10.07 (6.17)
Median (range)	10.00 (0–58)	7.50 (2–50)	11.00 (4–21)	12.00 (1–58)	12.00 (0–56)	8.00 (2–16)	12.00 (1–27)	8.00 (4–25)	8.00 (0–30)
<b>At diagnosis</b>									
Mean (SD)	20.81 (13.16)	19.07 (15.21)	17.69 (10.25)	22.16 (15.28)	22.78 (13.74)	12.71 (7.65)	22.90 (12.81)	22.38 (7.27)	18.95 (11.91)
Median (range)	19.00 (0–59)	16.00 (0–50)	21.00 (4–34)	20.50 (2–59)	21.00 (0–57)	16.00 (1–21)	23.00 (1–55)	24.50 (6–30)	18.00 (0–50)

**Table S2. Number of HAE attacks in the previous 6 months by country**

<b>Number of attacks</b>	<b>Total</b>	<b>AU</b>	<b>AT</b>	<b>CA</b>	<b>FR</b>	<b>DE</b>	<b>ES</b>	<b>CH</b>	<b>UK</b>
	<b>(N = 242)</b>	<b>(n = 28)</b>	<b>(n = 13)</b>	<b>(n = 32)</b>	<b>(n = 58)</b>	<b>(n = 7)</b>	<b>(n = 39)</b>	<b>(n = 8)</b>	<b>(n = 57)</b>
Mean (SD)	12.51 (14.10)	14.61 (16.50)	13.00 (7.19)	12.56 (11.67)	7.10 (8.88)	15.14 (6.49)	9.72 (13.32)	18.38 (19.00)	17.60 (17.83)
Median (range)	7.00 (0–90.00)	7.00 (0–60.00)	15.00 (3.00–25.00)	9.00 (1.00–40.00)	4.50 (0–52.00)	15.00 (2.00–22.00)	6.00 (0–78.00)	14.50 (4.00–61.00)	12.00 (1.00–90.00)

**Table S3. Number of patients visiting health care providers by country**

<b>Provider, no. of patients (%)</b>	<b>Total (N = 242)</b>	<b>AU (n = 28)</b>	<b>AT (n = 13)</b>	<b>CA (n = 32)</b>	<b>FR (n = 58)</b>	<b>DE (n = 7)</b>	<b>ES (n = 39)</b>	<b>CH (n = 8)</b>	<b>UK (n = 57)</b>
Allergist/immunologist	156 (64.5)	26 (92.9)	1 (7.7)	24 (75.0)	11 (19.0)	1 (14.3)	38 (97.4)	7 (87.5)	54 (94.7)
GP/internist	97 (40.1)	16 (57.1)	4 (30.8)	6 (18.8)	40 (69.0)	1 (14.3)	13 (33.3)	3 (37.5)	14 (24.6)
PA/nurse practitioner	23 (9.5)	2 (7.1)	0	5 (15.6)	6 (10.3)	0	8 (20.5)	0	2 (3.5)
Hematologist	18 (7.4)	0	0	6 (18.8)	4 (6.9)	3 (42.9)	0	4 (50.0)	1 (1.8)
Dermatologist	17 (7.0)	0	12 (92.3)	2 (6.3)	3 (5.2)	0	0	0	0
OB/GYN	11 (4.5)	1 (3.6)	0	0	6 (10.3)	0	2 (5.1)	0	2 (3.5)
Rheumatologist	4 (1.7)	0	0	1 (3.1)	1 (1.7)	0	1 (2.6)	0	1 (1.8)
Gastroenterologist	3 (1.2)	0	0	0	1 (1.7)	0	0	1 (12.5)	1 (1.8)

*GP* General practitioner, *PA* physician assistant, *OB/GYN* obstetrician-gynecologist

**Table S4. Number of emergency room visits, urgent care center visits, and hospitalizations by country**

<b>Facility, mean no. of visits (SD)</b>	<b>Total (N = 242)</b>	<b>AU (n = 28)</b>	<b>AT (n = 13)</b>	<b>CA (n = 32)</b>	<b>FR (n = 58)</b>	<b>DE (n = 7)</b>	<b>ES (n = 39)</b>	<b>CH (n = 8)</b>	<b>UK (n = 57)</b>
Emergency room/A&E visit	1.94 (6.02)	3.21 (5.61)	7.38 (17.12)	1.19 (2.47)	0.59 (1.53)	0.43 (1.13)	2.77 (4.32)	0.75 (1.75)	1.67 (6.93)
Urgent care center visit	1.03 (5.42)	1.25 (2.43)	0.08 (0.28)	0.09 (0.39)	0.09 (0.34)	0.14 (0.38)	3.95 (8.94)	0.75 (1.75)	0.30 (0.87)
Hospitalization	1.04 (5.10)	2.21 (11.33)	6.54 (17.49)	0.31 (0.74)	0.40 (1.39)	0.14 (0.38)	0.74 (2.47)	0.13 (0.35)	1.18 (5.38)

*A&E* accident and emergency

**Table S5. SF-12v2 scores by country**

SF-12v2 score, mean (SD)	AU (n = 28)	AT (n = 13)	CA (n = 32)	FR (n = 58)	DE (n = 7)	ES (n = 39)	CH (n = 8)	UK (n = 57)
Physical function	51.05 (9.70)	56.03 (2.97)	50.34 (9.78)	53.03 (8.65)	54.99 (5.97)	47.13 (11.31)	54.29 (4.09)	47.83 (10.17)
Role physical	47.29 (9.54)	47.02 (7.41)	47.98 (10.61)	47.48 (9.99)	51.05 (8.02)	42.16 (10.98)	47.59 (5.86)	43.91 (9.47)
Bodily pain	47.79 (9.49)	48.18 (9.86)	46.86 (11.55)	47.61 (9.82)	50.16 (7.18)	42.09 (13.92)	48.64 (7.93)	42.29 (12.05)
General health	49.10 (7.73)	49.86 (9.14)	48.85 (9.90)	49.10 (8.49)	50.28 (8.51)	42.68 (10.82)	51.22 (6.06)	44.82 (10.54)
Vitality	48.18 (8.57)	52.32 (9.49)	48.92 (9.03)	49.49 (9.75)	50.80 (9.84)	48.78 (10.63)	55.24 (4.76)	44.65 (11.01)
Social functioning	47.25 (10.83)	46.21 (8.83)	45.76 (11.22)	46.12 (9.55)	49.57 (4.52)	39.08 (10.94)	46.92 (8.57)	41.72 (10.79)
Role emotional	42.79 (12.61)	47.10 (12.07)	45.99 (11.52)	45.50 (12.46)	42.38 (8.58)	33.29 (14.05)	49.75 (7.51)	37.48 (13.29)
Mental health	45.07 (9.56)	50.27 (9.91)	48.86 (8.16)	48.64 (9.90)	48.03 (11.79)	41.50 (9.78)	49.21 (7.80)	41.81 (9.13)
Physical Health Composite	51.01 (8.21)	51.49 (4.93)	49.18 (10.92)	50.60 (7.42)	54.54 (6.65)	46.82 (11.15)	51.24 (4.15)	47.32 (10.24)
Mental Health Composite	43.63 (12.06)	47.56 (11.60)	46.80 (8.85)	46.08 (10.52)	44.50 (9.35)	37.91 (11.22)	49.33 (6.67)	39.18 (11.19)

*SF-12v2* 12-Item Short-Form Health Survey

**Table S6. HADS scores by country**

<b>HADS score, mean (SD)</b>	<b>Total (N = 242)</b>	<b>AU (n = 28)</b>	<b>AT (n = 13)</b>	<b>CA (n = 32)</b>	<b>FR (n = 58)</b>	<b>DE (n = 7)</b>	<b>ES (n = 39)</b>	<b>CH (n = 8)</b>	<b>UK (n = 57)</b>
Anxiety	8.05 (4.54)	8.82 (4.88)	4.15 (3.87)	6.75 (3.84)	6.57 (3.63)	6.29 (2.63)	10.23 (4.92)	5.75 (2.66)	9.82 (4.41)
Depression	5.39 (4.36)	5.36 (4.37)	3.62 (3.91)	4.34 (3.45)	4.16 (2.98)	2.43 (3.10)	7.59 (5.11)	2.38 (1.06)	6.93 (4.85)
Total	13.43 (8.17)	14.18 (8.52)	7.77 (7.63)	11.09 (6.33)	10.72 (5.70)	8.71 (5.22)	17.82 (9.59)	8.13 (3.27)	16.75 (8.22)

*HADS* Hospital Anxiety and Depression Scale

**Table S7. AECT scores by country**

<b>AECT score</b>	<b>Total</b>	<b>AU</b>	<b>AT</b>	<b>CA</b>	<b>FR</b>	<b>DE</b>	<b>ES</b>	<b>CH</b>	<b>UK</b>
	<b>(N = 242)</b>	<b>(n = 28)</b>	<b>(n = 13)</b>	<b>(n = 32)</b>	<b>(n = 58)</b>	<b>(n = 7)</b>	<b>(n = 39)</b>	<b>(n = 8)</b>	<b>(n = 57)</b>
Mean (SD)	8.00 (3.44)	8.86 (4.12)	6.23 (1.92)	9.06 (2.72)	9.69 (3.44)	7.00 (2.31)	6.77 (3.25)	6.63 (1.51)	6.82 (3.19)
Median	8.00	9.00	6.00	9.00	10.00	6.00	6.00	6.50	7.00
(range)	(0–16.00)	(2.00–16.00)	(3.00–10.00)	(1.00–16.00)	(2.00–16.00)	(4.00–11.00)	(0–14.00)	(4.00–9.00)	(0–13.00)

*AECT* Angioedema Control Test



**Table S8. AE-QoL scores by country**

<b>AE-QoL score, mean (SD)</b>	<b>Total (N = 242)</b>	<b>AU (n = 28)</b>	<b>AT (n = 13)</b>	<b>CA (n = 32)</b>	<b>FR (n = 58)</b>	<b>DE (n = 7)</b>	<b>ES (n = 39)</b>	<b>CH (n = 8)</b>	<b>UK (n = 57)</b>
Functioning	42.46 (27.39)	36.38 (28.47)	50.48 (22.02)	34.18 (24.95)	34.91 (30.80)	30.36 (17.09)	53.53 (24.95)	36.72 (27.02)	50.66 (23.88)
Fatigue/mood	46.24 (24.95)	48.21 (25.50)	39.62 (31.39)	44.69 (20.04)	35.17 (21.07)	28.57 (21.74)	55.77 (23.44)	36.25 (16.85)	55.96 (25.87)
Fears/shame	54.68 (24.67)	51.19 (26.30)	29.49 (20.59)	46.35 (19.74)	54.17 (24.51)	29.17 (19.69)	69.44 (19.03)	35.94 (21.59)	63.01 (21.78)
Nutrition	36.16 (28.62)	34.82 (25.08)	25.00 (21.65)	26.17 (21.38)	31.03 (28.22)	14.29 (19.67)	42.95 (32.16)	23.44 (33.70)	50.00 (27.35)
Total	47.14 (20.69)	44.91 (23.43)	36.88 (20.27)	40.63 (15.52)	41.33 (19.98)	27.52 (13.01)	58.56 (17.34)	34.74 (16.32)	56.50 (18.91)

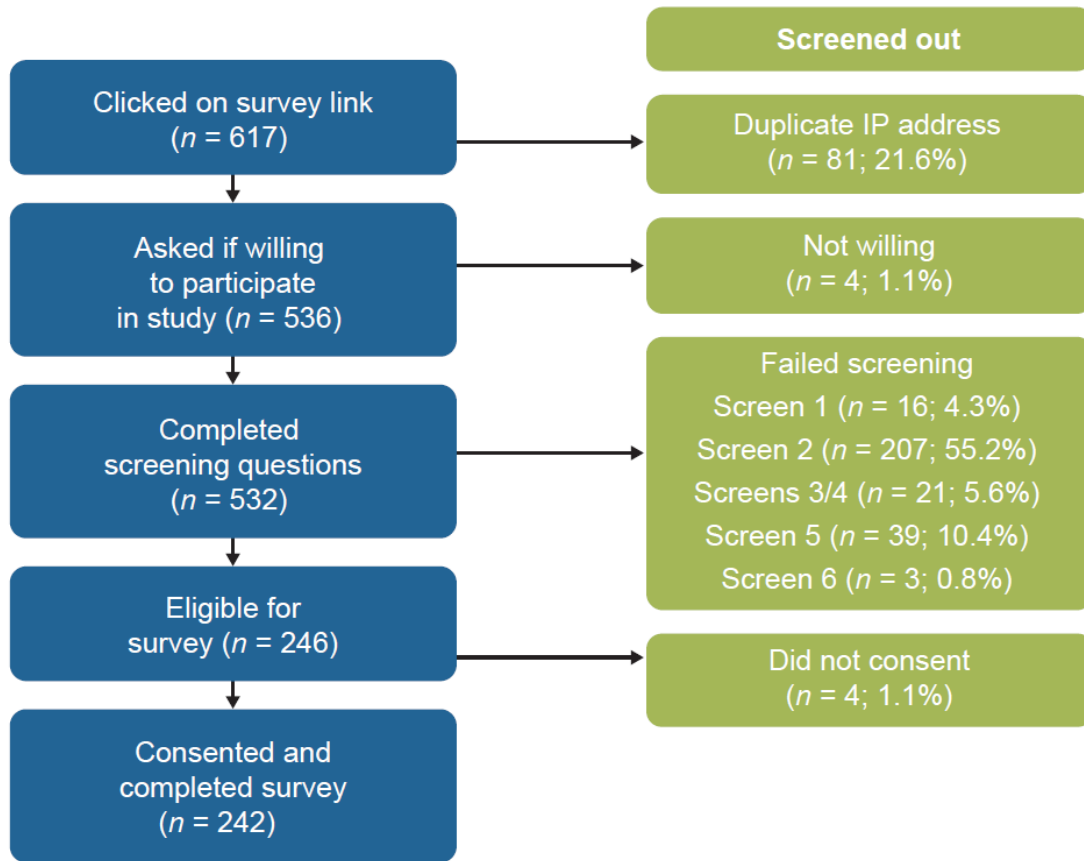
*AE-QoL* Angioedema Quality of Life questionnaire

**Table S9. WPAI scores by country**

<b>WPAI score, mean (SD)</b>	<b>Total (N = 242)</b>	<b>AU (n = 28)</b>	<b>AT (n = 13)</b>	<b>CA (n = 32)</b>	<b>FR (n = 58)</b>	<b>DE (n = 7)</b>	<b>ES (n = 39)</b>	<b>CH (n = 8)</b>	<b>UK (n = 57)</b>
Absenteeism	7.87 (20.01)	5.08 (15.57)	3.59 (9.04)	4.55 (16.11)	7.27 (20.61)	0	17.25 (29.83)	0	8.60 (19.06)
Presenteeism	24.59 (28.65)	25.56 (32.94)	18.89 (17.64)	20.00 (31.12)	19.23 (27.41)	10.00 (10.00)	33.33 (35.68)	12.00 (21.68)	29.76 (25.71)
Work productivity loss	24.18 (30.03)	27.22 (34.95)	21.51 (19.86)	19.17 (30.57)	15.47 (26.67)	10.00 (10.00)	32.86 (36.94)	10.00 (20.00)	32.18 (28.54)
Activity impairment	33.88 (31.20)	33.21 (30.07)	35.38 (27.57)	25.31 (29.29)	23.97 (31.06)	11.43 (10.69)	50.77 (34.52)	20.00 (26.19)	41.93 (26.95)

*WPAI* Work Productivity and Impairment questionnaire

**Figure S1. Patient flow**



Percentages for patients screened out are calculated from a total of 375 patients excluded. Screen

1: “Has a healthcare professional told you that you have hereditary angioedema, or HAE?”

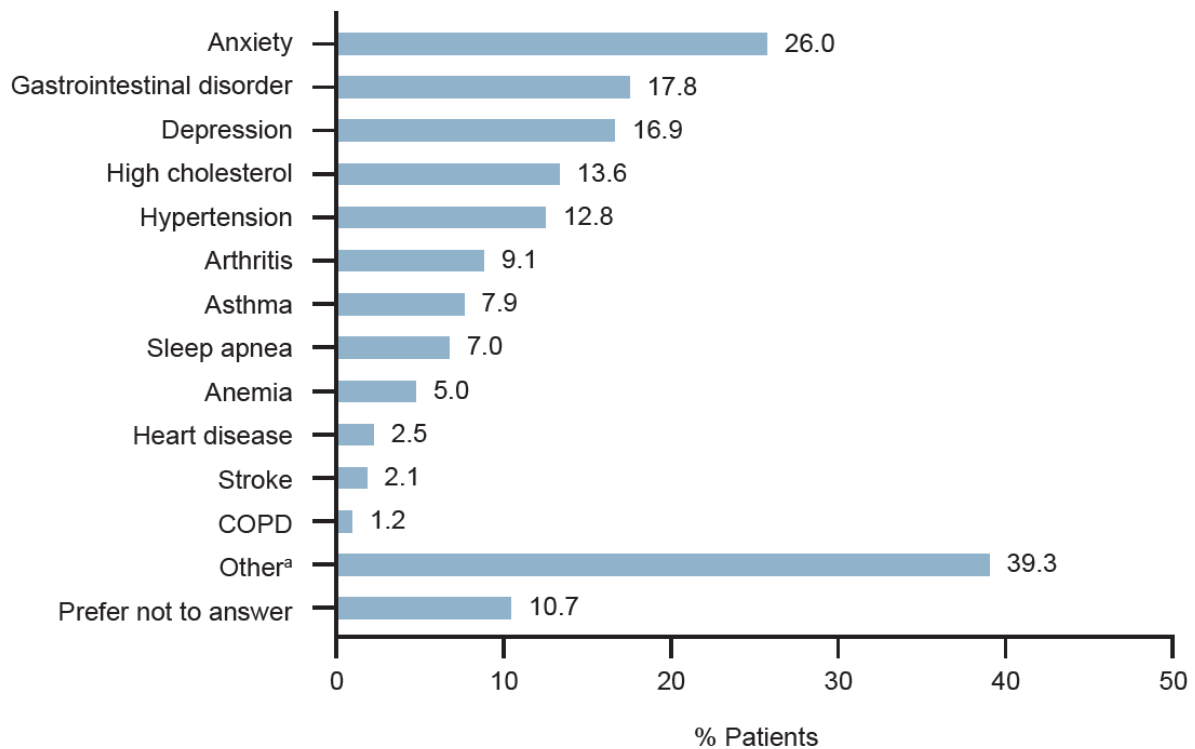
Screen 2: “What type of HAE do you have?” Screen 3: “In the past year (12 months), how many angioedema attacks did you have? Please include any attacks in which you experienced swelling, abdominal pain, nausea, vomiting, diarrhea, or other symptoms related to your attack.” Screen

4: “In the past year (12 months), how often did you have signs or symptoms that suggest that an attack was coming WITHOUT having an angioedema attack?” Screen 5: “Have you taken a

prescription medication to treat or prevent an angioedema attack in the past 2 years?” Screen 6:

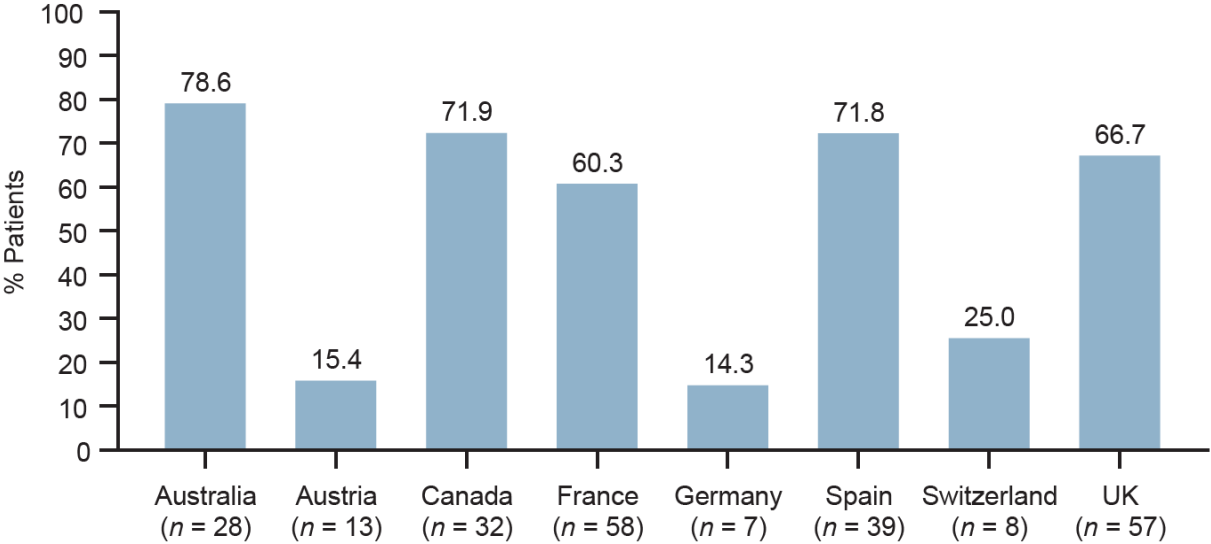
“What is your current age?”

**Figure S2. Comorbidities**

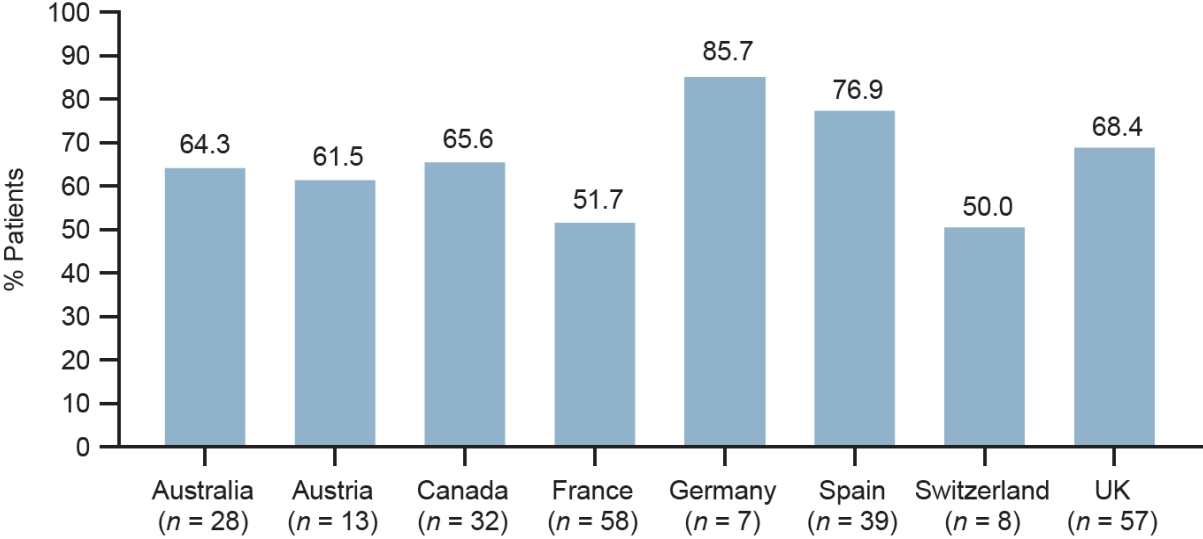


\*A total of 50 “other” comorbidities were reported by patients as free text, including thyroid conditions (n=7, 2.9%), arthritis (n=3, 1.2%), and diabetes (n=3, 1.2%). *COPD* chronic obstructive pulmonary disease.

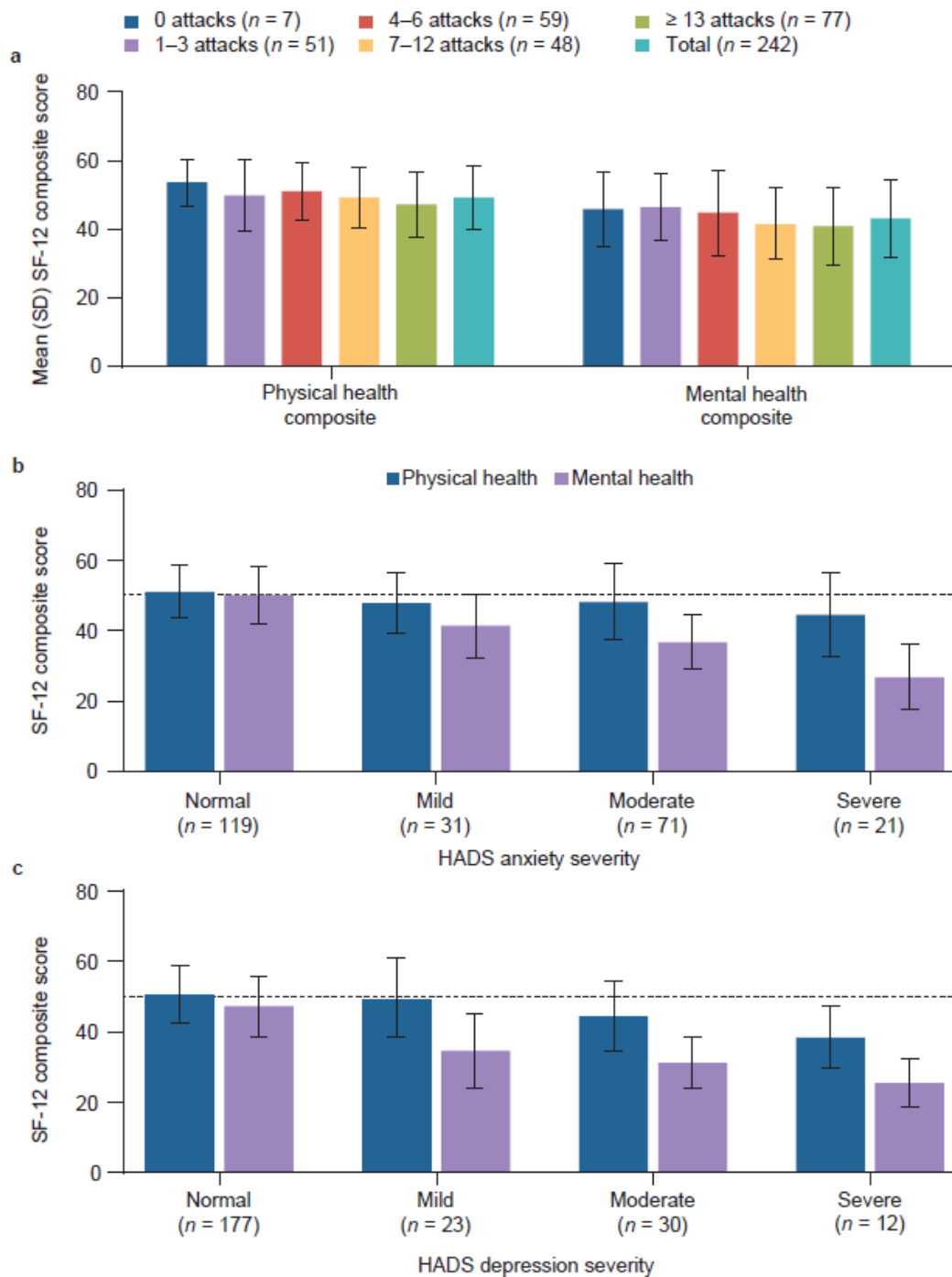
**Figure S3. Current LTP use by country**



**Figure S4. STP use by country**



**Figure S5. Mean SF-12v2 physical and mental health composite scores**



Scores are shown by number of HAE attacks in the previous 6 months (a) and by HADS anxiety (b) and depression (c) subscales. The dotted line indicates a mean score of 50 which represents

the general population. *HADS* Hospital Anxiety and Depression Scale, *HAE* hereditary angioedema, *SF-12v2* 12-Item Short-Form Health Survey



**Figure S6. AECT scores by number of attacks in the previous 6 months**

