Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax): Evaluation of Measurement Properties in Phase II Study Data

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Background

Primary focal axillary hyperhidrosis (AHH) is a disorder of excessive sweating. Appropriate patient care requires the ability to accurately evaluate symptoms and treatment responses.[1,2]

The Hyperhidrosis Disease Severity Measure-Axillary© (HDSM-Ax) is an 11-item measure of AHH severity in subjects ≥12 years of age (see Figure 1). Each question has 5 response categories scored 0-4. A child-specific HDSM-Ax was developed for children ≥9 to <12. The development process aimed to satisfy regulatory and scientific requirements for registrational clinical trials.[2] Content validity was supported by iterative rounds of qualitative and quantitative research.[3]

Figure 1: Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax) Scale

INSTRUCTIONS: We are interested in finding out about your current experience with excessive underarm sweating.

- Please consider excessive sweating in your underarms only when selecting the answer to each question.
- For each statement, please provide the response that best describes your experience since you woke up yesterday.
- Please answer ALL questions even if some seem similar to others or seem irrelevant to you.

1. Since you woke up yesterday, how often did you experience the following while you were awake?
(Please select the number that best describes your experience.)

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
a) Damp or wet clothing because of your underarm sweating?	0	1	2	3	4
b) Underarm sweating for no apparent reason?	0	1	2	3	4

2. Since you woke up yesterday, how severe was your experience with the following?
(Please select the number that best describes your experience.)

	I did not experience this	Mild	Moderate	Severe	Very severe
a) Underarm sweating when you felt nervous, stressed or anxious?	0	1	2	3	4
b) Damp or wet clothing because of your underarm sweating?	0	1	2	3	4
c) Underarm sweating after little or no physical exercise?	0	1	2	3	4
d) Underarm wetness?	0	1	2	3	4
e) Underarm sweating for no apparent reason?	0	1	2	3	4
f) Underarm sweating that was unmanageable?	0	1	2	3	4
g) Underarm sweating when you were cool?	0	1	2	3	4

3. Since you woke up yesterday, what was your experience with each of the following?
(Please select the number that best describes your experience.)

	Not at all	Slight	Moderate	Strong	Very strong
a) Feeling the need to change clothes because of underarm sweating?	0	1	2	3	4
b) Feeling the need to wipe sweat from your underarms?	0	1	2	3	4

Objective

To examine the reliability, validity and ability to detect change of the HDSM-Ax using Phase II (BBI-4000-CL-203) clinical trial data and two psychometric paradigms.

Table 1: Classical Test Theory Analyses Data Summary

Parameter	Estimate
Data availability	
Item missing data (max %)	0.2
Percent for whom total scores can be compute	100
Scale-to-sample targeting	
Possible scale range (mid-point)	0-44 (22)
Observed score range	0-44
Mean (SD; SE error mean)	26.5 (11.3; 0.34)
Median (IQR)	28.5 (19-35)
Floor effect: n (%)	55 (5.0)
Ceiling effect: n (%)	11 (1.0)
Skewness / Kurtosis	-0.3974 / -0.688
Reliability	
Cronbach's alpha^	0.98
Homogeneity coefficient^	0.80
Test-retest reliability*	
Correlations between screening and baseline	0.71 (n=189)
Difference between screening and baseline: mean (SD); SRM; ES**	-0.0699 (5.4196); -0.013; -0.010
Differential Responsiveness (total sample)	
Screening to baseline (n=189; T1 – T2)	
Paired samples t-test: t-value (p-value)	-0.177 (p=0.859)
Cohen's ES (mean change / SD screening)	(-0.010) -0.0699 / 7.0645
SRM (mean change / SD change)	(-0.013) -0.0699 / 5.4196
Baseline to Day29 (n=182; T1-T2)	
Paired samples t-test: t-value (p-value)	15.449 (p<0.001)
Cohen's effect size (mean change / SD baseline)	(1.85) 13.3475 / 7.2295
Standardised Response Mean (mean change / SD change)	(1.15) 13.3475 / 11.6555

^Computed from 1101 out of 1104 with complete data; *Agreement between total scores at screening and baseline; **SD Screening = 7.064515, SRM = Standard Response Mean, ES = Effect Size

Table 2: Rasch Measurement Theory Analyses Data Summary

EVALUATION	11-item HDSM axillary
No. items	11
SCALE-TO-SAMPLE TARGETING	
Item locations	
Item location range	-0.759 to +0.314
Threshold location range	-5.817 to +5.678
Person locations	
Person measure range	-7.629 to +7.525
Person measure mean (SD)	1.312 (3.345)
No. extreme scores: n (%)	66 (6.0%)
Floor / ceiling effect: n (%)*	55 (5.0%) / 11 (1%)
ITEM & SCALE PERFORMANCE	
Thresholds	
No items with disordered thresholds	0 of 11
Item fit statistics	
Item-person interaction	
Item fit residuals - range	-10.528 to +14.267
Item fit residuals exceeding +/-2.5 (item)	8 (n6 <-2.5; n2>+2.5)
Item bias	
No. of residual correlation^	55
Range of item residual correlations	-0.266 to +0.302
No. correlations > +/-0.30 (%)	1 (1.8%)
PERSON & GROUP MEASUREMENT	
Sample separation by these items	
Person separation index (reliability)**	0.964
Person fit statistics	
Person fit residuals - range	-4.846 to +5.973
Person fit residuals exceeding +/-2.5: n (%)	214/1038 (20.6%)
Person fit residuals: <-2.5 / >+2.5	173 (16.6%) / 41 (3.9)

Total data items = 1104; n = 66 extreme scores; n = 1038 item analysis; *: where floor effect = MAX possible score (worst hyperhidrosis); ceiling effect = MIN possible score (least hyperhidrosis); ^: Where number of correlations is given by the combination rule, nCr = n!/[(n-r)!r!] **: with n = 66 extreme scores included

Methods

Subjects (n=227, 23 sites) were randomized 1:1:1:1 to apply the retro-metabolically designed anticholinergic investigational drug sofpironium bromide gel, 5%, 10%, 15%, or vehicle, nightly to the axillae for 42 days. Eligible subjects were ≥18 years and had AHH for ≥6 months. Subjects had HDSM-Ax scores of >3 and >50 mg/5min of sweat production in each axilla, with a two-axilla combined total of >150 mg/5min.

Results

Classical Test Theory analyses showed good reliability (Cronbach's alpha = 0.98; test retest reproducibility = 0.71). Correlations and mean score differences supported validity and large effect sizes implied good ability to detect change. Rasch Measurement Theory analyses showed good targeting, ordered item thresholds, statistical cohesiveness, no item scoring bias or instability and good person fit (Person separation index 0.96). A 1-point improvement was found to be clinically meaningful.

Conclusion

HDSM-Ax satisfies psychometric criteria as a fit-for-purpose patient-reported outcome measure of AHH severity.

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