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Minimum important difference for validated instruments in women with urge incontinence

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Abstract

Aims—Minimum important difference (MID) estimates the minimum degree of change in an instrument's score that correlates with subjective sense of improvement. The aim of this study was to estimate the MID for the Urogenital Distress Inventory(UDI), Incontinence Impact Questionnaire(IIQ) and Overactive Bladder Questionnaire(OAB-q) using anchor and distribution-based approaches in patients with urge-predominant incontinence and whether MID changes over time.

Methods—This was a sub-analysis of a multi-center trial of 307 women with pure urge (11) or urge-predominant (296) incontinence who completed condition-specific instruments 10 weeks and 8 months after randomization to anticholinergic medication with or without behavioral therapy. We applied anchor-based methods only when the Kendall's rank correlations between the anchors (Global Perception of Improvement(GPI), Patient Satisfaction Questionnaire(PSQ) and incontinence episodes(IE)) and the incontinence instruments (UDI, UDI irritative subscale, IIQ and OAB-q subscales) were ≥0.3. We applied 3 distribution-based methods to all instruments: effect sizes of ±0.2 SD (small) and ±0.5 SD (medium) and standard error of measurement (SEM) of ±1. Analyses were performed at both time points.

Results—Anchor-based MIDs for the UDI ranged from -35 to -45 and -15 to -25 for the irritative subscale Distribution-based methods MIDs for UDI and IIQ ranged between -10 to -25 and -19 to -49 respectively, reflective of a reduction in bother and symptom severity. OAB-q subscale MIDs ranged from +5 to +12, denoting improved quality of life (HRQL) and -13 to -25, consistent with a reduction in symptom severity (SS).

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Conclusions—The MID in women with urge-predominant UI for the UDI and UDI irritative are -35 and -15. Our findings are consistent with previously reported MIDs for the OAB-q subscales. Distribution-based method MIDs are lower values than anchor-based values. The MID did not typically change over the time.

INTRODUCTION

Overactive bladder (OAB) is estimated to affect more than 10-15% of adult women and 5-10% of women experience urge urinary incontinence (UUI) at least monthly.[1] OAB carries a large personal and societal burden with major impacts on health related quality of life, productivity, healthcare utilization, and costs.[1-4] For this reason, questionnaires that measure UUI and OAB symptoms are valuable tools for research and patient care.

Three commonly used instruments that evaluate UUI and OAB symptoms are: 1) the Urogenital Distress Inventory (UDI); 2) the Incontinence Impact Questionnaire (IIQ); [5] and 3) the Overactive Bladder Questionnaire (OAB-q).[6] They are psychometrically sound based on reliability, validity and sensitivity-to-change data.[5-8] However, the data are limited with respect to the the minimum important difference (MID) for these instruments. The MID is a score change that reflects a clinically meaningful response to treatment. The MID is useful for interpreting questionnaire results for within-group or between-group differences and can be used to perform power calculations for future studies. MIDs have been reported in women with urge urinary incontinence for the OAB-q subscales and Kings Health Questionnaire.[9&10] Estimates for the UDI[11] have been suggested in women with stress-predominant incontinence; however, it is unclear whether these values apply to subjects with UUI. Furthermore, previous studies suggest that MIDs may vary over time with certain chronic conditions.[12&13] Our objectives were to estimate the MID for the UDI, IIQ, OAB-q and/or their selected subscales in patients with UUI and to determine whether the MID changes over time.

MATERIALS AND METHODS

This was an ancillary analysis of data from the BE-DRI study; the design and primary outcome of the trial have been published.[14] Methods of the trial relevant to this analysis include collection of the UDI, IIQ, OAB-q and 7-day bladder diary, Global Perception of Improvement (GPI) and Patient Satisfaction Questionnaire (PSQ) at baseline, 10 weeks and 8 months post-randomization in women enrolled in a randomized controlled trial of anticholinergic therapy with or without behavioral therapy for UUI.

The UDI, IIQ and OAB-q were the 3 instruments considered for MID analyses. The UDI measures the degree of bother with obstructive, irritative and stress symptoms. [5] The IIQ captures the impact of incontinence on activities, travel, emotional state, and social habits, while the OAB-q specifically assesses the impact of OAB on patients' lives. [5&6] They are all psychometrically sound based on reliability, validity and sensitivity-to-change data.[5-8] The OAB-q consists of 33 items: an 8-item symptom bother scale (SS) and a 25-item health-related quality of life (HRQL) scale. The quality of life items are composed of 4 subscales (concern, coping, social interaction & sleep) and based on these, a total HRQL score can be

assigned.[6] Higher scores represent better quality of life. For the other measures a lower score/value is indicative of less bother, symptom severity or fewer incontinence episodes

The concept of minimum important difference (MID) represents the magnitude of benefit for which randomized controlled trials should be powered in order to minimize type 1 and type 2 errors (false positives and false negatives). Likewise, they can be used as clinical markers of improvement, as well as gauges for interpreting future studies.[12] There are two methods of determining MID, anchor-based and distribution-based.

We utilized both methods to measure MID. Anchor-based MIDs are determined by evaluating the change in an instrument score or objective measure in relation to a global measure or satisfaction or improvement. Specifically, it is determined by calculating the difference between the mean instrument score for those individuals with the smallest amount of improvement and the mean instrument score of those individuals with no change. This analysis was performed for the following instruments/subscales: UDI, UDI irritative subscale, IIQ and OAB-q subscales [health related quality of life (HRQL) and symptom severity (SS)]. For all anchor-based analyses, Kendall's rank correlation coefficients were first calculated to determine whether the instruments and anchors were at least moderately correlated ($r \geq 0.3$).[16] Only if this criterion was met did we proceed with the calculation of an anchor based MID. We used subjective and objective anchors to evaluate whether the MIDs vary based on the type of anchors used. For the subjective anchors we used two global measures: the GPI and the PSQ. They ask the following: 1. "Overall, do you feel that you are: much better, better, about the same, worse or much worse?" and 2. "How satisfied are you with your progress: completely satisfied, somewhat satisfied, or not at all satisfied?".[15] We used the difference in mean questionnaire scores between patients reporting *"better"* and those reporting *"about the same"* on the GPI. Similarly, the difference in mean questionnaire scores between patients reporting *"somewhat satisfied"* and those reporting *"not at all"* satisfied on the PSQ was used. For the objective anchors, we compared the difference in scores between those patients with a ≥25% reduction in incontinence episodes (IE) on the 7-day diary to those with no change[14]. Since this 25% reduction was arbitrarily chosen, ≥50% and ≥75% reductions were also analyzed.[11]

The distribution-based method of MID assessment was applied using an effect size of 0.2 and 0.5 standard deviation (SD) as well as a standard error of measurement (SEM) of 1. [12] Cohen designated an effect size of 0.2 as small and 0.5 as medium, derived from absolute differences divided by the standard deviation. This approach is widely understood and central to many psychometric indices. Likewise, a standard error of measurement of 1 has also been shown to yield results consistent with the use of patient-centered anchors across a wide range of chronic conditions. [12&17-19]

Finally, we included a post-hoc threshold analysis using the UDI. We considered the possibility that once the post-treatment UDI score falls below a certain threshold the majority of subjects would consider themselves satisfied with treatment. Using the PSQ data, the responses were dichotomized to satisfied (n=258) *("completely"* and *"somewhat"*) versus *"not at all satisfied"* (n=14) and ROC (Receiver Operating Characteristic) analysis

was performed. This analysis allowed us to determine a threshold that would maximize the sensitivity and specificity.

RESULTS

Three hundred subjects were randomized with an average age of 57 ± 14 years. The majority of the participants were White and 19% were Non-Hispanic Black. Ten weeks and 8 months data were analyzed for 89% and 79% of the subjects, respectively. The UDI, IIQ, and OAB-q scores improved post-treatment at 10 weeks and 8 months. Likewise, the number of incontinence episodes (IE) ascertained from the bladder diaries declined after treatment (Table I).

The UDI, UDI irritative and OAB-q(symptom severity) met *a priori* criteria for further evaluation using an anchor-based approach (Kendall's rank correlation (r) of ≥0.3) for determining the MID at 8 weeks and 10 months for *all* anchors (GPI, PSQ and IE). The OAB-q (HRQL) met our criterion (r ≥0.3) for the following anchors at one of the two time points: GPI at 8 months and the IEF at 10 weeks. IIQ was not at least moderately correlated with any of the anchors and thus no further analysis was performed (Table II).

The mean UDI scores at 10 weeks and 8 months for the subjective (GPI and PSQ) and objective (IE) anchors by response levels, as well as the UDI MID for these anchors, are presented in Table IIIa. From the subjective anchors (GPI and PSQ), the MID values of the UDI varied from -35 to -43 at 10 weeks and 8 months, respectively. A similar variation was found in the MID values of the UDI from the objective anchor, the IE, at the same time points: -41 and -36, respectively. The MID for the UDI irritative subscale ranged from -15 to -25 (Table IIIb). When evaluating the OAB-q (HRQL), a MID of 11 (range 5 to 16) was obtained using the GPI anchor at 8 months and a MID value of 13 (range 3 to 23) was seen using IE with a 25% reduction cut-point at 10 weeks (data not shown) For the OAB-q (SS) the range was from -13 to -25 for both all anchors at both time points (Table IIIc).

When the alternate cut-points were used for IE (50% and 75% reduction), only the UDI at 8 months with the 75% reduction in IE met criterion for further analysis (r≥0.3). The MID value was consistent with all others at -45 (range -58 to -31). Given the similarities in the results obtained, none of the other instruments (IIQ or OAB-q) were analyzed with these alternate IE cut-points.

In Table IV, distribution-based MIDs are presented for the UDI, UDI irritative, IIQ, and OAB-q subscales using 0.2 SD, 0.5 SD and 1 SEM. When using the distribution-based methods, the MID values were lower than those obtained using anchor based methods (Table IIIa-c).

Threshold analysis was performed using the UDI values to determine if a particular cut-point in UDI score was correlated with patient satisfaction after treatment. At 10 weeks, a UDI score of 100 or less resulted in a sensitivity of 90% and specificity of 71%. However, at 8 months, a clear cut-point could not be readily established.

DISCUSSION

This analysis found that using both subjective and objective anchor-based methods, the range of MID for the UDI and UDI irritative subscale in urge-predominant incontinent patients ranged from -35 to -45 points and -15 to -25, respectively. This range represents an approximately 15% change in score and correlates well with the patient report of at least "better" on the GPI or "somewhat satisfied" on the PSQ. Likewise the OAB subscale MIDs ranged from +5 to +12 (HRQL) and -13 to -25 (SS) which is consistent with previously reported estimates of 10 by Coyne et al.[9] The IIQ did not meet our *a priori* inclusion criteria, restricting our ability to estimate the MID using anchor-based methods for these instruments.

One limitation of this analysis is that the data is "clumped" or not well distributed between the various responses. Using Kendall's Tau adjusts for this; nevertheless, an overestimation of the degree of correlation between the instruments and anchors may result. Given this limitation, using a strict cut-off of 0.3 may be somewhat stringent; however, this cut point is advocated in the literature.[16]

We noted that the UDI MID estimates were slightly smaller for patient-reported anchors than the objective anchor at 10 weeks, but this reversed in longer-term follow-up. It is important to note that active treatment was discontinued at 10 weeks, although participants were allowed to request additional treatment during follow-up. Nonetheless, although this finding will require additional study, we believe that longer-term follow-up is more important for assessing clinically relevant outcomes. The 7-day voiding diary, our objective anchor, gave similar MID estimates for the UDI at both time points as the patient reported anchors, suggesting that UDI alone (without 7 day bladder diary) may be adequate to describe clinically relevant outcomes. This is particularly important as maintaining bladder diaries are burdensome for patients and non-compliance can be an issue.

Using multiple anchor-based approaches, Barber, et al proposed the MID threshold of -11 for the UDI when measuring treatment of stress urinary incontinence .[11] This is considerably smaller than our estimate, suggesting that patient's perception of improvement required more clinical improvement for UUI than SUI. This may be due to the underlying differential in quality of life impact experienced by affected patients, with UUI patients experiencing more impact and bother than SUI patients. In addition, the baseline UDI score tends to be higher in women with UUI than SUI; for example, the mean baseline UDI score in our study was 120 and in Barber's study of women with SUI was 80. As many patients have elements of both stress and urge urinary incontinence, it will be important to estimate MID in women with mixed UI in future analyses.

This analysis compared anchor-based approaches that included two patient-reported measures (global perception of improvement and the patient satisfaction questionnaire) and one objective measures of incontinence severity (number of incontinence episodes recorded on the 7-day diary). Although it would be ideal to have a single value for the MID of each instrument used in clinical care or research, the use of multiple approaches provides ranges of estimates for the MID which will require additional refinement as data from other

research populations becomes available. We were able to estimate the distribution-based MID for all three instruments: the UDI, IIQ, and OAB-q at 10 weeks and 8 months. The distribution-based approach consistently resulted in small changes compared to the anchor-based approach. Given the similarity of the patient-reported outcome estimates, and the increasing awareness of patient-reported outcomes in assessing treatment of UUI, we propose that the anchor based estimates of MID may be useful to design and perform power calculations of future studies, in keeping with the recommendation of Revicki et al.[11&20] Furthermore, the FDA recently established clinical guidelines for patient-reported outcome (PRO) measures which states, “The empiric evidence for any responder definition is derived using anchor-based methods”.[21]

This analysis is the first to provide an estimate of the UDI MID for women undergoing UUI treatment. Our analysis is strengthened by the use of validated UUI measures from a large UUI multi-center study, as well as the analytic use of multiple approaches to estimate MID values. However, the lack of correlation of some validated UUI measures limited our ability to compare anchor-based and distribution-based methods for estimating MID for the IIQ.

CONCLUSIONS

In women undergoing treatment for UUI, the minimum important difference for the UDI and UDI irritative are -35 and -15, respectively. For the OAB-q (health related quality of life) and OAB-q (symptom severity) subscales, our findings were consistent with previous reports.[9] It is important to note that these are population estimates; an individual woman’s perception of her improvement may not correlate with these values. Furthermore, while MID provides a means of powering future studies, threshold analyses offers another method for analyzing patient centered outcome data. A particular target score can be used to dichotomize subjects as “success” or “failure” based on a given instrument. Patient centered outcome research remains important in describing response to treatment in clinical research and thus measures of satisfaction continue to be important to collect.

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Table I

Subjective and Objective Measures in the BE-DRI study at Baseline, 10 Weeks, and 8 Months

	Baseline (n=307)	10 weeks$^{\Delta}$ (n=272)	8 months$^{\Delta}$ (n=241)
Subjective Measures (Mean ± SD)			
• **UDI** (range 0-300)	120.5±49.6	54.1±43.4	72.7±50.4
• **UDI Irritative** (range 0-100)	58.4±21.8	26.4±22.9	36.5±25.6
• **IIQ** (range 0-400)	153.6±99.5	68.9±78.9	78.9±85.5
• **OAB-q** (HRQL) (range 25-150)	61.7±24.1	85.6±15.7	81.2±19.3
• **OAB-q** (SS) (range 8-48)	60.2±20.9	26.9±19.3	34.2±22.4
Objective Measures (Mean ± SD)			
• **Incontinence Episodes**(IE) per day	3.7±2.4	0.9±1.2	1.4±1.9

* Health-related quality of life subscale; higher score represents improved quality of life. For all other measures a lower score/value is indicative of a reduction in bother, symptom severity and incontinence episodes.

$^{\Delta}$P values all < 0.0001.

Table II

Correlations Between Instruments and Anchors at 10 Weeks and 8 Months

	GPI	PSQ	Incontinence Episodes
			r *
At 10 week			
Δ UDI	**0.29**	**0.28**	**0.38**
Δ UDI irritative	**0.31**	**0.30**	**0.35**
Δ IIQ	0.10	0.07	0.17
Δ OAB-q Symptom Severity	**0.28**	**0.30**	**0.38**
Δ OAB-q HRQL total	-0.21	-0.18	**-0.28**
At 8 month			
Δ UDI	**0.43**	**0.44**	**0.41**
Δ UDI irritative	**0.45**	**0.40**	**0.37**
Δ IIQ	0.22	0.24	0.19
Δ OAB-q Symptom Severity	**0.38**	**0.31**	**0.40**
Δ OAB-q HRQL total	**-0.29**	-0.21	-0.23

Correlations using Kendall's tau

*Correlation coefficient from Spearman.

Table III

a. Anchor-based Measures and the Change in the UDI by Response Level and the MID at 10 Weeks and 8 Months

Severity Measure	N	10 weeks	N	8 months
Global Percent Improvement (GPI), mean (±SD)				
Much better	109	-88.0 (60.4)	45	-96.6 (49.7)
Better	117	-65.1 (47.9)	89	-58.7 (47.6)
About the Same	41	-29.8 (40.9)	89	-16.2 (46.8)
Worse	5	0.1 (11.3)	15	-16.3 (46.1)
Much Worse	0		3	-42.8 (7.9)
Missing	35		66	
MID for UDI using GPI anchor		**-35.3** (-51.9, -18.8)		**-42.5** (-56.5, -28.6)
Patient Satisfaction Questionnaire (PSQ)				
Completely satisfied	126	-87.8 (59.7)	63	-88.8 (50.6)
Somewhat satisfied	132	-54.1 (46.1)	131	-43 (50.8)
Not at all satisfied	14	-16.1 (37.8)	44	-2.5 (35.8)
Missing	35		69	
MID for UDI using PSQ anchor		**-38.1** (-63.3, -12.8)		**-40.5** (-56.8, -24.1)
Incontinence Episode ($IE_{25\%}$)				
Improved (≥25% decrease)	241	-70.4 (55.7)	187	-54.9 (56.1)
No change (0 to 25%)	18	-29.1 (38.3)	34	-18.8 (50.3)
Worse (≥25% increase)	3	-27.6 (58.9)	8	-25.0 (23.3)
Missing	45		78	
MID for UDI using $IE_{25\%}$ anchor		**-41.2** (-67.6, -14.9)		**-36.2** (-56.5, -15.8)
Incontinence Episode ($IE_{75\%}$)				
Improved (≥75% decrease)			106	-72.3 (54.6)
No change (0 to 75%)			119	-27.7 (49.4)
Worse (≥75% increase)			4	-33.1 (11.5)
Missing			78	
MID for UDI using $IE_{75\%}$ anchor		**		**-44.6** (-58.3, -30.9)

b. Anchor-based Measures and the Change in the UDI Irritative Subscale by Response Level and the MID at 10 Weeks and 8 Months

Severity Measure	N	10 weeks	N	8 months
Global Percent Improvement (GPI), mean (±SD)				
Much better	109	-42.1 (26.8)	45	-44.8 (24.9)
Better	117	-33.5 (20.8)	89	-27.1 (20.5)
About the Same	41	-10.6 (21.5)	89	-9.2 (20.2)
Worse	5	-5.3 (5.8)	15	0.8 (20.8)
Much Worse	0		3	-7.4 (8.5)

Severity Measure	N	10 weeks	N	8 months
Missing	35		66	
MID for UDI using GPI anchor		-22.9 (-30.5, -15.4)		-17.9 (-23.9, -11.9)
Patient Satisfaction Questionnaire PSQ)				
Completely satisfied	126	-42.0 (26.6)	63	-38.9 (25.6)
Somewhat satisfied	132	-27.7 (21.7)	131	-21.0 (22.2)
Not at all satisfied	14	-2.3 (13.9)	44	-0.9 (15.9)
Missing	35		69	
MID for UDI using PSQ anchor		-25.3 (-37.1, -13.6)		-20.1 (-27.2, -12.9)
Incontinence Episode ($IE_{25\%}$)				
Improved (≥25% decrease)	241	-34.2 (25.5)	186	-25.7 (25.2)
No change (0 to 25%)	18	-19.7 (18.1)	34	-6.7 (22.1)
Worse (≥25% increase)	3	3.7 (25.7)	8	-16.7 (15.1)
Missing	45		79	
MID for UDI using $IE_{25\%}$ anchor		-14.5 (-26.6, -2.4)		-19.1 (-28.2, -10.0)
Incontinence Episode ($IE_{75\%}$)				
Improved (≥75% decrease)	153	-40.4 (24.8)	106	-32.6 (25.7)
No change (0 to 75%)	107	-22.3 (22.9)	118	-13.5 (21.8)
Worse (≥75% increase)	2	-11.1 (0)	4	-23.6 (16.0)
Missing	45		79	
MID for UDI using $IE_{75\%}$ anchor		-18.1 (-24.0, -12.1)		-19 (-25.3, -12.8)

c. Anchor-based Measures and the Change in the OAB-q Symptom Severity by Response Level and the MID at 10 Weeks and 8 Months

Severity Measure	N	10 weeks	N	8 months
Global Percent Improvement (GPI), mean (±SD)				
Much better	107	-41.1 (23.5)	45	-45.0 (24.2)
Better	117	-35.0 (20.1)	89	-28.6 (19.5)
About the Same	40	-14.4 (19.4)	89	-15.9 (19.0)
Worse	5	-2.5 (8.3)	15	-9.0 (20.9)
Much Worse	0		3	-5.8 (19.1)
Missing	38		66	
MID for UDI using GPI anchor		-20.6 (-27.8, -13.4)		-12.7 (-18.4, -7.0)
Patient Satisfaction Questionnaire PSQ)				
Completely satisfied	124	-42.1 (22.8)	63	-37.8 (23.0)
Somewhat satisfied	131	-29.1 (20.4)	131	-25.0 (21.6)
Not at all satisfied	14	-4.1 (18.2)	44	-10.1 (18.5)
Missing	38		69	
MID for UDI using PSQ anchor		-25.0 (-36.2, -13.7)		-14.9 (-22.1, -7.7)

Severity Measure	N	10 weeks	N	8 months
Incontinence Episode ($IE_{25\%}$)				
Improved (≥25% decrease)	238	-35.0 (22.9)	186	-29.2 (22.7)
No change (0 to 25%)	18	-18.6 (16.5)	34	-9.9 (20.5)
Worse (≥25% increase)	3	-12.5 (17.5)	8	-22.2 (18.5)
Missing	48		79	
MID for UDI using $IE_{25\%}$ anchor		-16.3 (-27.2, -5.5)		-19.3 (-27.6, -11.1)
Incontinence Episode ($IE_{75\%}$)				
Improved (≥75% decrease)	150	-40.5 (22.9)	106	-35.7 (22.2)
No change (0 to 75%)	107	-24.0 (19.4)	118	-17.5 (20.6)
Worse (≥75% increase)	2	-22.5 (3.5)	4	-21.9 (25.9)
Missing	48		79	
MID for UDI using $IE_{75\%}$ anchor		-16.5 (-21.9, -11.1)		-18.2 (-23.8, -12.5)

*The difference in mean between response group with no improvement/change and group with the smallest improvement.

**The Kendall's rank correlation did not reach 0.3, so results were not shown Note: The negative value reflects a reduction in the degree of bother for the UDI.

Table IV

Distribution-based MID Calculations

Effect size	ΔUDI	ΔUDI Irritative	ΔIIQ	ΔOAB-q (HRQL)	ΔOAB-q (SS)
0.2 SD *	-9.9	-4.4	-19.9	4.8	-4.2
0.5 SD *	-24.8	-10.9	-49.7	12.1	-10.4
1 SEM	-22.1	-11.9	-18.2	4.3	-7.5

* Baseline SD used.