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MINIMUM IMPORTANT DIFFERENCE FOR VALIDATED INSTRUMENTS IN WOMEN WITH URGENCY INCONTINENCE

Hypothesis / aims of study
Minimum important difference (MID) estimates the smallest change in an instrument's score that is associated with subjective improvement. The aim of this study was to determine the MID for the Urogenital Distress Inventory (UDI), Incontinence Impact Questionnaire (IIQ) and Overactive Bladder Questionnaire (OAB-q) in subjects with urge incontinence. A secondary aim was to determine whether MID changes over time. Previous reports suggest that the MID for the UDI ranges between -6.4 and -22.4 in women with stress urinary incontinence[1]; however, it is unclear if these values apply to subjects with urgency incontinence.

Study design, materials and methods
Data for this sub-analysis came from a multi-center trial of 307 women with pure urge (n=11) or urge-predominant (n=296) incontinence who were randomized to anticholinergic therapy with or without behavioral therapy. Condition specific instruments were completed at 10 weeks and 8 months post-randomization. The 3 instruments for planned MID analysis were the UDI, IIQ and OAB-q; all psychometrically sound based on reliability, validity and sensitivity to change data. The UDI measures the degree of bother related to urinary symptoms, while the IIQ captures the impact of incontinence on activities. The scores for both instruments range between 0 and 300. The OAB-q consists of 33 items, which includes a 25-item health-related quality of life (HRQL) scale (range 25-150) which measures coping, concern, sleep and social impact of overactive bladder symptoms. The concept of minimum important difference (MID) represents the magnitude of benefit as measured by a validated instrument for which randomized controlled trials should be powered in order to minimize type 1 (false positive) and type 2 (false negative) errors. Likewise MIDs can be used as clinical markers of improvement, as well as gauges for interpreting future studies. There are primarily two methods used to determine MID: anchor-based and distribution-based. Anchor-based MIDs estimate the change associated with improvement or satisfaction using a global or objective measure. Specifically, it is the difference between the mean instrument score for those individuals with the smallest amount of improvement and the mean score of those individuals with no change. For the subjective anchors we used two global measures: the Global Perception of Improvement (GPI) ["Overall, do you feel that you are: much better, better, about the same, worse or much worse?"] and the Patient Satisfaction Questionnaire (PSQ) ["How satisfied are you with your progress?"]. The MID was defined as 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 anchor, 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. For *all* anchor-based analyses Spearman's correlation coefficients were first calculated to determine whether the instruments (UDI, IIQ, OAB-q) and anchors (GPI, PSQ, and IE) were at least moderately correlated (r≥0.3).[2] MID analyses were performed using both time points (10 weeks and 8 months) to assess whether MID changes over time. We also applied 3 distribution-based methods to all instruments: effect sizes of ±0.2 standard deviation (SD) (small) and ±0.5 SD (medium) and standard error of measurement of ±1 SEM.[3] Finally, a post-hoc threshold analysis was also performed for the UDI. PSQ responses dichotomized to those who were satisfied (n=258) ("*completely*" and *"somewhat*") versus "*not at all satisfied*" (n=14). Receiver operating characteristic (ROC) analysis was performed to determine a threshold to maximize the sensitivity and specificity in detecting satisfaction.

Results
307 subjects were enrolled, with complete data available for 89% at 10 weeks and 79% at 8 months. The average age was 57 ±14years. Post-treatment, UDI, IIQ, and OAB-q scores reflected improvement and incontinence episodes (IE) declined. IIQ and OAB-q were less than moderately correlated with the anchors (r<0.3); therefore, only the UDI was analyzed using anchor-based analyses. Baseline mean UDI scores were 121±50. Anchor-based MIDs for the UDI ranged from -35 to -43 for both subjective (PGI and PSQ) and objective anchors (IE) at both time points. (Table 1) Distribution-based method MIDs for UDI and IIQ ranged between -10 to -25 and -18 to -50 respectively, reflective of a reduction in degree of bother and symptom severity. OAB-q MIDs ranged from +5 to +12, denoting an improvement in health related quality of life. The post-hoc threshold analysis determined that a UDI score of 100 or less had a sensitivity of 90% and specificity of 71% to detect satisfaction.

Interpretation of results
Only UDI consistently met *a priori* criteria for both anchor and distribution based analysis. There was no difference between the MID for the UDI using subjective and objective anchors. MID for the UDI did not change over the time points studied. Anchor-based values were lower (-35 to -43) than distribution-based (-10 to -25) methods. Finally, the minimum important difference is greater in subjects with UUI (-35-to 45) than those with SUI (-6.4 and -22.4) suggesting that patients with urge UI may require a higher magnitude of symptomatic improvement in order to achieve a global sense of improvement. The post-hoc threshold analysis may represent an alternate means of measuring patient centered outcomes, with a UDI score of 100 or less being the threshold that maximizes sensitivity and specificity to detect satisfaction.

Concluding message

In women undergoing treatment for UUI, the MID for UDI ranges between -35 and -43 points. This appears to be higher than in women undergoing non-surgical treatment for SUI and may represent differences in impact of these two incontinence conditions on quality of life. It is important to note that these are population estimates, and that an individual woman's perception of her improvement may not correlate with these values. Patient-centered outcome research remains important in describing response to treatment in clinical trials.

Table 1: Anchor-based Measures and Change in UDI by Response Level and the MID

Anchor	N	10 weeks	N	8 months
Global Percent Improvement (GPI)				
Better	117	-65.1 (47.9)	89	-58.7 (47.6)
About the Same	41	-29.8 (41.0)	89	-16.2 (46.8)
MID (GPI)		-35.3 (-51.9, -18.8)		-42.5 (-56.5, -28.6)
Patient Satisfaction Questionnaire (PSQ)				
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)
MID (PSQ)		-38.1 (-63.3, -12.8)		-40.5 (-56.8, -24.1)
Incontinence Episodes ($IE_{25\%}$)				
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)
MID ($IE_{25\%}$)		-41.2 (-67.6, -14.9)		-36.2 (-56.5, -15.8)

References

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Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**ClinicalTrials.gov registration number: NCT00090584**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**The institutional review boards of the participating clinical centers of the Urinary Incontinence Treatment Network: University of Alabama at Birmingham and Dept. of Veterans Affairs; University of Texas Health Sciences Center; University of California, San Diego; Duquesne University and Magee Women's Hospital, University of Pittsburgh; University of Texas Southwestern; University of Maryland; Oakwood Hospital; University of Utah Health Sciences Center; Loyola University Medical Center**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**