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Distribution-Based Estimates of Minimal Important Difference for Hospital Anxiety and Depression Scale and Impact of Event Scale-Revised in Survivors of Acute Respiratory Failure

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Abstract

Objective—This study will estimate distribution-based minimal important difference (MID) for the Hospital Anxiety and Depression Scale anxiety (HADS-A) and depression (HADS-D) subscales, and the Impact of Event Scale-Revised IES-R in survivors of acute respiratory failure (ARF).

Methods—Secondary analyses of data from two U.S. and three U.K. studies of ARF survivors (Total N=1,223). HADS-D and HADS-A were used to assess depression and anxiety symptoms. IES-R assessed PTSD symptoms. Standard error of measurement (SEM), minimal detectable change₉₀ (MDC₉₀), 0.5 standard deviation (SD), and 0.2 SD were used to estimate MID for the combined sample, by studies, 6- and 12-month follow-ups, country and mental health condition.

Results—Overall, MID estimates converged to 2.0-2.5 for the HADS-A, 1.9-2.3 for the HADS-D, and 0.17-0.18 for the IES-R. MID estimates were comparable across studies, follow-up, country and mental health condition.

Conclusion—Among ARF survivors, 2.0-2.5 is a reasonable range for the MID for both HADS subscales and 0.2 is reasonable for IES-R. Until anchor-based MIDs for these instruments are available, these distribution-based estimates can help researchers plan future studies and interpret the clinical importance of findings in ARF patient populations.

INTRODUCTION

Psychological symptoms are common in patients surviving acute respiratory failure (ARF) requiring mechanical ventilation in an intensive care unit (ICU).¹⁻⁴ A recent study of ARF survivors reported that >38% screened positive for general anxiety, >26% for depression, >22% for post-traumatic stress disorder (PTSD) during 2-year longitudinal follow-up.⁵ The Hospital Anxiety and Depression Scale (HADS)⁶ and Impact of Event Scale-Revised (IES-R)⁷ have been used in studies of ICU survivors^{3,5,8-10} to assess symptoms of these conditions. While the HADS and IES-R demonstrate good reliability and validity in ICU survivors^{2,11} and other populations¹²⁻¹⁴, the minimal important difference (MID) has not been reported in ARF survivors.

MID estimates are useful for determining the clinical relevance of group differences or patient change, and for sample size calculations for clinical trials. MIDs may be estimated using anchor-based or distribution-based approaches. Anchor-based approaches offer direct estimates of MIDs, but require additional data from patient ratings of change or other instruments with an established MID to serve as the anchor. If calculating anchor-based MIDs is not feasible, distribution-based approaches, which evaluate score difference or change relative to sampling variability, can provide indirect estimates of MID using only data from the target instrument. Cohen's thresholds for small and medium effect sizes, which assist in interpreting the magnitude of group differences,¹⁵ can also inform the determination of a MID¹⁶. Using a large sample of ARF survivors from five studies

conducted in the United States and United Kingdom, we estimate distribution-based MIDs for the HADS anxiety (HADS-A) and depression (HADS-D) subscales and the IES-R.

METHODS

Data Sources

Secondary analyses were performed using data from five studies. ALTOS (ARDSNet Long-Term Outcomes Study) is a multi-center national prospective study of ARF survivors recruited from 41 hospitals in the U.S., with 6- and 12-month follow-up between 2008 and 2012.¹⁷ ICAP (Improving Care of Acute Lung Injury Patients) is a prospective cohort study evaluating ARF survivors from 4 teaching hospitals in Baltimore, MD, with 6 and 12-month follow-up between 2005 and 2008.⁵ CESAR (Conventional ventilator support versus Extracorporeal membrane oxygenation for Severe Adult Respiratory failure) is a multi-center randomized trial of extracorporeal membrane oxygenation (ECMO) versus conventional ventilatory support in ARF, with 6-month follow-up between 2002 and 2007¹⁸. PRaCTICaL (Pragmatic Randomized, Controlled Trial of Intensive Care follow up programmes in improving Longer-term outcomes from critical illness) is a multi-center randomized trial of a nurse-led intensive care follow-up program versus standard care in ARF patients with 6- and 12-month follow-up between 2007 and 2008.¹⁹ The study by Jones et al.⁴ is a multi-centered randomized trial of a rehabilitation program in ARF survivors. Both intervention and control group participants from these trials were included.

Measures

The HADS-D and HADS-A subscales⁶ range 0-21 based on seven items, with scores ≥ 8 indicating at least mild anxiety or depression symptoms, respectively. The IES-R⁷ has 22 items and ranges 0-4, with scores ≥ 1.6 indicating substantial PTSD symptoms.² For this study, HADS data were available at 6-month follow-up from all 5 studies, and at 12-month follow-up from ALTOS, ICAP, and PRaCTICaL. IES-R data were available at 6 and 12 months, but only from ALTOS and ICAP. Baseline HADS and IES-R were not available. All studies obtained informed consent from participants, and had research ethics approval.

Statistical Analysis

Per recommendations¹⁶, we based the MID on the smallest estimate for which we observe convergence across different distribution-based methods. Distribution-based approaches include standard error of measurement (SEM) and 0.5 standard deviation (SD). The SEM provides the confidence interval around individual scores and is calculated as $\text{sample SD} \times (1 - \text{reliability})$.²⁰ Cronbach's alphas from prior studies were used as reliability estimates for the HADS¹¹ and IES-R². The 0.5 SD is based on the specified study sample and is consistent with the approach used to calculate effect sizes.^{21,22} The minimal detectable change, defined as the smallest score change that can be detected beyond random error²³, is calculated at the 90% confidence interval (CI) as $1.65 \times \text{SEM} \times \sqrt{2}$. Finally, 0.2 SD, reflecting Cohen's criterion for small effect size, was also calculated as MID as small as 0.25-0.33 SD have been reported¹⁶. MID based on the SEM and 0.5 SD have been shown to be meaningful to patients and to approximate anchor-based MID.²¹⁻²⁵ However, the 0.2 SD and MDC may help identify the MID if SEM and 0.5 SD estimates diverge²³. MID were

examined for the aggregated sample and by study, country, and follow-up to assess generalizability. MID estimates for patients with likely depression, anxiety or PTSD (HADS-A, HADS-D ≥ 8 ; IES-R ≥ 1.6) were also calculated.

RESULTS

Sample characteristics are presented in Table 1. MID estimates for each instrument were generally comparable across studies and across follow-up times (Table 2). For the overall sample, the SEM and 0.5 SD converged to 2.0-2.5 for HADS-A and 1.9-2.4 for HADS-D while SEM and 0.2 SD converged to 0.17-0.18 for IES-R. MID estimates were generally comparable across studies, follow-up, country, and mental health subgroups (see supplemental Tables S1-S4). MID for a measure was smaller if the measure was also used to define having the condition, as only scores above the threshold were included (e.g., HADS-D ≥ 8 for depressed patients).

DISCUSSION

This is the first study to estimate MID estimates of the HADS and IES-R in ARF survivors. Using data from U.S. and U.K. studies, the distribution-based MID was 2.0-2.5 for HADS-A and HADS-D and 0.2 for the IES-R. Results were generally similar across follow-ups, studies, and country, and mental health subgroups. Interventions which increase HADS scores by ≥ 2.5 or IES-R scores by ≥ 0.2 should yield differences perceivable by ARF survivors.

Our study has the following limitations. We used only distribution-based methods, which are indirect assessments of MID and can vary by estimation method¹⁶. Per recommendations¹⁶, we triangulated results to identify MID estimates for each instrument, but research using anchor-based approaches are needed to confirm our findings. Our study did not examine within-person change; hence, our MID estimates are recommended for between-group comparisons. Despite these limitations, our distribution-based MID estimates will be a useful resource for researchers planning future studies and interpreting the clinical importance of findings using these psychological instruments in ARF survivors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1**Participant Characteristics by Study**

Variables	Pooled (N=1223)	U.S. Studies		U.K. Studies		
		ALTOS (N=629)	ICAP (N=186)	PRaCTICa L (N=232)	Jones (N=102)	CESAR (N=74)
Age years, mean (sd)	51 (15)	49 (14)	49 (14)	58 (16)	53 (16)	44 (12)
Male, n (%)	646 (53)	306 (49)	105 (57)	133 (58)	59 (58)	43 (58)
Race, n (%)						
White	603 (74)	496 (79)	107 (58)	NA	NA	NA
Black	175 (22)	100 (16)	75 (41)	NA	NA	NA
Other	36 (4)	33 (5)	3 (2)	NA	NA	NA
APACHE II score, mean (sd)	23 (8)	26 (8) [†]	24 (8)	19 (7)	16 (5)	19 (6)
Ventilation duration, mean (sd)	11 (11)	11 (10)	14 (15)	7 (8)	NR	NR
ICU length of stay, mean (sd)	15 (15)	14 (11)	19 (17)	7 (9)	19 (20)	34 (27)
Hospital length of stay, mean (sd)	29 (27)	22 (16)	32 (23)	29 (24)	47 (41)	64 (49)
Mental Health, Overall Sample[‡]						
6-month HADS-A, mean (sd)	6.7 (4.8)	7.1 (4.9)	5.7 (4.8)	6.5 (4.6)	7.1 (4.7)	6.5 (4.5)
6-month Anxiety, n (%) ¹	469 (40)	260 (42)	52 (32)	86 (39)	46 (45)	25 (34)
6-month HADS-D, mean (sd)	5.7 (4.5)	6.1 (4.8)	5.2 (4.2)	5.3 (4.1)	5.6 (3.9)	4.9 (4.2)
6-month Depression, n (%) ²	370 (32)	222 (36)	41 (26)	60 (27)	31 (30)	16 (22)
6-month IES-R, mean (sd)	1.0 (0.9)	1.0 (0.9)	0.9 (0.8)	NA	NA	NA
6-month PTSD, n (%) ³	179 (23)	148 (25)	31 (19)	NA	NA	NA
12-month HADS-A, mean (sd)	6.7 (5.0)	7.0 (5.2)	6.4 (4.9)	6.0 (4.6)	NA	NA
12-month Anxiety, n (%) ¹	359 (40)	241 (42)	50 (35)	68 (35)	NA	NA
12-month HADS-D, mean (sd)	5.6 (4.7)	5.9 (4.9)	5.2 (4.1)	4.8 (4.3)	NA	NA
12-month Depression, n (%) ²	291 (32)	204 (36)	34 (24)	53 (28)	NA	NA
12-month IES-R, mean (sd)	1.0 (0.9)	1.0 (0.9)	0.9 (0.9)	NA	NA	NA
12-month PTSD, n (%) ³	163 (23)	132 (23)	31 (22)	NA	NA	NA

NA = Not available

¹Based on HADS-A 8.²Based on HADS-D 8.³Based on IES-R 1.6. Higher scores on HADS-A, HADS-D, IES-R indicate poorer mental health.[†]Originally reported as APACHE III (Mean=86, SD=26); presented as APACHE II using standard conversion (Reference: Schneider et al. J Crit Care. 2013 28(5):885.e1–8.)[‡]Ns for Pooled, ALTOS, ICAP, PRaCTICaL, Jones, CESAR—HADS-A (6m: 1170, 613, 161, 220, 102, 74; 12m: 910, 575, 142, 193, NA, NA), HADS-D (6m: 1170, 613, 161, 220, 102, 74; 12m: 909, 574, 142, 193, NA, NA), and IES-R (6m: 765, 621, 160, NA, NA, NA; 12m: 714, 573, 141, NA, NA, NA).

Table 2

Distribution-based Minimal Important Difference (MID)[†] for HAD-A, HAD-D, IES-R, 6 and 12 Month Follow-Up[‡]

	Pooled	Study					Country	
		ALTOS	ICAP	PRaCTICaL	Jones	CESAR	U.S.	U.K.
<u>HADS-A</u>								
Sample Size								
6 month	1170	613	161	220	102	74	774	396
12 month	910	575	142	193	NA	NA	717	193
Standard Error of Measurement								
6 month	2.0	2.0	2.0	1.9	2.0	1.9	2.0	1.9
12 month	2.1	2.1	2.0	1.9	NA	NA	2.1	1.9
Minimal Detectable Change 90								
6 month	4.6	4.7	4.6	4.4	4.5	4.3	4.7	4.4
12 month	4.8	5.0	4.7	4.4	NA	NA	4.9	4.4
Small Effect Size: 0.2 SD								
6 month	1.0	1.0	1.0	0.9	0.9	0.9	1.0	0.9
12 month	1.0	1.0	1.0	0.9	NA	NA	1.0	0.9
Moderate Effect Size: 0.5 SD								
6 month	2.4	2.5	2.4	2.3	2.4	2.2	2.5	2.3
12 month	2.5	2.6	2.4	2.3	NA	NA	2.6	2.3
<u>HADS-D</u>								
Sample Size								
6 month	1170	613	161	220	102	74	774	396
12 month	909	574	142	193	NA	NA	716	193
Standard Error of Measurement								
6 month	1.9	2.1	1.8	1.8	1.6	1.8	2.0	1.7
12 month	2.0	2.1	1.8	1.8	NA	NA	2.0	1.8
Minimal Detectable Change 90								
6 month	4.5	4.8	4.2	4.1	3.8	4.1	4.7	4.0
12 month	4.6	4.8	4.1	4.3	NA	NA	4.7	4.3
Small Effect Size: 0.2 SD								
6 month	0.9	1.0	0.8	0.8	0.8	0.8	0.9	0.8
12 month	0.9	1.0	0.8	0.9	NA	NA	1.0	0.9
Moderate Effect Size: 0.5 SD								
6 month	2.3	2.4	2.1	2.1	1.9	2.1	2.4	2.0
12 month	2.4	2.5	2.1	2.2	NA	NA	2.4	2.2
<u>IES-R</u>								
Sample Size								
6 month	765	605	160	NA	NA	NA	765	NA
12 month	714	573	141	NA	NA	NA	714	NA
Standard Error of Measurement								

	Pooled	Study					Country	
		ALTOS	ICAP	PRaCTICaL	Jones	CESAR	U.S.	U.K.
6 month	0.17	0.17	0.16	NA	NA	NA	0.17	NA
12 month	0.18	0.18	0.17	NA	NA	NA	0.18	NA
Minimal Detectable Change⁹⁰								
6 month	0.40	0.41	0.38	NA	NA	NA	0.40	NA
12 month	0.42	0.43	0.40	NA	NA	NA	0.42	NA
Small Effect Size: 0.2 SD								
6 month	0.17	0.17	0.16	NA	NA	NA	0.17	NA
12 month	0.18	0.18	0.17	NA	NA	NA	0.18	NA
Moderate Effect Size: 0.5 SD								
6 month	0.43	0.44	0.41	NA	NA	NA	0.43	NA
12 month	0.46	0.46	0.43	NA	NA	NA	0.46	NA

SD=standard deviation,

[†]Data for MID calculations: Cronbach's α : HADS-A=0.83, HADS-D=0.82 (Sukantarat et al.¹¹); IES-R=0.96 (Bienvenu et al.²); sample SD from Table 1; SD for U.S.at 6 and 12 month MID estimates are (HADS-A: 4.93, 5.21; HADS-D: 4.85, 4.92; IES-R: 0.88, 0.94) and for U.K are (HADS-A: 4.59, 4.58; HADS-D: 4.08, 4.34).

[‡]All 5 studies had subscale data for HADS at 6 month; Jones et al. and CESAR studies did not have HADS data at 12 month. IES-R data available only for U.S. studies (ALTOS, ICAP).