

Intra-class Correlation in Cluster Randomized Controlled Trials: A Meta- analysis of Studies on Major Depression

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- The pooled estimate of ICC 0.07 (95%CI: 0.05-0.09) can be used as a reference value for sample size estimation in for future CRTs targeting major depression.
- All scientific journals need to actively encourage future CRTs to adhere to CONSORT recommendations on reporting of ICC estimates used at the design and calculated at the analysis stage.

BACKGROUND

- Cluster Randomized Trials (CRTs) provide robust evidence for intervention by controlling contamination of interventions. However, there could be some loss of statistical efficiency.
- Though CONSORT recommends reporting intra-class correlation coefficients (ICC) to understand this phenomenon, not many studies seem to adhere it.

This study aims to explore the compliance of CRTs in major depression for reporting ICC besides deriving the pooled ICC and pooled mean differences of intervention outcomes.

METHODS

- Databases used: PubMed, Cochrane Library, Embase and PsychINFO
- Appropriate search terms were used in advanced search options in databases using a combination of main keywords, Boolean operators, and Mesh terms.
- Published between 1st January 2004 and 31st December 2020.
- Inclusion criteria: i). CRTs on major depression where in the study identified the CRT status either in the title, abstract or in the text, ii). studies conducted on humans, iii) Articles published in the English language
- The CRTs identified were imported into EndNote X9 to check for duplication.
- Two reviewers screened the studies independently for eligibility by evaluating the title and abstract and referred to a third reviewer when a discrepancy was noted.
- Accordingly, all the relevant articles were identified and accessed.

RESULTS

- Records identified through database search (n =305): PubMed: 58; Cochrane Library: 101; PsychInfo: 97; Embase: 49 [Excluded duplications: 137]
- Full-text articles assessed for eligibility : n = 37; Systematic review: 34
- Eligible number of studies for Meta-analysis:

Effectiveness of interventions (n=20) & ICC (n=8)

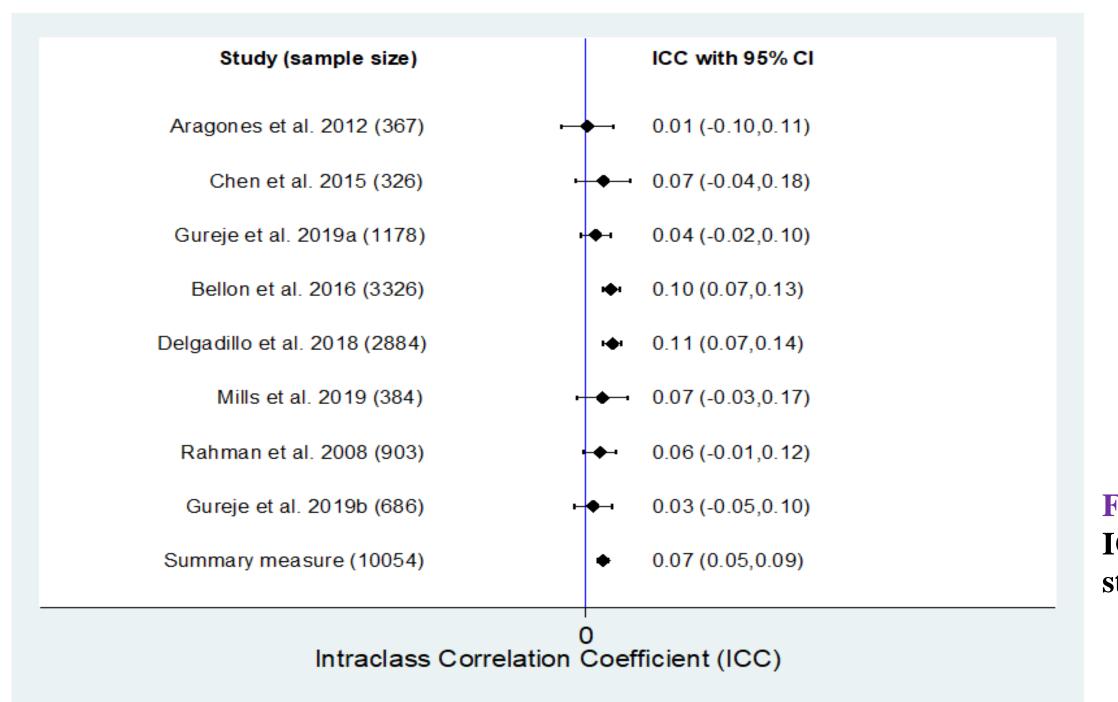


Fig 1: Forest plot for ICC with I^2 -statistic = 28%

	Inte	erventio	n	C	ontrol		9	Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI	ABCDEFG
Bolton et al. 2003	6.1	6.3	116	20.64	9	132	5.0%	-1.85 [-2.14, -1.55]	2003		• •
Richards et al. 2007	8.8	7.02	79	10.27	7.51	35	4.8%	-0.20 [-0.60, 0.20]	2007	→+	••• •••
Marvijk et al. 2008	10.8	2.85	70	10.09	2.5	75	5.0%	0.26 [-0.06, 0.59]	2008	 -	• •
Rahman et al. 2008	5.4	6.5	463	10.7	8.1	440	5.2%	-0.72 [-0.86, -0.59]	2008	+	
Gensichen et al. 2009	10.72	5.43	310	12.13	5.6	316	5.1%	-0.26 [-0.41, -0.10]	2009	+	$\bullet \bullet \bullet \bullet \bullet \bullet$
Chaney et al. 2011	11.5	6.5	386	11.6	6.7	375	5.2%	-0.02 [-0.16, 0.13]	2011	+	● ● ●
AcSweeney et al. 2012	9.47	5.57	21	14.23	4.6	23	4.4%	-0.92 [-1.54, -0.29]	2012		• •
Aragones et al. 2012	7.15	7.11	201	8.78	6.99	166	5.1%	-0.23 [-0.44, -0.02]	2012	*	
Berghofer et al. 2012	4.7	8	19	11.2	7.4	44	4.5%	-0.85 [-1.41, -0.29]	2012		• •
Pradeep et al. 2014	11.3	6.22	122	11.73	7.24	138	5.1%	-0.06 [-0.31, 0.18]	2014	+	
Chen et al. 2015	6.1	2.6	164	12.6	5.2	162	5.1%	-1.58 [-1.83, -1.33]	2015		$\bullet \bullet \bullet \bullet \bullet$
Keeley et al. 2016	9.09	1.48	88	11.8	0.82	80	4.9%	-2.23 [-2.61, -1.84]	2016		
Bellon et al. 2016	7.39	32.35	1663	9.4	33.09	1663	5.2%	-0.06 [-0.13, 0.01]	2016	•	
Perry et al. 2017	13.3	1	242	15.3	0.9	298	5.1%	-2.11 [-2.32, -1.90]	2017		lacktriangle
Beidler et al. 2018	24.7	2.3	31	24.1	2.4	28	4.6%	0.25 [-0.26, 0.77]	2018	+	$\bullet \bullet \bullet \bullet \bullet \bullet$
Delgadillo et al. 2018	8.61	6.6	1489	9.75	7.12	1395	5.2%	-0.17 [-0.24, -0.09]	2018	•	$\bullet \bullet \bullet \bullet \bullet$
Mills et al. 2019	5.48	5.5	246	6.64	5.3	138	5.1%	-0.21 [-0.42, -0.00]	2019		••• ••
∂ureje et al. 2019a	3.6	4.9	631	3.5	3.9	547	5.2%	0.02 [-0.09, 0.14]	2019a	+	
∋ureje et al. 2019b	3.5	3.9	452	4.6	4.6	234	5.1%	-0.26 [-0.42, -0.11]	2019b	+	•• •••
Nakimuli-Mpungu et al. 2020	9.87	0.86	578	5.94	2.94	562	5.2%	1.82 [1.69, 1.96]	2020	+	
Total (95% CI)			7371			6851	100.0%	-0.46 [-0.79, -0.13]		•	
Heterogeneity: Tau² = 0.55; Ch	i² = 1589	i.04, df=	= 19 (P	< 0.000	01); l²=	99%				+ + +	-
est for overall effect: Z = 2.71		-	· - V		171.1	· -				-4 -2 0 2 Favours [Intervention] Favours [contr	4

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

Fig 2: Forest plot for assessing the Effectiveness of intervention with I^2 – statistic = 99%

RESULTS CONTINUED

- 50% of the studies reported that ICC values were used at the design stage
- Only 44% of the studies reported ICC values for specific outcomes.
- About one-third of the eligible studies only complied with the CONSORT recommendation on reporting the ICC.
- The pooled SMD (95% CI): -0.46 (-0.79, -0.13) for the depression scores measured in psychosocial studies as well as studies with psychosocial combined with antidepressants was statistically significant (z = 2.71, p-value = 0.007).

	Inte	rventio	n	(Control			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
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Richards et al. 2007	8.8	7.02	79	10.27	7.51	35	0.0%	-0.20 [-0.60, 0.20]	2007	
Marvijk et al. 2008	10.8	2.85	70	10.09	2.5	75	0.0%	0.26 [-0.06, 0.59]	2008	
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Gensichen et al. 2009	10.72	5.43	310	12.13	5.6	316	0.0%	-0.26 [-0.41, -0.10]	2009	
Chaney et al. 2011	11.5	6.5	386	11.6	6.7	375	0.0%	-0.02 [-0.16, 0.13]	2011	
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Keeley et al. 2016	9.09	1.48	88	11.8	0.82	80	0.0%	-2.23 [-2.61, -1.84]	2016	
Bellon et al. 2016	7.39	32.35	1663	9.4	33.09	1663	13.1%	-0.06 [-0.13, 0.01]	2016	•
Perry et al. 2017	13.3	1	242	15.3	0.9	298	0.0%	-2.11 [-2.32, -1.90]	2017	
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Mills et al. 2019	5.48	5.5	246	6.64	5.3	138	12.0%	-0.21 [-0.42, -0.00]	2019	*
Gureje et al. 2019a	3.6	4.9	631	3.5	3.9	547	12.9%	0.02 [-0.09, 0.14]	2019a	†
Gureje et al. 2019b	3.5	3.9	452	4.6	4.6	234	12.5%	-0.26 [-0.42, -0.11]	2019b	+
Nakimuli-Mpungu et al. 2020	9.87	0.86	578	5.94	2.94	562	0.0%	1.82 [1.69, 1.96]	2020	
Total (95% CI)			5309			4745	100.0%	-0.39 [-0.62, -0.15]		•
Heterogeneity: Tau ² = 0.11; Ch	$i^2 = 207.9$	94. df=	7 (P < 0	0.00001); ² = 9?	7%				+ + + + + + + + + + + + + + + + + + + +

Fig 3: Sub-group Analyses- Forest plot for change in depression scores for studies that reported ICC.

	Inte	n	(Control Std. Mean Difference					Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI	
Bolton et al. 2003	6.1	6.3	116	20.64	9	132	8.4%	-1.85 [-2.14, -1.55]	2003	-	
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Gensichen et al. 2009	10.72	5.43	310	12.13	5.6	316	8.5%	-0.26 [-0.41, -0.10]	2009	-	
Chaney et al. 2011	11.5	6.5	386	11.6	6.7	375	8.5%	-0.02 [-0.16, 0.13]	2011	+	
McSweeney et al. 2012	9.47	5.57	21	14.23	4.6	23	8.0%	-0.92 [-1.54, -0.29]	2012		
Aragones et al. 2012	7.15	7.11	201	8.78	6.99	166	0.0%	-0.23 [-0.44, -0.02]	2012		
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Gureje et al. 2019b	3.5	3.9	452	4.6	4.6	234	0.0%	-0.26 [-0.42, -0.11]	2019b		
Nakimuli-Mpungu et al. 2020	9.87	0.86	578	5.94	2.94	562	8.5%	1.82 [1.69, 1.96]	2020	-	
Total (95% CI)			2062			2106	100.0%	-0.51 [-1.29, 0.27]			
Heterogeneity: Tau² = 1.85; Ch	i²= 1357	.68, df=	= 11 (P	< 0.000	01); l²=	99%				 	
Fest for overall effect: $Z = 1.28$					/// .					-4 -2 0 2 Favours [Intervention] Favours [control]	

Fig 4: Sub-group Analyses: Forest plot for change in depression scores for studies that did not report ICC.

CONCLUSIONS

- One-third of eligible studies only complied with the CONSORT recommendation on reporting of ICC, which is a serious concern too.
- Further, our study also revealed that the ICCs can affect the intervention outcomes.
- Hence, all journals need to actively encourage future CRTs to adhere to CONSORT recommendations on ICC as an essential criterion for publishing it.
- At a practical level, the pooled ICC estimated from the current study for future trials, as a reference value for sample size estimation, targeting major depression.

ADDITIONAL KEY INFORMATION

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