

Binukumar Bhaskarapillai<sup>1</sup>, Palash Kumar Malo<sup>2</sup>, M. Thomas Kishore<sup>3</sup>, Anoop Joseph<sup>4</sup>, Gobinda Majhi<sup>5</sup>, Thennarasu Kandavel<sup>1</sup>

<sup>1</sup> Department of Biostatistics, <sup>3</sup> Department of Clinical Psychology, <sup>5</sup> Department of Psychiatric Social Works, National Institute of Mental Health and Neuro Sciences, Bengaluru, India. <sup>2</sup>Centre for Brain Research, Indian Institute of Science, Bengaluru, India. <sup>4</sup>Careadd, St. John's Research Institute, Bengaluru, India.

**- 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 to 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 1<sup>st</sup> January 2004 and 31<sup>st</sup> 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)

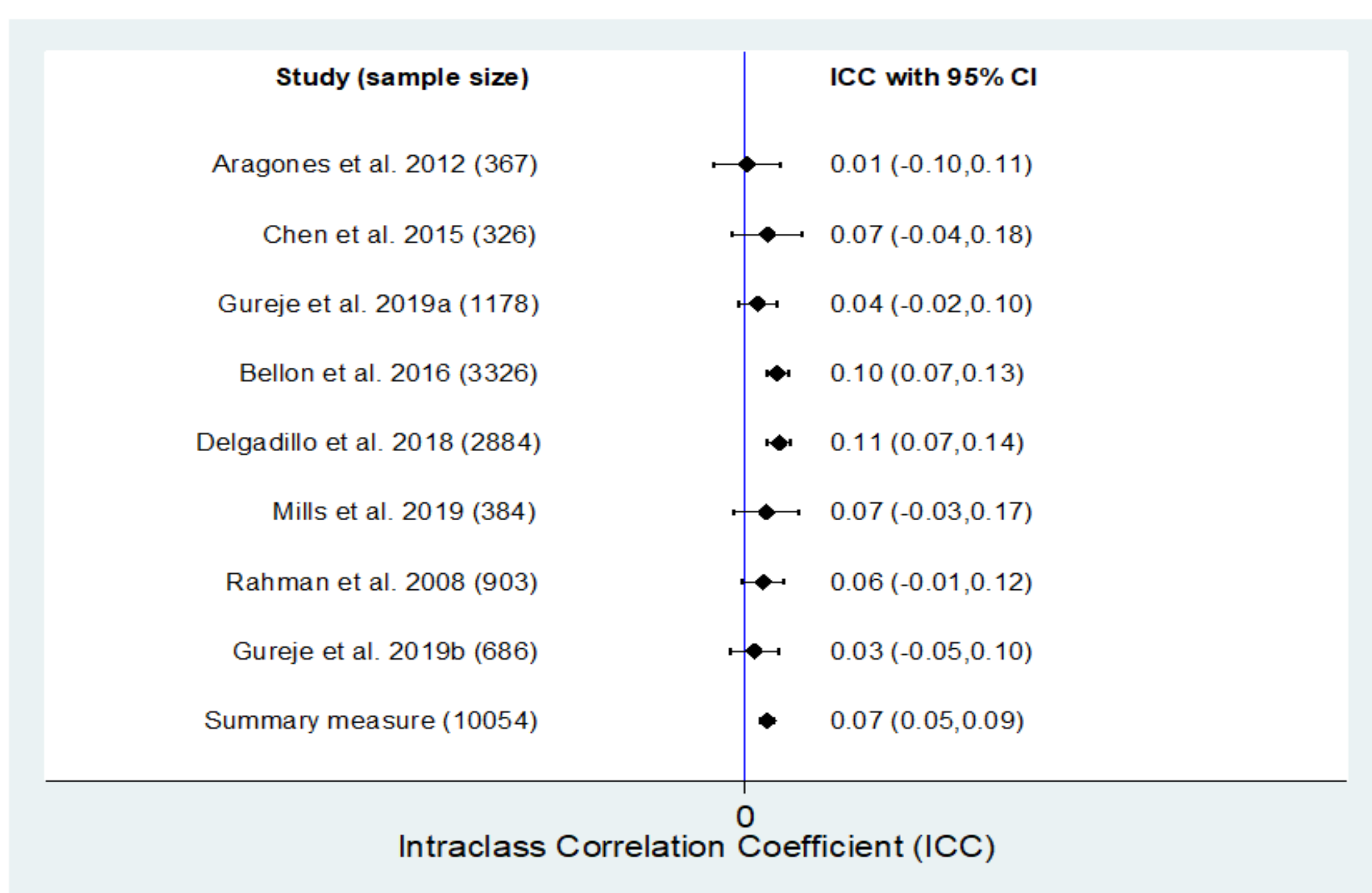


Fig 1: Forest plot for ICC with  $I^2$ -statistic = 28%

## 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).

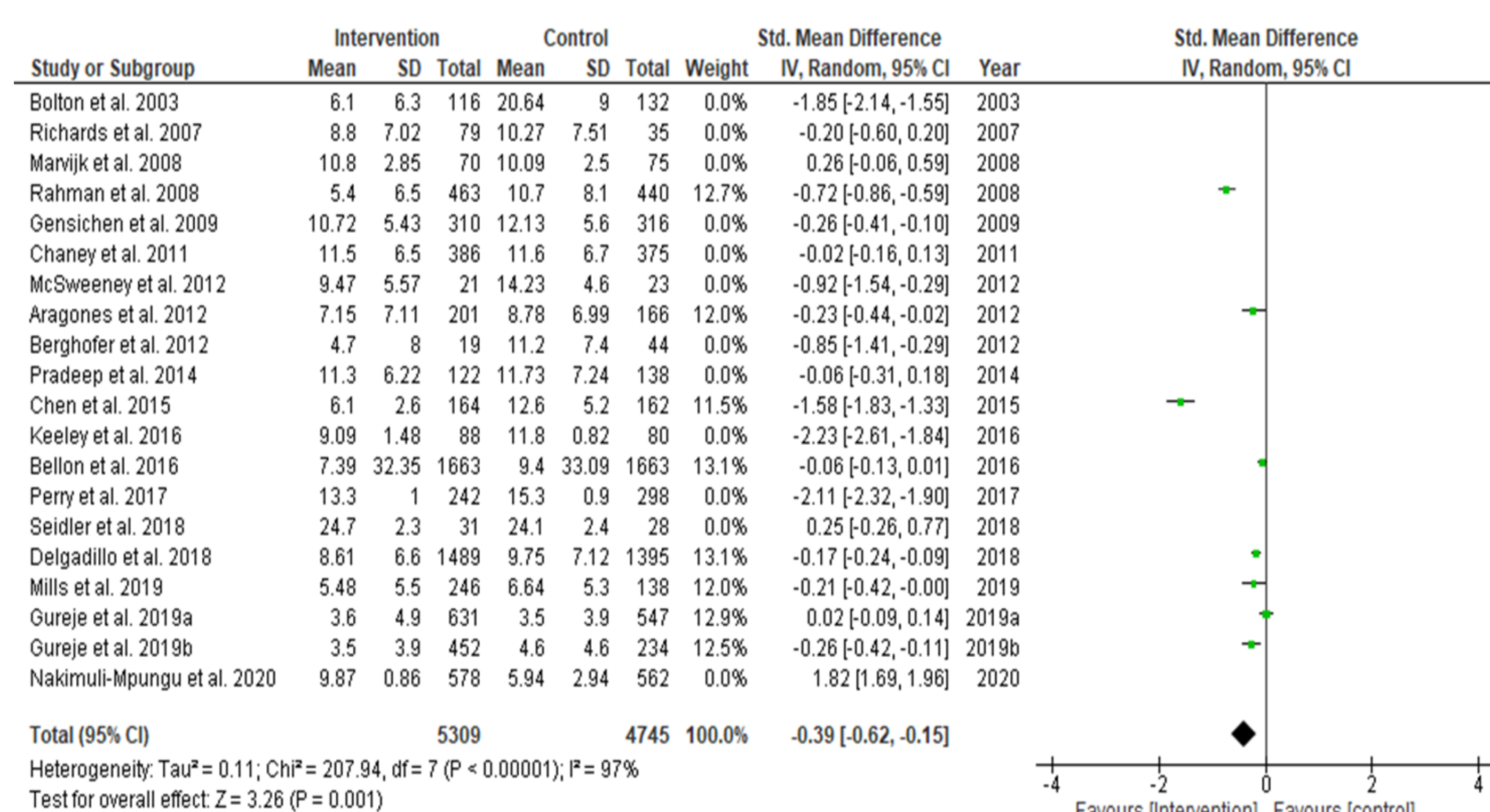


Fig 3: Sub-group Analyses- Forest plot for change in depression scores for studies that reported ICC.

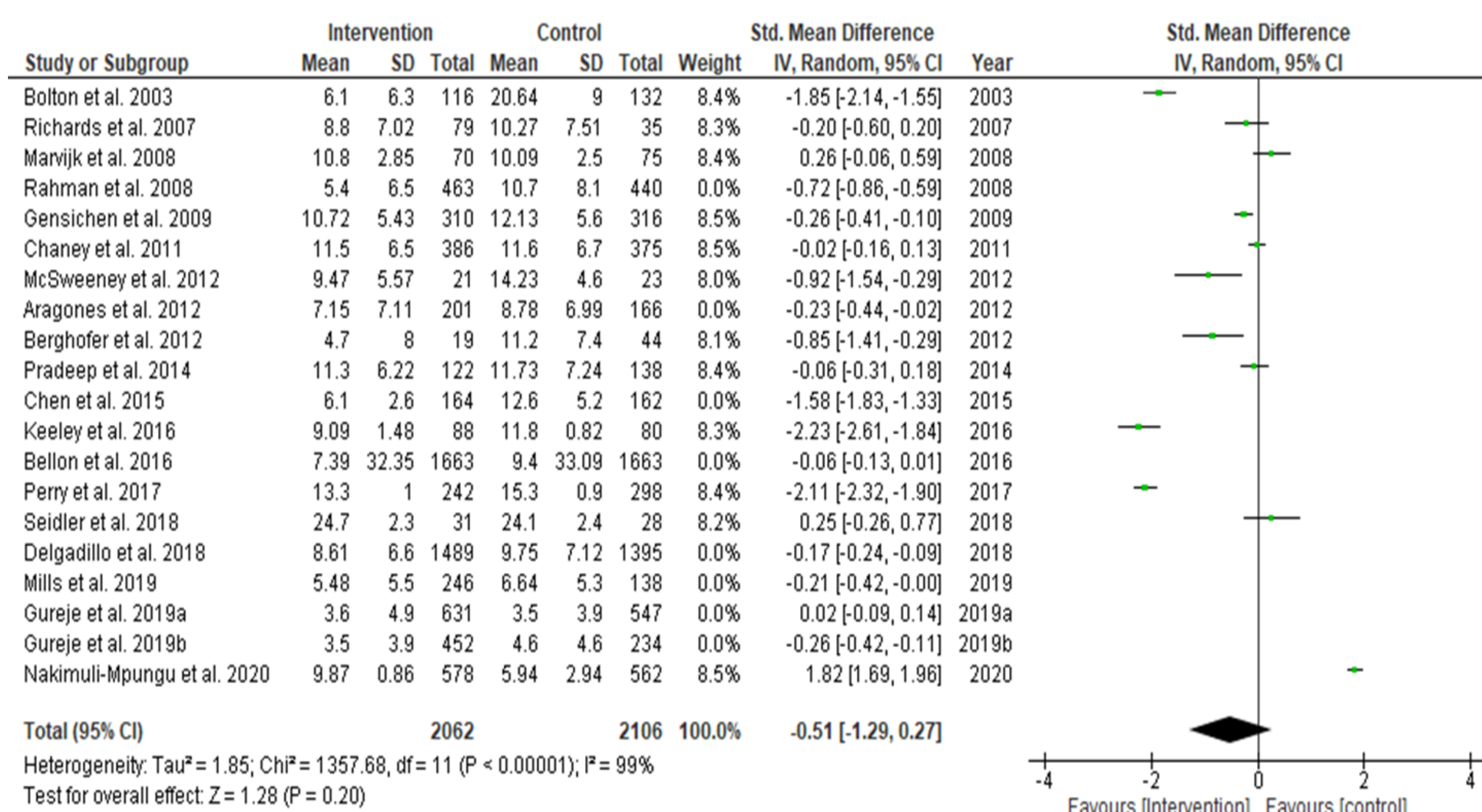


Fig 4: Sub-group Analyses: Forest plot for change in depression scores for studies that did not report ICC.

## 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

**Author Contact Information:** Additional Professor, Department of Biostatistics, National Institute of Mental Health and Neurosciences, Bengaluru, India. Email: [binukumarb@gmail.com](mailto:binukumarb@gmail.com)

**Funding Source:** Supported by the intramural grant of the National Institute of Mental Health and Neurosciences, Bengaluru, India.

**Conflicts of Interest:** None

**Acknowledgements:** None

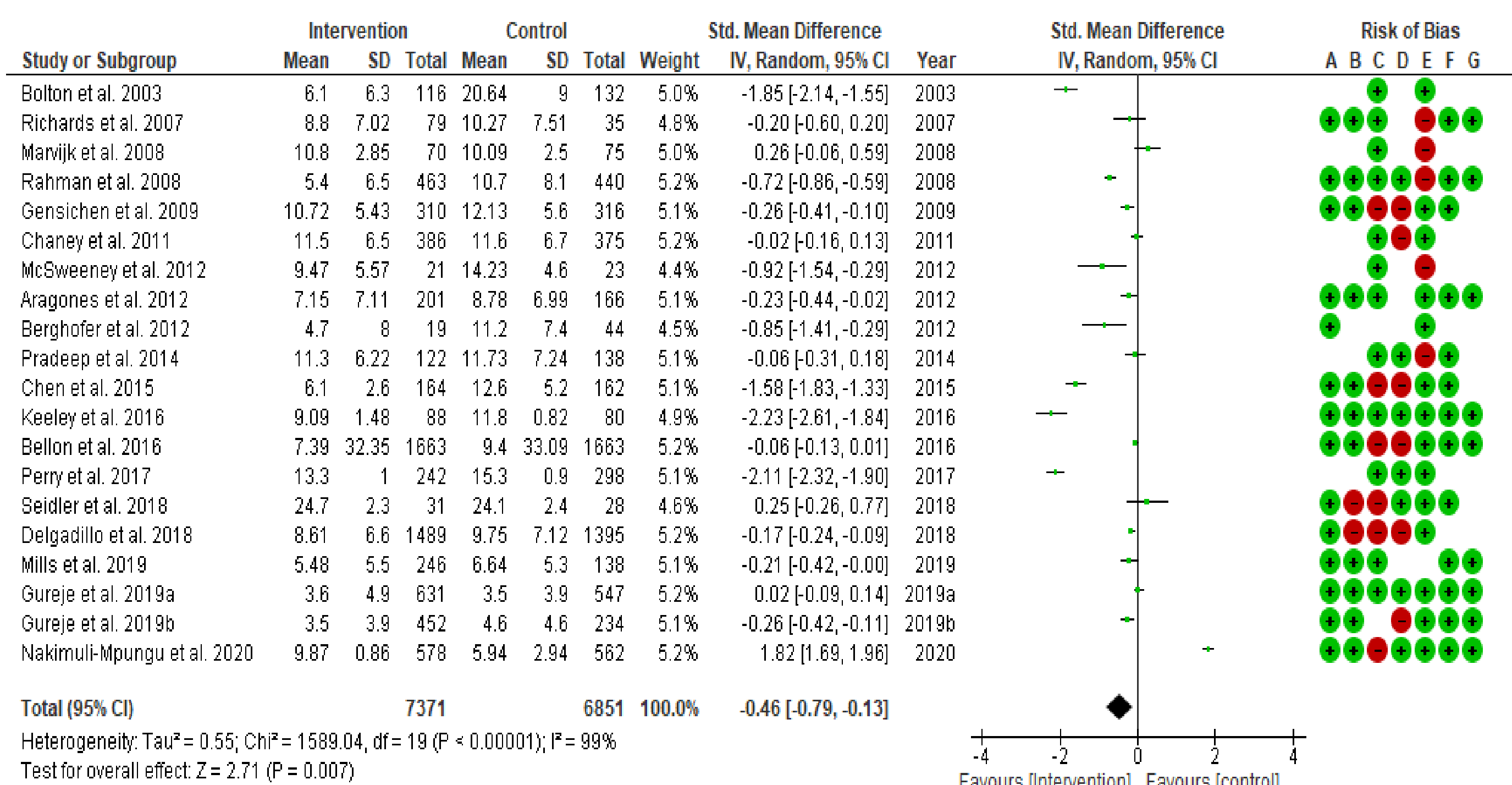


Fig 2: Forest plot for assessing the Effectiveness of intervention with  $I^2$ -statistic = 99%

**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