

# Cognitive impairment and neuropsychiatric symptoms in GBA-related Parkinson's Disease: a systematic review and meta-analysis

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## INTRODUCTION

GBA mutations, classified according to severity, are the main genetic risk factor for Parkinson's Disease (PD). GBA-PD is typically an early-onset disorder with fast-progressing and severe motor impairment and early cognitive and psychiatric involvement. Many studies focused on the correlation between GBA-PD and neuropsychological disturbances and new investigations are still ongoing.

## OBJECTIVE

To systematically review and meta-analyse the presence and severity of cognitive and neuropsychiatric symptoms in GBA-PD compared to non-GBA-PD.

## METHODS

- **Protocol registration:** CRD42023439774 (PROSPERO)
- **Reporting:** PRISMA guidelines
- **Search engines:** PubMed/MEDLINE, Web of Science, EMBASE (inception - 17/09/2025)
- **Inclusion criteria:** cohort and case-control studies and case-series published in English, with cognitive and neuropsychiatric symptoms assessed with validated scales and compared between GBA-PD and non-GBA-PD.
- **Exclusion criteria:** studies regarding non manifesting GBA carriers, not reporting information about genetic status or cognitive/neuropsychiatric features of PD.
- **Methods:** risk of bias evaluated with Newcastle-Ottawa-Scale (NOS), qualitative data with systematic descriptive analysis and quantitative data with Review Manager (random effect statistical model with 95% CI).
- **Clinical evaluation:** neuropsychological (global cognition, attention-working memory, executive function, memory and visuospatial abilities) and neuropsychiatric investigation (depression, anxiety, apathy and impulse control disorders).

## RESULTS

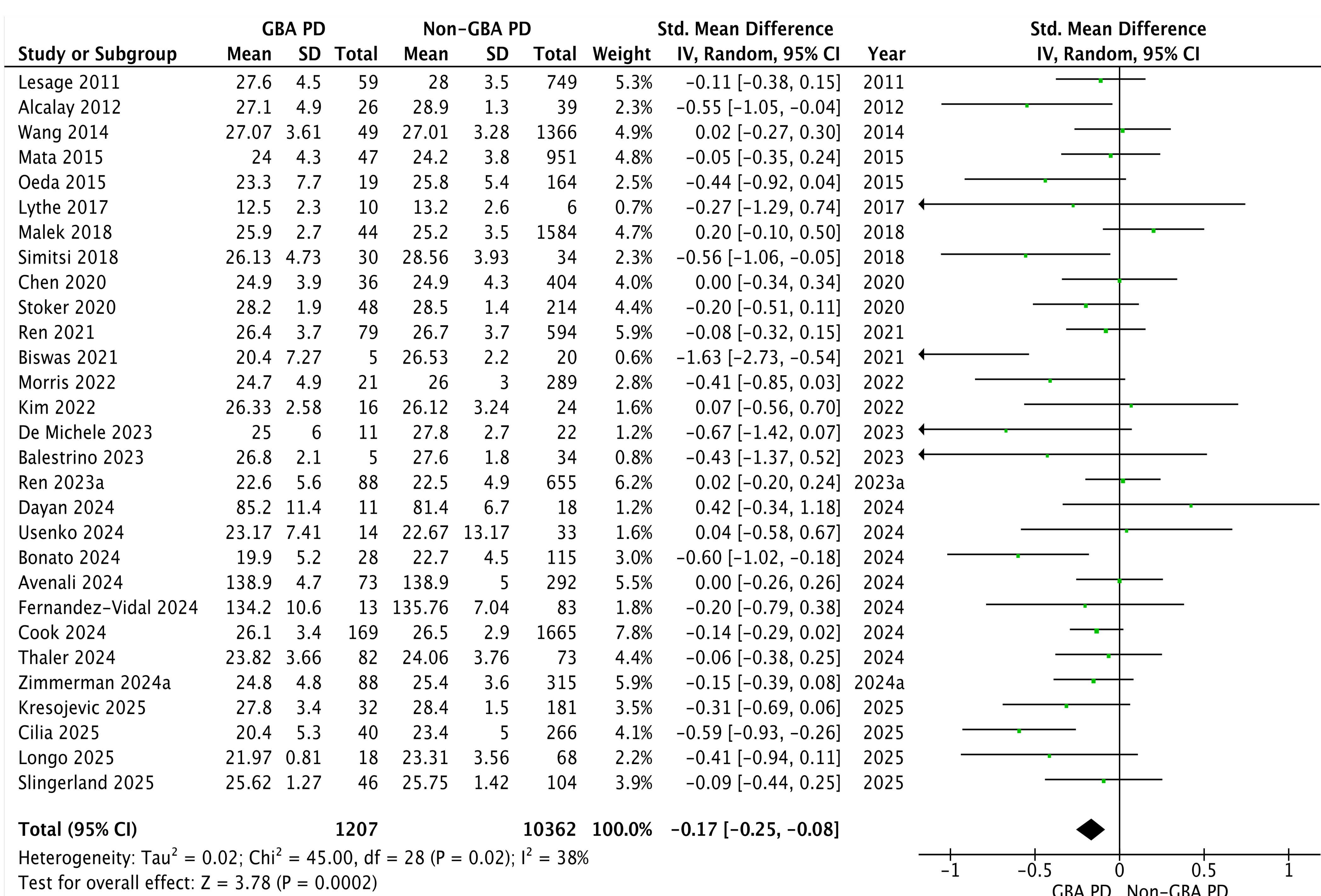
- **103 studies** (85 cross-sectional/cohort, 13 longitudinal, 5 case-series) included in the systematic review, **35** in the meta-analysis.
- Worse **global cognition** ( $p=0.0002$ , **26 studies**) and higher levels of **anxiety** ( $p=0.0005$ , **6 studies**) and **depression** ( $p=0.009$ , **16 studies**) in GBA-PD patients compared to non-GBA-PD patients.
- No significant differences in terms of apathy and ICD presence and severity between the two groups.
- NOS yielded good methodological quality of the included studies ( $6.8 \pm 1.0$ ).

## CONCLUSIONS

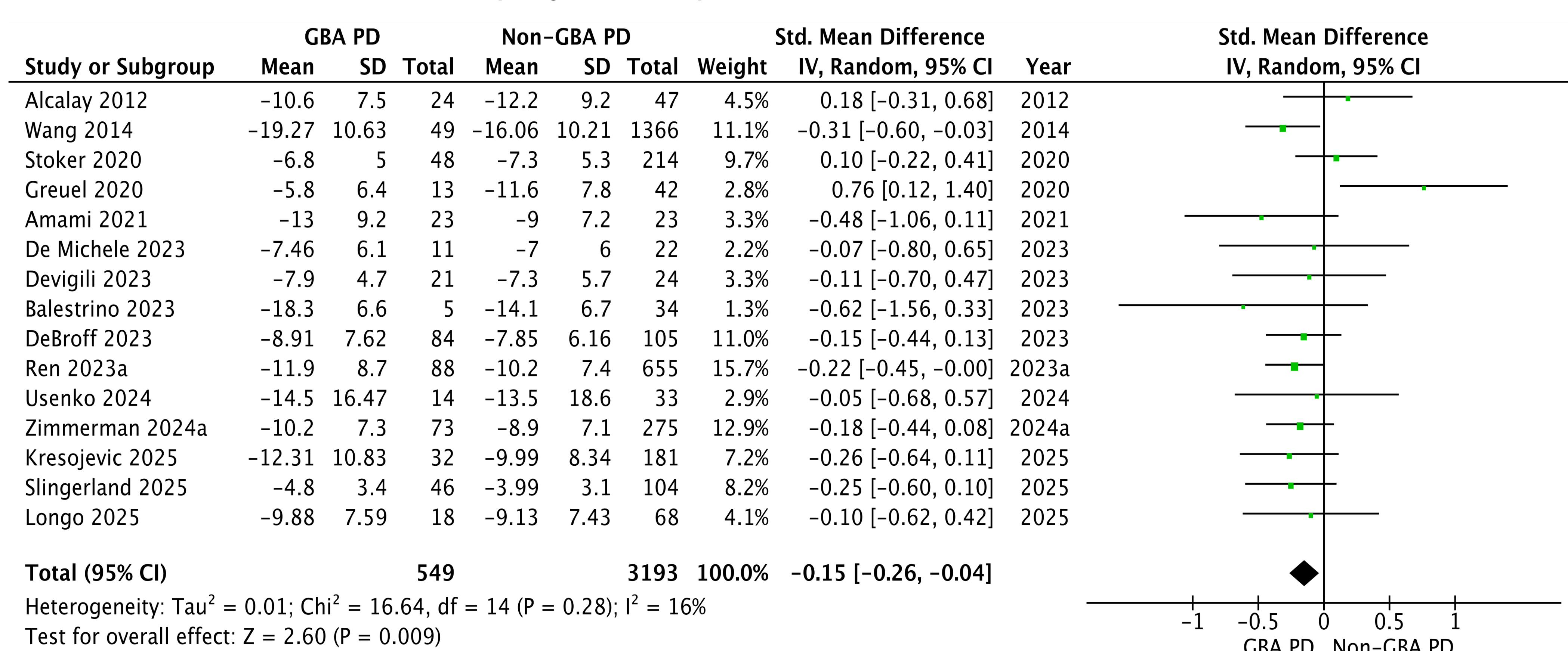
The meta-analysis showed worse global cognition and higher anxiety and depression levels in GBA-PD patients.

This study is still in progress, so further analysis will probably display additional significant results, in particular regarding mutation severity status and specific cognitive domains. These data may help understanding and treating GBA-PD.

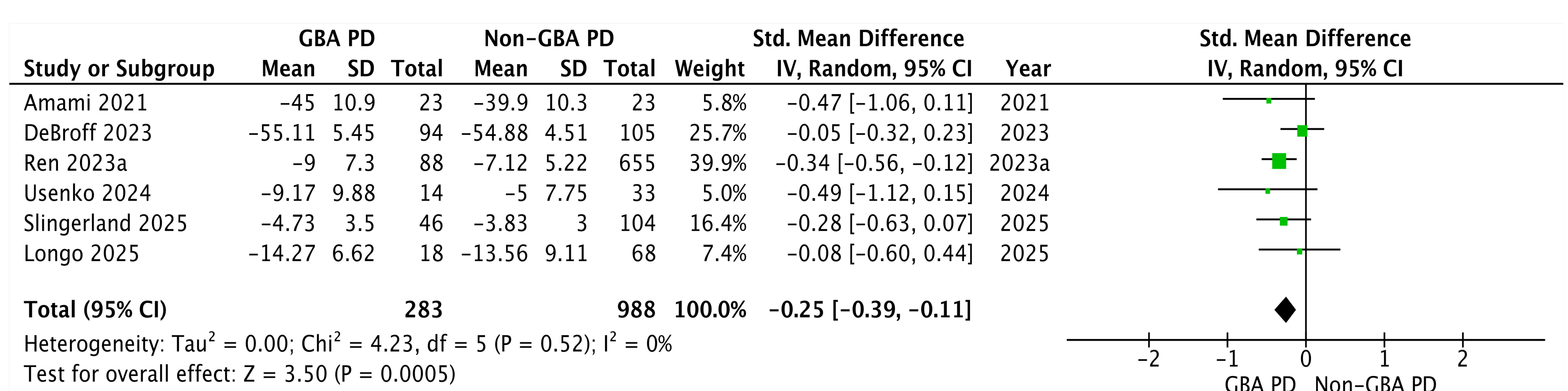
### A: GBA-PD vs non-GBA-PD (global cognition)



### B: GBA-PD vs non-GBA-PD (depression)

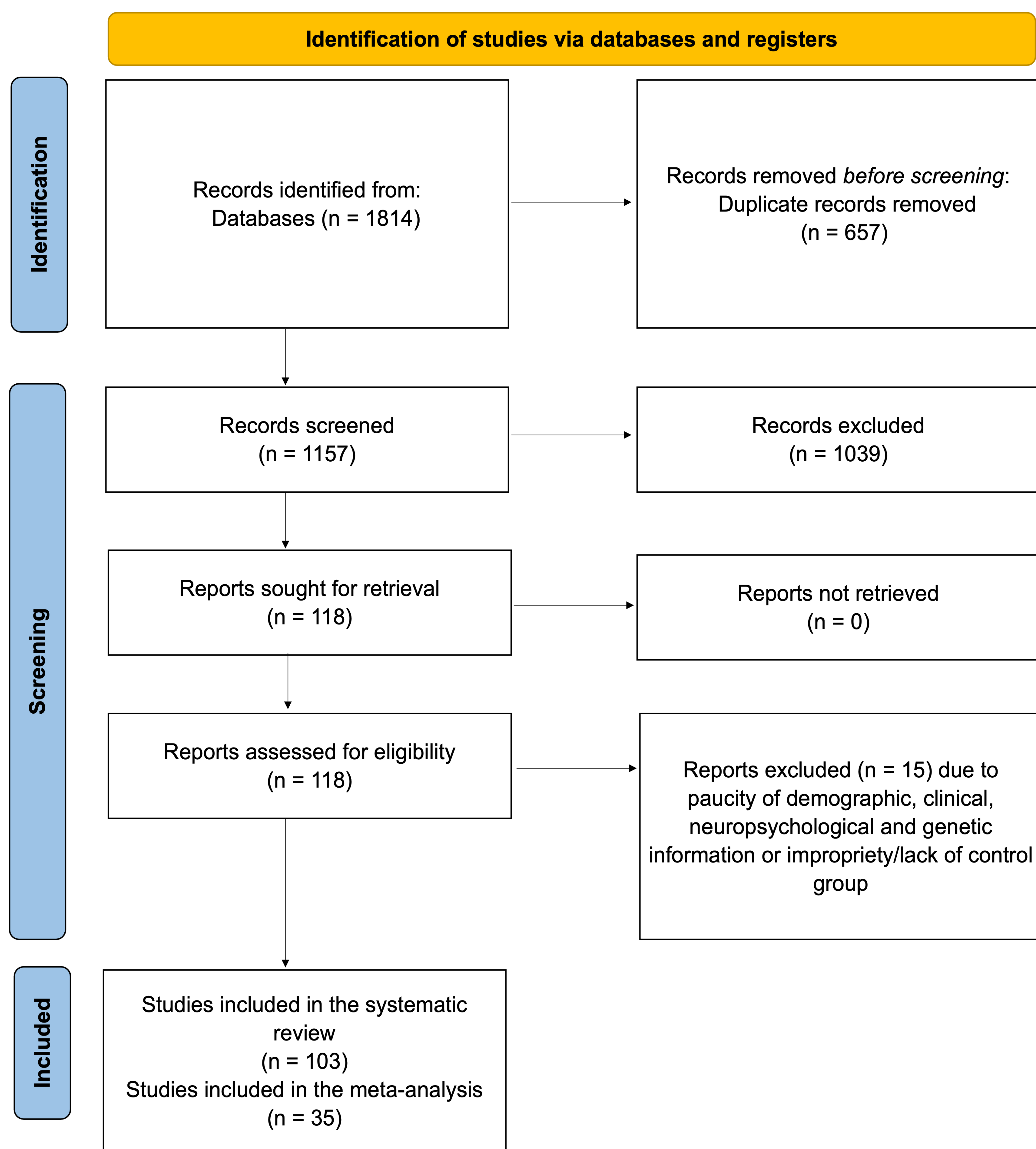


### C: GBA-PD vs non-GBA-PD (anxiety)



Panels A-C: Forest plots of the meta-analyses yielding significant results (P ≤ 0.05)

### PRISMA flow-diagram of the studies included in the review.



### BIBLIOGRAPHY

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