Exploring the Causal Effect of Omega-3 Polyunsaturated Fatty Acid Levels on Risk of Type 1 Diabetes: A Mendelian Randomization Study

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Background

- The burden of Type 1 diabetes (T1D) is vast and as of 2021, an estimated 8.4 million people were living with the disease worldwide. This number could increase to 17.4 million people by 2040.

- Despite nearly a century of insulin therapy for the management of hyperglycaemia in T1D, no therapies exist to treat its underlying etiopathology.

- Adequate dietary intake of omega-3 fatty acids (ω-3) has been reported to be associated with reduced risk of developing T1D.

- Given the inconclusive evidence from observational studies and RCTs, we conducted a Mendelian randomization (MR) study to explore the relationship between ω-3 intake and T1D
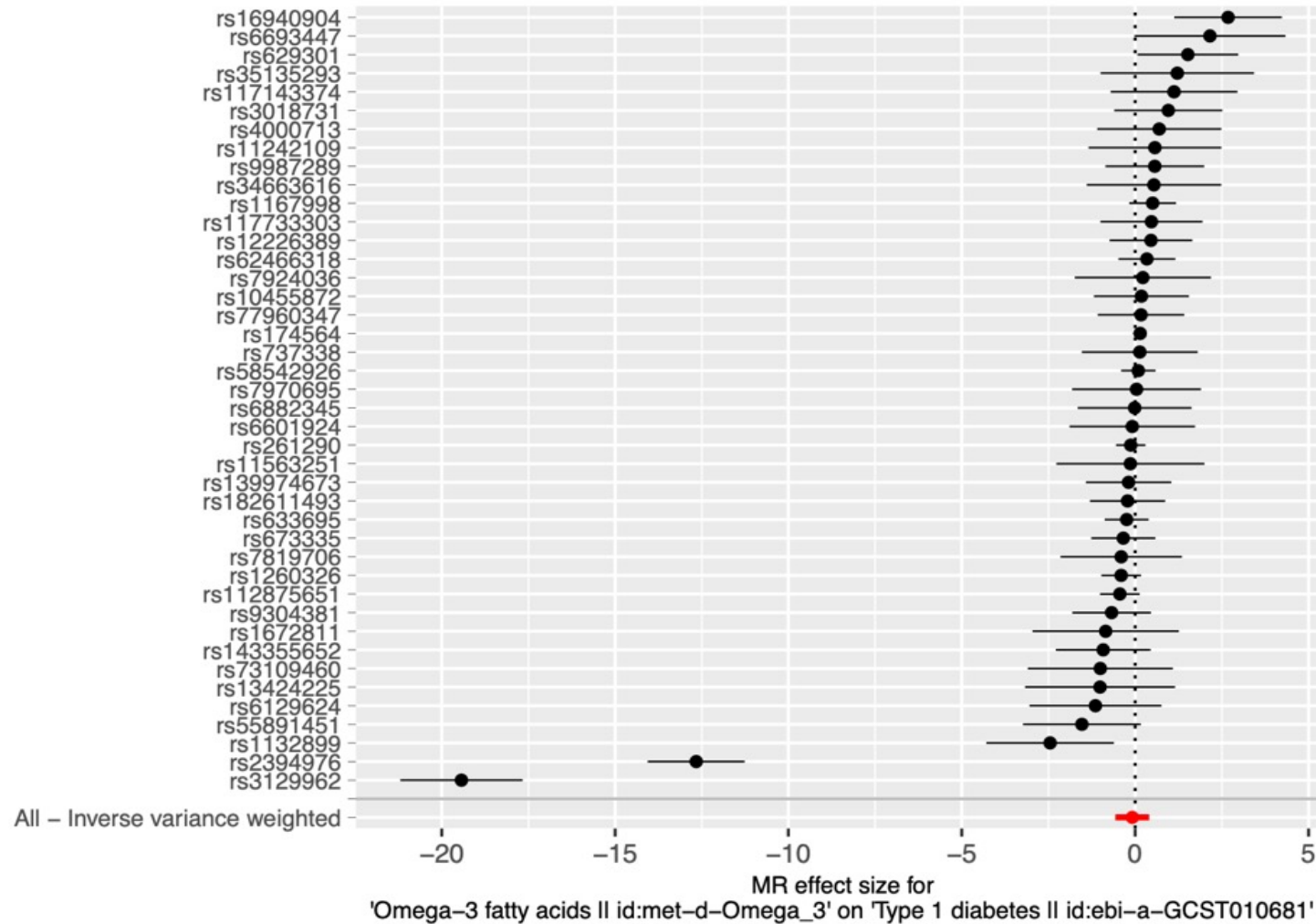
Methods & Analytical approach
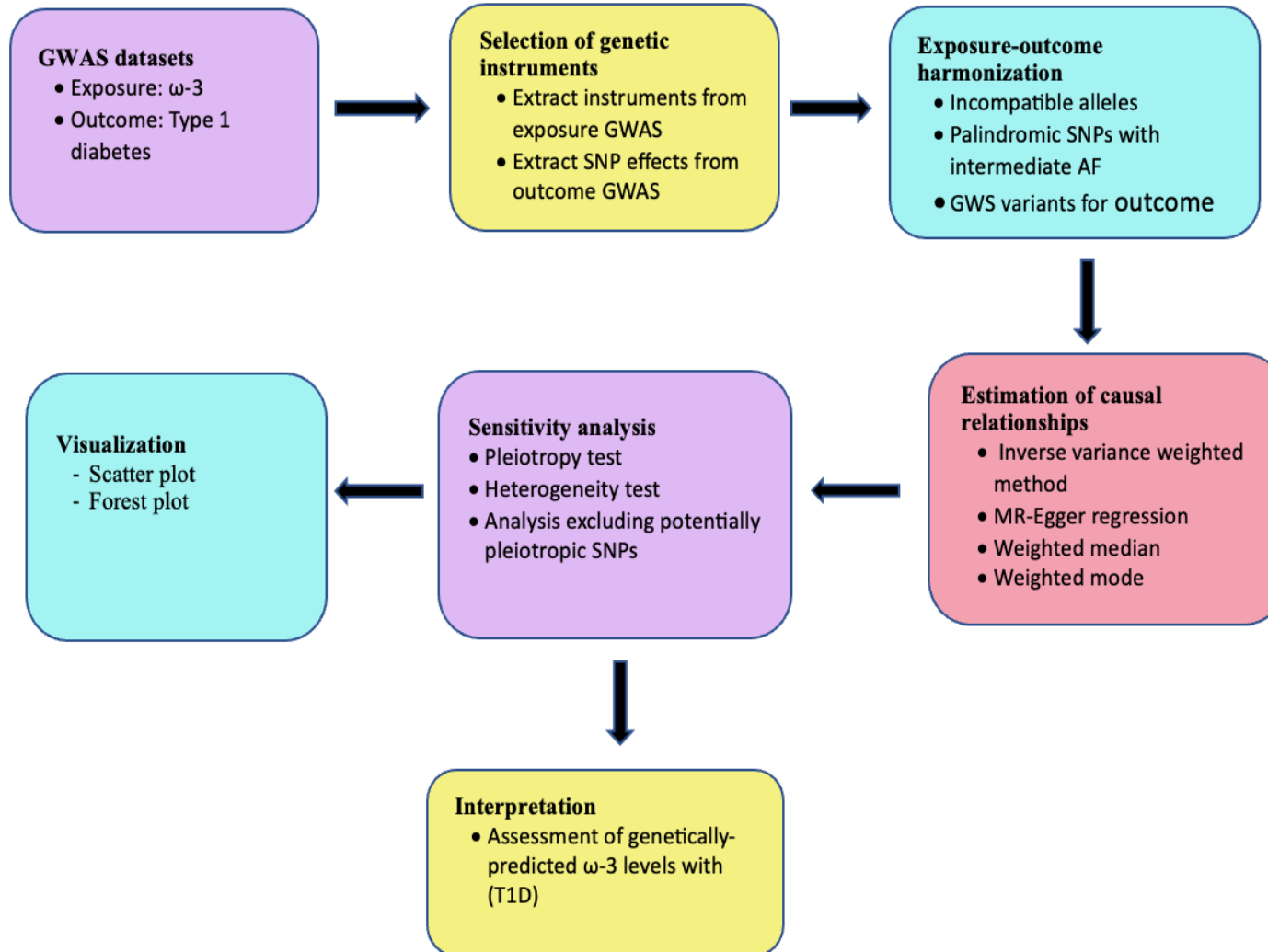
Data:
- Exposure: omega-3 GWAS summary data (OpenGWASID: met-d-Omega_3)
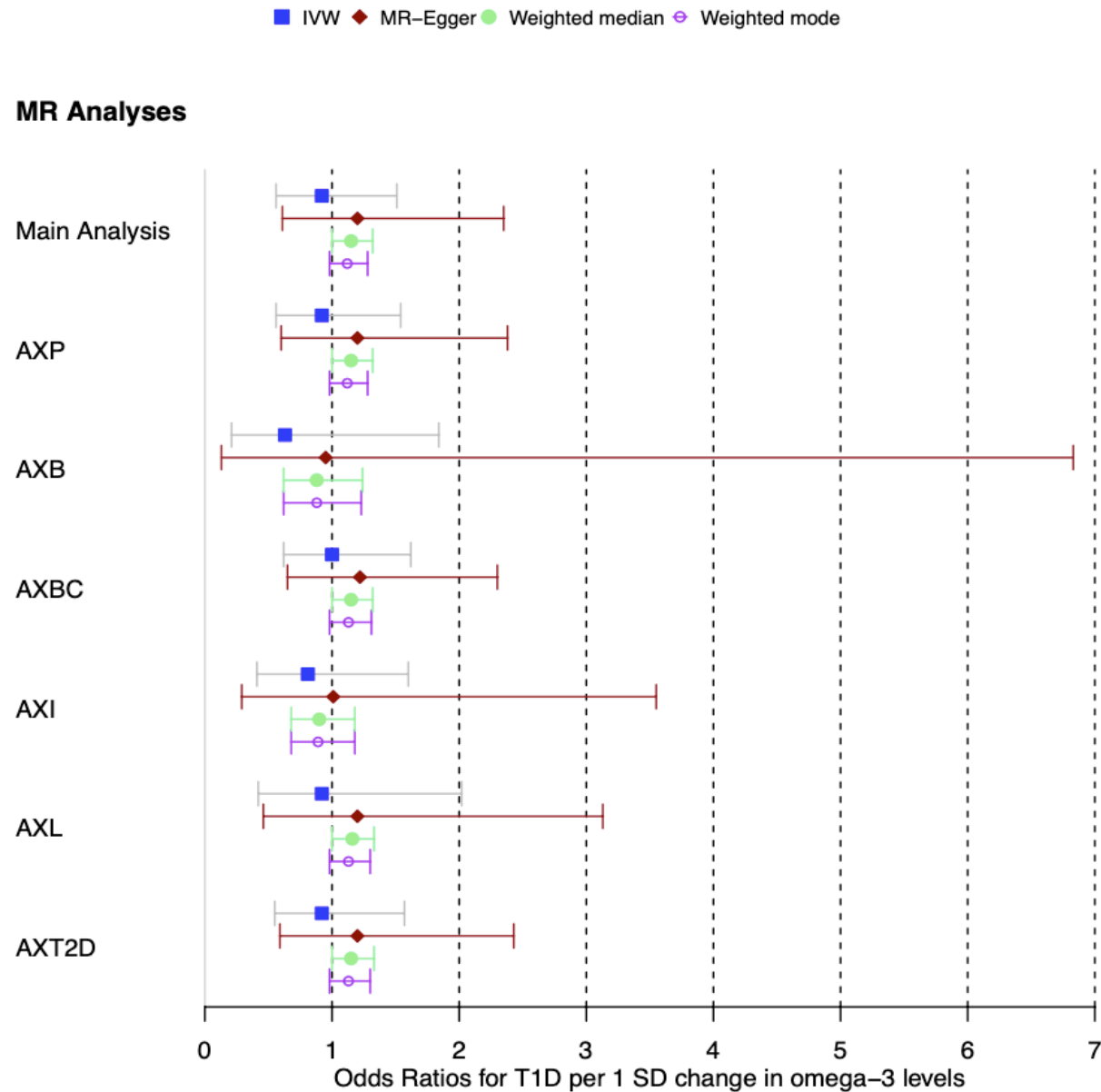- Outcome: T1D GWAS meta-analysis summary data(ID: ebi-a-GCST010681)

Analysis was done in R using the **TwoSampleMR** package (*version 0.5.6*)

Results: Main MR analysis

Forest plot of MR effect size for IVW single SNP and all SNPs analysis. RSIDs are shown on the y-axis and their corresponding MR effect sizes on the x-axis. The summary estimate for all IVs is represented as a red plotted point at the bottom of the graph. The vertical line through effect size of 0 represents the line of no effect.

Results: Sensitivity analyses

MR Analyses

Legend: ■ IVW ◆ MR–Egger ● Weighted median ○ Weighted mode

X-axis: Odds Ratios for T1D per 1 SD change in omega–3 levels

Rows: Main Analysis, AXP, AXB, AXBC, AXI, AXL, AXT2D

Analysis excluding;
AXP: proxy SNPs **AXB**: blood-associated SNPs
AXBC: body composition-associated SNPs
AXI: inflammation-associated SNPs
AXL: lipid-associated SNPs
AXT2D: Type 2 diabetes-associated SNPs

Forest plot of main MR analysis and sensitivity analyses excluding potentially pleiotropic variants.

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Discussion and Conclusion

- Our study found limited evidence of a causal association between ω-3 and T1D

- Findings from this study are contradictory to those from several observational studies

- This challenges the proposition that ω-3 -rich diets are of substantial benefit for the prevention and management of T1D

- Study limitations: Potential bias due to unmeasured pleiotropy, canalization and limited generalizability

- While this study provides important information regarding the ω-3-T1D link, further evidence is required to explore the minor effects that ω-3 may have on T1D risk