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Trans-biobank genome-wide association analysis of pregnancy complications

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Motivation: For the last two decades an increasing number of genome-wide association studies (GWAS) were successfully conducted to identify the genetic variants associated with human traits and predispositions to different diseases. Since many biobanks and consortia are currently investigating identical or related traits in different populations, it is promising to aggregate the results of large-scale GWAS and conduct trans-biobank meta-analyses. It seems important to meta-analyze summary statistics from different studies to better understand genetics of complex diseases and traits in humans.

Methods: In our current study, we aggregated summary statistics of several GWASes of pregnancy-related traits from the UK Biobank and FinnGen projects. We used METAL and MTAG, Multi-Trait Analysis of GWAS, for meta-analysis of genome-wide summary statistics of 24 pregnancy-related traits (with different preprocessing approaches and settings). We also used HuGE Navigator Phenopedia tool to search for genes implicated in pregnancy complications in other gene-level association studies.

Results and Conclusions: 1 and 339 variants with genome-wide significant association with pregnancy complications were identified in UK Biobank and Finngen data, respectively. When meta-analysis methods were used, results of the analysis with different meta-analysis tools tend to be highly similar (Pearson's correlation coefficient is almost 1). However, METAL was chosen as the best option as its results did not show over-inflation of the association statistics. Meta-analysis of pregnancy-related traits identified 6 variants with genome-wide significant association for three traits. Some of the identified loci overlapped with earlier genome-wide association efforts and gene-level association studies according to HuGE Navigator. The results point to a great role of immunity-related processes in driving pregnancy complications.