# Regulatory T-cells in the peripheral blood of women with gestational diabetes; a systematic review and meta-analysis

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## Background

Gestational diabetes (GDM) affects approximately 5-10% of pregnancies globally and is associated with short- and long-term complications for mother and child. GDM is linked to chronic low-grade inflammation and recent research indicates a potential immune dysregulation in the pathophysiology and a disparity in Treg levels which are key in immune-modulation. Treg dysregulation has previously been implicated in pregnancy complications such as pre-eclampsia and recurrent pregnancy loss as well as TD1 and TD2M

## Objective

This systematic review and meta-analysis aimed to determine whether there is an association between GDM and the level of Tregs in the peripheral blood.

## Methods

Literature searches were conducted in PubMed, Embase and Ovid. Inclusion criteria were original articles published in the English Language measuring differentiated Tregs in women with GDM compared to glucose-tolerant pregnant women. Meta-analysis was performed between comparable Treg markers. Statistical tests were used to quantify heterogeneity: Tau$^2$, X$^2$ and I$^2$. Study quality was assessed using a modified version of the Newcastle-Ottawa scale.

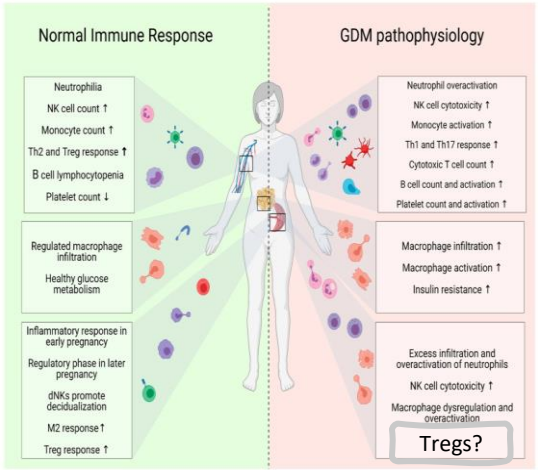


Figure 1 Immune Pathophysiology of GDM, adapted from McElwain et al., 2021

## Results

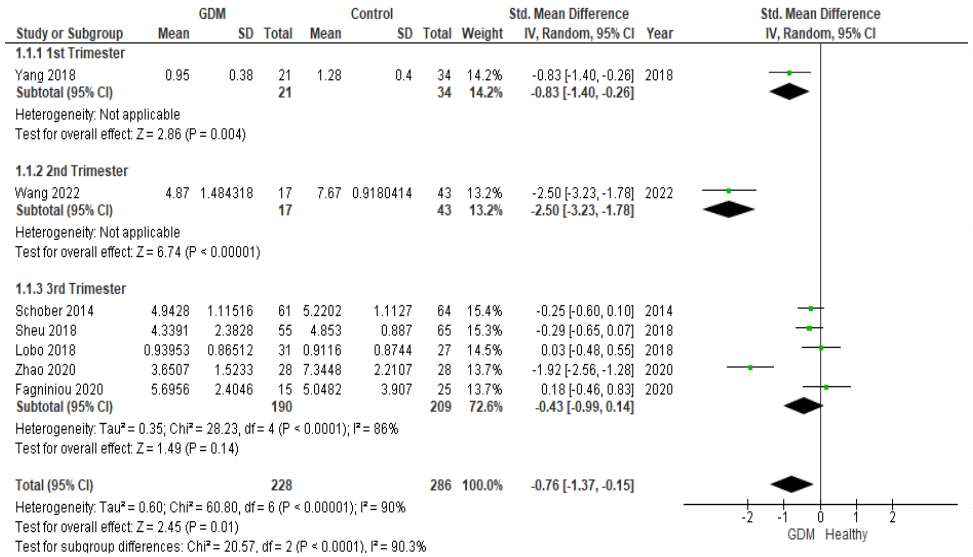


Figure 2 shows a forest plot of Tregs in women with GDM in all trimesters versus healthy pregnant women

The search yielded 223 results: eight studies were included in the review and seven in the Meta-analysis (GDM = 228, Control = 286). Analysis of Tregs across all trimesters showed significantly lower Treg numbers in women with GDM (SMD, -0.76; 95% CI, -1.37, -0.15; I$^2$ = 90%). This was reflected in analysis by specific Treg markers (SMD -0.55; 95% CI, -1.04, -0.07; I$^2$ = 83%; third-trimester, five studies). Non-significant differences were found within subgroups of both analyses indicating underlying differences between Treg subpopulations

## Conclusion

GDM is associated with lower Treg numbers in the peripheral maternal blood. There is clinical potential to use Treg levels, in early pregnancy, as a predictive tool for later complications such as GDM. The therapeutic potential is also indicated through interventions aimed at increasing Treg populations. However, the precise mechanism by which Tregs mediate GDM remains unclear. Further research is required to aid our understanding, emphasising the role of Treg subpopulations and maternal ethnicity in disease pathophysiology.

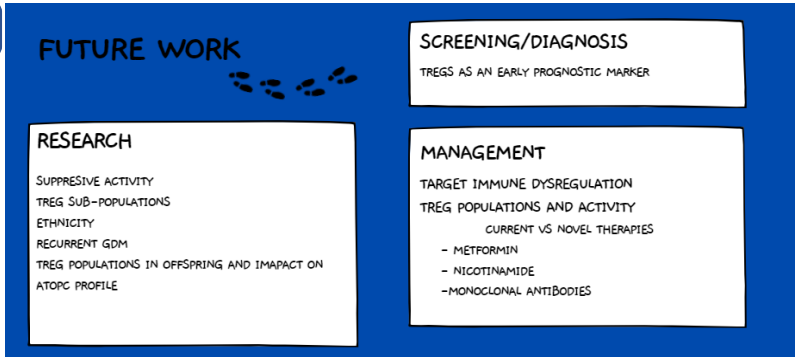


Figure 3 Potential future research and clinical potential.

**References**

1. Behboudi-Gandevani, S. et al. (2019) The impact of diagnostic criteria for gestational diabetes on its prevalence: a systematic review and meta-analysis. *Diabetology & Metabolic Syndrome;*

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*3.* McElwain, C. J. et al. (2021) Gestational Diabetes Mellitus and Maternal Immune Dysregulation: What We Know So Far. *International Journal of Molecular Sciences*. [Online] 22 (8),