

The Role of the Immune Microenvironment in Endometriosis-Associated Infertility: A Systematic Review

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Introduction

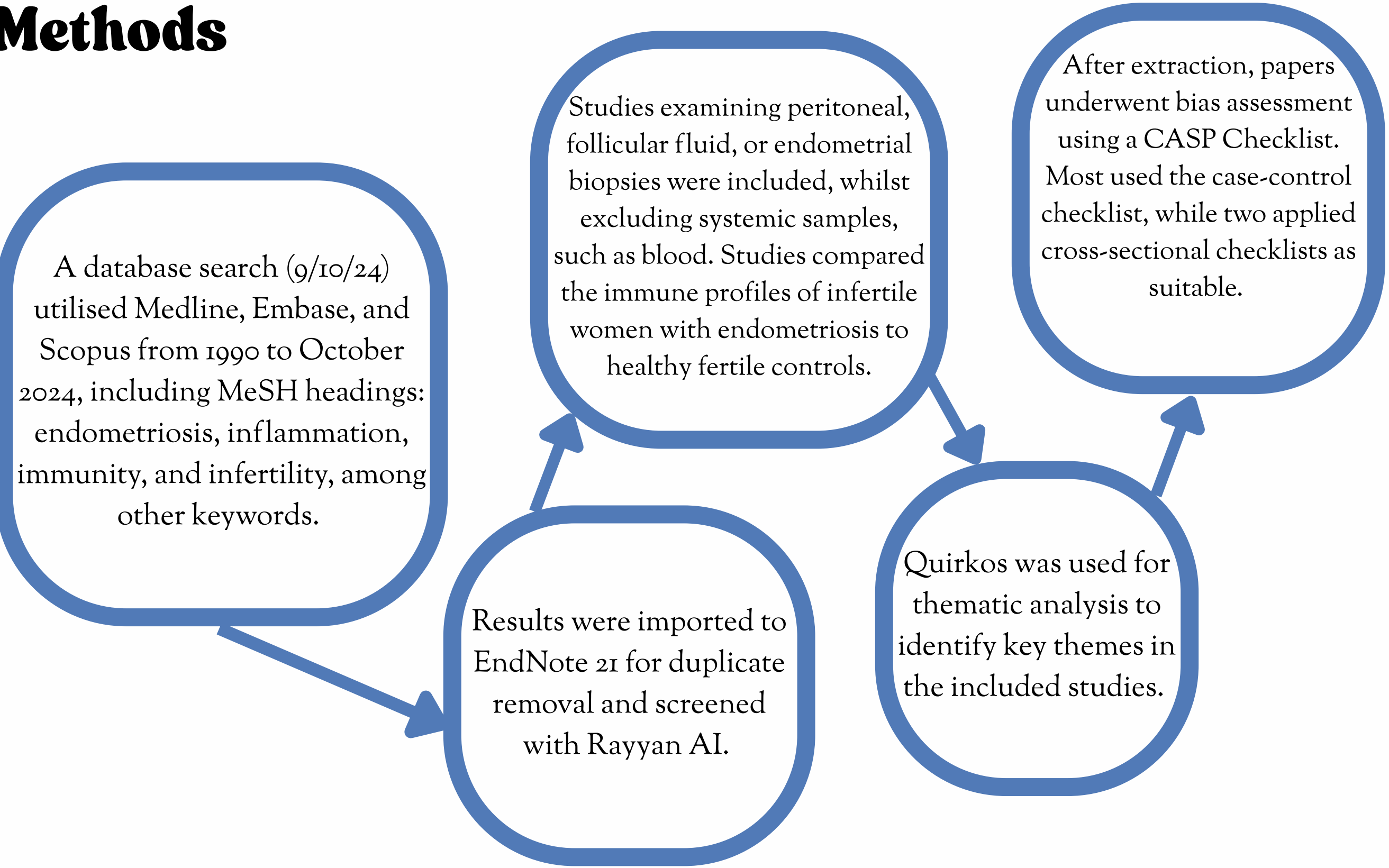
Endometriosis is a reproductive disease characterised by ectopic endometrial tissue growth, primarily on the outer uterine walls and ovaries. It affects approximately 190 million women globally, around 10% of reproductive-age women (1).

Many women are diagnosed only when they face subfertility, with endometriosis prevalence in infertile women as high as 50% (2). Studies examining the link between endometriosis and infertility examined structural changes caused by the disease and treatment options (3,4). Endometriosis-associated infertility is a multifactorial condition, and several studies have postulated that an altered immune system could play a role in this due to the role of inflammation in the pathogenesis of endometriosis (1; 5; 6).

Aims

This systematic review aimed to explore the role of the localised immune microenvironment in endometriosis-associated infertility and propose mechanisms through which inflammation may contribute to infertility.

Methods



Results

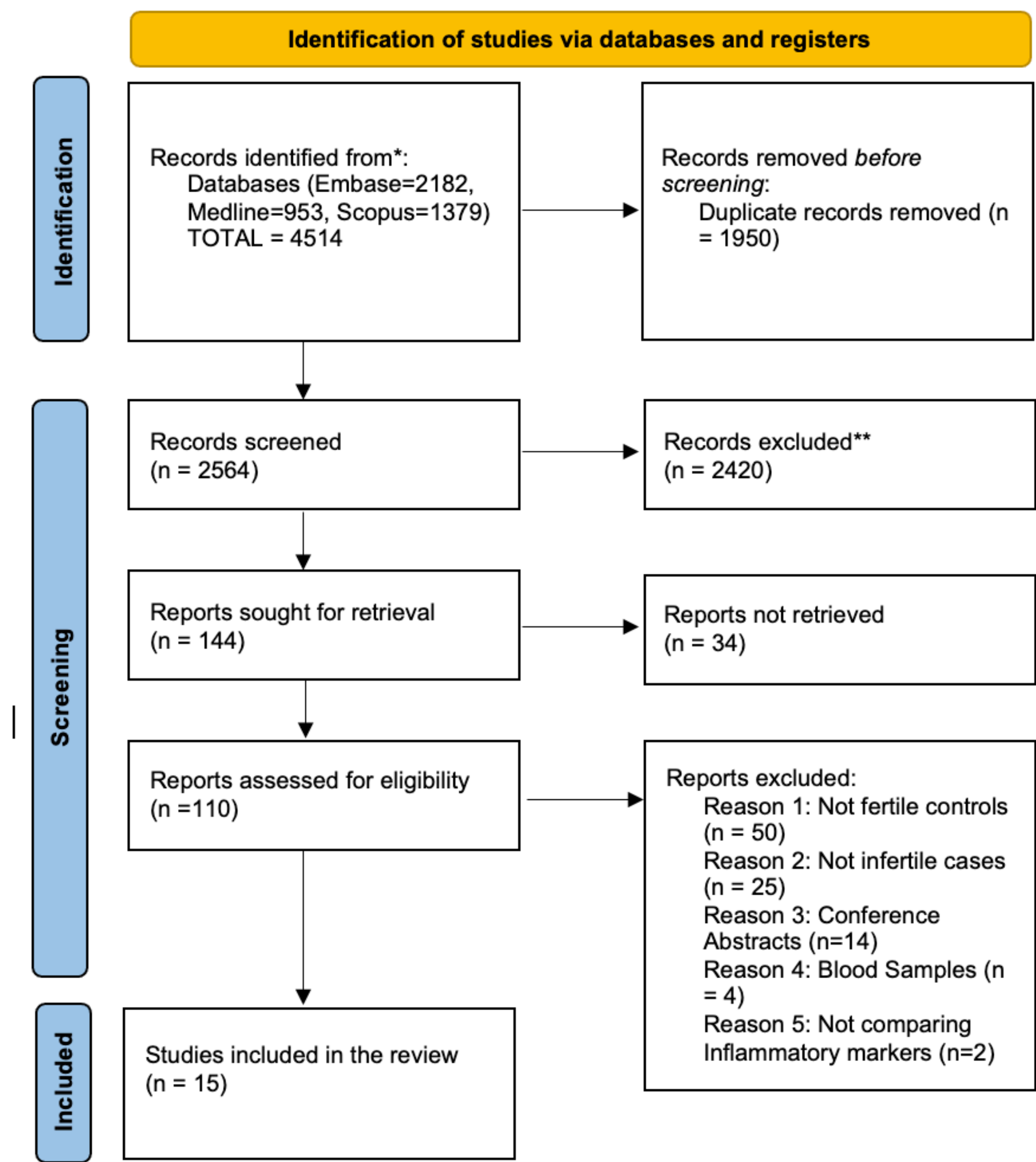


Figure 1 – PRISMA flowchart indicating the selection process for studies, in total, 15 studies were selected for this systematic review

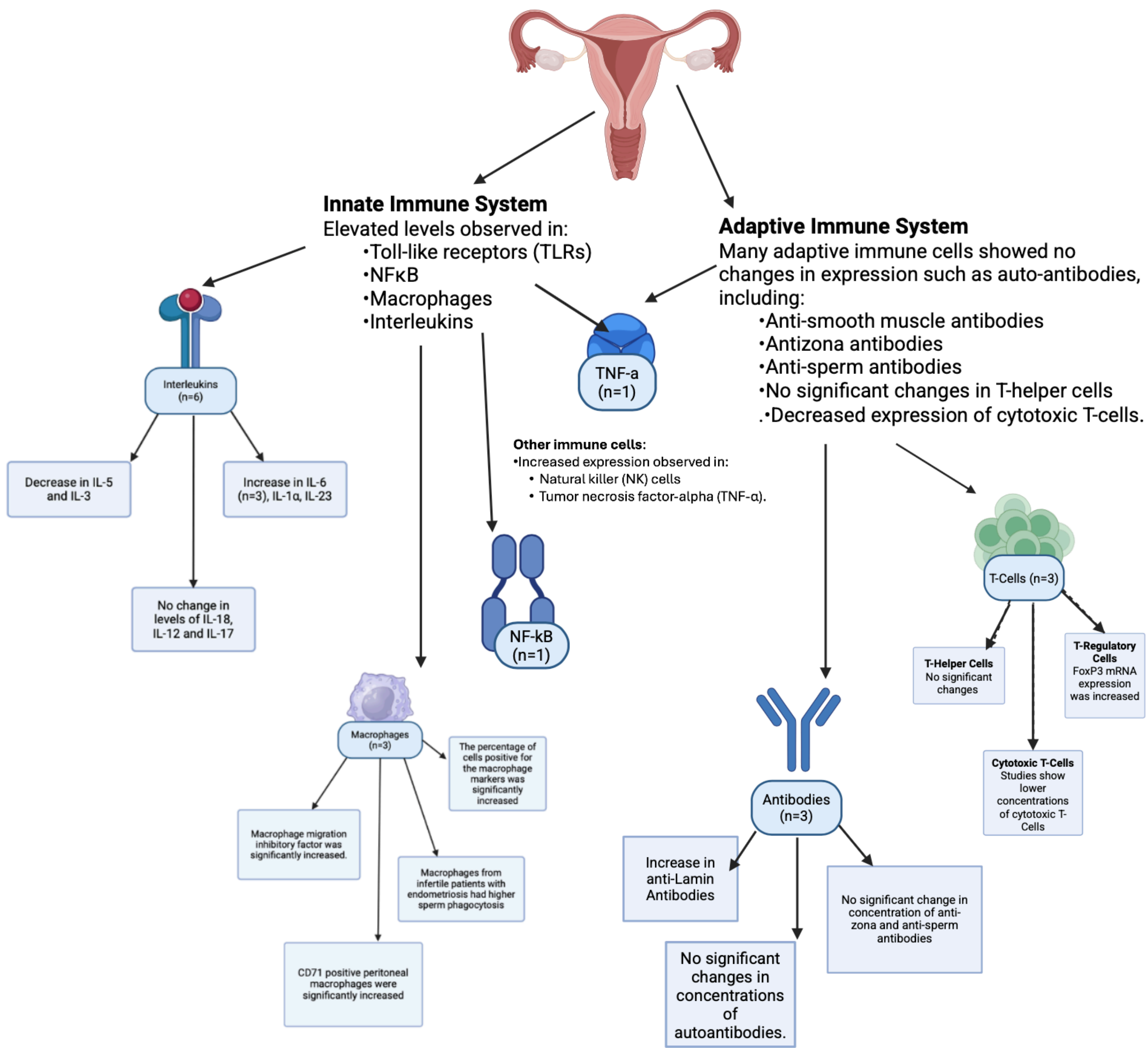


Figure 2 – Flowchart demonstrating key results from the studies; the results were organised depending on whether they fit into the adaptive or innate immune system. Created using Biorender.

Clinical Applicability

- The common theme throughout all the results was IL-6. IL-6 plays a central role in the inflammatory microenvironment of endometriosis, whether through downregulating anti-inflammatory markers or upregulating reactive oxygen species.
 - This suggests that targeting IL-6 may lead to increased fertility.
- Monoclonal antibodies against IL-6 are already used in several autoimmune diseases, such as rheumatoid arthritis and juvenile idiopathic arthritis, and they are being investigated as effective treatments for more acute conditions (7).
- The results suggest that blocking the IL-6 pathway helps reduce the burden of infertility or could be used as an adjunct to IVF to improve outcomes.
 - Tocilizumab is a recombinant humanised anti-IL-6 receptor currently on the market that could be used for this purpose (8). This could reduce the number of IVF cycles needed, which would also have economic benefits.
 - Studies looking at the effect of Tocilizumab in pregnancy showed no increased rates of adverse events in pregnancies (9).

Discussion

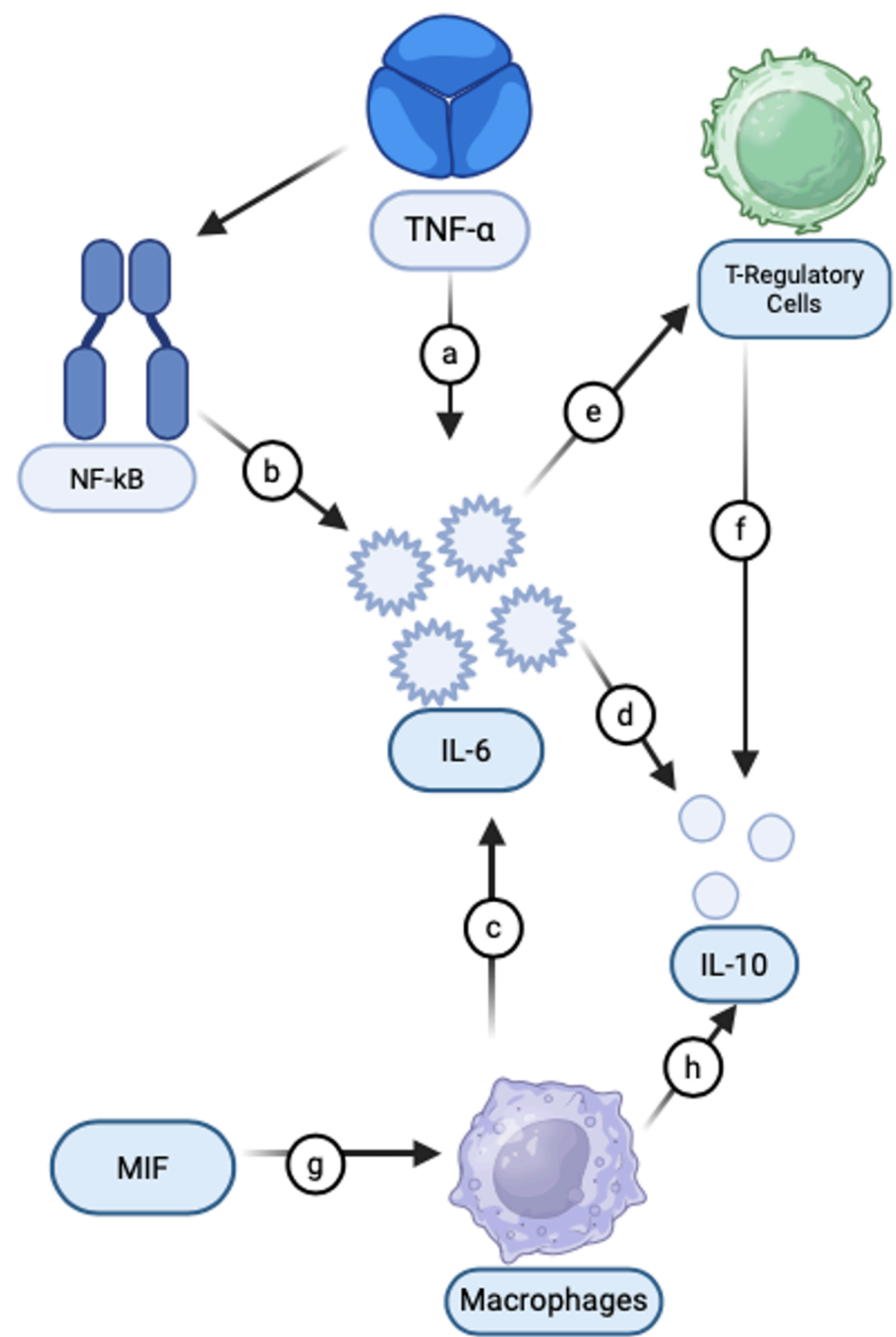


Figure 3 – Figure showing the linkages between the results. Image created using Biorender.

The results demonstrated that the localised immune response in endometriosis-associated infertility centred around IL-6, and this inflammation could damage/impair fallopian tubes and sperm motility.

References

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