SWEDISH AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT AND ASSESSMENT OF SOCIAL SERVICES

English Summary

Effectiveness, complications, and health economic and ethical aspects of preimplantation genetic testing for aneuploidy (PGT-A) during in vitro fertilisation (IVF)

An HTA Report

June 2025. The full report is available in Swedish (www.sbu/393)

Main message

The scientific evidence shows a comparable number of live births after in vitro fertilisation (IVF) with or without preimplantation genetic testing for aneuploidy (PGT-A).

Conclusions

After reviewing the scientific literature, SBU draws the following conclusions:

- The proportion of deliveries with at least one live birth after IVF with PGT-A seems to be comparable to IVF without PGT-A. This is also the case for women over 35 years, although the results are more uncertain for this group.
- Adding PGT-A to IVF almost doubles the cost of an IVF-treatment (defined as an oocyte retrieval and the first embryo transfer) without any increase in live births.
- It is not possible to evaluate if the miscarriage rate is affected when adding PGT-A to IVF since the certainty of evidence is very low.
- There are too few studies to evaluate if PGT-A can reduce the time for IVF treatment to lead to a live born child.
- When comparing biopsy of the embryo with no biopsy in IVF, there does not seem to be any difference in complications for the pregnant women or children.

Aim

The purpose of this systematic review was to evaluate if IVF with PGT-A results in more live births than IVF without PGT-A, and to investigate possible complications from the biopsy. It also includes an analysis of health economic and ethical aspects.

Background

In IVF, embryos are traditionally selected based on morphology to determine which embryo should be transferred to the woman. PGT-A is an additional method for embryo selection that has been suggested to increase the pregnancy and live birth rates. PGT-A involves a biopsy of the embryo (a few cells are taken out) and an analysis of the number of chromosomes. Only embryos with a normal number of chromosomes are transferred to the woman, potentially leading to a higher probability of pregnancy. However, PGT-A also leads to fewer embryos available for transfer and some women will not receive any embryo transfer and it cannot be ruled out that some of the excluded embryos could have resulted in a live birth. The question is therefore whether IVF with PGT-A increases the live birth rate or not. In older women it is more common to have embryos with an abnormal number of chromosomes, suggesting that older women might benefit more from this method. PGT-A is not legally permitted in Sweden but is used in many other countries.

Method

We conducted a systematic review for three separate research questions and reported it in accordance with the PRISMA statement. The protocol is registered in Prospero (CRD42024529876). The certainty of evidence was assessed using GRADE.

Research questions

1. What effect does IVF with PGT-A have on outcomes related to pregnancy and quality of life?
2. Does embryo biopsy during IVF treatment with preimplantation genetic testing (PGT) result in any complications for the child or the pregnant woman?
3. What is the relationship between costs and effects of IVF with PGT-A compared to IVF without PGT-A?

Inclusion criteria:

PICO 1: Effectiveness of PGT-A

- Population: Women undergoing IVF treatment .
- Intervention: IVF treatment with PGT-A, where all chromosomes are analysed.
- Control: IVF treatment without PGT-A.
- Outcome: *Primary outcomes*: Proportion of deliveries with at least one live born child per randomized woman, after the first planned embryo transfer and cumulatively for all embryo transfers from one oocyte retrieval. *Secondary outcomes*: Proportion of deliveries with at least one live born child per embryo transfer, pregnancy rate, miscarriage rate, ectopic pregnancies, time to a live born child and quality of life for the woman and partner.
- Study design: Randomized controlled trials and systematic reviews following PRISMA.

PICO 2: Complications of PGT

- Population: Children who have been conceived through IVF and women who have undergone an IVF treatment and achieved a pregnancy or delivery.
- Intervention: IVF treatment with biopsy of the embryo to perform any form of preimplantation genetic testing (PGT).
- Control: IVF treatment without biopsy of the embryo.
- Outcome: Perinatal and long-term outcomes for children and placenta-related complications for pregnant women.
- Study design: Controlled studies with or without randomization that compare the outcomes between the intervention and control group. Can be prospective or retrospective studies. Systematic reviews following PRISMA.

PICO 3: Health economic aspects of PGT-A

- Same population, intervention and control as PICO 1.
- Outcomes: Costs, Resource use, Cost per effect
- Study design: Comparative cost analyses and health economic evaluations.

All PICO:s

- Language: Scandinavian or English

- Databases searched: CINAHL (EBSCO), Cochrane Library (Wiley), EMBASE (Embase.com), Medline (Ovid), PsycINFO (EBSCO), PubMed (NLM), Scopus (Elsevier)

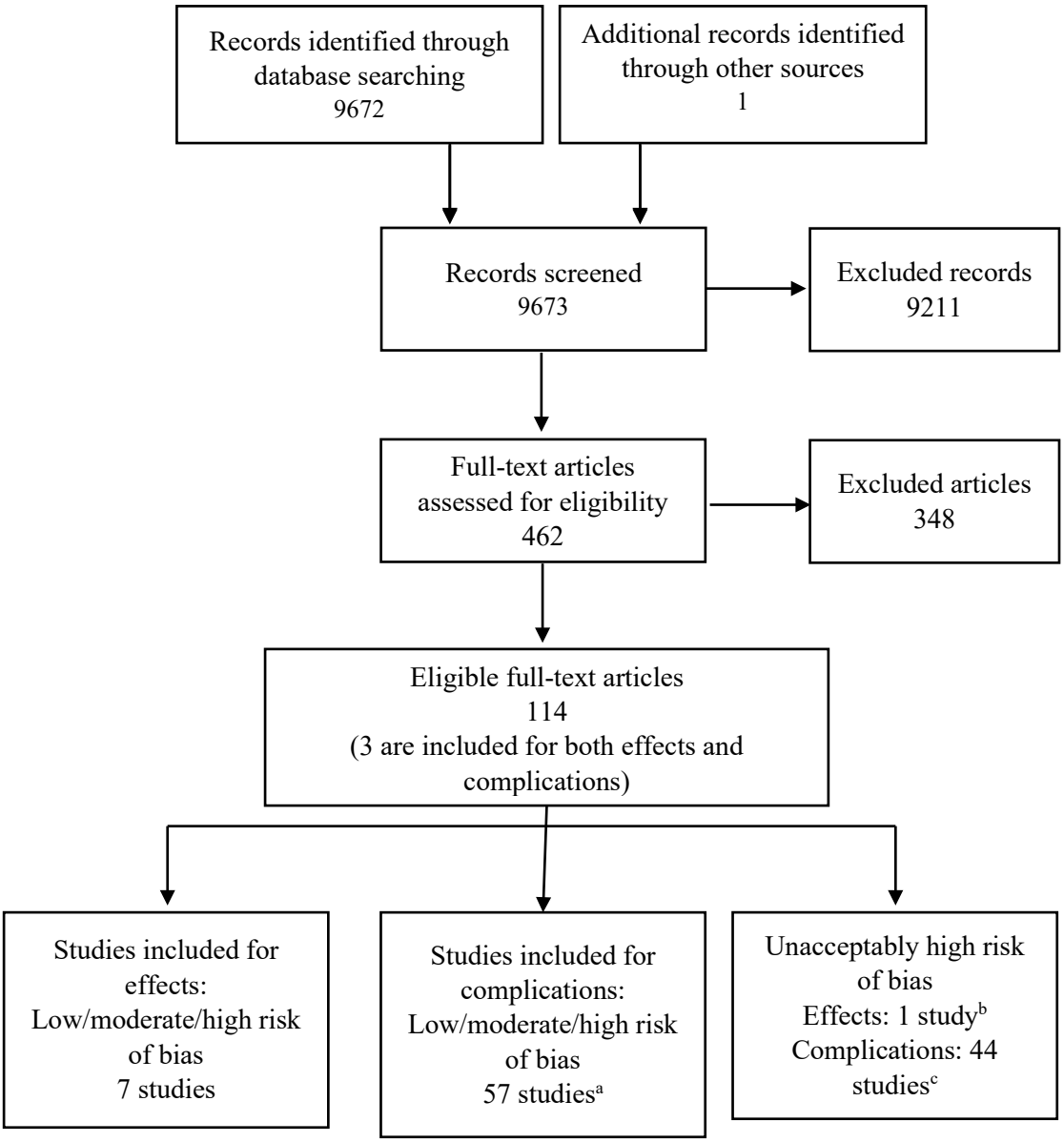
In addition to research questions 1-3, we examined ethical issues of relevance for performing IVF with PGT-A in a Swedish context. These issues were identified from qualitative literature found in searches for PICO 1-3, complementary literature searches, discussions in the group working with the report and discussions with patient advocacy groups.
Patient involvement: yes

Result

The search for effect and complications resulted in 9 673 references (Figure 1). We included 7 RCTs on the effect of PGT-A and 57 studies on complications from embryo biopsy. Three studies were included for both research questions, see figure 1.

The effect of IVF with PGT-A compared to IVF without PGT-A is presented in table 1. The certainty of evidence (GRADE) was mainly affected by limitations in the included studies that may result in bias, precision due to few studies, or heterogeneity. For complications, a synthesis without meta-analysis was used, and no assessment of the certainty of evidence (GRADE) was done. However, the results do not seem to differ between those women that had IVF with or without biopsy for any of the included complications.

Figure 1 Flowchart.



[a] Reported in 60 articles
[b] Reported in 2 articles
[c] Reported in 48 articles

Table 1 Summary of findings (main results) for the effect of IVF with PGT-A compared with regular IVF on different outcomes.

Outcome	Results	GRADE
Deliveries with live birth		
After first planned embryo transfer (ITT) All ages ≥35 years	 Comparable effect Cannot be determined	 ⨁⨁◯◯ ⨁◯◯◯
All embryo transfers from an oocyte retrieval (ITT) All ages ≥35 years	 Comparable effect Comparable effect	 ⨁⨁◯◯ ⨁⨁◯◯
For those that had an embryo transfer All ages ≥35 years	 In favour of PGT-A In favour of PGT-A	 ⨁⨁◯◯ ⨁⨁◯◯
Miscarriage		
Miscarriage per clinical pregnancy All ages ≥35 years	 Cannot be determined Cannot be determined	 ⨁◯◯◯ ⨁◯◯◯

Abbreviations: ITT = intention to treat analysis.
⨁⨁◯◯= low certainty of evidence, ⨁◯◯◯= very low certainty of evidence

Health Economic Assessment

Twelve relevant studies were identified in the literature search, but only two had sufficient quality (at least low to medium quality) and were included in the report. Since these studies were from China and the USA, respectively, the results are expected to have limited transferability to a Swedish context if PGT-A were to be made available. Thus, a health economic model was constructed using data from Swedish registry data for IVF treatment and Swedish costs. Based on the results of the systematic review on the effect of adding PGT-A to IVF, our analyses showed an increase in costs by 37 500 Swedish kronor when adding PGT-A to IVF, without any increase in live births. This result was consistent for the subgroup of women 35 years and older.

Ethics

A healthcare intervention needs to have benefits to patients that outweigh its potential disadvantages. PGT-A does not fulfil this condition as there is no evidence of any relevant patient benefits in our systematic review.

If PGT-A were nevertheless to be offered within publicly funded healthcare in Sweden, priority setting decisions would be needed. Additionally, patients' informed consent to PGT-A may be threatened by unrealistic expectations. It would therefore be essential that healthcare providers are well informed about the state of scientific knowledge in this area and able to communicate this accurately to patients.

Discussion

In this systematic review we did not find any support for the hypothesis that adding PGT-A to IVF treatment increases the live birth rate when considering all randomised women in the included trials. In addition, no increased live birth rate could be found for women 35 years or

older, even though older women have a higher proportion of aneuploid embryos. Our results may be due to fewer women in the group that had IVF with PGT-A having an embryo transfer. It is also possible that some of the embryos excluded after PGT-A analysis could have resulted in a live birth.

For the outcome miscarriage rate no conclusions could be drawn as the result was too uncertain, which may be due to too few studies and events. No synthesis of the result could be performed for the outcome time to live birth as there were too few studies. There is a need for more well-conducted studies focusing on specific groups of patients, to assess whether PGT-A offers benefit to particular populations.

Our results for complications related to the biopsy of the embryo did not show any differences, but the certainty of evidence was not assessed, as the studies were too heterogenous.

In conclusion, PGT-A does not increase the proportion of successful IVF treatments, but adding PGT-A to an IVF treatment nearly doubles the costs. From an ethical perspective, PGT-A thereby does not fulfil the requirement that healthcare interventions should have clear benefits that outweigh their disadvantages.

Conflict of Interest

In accordance with SBU's requirements, the experts and scientific reviewers participating in this project have submitted statements about conflicts of interest. These documents are available at SBU's secretariat. SBU has determined that the conditions described in the submissions are compatible with SBU's requirements for objectivity and impartiality.

Appendices

- Search strategies
- Excluded studies after full text review and studies not included in analysis due to Risk of Bias
- Characteristics of included studies
- References included in analysis