Bilaga till rapport

Undersökning av kromosomavvikelser i embryot vid assisterad befruktning/Effectiveness, complications and health economic and ethical aspects of preimplantation genetic testing for aneuploidy (PGT-A) during *in vitro* fertilisation (IVF) report 393 (2025)

# Appendix 4 Risk of bias assessments for included studies

## Table of contents

Table 1 Risk of bias assessments for studies of efficacy.

| Study | Overall risk of bias assessment | Reasons for the assessment |
|---|---|---|
| **Munne 2019** **[1]** | Low/ Moderate | Low risk of bias for all outcomes for the entire population.<br><br>Subgroup 35-40 years: Moderate risk of bias because baseline data is not reported separately for this group. |
| **Ozgur 2019** **[2]** | Serious | Only per protocol analyses. The difference in dropouts between the groups was not considered in analysis.<br>We have calculated a modified ITT analysis that includes all participants and made assumptions for those who were missing. Those who received embryos with unknown ploidy are included in the PGT-A group in our analyses, which affects the results for this group. It is not clear in the protocol how they intended to handle and analyse those who did not have any euploid embryos. |
| **Rubio 2017** **[3]** | Moderate/ Serious/ Critical | Critical risk of bias for time to pregnancy/childbirth due to how the results are calculated.<br><br>Serious risk of bias for cumulative outcomes due to possible difference in the number of embryos left in the groups since the study is completed 6 months after the last recruitment.<br><br>Moderate risk of bias for other outcomes because randomization was done early and it was unclear whether the therapists and participants were blinded, age is only reported as mean and baseline data is only reported for per protocol patients. |
| **ScottJr 2013** **[4]** | Serious | Different days of embryo transfer in the groups (days 5 vs. 6). The outcome measures were not specified in the protocol. |
| **Verpoest 2018** **[5]** | Moderate | Those who received embryos with unknown ploidy are included in the PGT-A group, which affects the results for this group. |
| **Wang 2022** **[6]** | Serious | Poor description of randomization, baseline values and how the study was conducted. Missing protocol. |
| **Yan 2021** **[7] [8]** | Low/ Moderate/ Serious | Moderate risk of bias for cumulative efficacy outcomes and time to delivery as the biopsy of maximum three embryos may affect the possibility to fully assess the effect of PGT-A.<br><br>Low risk of bias for other efficacy outcomes and outcomes related to complications.<br><br>For the subgroup over 35 years of age; serious risk of bias because baseline data for this group is missing, randomization was not done specifically for this age group and the subgroup analysis was not planned in advance. |

Table 2 Risk of bias assessments per domain for the subgroup of women aged 35 years and older.

| Study | Randomi-zation | Differences in treatment | Drop-out: | Measure-ment of outcomes | Reporting of results | Conflict of interests | Overall |
|---|---|---|---|---|---|---|---|
| **Munne et al. 2019 [1]** | Moderate | Low | Low | Low | Low | Yes | Moderate |
| **Rubio et al. 2017 [3]** | Moderate | Moderate[a] Serious[b] | Low | Low | Low | Yes | Moderate[a] Serious[b] |
| **Verpoest et al. 2018 [5]** | Low | Moderate | Low | Low | Low | No | Moderate |
| **Yan et al. 2021 [8]** | Serious | Moderate | Low | Low | Moderate | No | Serious |

[a] for the outcomes per planned embryo transfer and per performed embryo transfer and miscarriage

[b] for the outcome cumulative birth rate per egg retrieval

Table 3 Risk of bias assessments for studies of complications.

| Study | Risk of bias assessment for included outcomes | Reasons for the assessment |
|---|---|---|
| Awadalla 2021 [9] | Moderate | Subgroup analyses instead of adjustment to confounders.<br>No information on potentially missing data.<br>No protocol. |
| Belva 2018 [10] | Moderate | Matching on pediatric variables, possible confounders slightly different<br>Missing data without explanation.<br>No protocol |
| Belva 2023 [11] | Moderate | Baseline differences particularly in rate of nulliparous but adjusted for in analysis.<br>Significant drop out.<br>No protocol |
| Cozzolino 2023 [12] | Moderate | Information on parity missing but adjusted for in addition to age in analyses.<br>No information on potentially missing data.<br>Unclear selection of control group.<br>No protocol. |
| Desmyttere 2009 [13] | Serious | No information about groups before matching.<br>No information on fresh or frozen embryo transfers.<br>Missing data without explanation.<br>No protocol.<br>Some outcomes reported partly by parents.<br><br>Critical risk of bias for gestational age, birthweight, gestational hypertension, Apgar score, and reason and duration of admission to a neonatal care unit because proportion of fresh or frozen transfers is not reported. Length and head circumference at birth not relevant |
| Desmyttere 2012 [14] | Serious | Differences in age and parity and no adjustment.<br>No information on fresh or frozen transfers.<br>No information on potentially missing data.<br>No protocol.<br><br>Critical risk of bias for birth weight, gestational age, and length of stay at intensive care unit because of no information on the proportion of fresh or frozen embryos. Birth defects not reported separately for singletons. |
| DeVos 2009 [15] | Serious | Unclear how monozygotic twins were accounted for.<br>No information on parity.<br>No information on potentially missing data.<br>No protocol.<br><br>Critical risk of bias for still born because no information on parity. |
| Eldar-Geva 2014 [16] | Moderate for caesarean section | Sparse data on matching and baseline data<br>No protocol.<br>Differential ratio of fresh or frozen transfers (not relevant for caesarean section). |

| | | |
|---|---|---|
| | Serious for all other outcomes | Critical risk of bias for gestational hypertension as not separately reported for singletons. |
| El-Toukhy 2009 [17] | Serious | Do not take confounders into account.<br>Monozygotic twins unclearly described.<br>No information on potentially missing data.<br>No protocol. |
| Feldman 2020 [18] | Moderate | No information on proportion of fresh or frozen transfers, no information on day of transfer.<br>No information on potentially missing data.<br>No protocol.<br><br>Critical risk of bias for gestational length, birth weight, length of stay in intensive care unit and gestational hypertension because proportion of fresh or frozen transfers is not reported. |
| Forman 2012 [19] | Moderate for monozygotic twins<br><br>Serious for birth defects | Age difference (mainly affects birth defects)<br>Do not take confounders into account.<br>Ratio of fresh or frozen transfers unclear.<br>No protocol.<br><br>Critical risk of bias for all outcomes except for monozygotic twins and birth defects which are reported separately for singletons. |
| Ginstrom Ernstad 2023 [20] | Moderate<br><br>Serious for placenta previa | Differential day of transfer (mainly affects placenta previa)<br>Potentially missing data.<br>No protocol.<br>Some outcomes may be underdiagnosed. |
| Gulersen 2021 [21] | Moderate | Day of transfer not reported in control group.<br>No information on potentially missing data.<br>Differential fresh or frozen transfers in the groups which is accounted for in the analysis.<br><br>Critical risk of bias for placenta previa because of no information on day of transfer. |
| Gulersen 2022 [22] | Moderate | No information on potentially missing data per group.<br>No protocol. |
| Hao 2022 [23] | Moderate | Significant proportion of excluded patients. Some outcome data have been collected via phone interviews.<br>No protocol. |
| Hasson 2017 [24] | Serious | Matching on age and BMI, but parity differs in the groups. No information about groups before matching.<br>No information on potentially missing data.<br>Outcomes may have been collected by phone calls.<br>No protocol. |
| He 2019 [25] | Moderate for birth defects<br><br>Serious for all other outcomes | Confounders accounted for but no information on parity (does not affect birth defects).<br>No information on potentially missing data.<br>Outcomes for children reported by parents.<br>No protocol. |
| Ji 2023 [26] | Moderate | Propensity score matching may lead to differential missing data.<br>No protocol, |

| | | |
|---|---|---|
| Kamath 2020 [27] | Moderate | No protocol |
| Kato 2023 [28] | Moderate | Large loss at propensity score matching, which leads to potentially missing data.<br>No information on parity but given the population probably no previous children.<br>No protocol. |
| Kato 2023 [29] | Moderate | Single embryo transfer but no information on eventual monozygotic twins, which might be expected in such a large study.<br>No protocol, |
| Lewis 2021 [30] | Serious | Lack information on parity. Matched cohort.<br>Exclusion of those born before v 30.<br>Differential loss, potentially missing data.<br>No protocol.<br><br>Critical risk of bias for all outcomes except for caesarean section due to lack of information on parity. |
| Li 2021 [31] | Moderate | No information on potentially missing data per group. |
| Li 2022 [32] | Moderate | Missing data due to matching.<br>Maternal outcomes may be affected by only selecting those with live born children.<br>No protocol. |
| Li 2022 [33] | Serious | No information on parity, regression analyses for other confounders.<br>Unclear selection on study participants.<br>Unclear information on potentially missing data.<br>No protocol. |
| Liu 2024 [34] | Moderate | Scanty description of treatment.<br>No information on potentially missing data.<br>No protocol. |
| Liu 2024 [35] | Moderate | Do not take confounders into account. Some difference in parity.<br>No information on potentially missing data.<br>No protocol<br><br>Critical risk of bias for all outcomes except birth weight in the group <38 years because singletons not reported separately |
| Lu 2020 [36] | Moderate | Do not take confounders into account but baseline data similar.<br>More hormone treatment in one group may affect hypertension.<br>No information on potentially missing data.<br>No protocol. |
| Makhijani 2021 [37] | Moderate | Take confounders into account, but big difference in unadjusted data.<br>No information on potentially missing data.<br>Outcomes collected from parents which may lead to uncertainty for certain outcomes.<br>No protocol. |

| | | |
|---|---|---|
| Mastenbroek 2007<br>[38]<br>[39] [40] | Moderate<br><br>Serious for gestational length and birth weight | Differential loss, potentially missing data.<br>Outcomes for complications not specified in the protocol<br>Ratio of fresh or frozen transfers unclear in PGS group (affects gestational length and birth weight.)<br><br>Critical risk of bias for all outcomes not reported separately for singletons. |
| Mejia 2022<br>[41] | Moderate | Do not take confounders into account, but parity and age similar.<br>No information on fresh or frozen transfer.<br>Significant loss in both groups, potentially missing data.<br>No protocol.<br><br>Critical risk of bias for gestational length and birth weight due to no information on proportion of fresh or frozen transfers. |
| Meyer 2009<br>[42] | Moderate | Unclarities in the randomization procedure.<br>No protocol. |
| Nekkebroeck 2008<br>[43] | Moderate | No information about groups before matching.<br>No information of fresh or frozen embryos in control group.<br>Potentially missing data due to some loss, but similar between groups.<br>No protocol. |
| Nekkebroeck 2008<br>[44] | Serious | No information about groups before matching. For some outcomes no account of age, but fairly similar.<br>No information on ratio of fresh or frozen transfers and day of transfer in control group.<br>Possible selection of patients.<br>Potentially missing data due to some loss.<br>Measures of some outcomes problematic if not blinded.<br>No protocol.<br><br>Critical risk of bias for gestational length and birth weight due to no information on proportion of fresh or frozen transfers. |
| Ricciarelli 2013<br>[45] | Serious | No information on parity and no account of confounders.<br>Unclear if fresh or frozen transfers.<br>Potentially missing data due to loss.<br>Outcome data collected via questionnaires.<br>No protocol<br><br>Critical risk of bias for prematurity and stillbirth because of no information on parity. |
| Richardson 2022<br>[46] | Serious | Do not take confounders into account. Some differences in baseline data.<br>Transfer at different days.<br>No information on potentially missing data.<br>No protocol. |
| Riestenberg 2021<br>[47] | Serious | Do not take confounders into account. Difference in age since more donated eggs in one group.<br>Abortions due to fetal anomalies excluded, but no information on how many.<br>No information on treatment.<br>No protocol |

| | | |
|---|---|---|
| | | Placenta previa not relevant as it cannot be assessed in second trimester. |
| Roeca 2020 [48] | Serious | Unclarities regarding baseline data, treatment and reporting of data for singletons.<br>No information on potentially missing data.<br>No protocol.<br><br>Critical risk of bias for all outcomes not reported separately for singletons. |
| Sarkar 2023 [49] | Moderate | Take confounders into account, but parity is missing.<br>Unclear selection and loss of participants. Potentially missing data.<br>No protocol. |
| Shi 2023 [50] | Moderate | Do not take confounders into account, but age and parity similar.<br>No information on potentially missing data.<br>No protocol. |
| Sites 2021 [51] | Moderate | No information on potentially missing data.<br>No protocol. |
| Snelgrove 2024 [52] | Moderate | Do not take confounders into account, but age and parity similar.<br>No information on potentially missing data.<br>No protocol. |
| Srebnik 2023 [53] | Serious | No adjustment for confounders, but similar between groups.<br>Stillborn children excluded, unclear if different in the groups.<br>Unclear if day of transfer differs between groups.<br>No information on potentially missing data.<br>No protocol |
| Staessen 2004 [54] | Serious | Randomization process not described.<br>Unclear reporting of monozygotic twins.<br>No protocol, study terminated before finished. |
| Staessen 2008 [55] | Moderate | Sparse information on the randomization procedure. |
| Sun 2024 [56] | Moderate | No information on parity and do not take this confounder into account.<br>No information on potentially missing data.<br>Outcomes assessed by phone.<br><br>Critical risk of bias for preterm delivery, perinatal death, caesarean section, fetal distress, birthweight, hypertension and placenta related problems due to unadjusted data and information on parity missing. |
| Sunkara 2017 [57] | Moderate | Do not take parity into account as a confounder.<br>No protocol. |
| Verpoest 2009 [58] | Moderate | Not clear if embryos were frozen or fresh.<br>No information on potentially missing data.<br>No protocol. |
| Winter 2014 [59] | Serious | No information on fresh or frozen transfer and day of transfer.<br>Possible selection of study participants.<br>Potentially missing data as comparatively large loss in both groups.<br>Assessors not blinded.<br>No protocol. |

| | | |
|---|---|---|
| Winter 2015<br>[60] | Serious | No information on ratio fresh or frozen transfers and day of transfer.<br>Possible selection of study participants.<br>Potentially missing data as comparatively large loss in both groups.<br>Assessors not blinded.<br>No protocol. |
| Wu 2021<br>[61] | Moderate for birth defects<br><br>Serious for all other outcomes | Matched, but not for parity (does not affect birth defects).<br>Possible selection of study participants.<br>No protocol. |
| Zhang 2019<br>[62] | Moderate<br><br>Serious for birth defects | Possible selection as terminations for fetal anomalies and maternal health were excluded. One case with birth defects (terminated) were excluded.<br>No protocol. |
| Zheng 2022<br>[63] | Moderate | Large loss, potentially missing data.<br>No protocol. |
| Zheng 2022<br>[64] | Moderate | No information on potentially missing data<br>No protocol |

# References


1. Munne S, Kaplan B, Frattarelli JL, Child T, Nakhuda G, Shamma FN, et al. Preimplantation genetic testing for aneuploidy versus morphology as selection criteria for single frozen-thawed embryo transfer in good-prognosis patients: a multicenter randomized clinical trial. Fertility and sterility. 2019;112(6):1071-9.e7. Available from: https://doi.org/10.1016/j.fertnstert.2019.07.1346
2. Ozgur K, Berkkanoglu M, Bulut H, Yoruk GDA, Candurmaz NN, Coetzee K. Single best euploid versus single best unknown-ploidy blastocyst frozen embryo transfers: a randomized controlled trial. Journal of Assisted Reproduction and Genetics. 2019;36(4):629-36. Available from: https://doi.org/10.1007/s10815-018-01399-1
3. Rubio C, Bellver J, Rodrigo L, Castillon G, Guillen A, Vidal C, et al. In vitro fertilization with preimplantation genetic diagnosis for aneuploidies in advanced maternal age: a randomized, controlled study. Fertility and sterility. 2017;107(5):1122-9. Available from: https://doi.org/10.1016/j.fertnstert.2017.03.011
4. Scott Jr RT, Upham KM, Forman EJ, Hong KH, Scott KL, Taylor D, et al. Blastocyst biopsy with comprehensive chromosome screening and fresh embryo transfer significantly increases in vitro fertilization implantation and delivery rates: A randomized controlled trial. Fertility and Sterility. 2013;100(3):697-703. Available from: https://doi.org/10.1016/j.fertnstert.2013.04.035
5. Verpoest W, Staessen C, Bossuyt PM, Goossens V, Altarescu G, Bonduelle M, et al. Preimplantation genetic testing for aneuploidy by microarray analysis of polar bodies in advanced maternal age: a randomized clinical trial. Human reproduction (Oxford, England). 2018;33(9):1767-76. Available from: https://doi.org/10.1093/humrep/dey262
6. Wang L, Wang X, Li M, Liu Y, Ou X, Chen L, et al. PGT-A: The biology and hidden failures of randomized control trials. Prenatal Diagnosis. 2022;42(9):1211-21. Available from: https://doi.org/10.1002/pd.6199
7. Guo L, Li X, Guo A, Wang Y, Liang Y, Li Y, et al. Comparative study on pregnancy complications: PGT-A vs. IVF-ET with gender-specific outcomes. Front Endocrinol (Lausanne). 2024;15:1453083. Available from: https://doi.org/10.3389/fendo.2024.1453083
8. Yan J, Qin Y, Zhao H, Sun Y, Gong F, Li R, et al. Live Birth with or without Preimplantation Genetic Testing for Aneuploidy. The New England journal of medicine. 2021;385(22):2047-58. Available from: https://doi.org/10.1056/NEJMoa2103613
9. Awadalla MS, Park KE, Latack KR, McGinnis LK, Ahmady A, Paulson RJ. Influence of Trophectoderm Biopsy Prior to Frozen Blastocyst Transfer on Obstetrical Outcomes. Reproductive Sciences. 2021;28(12):3459-65. Available from: https://doi.org/10.1007/s43032-021-00552-z
10. Belva F, Roelants M, Kluijfhout S, Winter C, De Schrijver F, Desmyttere S, et al. Body composition and blood pressure in 6-year-old singletons born after pre-implantation genetic testing for monogenic and structural chromosomal aberrations: a matched cohort study. Human Reproduction Open. 2018;2018(4). Available from: https://doi.org/10.1093/hropen/hoy013
11. Belva F, Kondowe F, De Vos A, Keymolen K, Buysse A, Hes F, et al. Cleavage-stage or blastocyst-stage embryo biopsy has no impact on growth and health in children

up to 2 years of age. Reproductive Biology and Endocrinology. 2023;21(1):87. Available from: https://doi.org/10.1186/s12958-023-01140-3
12. Cozzolino M, Cecchino GN, Garcia Velasco JA, Pellicer N, Galliano D, Pellicer A. Preimplantation genetic testing for aneuploidy is not related to adverse obstetric and neonatal outcomes in singleton pregnancies. Human Reproduction. 2023;38(8):1621-7. Available from: https://doi.org/10.1093/humrep/dead123
13. Desmyttere S, De Schepper J, Nekkebroeck J, De Vos A, De Rycke M, Staessen C, et al. Two-year auxological and medical outcome of singletons born after embryo biopsy applied in preimplantation genetic diagnosis or preimplantation genetic screening. Human Reproduction. 2009;24(2):470-6. Available from: https://doi.org/10.1093/humrep/den402
14. Desmyttere S, De Rycke M, Staessen C, Liebaers I, De Schrijver F, Verpoest W, et al. Neonatal follow-up of 995 consecutively born children after embryo biopsy for PGD. Hum Reprod. 2012;27(1):288-93. Available from: https://doi.org/10.1093/humrep/der360
15. De Vos A, Staessen C, De Rycke M, Verpoest W, Haentjens P, Devroey P, et al. Impact of cleavage-stage embryo biopsy in view of PGD on human blastocyst implantation: a prospective cohort of single embryo transfers. Human Reproduction. 2009;24(12):2988-96. Available from: https://doi.org/10.1093/humrep/dep251
16. Eldar-Geva T, Srebnik N, Altarescu G, Varshaver I, Brooks B, Levy-Lahad E, et al. Neonatal outcome after preimplantation genetic diagnosis. Fertility and sterility. 2014;102(4):1016-21. Available from: https://doi.org/10.1016/j.fertnstert.2014.06.023
17. El-Toukhy T, Kamal A, Wharf E, Grace J, Bolton V, Khalaf Y, et al. Reduction of the multiple pregnancy rate in a preimplantation genetic diagnosis programme after introduction of single blastocyst transfer and cryopreservation of blastocysts biopsied on Day 3. Human Reproduction. 2009;24(10):2642-8. Available from: https://doi.org/10.1093/humrep/dep172
18. Feldman B, Orvieto R, Weisel M, Aizer A, Meyer R, Haas J, et al. Obstetric and Perinatal Outcomes in Pregnancies Conceived After Preimplantation Genetic Testing for Monogenetic Diseases. Obstetrics & Gynecology. 2020;136(4):782-91. Available from: https://doi.org/10.1097/aog.0000000000004062
19. Forman EJ, Tao X, Ferry KM, Taylor D, Treff NR, Scott RT, Jr. Single embryo transfer with comprehensive chromosome screening results in improved ongoing pregnancy rates and decreased miscarriage rates. Human Reproduction. 2012;27(4):1217-22. Available from: https://doi.org/10.1093/humrep/des020
20. Ginstrom Ernstad E, Hanson C, Wanggren K, Thurin-Kjellberg A, Hulthe Soderberg C, Syk Lundberg E, et al. Preimplantation genetic testing and child health: a national register-based study. Human reproduction (Oxford, England). 2023;38(4):739-50. Available from: https://doi.org/10.1093/humrep/dead021
21. Gulersen M, Peyser A, Ferraro A, Goldman R, Mullin C, Li X, et al. Maternal and neonatal outcomes in pregnancies conceived after preimplantation genetic testing. Prenatal Diagnosis. 2021;41(7):835-42. Available from: https://doi.org/10.1002/pd.5937
22. Gulersen M, Peyser A, Kim J, Ferraro A, Goldman R, Mullin C, et al. The impact of preimplantation genetic testing for aneuploidy on prenatal screening. 2022;50(3):300-4. Available from: https://doi.org/10.1515/jpm-2021-0495
23. Hao Y, Long X, Kong F, Chen L, Chi H, Zhu X, et al. Maternal and neonatal outcomes following blastocyst biopsy for PGT in single vitrified-warmed embryo transfer cycles. Reproductive BioMedicine Online. 2022;44(1):151-62. Available from: https://doi.org/10.1016/j.rbmo.2021.07.016

24. Hasson J, Limoni D, Malcov M, Frumkin T, Amir H, Shavit T, et al. Obstetric and neonatal outcomes of pregnancies conceived after preimplantation genetic diagnosis: cohort study and meta-analysis. Reproductive BioMedicine Online. 2017;35(2):208-18. Available from: https://doi.org/10.1016/j.rbmo.2017.05.003
25. He H, Jing S, Lu CF, Tan YQ, Luo KL, Zhang SP, et al. Neonatal outcomes of live births after blastocyst biopsy in preimplantation genetic testing cycles: a follow-up of 1,721 children. Fertility and sterility. 2019;112(1):82-8. Available from: https://doi.org/10.1016/j.fertnstert.2019.03.006
26. Ji H, Zhang MQ, Zhou Q, Zhang S, Dong L, Li XL, et al. Trophectoderm biopsy is associated with adverse obstetric outcomes rather than neonatal outcomes. BMC Pregnancy Childbirth. 2023;23(1):141. Available from: https://doi.org/10.1186/s12884-023-05466-z
27. Kamath M, Antonisamy B, Sunkara S. Zygotic splitting following embryo biopsy: a cohort study of 207 697 single-embryo transfers following IVF treatment. BJOG: An International Journal of Obstetrics & Gynaecology. 2020;127(5):562-9. Available from: https://doi.org/10.1111/1471-0528.16045
28. Kato K, Kuroda T, Yamadera-Egawa R, Ezoe K, Aoyama N, Usami A, et al. Preimplantation Genetic Testing for Aneuploidy for Recurrent Pregnancy Loss and Recurrent Implantation Failure in Minimal Ovarian Stimulation Cycle for Women Aged 35–42 Years: Live Birth Rate, Developmental Follow-up of Children, and Embryo Ranking. Reproductive Sciences. 2023;30(3):974-83. Available from: https://doi.org/10.1007/s43032-022-01073-z
29. Kato K, Ezoe K, Onogi S, Ito S, Egawa R, Aoyama N, et al. Comparison of 1-year cumulative live birth and perinatal outcomes following single blastocyst transfer with or without preimplantation genetic testing for aneuploidy: a propensity score-matched study. Journal of assisted reproduction and genetics. 2023;40(11):2669-80. Available from: https://doi.org/10.1007/s10815-023-02926-5
30. Lewis S, Amor DJ, Glynn A, Wilton L, Halliday J. Child health after preimplantation genetic testing. Reproductive BioMedicine Online. 2021;42(3):609-19. Available from: https://doi.org/10.1016/j.rbmo.2020.11.014
31. Li M, Kort J, Baker VL. Embryo biopsy and perinatal outcomes of singleton pregnancies: an analysis of 16,246 frozen embryo transfer cycles reported in the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System. American Journal of Obstetrics & Gynecology. 2021;224(5):500.e1-.e18. Available from: https://doi.org/10.1016/j.ajog.2020.10.043
32. Li S, Ma S, Zhao J, Hu J, Li H, Zhu Y, et al. Non-Assisted Hatching Trophectoderm Biopsy Does Not Increase The Risks of Most Adverse Maternal and Neonatal Outcome and May Be More Practical for Busy Clinics: Evidence From China. Front Endocrinol (Lausanne). 2022;13:819963. Available from: https://doi.org/10.3389/fendo.2022.819963
33. Li Y, Wen Q, Liao J, Ma S, Zhang S, Gu Y, et al. Trophectoderm Biopsy Differentially Influences the Level of Serum β-Human Chorionic Gonadotropin With Different Embryonic Trophectoderm Scores in Early Pregnancy From 7847 Single-Blastocyst Transfer Cycles. Frontiers in Endocrinology. 2022;13. Available from: https://doi.org/10.3389/fendo.2022.794720
34. Liu AH-C, Shah T, Wu H, Lieman HJ, Singh M, Pollack SE, et al. Trophectoderm biopsy is associated with lower risks of moderate to extreme prematurity and low birthweights: a national registry cohort study of singleton livebirths from frozen-thawed blastocyst transfers. American journal of obstetrics and gynecology. 2024. Available from: https://doi.org/10.1016/j.ajog.2024.07.007

35. Liu D, Chen C, Huang Q, Dong Y, Xu L, Dong M, et al. Preimplantation genetic testing for complex chromosomal rearrangements: clinical outcomes and potential risk factors. Frontiers in Genetics. 2024;15. Available from: https://doi.org/10.3389/fgene.2024.1401549
36. Lu M-m, Wen Y-x, Liu Y-l, Ding C-h, Zhou C-q, Xu Y-w. Trophectoderm biopsy reduces the level of serum β-human chorionic gonadotropin in early pregnancy. Fertility and Sterility. 2020;114(4):801-8. Available from: https://doi.org/10.1016/j.fertnstert.2020.05.015
37. Makhijani R, Bartels CB, Godiwala P, Bartolucci A, DiLuigi A, Nulsen J, et al. Impact of trophectoderm biopsy on obstetric and perinatal outcomes following frozen–thawed embryo transfer cycles. Human Reproduction. 2021;36(2):340-8. Available from: https://doi.org/10.1093/humrep/deaa316
38. Mastenbroek S, Twisk M, van Echten-Arends J, Sikkema-Raddatz B, Korevaar JC, Verhoeve HR, et al. In Vitro Fertilization with Preimplantation Genetic Screening. New England Journal of Medicine. 2007;357(1):9-17. Available from: https://doi.org/10.1056/NEJMoa067744
39. Middelburg KJ, Heineman MJ, Haadsma ML, Bos AF, Kok JH, Hadders-Algra M. Neurological Condition of Infants Born After In Vitro Fertilization With Preimplantation Genetic Screening. Pediatric Research. 2010;67(4):430-4. Available from: https://doi.org/10.1203/PDR.0b013e3181d2273e
40. Schendelaar P, Middelburg KJ, Bos AF, Heineman MJ, Kok JH, La Bastide-Van Gemert S, et al. The effect of preimplantation genetic screening on neurological, cognitive and behavioural development in 4-year-old children: follow-up of a RCT. Hum Reprod. 2013;28(6):1508-18. Available from: https://doi.org/10.1093/humrep/det073
41. Mejia RB, Capper EA, Summers KM, Mancuso AC, Sparks AE, Van Voorhis BJ. Cumulative live birth rate in women aged </=37 years after in vitro fertilization with or without preimplantation genetic testing for aneuploidy: a Society for Assisted Reproductive Technology Clinic Outcome Reporting System retrospective analysis. F S Rep. 2022;3(3):184-91. Available from: https://doi.org/10.1016/j.xfre.2022.05.004
42. Meyer LR, Klipstein S, Hazlett WD, Nasta T, Mangan P, Karande VC. A prospective randomized controlled trial of preimplantation genetic screening in the "good prognosis" patient. Fertility and sterility. 2009;91(5):1731-8. Available from: https://doi.org/10.1016/j.fertnstert.2008.02.162
43. Nekkebroeck J, Bonduelle M, Desmyttere S, Van den Broeck W, Ponjaert-Kristoffersen I. Mental and psychomotor development of 2-year-old children born after preimplantation genetic diagnosis/screening. Human Reproduction. 2008;23(7):1560-6. Available from: https://doi.org/10.1093/humrep/den033
44. Nekkebroeck J, Bonduelle M, Desmyttere S, Van den Broeck W, Ponjaert-Kristoffersen I. Socio-emotional and language development of 2-year-old children born after PGD/PGS, and parental well-being. Human Reproduction. 2008;23(8):1849-57. Available from: https://doi.org/10.1093/humrep/den179
45. Ricciarelli E, Bruna I, Verdú V, Torrelló MJ, Herrer R, Gris JM, et al. Impact of assisted reproduction treatments on Spanish newborns: report of 14,119 pregnancies. Journal of Assisted Reproduction and Genetics. 2013;30(7):897-905. Available from: https://doi.org/10.1007/s10815-013-0023-0
46. Richardson H, Kalliora C, Mainigi M, Coutifaris C, Sammel MD, Senapati S. Impact of mode of conception on early pregnancy human chorionic gonadotropin rise and birth weight. F&S reports. 2022;3(1):13-9. Available from: https://doi.org/10.1016/j.xfre.2021.12.006

47. Riestenberg CK, Mok T, Ong JR, Platt LD, Han CS, Quinn MM. Sonographic abnormalities in pregnancies conceived following IVF with and without preimplantation genetic testing for aneuploidy (PGT-A). Journal of Assisted Reproduction and Genetics. 2021;38(4):865-71. Available from: https://doi.org/10.1007/s10815-021-02069-5
48. Roeca C, Johnson R, Carlson N, Polotsky AJ. Preimplantation genetic testing and chances of a healthy live birth amongst recipients of fresh donor oocytes in the United States. Journal of Assisted Reproduction and Genetics. 2020;37(9):2283-92. Available from: https://doi.org/10.1007/s10815-020-01874-8
49. Sarkar P, New EP, Jindal S, Tanner JP, Imudia AN. The effect of trophectoderm biopsy for preimplantation genetic testing on fetal birth weight and preterm delivery. Minerva Obstet Gynecol. 2023. Available from: https://doi.org/10.23736/s2724-606x.22.05196-x
50. Shi X, Tang Y, Liu C, Li W, Lin H, Mao W, et al. Effects of NGS-based PGT-a for idiopathic recurrent pregnancy loss and implantation failure: a retrospective cohort study. Systems Biology in Reproductive Medicine. 2023;69(5):354-65. Available from: https://doi.org/10.1080/19396368.2023.2225679
51. Sites CK, Bachilova S, Gopal D, Cabral HJ, Coddington CC, Stern JE. Embryo biopsy and maternal and neonatal outcomes following cryopreserved-thawed single embryo transfer. American Journal of Obstetrics and Gynecology. 2021;225(3):285.e1-.e7. Available from: https://doi.org/10.1016/j.ajog.2021.04.235
52. Snelgrove JW, Lee R, Jeyakumar Y, Greenblatt EM, Kingdom JC, Zwingerman R, et al. Maternal Placental Growth Factor (PlGF) levels, sonographic placental parameters, and outcomes of IVF pregnancies with and without embryo trophectoderm biopsy. Journal of assisted reproduction and genetics. 2024;41(10):2721-6. Available from: https://doi.org/10.1007/s10815-024-03193-8
53. Srebnik N, Sverdlik Kislasi Y, Amosi-Victor D, Rotshenker-Olshinka K, Eldar-Geva T, Ben-Ami I, et al. PGT pregnancies have a similar risk for post-partum complications as naturally conceived pregnancies. Reproductive BioMedicine Online. 2023;46(1):189-95. Available from: https://doi.org/10.1016/j.rbmo.2022.09.009
54. Staessen C, Platteau P, Van Assche E, Michiels A, Tournaye H, Camus M, et al. Comparison of blastocyst transfer with or without preimplantation genetic diagnosis for aneuploidy screening in couples with advanced maternal age: a prospective randomized controlled trial. Hum Reprod. 2004;19(12):2849-58. Available from: https://doi.org/10.1093/humrep/deh536
55. Staessen C, Verpoest W, Donoso P, Haentjens P, Van der Elst J, Liebaers I, et al. Preimplantation genetic screening does not improve delivery rate in women under the age of 36 following single-embryo transfer. Human Reproduction. 2008;23(12):2818-25. Available from: https://doi.org/10.1093/humrep/den367
56. Sun N, Fang X, Jiao Y, Wang Y, Wan Y, Wu Z, et al. Adverse maternal and neonatal outcomes of preimplantation genetic testing with trophectoderm biopsy: a retrospective cohort study of 3373 intracytoplasmic sperm injection single frozen-thawed blastocyst transfer cycles. Arch Gynecol Obstet. 2024;309(6):2427-37. Available from: https://doi.org/10.1007/s00404-023-07120-7
57. Sunkara SK, Antonisamy B, Selliah HY, Kamath MS. Pre-term birth and low birth weight following preimplantation genetic diagnosis: analysis of 88 010 singleton live births following PGD and IVF cycles. Human Reproduction. 2017;32(2):432-8. Available from: https://doi.org/10.1093/humrep/dew317
58. Verpoest W, Van Landuyt L, Desmyttere S, Cremers A, Devroey P, Liebaers I. The incidence of monozygotic twinning following PGD is not increased. Human

Reproduction. 2009;24(11):2945-50. Available from: https://doi.org/10.1093/humrep/dep280
59. Winter C, Van Acker F, Bonduelle M, Desmyttere S, De Schrijver F, Nekkebroeck J. Cognitive and psychomotor development of 5- to 6-year-old singletons born after PGD: a prospective case–controlled matched study. Human Reproduction. 2014;29(9):1968-77. Available from: https://doi.org/10.1093/humrep/deu165
60. Winter C, Van Acker F, Bonduelle M, Desmyttere S, Nekkebroeck J. Psychosocial development of full term singletons, born after preimplantation genetic diagnosis (PGD) at preschool age and family functioning: a prospective case-controlled study and multi-informant approach. Human Reproduction. 2015;30(5):1122-36. Available from: https://doi.org/10.1093/humrep/dev036
61. Wu Y, Ying Y, Cao M, Liu J, Liu H. Trophectoderm biopsy of blastocysts for a preimplantation genetic test does not affect serum β-hCG levels in early pregnancy: a study using propensity score matching. Journal of Ovarian Research. 2021;14(1):78. Available from: https://doi.org/10.1186/s13048-021-00824-x
62. Zhang WY, von Versen-Höynck F, Kapphahn KI, Fleischmann RR, Zhao Q, Baker VL. Maternal and neonatal outcomes associated with trophectoderm biopsy. Fertility and Sterility. 2019;112(2):283-90.e2. Available from: https://doi.org/10.1016/j.fertnstert.2019.03.033
63. Zheng W, Yang SH, Yang C, Ren BN, Sun SM, Liu YL, et al. Perinatal outcomes of singleton live births after preimplantation genetic testing during single frozen-thawed blastocyst transfer cycles: a propensity score-matched study. Fertility and sterility. 2022;117(3):562-70. Available from: https://doi.org/10.1016/j.fertnstert.2021.12.020
64. Zheng W, Ren B, Mu M, Liu Y, Liu X, Yang C, et al. Perinatal Outcomes of Singleton Live Births Following Preimplantation Genetic Testing for Chromosomal Structural Rearrangements in Single Frozen-Thawed Blastocyst Transfer Cycles: a Retrospective Cohort Study. Reprod Sci. 2022;29(10):3039-46. Available from: https://doi.org/10.1007/s43032-021-00732-x