Caesarean Section in Pregnancies Conceived by Assisted Reproductive Technology: A Systematic Review and Meta-analysis

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Research article

Keywords: elective caesarean section, emergent caesarean section, frozen embryo transfer, fresh embryo transfer, in-vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), maternal outcomes.

Posted Date: December 21st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-131014/v1

Version of Record: A version of this preprint was published on March 22nd, 2021. See the published version at https://doi.org/10.1186/s12884-021-03711-x.

Abstract

Background: Caesarean section rates are higher among pregnancies conceived by assisted reproductive technology (ART) compared to spontaneous conceptions (SC), implying an increase in neonatal and maternal morbidity. We aimed to compare caesarean section rates in ART pregnancies versus SC, overall, by indication (elective versus emergent), and by type of ART treatment (in-vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), fresh embryo transfer, frozen embryo transfer) in a systematic review and meta-analysis.

Methods: We searched Medline, EMBASE and CINAHL databases using the OVID Platform from 1993-2019, and the search was completed in January 2020. The eligibility criteria were cohort studies with singleton conceptions after in-vitro fertilization and/or intracytoplasmic sperm injection using autologous oocytes versus spontaneous conceptions. The study quality was assessed using the Newcastle Ottawa Scale. Meta-analyses were performed using odds ratios (OR) with a 95% confidence interval (CI) using random effect models in RevMan 5.3, and I-squared (I^2) test > 75% was considered as high heterogeneity.

Results: 1750 studies were identified from the search of which 34 met the inclusion criteria. Compared to spontaneous conceptions, IVF/ICSI pregnancies were associated with a 1.93-fold increase of odds of caesarean section (95% CI 1.78, 2.09). When stratified by indication, IVF/ICSI pregnancies were associated with a 2.12-fold increase of odds of elective caesarean section (95% CI 1.63, 2.77) and 1.57-fold increase of odds of emergent caesarean section (95% CI 1.27, 1.95).

Conclusions: The odds of delivering by caesarean section are greater for ART singleton pregnancies compared to spontaneous conceptions. Preconception and pregnancy care plans should focus on minimizing the risks that may lead to emergency caesarean sections and finding strategies to understand and decrease the rate of elective caesarean sections.

Background

Infertility, defined as the inability to conceive after 12 or more months of regular unprotected intercourse, affects 12–15% of couples. [1, 2] Between 1% and 5% of children in industrialized countries are born following assisted reproductive technologies (ART). [3] ART has been associated with higher caesarean section rates compared to women who conceive spontaneously. [4]

The overall rate of caesarean sections continues to increase at a rapid rate. The ideal caesarean section rate is 10–15% according to the World Health Organization (WHO), [5] which states that population level rates higher than 10% are not associated with reductions in maternal and neonatal mortality. [5] Globally, the rate of caesarean section has increased from 12.1% in 2000 to 21.1% in 2015. [6]

Previous studies have compared caesarean sections between fresh and frozen embryo transfer in ART pregnancies, [7] in oocyte donation pregnancies, [8] and in multiple pregnancies conceived by IVF. [9, 10] Two systematic reviews and meta-analyses published in 2004 estimated an increased risk of caesarean delivery among the IVF/ICSI population, [11, 12] followed by a third meta-analysis published in 2012 which confirmed those findings. [4] However, the identification of associated treatment factors has not been addressed in previous meta-analyses. This can help to establish care plans for women undergoing ART to

improve pregnancy deliveries and to reduce possible harm in unnecessary caesarean sections in these pregnancies.

The objective of the present study is to conduct a systematic review and meta-analysis to assess the risk of caesarean section in IVF/ICSI singleton pregnancies compared to spontaneous conceptions, overall and by indication (elective versus emergent), and by type of ART treatment (IVF, ICSI, fresh embryo transfer, and frozen embryo transfer).

Methods

Search Strategy and Information Sources

We conducted a literature search from 1993 to 2019 on MEDLINE, EMBASE and the cumulative index to nursing and allied health literature (CINAHL) database using the OVID Platform. The search was completed in January 2020. MeSH terms and the indexing of terms were used. The keywords used in database searches were; in vitro fertilization/or intracytoplasmic sperm injection/, fertilization in vitro, in vitro fertilization*.mp., reproductive techniques assisted, caesarean section/ or repeat caesarean section/, caesarean section*mp., caesarean section*.mp., caesarean section*.mp., c-section*.mp., caesarean delivery, caesarean section, elective. Keywords with the notation "*mp" indicate the plural form of that term was searched, and the term was also searched as a keyword (See supplementary materials, Additional file 1). Additionally, search criteria included studies after 1990 limited to only English and French literature and grey literature. References of past systematic reviews were also searched for relevant articles to include in the review. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) Statement [13] was followed in preparation of this manuscript. PROSPERO register (CRD42020165075).

Study Selection and Eligibility Criteria

Two team members independently performed the title and abstract screening and conducted full text screening (NL, FTSE). Conflicts were resolved by consensus or by a third team member (MPV). Criteria to identify eligible publications for the current review were established using the PICOS (Population-Intervention- Comparators-Outcomes-Study design) framework. The inclusion criteria were singleton pregnancies conceived using ART (IVF and/or ICSI) with autologous oocytes compared to spontaneously conceived singleton pregnancies. The exclusion criteria were pregnancies conceived using intrauterine insemination (IUI), exclusive ovulation induction, or IVF/ICSI using donor gametes (oocyte, embryo or sperm), gestational surrogacy and twins or higher order multiples pregnancies.

Exposure and Outcome Measures

The main exposure was IVF and/or ICSI combined. Additional analyses were conducted by type of fertilization (IVF or ICSI), and type of embryo transfer (fresh or frozen). The outcomes of interest were caesarean section, overall and by indication (e.g. elective and emergent caesarean section). We used the Lucas et al. classification of urgency of caesarean section, [14] grouped as emergent (grade I: emergent and grade II: urgent) and elective (grade III: scheduled and grade IV: elective). Most literature classifies caesarean section as elective or emergent, where an elective caesarean section is one performed for nonclinical reasons and an emergent caesarean section is one performed due to an immediate threat to the life of the woman or fetus. [14]

Assessment of Heterogeneity

The similarity between the included studies (mainly regarding study design and clinical characteristics) was assessed to ensure pooling was appropriate. The I^2 statistic was used to analyze heterogeneity. High heterogeneity is indicated by a percentage greater than 75%.

Risk of Bias and Quality Assessment

Risk of bias and quality assessment of included studies was performed independently by two authors (NL, FTSE). Conflicts were resolved by consensus or by a third team member (MPV). Study quality was assessed by two reviewers using the Newcastle-Ottawa Scale (NL, FTSE). This system involves eight scored items, each included study was evaluated in these categories and received a total score ranging from 0 to 9 points. A score of 8 or 9 indicates a high-quality study and a score of 6 to 7 indicates a moderate quality study. [15] Publication bias was assessed by Funnel Plot graphics using RevMan 5.3 software if the pooled analysis included more than 10 studies (Additional file 2). [16]

Statistical Analysis

Data extracted from included studies was composed into 2 × 2 tables to conduct a meta-analysis using RevMan 5.3 software. Studies with similar outcomes were pooled together and the tables were used to calculate crude odds ratio. For the outcome of caesarean section, measures of association were reported as odds ratios with a 95% confidence interval. Data was analyzed using the random effect model which assumes heterogeneity and the significance of the pool odds ratio was analyzed using the Mantel-Haenszel statistical method. When conducting the meta-analysis, the number of individuals undergoing caesarean section for five studies [17–21] needed to be estimated based on percentages provided as no explicit number was stated in the study.

This systematic review and meta-analysis did not involve consumer and community participation. The study was approved by the Queen’s University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board on October 29, 2019 (Reference number OBGY-357-19). Additionally, informed consent was not applicable in this study as there were no human participants involved.

Results

Search Results

There were a total of 1750 studies resulting from the search of MEDLINE, EMBASE and CINAHL databases. An additional 12 studies were identified through manual examination of the references from the initial search. Figure 1 displays the process of screening and selecting the studies for the review and meta-analysis. During full text screening, three studies were identified as having used the same cohort study and as such the most recent study was included [22] and the other two studies removed. [23, 24] A total of 34 studies were included in the review and meta-analysis, of which 18 were matched cohort studies [17, 19, 22, 25–39] and 16 unmatched cohort studies. [18, 20, 21, 40–52] Excluded manuscripts are listed in Additional file 3.

Study Characteristics

The characteristics of each study selected for this review are presented in Table 1. Studies were conducted in Europe (n = 23), Canada (n = 3), The United States (n = 2) and Asia (n = 6). Twenty-nine studies were retrospective cohort studies, [17, 19, 20, 22, 25–27, 29–43, 46–52] while five were prospective cohort studies. [18, 21, 28, 44, 45] Twenty-two of the selected studies were hospital based cohort studies, [18–21, 25–28, 31–34, 36–41, 44, 46, 51, 52] while twelve of the selected studies were population based cohort studies. [17, 22, 29, 30, 35, 42, 43, 45, 47–50] Fourteen studies provided data on exclusively IVF procedures, [17, 19–21, 27–29, 32, 35, 39, 43, 44, 46, 47] and six studies on ICSI procedures. [17, 18, 27, 35, 44, 47] Five studies reported data on fresh embryo transfer and frozen embryo transfer. [22, 25, 35, 40, 50] Additionally, ten studies reported on the type of caesarean section performed, either elective or emergent. [19, 29, 34, 36, 37, 39, 41, 47, 48, 51]

1. IVF/ICSI versus spontaneous conception. Thirty-four studies met the inclusion criteria, [17–22, 25–52] resulting in 164,603 pregnancies following IVF/ICSI compared to 5,702,123 spontaneous conceptions. The pooled OR was 1.93 (95% CI 1.78, 2.09) with high heterogeneity between the studies I^2 = 96% (Fig. 2). Eighteen studies were matched cohorts, [17, 19, 22, 25–39] and sixteen unmatched cohorts. [18, 20, 21, 40–52] The quality of studies according to the NOS was moderate to high with NOS scores ranging from 4–9, of which 25 studies had scores of 8 or 9 (Table 1). Publication bias was low as demonstrated by a funnel plot with symmetric distribution (Additional file 2, Fig. 1).

Elective caesarean section. Ten studies met the inclusion criteria and reported data on elective caesarean sections (n = 27,799 pregnancies following IVF/ICSI compared to 2,193,608 spontaneous conceptions). [19, 29, 34, 36, 37, 39, 41, 47, 48, 51] The pooled OR was 2.12 (95% CI 1.63, 2.77) with high heterogeneity between the studies I^2 = 96% (Fig. 3). Six studies were matched cohorts, [19, 29, 34, 36, 37, 39] and four unmatched cohorts. [41, 47, 48, 51] The quality of studies was moderate to high with NOS scores ranging from 7–9 (Table 1).

Emergent Caesarean Section. Eight studies also met the inclusion criteria and reported data on emergent caesarean sections (n = 19,862 pregnancies following IVF/ICSI compared to 1,955,866 spontaneous conceptions). [19, 29, 34, 36, 37, 39, 48, 51] The pooled OR was 1.57 (95% CI 1.27, 1.95) with high heterogeneity between the studies I^2 = 87% (Fig. 3). Six studies were matched cohorts, [19, 29, 34, 36, 37, 39] and two unmatched cohorts. [48, 51] The quality of studies was high with NOS scores ranging from 8–9 (Table 1).

2. In vitro fertilization (IVF) versus spontaneous conception. Fourteen studies met the inclusion criteria (n = 71,685 IVF pregnancies vs. 3,419,104 spontaneous conceptions). [17, 19–21, 27–29, 32, 35, 39, 43, 44, 46, 47] The pooled OR was 2.07 (95% CI 1.87, 2.30) with high heterogeneity between the studies I^2 = 94% (Fig. 4). Eight studies were matched cohorts, [17, 19, 27–29, 32, 35, 39] and six unmatched cohorts. [20, 21, 43, 44, 46, 47] The quality of studies according to the NOS was moderate to high with NOS scores ranging from 6–9 (Table 1).

3. Intracytoplasmic sperm injection (ICSI) versus spontaneous conception. Six studies met the inclusion criteria (n = 15,926 ICSI pregnancies vs. 277,187 spontaneous conceptions). [17, 18, 27, 35, 44, 47] The pooled OR was 1.66 (95% CI 1.29, 2.15) with high heterogeneity between the studies I^2 = 97% (Fig. 4). Three studies were matched cohorts, [17, 27, 35] and three unmatched cohorts. [18, 44, 47] The quality of studies according to the NOS was moderate to high with NOS scores ranging from 6–9 (Table 1).

4. Fresh embryo transfer versus spontaneous conception. Five studies met the inclusion criteria (n = 60,767 following fresh embryo transfer compared to 878,654 spontaneous conceptions). [22, 25, 35, 40, 50] The pooled OR was 1.55 (95% CI 1.42, 1.69) with high heterogeneity between the studies I^2 = 85% (Fig. 5). Three studies were matched cohorts, [22, 25, 35] and two unmatched cohorts. [40, 50] The quality of studies was moderate to high with NOS scores ranging from 7–9 (Table 1).

5. Frozen embryo transfer versus spontaneous conception. Five studies met the inclusion criteria (n = 9,597 pregnancies following frozen embryo transfer compared to 878,654 spontaneous conceptions). [22, 25, 35, 40, 50] The pooled OR was 1.68 (95% CI 1.41, 2.00) with high heterogeneity between the studies I^2 = 86% (Fig. 5). Three studies were matched cohorts, [22, 25, 35] and two unmatched cohorts. [40, 50] The quality of studies was moderate to high with NOS scores ranging from 7–9 (Table 1).

Conclusions

Main Findings

Our study indicates that IVF/ICSI pregnancies are associated with higher odds of caesarean section compared to spontaneous conceptions. The odds were also greater for elective caesarean sections compared to spontaneous conceptions than for emergent caesarean sections. This trend was also apparent, in IVF or ICSI, and fresh or frozen embryo transfer, compared to spontaneous conception. Our study presents updated rates of caesarean section between ART and spontaneous pregnancies, with 16 studies conducted after 2012. In addition, we considered type of treatment (IVF, ICSI, fresh, and frozen embryo transfer) as independent factors. A strength of the study is the type of included studies. While the quality scores ranged from low to high with scores from 4–9, 25 studies (75%) were considered high quality studies. Furthermore, majority of the included studies, with the exception of two studies, considered potential confounders in the analysis. Limitations include variations in the definitions of outcomes and different inclusion and exclusion criteria between studies, and the significantly high heterogeneity between pooled studies.

Comparison with Existing Literature

These results are consistent with the findings of three past systematic reviews and meta-analyses which examined obstetric and perinatal outcomes among the IVF/ICSI population compared to spontaneous conceptions. [4, 11, 12] Pandey et al. (2012) reported that the relative risk of having a caesarean section was 1.56 (95% CI 1.51–1.60) in IVF/ICSI conceptions compared to spontaneous conceptions. [4] They also reported a statistically increased risk of caesarean section in singleton frozen embryo transfer pregnancies compared with singletons from spontaneous conception with a relative risk ratio of 1.76 (95% CI 1.65–1.87). [4] However, they did not evaluate and present findings on the caesarean section rates based on fertilization mode (IVF or ICSI), or other fresh embryo transfer. Helmerhorst et al. (2004) reported that rates of caesarean section were significantly higher after ART compared to spontaneous conception, with a relative risk ratio of 1.54 (95% CI 1.44–1.66) in singleton matched births. [12] The findings of these two systematic reviews support the results in this study which exhibited that there is an increased risk for caesarean section in singleton IVF/ICSI populations and frozen embryo transfer populations compared to spontaneous conception groups. Additionally, our results are similar to a meta-analysis conducted by Jackson et al. (2004) reporting a 2.13-fold increased risk of caesarean delivery among the IVF/ICSI population (OR = 2.13, 95% CI 1.72, 2.63). [11] They also reported a 1.92-fold increased risk of elective caesarean section (OR = 1.92, 95% CI 1.49, 2.48) and a 1.47-fold increased risk of emergent caesarean section (OR = 1.47, 95% CI 1.09, 1.98) among the IVF/ICSI population compared to the spontaneous conception group. [11] However, Helmerhorst et al. (2004) and Jackson et al. (2004) did not analyze and present findings on the caesarean section rates based on fertilization mode (IVF or ICSI), or by fresh or frozen embryo transfer.

Interpretation

Pregnancies following ART have a higher risk of adverse maternal and neonatal outcomes, which can explain the higher rate of emergent caesarean sections compared to spontaneous conceptions. [53, 54] However, provider or patient factors associated with a higher rate of elective caesarean section in ART pregnancies need to be further investigated.

Conclusions and Implications

The probability of singleton pregnancies ending in delivery by caesarean section is higher in women who conceive using ART compared to spontaneous conceptions. Preconception and pregnancy care plans should focus on minimizing the risks that may lead to emergency caesarean sections and finding strategies to understand and decrease the rate of elective caesarean sections.

Abbreviations

ART (Assisted reproductive Technologies), IVF (In vitro fertilization), ICSI (Intracytoplasmic sperm injections), CINAHL (Cumulative index to nursing and allied health literature), PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses), PICOS (Population-Intervention-Comparators-Outcomes-Study design), IUI (Intrauterine insemination), NOS (Newcastle Ottawa Scale), and OR (Odds ratio).

Declarations

Ethics approval and consent to participate

This systematic review and meta-analysis did not involve consumer and community participation. The study was approved by the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board on October 29, 2019 (Reference number OBGY-357-19).

Consent for publication

Not applicable.

Availability of data and materials

The datasets supporting the conclusions of this article are included within the article and its additional files.

Competing interests

The authors report no competing interests.

Funding

This study was supported by the Canadian Institutes of Health Research (CIHR) Institute of Human Development, child and Youth Health (IHDCYH), Clinician Investigators Program, Grant number MFM – 146444. The opinions, results and conclusions reported in this article are those of the authors and are independent from the funding sources.

Author Contributions

Study concept and design: MPV. Acquisition of data: NL, FTSE and MPV. Analysis and interpretation of data: NL, FTSE, JP, LG, and MPV. Drafting of the manuscript: NL, FTSE and MPV. Critical revision of the manuscript for important intellectual content: NL, FTSE, JP, LG, MW, GS, MPV. Obtaining funding: LG, MPV. Study supervision: FTSE and MPV. All authors have read and approved the manuscript

Acknowledgements

Not applicable.

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Tables

Table 1. Characteristics of Included Studies

Study ID and Location	Study Design	Number of Participants, n	Exposure	NOS Score
Anzola et al. (2019) [25] France	Retrospective hospital-based	Fresh=5883 Frozen=366 SC=6981	IVF and IVF+ICSI, Fresh Embryo Transfer (ET) or Frozen Embryo Transfer (ET)	8
Apantaku et al. (2008) [26] England	Retrospective hospital-based	ART=88 SC=88	IFV/ICSI	8
Beyer et al. (2016) [40] Germany	Retrospective hospital-based	ART=467 SC=6417	ART (Fresh ET, Slow-rate Freezing, Vitrification)	7
Buckett et al. (2007) [27] Canada	Retrospective hospital-based	IVF=133 ICSI=104 SC=338	Fresh (ET) after IVF Fresh (ET) after ICSI	9
Carbillon et al. (2017) [41] France	Retrospective hospital-based	IVF/ICSI=119 SC=7993	IFV/ICSI (Excluded oocyte donation, previous diabetes)	7
Dayan et al. (2018) [42] Canada	Retrospective population-based	IVF=1596 SC=112813	IVF including (ICSI both fresh and frozen embryo transfer)	9
D'Souza et al. (1997) [28] England	Prospective hospital-based	IVF=150 SC=150	Frozen ET after IVF	9
Ensing et al. (2015) [29] Netherlands	Retrospective population- based	MAR=16177 SC=1905011	MAR (including IVF as a subgroup)	9
Ernstad et al. (2016) [43] Sweden	Retrospective population-based	Fresh ET=22771 Frozen ET=7795 SC=1196394	Fresh ET after IVF Frozen ET after IVF (excluded oocyte donation)	7
Farhi et al. (2013) [44] Israel	Prospective hospital-based	IVF=202 ICSI=307 SC=587	ART (IVF and ICSI)	6

Fedder et al. (2013) [17] Denmark	Retrospective population-based	ICSI= 6156 IVF=11060 SC=33852	IVF and ICSI	9
Gambadauro et al. (2017) [45] Sweden	Longitudinal Observational Study/Prospective population-based	IVF=167 SC=3116	IVF with or without ICSI	7
Gillet et al. (2011) [30] Belgium	Retrospective population-based	IVF/ICSI=1866 SC=15228	IFV/ICSI	9
Harlev et al. (2018) [46] Israel	Retrospective hospital-based	IVF=229 SC=7929	IVF and Ovulation induction (OI)	9
Katalinic et al. (2004) [18] Germany	Prospective hospital-based	ICSI=2055 SC=7861	Fresh embryo transfer (ET) after ICSI	7
Koudstaal et al. (2000) [19] Netherlands	Retrospective hospital-based	IVF=307 SC=307	Fresh ET after IVF (excluded frozen and embryo reduction)	9
Liu et al. (2015) [31] China	Retrospective hospital-based	IVF=380 SC=405	IVF/ICSI	4
Malchau et al. (2014) [47] Denmark	Retrospective population-based	IVF=4135 ICSI=3635 SC=229749	IUI IVF and ICSI	9
Ochsenkuhn et al. (2003) [32] Germany	Retrospective hospital-based	IVF=163 SC=322	IVF GIFT	9
Olivennes et al. (1993) [20] France	Retrospective hospital-based	IVF=162 SC=5096	IVF	7

Olson et al. (2005) [33] United States	Retrospective hospital-based	IVF/ICSI=645 SC=4590	IVF/ICSI	8
Perri et al. (2001) [34] Israel	Retrospective hospital-based	ART=95 SC=190	IFV/ICSI Transferring both IVF- and ICSI-derived embryos	9
Pinborg et al. (2010) [35] Denmark	Retrospective population-based	Frozen=957 Fresh =10329	Frozen ET after IVF/ICSI Fresh ET after IVF/ICSI	8
Poikkeus et al. (2007) [36] Finland	Retrospective hospital-based	IVF/ICSI=499 (SET=269; DET=230) SC=15037	IFV/ICSI (Single ET or Double ET)	8
Rahu et al. (2019) [48] Estonia	Retrospective population-based	IVF/ICSI=1778 SC=33555	IVF/ICSI, autologous	9
Romundstad et al. (2008) [49] Norway	Retrospective population-based	ART=8229 SC=1200922	IFV/ICSI	9
Sazonova et al. (2012) [50] Sweden	Retrospective population-based	Frozen=2348 Fresh=8944 SC=571914	Frozen ET after IVF/ICSI Fresh ET after IVF/ICSI (excluded oocytes donation)	9
Shevell et al. (2005) [21] United States	Prospective hospital-based	ART=554 SC=34286	IVF ICSI GFIT/ZIFT	8
Stojnic et al. (2013) [37] Serbia	Retrospective hospital-based	IVF=351 ICSI=283 SC=634	IVF/ICSI (excluded oocyte donation, frozen and vanishing twins)	9
Sun et al. (2014) [38]	Retrospective hospital-based	ART=1327 SC=5222	IFV/ICSI	9

Canada				
Suzuki et al. (2007) [51] Japan	Retrospective hospital-based	IVF-ET=89 (including 24 ICSI-ET) SC=849	IVF/ICSI	8
Tomic et al. (2011) [39] Croatia	Retrospective hospital-based	IVF=283 SC=283	IVF in advanced age (excluded oocyte donation, cryopreservation, vanishing twins)	9
Toshimitsu et al. (2014) [52] Tokyo	Retrospective hospital-based	IVF/ICSI=116 SC=662	IVF/ICSI, autologous	7
Wennerholm et al. (2013) [22] Denmark, Norway and Sweden	Retrospective population-based	Frozen ET=6647 Fresh ET=42242 SC=288542	Frozen ET after IVF/ICSI	9

Legend: ET (Embryo Transfer), IVF (In vitro fertilization), ICSI (Intracytoplasmic sperm injections), ART (Assisted reproductive Technologies), IUI (Intrauterine insemination), GFIT (Gamete intrafallopian transfer), NOS (Newcastle Ottawa Scale), SET(Single Embryo Transfer), DET (Doble Embryo Transfer).

Figures

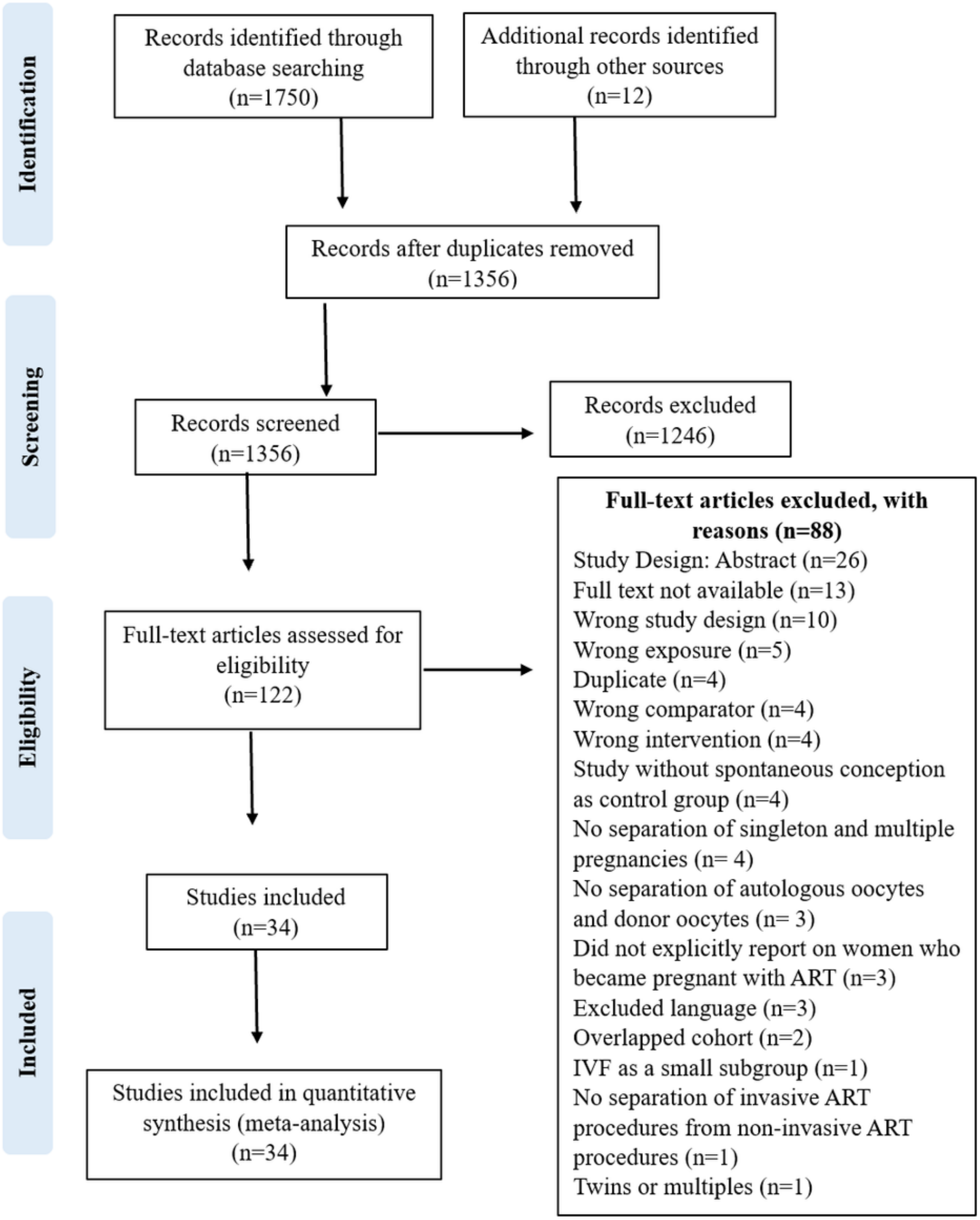

Figure 1

PRISMA Flowchart Flowchart showing identification and selection of studies included in the systematic review and meta-analysis.

Study or Subgroup	IVF/ICSI Events	IVF/ICSI Total	SC Events	SC Total	Weight	Odds Ratio M-H, Random, 95% CI
Anzola 2019	600	2327	1652	6981	3.8%	1.12 [1.01, 1.25]
Rahu 2019	620	1778	7715	33555	3.8%	1.79 [1.62, 1.98]
Dayan 2018	651	1596	29220	112813	3.8%	1.97 [1.78, 2.18]
Harlev 2018	162	229	2116	7929	2.7%	6.64 [4.98, 8.87]
Carbillon 2017	34	167	1745	7993	2.1%	0.92 [0.63, 1.34]
Gambadauro 2017	34	167	332	3116	2.1%	2.14 [1.45, 3.18]
Beyer 2016	206	467	2798	6417	3.3%	1.02 [0.84, 1.23]
Ernstad 2016	7907	30566	195486	1196394	4.0%	1.79 [1.74, 1.83]
Ensing 2015	3938	16177	248156	1905011	4.0%	2.15 [2.07, 2.23]
Liu 2015	317	380	182	405	2.4%	6.17 [4.42, 8.61]
Malchau 2014	2073	7770	45799	229749	4.0%	1.46 [1.39, 1.54]
Sun 2014	566	1327	1786	5222	3.7%	1.43 [1.27, 1.62]
Toshimitsu 2014	29	116	76	662	1.6%	2.57 [1.58, 4.17]
Farhi 2013	133	509	125	587	2.7%	1.31 [0.99, 1.73]
Stojnic 2013	512	634	199	634	2.9%	9.17 [7.08, 11.89]
Wennerholm 2013	11284	48889	44446	288542	4.0%	1.65 [1.61, 1.69]
Fedder 2012	4539	17216	5924	33852	4.0%	1.69 [1.62, 1.76]
Sazonova 2012	1861	7580	92676	571914	4.0%	1.68 [1.60, 1.77]
Gillet 2011	473	1866	3472	15228	3.8%	1.15 [1.03, 1.28]
Tomic 2011	113	283	71	283	2.2%	1.98 [1.39, 2.84]
Pinborg 2010	3021	11286	801	4800	3.9%	1.82 [1.67, 1.99]
Apantaku 2008	18	88	11	88	0.8%	1.80 [0.80, 4.07]
Romundstad 2008	1983	8229	150691	1200922	4.0%	2.21 [2.10, 2.33]
Buckett 2007	85	237	88	338	2.2%	1.59 [1.11, 2.28]
Poikkeus 2007	131	499	2601	15037	3.2%	1.70 [1.39, 2.09]
Suzuki 2007	29	89	216	849	1.7%	1.42 [0.89, 2.26]
Olson 2005	198	645	1086	4590	3.4%	1.43 [1.19, 1.71]
Shevell 2005	262	554	8092	34286	3.4%	2.90 [2.45, 3.44]
Katalinic 2004	688	2055	1093	7861	3.8%	3.12 [2.79, 3.48]
Ochsenkuhn 2003	50	163	73	322	1.9%	1.51 [0.99, 2.30]
Perri 2001	40	95	39	190	1.4%	2.82 [1.64, 4.82]
Koudstaal 2000	51	307	40	307	1.8%	1.33 [0.85, 2.08]
D'Souza 1997	40	150	14	150	1.1%	3.53 [1.83, 6.82]
Olivennes 1993	47	162	749	5096	2.3%	2.37 [1.67, 3.36]
Total (95% CI)		**164603**		**5702123**	**100.0%**	**1.93 [1.78, 2.09]**
Total events	42695		849570			

Heterogeneity: Tau² = 0.04; Chi² = 917.70, df = 33 (P < 0.00001); I² = 96%
Test for overall effect: Z = 16.04 (P < 0.00001)

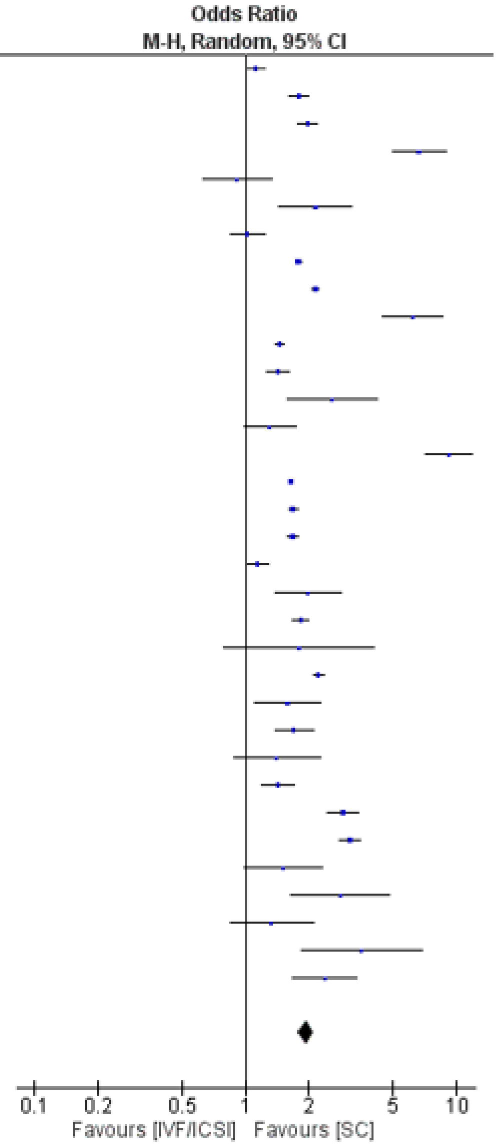

Figure 2

Caesarean Section Meta-analysis Forest plot displaying the results of a meta-analysis comparing caesarean sections after in vitro fertilization (IVF) / intracytoplasmic sperm injection (ICSI) versus spontaneous conception.

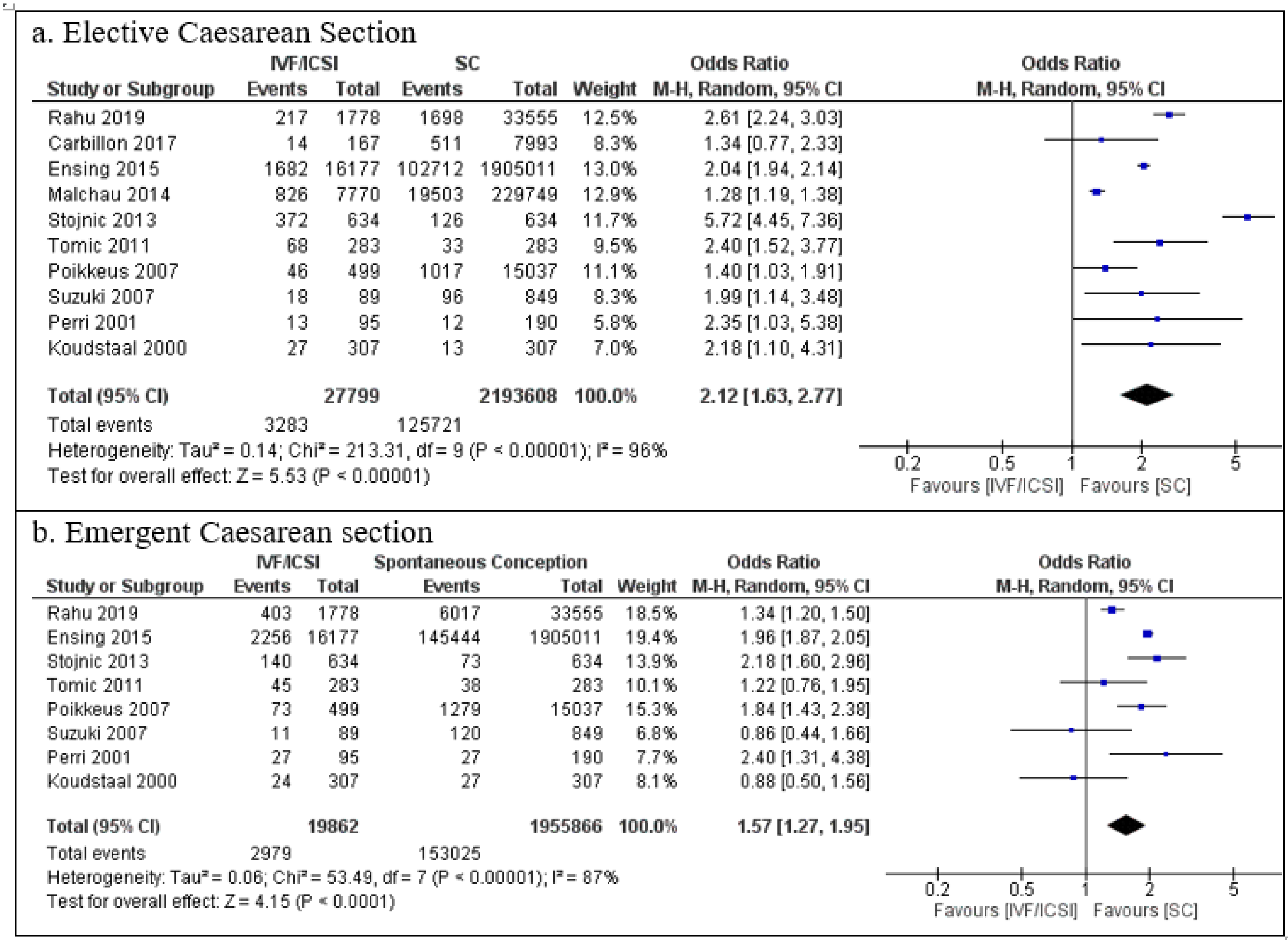

Figure 3

Elective Caesarean Section and Emergent Caesarean Section Meta-analyses Forest plots displaying the results of meta-analyses comparing elective caesarean sections after in vitro fertilization (IVF) / intracytoplasmic sperm injection (ICSI) treatment versus spontaneous conception and comparing emergent caesarean sections after in vitro fertilization (IVF) / intracytoplasmic sperm injection (ICSI) treatment versus spontaneous conception.

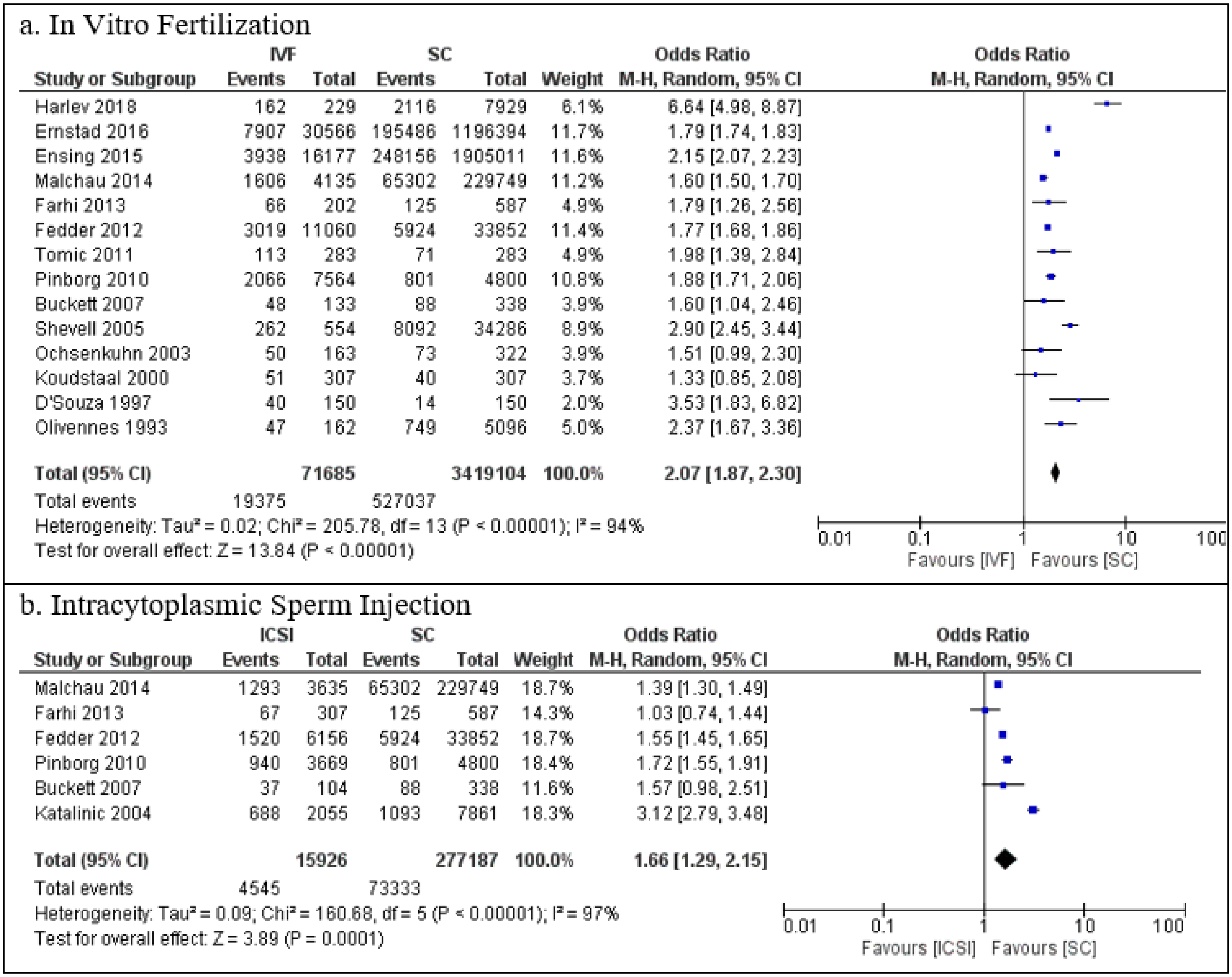

Figure 4

Fertilization Mode (a. IVF, b. ICSI) Meta-analysis Forest plot displaying the meta-analyses comparing caesarean sections after exclusively in vitro fertilization procedures versus spontaneous conception and comparing exclusively intracytoplasmic sperm injection procedures versus spontaneous conception.

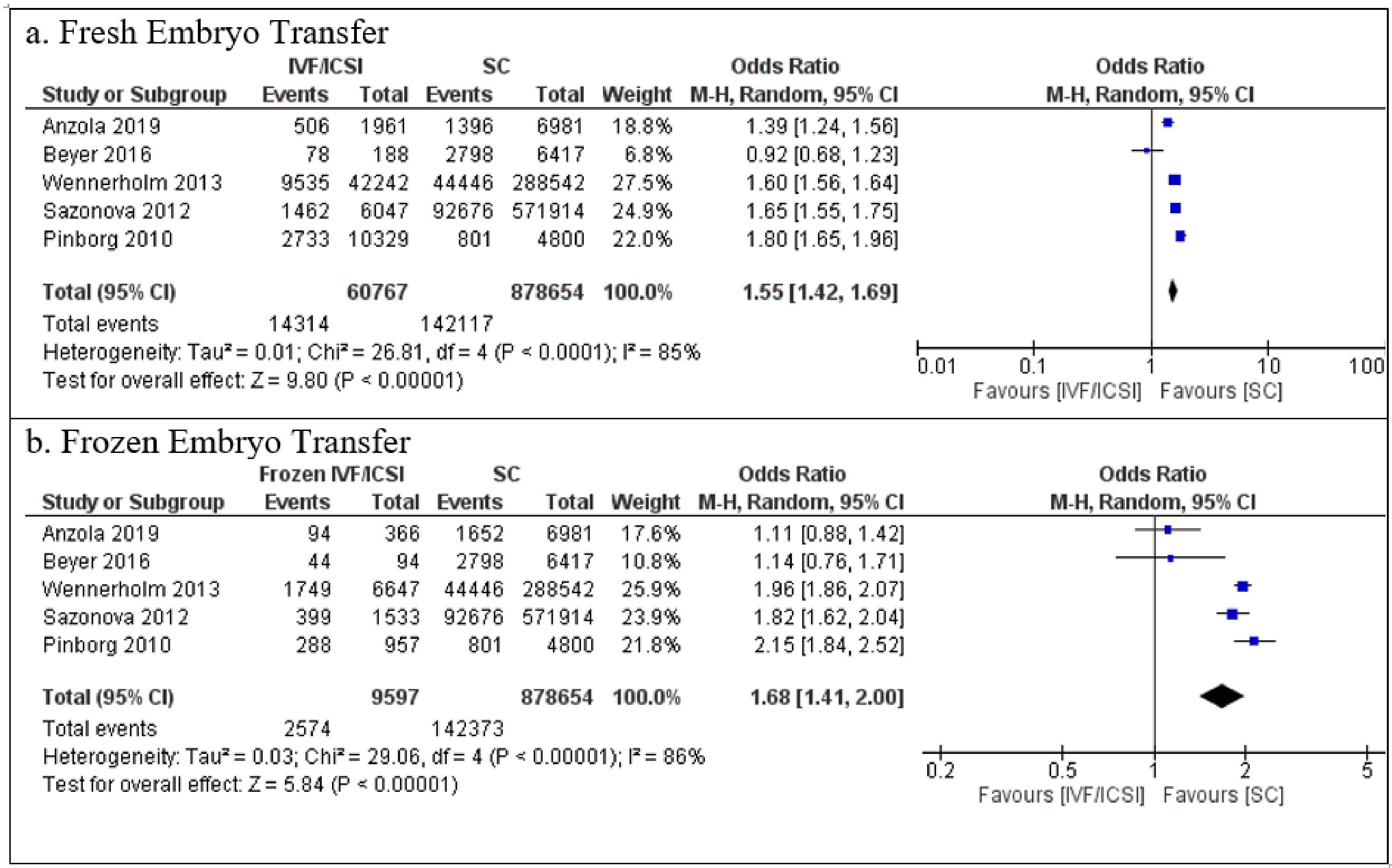

Figure 5

Fresh and Frozen in vitro fertilization (IVF) / intracytoplasmic sperm injection (ICSI) Meta-analysis Forest plot displaying the meta-analyses comparing caesarean sections after frozen in vitro fertilization (IVF) / intracytoplasmic sperm injection (ICSI) treatment versus spontaneous conception and comparing fresh in vitro fertilization (IVF) / intracytoplasmic sperm injection (ICSI) treatment versus spontaneous conception.

Supplementary Files

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