

Neonatal Outcomes by Mode of Conception in a NICU Population: An Interim Analysis of a Two-Centre Cohort Study

CHAITANYA DARSHAN BHATTARAI

dr.chaitanyadarshan@gmail.com

Baidya and Banskota Hospital

Arun Bajgain

Tree Top Hospital

Sangita Shakya

Baidya and Banskota Hospital

Prerana Kansakar

Patan Academy of Health Sciences

Akriti Bharati

Vatsalya Natural IVF & Fertility Center, Nepal

Bikash Shrestha

Nepalese Army Institute of Health Services

Research Article

Keywords: Assisted reproductive techniques, in vitro fertilization, infant, newborn, intensive care units, neonatal, infant, premature, infant, low birth weight

Posted Date: September 29th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10929551/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background: IVF-conceived singletons are internationally reported to carry a higher risk of preterm birth and low birth weight than spontaneously conceived singletons, but comparable data from Nepal and South Asia are limited

Methods: Retrospective observational cohort study of 559 neonates admitted to the NICU at two centres (2020–2025), compared by mode of conception (spontaneous, IUI, IVF). Composite adverse neonatal outcome analyzed by multivariable logistic regression adjusting for maternal age, comorbidity, and mode of delivery.

Results: Of 556 neonates with documented conception mode, 292 (52.5%) were spontaneously conceived, 6 (1.1%) via IUI, and 258 (46.4%) via IVF. IVF-conceived neonates had higher rates of preterm birth (57.8% vs 35.6%), low birth weight (58.1% vs 30.1%), and composite adverse outcome (73.6% vs 42.8%) than spontaneously conceived neonates (all $p < 0.001$). IVF remained independently associated with the composite adverse outcome after adjustment (adjusted OR 3.58, 95% CI 2.46–5.21, $p < 0.001$).

Conclusion: *IVF-conceived neonates had significantly higher rates of preterm birth, low birth weight, and composite adverse outcome than spontaneously conceived neonates, with IVF remaining an independent risk factor after adjustment (adjusted OR 3.58); findings are hypothesis-generating completion of the full multicentre cohort.*

Introduction

Preterm birth remains the leading cause of death in children under five worldwide. An estimated 13.4 million babies were born preterm in 2020, and preterm birth rates have shown no measurable improvement globally over the past decade (1,2). Low birth weight, closely linked to preterm birth, is similarly a major determinant of neonatal morbidity and mortality.

The burden of preterm birth is not evenly distributed. Southern Asia and sub-Saharan Africa together account for more than 65% of preterm births worldwide, and Southern Asia has among the highest age-standardized preterm birth incidence of any region (1,2). Within this regional picture, hospital-based data from another Nepali tertiary centre (Bharatpur Hospital, Chitwan) similarly identify preterm birth as one of the leading causes of NICU admission, with reported preterm prevalence among NICU-admitted neonates broadly consistent with the wider South Asian pattern (8); comparable site-specific data from our own two study centres have not previously been published.

At the same time, infertility affects an estimated 1 in 6 people globally during their lifetime, with broadly similar prevalence across high-, middle-, and low-income countries (3). Use of assisted reproductive technologies such as intrauterine insemination (IUI) and in vitro fertilization (IVF) has expanded accordingly, including in South Asia. A substantial international literature, mainly from high-income

settings, indicates that IVF-conceived singletons carry a higher risk of preterm birth and low birth weight than spontaneously conceived singletons, even after accounting for maternal age (4,5,6).

However, most of this evidence originates outside South Asia, and there is limited published data from Nepal directly comparing neonatal outcomes by mode of conception among NICU-admitted neonates. It is unclear whether the risk estimates reported internationally are reflected in local tertiary NICU populations, and how far any observed differences reflect the conception method itself as opposed to baseline maternal differences and referral patterns between groups. Characterizing this locally is relevant both for antenatal counselling of patients undergoing ART and for NICU resource and staffing planning as access to ART expands in the region.

We hypothesized that IVF-conceived neonates would show higher rates of preterm birth, low birth weight, and a composite adverse neonatal outcome compared with spontaneously conceived neonates, and that this association would persist after adjustment for maternal age, comorbidity, and mode of delivery. The objective of this study was to compare baseline maternal characteristics and neonatal outcomes among neonates conceived spontaneously, via IUI, and via IVF and admitted to the NICUs of two participating centres, and to determine whether mode of conception is independently associated with a composite adverse neonatal outcome after adjustment for major maternal confounders.

Methods

Study design

This was a retrospective, observational cohort study comparing neonatal outcomes by mode of conception (spontaneous conception, intrauterine insemination [IUI], and in vitro fertilization [IVF]).

Study setting

B and B Hospital, Gwarko, Lalitpur; Grandy City Hospital, Kantipath, Kathmandu.

Study duration

NICU admissions from 2020–2025, per admission dates referenced in the results.

Participants

Neonates admitted to the NICU at the two participating centres during the study period. Of 559 total NICU admissions, 556 (99.5%) had a documented mode of conception and were included in group comparisons; 3 records with undocumented conception mode were excluded (Fig 1, participant flow diagram).

Eligibility criteria

Inclusion criteria: live births ≥ 28 weeks gestation at participating centres; known mode of conception (IVF, IUI, or spontaneous); singleton and multiple births. **Exclusion criteria:** unknown conception status; refusal for participation; major missing data impacting primary outcomes. Multiple births were included in the eligibility criteria; each neonate was analyzed as an independent observation, which does not account for clustering within mother (see Limitations).

Sampling

Consecutive sampling of eligible neonates born during the study period at each centre.

Sample size

Analytic sample: $n=556$ for group comparisons (292 spontaneous, 6 IUI, 258 IVF); $n=546$ for the multivariable regression model (13 cases excluded for missing predictor data). This is an interim/pilot analysis; the study protocol's target sample size was $n=3,000$ across all planned centres, calculated to achieve 80% power to detect a 10% difference in preterm birth rate.

Post-hoc power calculation: Using a two-proportion z-test ($\alpha=0.05$, two-sided) anchored to the spontaneous-conception group's observed preterm birth rate in this pilot (35.6%), the current interim sample ($n=292$ spontaneous vs. $n=258$ IVF) provided 66.5% power to detect a 10-percentage-point absolute difference — below the conventional 80% threshold, confirming the interim analysis is underpowered for a modest effect of this size. However, post-hoc power to detect the substantially larger difference actually observed in this cohort (35.6% vs. 57.8%, a 22.2-percentage-point difference) exceeded 99.9%. A sample of 378 per arm (756 total, 1:1 allocation) would be required for 80% power to detect a 10-percentage-point difference from this baseline; smaller total samples would suffice to detect larger effects (e.g., 194 total for a 20-point difference).

Variables

Exposure: mode of conception (spontaneous / IUI / IVF).

Outcomes: preterm birth (<37 weeks), birth weight, low birth weight (LBW, $<2500\text{g}$), very low birth weight (VLBW, $<1500\text{g}$), congenital anomaly, respiratory distress syndrome (RDS), neonatal sepsis, hypoglycemia, NICU length of stay, mortality, and a composite adverse neonatal outcome.

Composite adverse neonatal outcome: A composite adverse neonatal outcome was predefined as the occurrence of one or more clinically significant neonatal complications before hospital discharge, including preterm birth (<37 completed weeks of gestation), low birth weight ($<2500\text{ g}$), very low birth

weight (<1500 g), small for gestational age, a 5-minute Apgar score <7, respiratory distress syndrome requiring respiratory support, neonatal sepsis, hypoxic–ischemic encephalopathy, intraventricular hemorrhage, necrotizing enterocolitis, NICU admission, major congenital anomalies, or neonatal death. Infants experiencing at least one of these events were classified as having a composite adverse neonatal outcome.

Covariates: maternal age, primigravida status, socioeconomic status, antenatal care (ANC) visits, maternal comorbidity, antenatal corticosteroid administration, mode of delivery (LSCS vs. NVD).

Data collection

Data were extracted retrospectively from discharge charts by a medical officer and a dedicated data abstractor. No formal inter-rater reliability assessment was performed for this interim analysis.

Outcome measures

Definitions follow standard neonatal criteria (WHO birth-weight thresholds for LBW/VLBW; WHO gestational-age threshold for preterm birth).

Birth weight was classified according to the World Health Organization (WHO) criteria. Low birth weight (LBW) was defined as a birth weight of <2,500 g (2.5 kg), irrespective of gestational age. Very low birth weight (VLBW) was defined as a birth weight of <1,500 g (1.5 kg), while extremely low birth weight (ELBW) was defined as a birth weight of <1,000 g (1.0 kg).

Preterm birth was defined according to WHO as live birth occurring before 37 completed weeks of gestation (<37+0 weeks). WHO further classifies preterm birth into extremely preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate to late preterm (32 to <37 weeks)

Respiratory distress syndrome (RDS) was considered present if the diagnosis was documented by the treating neonatologist based on compatible clinical features (tachypnea, grunting, nasal flaring, chest retractions, and oxygen requirement) together with characteristic chest radiographic findings.

Neonatal sepsis was considered present if the diagnosis was documented in the medical record by the treating neonatologist based on clinical features suggestive of systemic infection, with or without laboratory confirmation, and treatment with intravenous antibiotics was initiated. Clinical diagnosis followed WHO recommendations for possible serious bacterial infection (PSBI).

Statistical analysis

Continuous variables were tested for normality using the Shapiro-Wilk test; all continuous outcomes were non-normally distributed and are reported as median [IQR], analyzed using the Kruskal-Wallis test.

Categorical variables are reported as n(%) and compared using the chi-square test, with Fisher-Freeman-Halton exact tests used where expected cell counts were <5. The composite adverse neonatal outcome was analyzed using binary logistic regression, first unadjusted and then adjusted for maternal age, comorbidity, and mode of delivery; model fit was assessed with the Hosmer-Lemeshow test and Nagelkerke R². Statistical significance was set at p<0.05.

Statistical analyses were performed using IBM SPSS Statistics, version 31.0.2.0.

Results

Of 559 neonates admitted to the NICU across the two participating centres during the study period, 556 (99.5%) had a documented mode of conception and were included in the analysis: 292 (52.5%) were spontaneously conceived, 6 (1.1%) were conceived via IUI, and 258 (46.4%) were conceived via IVF; 3 records with undocumented conception mode were excluded from group comparisons (Fig 1).

Baseline characteristics

The three groups differed significantly on several baseline characteristics (Table 1). Maternal age was higher in the IVF group (median 32.0 years, IQR 30.0–36.0) than the spontaneous group (median 30.0 years, IQR 28.0–34.0; Kruskal-Wallis p<0.001). Primigravida status was more common in the IVF group (63.2%) than the spontaneous group (51.3%; p=0.024 chi-square, p=0.008 exact, ART vs. spontaneous). Maternal comorbidity was present in 40.6% of the IVF group versus 30.6% of the spontaneous group (p=0.040 chi-square, p=0.016 exact). Antenatal corticosteroids were administered far more frequently in the IVF group (50.8%) than the spontaneous group (18.9%; p<0.001). Socioeconomic status distribution and ANC visit frequency did not differ significantly between groups (p=0.264 and p=0.731, respectively). Mode of delivery (LSCS) was near-universal across all groups (98.6–100%) with no significant difference (p=0.769 chi-square, p=0.688 exact).

Characteristic	Spontaneous (n=292)	IUI (n=6)	IVF (n=258)	p-value
Maternal age, yrs, median[IQR]	30.0 [28.0-34.0]	31.5 [31.0-32.0]	32.0 [30.0-36.0]	<0.001 (KW)
Primigravida, n(%)	139 (51.3%)	2 (50.0%)	153 (63.2%)	0.024; 0.008 exact
Socioeconomic status (Low/Mid/Upper), n	5 / 265 / 22	0 / 5 / 1	0 / 238 / 20	0.264 (33% cells <5)
ANC visits, median[IQR]	9.0 [9.0-10.0]	9.5 [9.0-10.0]	9.0 [8.0-10.0]	0.731 (KW)
Maternal comorbidity, n(%)	89 (30.6%)	3 (50.0%)	103 (40.6%)	0.040; 0.016 exact
Antenatal steroid given, n(%)	55 (18.9%)	3 (50.0%)	131 (50.8%)	<0.001
Delivery by LSCS, n(%)	286 (98.6%)	6 (100.0%)	255 (99.2%)	0.769; 0.688 exact

Table 1. Baseline maternal characteristics by mode of conception. KW = Kruskal-Wallis test.

Neonatal outcomes

Preterm birth occurred in 57.8% of IVF-conceived neonates, 50.0% of IUI-conceived neonates, and 35.6% of spontaneously conceived neonates ($p<0.001$) (Table 2). Birth weight was lower in the IVF group (median 2380g, IQR 1983–2770) than the spontaneous group (median 2800g, IQR 2348–3200; Kruskal-Wallis $p<0.001$). LBW occurred in 58.1% of the IVF group versus 30.1% of the spontaneous group ($p<0.001$), and VLBW occurred in 11.2% of the IVF group versus 1.7% of the spontaneous group ($p<0.001$). Congenital anomaly rates did not differ significantly between groups (5.1% IVF vs. 2.1% spontaneous, $p=0.141$ chi-square, $p=0.099$ exact) (Fig 2, Fig 3).

Outcome	Spontaneous	IUI	IVF	p-value
Preterm birth (<37wk), n(%)	104 (35.6%)	3 (50.0%)	149 (57.8%)	<0.001
Birth weight (g), median[IQR]*	2800 [2348-3200]	2525 [1920-2838]	2380 [1983-2770]	<0.001 (KW)
LBW <2500g, n(%)	88 (30.1%)	3 (50.0%)	150 (58.1%)	<0.001
VLBW <1500g, n(%)	5 (1.7%)	0 (0.0%)	29 (11.2%)	<0.001
Congenital anomaly, n(%)	6 (2.1%)	0 (0.0%)	13 (5.1%)	0.141; 0.099 exact

Table 2. Neonatal outcomes by mode of conception. *Birth weight was non-normally distributed in every group (Shapiro-Wilk $p < 0.05$); Kruskal-Wallis (KW) used rather than ANOVA.

Neonatal morbidity and NICU course

RDS (19.5% IVF vs. 13.7% spontaneous, $p = 0.192$), sepsis (7.8% vs. 4.1%, $p = 0.152$), hypoglycemia (0.4% vs. 0.7%, $p = 0.880$), and mortality (5.4% vs. 3.4%, $p = 0.449$) did not differ significantly between the IVF and spontaneous groups (Table 3). NICU length of stay was longer in the IVF group (median 3.0 days, IQR 0.2–6.0) than the spontaneous group (median 0.2 days, IQR 0.2–4.0; Kruskal-Wallis $p < 0.001$) (Fig 4). The composite adverse neonatal outcome occurred in 73.6% of the IVF group, 50.0% of the IUI group, and 42.8% of the spontaneous group ($p < 0.001$) (Fig 5).

Variable	Spontaneous	IUI	IVF	p-value
RDS, n(%)	40 (13.7%)	1 (16.7%)	50 (19.5%)	0.192; 0.085 exact
Sepsis, n(%)	12 (4.1%)	0 (0.0%)	20 (7.8%)	0.152; 0.100 exact
Hypoglycemia, n(%)	2 (0.7%)	0 (0.0%)	1 (0.4%)	0.880; 1.000 exact
NICU stay, days, median[IQR]	0.2 [0.2-4.0]	1.0 [0.4-3.2]	3.0 [0.2-6.0]	<0.001 (KW)
Mortality, n(%)	10 (3.4%)	0 (0.0%)	14 (5.4%)	0.449; 0.302 exact
Composite adverse outcome, n(%)	125 (42.8%)	3 (50.0%)	190 (73.6%)	<0.001

Table 3. Neonatal morbidity and NICU course by mode of conception.

Regression analysis

On univariable analysis, IVF (vs. spontaneous conception) was associated with the composite adverse outcome (unadjusted OR 3.73, 95% CI 2.60–5.36, $p < 0.001$), as was maternal age per year (OR 1.04, 95% CI 1.01–1.08, $p = 0.025$) and presence of comorbidity (OR 1.56, 95% CI 1.09–2.23, $p = 0.015$). IUI (vs. spontaneous) was not significantly associated with the outcome (OR 1.34, 95% CI 0.27–6.73, $p = 0.725$).

On multivariable logistic regression adjusting for maternal age, comorbidity, and mode of delivery, IVF remained independently associated with the composite adverse outcome (adjusted OR 3.58, 95% CI 2.46–5.21, $p < 0.001$). Maternal age (adjusted OR 1.01, 95% CI 0.97–1.05, $p = 0.590$) and comorbidity (adjusted OR 1.43, 95% CI 0.98–2.10, $p = 0.064$) were not independently significant after adjustment. The IUI estimate remained statistically unstable given the small subgroup size (adjusted OR 1.26, 95% CI

0.25–6.43, $p=0.778$; $n=6$) (Fig 6). The final model included $n=546$ neonates (13 excluded for missing predictor data); the overall model was significant (likelihood ratio $p<0.001$), with adequate fit (Hosmer-Lemeshow $\chi^2=5.64$, $df=8$, $p=0.688$) but modest discrimination (Nagelkerke $R^2=0.139$).

Predictor	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
IUI vs Spontaneous	1.34 (0.27-6.73)	0.725	1.26 (0.25-6.43)	0.778
IVF vs Spontaneous	3.73 (2.60-5.36)	<0.001	3.58 (2.46-5.21)	<0.001
Maternal age (per year)	1.04 (1.01-1.08)	0.025	1.01 (0.97-1.05)	0.590
Comorbidity present	1.56 (1.09-2.23)	0.015	1.43 (0.98-2.10)	0.064
LSCS vs NVD	0.26 (0.03-2.27)	0.225	0.17 (0.02-1.57)	0.119

Table 4. Logistic regression – composite adverse neonatal outcome. $n=546$ (13 dropped for missing predictor data). Model likelihood-ratio $p<0.001$. Nagelkerke $R^2=0.139$. Hosmer-Lemeshow $\chi^2=5.64$, $df=8$, $p=0.688$ (adequate fit).

Predictor	aOR	95% CI	p
IVF vs Spontaneous	3.58	2.46-5.21	<0.001
IUI vs Spontaneous	1.26	0.25-6.43	0.778 (unstable, $n=6$)
Maternal age (per year)	1.01	0.97-1.05	0.590
Comorbidity present	1.43	0.98-2.10	0.064
LSCS vs NVD	0.17	0.02-1.57	0.119

Table 5. Final adjusted model summary. Hosmer-Lemeshow $p=0.688$; Nagelkerke $R^2=0.139$; $n=546$.

Discussion

Principal findings

In this interim analysis of a two-centre NICU cohort, neonates conceived by IVF had significantly higher rates of preterm birth, low birth weight, very low birth weight, and a composite adverse neonatal outcome than spontaneously conceived neonates, and IVF-conceived neonates also had a longer NICU stay. The association between IVF and the composite adverse outcome persisted after adjustment for maternal age, comorbidity, and mode of delivery (adjusted OR 3.58, 95% CI 2.46–5.21). The IUI group was too small ($n=6$) to draw reliable conclusions. Baseline characteristics differed substantially between groups: IVF mothers were older, more often primigravida, more often had a documented comorbidity, and far more often received antenatal corticosteroids than the spontaneous-conception group – the last of these consistent with clinicians anticipating preterm delivery in this group before birth occurred.

Comparison with previous studies

These findings are directionally consistent with the existing international literature on IVF and neonatal outcomes, although the magnitude observed here is larger than most published estimates. A systematic review and meta-analysis of controlled studies found that IVF-conceived singletons had a higher relative risk of preterm birth and low birth weight compared with spontaneously conceived singletons after accounting for maternal age (4). A subsequent, larger systematic review of obstetric and perinatal outcomes in IVF/ICSI singleton pregnancies similarly reported consistently elevated risks of preterm birth, low birth weight, and perinatal mortality relative to spontaneous conception (5). A narrative review of the obstetric and perinatal literature likewise concluded that singleton IVF pregnancies carry a higher incidence of adverse outcomes than unassisted singleton pregnancies, independent of the well-established risk from multiple gestation (6). The composite adverse outcome rate and adjusted odds ratio observed in the present cohort (73.6% in the IVF group; adjusted OR 3.58) are higher than the pooled relative risks reported in these reviews, which is plausible given that this cohort is drawn exclusively from NICU admissions rather than all live births – a distinction addressed further under Limitations.

Explanation of findings

Several explanations have been proposed for the excess perinatal risk observed after IVF, and this cohort cannot distinguish between them. One line of evidence suggests that the underlying subfertility of the parents – rather than the IVF procedure itself – accounts for at least part of the excess risk, since subfertile women who conceive without assisted reproduction also show elevated rates of adverse perinatal outcomes relative to fertile women (3). A second line of evidence points to features of the IVF procedure itself, including ovarian stimulation and laboratory embryo culture, as independently contributing to risk (6). A third, and highly relevant explanation for the present dataset, is referral and surveillance bias intrinsic to this study's design (see Limitations): because this is a NICU-register cohort rather than a delivery-register cohort, it captures only neonates unwell enough to be admitted, and IVF pregnancies – being more closely monitored and more often delivered at tertiary centres – may be systematically over-represented relative to their true population risk. The very high rate of antenatal corticosteroid use in the IVF group (50.8% vs. 18.9%) is consistent with clinicians anticipating preterm delivery in this group, which may reflect either genuinely higher risk or a lower threshold for referral and intervention. This cohort's design cannot separate a true biological effect of IVF from these referral and surveillance pathways.

Clinical implications

If confirmed in the full multicentre cohort, these findings support continued heightened antenatal and neonatal surveillance for IVF-conceived pregnancies, including anticipation of preterm delivery and NICU

bed planning at tertiary centres. They also support pre-conception and antenatal counselling of IVF patients regarding the observed excess risk of preterm birth and low birth weight, framed alongside the uncertainty about how much of this risk reflects the procedure itself versus the underlying subfertility being treated.

Public health implications

Preterm birth remains the leading cause of neonatal mortality worldwide, and South Asia carries a disproportionate share of the global burden alongside sub-Saharan Africa (5,6). As access to assisted reproduction expands in this region, understanding the perinatal risk profile of ART-conceived pregnancies – and ensuring NICU capacity and antenatal referral pathways anticipate this risk – is a relevant health-system planning question, not only a clinical one.

Strengths

This analysis draws on a real, two-centre clinical dataset with individually adjudicated maternal and neonatal variables rather than administrative coding alone, allowing adjustment for clinically meaningful confounders (maternal age, comorbidity, mode of delivery) rather than relying on unadjusted comparisons. Non-normally distributed continuous variables were identified explicitly (Shapiro-Wilk testing) and analyzed with appropriate non-parametric methods rather than assuming normality, and small-cell categorical comparisons were supplemented with exact tests rather than relying on chi-square alone.

Limitations

Documented, real limitations already identified in your pilot review, safe to retain:

- Underpowered: interim analysis of $n=559$ vs. the protocol's target $n=3,000$ (calculated for 80% power to detect a 10% preterm-rate difference).
- No true denominator: this is a NICU-register dataset only; the all-live-birth denominator by conception mode is not available, so absolute risk cannot be estimated.
- Selection bias: only NICU-admitted neonates are captured, systematically excluding well spontaneous-conception babies never admitted, likely inflating apparent severity in that comparator group.
- Confounding by indication / referral bias: IVF/IUI pregnancies are more likely to be monitored or referred to tertiary NICUs regardless of true morbidity.
- Small cell counts in several sub-analyses (e.g., anomaly type); exact tests and Clopper-Pearson CIs recommended where counts are small.

- Non-independence: multiple births from the same mother are not statistically independent; each neonate was treated as an independent unit, a limitation to note.
- Embryo-transfer detail (fresh vs. frozen, number of embryos transferred) was not captured in this interim dataset.

Future research

Completion of full multicentre recruitment to the protocol target (n=3,000); addition of a delivery-register comparator arm to estimate true denominators; capture of embryo-transfer detail (fresh vs. frozen, number transferred) – a distinction reported to influence perinatal outcomes in prior systematic review (7); sensitivity analysis excluding multiple births; subgroup analysis of fresh vs. frozen IVF; interaction analysis of mode of conception × maternal age; and treatment of centre as a covariate or random effect once multiple centres are pooled (mixed-effects logistic regression).

Conclusion

In this interim two-centre NICU cohort, IVF-conceived neonates had substantially higher rates of preterm birth, low birth weight, and a composite adverse neonatal outcome than spontaneously conceived neonates, an association that persisted after adjustment for measured confounders and that is directionally consistent with the international literature. Because this is a pilot, NICU-admission-only sample drawn from 2 of the planned centres, these findings should be regarded as hypothesis-generating rather than definitive, pending completion of the full multicentre cohort with a proper delivery-register denominator.

Abbreviations

ANC: Antenatal care

ART: Assisted reproductive technology

CI: Confidence interval

ELBW: Extremely low birth weight

ICSI: Intracytoplasmic sperm injection

IQR: Interquartile range

IUI: Intrauterine insemination

IVF: In vitro fertilization

LBW: Low birth weight

LSCS: Lower segment caesarean section

NHRC: Nepal Health Research Council

NICU: Neonatal intensive care unit

NVD: Normal vaginal delivery

OR: Odds ratio

RDS: Respiratory distress syndrome

VLBW: Very low birth weight

WHO: World Health Organization

Declarations

Clinical Trial Number

Clinical trial number: not applicable.

Ethics approval and consent to participate

This study was approved by the Ethical Review Board of the Nepal Health Research Council (NHRC), under expedited review, via the official NHRC Integrated Research Ethics Review Platform (IRERP) (Reference No. 1843). As this was a retrospective analysis of anonymised NICU register data, informed consent — including parental/guardian consent for participants younger than 16 years — was waived by the Ethical Review Board, as no participants were contacted and no identifiable data were used. All procedures involving human data were performed in accordance with the relevant guidelines and regulations, including the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

Data Sharing Statement: De-identified participant data that support the findings of this study are available from the corresponding author upon reasonable request for scientifically sound research purposes, subject to institutional approval and applicable ethical and data protection requirements.

Competing Interests

The authors declare no conflict of interest.

Funding

This research received no specific grant from any funding agency.

Authors' contributions

Dr. Chaitanya Darshan Bhattarai: Conceptualization of the study, development of the research question and study design, interpretation of the findings, and preparation and critical revision of the manuscript.

Dr. Arun Bajgain: Contribution to the study methodology, clinical input, interpretation of findings, and critical revision of the manuscript. **Dr. Sangita Shakya:** Contribution to data analysis, interpretation of findings, and critical revision of the manuscript. **Dr. Prerana Kansakar:** Contribution to data analysis, interpretation of findings, and critical revision of the manuscript. **Dr. Akriti Bharati:** Contribution to data analysis, interpretation of findings, and critical revision of the manuscript. **Dr. Bikash Shrestha:** Guidance and supervision of data analysis, statistical interpretation, and critical revision of the manuscript. All authors reviewed and approved the final manuscript and agree to be accountable for the accuracy and integrity of the work.

Acknowledgements

Dr. Sangita Shakya, HOD, Department of Pediatric B and B Hospital and Dr Prerana Kansakar, HOD NICU Patan Academy of Health Sciences and B and B Hospital; Dr. Aakriti Bharati is a leading IVF and Fertility Specialist at Vatsalya IVF and Fertility Clinic Dr. Bikash Shrestha, Nepalese Army Institute of Health Sciences, HOD, Department of NICU Grandi City Hospital.

References

1. World Health Organization, UNICEF, Partnership for Maternal, Newborn & Child Health. Born too soon: decade of action on preterm birth. Geneva: World Health Organization; 2023.
2. Ohuma EO, Moller AB, Bradley E, Chakwera S, Hussain-Alkhateeb L, Lewin A, et al. National, regional, and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis. Lancet. 2023;402(10409):1261-71.
3. Pinborg A, Wennerholm UB, Romundstad LB, Loft A, Aittomaki K, Söderström-Anttila V, et al. Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis. Hum Reprod Update. 2013;19(2):87-104.
4. McDonald SD, Han Z, Mulla S, Murphy KE, Beyene J, Ohlsson A; Knowledge Synthesis Group. Preterm birth and low birth weight among in vitro fertilization singletons: a systematic review and meta-analyses. Eur J Obstet Gynecol Reprod Biol. 2009;146(2):138-48.
5. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. Hum Reprod Update. 2012;18(5):485-503.

6. Sullivan-Pyke CS, Senapati S, Mainigi MA, Barnhart KT. In vitro fertilization and adverse obstetric and perinatal outcomes. *Semin Perinatol.* 2017;41(6):345-53.
7. Maheshwari A, Pandey S, Shetty A, Hamilton M, Bhattacharya S. Obstetric and perinatal outcomes in singleton pregnancies resulting from the transfer of frozen thawed versus fresh embryos generated through in vitro fertilization treatment: a systematic review and meta-analysis. *Fertil Steril.* 2012;98(2):368-77.
8. Sharma Y, Pathak OK, Poudel B, Sharma A, Sapkota RP, Devkota K. Preterm neonates admitted in the neonatal intensive care unit at a tertiary care centre: a descriptive cross-sectional study. *JNMA J Nepal Med Assoc.* 2023;61(260):320-4.

Figures

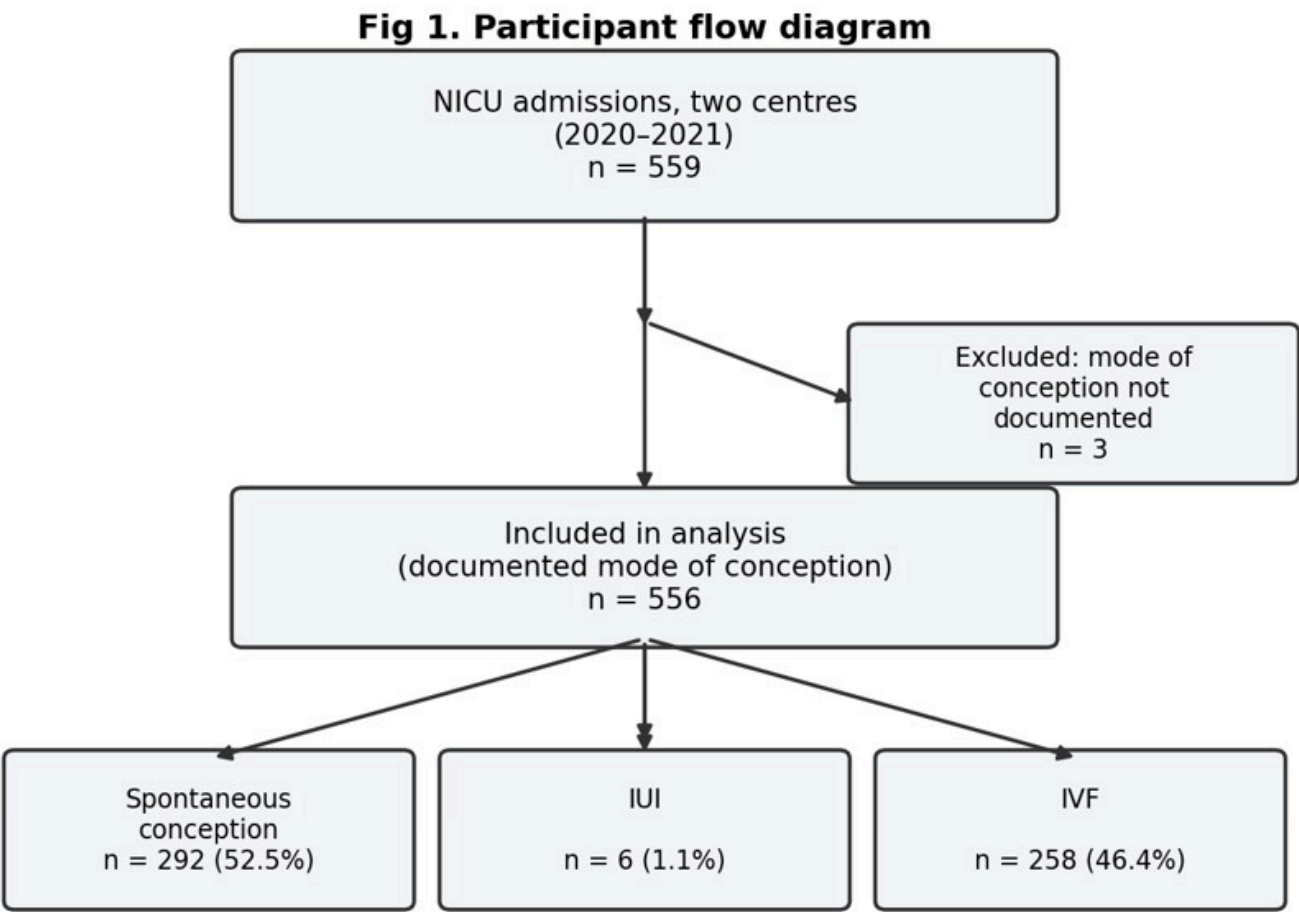


Figure 1

(CONSORT-style flow diagram): Flow of participants from total NICU admissions (n=559) to final analytic sample (n=556), by exclusion reason (n=3 undocumented conception mode).

Fig 2. Birth weight category by mode of conception

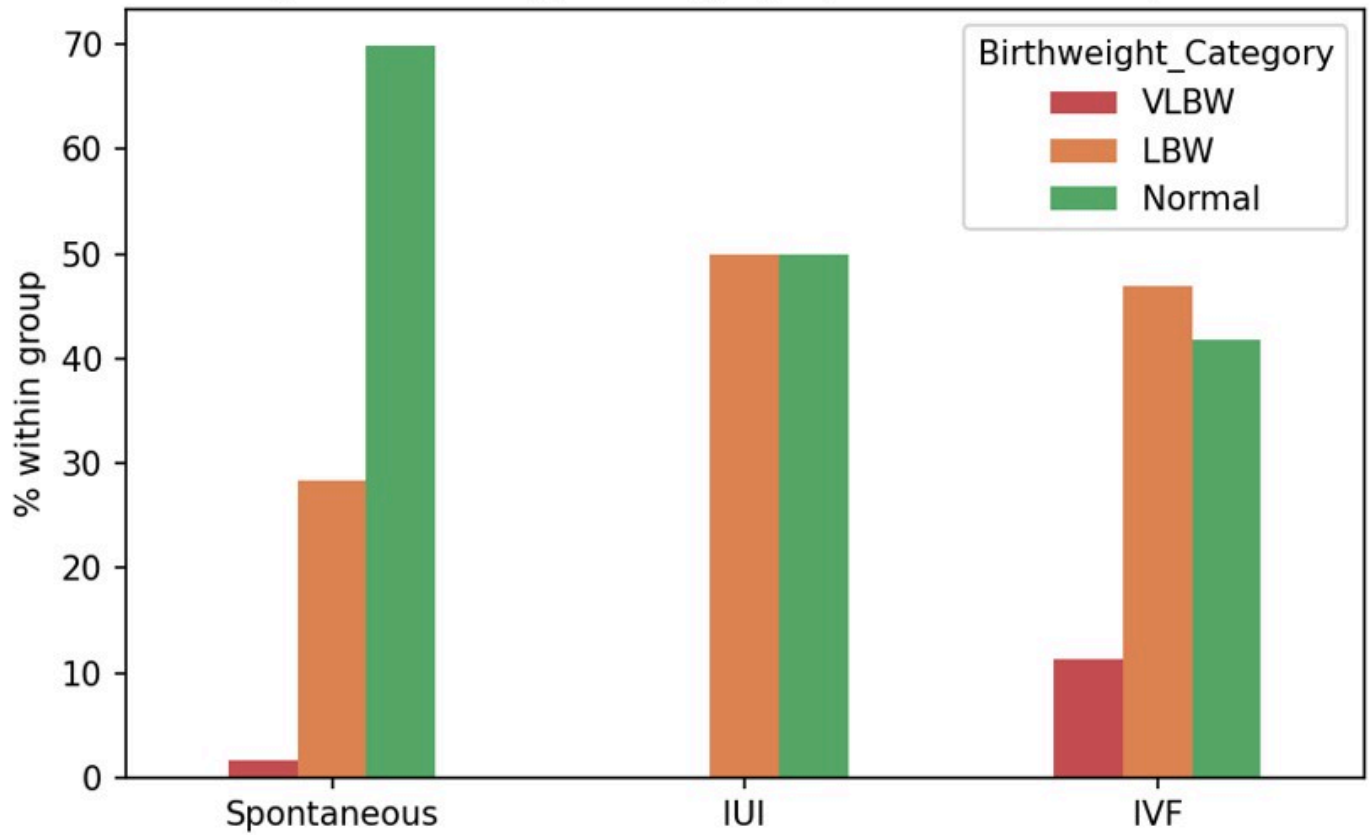


Figure 2

(Clustered bar chart): Distribution of birth weight category (VLBW/LBW/Normal) by mode of conception.

Fig 3. Gestational age at birth by mode of conception

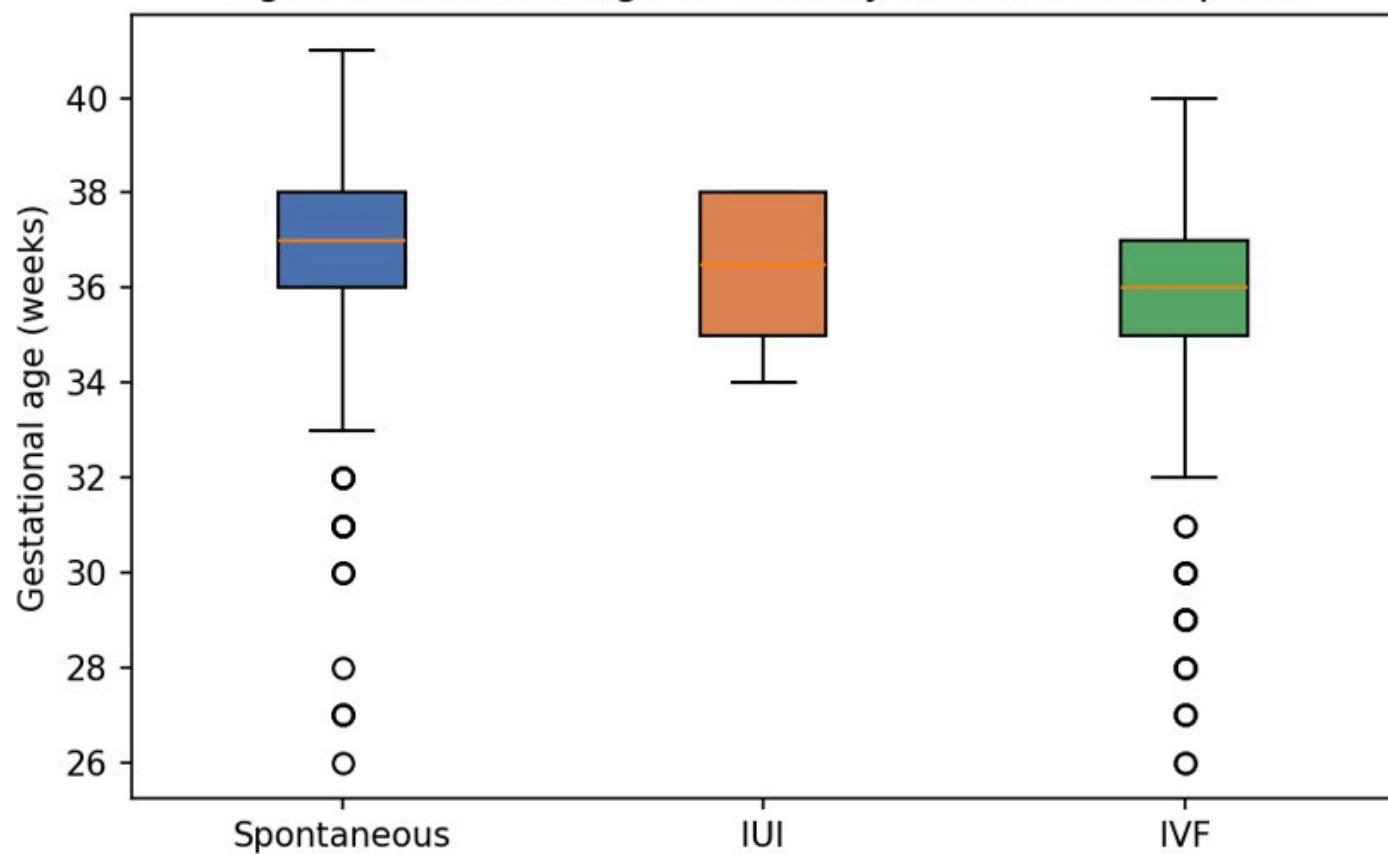


Figure 3

(Box plot): Gestational age at birth by mode of conception.

Fig 4. NICU length of stay by mode of conception

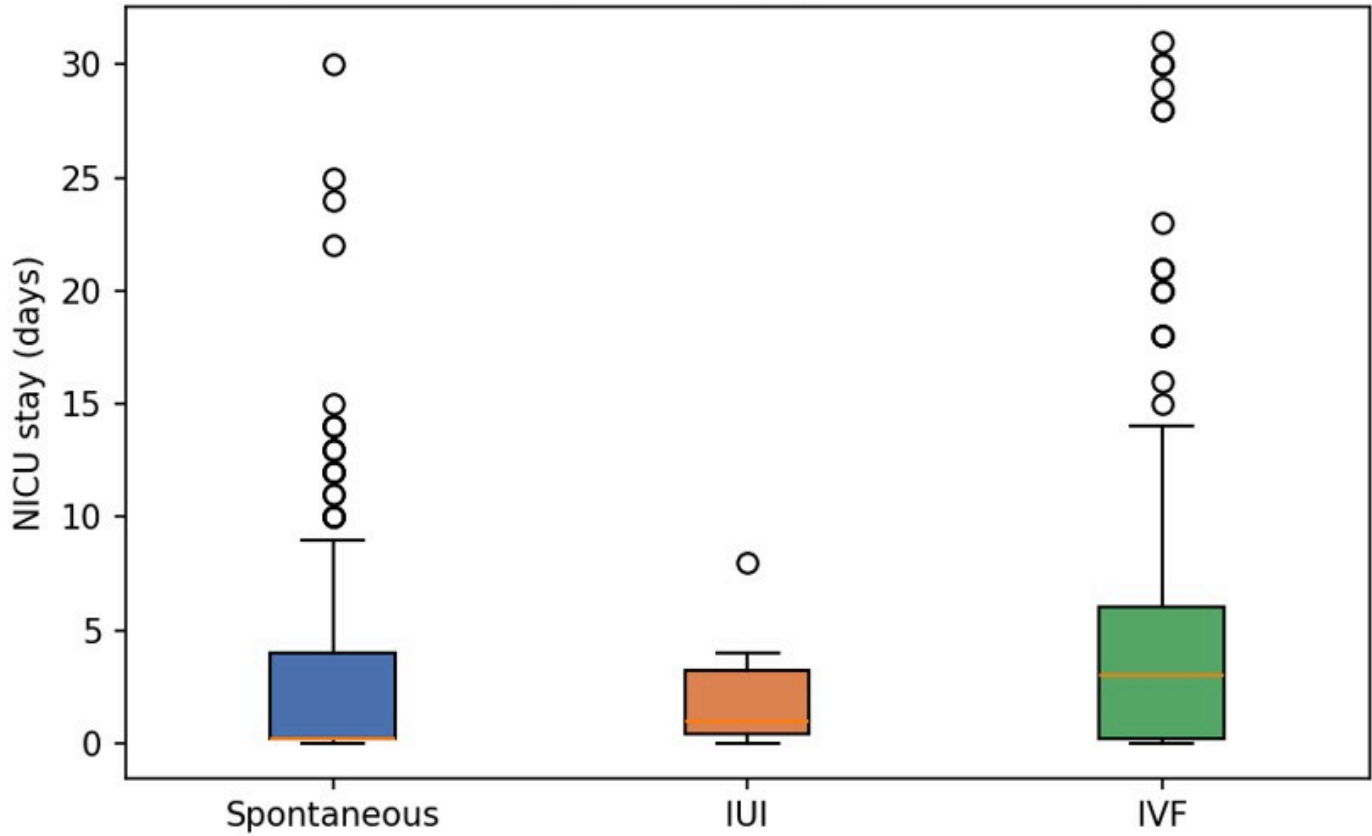


Figure 4

(Box plot): NICU length of stay (days) by mode of conception.

Fig 5. Composite adverse outcome rate by mode of conception
(error bars = 95% Wilson CI)

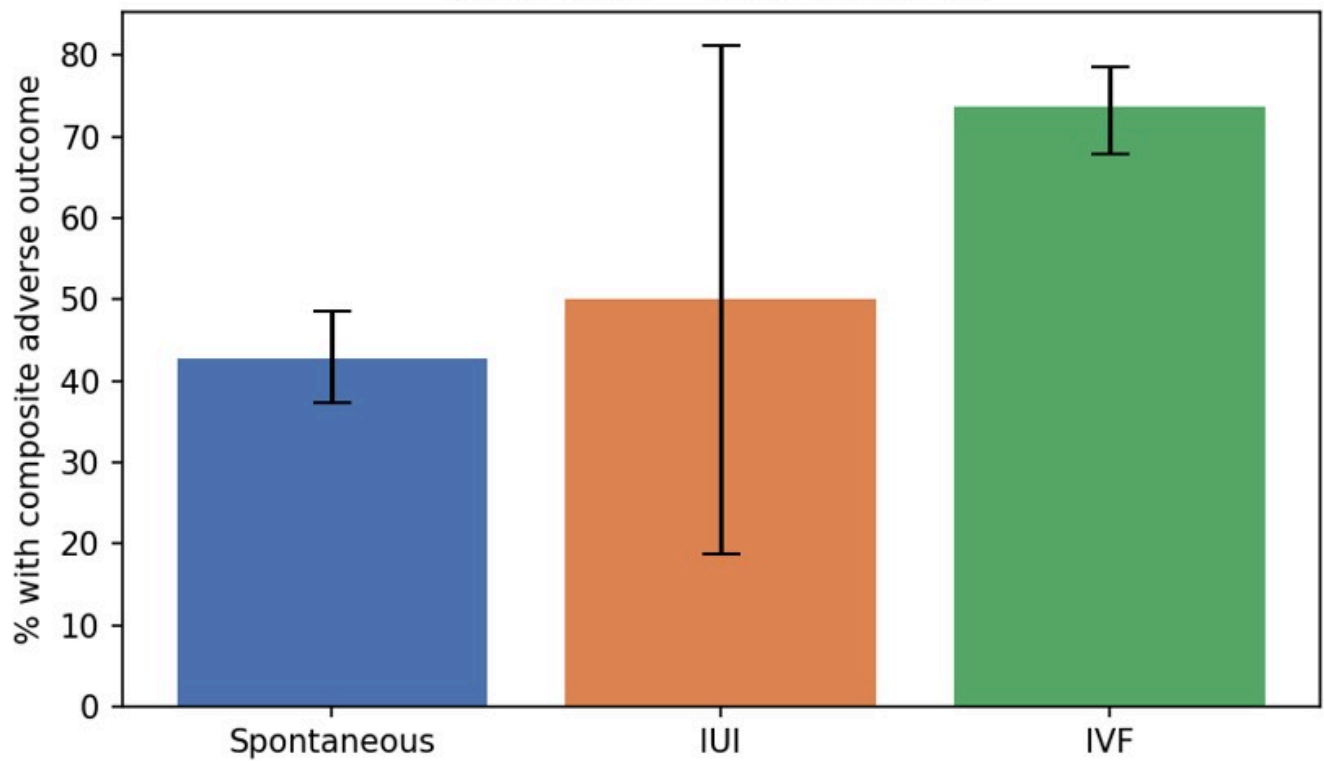


Figure 5

(Bar chart with 95% CI error bars): Rate of composite adverse neonatal outcome by mode of conception.

Fig 6. Adjusted ORs for composite adverse neonatal outcome

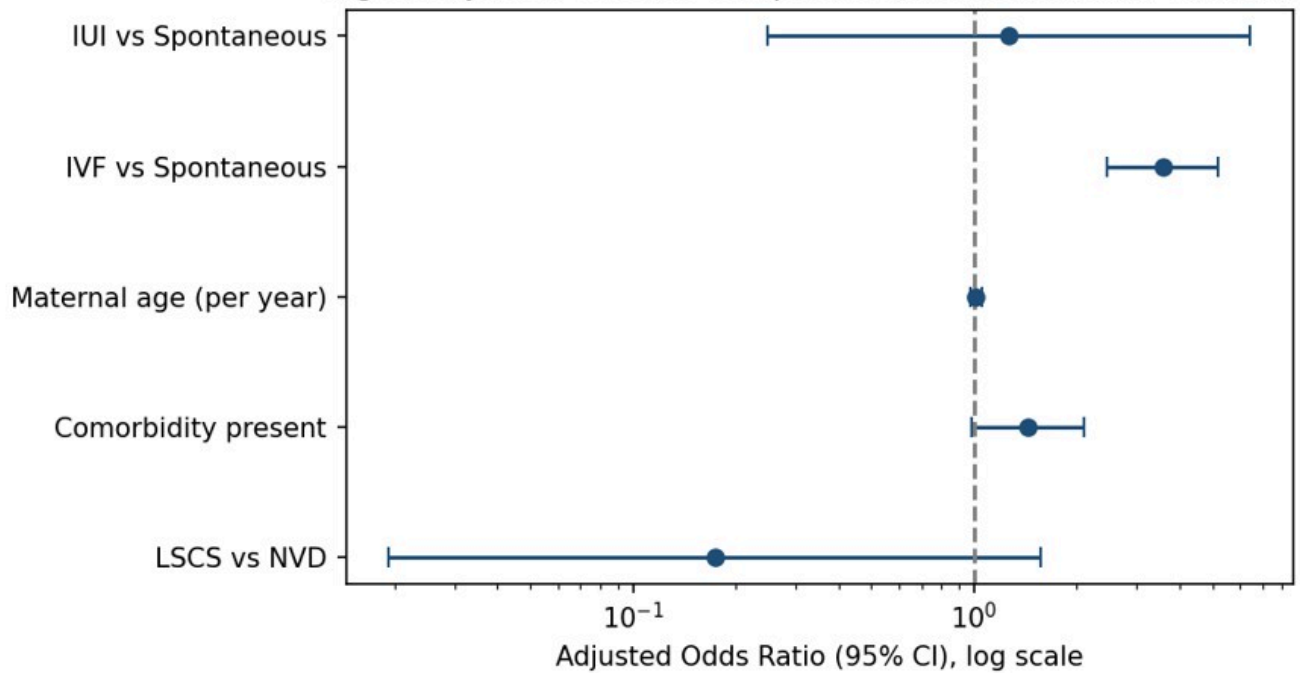


Figure 6

(Forest plot): Adjusted odds ratios (95% CI) for composite adverse outcome, IUI and IVF vs. spontaneous reference.