

# **Birth outcomes following assisted reproductive technologies conception in same-sex lesbian couples vs natural conception and assisted reproductive technologies conception in heterosexual couples**

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Word count: 658

Date of revisions: 20<sup>th</sup> of January 2023

Introduction | Higher rates of adverse birth outcomes have been consistently reported among children conceived via Assisted Reproductive Technologies (ART) compared with children conceived naturally.<sup>1</sup> Higher rates of multiple births in ART pregnancies partially explain the increased risk.<sup>2,3</sup> It remains unclear to what extent the remaining difference can be attributed to the reproductive technology or to factors related to infertility, which is associated with an elevated risk of poorer birth outcomes.<sup>4,5</sup> Same-sex lesbian couples undergo ART treatments generally without experiencing infertility. To distinguish the effects of reproductive treatment and infertility, we compared birth

outcomes in ART pregnancies in same-sex lesbian couples with natural conceptions and ART pregnancies in heterosexual couples.

**Method** | In Sweden, same-sex lesbian couples have been eligible to receive publicly funded ART treatments with donated sperm since 2005. This study includes all births in Sweden during 2007-2018. Using pseudonymized personal identifiers, the Swedish National Quality Registry for Assisted Reproduction, which includes all ART treatments (in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI) and intrauterine insemination (IUI)), was linked to the medical birth register and the total population registers, which include information on birth outcomes and sociodemographic characteristics. We focused on first live births for ART and naturally conceived births since 97.3% of ART births in same-sex lesbian couples were first births. We analyzed 4 outcomes: birth weight (continuous), gestational age (continuous), low birth weight (LBW) (binary, < 2500 gr.), and preterm delivery (binary, < 37 weeks of gestation). We estimated linear models on the continuous outcomes and linear probability models on the binary outcomes comparing ART conceived births in same-sex lesbian couples (reference category) to ART births in heterosexual couples and naturally conceived births. For each outcome, we estimated unadjusted and adjusted (controlling for child sex, multiplicity and maternal age at birth) models. We also estimated differences focusing on children conceived via IVF/ICSI, since 99.4% of ART births in heterosexual couples were conceived via IVF/ICSI compared with 63.3% in same-sex couples, as same-sex couples often start treatments with IUI, which has a lower chance of success regardless of subfertility.<sup>6</sup> Analyses were conducted using R, version 4.1.1. Statistical significance was set at  $P < .05$  (2-sided). This study was approved by the Regional Ethical Review Board of Stockholm. Informed consent was not required for pseudonymized data.

**Results** | During the study period there were 868 ART births in same-sex lesbian couples, 23488 ART births in heterosexual couples and 456898 naturally conceived births. ART conceived children in same-sex and heterosexual couples showed a higher proportion of multiplicity (7.5% and 5.8%, respectively), compared with naturally conceived births (2.1%) (Table 1). Couples who conceived naturally had significantly lower birth weight and gestational age and similar risk of LBW and

preterm delivery compared with same-sex couples who conceived via ART (Table 2). For example, birth weight was 3429 g in naturally conceived births vs 3460 g in same-sex ART births, adjusted difference -76.2 g (95% CI, -113, -39.3),  $P < 0.001$ ; LBW, 4.9% vs. 6.7%, adjusted difference 0.28 percentage points (95% CI, -1.11, 1.66),  $P = 0.70$ . Heterosexual couples who conceived via ART had statistically significantly lower birth weight and gestational age compared with same-sex couples (e.g. birth weight: 3343 g vs. 3460 g, adjusted difference -97.4 (95% CI, -134.8, -59.9),  $P < 0.001$ ). Percentages with LBW and preterm birth were higher among ART conceptions in heterosexual couples vs same-sex couples but did not reach statistical significance (e.g., LBW: 8.9% vs. 6.7%, adjusted difference 1.23 percentage points, 95% CI, -0.17, 2.65,  $P = 0.09$ ). The results were qualitatively similar when only considering IVF/ICSI conceived children (Table 2).

Discussion | This study demonstrated that same-sex lesbian couples undergoing ART had more favorable or similar birth outcomes to heterosexual couples who conceived naturally or underwent ART to conceive, suggesting infertility related factors rather than reproductive treatments contribute to higher rates of adverse birth outcomes in ART pregnancies. A limitation was that the relatively small sample size of same-sex couples reduced the statistical power of the study, particularly in the binary outcomes analyses.

**Data sharing statement:** The data used in this study cannot be shared by the authors but are directly available from the Swedish register holding authorities (Statistics Sweden, the National Board of Health and Welfare, and Swedish National Quality Registry for Assisted Reproduction).

### **Acknowledgment section**

Agneta Cederström had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Alice Goisis conceived the idea. All authors were involved in the design of the study and in interpreting the results. Agneta Cederström conducted the analyses. Alice Goisis wrote the first draft

and all authors contributed to critically revising the manuscript and approved the final version of the study.

**Conflict of interest disclosure:** None reported.

**Founding/support:** This work was supported by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 803958 to Alice Goisis). Pekka Martikainen was supported by the Academy of Finland (#308247, # 345219), the European Research Council under the European Union's Horizon 2020 research and innovation programme (grant agreement No 101019329), and the Max Planck – University of Helsinki Center for Social Inequalities in Population Health.

**Role of Funder/sponsor:** The funders had no role in the design and conduct of the study, collection, management, analysis, and interpretation of the data, preparation, review, or approval of the manuscript, and decision to submit the manuscript for publication.

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## Tables

**Table 1. Descriptive characteristics of the analytical samples, by mode of conception (first births 2007-2018)**

	<b>ART conceived - same-sex lesbian couple</b>	<b>ART conceived - heterosexual couple</b>	<b>Natural conceptions</b>
Number of observations	868	23488	456898
Multiple births (%)	5.8 <sup>a</sup>	7.5 <sup>c</sup>	2.1
Maternal age at birth (mean)	32.9 <sup>ab</sup>	33.2 <sup>c</sup>	28.3
Infant sex (%)			
Female	50.9	48.4	48.5
Male	49.1	51.6	51.5

<sup>a</sup> ART births in same sex couples statistically different from naturally conceived births (P<0.05); <sup>b</sup> ART births in same sex couples statistically different from ART conceived births in heterosexual couples (P<0.05); <sup>c</sup> ART conceived births in heterosexual couples statistically different from naturally conceived births (P<0.05).

**Table 2. Comparison of birth outcomes between the analytical samples, by mode of conception (first births 2007-2018)**

	<b>Absolute values</b>	<b>(1) Unadjusted Model</b>			<b>(2) Adjusted Model (by child sex, maternal age and multiple birth)</b>			<b>(3) Adjusted Model for IVF/ICSI conceived births ***</b>		
<b>Birth weight (gr.)*</b>	<b>Mean</b>	<b>Mean Difference</b>	<b>95% CI</b>	<b>P</b>	<b>Mean Difference</b>	<b>95% CI</b>	<b>P</b>	<b>Mean Difference</b>	<b>95% CI</b>	<b>P</b>
ART conception in same-sex lesbian couple	3460.2 <sup>b</sup>	reference category			reference category			reference category		
ART conception in heterosexual couple	3342.9 <sup>c</sup>	-117.3	(-156.5, -78.1)	< 0.001	-97.4	(-134.8, -59.9)	< 0.001	-88.2	(-135.9, -40.4)	< 0.001
Natural conception	3429.5	-30.7	(-69.2, 7.9)	0.12	-76.2	(-113.0, -39.3)	< 0.001	-66.9	(-114.14, -19.6)	0.006
<b>Gestational age (in days) *</b>	<b>Mean</b>									
ART conception in same-sex lesbian couple	278.1 <sup>b</sup>	reference category			reference category			reference category		
ART conception in heterosexual couple	274.7 <sup>c</sup>	-3.5	(-4.4, -2.5)	< 0.001	-2.9	(-3.8, -2.0)	< 0.001	-2.5	(-3.7, -1.4)	< 0.001
Natural conception	277.6	-0.50	(-1.5, 0.5)	0.310	-1.3	(-2.2, -0.4)	0.004	-0.9	(-2.2, 0.19)	0.10
<b>Low birth weight (&lt; 2500 gr.) **</b>	<b>Percent</b>									
ART conception in same-sex lesbian couple	6.7 <sup>ab</sup>	reference category			reference category			reference category		
ART conception in heterosexual couple	8.9 <sup>c</sup>	2.23	(0.73, 3.72)	0.004	1.23	(-0.17, 2.65)	0.09	0.86	(-0.94, 2.66)	0.35
Natural conception	4.9	-1.76	(-3.23,-0.29)	0.02	0.28	(-1.11, 1.66)	0.70	-0.1	(-1.88, 1.68)	0.91
<b>Preterm delivery (&lt; 37 weeks gestation) **</b>	<b>Percent</b>									
ART conception in same-sex lesbian couple	9.1 <sup>a</sup>	reference category			reference category			reference category		
ART conception in heterosexual couple	11.2 <sup>c</sup>	2.14	(0.40,3.88)	0.02	1.25	(-0.42, 2.92)	0.14	0.84	(-1.29, 2.97)	0.44
Natural conception	6.9	-2.18	(-3.89,-0.47)	0.01	-0.29	(-1.94, 1.36)	0.73	-0.67	(-2.78, 1.45)	0.54

Legend for the absolute values column: <sup>a</sup> ART births in same sex couples statistically different from naturally conceived births (P<0.05); <sup>b</sup> ART births in same sex couples statistically different from ART conceived births in heterosexual couples (P<0.05); <sup>c</sup> ART conceived births in heterosexual couples statistically different from naturally conceived births (P<0.05); \* Linear model; \*\* Linear Probability Models. \*\*\* IVF/ICSI births in same-sex lesbian couples N=527; IVF/ICSI births in heterosexual couples N=23001.