

Supplementary Table S4. Effect of frozen-ET and fresh-ET on preterm birth (using transfer date as basis for gestational age in the ART pregnancies) overall (total), through HDP^a (mediated) and independent of HDP^a (direct). Odds ratios (OR) with 95% CIs.

	Cases/deliveries (%)	Total effect OR ^b	Direct effect OR ^b	Mediated OR ^b	% Mediated ^c
<i>Any preterm birth (<37 weeks)</i>					
Natural conception	219 454/4 426 682 (5.0%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	–
Frozen-ET	1195/18 037 (6.6%)	1.28 (1.28 to 1.36)	1.22 (1.19 to 1.26)	1.048 (1.048 to 1.049)	20.9
Fresh-ET	6359/78 300 (8.1%)	1.49 (1.45 to 1.53)	1.49 (1.44 to 1.53)	1.001 (1.000 to 1.003)	0.5
<i>Spontaneous preterm birth (<37 weeks)^d</i>					
Natural conception	139 894/4 267 470 (3.3%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	–
Frozen-ET	700/18 033 (3.9%)	1.18 (1.09 to 1.27)	1.17 (1.13 to 1.22)	1.003 (1.001 to 1.005)	2.1
Fresh-ET	3668/78 003 (4.7%)	1.34 (1.29 to 1.39)	1.34 (1.29 to 1.39)	1.000 (0.999 to 1.001)	0
<i>Medically indicated preterm birth (<37 weeks)^d</i>					
Natural conception	69 767/4 267 470 (1.6%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	–
Frozen-ET	494/18 033 (2.7%)	1.48 (1.34 to 1.62)	1.30 (1.24 to 1.36)	1.136 (1.133 to 1.138)	37.1
Fresh-ET	2640/78 003 (3.4%)	1.71 (1.64 to 1.79)	1.71 (1.64 to 1.78)	1.005 (1.003 to 1.006)	1.1
<i>Extremely or very preterm birth (<32 weeks)</i>					
Natural conception	31 634/4 426 682 (0.7%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	–
Frozen-ET	224/18 037 (1.2%)	1.49 (1.30 to 1.70)	1.38 (1.29 to 1.48)	1.074 (1.072 to 1.077)	21.2
Fresh-ET	1221/78 300 (1.6%)	1.78 (1.68 to 1.89)	1.78 (1.68 to 1.89)	1.002 (1.001 to 1.004)	0.6
<i>Extremely preterm birth (<28 weeks)</i>					
Natural conception	10 423/4 426 682 (0.2%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	–
Frozen-ET	90/18 037 (0.5%)	1.68 (1.37 to 2.08)	1.61 (1.45 to 1.79)	1.047 (1.044 to 1.050)	11.1
Fresh-ET	453/78 300 (0.6%)	1.96 (1.78 to 2.16)	1.96 (1.78 to 2.16)	1.002 (1.000 to 1.003)	0.3

Models are adjusted for year of delivery, maternal age, parity, and country.

^a Hypertensive disorders in pregnancy, i.e. gestational hypertension, preeclampsia, eclampsia, or chronic hypertension with superimposed preeclampsia.

^b The total effect decomposes into the product of the direct effect odds ratio and the mediated effect odds ratio.

^c Proportion mediated = DE × (ME – 1)/(DE × ME – 1), where DE is direct effect and ME is mediated effect.

^d For Sweden, the study population was restricted to deliveries 1991–2015.

Models are adjusted for year of delivery, maternal age, parity, and country.