### **Charlers Chapron**

Bruno Borghese Hervé Foulot Antoine Bouret Paul Mazurk Guillaume Pierre Marie Christine Lafay Fouzia Decupere Francois X. Aubriot

#### Dominique de Ziegler

Vanessa Gayet Pietro Santulli Chloe Meignien Mathilde Bourdon François Aubriot Ann Marszalek Alessandra Fubini Catarina Feretti

### Université Paris-Descartes, Hôpital Cochin, Paris, France



COS and ART: wed by necessity

ART and obstetrical outcome: a little small, a little early

Fresh and frozen embryo transfers: the unexpected

COS and oocyte quality

COS and obstetrical outcome

Window of receptivity and endometrial vulnerability

COS and ART: wed by necessity

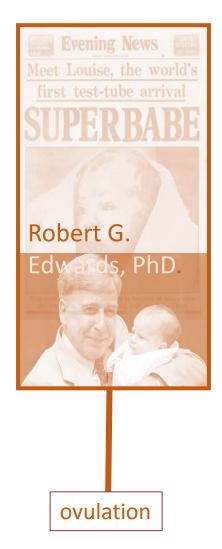
ART and obstetrical outcome: a little small, a little early

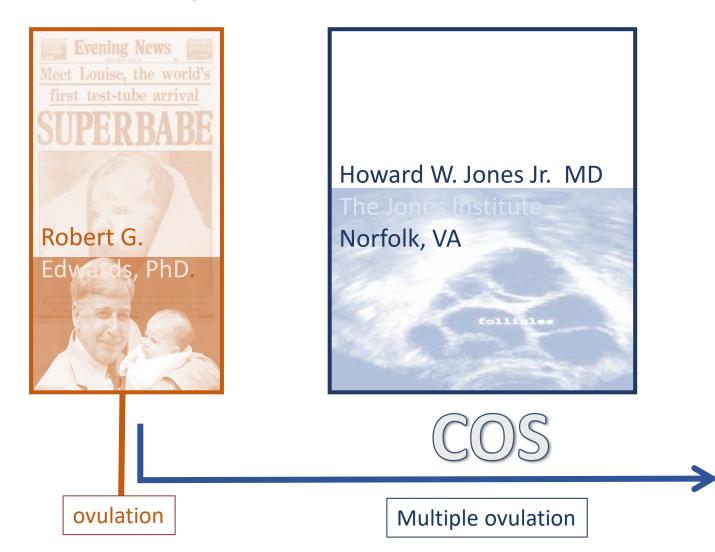
Fresh and frozen embryo transfers: the unexpected

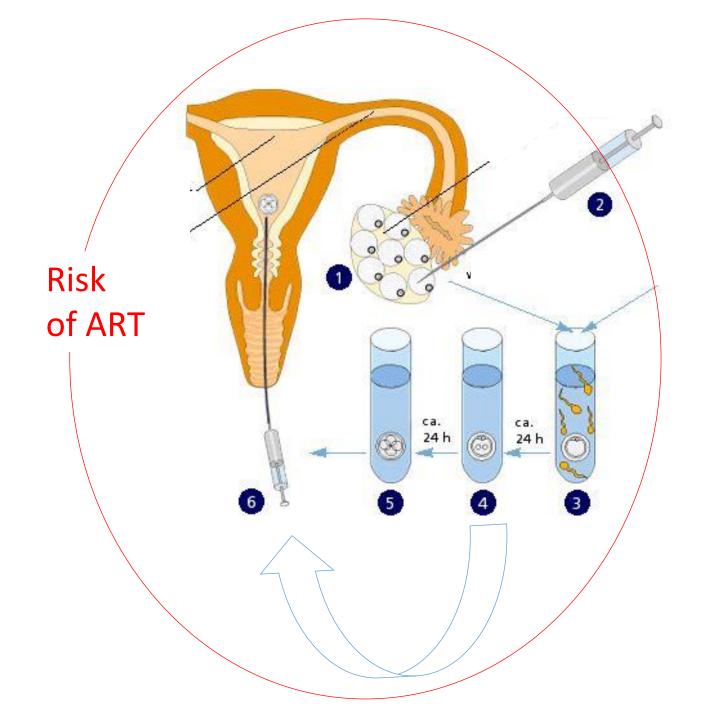
COS and oocyte quality

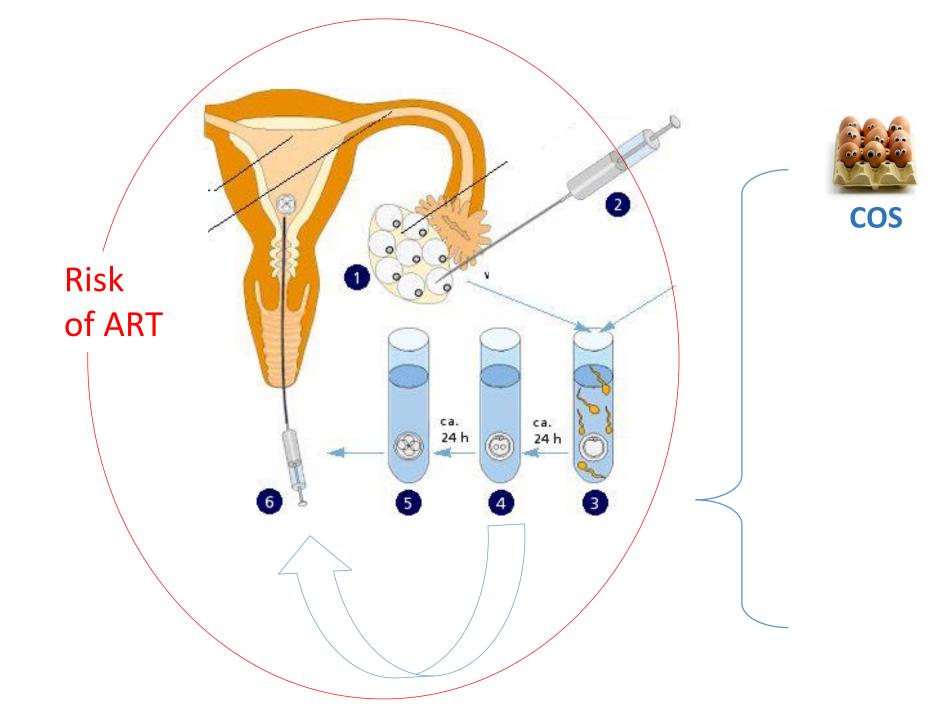
COS and obstetrical outcome

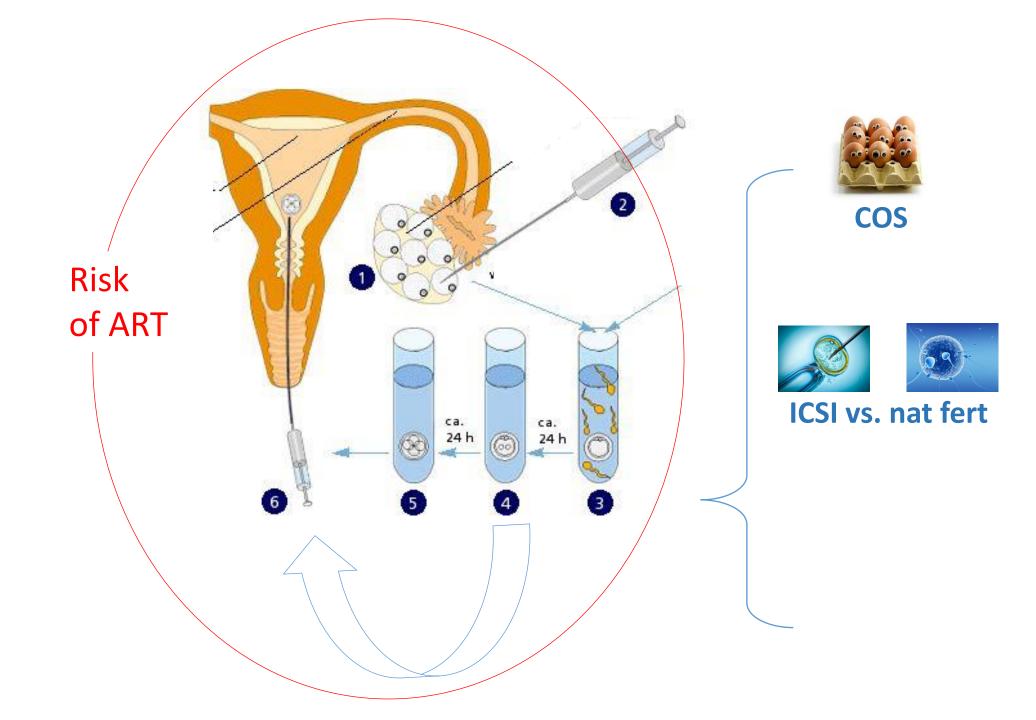
Window of receptivity and endometrial vulnerability

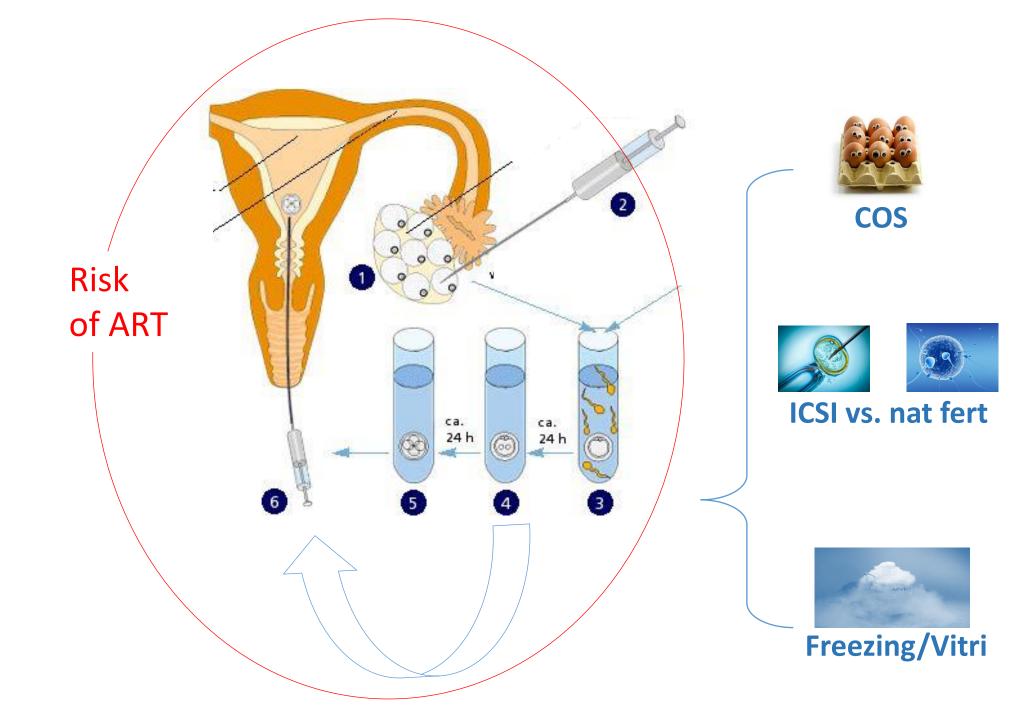












COS and ART: wed by necessity

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Window of receptivity and endometrial vulnerability

# Assisted reproductive technology and the risk of preterm birth among primiparas

Galit Levi Dunietz, M.A., M.P.H.,<sup>a</sup> Claudia Holzman, Ph.D., D.V.M.,<sup>a</sup> Patricia McKane, M.P.H., D.V.M.,<sup>b</sup>

Fertil Steril 2015;103:974-9.

## Singletons born to primiparas conceived naturally or by ART

(female or male infertility)

Maternal and pregnancy characteristics for ART and non-ART primiparas with live births of singletons in Florida and Massachusetts 2000–2010 and Michigan 2000–2009.

	$\square$	$\frown$		ART					
Characteristic	Non-ART	Female infertility	Male infertility	Combined infertility U	Inexplained infertility	<b>P</b> value			
Sample size, N (%) Maternal age, mean (SD)	1,804,100 (98.8 25.5 (6.1)	9,891 (0.5) 35.6 (5.2)	4,819 (0.3) 33.4 (4.1)	3,688 (0.2) 34.8 (5.0)	2,930 (0.2) 35.3 (4.1)	<.01			
Outcome	Non-ART	Female infertility	Male infertility	Combined inferti	lity Unexplained	infertility			
PTB <37 wk cOR (95% CI) aOR (95% CI) <sup>a</sup> PTB/early term <39 wk cOR (95% CI)	Reference Reference Reference	1.69 (1.59, 1.79) 1.60 (1.50, 1.70) 1.47 (1.41, 1.53)	1.21 (1.10, 1.33) 1.24 (1.13, 1.37) 1.12 (1.06, 1.19)	1.49 (1.35, 1.64	4) 1.26 (1.12	, 1.43)			
aOR (95% Cl) <sup>a</sup>	Reference	1.48 (1.42, 1.54)	1.19 (1.12, 1.26)	1.39 (1.30, 1.49	9) 1.23 (1.14	, 1.33)			
				Fertil Steril 2015;103:974-9.					

### Human Reproduction Update, Vol.19, No.2 pp. 87-104, 2013

Advanced Access publication on November 14, 2012 doi:10.1093/humupd/dms044

human reproduction update

## Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis

## A. Pinborg<sup>1,\*</sup>, U.B. Wennerholm<sup>2</sup>, L.B. Romundstad<sup>3</sup>, A. Loft<sup>1</sup>, K. Aittomaki<sup>4</sup>, V. Söderström-Anttila<sup>5</sup>, K.G. Nygren<sup>6</sup>, J. Hazekamp<sup>7</sup>, and C. Bergh<sup>8</sup>

<sup>1</sup>Fertility Clinic, Section 4071, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK – 2100 Copenhagen, Denmark <sup>2</sup>Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Sahlgrenska University Hospital/East, Gothenburg, Sweden <sup>3</sup>Department of Obstetrics and Gynaecology, IVF Unit, St Olav's University Hospital, Trondheim NO-7006, Norway and Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway <sup>4</sup>Department of Medical Genetics, Helsinki University Central Hospital (HUCH) and University of Helsinki, 00029 HUS, Helsinki, Finland <sup>5</sup>Familiy Federation of Finland, Fertility Clinic, Helsinki, 00100 Helsinki, Finland <sup>6</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden <sup>7</sup>IVF-Klinikken Oslo, Norway <sup>8</sup>Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Reproductive Medicine, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden

## Effects of infertility

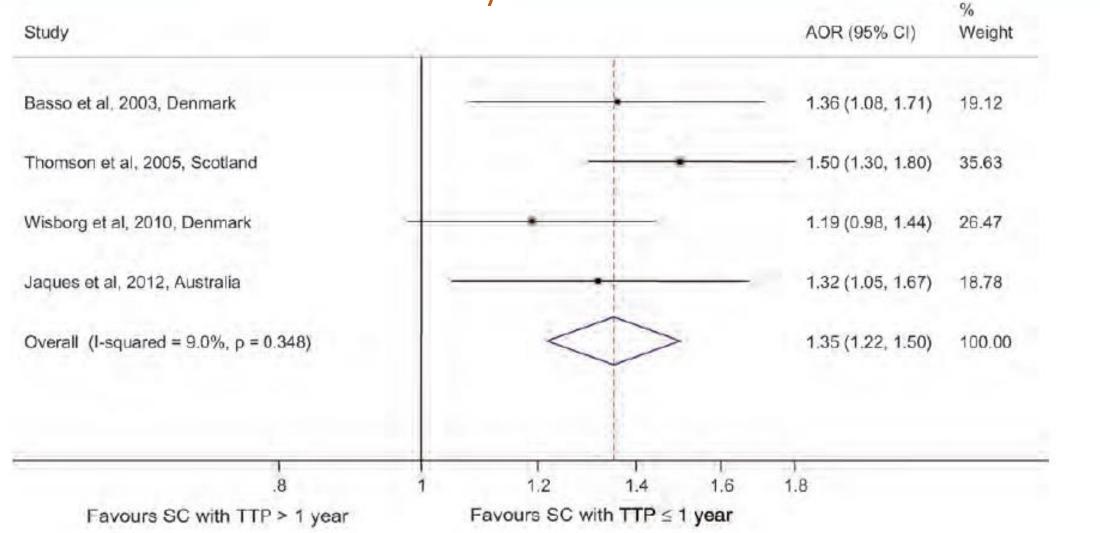


Figure 1 Pooled estimate on the risk of PTB in SC singletons of subfertile women with TTP > 1 year versus SC singletons of fertile women with TTP  $\leq$  1 year.  $\tau^2 = 0.0010$ . SC, spontaneous conception; AOR, adjusted odds ratio; Cl, confidence interval.

## ART vs. infertility

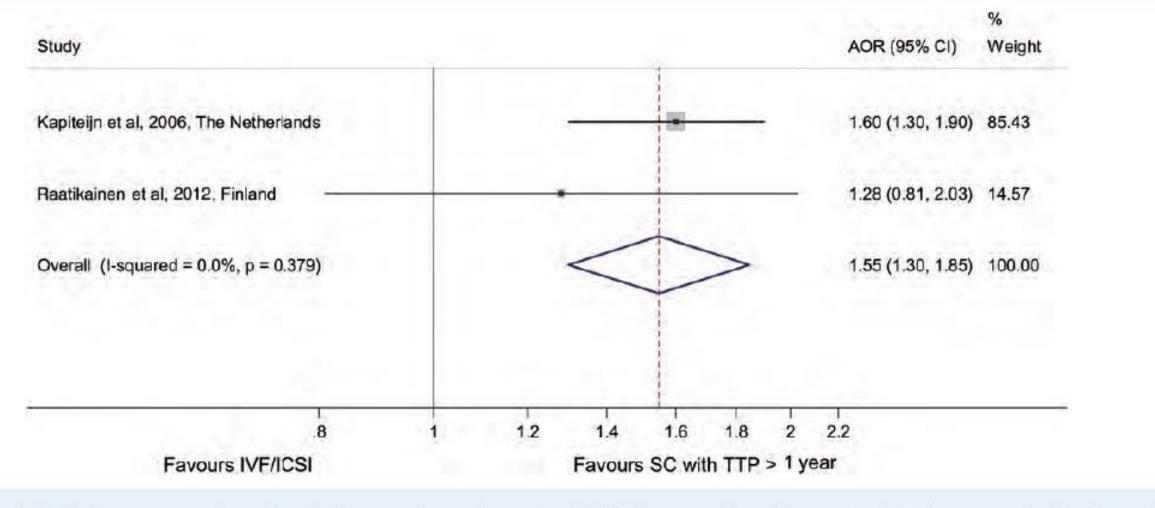


Figure 2 Pooled estimate on the risk of PTB in singletons born after IVF/ICSI versus SC singletons of subfertile women (TTP > I year).  $\tau^2 = 0.0000$ .

## ART vs. SC siblings

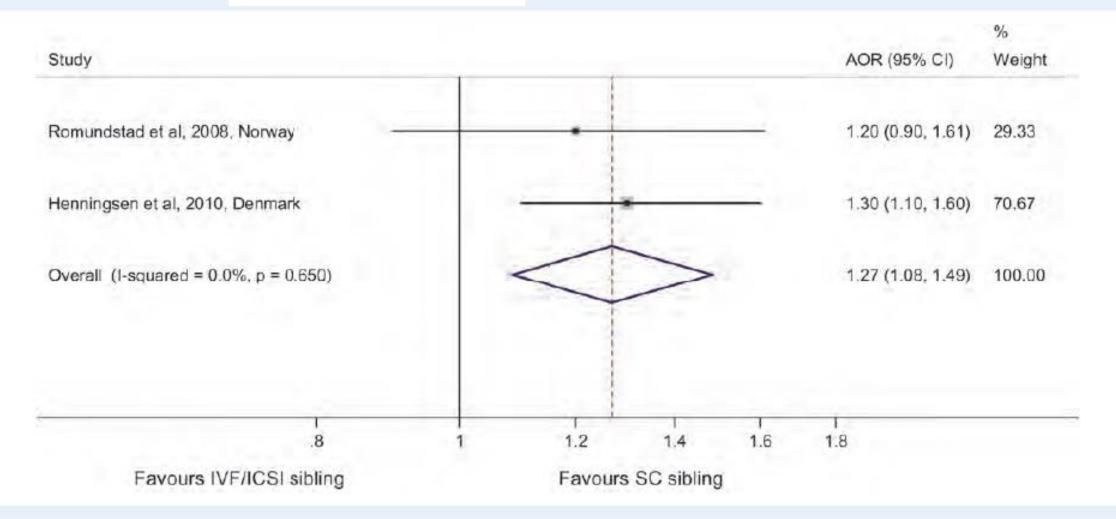


Figure 3 Pooled estimate on the risk of PTB in sibling studies of mothers to consecutive-singleton siblings of an IVF/ICSI child and an SC child.  $\tau^2 = 0.0000$ .

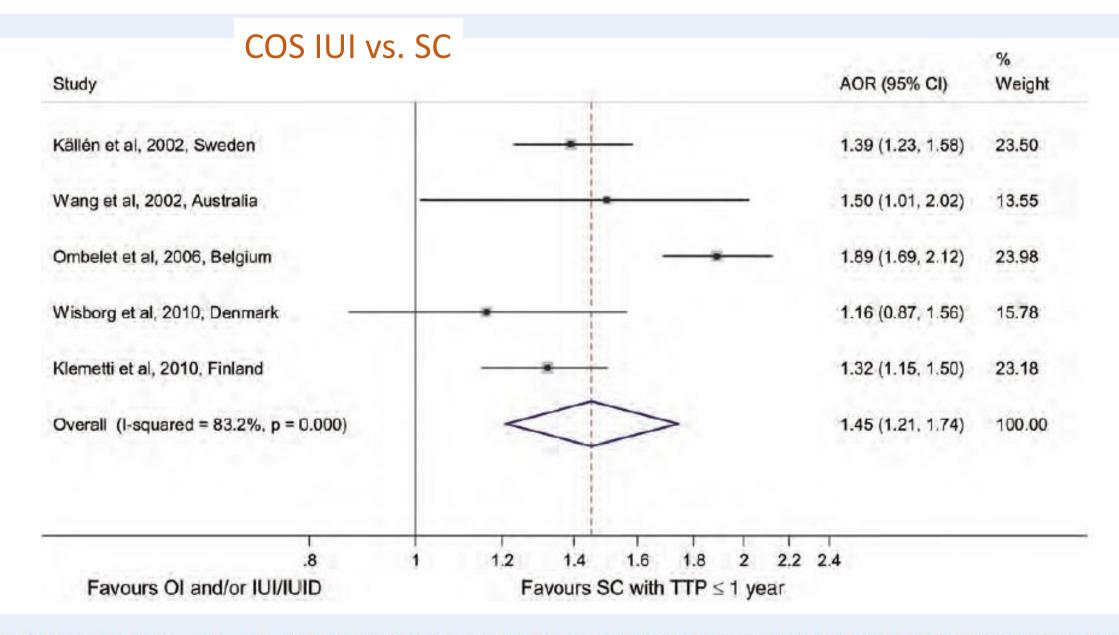


Figure 4 Pooled estimate on the risk of PTB in singletons born after OI and/or intrauterine insemination/donor (IUI/IUID) versus SC singletons of fertile women with TTP  $\leq$  I year.  $\tau^2 = 0.0329$ .

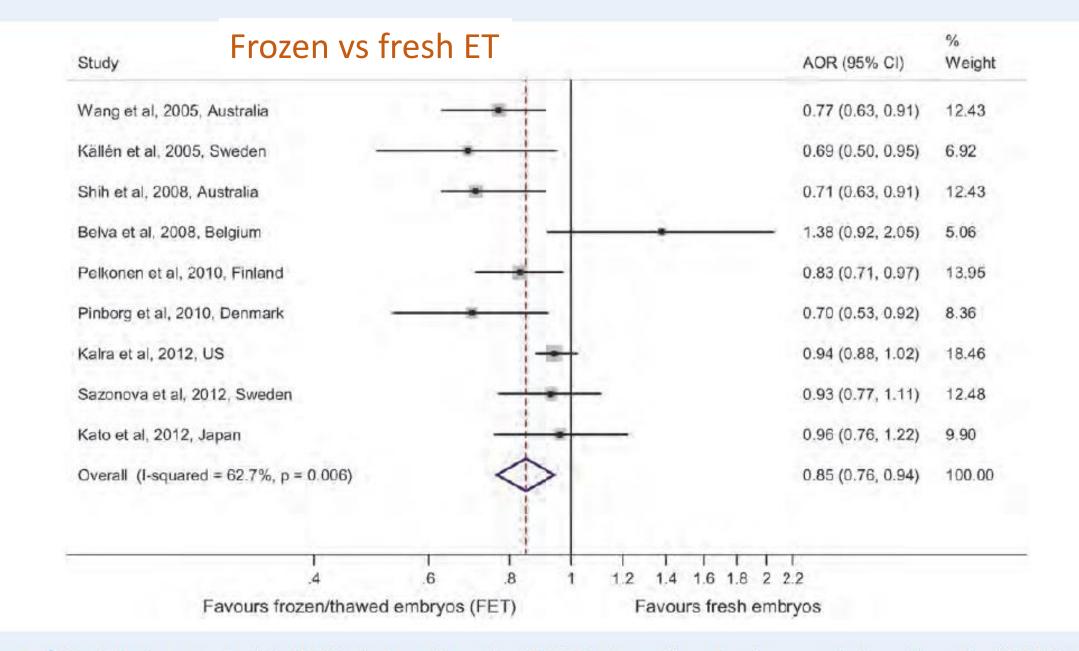


Figure 6 Pooled estimate on the risk of PTB in singletons born after IVF/ICSI in frozen/thawed cycles versus singletons born after IVF/ICSI in fresh cycles.  $\tau^2 = 0.0138$ .

COS and ART: wed by necessity

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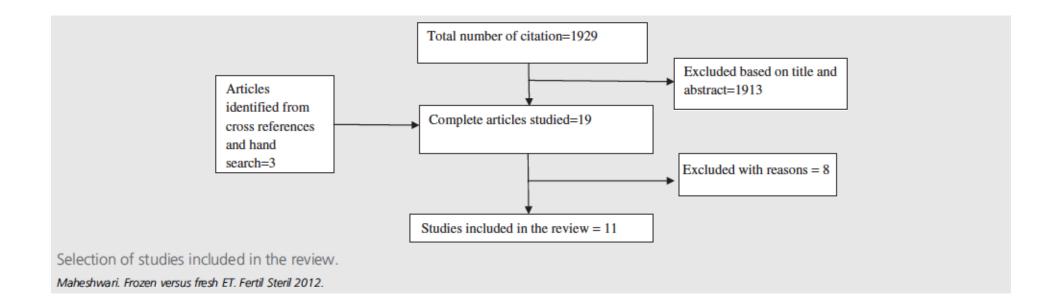
Fresh and frozen embryo transfers: the unexpected

- COS and oocyte quality
- COS and obstetrical outcome

Window of receptivity and endometrial vulnerability

> 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

Abha Maheshwari, M.D.,<sup>a</sup> Shilpi Pandey, M.R.C.O.G.,<sup>b</sup> Ashalatha Shetty, M.D.,<sup>b</sup> Mark Hamilton, M.D.,<sup>b</sup> and Siladitya Bhattacharya, M.D.<sup>a</sup>



## **Preterm labor**

### SUPPLEMENTAL FIGURE 2

	Frozen Fresh				Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
5.8.1 matched cohort							
Pinborg 2010	59	957	940	10,329	10.7%	0.68 [0.53, 0.87]	-
Shih 2008	220	2,387	383	3110	22.3%	0.75 [0.64, 0.88]	=
Wennerholm 1997 Subtotal (95% Cl)	9	160 3,504	18	160 13,599	1.2% 34.2%	0.50 [0.23, 1.08] 0.72 [0.63, 0.82]	•
Total events	288		1,341				
Heterogeneity: χ <sup>2</sup> = 1.3	2, df = 2 (/	P = .52)	; l <sup>2</sup> = 0%				
Test for overall effect:	Z = 4.93 (F	<.000	01)				
5.8.2 unmatched coh	ort						
Aflatoonian2010	11	84	18	252	0.6%	1.83 [0.90, 3.72]	<b></b>
Belva 2008	78	662	266	2,999	6.4%	1.33 [1.05, 1.69]	
Pelkonen 2010	120	1,830	258	2,942	13.3%	0.75 [0.61, 0.92]	-
Wang 2005	437	3,834	1,008	7,695	44.9%	0.87 [0.78, 0.97]	-
Wikland 2010	7	103	14	199	0.6%	0.97 [0.40, 2.32]	
Subtotal (95% CI)		6,513		14,087	65.8%	0.90 [0.83, 0.98]	•
Total events	653		1,564				
Heterogeneity: $\chi^2 = 17$ .	.62, df = 4	(P = .00	)1); l² = 7	7%			
Test for overall effect: 2	Z = 2.40 (F	P=.02)					
Total (95% CI)		10,017		27,686	100.0%	0.84 [0.78, 0.90]	•
Total events	941		2,905				
Heterogeneity: $\chi^2 = 27$ .	.25, df = 7	(P = .00	03); l <sup>2</sup> =	74%			0.01 0.1 1 10 10
Test for overall effect: 2	Z = 4.82 (#	<.000	01)				Frozen Fresh
Test for subgroup diffe	rences: χ²	= 7.95,	df = 1 (P	= .005),	l <sup>2</sup> = 87.4%	6	Hozori Hoan
eterm labor. CI = confide	ence interva	l; M-H =	Mantel-H	laenszel.			
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Maheshwari. Frozen versus fresh ET. Fertil Staril 2012.

## SGA

#### SUPPLEMENTAL FIGURE 4

	Frozen Fresh		Risk Ratio			Risk Ratio			
Study or Subgroup	Events 1	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl	
Pelkonen 2010	28	1,830	91	2,942	81.0%	0.49 [0.33, 0.75]			
Wikland 2010	3	103	24	199	19.0%	0.24 [0.07, 0.78]			
Total (95% CI)	1	1,933		3,141	100.0%	0.45 [0.30, 0.66]		•	
Total events	31		115						
Heterogeneity: χ <sup>2</sup> = 1.2	28, df = 1 (P	e .26	); I <sup>2</sup> = 229	6			0.04		100
Test for overall effect:	< .000	)1)		0.01	0.1 1 10 frozen fresh	100			
Small for gestational age. CI = confidence interval; M-H = Mantel-Haenszel.									

Maheshwari. Frozen versus fresh ET. Fertil Steril 2012.

## Low birth weight

### SUPPLEMENTAL FIGURE 5

	Froze	en 👘	Fres	h		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl	
5.6.1 matched cohort								
Henningsen 2011	11	716	20	716	2.0%	0.55 [0.27, 1.14]		
Pinborg 2010	42	957	764	10,329	13.0%	0.59 [0.44, 0.80]	+	
Wennerholm 1997 Subtotal (95% CI)	8	160 1,833	12	160 11,205	1.2% 16.3%	0.67 [0.28, 1.59] 0.59 [0.45, 0.78]	•	
Total events	61		796					
Heterogeneity: $\chi^2 = 0.1^{\circ}$	1, df = 2 (	P = .95	); l² = 0%	i i				
Test for overall effect: Z	= 3.83 (	P = .001	i)					
	-							
5.6.2 unmatched coho	ort							
Aflatoonian2010	16	84	40	252	2.0%	1.20 [0.71, 2.03]	+	
Belva 2008	44	662	227	2,999	8.3%	0.88 [0.64, 1.20]		
Pelkonen 2010	76	1,830	177	2,942	13.7%	0.69 [0.53, 0.90]		
Wada et al., 1994	13	177	68	527	3.4%	0.57 [0.32, 1.00]		
Wang 2005	277	3,847	829	7,676	55.7%	0.67 [0.59, 0.76]		
Wikland 2010	7	103	9	199	0.6%	1.50 [0.58, 3.92]		
Subtotal (95% CI)		6,703		14,595	83.7%	0.71 [0.64, 0.78]	* I	
Total events	433		1,350					
Heterogeneity: $\chi^2 = 9.5^{\circ}$	1, df = 5 (	P = .09	); $1^2 = 479$	%				
Test for overall effect: Z								
Total (95% CI)		8,536		25,800	100.0%	0.69 [0.62, 0.76]	*	
Total events	494		2,146					
Heterogeneity: $\chi^2 = 11.2$	16, df = 8	(P = .1)	9); F = 28	3%				
Test for overall effect: Z							0.01 0.1 1 10 100 Frozen Fresh	
Test for subgroup differ				P=.23),	l <sup>2</sup> = 29.5%		FI02en Fiesh	

Low birth weight (birth weight <2,500 g). CI = confidence interval; M-H = Mantel-Haenszel.

Maheshwari. Frozen versus fresh ET. Fertil Staril 2012.

### SUPPLEMENTAL FIGURE 7

	-		-						
	Froze		Fres			Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl		
5.1.1 Matched cohort									
Pinborg 2010	288	957	2,733	10,329	21.0%	1.14 [1.03, 1.26]	•		
Shih 2008	1,031	2,387	1,207	3,110	47.6%	1.11 [1.04, 1.19]	<b>—</b>		
Wennerholm 1997	42	160	36	160	1.6%	1.17 [0.79, 1.72]	+-		
Subtotal (95% CI)		3,504		13,599	70.3%	1.12 [1.06, 1.18]			
Total events	1,361		3,976						
Heterogeneity: $\chi^2 = 0.1$	7, df = 2 (/	P = .92	); l <sup>2</sup> = 0%						
Test for overall effect: 2	:= 4.19 (F	<.000	01)						
5.1.2 unmatched coho	urt								
Pelkonen 2010	519	1,830	818	2,942	28.5%	1.02 [0.93, 1.12]	•		
Wildand 2010	30	101	41	199	1.3%	1.44 [0.96, 2.16]	+		
Subtotal (95% CI)		1,931		3,141	29.7%	1.04 [0.95, 1.14]	•		
Total events	549		859						
Heterogeneity: χ <sup>2</sup> = 2.60	6, df = 1 (/	P = .10	); l <sup>2</sup> = 629	6					
Test for overall effect: 2	= 0.80 (F	<sup>2</sup> = .42)							
Total (95% CI)		5,435		16,740	100.0%	1.10 [1.05, 1.15]			
Total events	1,910		4835						
Heterogeneity: χ <sup>2</sup> = 4.86	6, df = 4 (/	P = .30	); l² = 189	6			0.01 0.1 1 10 100		
Test for overall effect: Z	= 3.90 (F	<.000	01)				Frozen Fresh		
Test for subgroup differences: $\chi^2 = 2.08$ , df = 1 (P = .15), l <sup>2</sup> = 51.9%									
Cesarean section. CI = confi	idence inte	rval: M.	H = Mant	el-Haers	70				
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Human Reproduction, Vol.28, No.9 pp. 2545-2553, 2013

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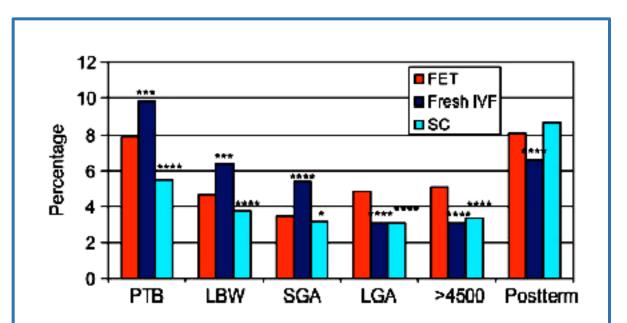
reproduction

Advanced Access publication on July 5, 2013 doi:10.1093/humrep/det272

**ORIGINAL ARTICLE Reproductive epidemiology** 

## Perinatal outcomes of children born after frozen-thawed embryo transfer: a Nordic cohort study from the CoNARTaS group

Ulla-Britt Wennerholm<sup>1,†\*</sup>, Anna-Karina Aaris Henningsen<sup>2,†</sup>, Liv Bente Romundstad<sup>3,4</sup>, Christina Bergh<sup>1</sup>, Anja Pinborg<sup>2</sup>, Rolv Skjaerven<sup>5,6</sup>, Julie Forman<sup>7</sup>, Mika Gissler<sup>8,9</sup>, Karl Gösta Nygren<sup>10</sup>, and Aila Tiitinen<sup>11</sup>



**Figure 3** Distribution of gestational age and birthweight in children born after FET, fresh IVF (IVF, ICSI, IVF/ICSI) and spontaneous conception (SC). FET versus fresh IVF: PTB: P = 0.0003, LBW: P = 0.0007, SGA: P < 0.0001, LGA: P < 0.0001,  $\geq 4500$  g: P < 0.0001, post-term birth: P < 0.0001 (adjusted *P* values). FET versus SC: PTB: P < 0.0001, LBW: P < 0.0001, SGA: P = 0.02, LGA: P < 0.0001,  $\geq 4500$  g: P < 0.0001 (adjusted *P* values). PTB, preterm birth; LBW, low birthweight; SGA, small for gestational age; LGA, large for gestational age;  $\geq 4500$ , birth weight  $\geq 4500$  g; postterm,  $\geq 42$  weeks. \* P < 0.05, \*\*\*P < 0.001, \*\*\*\*P < 0.0001.

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### Human Reproduction, Vol.29, No.6 pp. 1218-1224, 2014

human

reproduction

Advanced Access publication on March 20, 2014 doi:10.1093/humrep/deu053

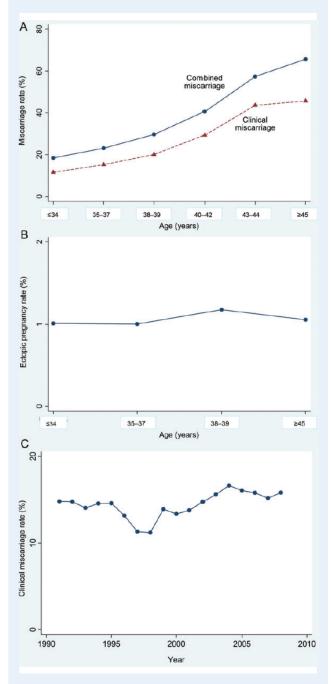
**ORIGINAL ARTICLE Infertility** 

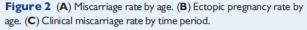
# Association between response to ovarian stimulation and miscarriage following IVF: an analysis of 124351 IVF pregnancies

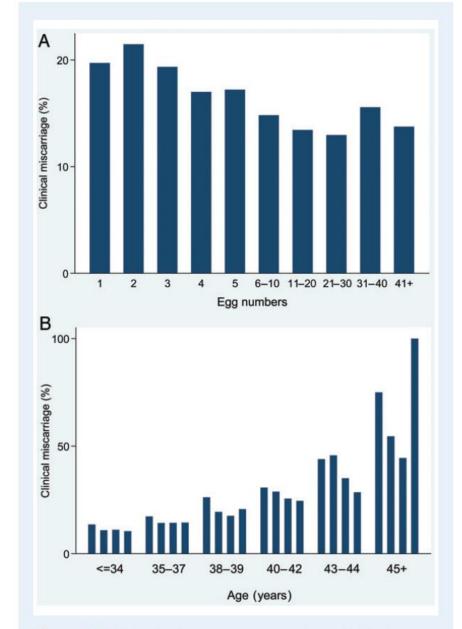
Sesh Kamal Sunkara<sup>1,\*</sup>, Yacoub Khalaf<sup>1</sup>, Abha Maheshwari<sup>2</sup>, Paul Seed<sup>1</sup>, and Arri Coomarasamy<sup>3</sup>

<sup>1</sup>King's College London, London, UK <sup>2</sup>University of Aberdeen, Aberdeen, UK <sup>3</sup>University of Birmingham, Birmingham, UK

\*Correspondence address. E-mail: sksunkara@hotmail.com







**Figure 3** Relationship between oocyte number and clinical miscarriage rate. (**A**) Overall association. (**B**) Stratified by age group. Each age group was divided according to oocyte number; from left to right: 1-3 oocytes, 4-9 oocytes, 10-14 oocytes,  $\geq 15$  oocytes.

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# Association of number of retrieved oocytes with live birth rate and birth weight: an analysis of 231,815 cycles of in vitro fertilization

Valerie L. Baker, M.D.,<sup>a</sup> Morton B. Brown, Ph.D.,<sup>b</sup> Barbara Luke, Sc.D., M.P.H.,<sup>c</sup> and Kirk P. Conrad, M.D.<sup>d</sup>

Fresh ET cycles with either **autologous** (n=194,627) or **donor** (n=37,188) oocytes reported to SART in the years 2004–2010

Fertil Steril 2015;103:931-8.

Oocyte source	Day of transfer	No. of retrieved oocytes	n	Length of gestation, wk (mean ± SD)	Birth weight, g (mean ± SD)	z-score (mean ± SD)	SGA, %	LB <b>W</b> , %
Autologus	Day/2-3	1–5	3,007	$38.3 \pm 2.1$	$3,263 \pm 580$	$0.02 \pm 0.96$	8.1	8.3
		6–10	7,352	$38.4 \pm 2.1$	$3,257 \pm 581$	$-0.02 \pm 0.97$	8.9	8.7
Trend		11–15	6,388	$38.4 \pm 2.2$	$3,244 \pm 591$	$-0.05 \pm 0.96$	9.3	8.8
w/ increasi	ng oocytes	16-25	5,538	$38.3 \pm 2.3$	$3,229 \pm 605$	$-0.04 \pm 0.95$	8.4	9.7
		≥26	1,310	$38.2 \pm 2.3$	3,193 ± 608	$-0.07 \pm 0.98$	9.5	11.5
		P value for trend		.002	< .0001	.0009	.43	.0001
		Adjusted P value <sup>a</sup>		.01	.0001	.005	.31	.0002
Donor	Days 2–3	1–5	138	$37.9 \pm 2.9$	3,222 ± 723	$0.05 \pm 1.08$	14.0	14.6
		6–10	810	$38.1 \pm 2.3$	3,229 ± 619	$0.06 \pm 0.95$	8.3	11.4
		11–15	1,150	$38.2 \pm 2.3$	3,280 ± 630	$0.12 \pm 1.02$	8.0	10.1
		16–25	1,596	$38.1 \pm 2.5$	$3,220 \pm 646$	$0.04 \pm 0.99$	7.8	11.4
		≥26	710	$38.2 \pm 2.1$	3,291 ± 586	$0.13 \pm 0.97$	7.6	8.9
		P value for trend		.59	.41	.42	.17	.21
		Adjusted <i>P</i> value <sup>a</sup>		.62	.39	.37	.16	.19
Autologus	Day/55-6	1–5	453	$38.0 \pm 2.1$	3,260 ± 603	$0.18 \pm 0.98$	6.7	8.8
		6–10	4,207	$37.9 \pm 2.1$	$3,243 \pm 583$	$0.15 \pm 0.99$	6.8	9.4
Trend		11–15	6,789	$37.9 \pm 2.3$	$3,209 \pm 603$	$0.07 \pm 0.95$	6.9	9.9
w/ increasir	ng oocytes	16-25	9,081	$37.9 \pm 2.4$	3,194 ± 625	$0.05 \pm 0.97$	7.8	10.8
		<u>∨</u> ≥26	2,951	$37.8 \pm 2.6$	3,178 ± 641	$0.07 \pm 0.96$	7.4	12.3
		P value for trend		.006	<.0001	<.0001	.06	<.0001
		Adjusted P value <sup>a</sup>		.01	<.0001	<.0001	.06	<.0001
Donor	Days 5–6	1–5	36	$38 \pm 2.7$	$3,260 \pm 694$	$0.20 \pm 1.05$	5.6	8.3
		6–10	589	$38 \pm 2.7$	$3,226 \pm 677$	$0.10 \pm 1.03$	8.9	10.5
		11–15	1,356	$38 \pm 2.4$	$3,255 \pm 615$	$0.13 \pm 0.99$	6.1	9.3
		16–25	2,743	$38 \pm 2.4$	3,236 ± 638	$0.11 \pm 1.00$	7.3	10.6
		≥26	1,768	$38 \pm 2.5$	3,223 ± 660	0.07 ± 0.96	8.1	10.7
		P value for trend		.80	.51	.14	.34	.73
		Adjusted P value <sup>a</sup>		.80	.58	.19	.37	.77

Birth outcomes by number of retrieved oocytes, oocyte source, and day of transfer for cycles with transfer of two embryos.

<sup>a</sup> The P value for trend was adjusted for female age and previous births.

Baker. Oocyte number and IVF outcomes. Fertil Steril 2015.

Oocyte source	Day of transfer	No. of retrieved oocytes	n	Length of gestation, wk (mean ± SD)	Birth weight, g (mean ± SD)	z-score (mean ± SD)	SGA, %	LB <mark>W</mark> , %
Autologus	Day/2-3	1–5	3,007	$38.3 \pm 2.1$	$3,263 \pm 580$	0.02 ± 0.96	8.1	8.3
		6–10	7,352	$38.4 \pm 2.1$	3,257 ± 581	$-0.02 \pm 0.97$	8.9	8.7
Trend		11-15	6,388	$38.4 \pm 2.2$	$3,244 \pm 591$	$-0.05 \pm 0.96$	9.3	8.8
w/ increasin	ig oocytes	16-25	5,538	$38.3 \pm 2.3$	$3,229 \pm 605$	$-0.04 \pm 0.95$	8.4	9.7
		√ ≥26	1,310	38.2 ± 2.3	3,193 ± 608	$-0.07 \pm 0.98$	9.5	11.5
		P value for trend		.002	<.0001	.0009	.43	.0001
6	D	Adjusted P value <sup>a</sup>	420	.01	.0001	.005	.31	.0002
Clonoor	Days 2–3	1-5	138	$37.9 \pm 2.9$	3,222 ± 723	$0.05 \pm 1.08$	14.0	14.6
Trend		6-10	810	38.1 ± 2.3	$3,229 \pm 619$	$0.06 \pm 0.95$	8.3	11.4
		11-15	1,150	$38.2 \pm 2.3$	$3,280 \pm 630$	$0.12 \pm 1.02$	8.0	10.1
w/ increasi	ng oocytes	16-25	1,596	$38.1 \pm 2.5$	$3,220 \pm 646$	$0.04 \pm 0.99$	7.8	11.4
		$\sqrt{\geq}26$	710	38.2 ± 2.1	3,291 ± 586	$0.13 \pm 0.97$	7.6	8.9
		P value for trend		.59	.41	.42	.17	.21
Autologue	Day 5 6	Adjusted P value <sup>a</sup>	450	.62	.39	.37	.16	.19
Autologus	Dayso-0	1–5 6–10	453	$38.0 \pm 2.1$	$3,260 \pm 603$	$0.18 \pm 0.98$	6.7	8.8 9.4
Trend			4,207	$37.9 \pm 2.1$	$3,243 \pm 583$	$0.15 \pm 0.99$	6.8	
		11-15	6,789	$37.9 \pm 2.3$	$3,209 \pm 603$	$0.07 \pm 0.95$	6.9	9.9
w/ increasin	g oocytes	16-25	9,081	$37.9 \pm 2.4$	$3,194 \pm 625$	$0.05 \pm 0.97$	7.8 7.4	10.8 12.3
		$\vee \geq 26$ <i>P</i> value for trend	2,951	37.8 ± 2.6	3,178 ± 641	0.07 ± 0.96 <.0001	.06	
				.006	<.0001 <.0001	<.0001	.06	<.0001 <.0001
Domor	Days 5–6	Adjusted P value <sup>a</sup> 1–5	36	$38 \pm 2.7$	$3,260 \pm 694$	$0.20 \pm 1.05$	5.6	8.3
	Days 5-0	6–10	589	$38 \pm 2.7$ $38 \pm 2.7$	$3,220 \pm 694$ $3,226 \pm 677$	$0.20 \pm 1.03$ $0.10 \pm 1.03$	5.6 8.9	10.5
Trend	\	11–15	1,356	$38 \pm 2.4$	$3,220 \pm 677$ $3,255 \pm 615$	$0.10 \pm 1.03$ $0.13 \pm 0.99$	6.1	9.3
w/ increasi	ng oocytes	16-25	2,743	$38 \pm 2.4$	$3,235 \pm 613$ $3,236 \pm 638$	$0.13 \pm 0.99$ $0.11 \pm 1.00$	7.3	10.6
	ing outytes	√ ≥26	1,768	$38 \pm 2.4$ $38 \pm 2.5$	$3,230 \pm 038$ $3,223 \pm 660$	$0.07 \pm 0.96$	8.1	10.8
		P value for trend	1,700	.80	.51	.14	.34	.73
		Adjusted P value <sup>a</sup>		.80	.51	.14	.34	.75
				.00		.12	, <u>,</u> , , , , , , , , , , , , , , , , ,	.//

Birth outcomes by number of retrieved oocytes, oocyte source, and day of transfer for cycles with transfer of two embryos.

<sup>a</sup> The P value for trend was adjusted for female age and previous births.

Baker. Oocyte number and IVF outcomes. Fertil Steril 2015.

### Human Reproduction Update, Vol.20, No.3 pp. 439-448, 2014

Advanced Access publication on January 30, 2014 doi:10.1093/humupd/dmu001

human reproduction update

## Neonatal outcomes among singleton births after blastocyst versus cleavage stage embryo transfer: a systematic review and meta-analysis

### S. Dar<sup>1,2,\*</sup>, T. Lazer<sup>1,2</sup>, P.S. Shah<sup>3</sup>, and C.L. Librach<sup>1,2,4</sup>

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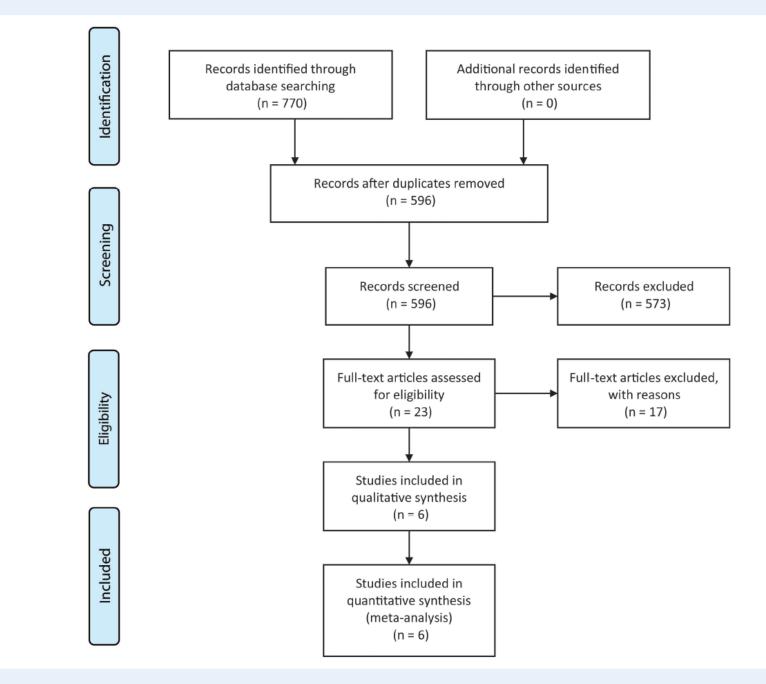


Figure | Flowchart for the selection of eligible studies.

## Preterm birth <37 weeks GA

## (a) Unadjusted data

	Blastocyst		Cleavage stage		Odds Ratio		Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Rando	om, 95% Cl	
Dar	548	3194	1335	9442	27.7%	1.26 [1.13, 1.40]			
Fernando	165	1716	228	2486	11.5%	1.05 [0.85, 1.30]		-	
Kallen	97	1071	757	10513	10.6%	1.28 [1.03, 1.60]			
Karla	2743	14743	4645	32351	45.8%	1.36 [1.29, 1.44]		-	
Martin	41	433	64	750	3.5%	1.12 [0.74, 1.69]	3 <del></del>		93
Wikland	21	302	9	194	1.0%	1.54 [0.69, 3.43]		-	
Total (95% CI)		21459		55736	100.0%	1.28 [1.18, 1.39]		•	
Total events	3615		7038						
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Ch	i <sup>2</sup> = 7.45	, df = 5 (P =	: 0.19); I <sup>≥</sup>	= 33%			1 5	
Test for overall effect	Z = 6.04	(P < 0.00	0001)	eter e			0.5 0.7 1 Cleavge stage	1.5 Blastocyst	2

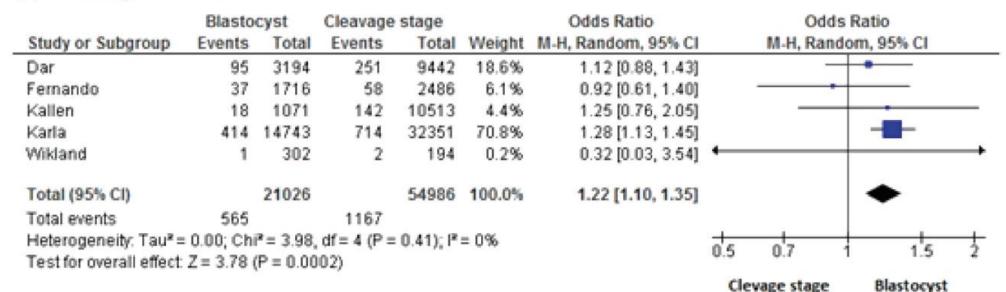
### (b) Adjusted data

				Adjusted OR	Adjust	ed OR	
Study or Subgroup	log[Adjusted OR]		SE Weight	IV, Random, 95% CI	I IV, Random, 95% CI		
Dar	0.277632	0.061677	32.5%	1.32 [1.17, 1.49]			
Fernando	-0.07257	0.172928	7.8%	0.93 [0.66, 1.31]			
Kallen	0.300105	0.119601	14.3%	1.35 [1.07, 1.71]			
Karla	0.329304	0.038475	45.4%	1.39 [1.29, 1.50]			
Total (95% CI)			100.0%	1.32 [1.19, 1.46]		•	
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi <sup>z</sup> = 5.35, d	f = 3 (P = 0.1	15); I <sup>2</sup> = 4	4%			
Test for overall effect: Z = 5.35 (P < 0.00001)					0.5 0.7 1 Cleavge stage	1.5 2 Blastocyst	

Figure 2 Meta-analysis of blastocyst versus cleavage stage embryo transfer for preterm birth <37 weeks. GA, gestational age.

## Preterm birth at <32 weeks GA

### (a) Unadjusted data



(b) Adjusted data

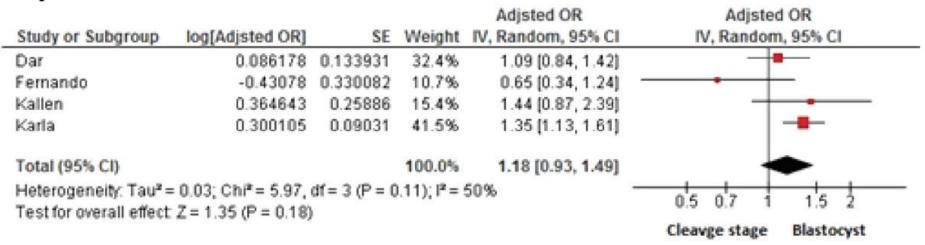


Figure 3 Meta-analysis of blastocyst versus cleavage stage embryo transfer for very preterm birth <32 weeks. GA, gestational age.

Human Reproduction, Vol.29, No.12 pp. 2794-2801, 2014

Advanced Access publication on October 14, 2014 doi:10.1093/humrep/deu246

human reproduction

**ORIGINAL ARTICLE** Reproductive epidemiology

## Clinical outcomes following cryopreservation of blastocysts by vitrification or slow freezing: a population-based cohort study

Z. Li<sup>1,2</sup>, Y.A. Wang<sup>1,3</sup>, W. Ledger<sup>1</sup>, D.H. Edgar<sup>4</sup>, and E.A. Sullivan<sup>1,2,\*</sup>

Table IVAdjusted relative risk for pregnancy outcomesfollowing transfer of slow frozen and vitrified blastocysts,Australia and New Zealand, 2009–2011.

	Slow freezing	Vitrification ARR (95% CI)
Thawed cycles result in transfer <sup>a</sup>	Ref	1.05 (1.03, 1.08)*
Pregnancy outcomes <sup>b</sup>		
Clinical pregnancies/thaw cycle <sup>a</sup>	Ref	1.43 (1.37, 1.50)*
Clinical pregnancies/embryo transfer	Ref	1.38 (1.32, 1.45)*
Live deliveries/thaw cycle <sup>a</sup>	Ref	1.47 (1.39, 1.55)*
Live deliveries/embryo transfer	Ref	1.41 (1.34, 1.49)*
Live deliveries/clinical pregnancy	Ref	1.02 (0.97, 1.08)
Miscarriage/clinical pregnancy	Ref	0.91 (0.82, 1.01)
Perinatal outcomes <sup>b</sup>		
Perinatal mortality	Ref	1.10 (0.64, 1.89)
Preterm delivery	Ref	0.97 (0.75, 1.25)
LBW births	Ref	1.08 (0.89, 1.31)
SGA births <sup>c</sup>	Ref	0.88 (0.70, 1.10)
LGA births <sup>c</sup>	Ref	0.89 (0.78, 1.02)

Compared with slow frozen blastocysts, vitrified blastocysts resulted in significantly higher clinical pregnancy and live delivery rates with similar perinatal outcomes.

COS and ART: wed by necessity

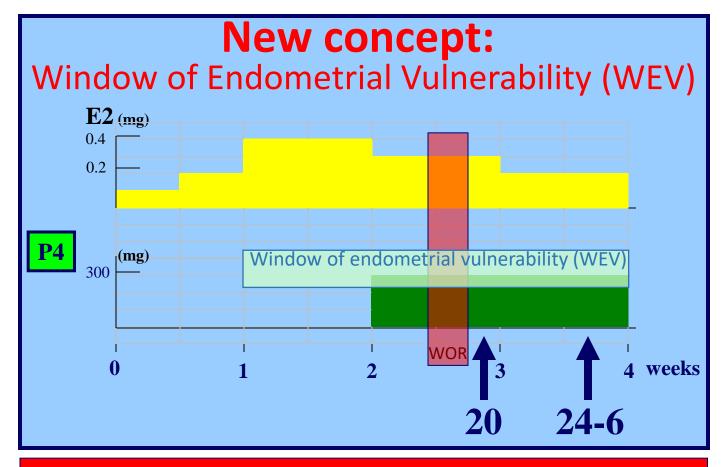
ART and obstetrical outcome: a little small, a little early

Fresh and frozen embryo transfers: the unexpected

COS and oocyte quality

COS and obstetrical outcome

Window of receptivity and endometrial vulnerability



<u>Window of receptivity (WOR)</u>: controlled by duration of exposure to P4

## Why we should transfer frozen instead of fresh embryos: the translational rationale

Rachel Weinerman, M.D. and Monica Mainigi, M.D.

KeyWords an vit. Fert. ration, Fize

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Division of Reproductive Endocrinology and Infertility, University of Pennsylvania, Philadelphia, Pennsylvania

asfer, superovulation, implantation, placentation

e with its authors and other ASRM members at http://

Epidemiologic studies have shown an increased rate of adverse perinatal outcomes, including smaller r getationa age (SGA) births, in fresh in vitro fertilization (IVF) cycles compared with frozen embryo transfer cycles. This acrease is no converte donor ocyte population, suggesting that it is the peri-implantation environment created after super vulation that responsible for these changes. population, suggesting that it is the peri-implantation environment created after supervisible vulation that a responsible for these changes. During a fresh IVF cycle, multiple corpora lutea secrete high levels of horizones and any factor that can affect the endometrium and the implanting embryo. In this review, we discuss both animals of hum in data lemo grating that superovulation has significant effects on the endometrium and embryo. Additionally, potential me tanks is for conductive effects of gonadotropin stimulation on implantation and placental development are proprise. We wink that the totata, along with the growing body of epidemiologic evidence, support the proposal that frozen embryor ransp ishold be considered preferentially, particularly in high responders, as a means to potentially decreate at least some of the adverse perinatal outcomes allociated with IVF. Fertil Steric 2014/02:10–8. ©2014 by American So-ciety for Reproductive fedicate.)



\* Download a free QR code scanner by searching for "QR scanner" in your smanphone's app store or app marketpla

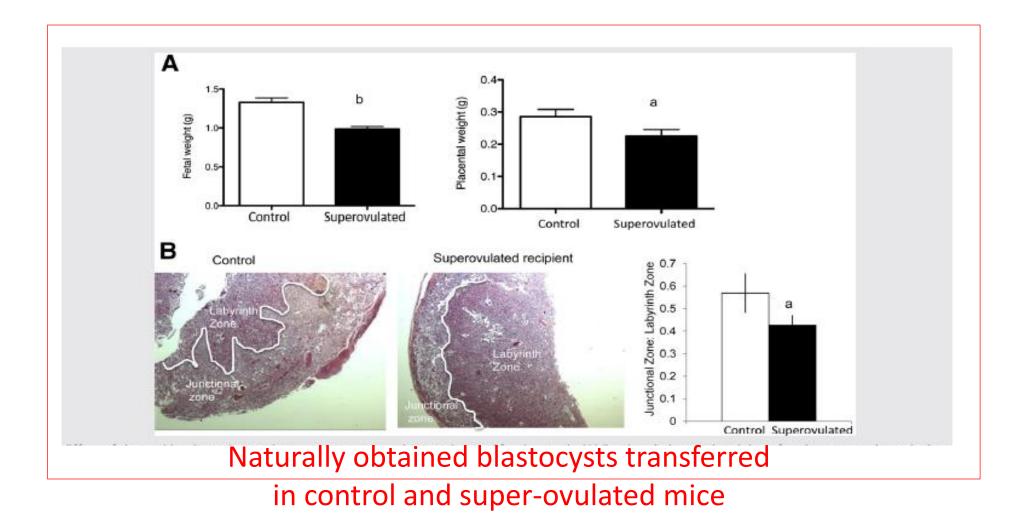
#### EFFECT OF SUPEROVULATION ON THE ENDOMETRIAL-EMBRYO INTERACTION Effect on Embryonic Development and Fetal Growth

#### Gene expression profiles of simulated and nonstimulated human endometrium during the window of embryo implantation.

	No. of	Fold change considered to	Number of genes		
Study		be significant	Up	Down	
Mirkin et al. (45)	13	≥1.2	5-6 <sup>a</sup>	1–6 <sup>a</sup>	
Horcajadas et al. (46)	19	≥3	281	277	
Simon et al. (47)	28	≥2	22-88ª	24–100 <sup>a</sup>	
Horcajadas et al. (48)	49	-	69	73	
iu et al. (49)	13	≥2	5-244ª	2-159 <sup>a</sup>	
Haouzi et al. (50)	84	≥2	321–657ª	0–4 <sup>a</sup>	

\* Ranges represent variation seen between different stimulation protocols.

Weinerman, Frozen vs. fresh ET: translational rationale, Fertil Steril 2014



Trimble Spitzer, MD<sup>1</sup> Victor Y. Fujimoto, MD<sup>2</sup>

## Year-one activity at FCC

# Thirty-five years later, the first assisted reproductive technology program opens in Cambodia

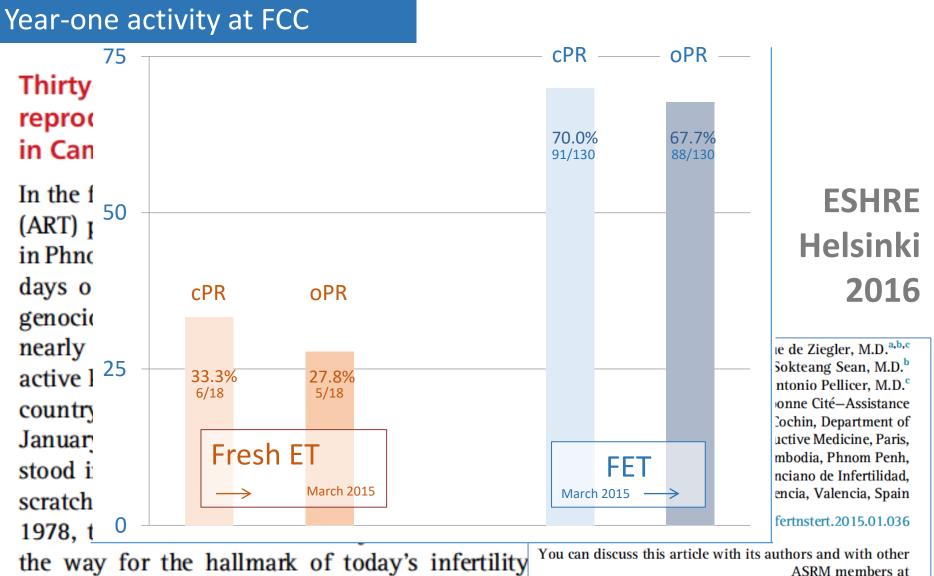
In the fall of 2014, the first assisted reproductive technology (ART) program opened in Cambodia. This event took place in Phnom Penh 35 years after Cambodia emerged—in the early days of 1979—from the worst geopolitical nightmare and genocide that the world has known since the Holocaust. In

nearly 4 years of abuse, the Khmer Rouge regi active killing and starvation had exterminated a country's population, who perished in the Killir January 1979—the nightmare suddenly over—t stood in rags and tears, with all needing to be scratch while wounds healed. Nearly concor 1978, the birth of the first baby conceived in the way for the hallmark of today's infertility worldwide, assisted reproductive technology, or 4

## Fertility Sterility 2015

Dominique de Ziegler, M.D.<sup>a,b,c</sup> Sokteang Sean, M.D.<sup>b</sup> Antonio Pellicer, M.D.<sup>c</sup> <sup>a</sup> Université Paris Descartes, Paris Sorbonne Cité—Assistance Publique Hôpitaux de Paris, CHU Cochin, Department of Obstetrics and Gynecology and Reproductive Medicine, Paris, France; <sup>b</sup> Fertility Clinic of Cambodia, Phnom Penh, Cambodia; and <sup>c</sup> Instituto Valenciano de Infertilidad, Universidad de Valencia, Valencia, Spain http://dx.doi.org/10.1016/j.fertnstert.2015.01.036

You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/dezieglerd-first-art-programcambodia/



worldwide, assisted reproductive technology, or

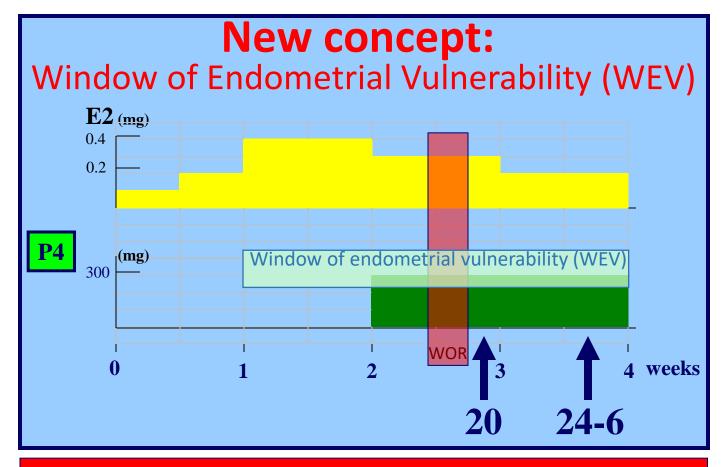
http://fertstertforum.com/dezieglerd-first-art-programcambodia/

## Ethnic variation in estradiol metabolism in reproductive age Asian and white women treated with transdermal estradiol

Heather G. Huddleston, M.D.,<sup>a</sup> Mitchell P. Rosen, M.D.,<sup>a</sup> Mark Gibson, M.D.,<sup>b</sup> Marcelle I. Cedars, M.D.,<sup>a</sup> and Victor Y. Fujimoto, M.D.<sup>a</sup>

<sup>a</sup> Department of Obstetrics, Gynecology and Reproductive Sciences, University of California at San Francisco, San Francisco, California; and <sup>b</sup> Department of Obstetrics and Gynecology, University of Utah, Salt Lake City, Utah

Asian women have significantly higher serum  $E_2$  levels during treatment with transdermal  $E_2$  compared with white women. This finding suggests altered metabolic clearance of this steroid hormone. (Fertil Steril<sup>®</sup> 2011;96:797–9. ©2011 by American Society for Reproductive Medicine.)



<u>Window of receptivity (WOR)</u>: controlled by duration of exposure to P4

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