



Ska vi frysa alla embryon vid IVF?

Christina Bergh

Reproduktionsmedicin, Sahlgrenska

Universitetssjukhuset, Göteborg

SFOG, Göteborg 2021

Inga jäv att deklarera

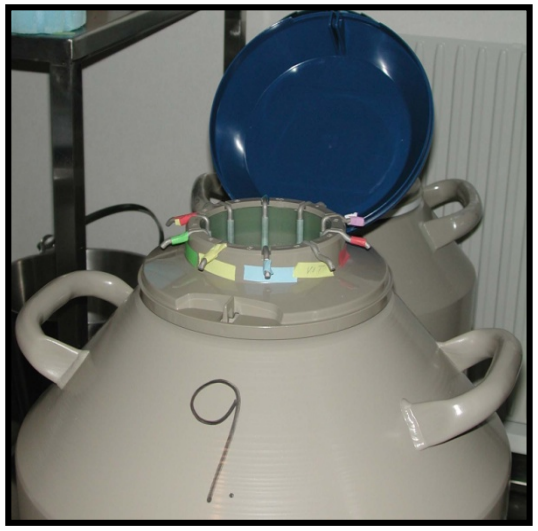
BAKGRUND

- >9 milj ART barn födda i världen *(ESHRE, 2021)*
- Upp till 7.7 % av nationella kohorter i Europa 2016 (Sverige 4.3 %)

  (ESHRE /EIM data, Wyns et al, Hum Reprod Open, 2020)
- 80 000 barn födda i Sverige (*www.qivf.se)*

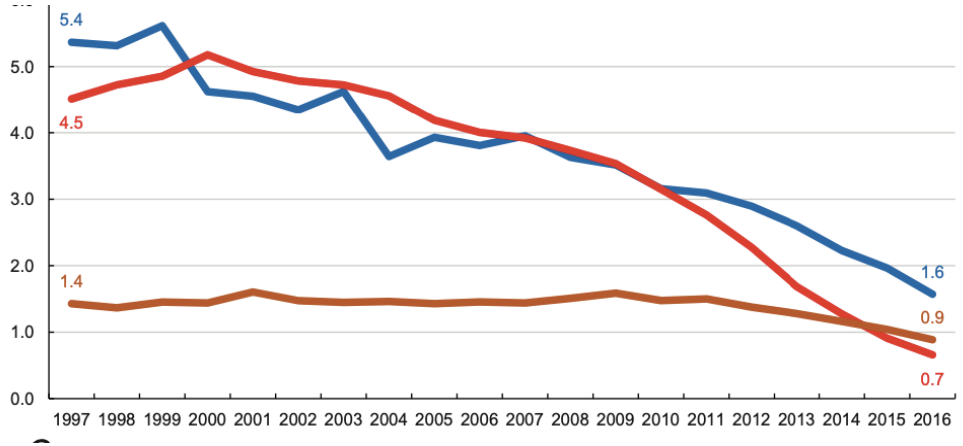
1983 första rapporten om graviditet och födsel efter frysning av embryon

Trounson and Mohr 1983, Zeilmaker et al, 1984

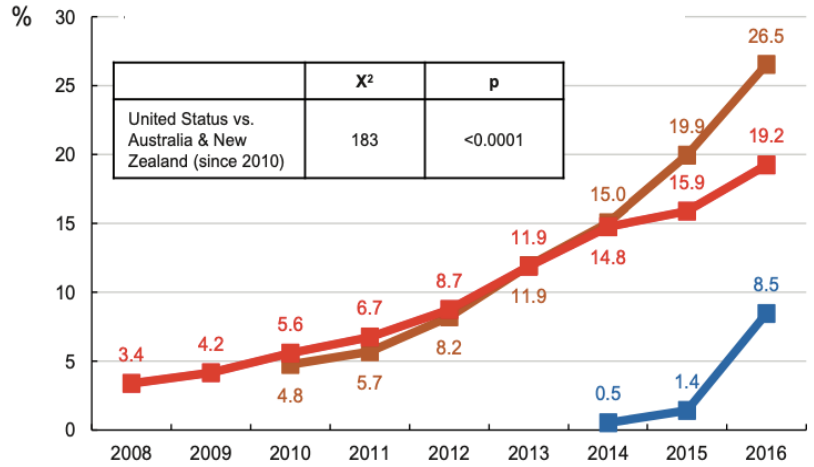


Färsk och frys embryo transfer-utveckling över tid

Ratio fresh cycle/frozen-thawed cycle



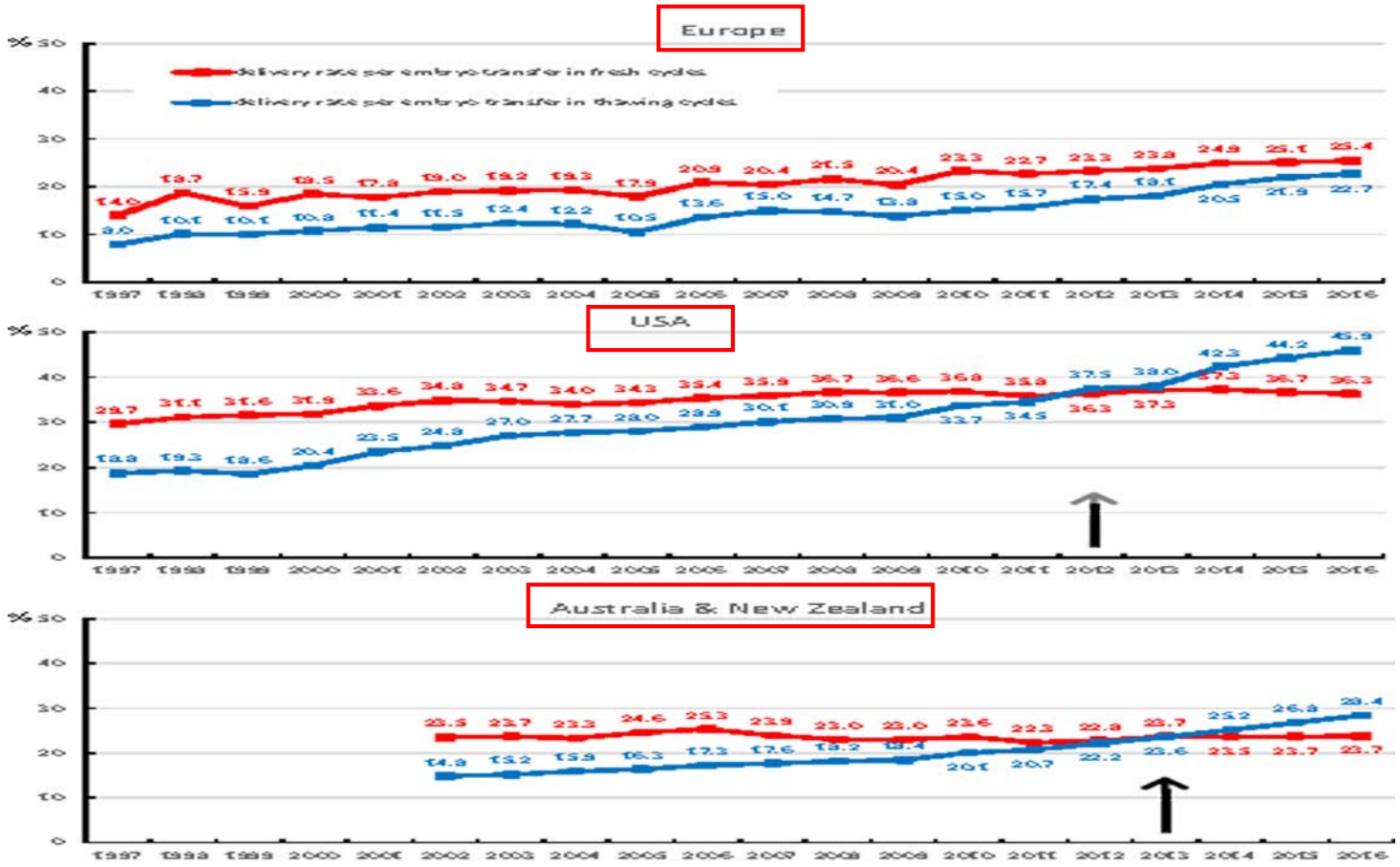
Freeze-all per oocyte retrieval, IVF/ICSI (%)



Europé
USA
Australia and New Zeeland

Hum Reprod 2020:35 (12): 2832–2849

Födsel per embryo transfer, färsk och fryst cykel

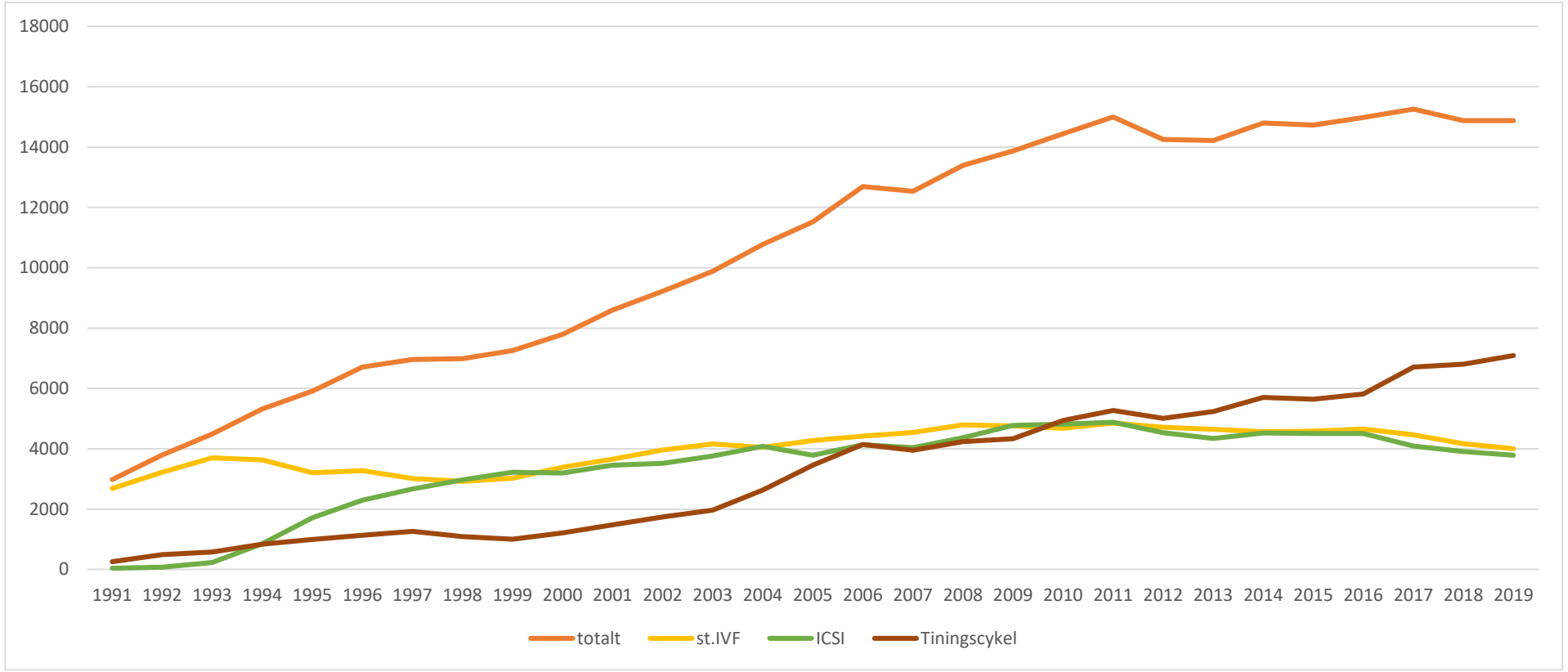


=färsk

=frys

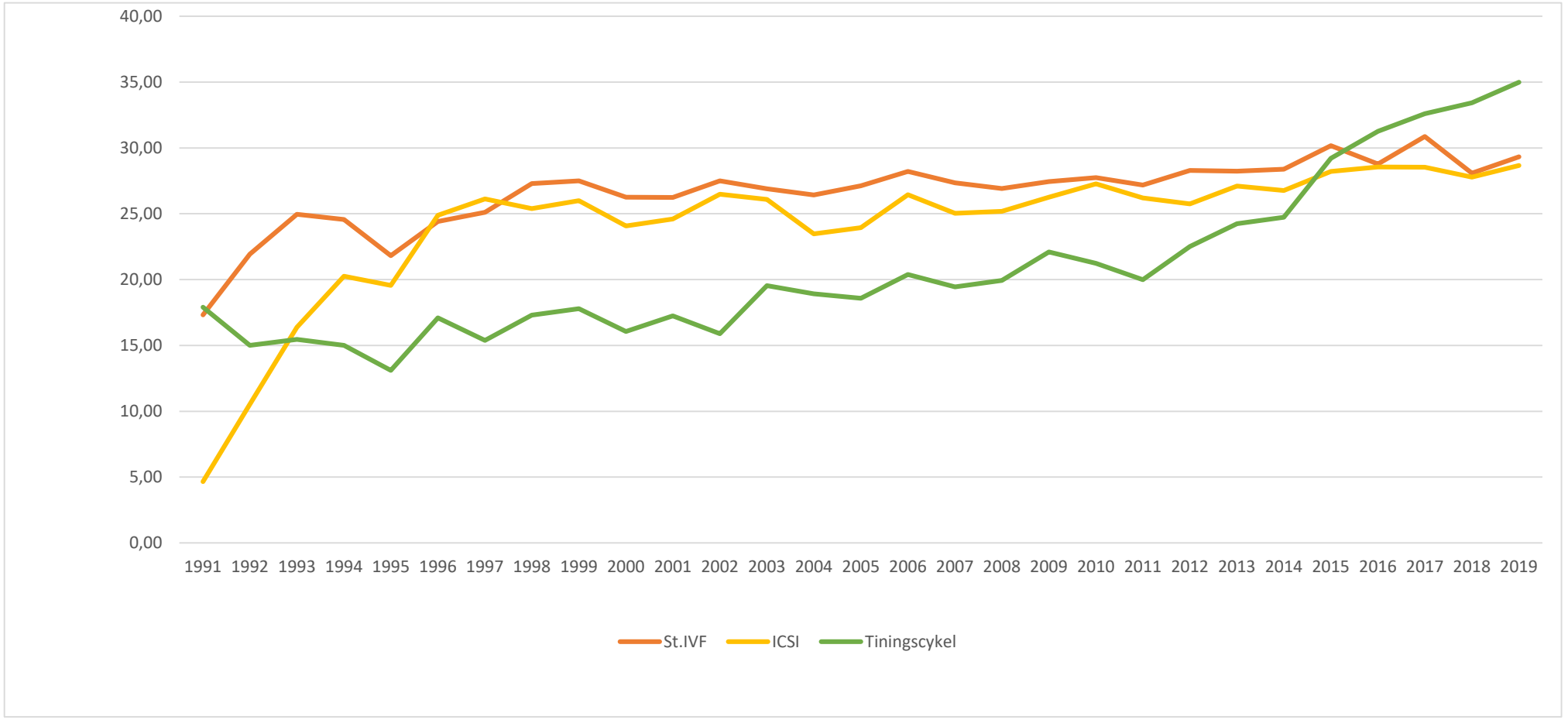
Hum Reprod 2020:35 (12): 2832–2849

Antal embryo återföranden med egna gameter och olika IVF tekniker
Sverige, 1991-2019



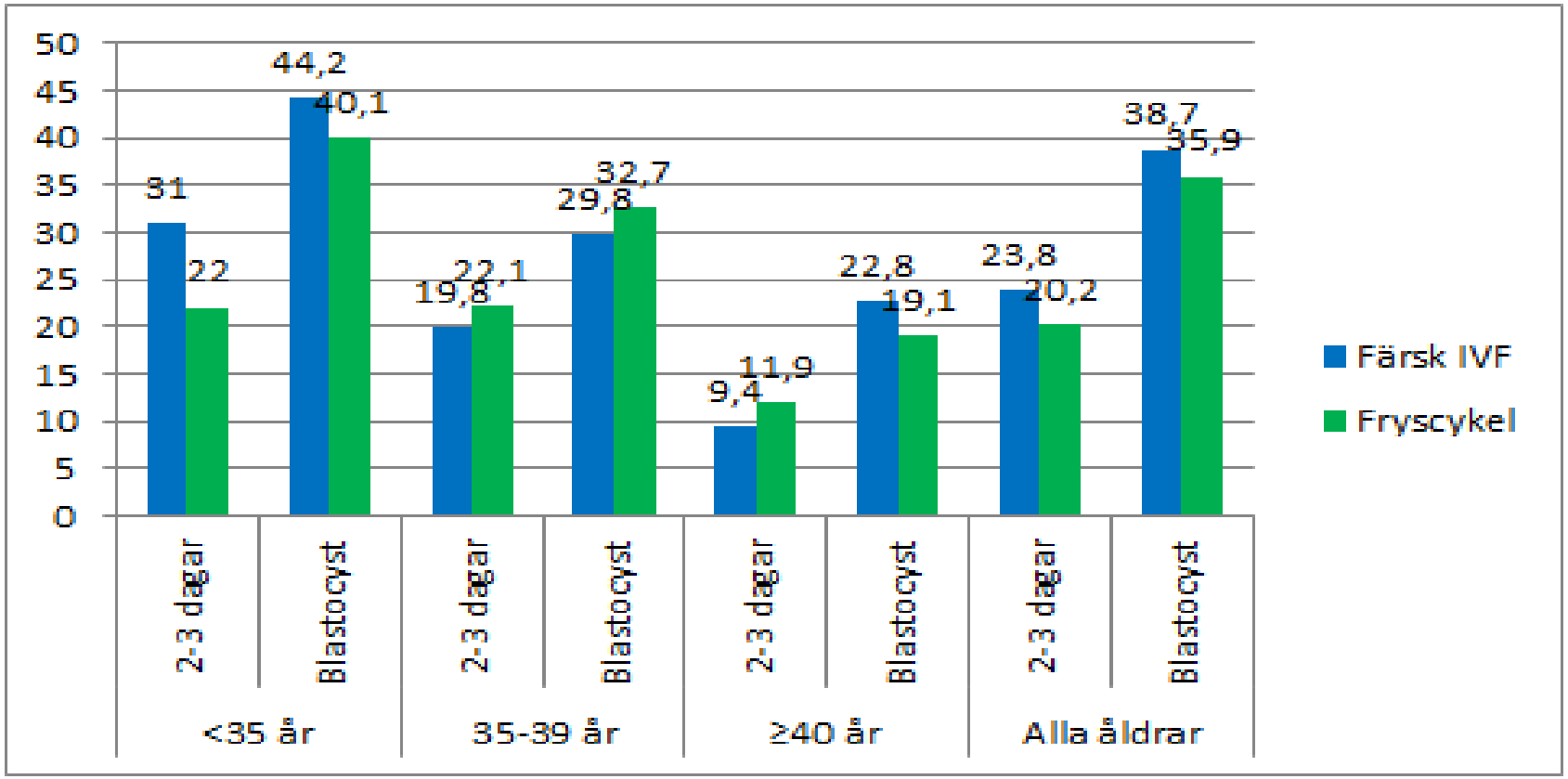
www.qivf.se

Andel förlossningar per embryo återförande och år, färsk IVF/ICSI och frysbehandling Sverige 1991-2019



www.qivf.se

Förlossning per ET: blastocyst vs dag 2-3, färsk IVF och fryscykel, 2019 Sverige



www.qivf.se

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fresh versus Frozen Embryos for Infertility in the Polycystic Ovary Syndrome

Z.-J. Chen, Y. Shi, Y. Sun, B. Zhang, X. Liang, Y. Cao, J. Yang, J. Liu, D. Wei, N. Weng, L. Tian, C. Hao, D. Yang, F. Zhou, J. Shi, Y. Xu, J. Li, J. Yan, Y. Qin, H. Zhao, H. Zhang, and R.S. Legro

ABSTRACT

Fresh ET-2 embryos, day 3, Cryo day 3 -vitrification

	Frozen ET n=746	Fresh ET n=762	Absolute difference, 95% CI
Live birth	368 (49.3%)	320 (42.0%)	7.3 (2.3-12.4)

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ABSTRACT

n=1508

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

IVF Transfer of Fresh or Frozen Embryos in Women without Polycystic Ovaries

Lan N. Vuong, M.D., Ph.D., Vinh Q. Dang, M.D., Tuong M. Ho, M.D., Bao G. Huynh, M.Sc., Duc T. Ha, M.D., Toan D. Pham, B.Sc., Linh K. Nguyen, M.D., Robert J. Norman, M.D., and Ben W. Mol, M.D., Ph.D.

ABSTRACT

n=782
Live birth 36.3% and 34.5%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transfer of Fresh versus Frozen Embryos in Ovulatory Women

Yuhua Shi, M.D., Ph.D., Yun Sun, M.D., Ph.D., Cuifang Hao, M.D., Ph.D., Heping Zhang, Ph.D., Daimin Wei, M.D., Ph.D., Yunshan Zhang, M.D., Yimin Zhu, M.D., Ph.D., Xiaohui Deng, M.D., Xiujuan Qi, M.D., Hong Li, M.D., Xiang Ma, M.D., Ph.D., Haiqin Ren, M.D., Yaqin Wang, M.D., Ph.D., Dan Zhang, M.D., Ph.D., Bo Wang, M.S., Fenghua Liu, M.D., Qiongfang Wu, M.D., Ze Wang, M.S., Haiyan Bai, Ph.D., Yuan Li, M.D., Ph.D., Yi Zhou, M.D., Mei Sun, M.D., Ph.D., Hong Liu, M.D., Ph.D., Jing Li, M.S., Lin Zhang, M.S., Xiaoli Chen, M.D., Ph.D., Songying Zhang, M.D., Ph.D., Xiaoxi Sun, M.D., Ph.D., Richard S. Legro, M.D., and Zi-Jiang Chen, M.D., Ph.D.

ABSTRACT

n=2157
Live birth 48.7% and 50.2%

Articles

Frozen versus fresh single blastocyst transfer in ovulatory women: a multicentre, randomised controlled trial

Daimin Wei*, Jia-Yin Liu*, Yun Sun*, Yuhua Shi*, Bo Zhang*, Jian-Qiao Liu, Jichun Tan, Xiaoyan Liang, Yunxia Cao, Ze Wang, Yingying Qin, Han Zhao, Yi Zhou, Haiqin Ren, Guimin Hao, Xiufeng Ling, Junzhao Zhao, Yunshan Zhang, Xiujuan Qi, Lin Zhang, Xiaohui Deng, Xiaoli Chen, Yimin Zhu, Xiaohong Wang, Li-Feng Tian, Qun Lv, Xiang Ma, Heping Zhang, Richard S Legro, Zi-Jiang Chen

Lancet 2019; 393: 1310–18

Summary

Background Elective single embryo transfer (eSET) has been increasingly advocated, but concerns about the lower

n=1650

Live birth 50.0% and 40.0%

Freeze-all versus fresh blastocyst transfer strategy during in vitro fertilisation in women with regular menstrual cycles: multicentre randomised controlled trial

Sacha Stormlund,[1] Negjyp Sopa,[1] Anne Zedeler,[1] Jeanette Bogstad,[2] Lisbeth Prætorius,[1] Henriette Svarre Nielsen,[2] Margaretha Laczna Kitlinski,[3] Sven O Skouby,[4] Anne Lis Mikkelsen,[5] Anne Lærke Spangmose,[2] Janni Vikkelsø Jeppesen,[2] Ali Khatibi,[6] Nina la Cour Freiesleben,[1] Søren Ziebe,[2] Nikolaos P Polyzos,[7] Christina Bergh,[6] Peter Humaidan,[8] Anders Nyboe Andersen,[2] Kristine Løssl,[2] Anja Pinborg[1,2]

BMJ, first published as 10.113

Table 3 | Reproductive outcomes for women in freeze-all and fresh transfer groups (intention-to-treat analysis). Data are number/total number (%) of women

Outcomes	Freeze-all group (n=223)	Fresh embryo transfer (n=230)	Difference between groups (percentage points (95% CI))	Risk ratio (95% CI)	P value
Primary outcome: ongoing pregnancy*					
Ongoing pregnancy rate/No of randomised women	62/223 (27.8)	68/230 (29.6)	−1.8 (−10.5 to 7.0)	0.98 (0.87 to 1.10)	0.76
Ongoing pregnancy rate/No of women who started stimulation	62/223 (27.8)	68/230 (29.6)	−1.8 (−10.5 to 7.0)	0.98 (0.87 to 1.10)	0.76
Ongoing pregnancy rate/No of oocyte retrievals	62/221 (28.1)	68/227 (30.0)	−1.9 (−10.8 to 6.9)	0.97 (0.86 to 1.10)	0.73
Ongoing pregnancy rate/No of embryo transfers	57/162 (35.2)	68/181 (37.6)	−2.4 (−13.2 to 8.4)	0.96 (0.82 to 1.13)	0.73
Secondary outcome: live birth†					
Live birth rate/No of randomised women	61/223 (27.4)	66/230 (28.7)	−1.3 (−10.1 to 7.4)	0.98 (0.87 to 1.10)	0.83
Live birth rate/No of women started stimulation	61/223 (27.4)	66/230 (28.7)	−1.3 (−10.1 to 7.4)	0.98 (0.87 to 1.10)	0.83
Live birth rate/No of oocyte retrievals	61/221 (27.6)	66/227 (29.1)	−1.5 (−10.3 to 7.3)	0.98 (0.87 to 1.10)	0.81
Live birth rate/No of embryo transfers	56/162 (34.6)	66/181 (36.5)	−1.9 (−12.6 to 8.8)	0.97 (0.83 to 1.14)	0.80

Not including women who withdrew their consent. All analyses by intention to treat.
*Ongoing pregnancy was defined as a detectable fetal heart beat after eight weeks of gestation.
†Live birth was defined as any sign of life following birth after 22 weeks of gestation.

Stormlund BMJ, 2020

Cochrane Library

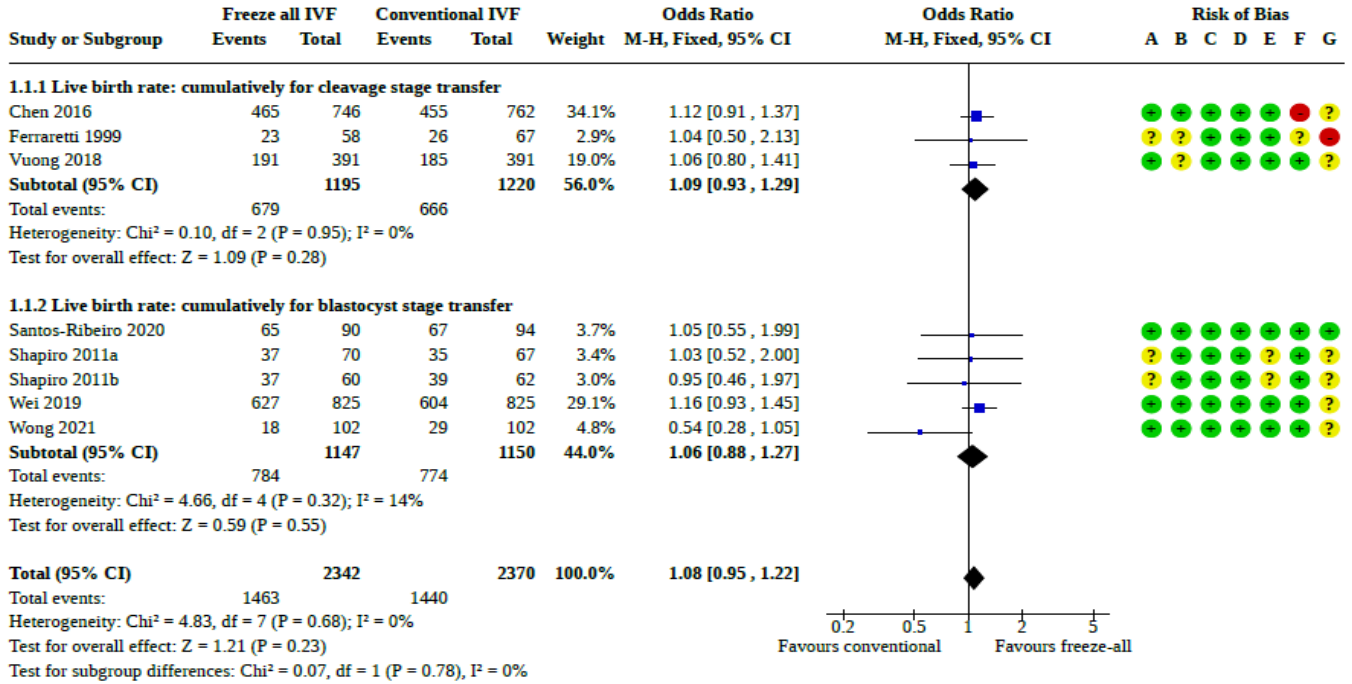
Cochrane Database of Systematic Reviews

Fresh versus frozen embryo transfers in assisted reproduction (Review)

Zaat T, Zagers M, Mol F, Goddijn M, van Wely M, Mastenbroek S

Cochrane Database of Systematic Reviews 2021, Issue 2. Art. No.: CD011184.
DOI: 10.1002/14651858.CD011184.pub3.

Figure 4. Forest plot of comparison 1. Freeze-all versus conventional IVF, outcomes per woman, outcome 1.1 live birth rate



Human Reproduction Open, Vol.00, No.0, pp. 1–9, 2021
doi:10.1093/hropen/hoab021

human reproduction open
ORIGINAL ARTICLE

Cumulative live birth rate after IVF: trend over time and the impact of blastocyst culture and vitrification

Zoha Saket [1,*], Karin Källén[2], Kersti Lundin[1,3], Åsa Magnusson [1,3], and Christina Bergh[3]

[1]Department of Reproductive Medicine, Sahlgrenska University Hospital, Göteborg, Sweden [2]Unit of Reproduction Epidemiology, Department of Obstetrics and Gynecology, Tornblad Institute, Institution of Clinical Sciences, Lund University, Lund, Sweden [3]Reproductive Medicine, Department of Obstetrics and Gynecology, Institute of Clinical Sciences, Sahlgrenska Academy, Sahlgrenska University Hospital, Göteborg University, Göteborg, Sweden

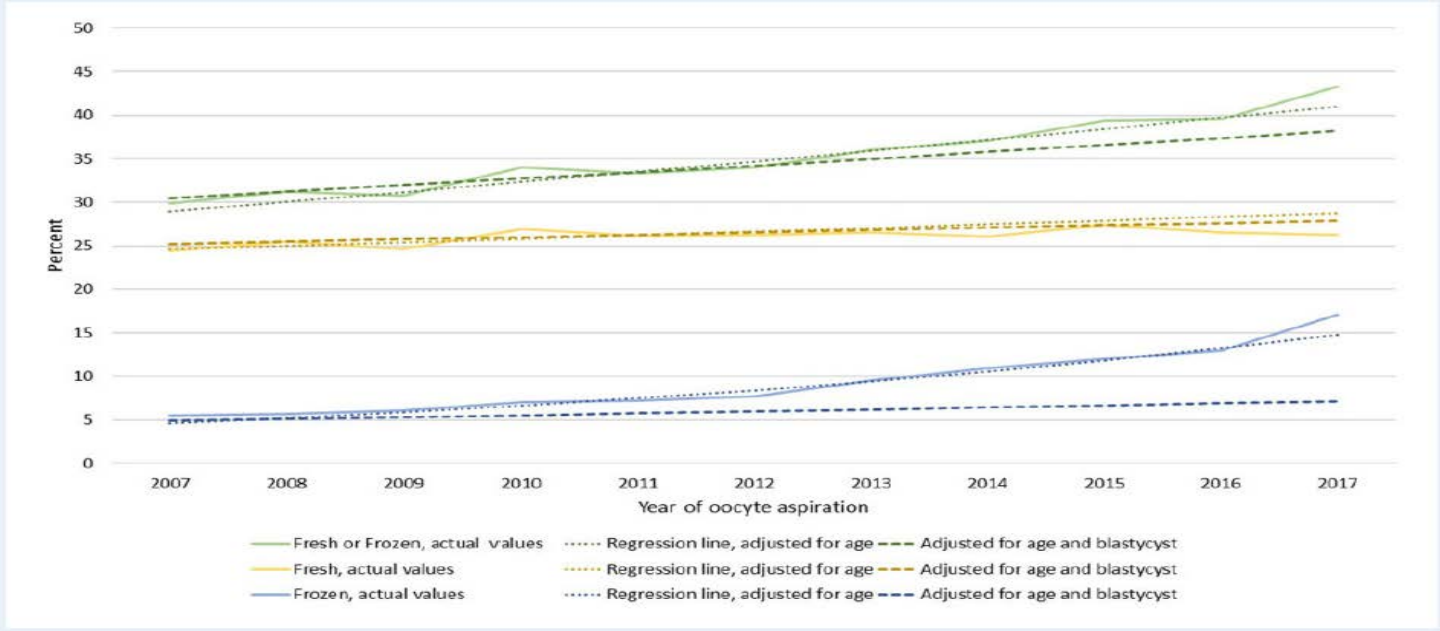


Figure 4. CLBR per oocyte aspiration by year of treatment, with oocyte aspirations not amounting to any ET excluded. Data separated for live birth rate after fresh ET (yellow) and the additive live birth rate after transfer of frozen embryos (blue) from the same oocyte retrieval, and live birth rate after fresh or frozen cycles from the same oocyte retrieval (green). Actual rates and regression lines with adjustment for age and blastocyst transfer. CLBR, cumulative live birth rate. ET, embryo transfer.

n=124 700
2007-2017

Year of treatment	2007	2011	2017
Number of oocyte aspirations	9782	11 467	11 931
Maternal age≥ 35 years, %	38.5	43.3	40.1
ICSI, %	48	50	48
SET, fresh, %	70	74	84
SET, FET, %	74	89	98
Blastocyst transfer rate, fresh, %	5	11	31
Blastocyst transfer rate, FET, %	6	30	88
Number of oocytes retrieved, median (IQR)	9 (7)	8 (7)	9 (7)

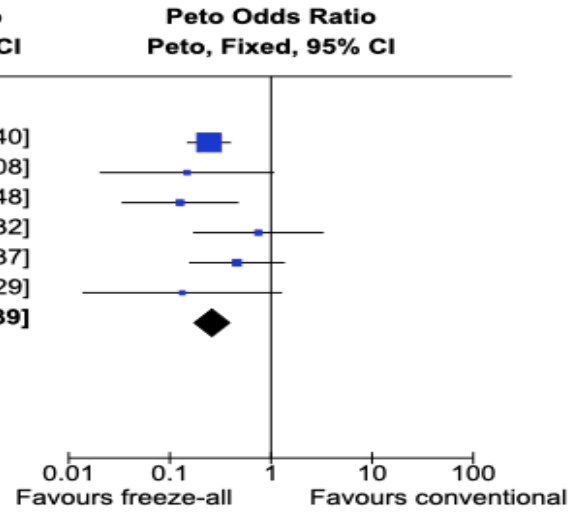
CLBR (per OPU):27.0% till 36.3%
CLBR (minst en ET): 30.0% till 43.3%

”Freeze-all” jämfört med konventionell IVF: Ovariellt hyperstimulerings -syndrom (OHSS)

Study or Subgroup	Freeze all IVF Events	Total	Conventional IVF Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
1.2.1 Per cycle with ovarian hyperstimulation						
Chen 2016	10	746	54	762	63.4%	0.24 [0.15 , 0.40]
Ferraretti 1999	0	58	4	67	4.0%	0.15 [0.02 , 1.08]
Santos-Ribeiro 2020	0	104	9	105	9.0%	0.13 [0.03 , 0.48]
Vuong 2018	3	391	4	391	7.2%	0.75 [0.17 , 3.32]
Wei 2019	4	825	9	825	13.3%	0.46 [0.15 , 1.37]
Wong 2021	0	102	3	102	3.1%	0.13 [0.01 , 1.29]
Subtotal (95% CI)		**2226**		**2252**	**100.0%**	**0.26 [0.17 , 0.39]**
Total events:	17		83			

Heterogeneity: Chi² = 4.85, df = 5 (P = 0.43); I² = 0%

Test for overall effect: Z = 6.61 (P < 0.00001)



Zaat *et al* Cochrane Syst Rev 2021 Feb 4;2(2):CD011184

Enkelbörd: ART vs spontan konception

Systematiska översikter and meta-analyser

AOR or RR, 95% CI	Helmerhorst 2004	Jackson 2004	McGovern 2004	McDonald 2009	Pandey 2012	Qin 2017
No of studies, no of children	12* 5361	14* 12 114	27 14 748	15* 31 032	22** 27 819	52 181 741
<37 w	2.0 (1.8-2.3)	2.0 (1.7-2.2)	2.0 (1.8-2.2)	1.8 (1.5-2.2)	1.5 (1.5-1.6)	1.7
<32 w	3.3 (2.0-5.3)	3.1 (2.0-4.8)	2.5 (0.9-7.2)	2.3 (1.7-3.0)	1.7 (1.5-1.9)	2.0
<2500 g	1.7 (1.5-1.9)	1.8 (1.4-2.2)	-	1.6 (1.3-2.0)	1.6 (1.6-1.8)	1.5
<1500 g	3.0 (2.1-4.4)	2.7 (2.3-3.1)	-	2.6 (1.8-3.8)	1.9 (1.7-2.2)	2.0
SGA	1.4 (1.2-2.7)	1.6 (1.3-2.0)	-	1.4 (1.0-2.0)	1.4 (1.3-1.5)	1.2

*Cohort studies, matched or adjusted for at least maternal age

Human Reproduction, Vol.30, No.3 pp. 710–716, 2015
Advanced Access publication on January 20, 2015 doi:10.1093/humrep/deu345

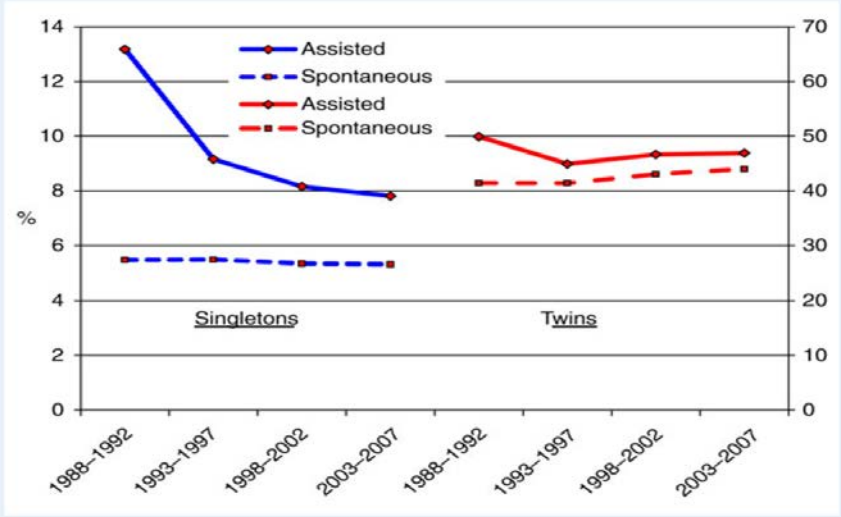
human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Trends in perinatal health after assisted reproduction: a Nordic study from the CoNARTaS group

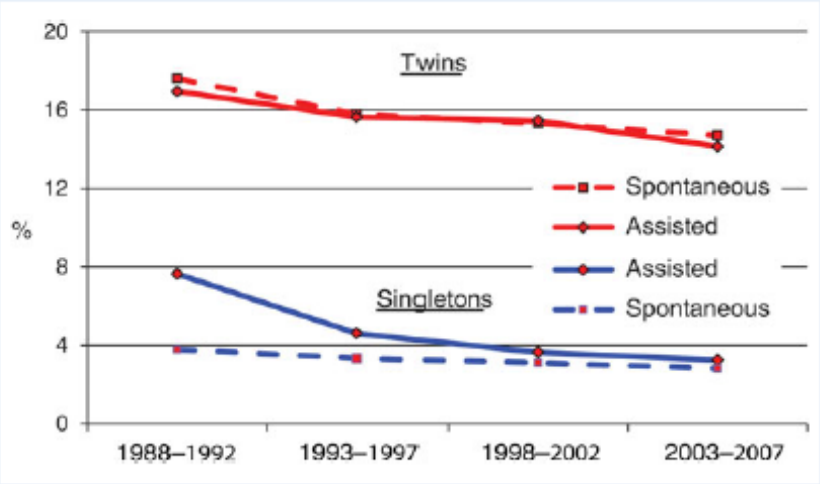
A.A. Henningsen[1,*], M. Gissler[2,3], R. Skjaerven[4,5], C. Bergh[6,7], A. Tiitinen[8], L.B. Romundstad[9,10], U.B. Wennerholm[11], O. Lidegaard[12], A. Nyboe Andersen[1], J.L. Forman[13], and A. Pinborg[14]

CoNARTaS
Committee of Nordic Assisted Reproductive Technology and Safety

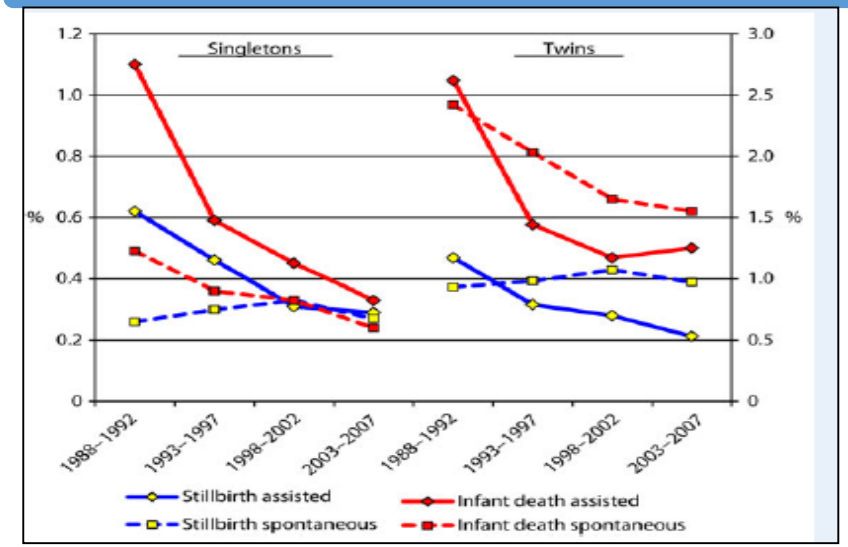
ART singleton and twins : <37 weeks



ART singleton and twins: SGA



ART singleton and twins: IUFD and death <1year



Human Reproduction, Vol.28, No.9 pp. 2545–2553, 2013
Advanced Access publication on July 5, 2013 doi:10.1093/humrep/det272

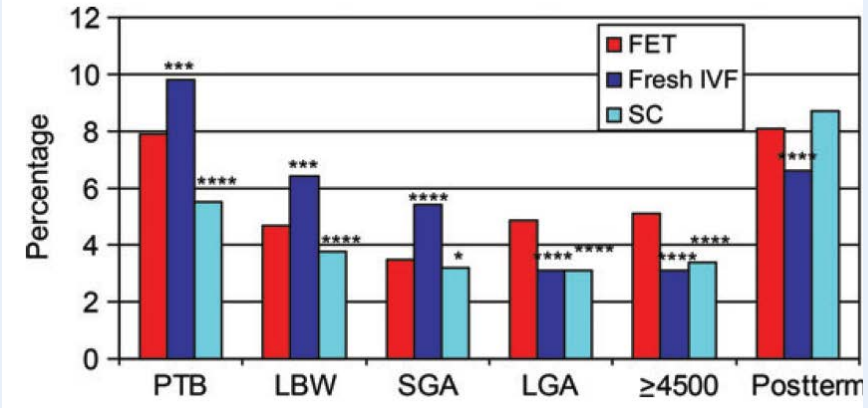
human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

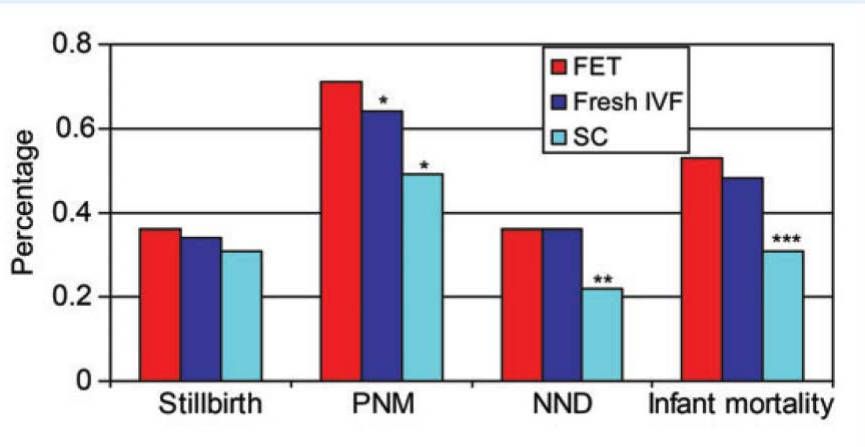
Perinatal outcomes of children born after frozen-thawed embryo transfer: a Nordic cohort study from the CoNARTaS group

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

CoNARTaS
Committee of Nordic Assisted Reproductive Technology and Safety

Singletons:
IVF- frozen/thawed embryos (FET): 6 647
IVF – fresh embryos: 42 242
SC: 288 547





FET vs fresh IVF and FET vs SC
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001
Adjusted for maternal age, parity, year of birth, gender and country

Human Reproduction Update, Vol.24, No.1 pp. 35–58, 2018
Advanced Access publication on November 13, 2017 doi:10.1093/humupd/dmx031

human reproduction update

Is frozen embryo transfer better for mothers and babies? Can cumulative meta-analysis provide a definitive answer?

Abha Maheshwari [1,*], Shilpi Pandey[2], Edwin Amalraj Raja[3], Ashalatha Shetty[1], Mark Hamilton[1], and Siladitya Bhattacharya[3]

[1]Aberdeen Maternity Hospital NHS Grampian, AB 25 2ZL, Scotland, UK [2]CARE Fertility Nottingham, John Webster House, 6 Lawrence Drive, Nottingham Business Park, Nottingham NG8 6PZ, UK [3]School of Medicine and Dentistry, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, UK

*Correspondence address. Aberdeen Maternity Hospital NHS Grampian, AB 25 2ZL, Scotland, UK. E-mail: abha.maheshwari@abdn.ac.uk
orcid.org/0000-0002-3652-2447

Submitted on July 31, 2017; resubmitted on September 19, 2017; editorial decision on October 5, 2017; accepted on October 9, 2017

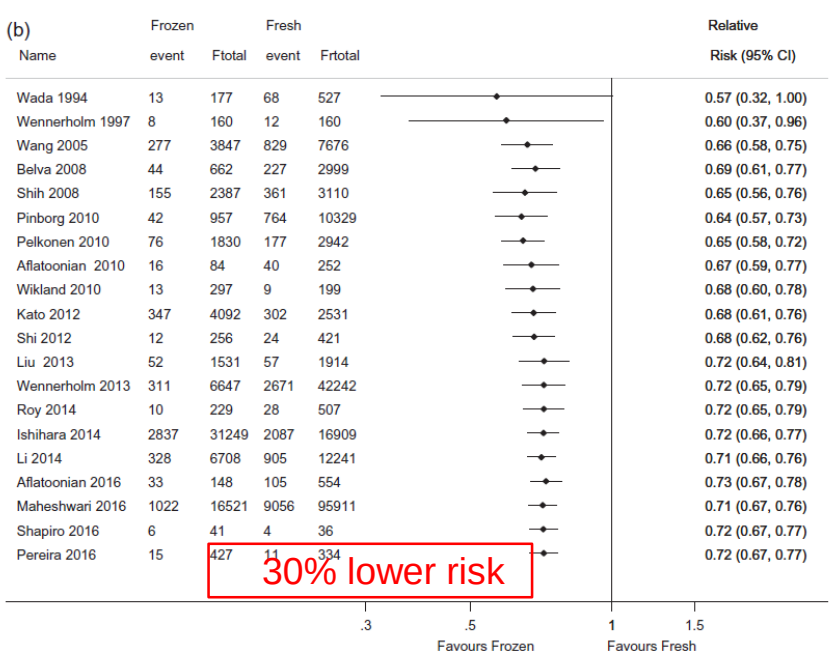


Figure 3 Low birth weight (less than 2500g): (**a**) meta-analysis and (**b**) cumulative meta-analysis.

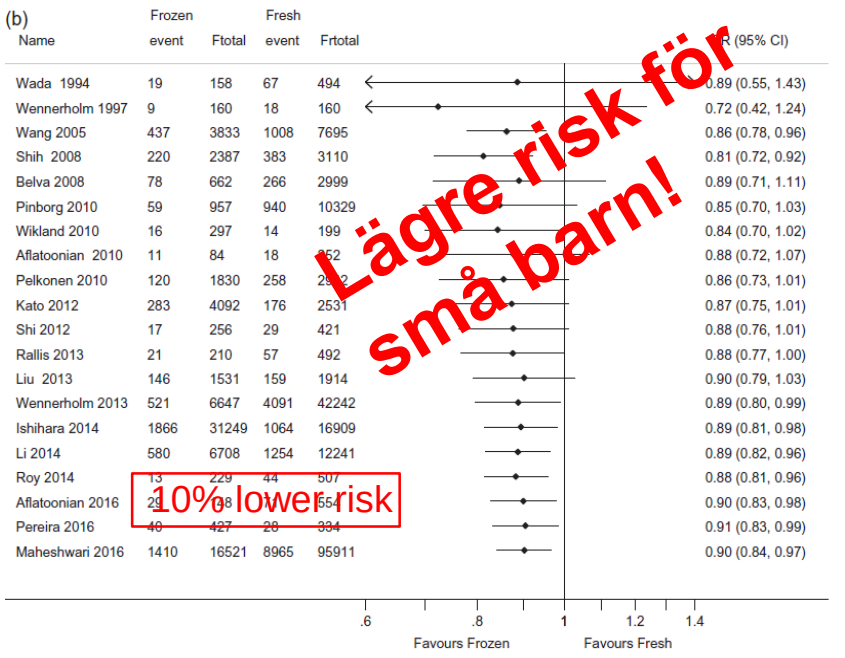


Figure 4 Preterm delivery (at less than 37 weeks): (**a**) meta-analysis and (**b**) cumulative meta-analysis.

Human Reproduction Update, Vol.24, No.1 pp. 35–58, 2018
Advanced Access publication on November 13, 2017 doi:10.1093/humupd/dmx031

human reproduction update

Is frozen embryo transfer better for mothers and babies? Can cumulative meta-analysis provide a definitive answer?

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[1]Aberdeen Maternity Hospital NHS Grampian, AB 25 2ZL, Scotland, UK [2]CARE Fertility Nottingham, John Webster House, 6 Lawrence Drive, Nottingham Business Park, Nottingham NG8 6PZ, UK [3]School of Medicine and Dentistry, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, UK

*Correspondence address. Aberdeen Maternity Hospital NHS Grampian, AB 25 2ZL, Scotland, UK. E-mail: abha.maheshwari@abdn.ac.uk
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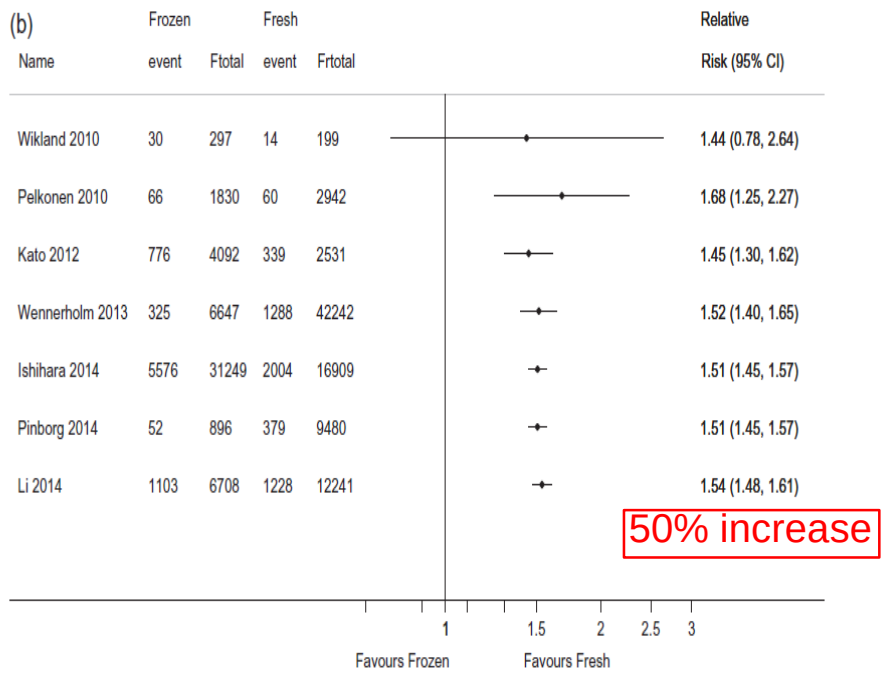


Figure 5 Large for gestational age: (**a**) meta-analysis and (**b**) cumulative meta-analysis.

Högre risk för stora barn!

Figure 6 High birth weight (more than 4000g): (**a**) meta-analysis and (**b**) cumulative meta-analysis.

Large for gestational age (LGA) och Small for gestational age (SGA)

Figure 7. Forest plot of comparison 1. Freeze-all versus conventional IVF, outcomes per woman, outcome 1.13 large for gestational age (birth weight above 90th percentile)

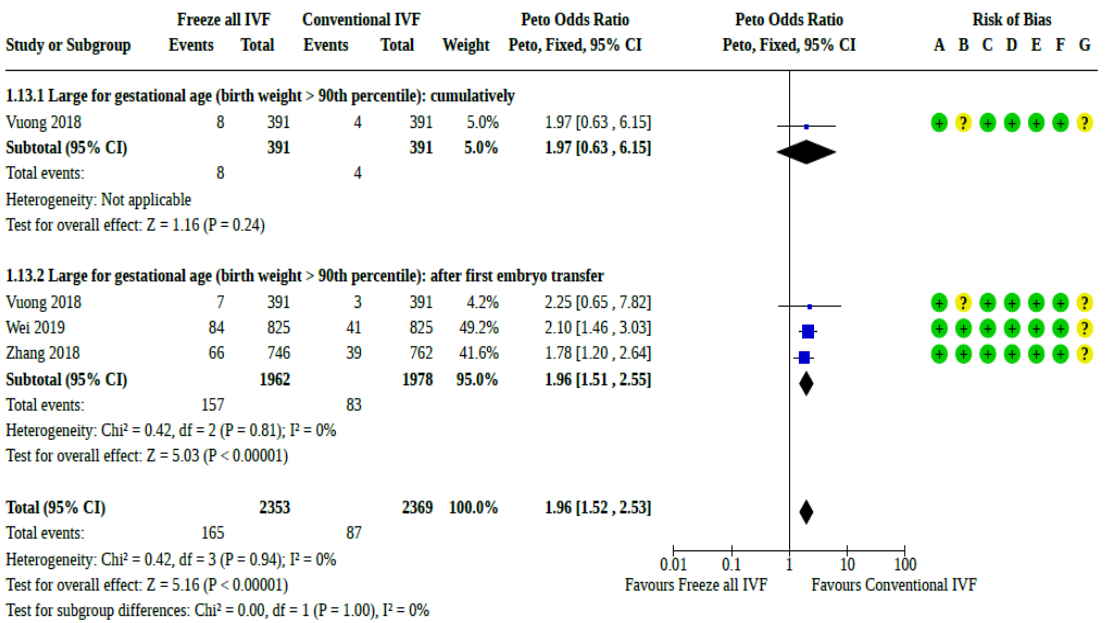
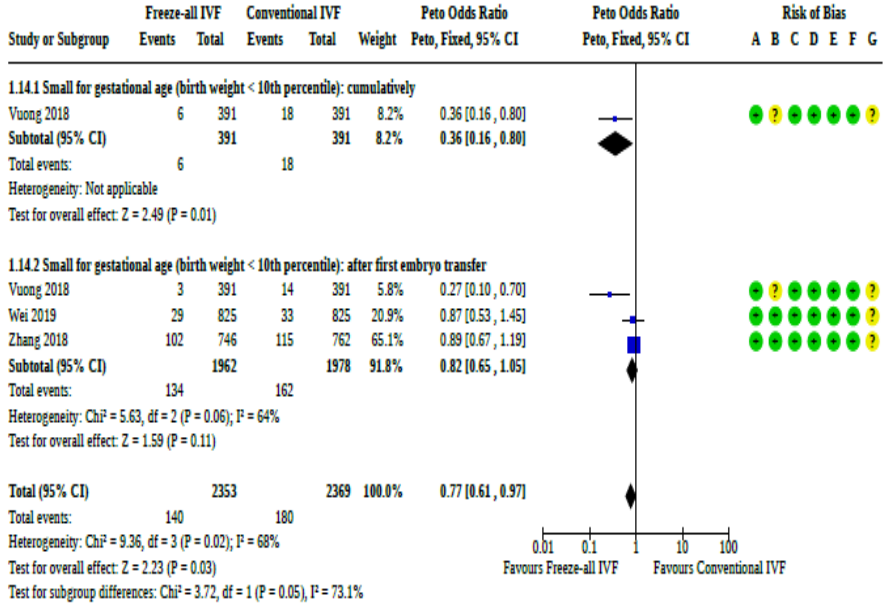


Figure 8. Forest plot of comparison 1. Freeze-all versus conventional IVF, outcomes per woman, outcome 1.14 small for gestational age (birth weight below 10th percentile)



Zaat *et al* Cochrane Syst Rev 2021 Feb 4;2(2):CD011184

Human Reproduction, Vol.00, No.00, pp. 1–8, 2019
Advance Access Publication on doi:10.1093/humrep/dez212

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Perinatal and maternal outcome after vitrification of blastocysts: a Nordic study in singletons from the CoNARTaS group

Erica Ginström Ernstad[1,*], Anne Lærke Spangmose[2], Signe Opdahl[3], Anna-Karina Aaris Henningsen[2], Liv Bente Romundstad[3], Aila Tiitinen[4], Mika Gissler[5,6], Ulla-Britt Wennerholm[1], Anja Pinborg[2], Christina Bergh[7,†], and Sara Sofia Malchau[1,†]

2002-2015
Singletons
Vitrified blastocysts: 3650
Slow-frozen embryos. 8123
Fresh blastocyst: 4469

PTB: aOR 1.33 (1.09-1.62) vitrified blastocysts vs slow frozen embryos

Risker på längre sikt

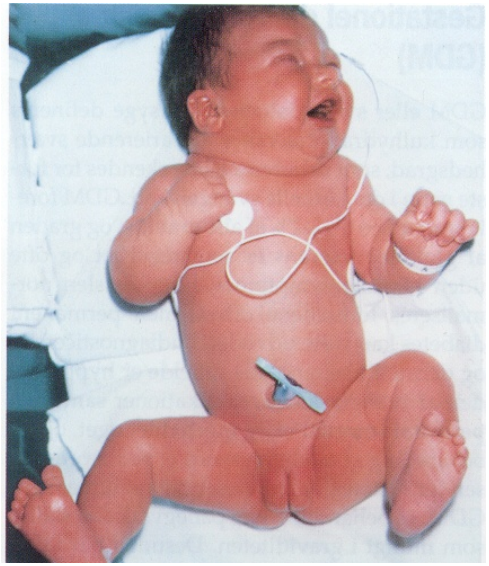
Diseases later in life?
(Developmental Origins of Health and Disease; Barker hypothesis)

SGA predisposes for

- Cardiovascular diseases
- Diabetes
- Hypertonia
- Stroke

Hög födelsevikt är associerad med

- Asfyxia
- Shoulder dystocia
- Hypoglycemia
- Respiratory problems
- Mortality



Henriksen et al., AOGS, 2008

frontiers in Pediatrics

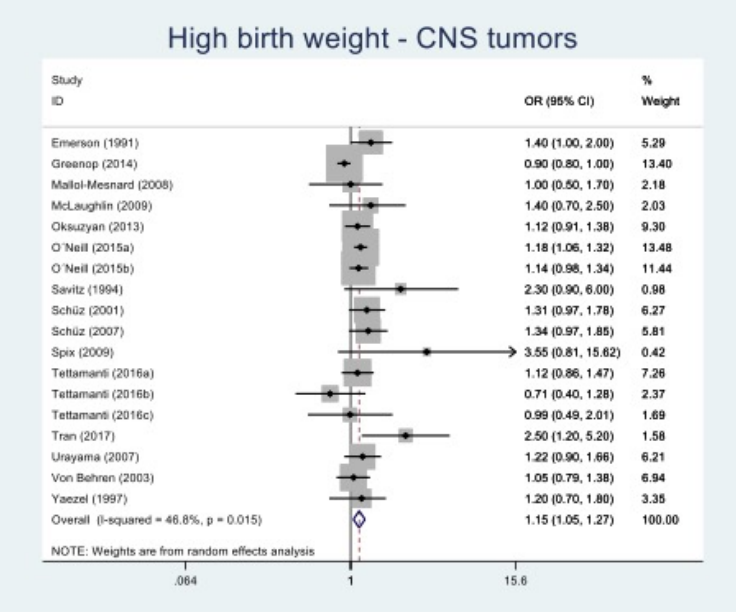
SYSTEMATIC REVIEW
published: 23 June 2021
doi: 10.3389/fped.2021.675775

The Association Between High Birth Weight and Long-Term Outcomes—Implications for Assisted Reproductive Technologies: A Systematic Review and Meta-Analysis

Ása Magnusson[1*], Hannele Laivuori[2,3,4], Anne Loft[5], Nan B. Oldereid[6], Anja Pinborg[5], Max Petzold[7], Liv Bente Romundstad[8,9], Viveca Söderström-Anttila[10] and Christina Bergh[1]

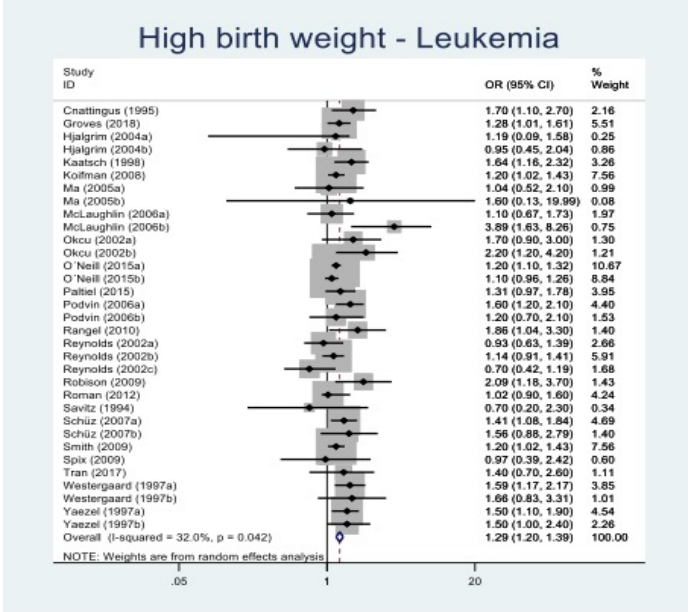
High birth weight and child cancer

CNS tumors



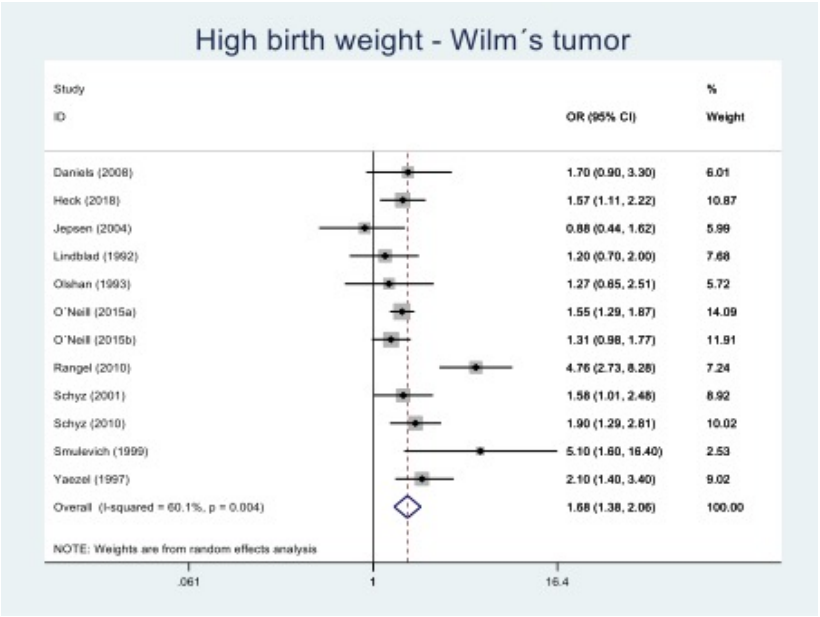
+15%

Leukemia



+29%

Wilm's tumor



+68%

Magnusson, Frontiers in Pediatrics 2021

frontiers in Pediatrics

SYSTEMATIC REVIEW
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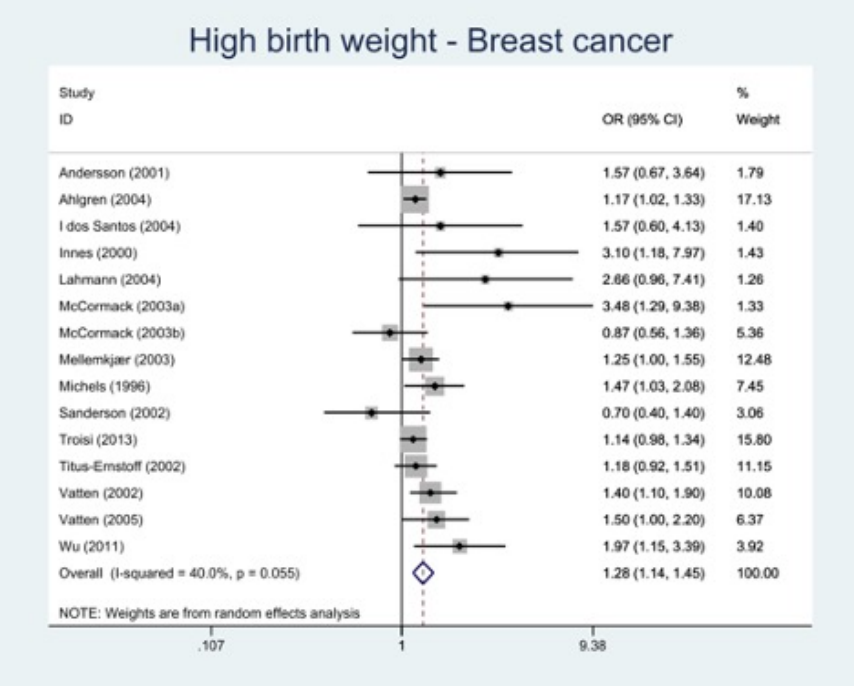
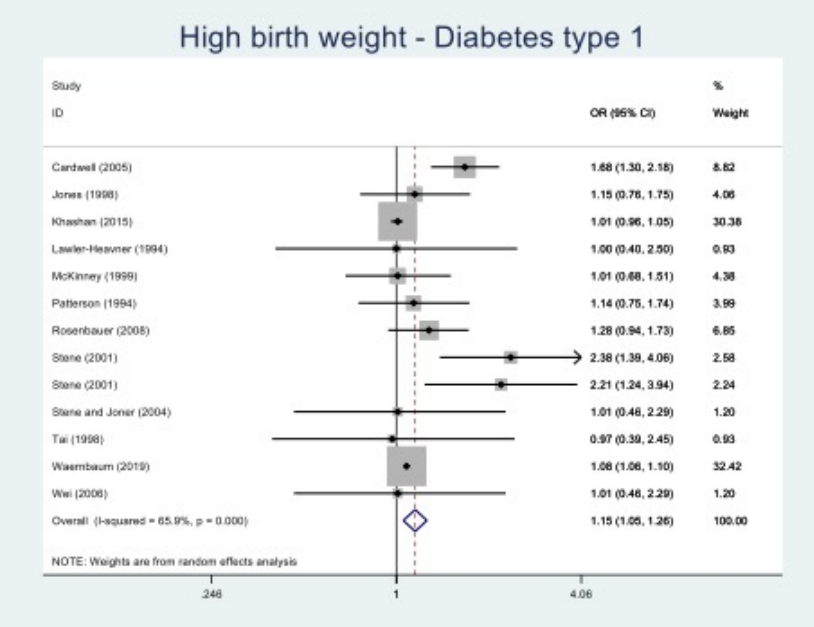
High birth weight and breast cancer



+28%

Diabetes Type 1



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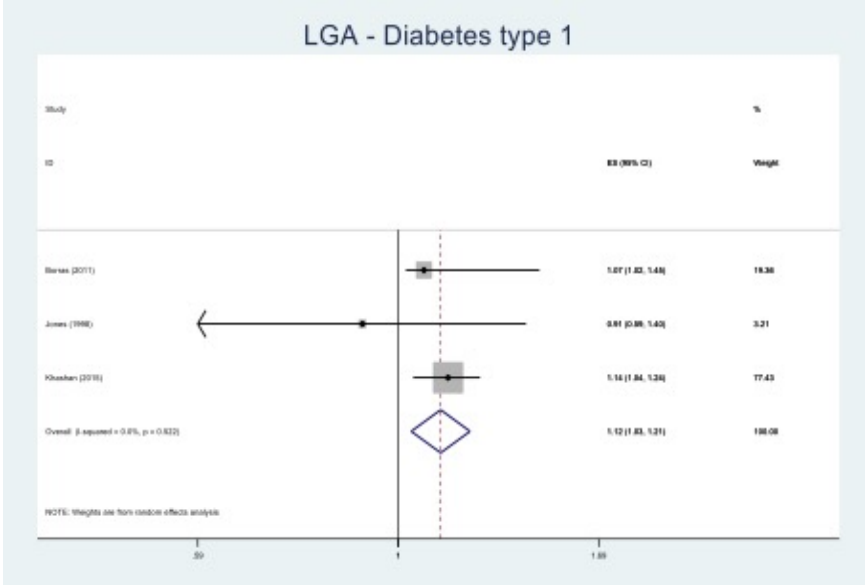


+12%

Psychiatric diseases

- Schizophrenia and depression
- Behavioral problems
- Positively associated with cognitive ability

Cardiovascular disease

- Hypertension in childhood, inverse association in adulthood
- No difference in the risk of coronary heart disease

Missbildningar

Singletons: ART vs spontan konception
Systematic reviews och meta-analyses

	Rimm 2004	Hansen 2005*	McDonald 2005	Pandey 2012*	Hansen 2013*
No of studies and ART children	IVF:8 2 064 ICSI:6 3 948	15 13 059	7 4 031	7 4 382	23 48 944
Birth defects AOR or RR (95% CI)	IVF: 1.5 (0.8-2.7) ICSI: 1.3 (0.9-2.0)	**1.3** (1.2-1.5)	**1.4** (1.1-1.9)	**1.7** (1.3-2.1)	**1.4** (1.3-1.4)

*Cohort studies, matched or adjusted

ART 30-70% increased risk

Human Reproduction, Vol.29, No.7 pp. 1552–1557, 2014
Advanced Access publication on May 7, 2014 doi:10.1093/humrep/deu088

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Major congenital anomalies in children born after frozen embryo transfer: a cohort study 1995–2006

S. Pelkonen[1,*], A.-L. Hartikainen[1], A. Ritvanen[2], R. Koivunen[3], H. Martikainen[1], M. Gissler[2,4], and A. Tiitinen[5]

[1]Department of Obstetrics and Gynecology, Oulu University Hospital, PO Box 24, Oulu 90029 OYS, Finland [2]National Institute for Health and Welfare (THL), PO Box 30, Helsinki 00271, Finland [3]Väestöliitto Fertility Clinics Ltd, Kiviharjuntie 11, Oulu 90220, Finland [4]NHV, Nordic School of Public Health, Box 12133, Gothenburg SE-40242, Sweden [5]Department of Obstetrics and Gynecology, Helsinki University Central Hospital and Helsinki University, PO Box 140, Helsinki 00029 HUS, Finland

*Correspondence address. Tel: +358-8-3153040; Fax: +358-8-3154310; E-mail: sari.pelkonen@fimnet.fi

Submitted on September 3, 2013; resubmitted on February 17, 2014; accepted on March 10, 2014

FET :1830	4.2%
Fresh:2942	4.5%
SC:31 243	3.2%

ART vs SC: AOR 1.23 (1.05-1.47)
FET vs fresh: AOR 0.95 (0.71-1.27)

Långtids uppföljning

1984-2015, 172,161 ART barn,
ART mammor och 7 681,792 kontroller

Diabetes mellitus
Kardiovaskulära risker
Pubertets utveckling
Cancer

Skolprestationer
Psykiatriska sjukdomar, ADHD
etc

Cancer hos barn födda efter ART

First author and year of publication	Country	Number of ART children	Overall cancer risk (95% CI)	Specific cancers at increased risk
Observational studies				
Williams , 2013	United Kingdom	106 013	SIR 0.98 (0.81 to 1.19)	Hepatoblastoma, rhabdomyosarcoma
Sundh, 2014	Nordic countries	91 796	aHR 1.08 (0.91 to 1.27)	CNS, malignant epithelial neoplasms
Reigstadt, 2016	Norway	25 782	HR 1.21 (0.90 to 1.63)	
Gilboa, 2018	Israel	64 317	RR 1.09 (0.79 to 1.48)	
Williams, 2018	United Kingdom	12 137	RR 0.83 (0.47 to 1.47)	
Spaan, 2019	Netherland	24 269	HR 1.00 (0.72 to 1.38)	
Spector, 2019	United States	275 686	HR 1.17 (1.0 to 1.36)	Hepatic tumors
Hargreave, 2019	Denmark	19 448 IVF 13 427 ICSI 3 356 FET	ART: aHR 1.20 (0.96 to 1.49) IVF: aHR 0.96 (0.70 to 1.32) ICSI: aHR 1.33 (0.94 to 1.89) FET: aHR 2.43 (1.44 to 4.11)	Leukemia

Research

JAMA | Original Investigation

Association Between Fertility Treatment and Cancer Risk in Children

Marie Hargreave, PhD; Allan Jensen, PhD; Merete Kjær Hansen, PhD; Christian Dehlendorff, PhD; Jeanette Falck Winther, DMSc; Kjeld Schmiegelow, DMSc; Susanne K. Kjær, DMSc

Denmark, 1996-2012
1,085,172 children, 37156 ART
2217 cancer

	Person-years	No of children	No of cancer cases	HR (95% CI)
Any type of maternal fertility treatment	943 199	89 981	178	1.03 (0.88 to 1.20)
Types of maternal fertility treatment[e]				
Any type of fertility drugs	934 946	89 334	173	1.01 (0.86 to 1.18)
Types of fertility drugs				
Clomiphene	372 402	33 835	64	0.95 (0.74 to 1.22)
Gonadotropins[f]	572 515	57 136	112	1.06 (0.88 to 1.29)
Human chorionic gonadotropin	682 288	68 181	129	1.02 (0.86 to 1.23)
Gonadotropin-releasing hormone analogs	393 199	38 653	81	1.12 (0.90 to 1.40)
Progesterone	429 787	41 628	85	1.08 (0.87 to 1.34)
Estrogen	123 958	16 948	23	0.91 (0.60 to 1.38)
Other or unspecified	73 129	8867	15	1.04 (0.63 to 1.74)
Any type of assisted reproductive technology	388 681	37 156	<90[g]	1.20 (0.96 to 1.49)
Types of assisted reproductive technology				
In vitro fertilization	220 159	19 448	38	0.96 (0.70 to 1.32)
Intracytoplasmic sperm injection	130 726	13 417	32	1.33 (0.94 to 1.89)
Frozen embryo transfer	30 260	3356	14	2.43 (1.44 to 4.11)

Hargreave JAMA 2019

Human Reproduction, pp. 1–11, 2020
doi:10.1093/humrep/dez227

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Type 1 diabetes in children born after assisted reproductive technology: a register-based national cohort study

E. Norrman[1,*], M. Petzold[2], T.D. Clausen[3], A-K. Henningsen[4], S. Opdahl[5], A. Pinborg[4], A. Rosengren[6], C. Bergh[7,†], and U-B. Wennerholm[1,†]

	ART n=47,938	SC n=3,090,602
DM1	202	17,916
per 100 000 person years	43.4	35.5

aHR (ART vs SC):1.07 (0.93-1.23)

aHR (FET vs fresh): 1.52 (1.08-2.14)
aHR (FET vs SC):1.41 (1.05 to 1.89)

BJOG An International Journal of Obstetrics and Gynaecology

DOI: 10.1111/1471-0528.15484
www.bjog.org

Epidemiology

Academic performance in adolescents aged 15–16 years born after frozen embryo transfer compared with fresh embryo transfer: a nationwide registry-based cohort study

AL Spangmose,[a] SS Malchau,[a] AA Henningsen,[b] JL Forman,[c] S Rasmussen,[b] A Loft,[b] L Schmidt,[d] A Pinborg[b]

Denmark, 1995-2001
15-16 years old singletons
Cryo: 423
Fresh: 6072

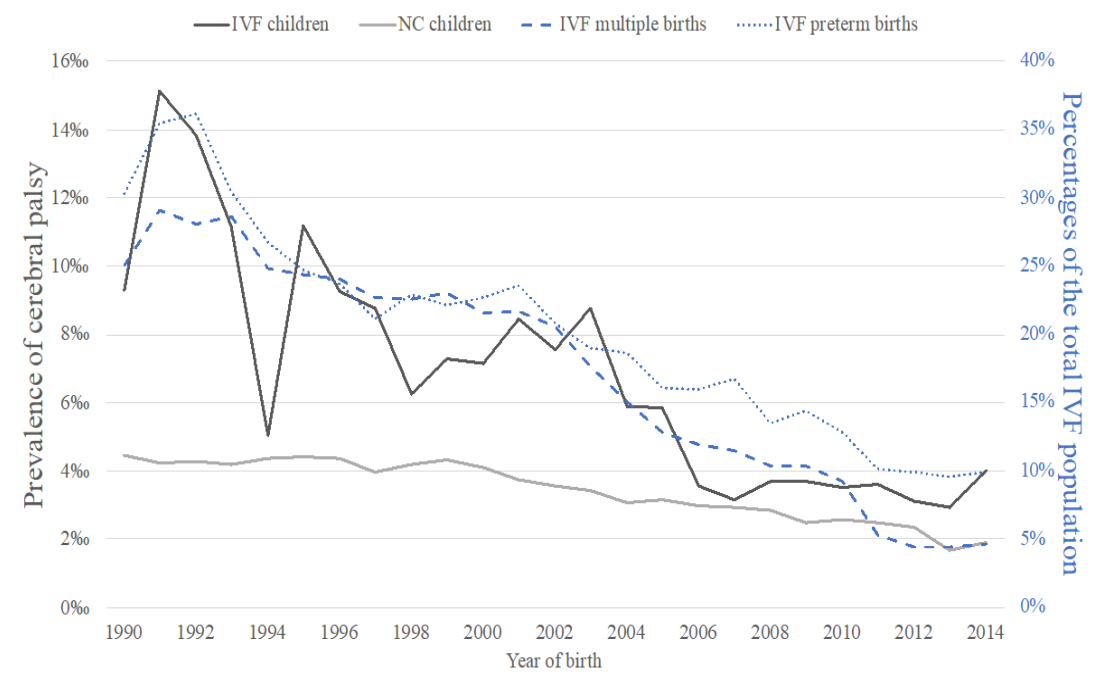
No differences in academic performance

Human Reproduction, Vol.00, No.0, pp. 1–13, 2021
doi:10.1093/humrep/deab122

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Cerebral palsy in ART children has declined substantially over time: a Nordic study from the CoNARTaS group

Anne Lærke Spangmose [1,*], Lene Hee Christensen [1], Anna-Karina Aaris Henningsen [1], Julie Forman [2], Signe Opdahl [3], Liv Bente Romundstad [3,4], Kate Himmelmann [5], Christina Bergh [6], Ulla-Britt Wennerholm [6], Aila Tiitinen [7], Mika Gissler [8,9], and Anja Pinborg [1]



Spangmose, 2021 Hum Reprod

N=97,614 ART
N=4,875,998 SC
1985-2010

	AOR (95% CI)
All children	2.76 (2.03-3.67)
	1.39 (1.01-1.87)
Total	1.56 (1.44-1.70)
Singletons	2.02 (1.22-3.14)
	1.28 (0.89-1.78)
Total	1.11 (0.98-1.24)

Human Reproduction, Vol.30, No.7 pp. 1724–1731, 2015
Advanced Access publication on April 29, 2015 doi:10.1093/humrep/dev090

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Risk of hypertensive disorders in pregnancies following assisted reproductive technology: a cohort study from the CoNARTaS group

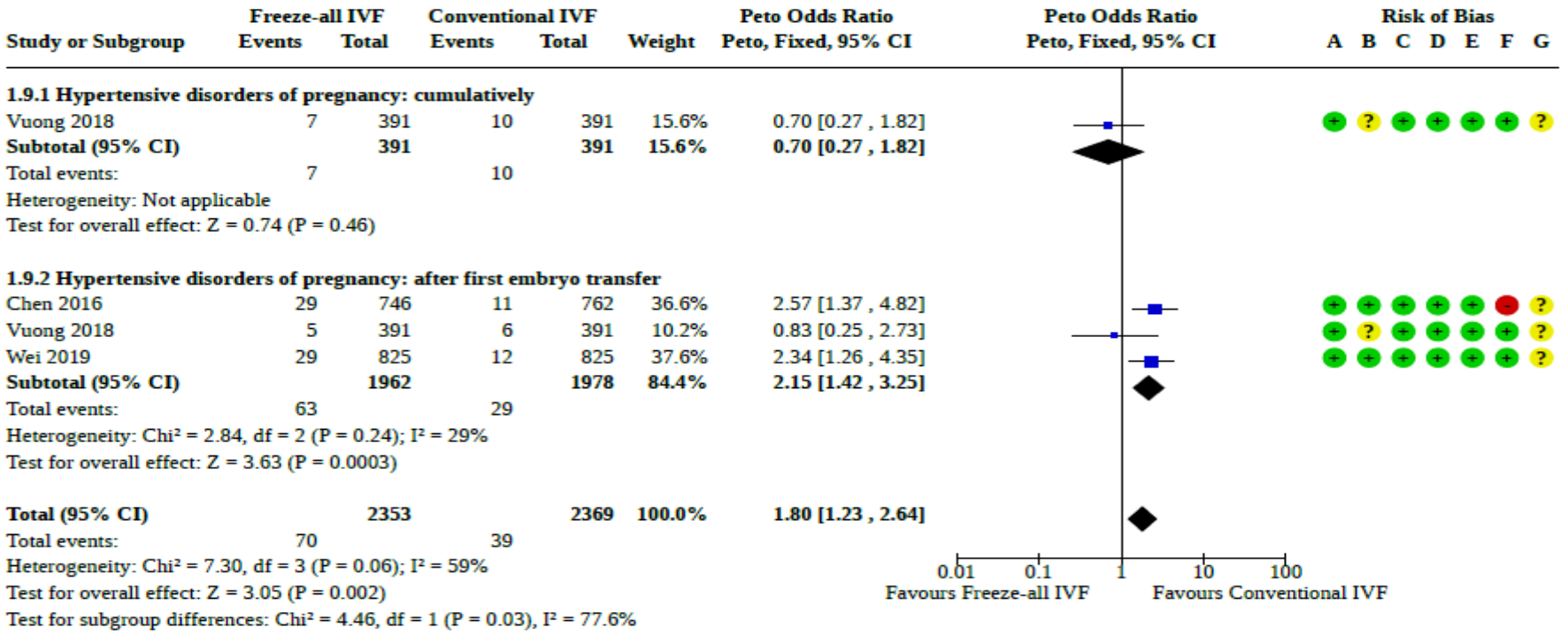
S. Opdahl[1,*], A.A. Henningsen[2], A. Tiitinen[3], C. Bergh[4], A. Pinborg[5], P.R. Romundstad[1], U.B. Wennerholm[4], M. Gissler[6,7], R. Skjærven[8,9], and L.B. Romundstad[1,10]

Table II Risk of hypertensive disorders in ART pregnancies, according to type of ART procedure.

	Singletons					Twins				
	Risk[1], %	Risk difference[2], % (95% CI)		Odds ratio[2] (95% CI)		Risk[1], %	Risk difference[2], % (95% CI)		Odds ratio[2] (95% CI)	
SC pregnancies	4.7	0	(Ref)	1	(Ref)	10.4	0	(Ref)	1	(Ref)
All ART pregnancies	5.9	0.7	(0.5–0.9)	1.16	(1.10–1.21)	12.6	−0.4	(−1.0–0.3)	0.96	(0.89–1.03)
Fresh cycle pregnancies	5.7	0.5	(0.3–0.8)	1.12	(1.06–1.18)	11.8	−0.9	(−1.6–−0.3)	0.90	(0.84–0.97)
Frozen cycle pregnancies	7.0	1.8	(1.2–2.4)	1.41	(1.27–1.56)	19.6	5.1	(3.0–7.1)	1.57	(1.34–1.85)
IVF pregnancies	5.7	0.5	(0.3–0.8)	1.12	(1.06–1.19)	12.4	−0.4	(−1.1–0.4)	0.96	(0.88–1.04)
ICSI pregnancies	6.2	1.0	(0.6–1.4)	1.23	(1.14–1.32)	13.1	−0.2	(−1.2–0.9)	0.98	(0.88–1.10)
IVF fresh cycle pregnancies	5.7	0.4	(0.1–0.7)	1.09	(1.02–1.16)	11.9	−0.9	(−1.6–−0.1)	0.91	(0.83–0.99)
IVF frozen cycle pregnancies	6.5	1.7	(0.9–2.6)	1.39	(1.21–1.60)	18.9	6.5	(3.3–9.7)	1.75	(1.39–2.21)
ICSI fresh cycle pregnancies	5.8	0.8	(0.4–1.2)	1.18	(1.09–1.28)	11.7	−1.1	(−2.2–0.0)	0.88	(0.78–1.00)
ICSI frozen cycle pregnancies	7.6	1.9	(1.0–2.7)	1.42	(1.23–1.64)	20.5	4.0	(1.3–6.7)	1.45	(1.16–1.81)

[1]Unadjusted.
[2]All analyses are adjusted for parity (0, ≥1), year of birth (one-year categories), maternal age (<25, 25–44 in 1-year categories, ≥45 years), country and offspring sex (singletons: male, female; twins: both male, both female, opposite sexes). CI, confidence interval.

Figure 6. Forest plot of comparison: 1 Freeze-all versus conventional IVF, outcomes per woman, outcome 1.9 hypertensive disorders of pregnancy



Zaat *et al* Cochrane Syst Rev 2021 Feb 4;2(2):CD011184

KEY MESSAGES –
IVF resultat Frys vs färsk

- Liknande födelsefrekvens
- Lägre risk för OHSS
- Längre tid till förlossning

KEY MESSAGES –barn och mamma utfall
Frys vs färsk

- Neonatala utfall (PTB, LBW) –lägre frekvens
- Neonatala utfall (LGA, hög födelsevikt)-ökad frekvens
- Missbildningar- Inga skillnader
- Cancer –oklart?
- Akademiska prestationer-ingen skillnad
- Typ 1 Diabetes-något ökad? för frys
- Mamma utfall –ökad risk för HDP (hypertensive disorders of pregnancy)

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Tack!