Rīgas Stradiņa Universitāte

VITA BREVIS ARS LONGA

Pēcdiploma lekciju cikls Aktualitātes dzemdniecībā un ginekoloģijā

Grūtniecība pēc ART

Vai ir nepieciešama specifiska antenatālā aprūpe?

Dr. med., doc. Anna Miskova

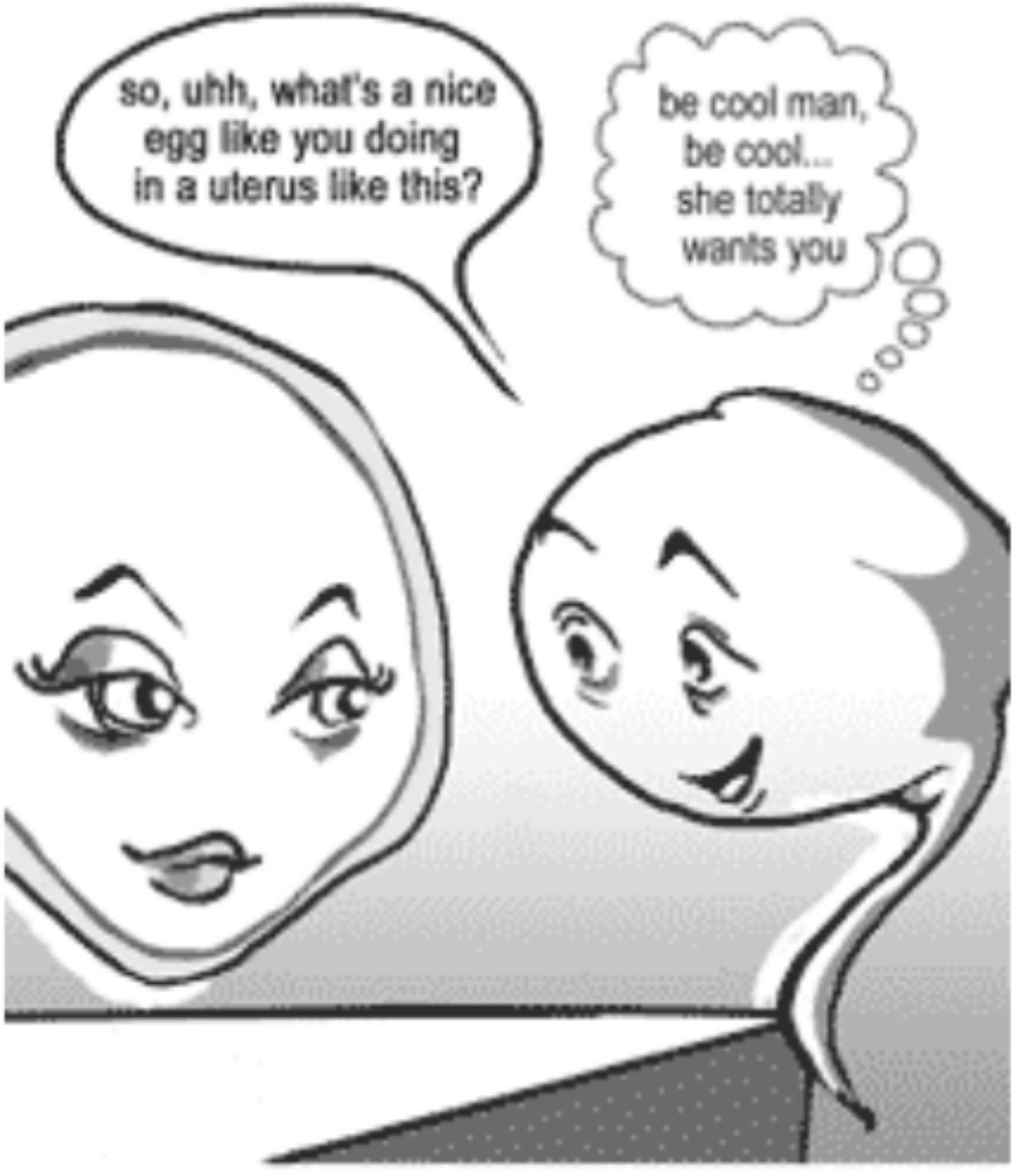
65 RSU IZAUGSMES GADI

Lekcijas plāns

- ART metodes
- Asistētas grūtniecības fizioloģija
- Raksturīgas problēmas 1., 2. un 3. trimestrī
- Asistēta DAG
- Iedzimtas anomālijas pēc ART

Kāpēc ART

- Anovulācija (PCOS, PON, hipotalāmiska)
- Endometrioze - neietekmē mātes un perinatālo M&S Benaglia et al., 2011
- Dzemdes strukturāla patoloģija - NI/ĀGN
- Olvadu faktors
- Vīrieša faktors
- Endokrinopātija - NI/ĀGN
- Antifosfolipīdu sindroms - NI/ĀGN
- Trombofīlija - NI/ĀGN
- Vecāku hromosomāla patoloģija - NI/ĀGN



why it can take ages
to get pregnant

Folskābe

Laparoskopija

Histeroskopija

Progesterons

Tiroksīns

IVIG

Aspirīns

Metformīns

Miomektomija

PCOS

MMH

Depresija

Vai cita grūtniece?

- priekšlaicīgas dzemdības
- zems jaundzimušā svars
- preeklampsija/eklampsija
- dvīņi
- perinatāla mirstība
- ķeizargrieziens
- placenta praevia/accreta
- cerebrāla trieka
- attīstības anomālijas?

Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Obstetric andperinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematicreview and meta-analysis. Hum Reprod Update.

Farhi A, Reichman B, Boyko V, Hourvitz A, Ron-El R, Lerner-Geva L. Maternaland neonatal health outcomes following assisted reproduction. Reprod BiomedOnline. 2013 May;26(5):454-61
Stojnic J, Radunovic N, Jeremic K, Kotlica BK, Mitrovic M, Tulic I. Perinatal outcome of singleton pregnancies following in vitro fertilization. Clin ExpObstet Gynecol. 2013;40(2):277-83

Kāpēc?

- pacientes veselības stāvoklis un dzīves veids
- ART per se
- OPU tehnika
- protokoli
- laboratorija
- ET tehnika

VECUMS

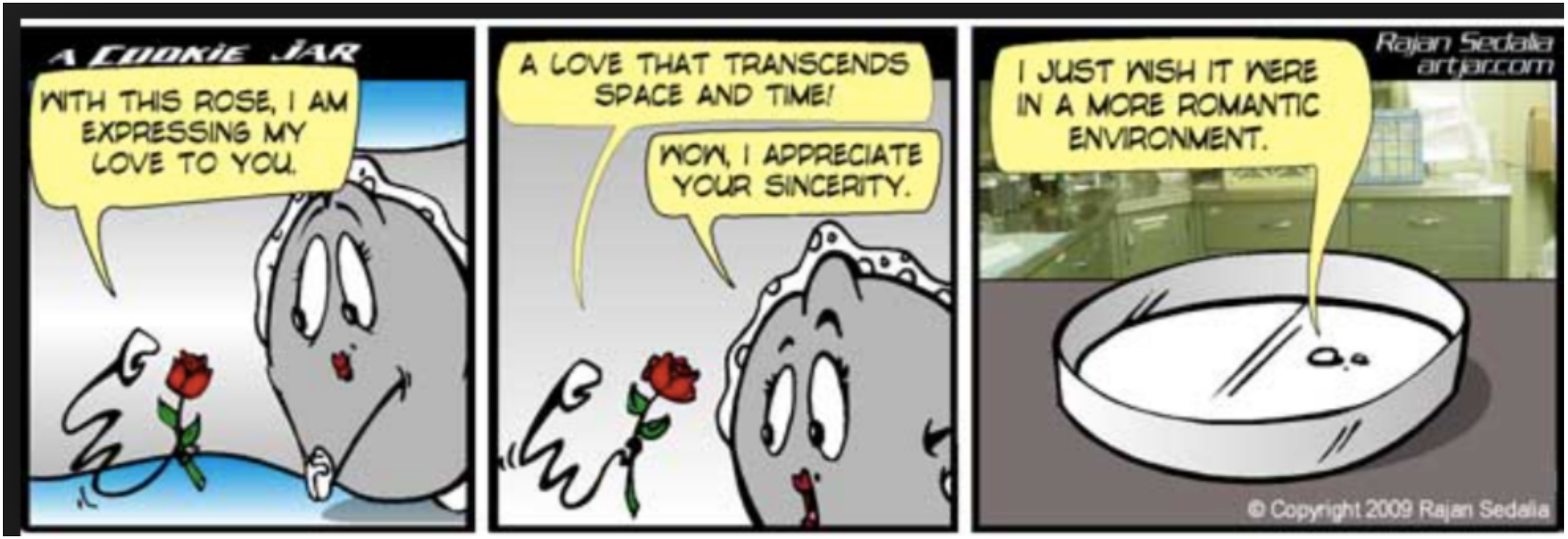
Riska faktori

- **vecums**
- ĶMI
- paritāte
- ART veids: stimulācija/IVF/ICSI
- embriju daudzums uz ET
- vīriešu dzimtas jaundzimušais
- dzemdību veids
- pazudušais dvīnis

Outcomes of singleton births after blastocyst versus nonblastocyst transfer in assisted reproductive technology

Dhanushi Fernando, B.Med.Sci., Jane L. Halliday, Ph.D., Susan Breheny, B.S., David Lindsay Healy, B.Med.Sci., M.B.B.S., Ph.D.

Adverse outcome	Odds ratio (95% CI)	*P* value	Adjusted odds ratio (99% CI)	*P* value
Days 2 to 4	1.00		1.00	
Days 5 to 6				
Very preterm	0.92 (0.61–1.40)	.70	0.65 (0.34–1.24)[a]	.08
Preterm	1.05 (0.85–1.30)	.63	0.93 (0.66–1.30)[a]	.57
VLBW	0.95 (0.60–1.51)	.84	0.73 (0.35–1.52)[b]	.26
LBW	1.02 (0.80–1.29)	.88	0.91 (0.62–1.33)[b]	.52
SGA	0.95 (0.76–1.19)	.65	1.05 (0.73–1.52)[a]	.71
LGA	0.99 (0.81–1.21)	.95	1.17 (0.83–1.64)[a]	.23
Preeclampsia	1.28 (0.91–1.80)	.15	1.72 (0.93–3.20)[a]	.02
APH	0.75 (0.50–1.14)	.18	0.75 (0.39–1.44)[a]	.25
PA	1.81 (0.49–6.76)	.38	0.65 (0.11–3.93)[a]	.53
PP	1.30 (0.92–1.83)	.13	1.65 (0.92–2.98)[a]	.03
PPH	3.73 (1.96–7.11)	<.001	0.97 (0.40–2.37)[c]	.94


A Cookie Jar
WITH THIS ROSE, I AM EXPRESSING MY LOVE TO YOU.
A LOVE THAT TRANSCENDS SPACE AND TIME!
WOW, I APPRECIATE YOUR SINCERITY.
I JUST WISH IT WERE IN A MORE ROMANTIC ENVIRONMENT.
Rajan Sedalia
artjar.com
© Copyright 2009 Rajan Sedalia

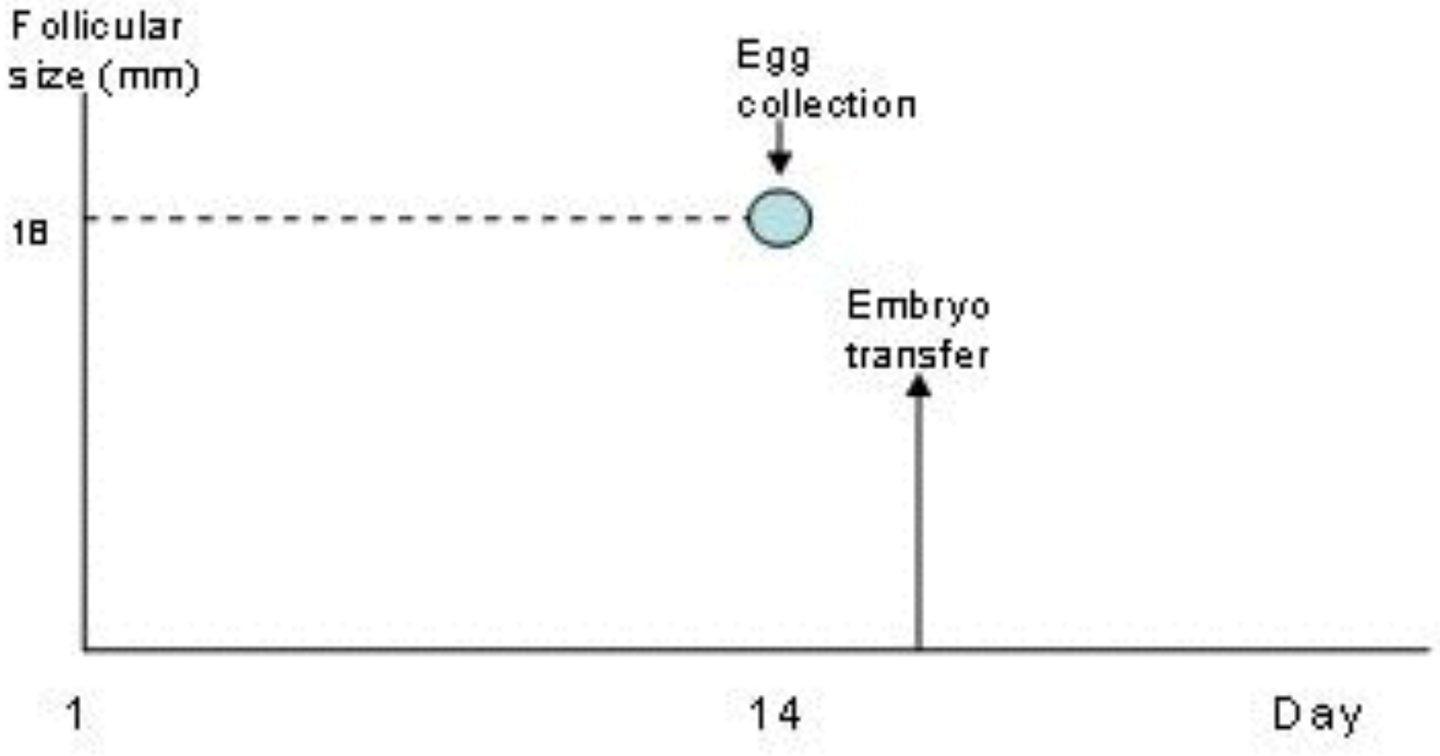
ART

- Naturālais cikls
- Ovulācijas indukcija
- IUI
- IVF
- ICSI
- SET
- FET

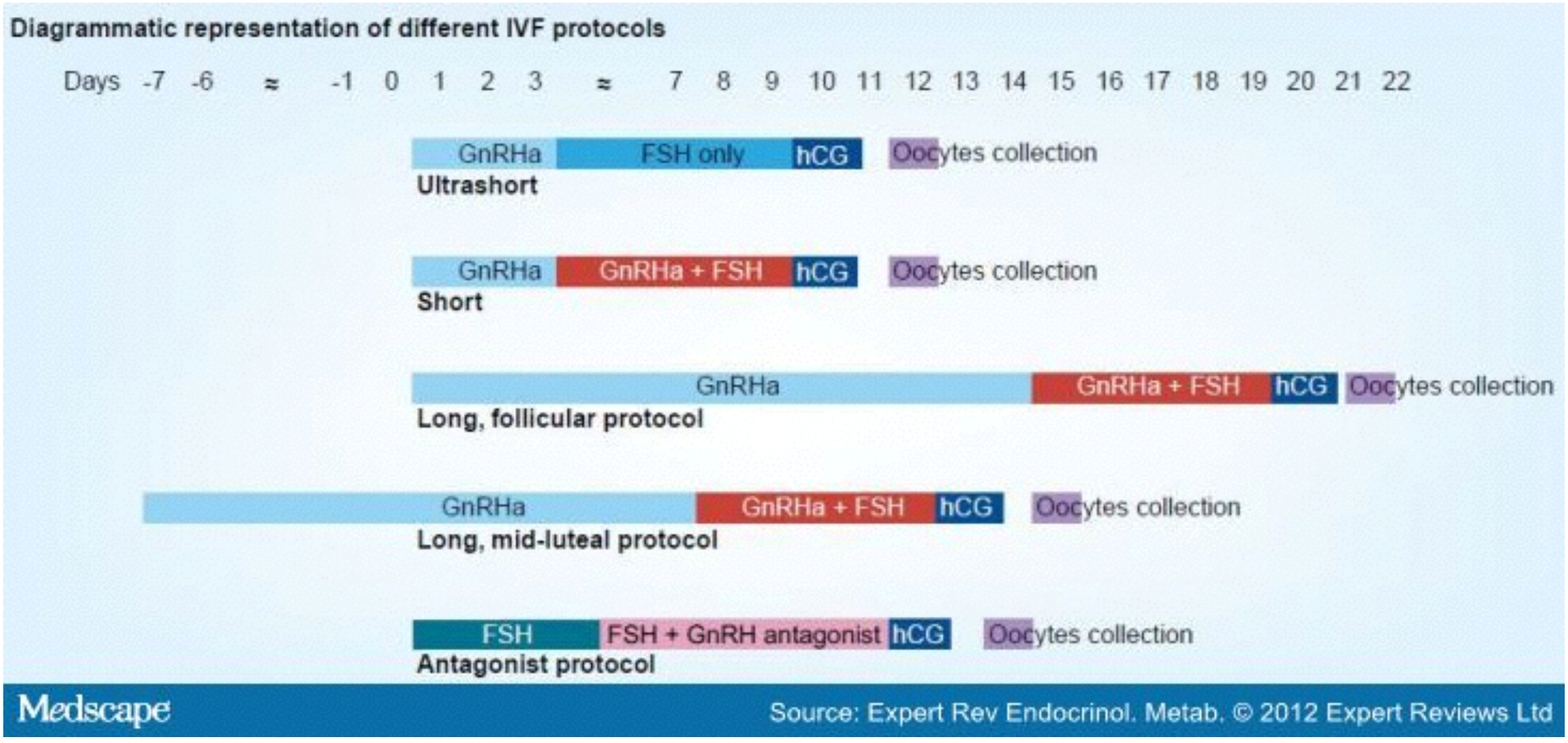
ART etapi

- Pacientes sagatavošana - kontrolēta olnīcu stimulācija - KOS
- Olšūnas iegūšana, spermas sagatavošana, apaugļošana (sasaldēšana)
- ET/FET

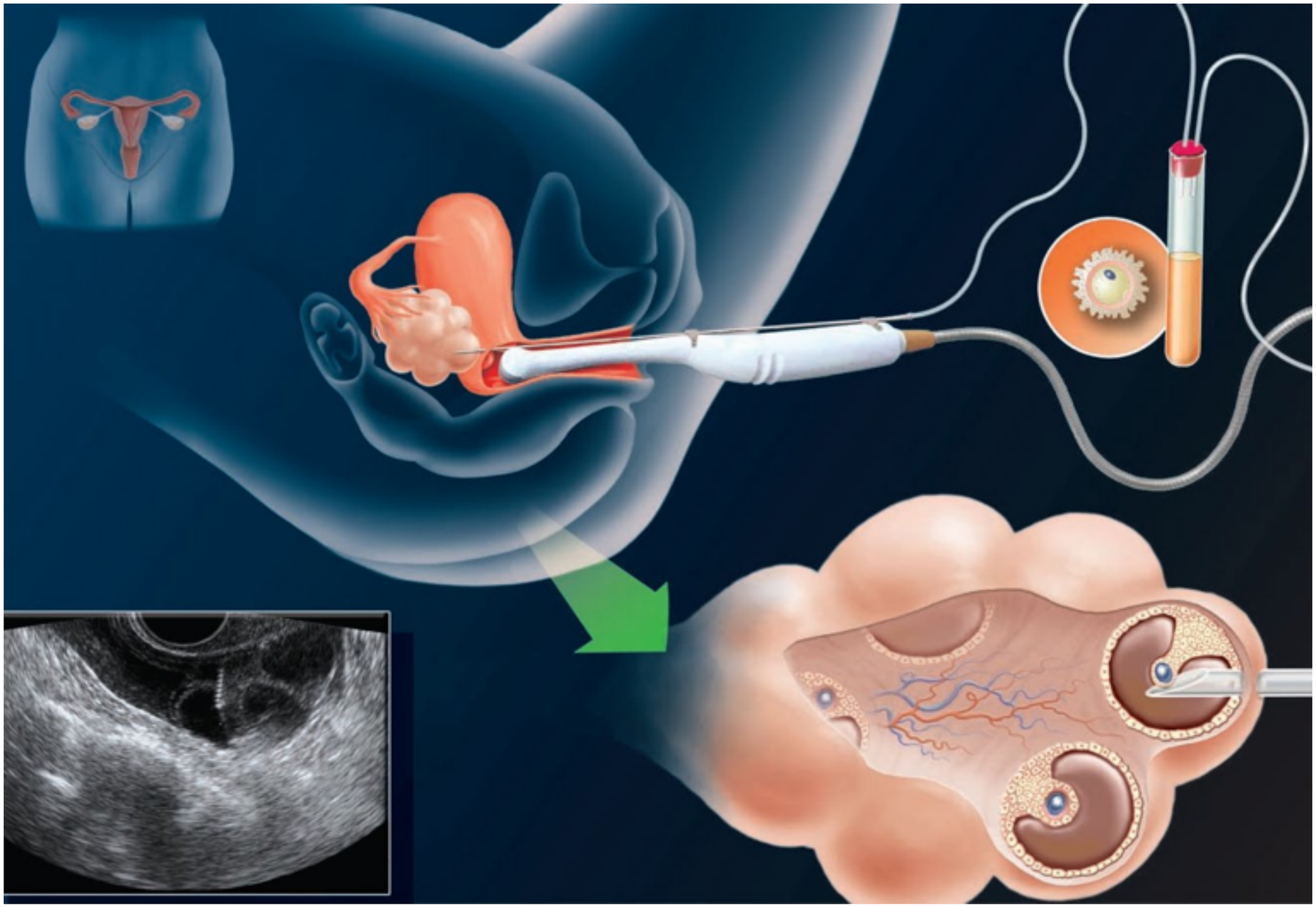
Naturālais cikls



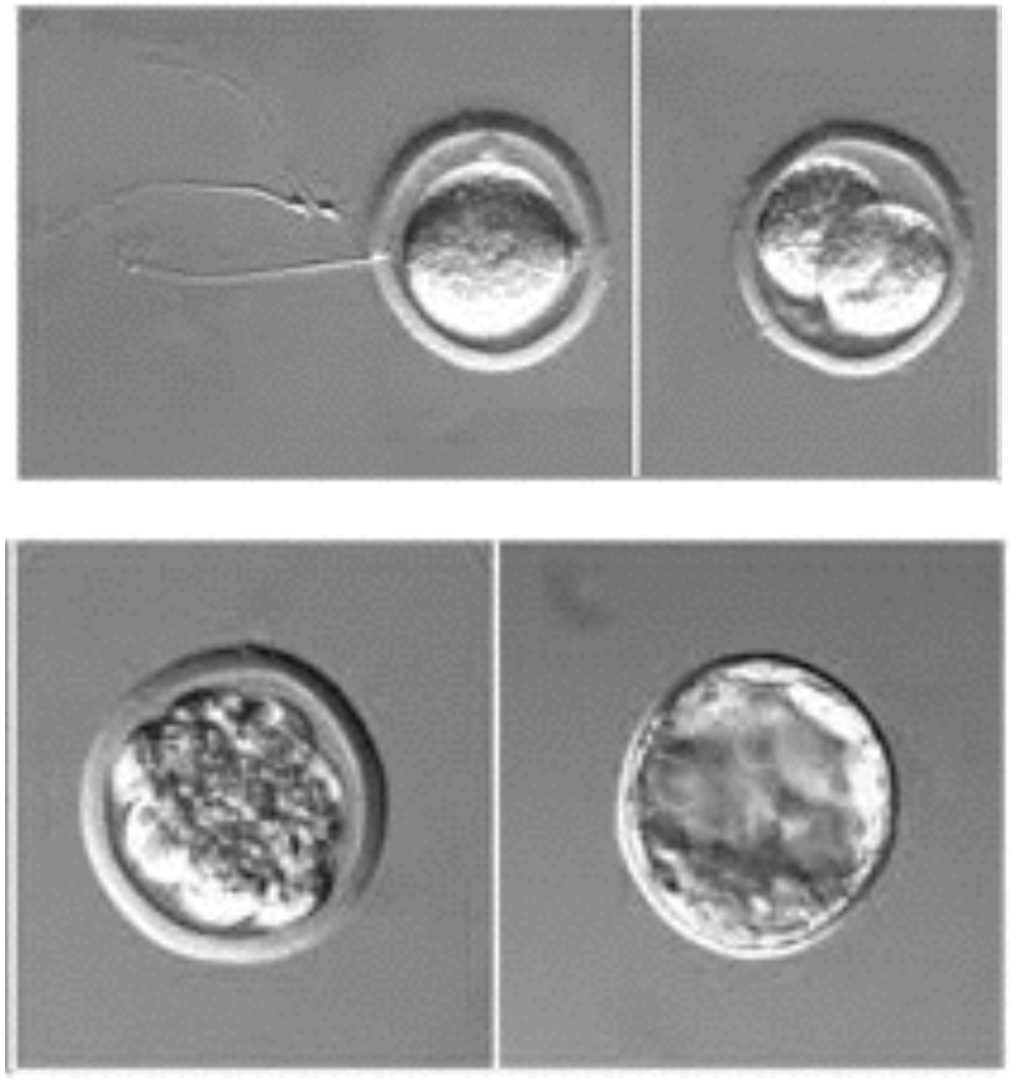
Kontrolēta olnīcu stimulācija

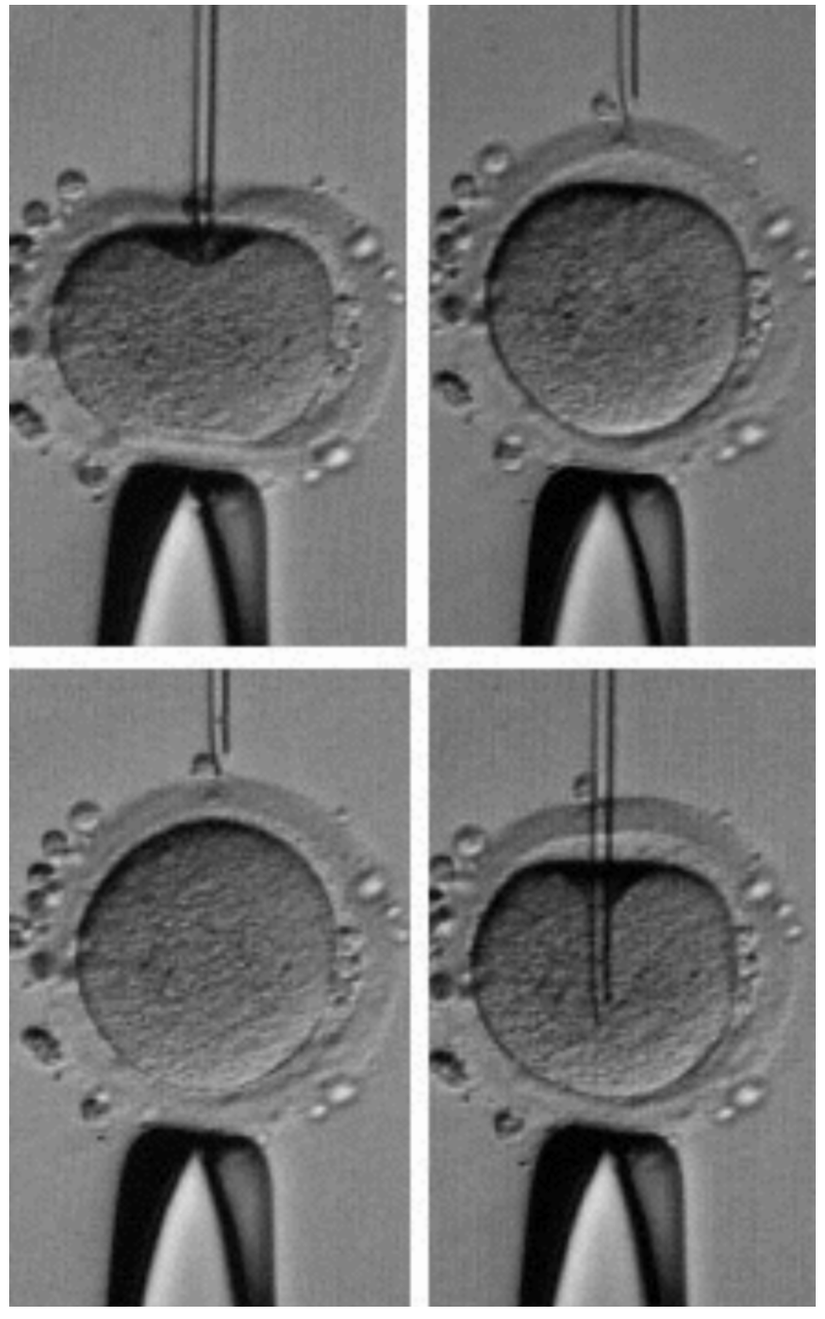


Olšūnu iegūšana - olnīcu punkcija



IVF/ICSI

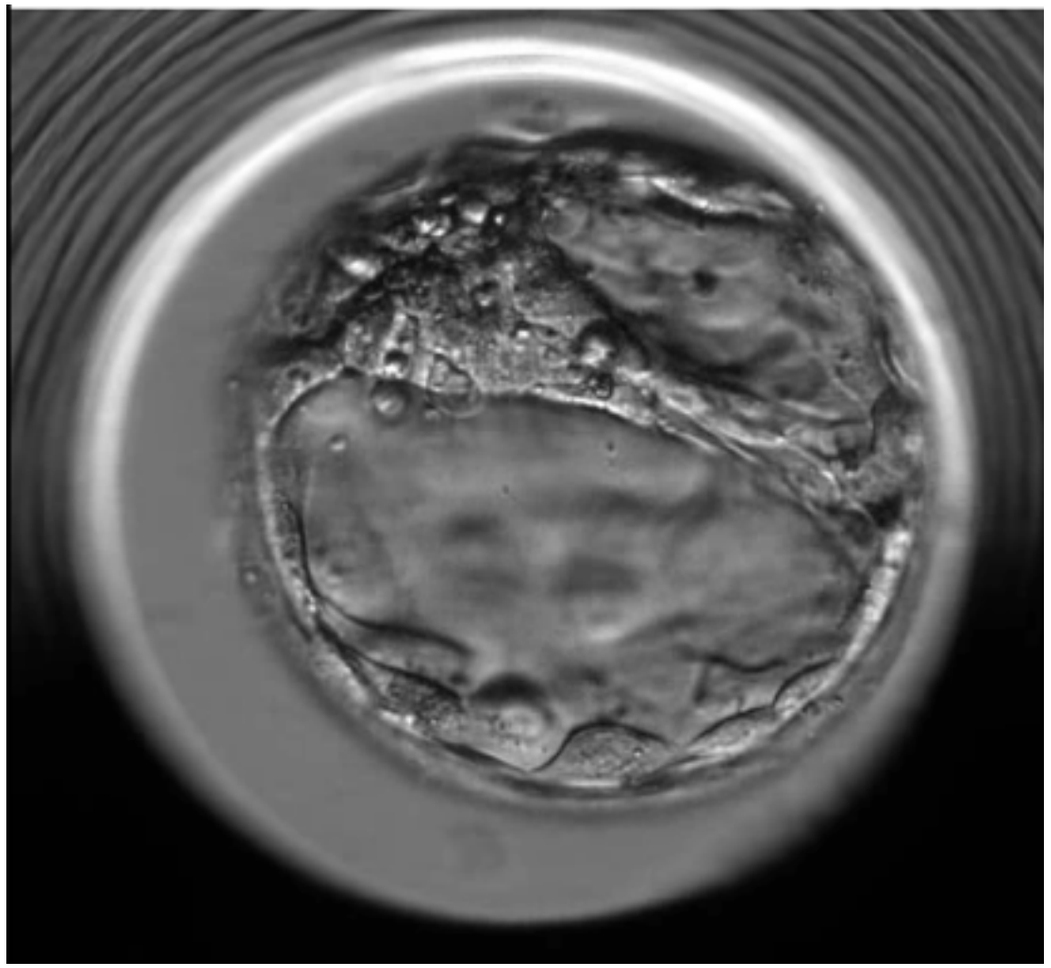




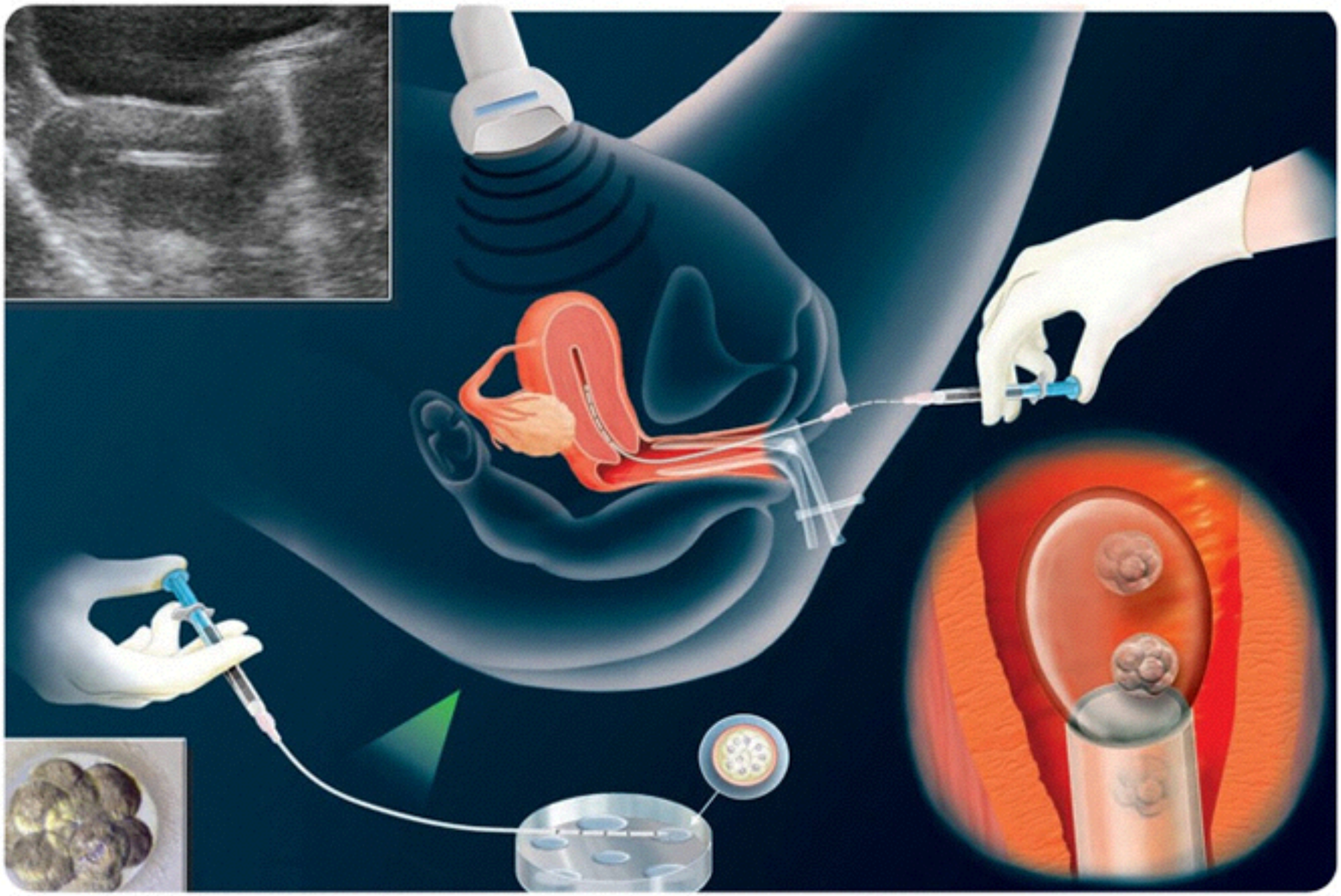
Embriju kultivēšana

- Konservatīvā kultivēšana un morfoloģiska embriju selekcija

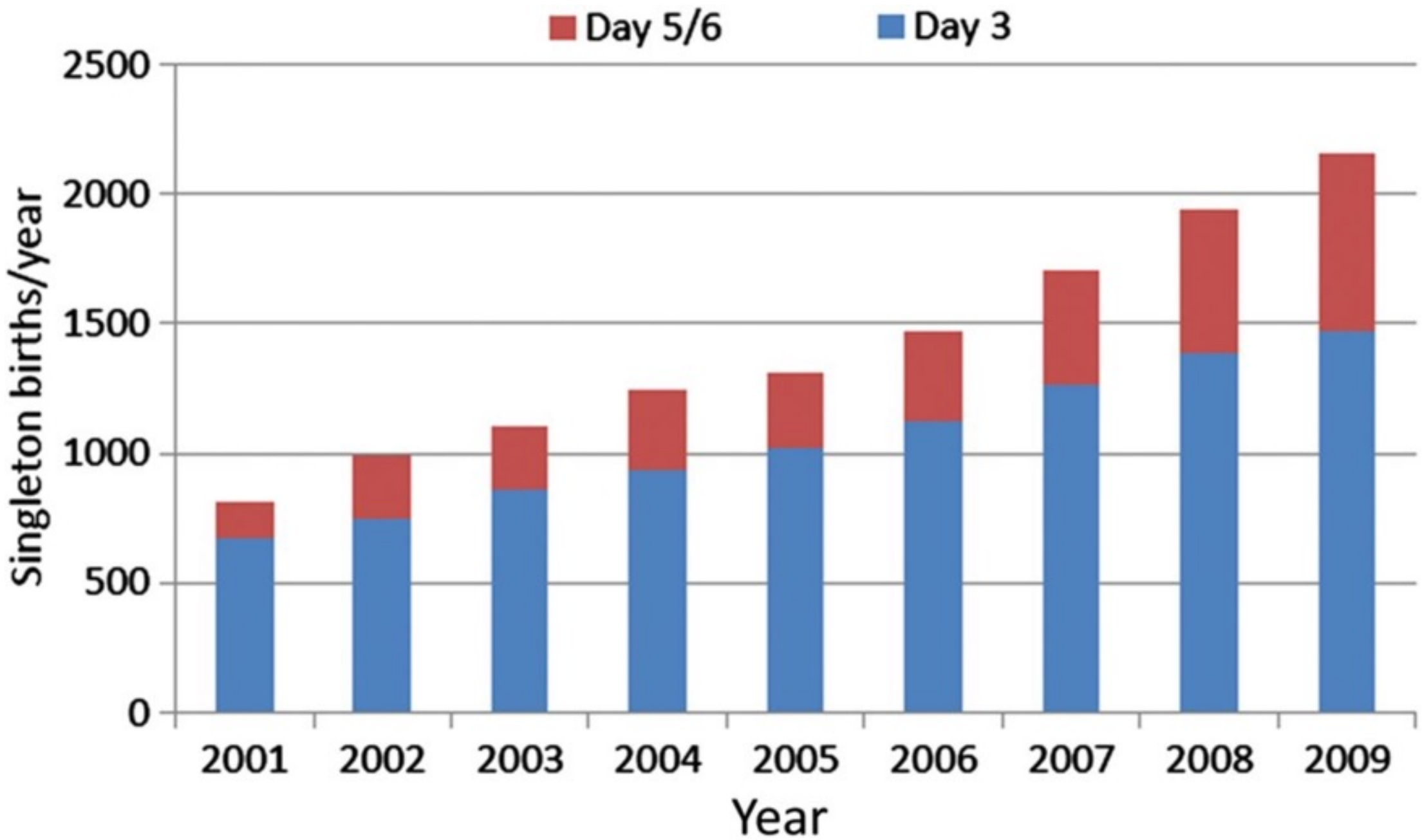
- Morfokinētiska embriju selekcija time-lapse sistēmā



ET3/ET5/FET



The number of singleton births per year from IVF/ICSI in Canada, showing proportions following transfer on Day 3 (blue) or Day 5/6 (red).



Dar S et al. Hum. Reprod. 2013;28:924-928

human reproduction

SET

- stratēģija samazināt daudzaugļu grūtniecību
- parasti blastocitas stādijā
- take home baby rate?
- drostalošanās stadija vai blastocista?

SET3/SET5

- priekšlaicīgo dzemdību risks 14.4% vs. 18.6%

- Iedzimto anomāliju risks?

SET/DET

Number of embryos for transfer following in vitro fertilisation or intra-cytoplasmic sperm injection (Review)

Pandian Z, Marjoribanks J, Ozturk O, Serour G, Bhattacharya S

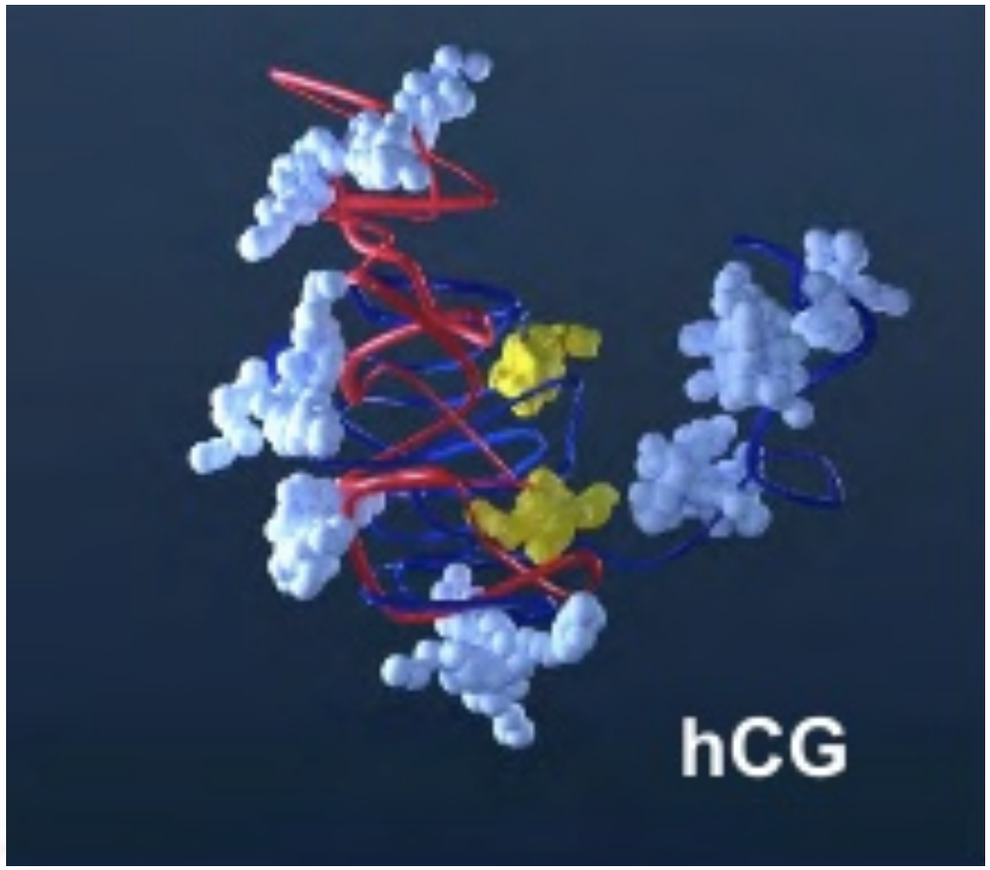
Authors' conclusions

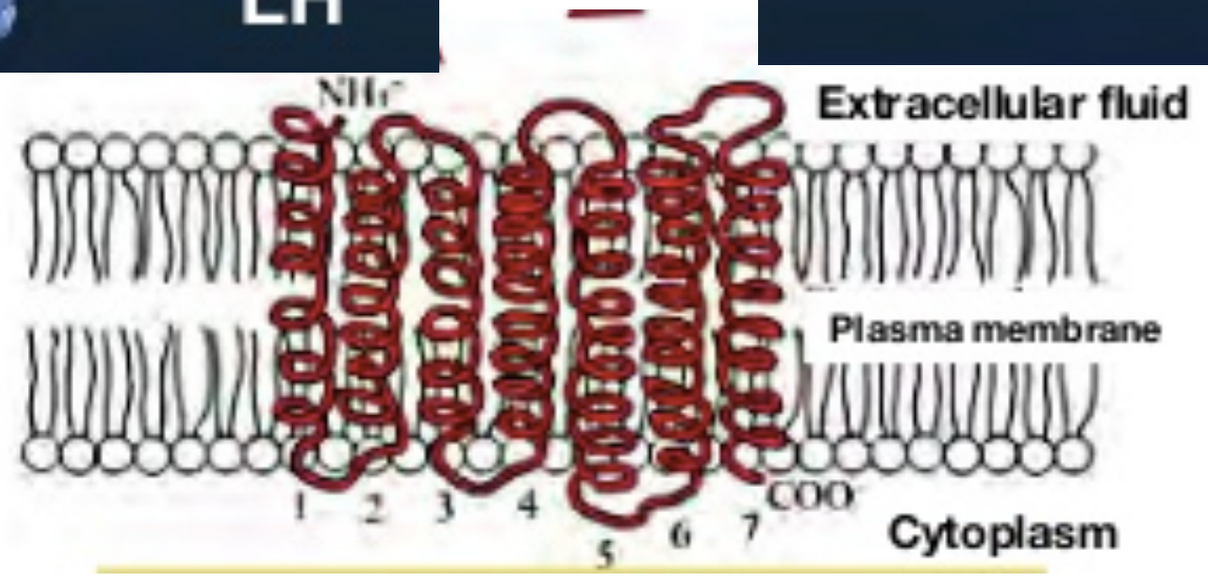
In a single fresh IVF cycle, single embryo transfer is associated with a lower live birth rate than double embryo transfer. However, there is no evidence of a significant difference in the cumulative live birth rate when a single cycle of double embryo transfer is compared with repeated SET (either two cycles of fresh SET or one cycle of fresh SET followed by one frozen SET in a natural or hormone-stimulated cycle). Single embryo transfer is associated with much lower rates of multiple pregnancy than other embryo transfer policies. A policy of repeated SET may minimise the risk of multiple pregnancy in couples undergoing ART without substantially reducing the likelihood of achieving a live birth. Most of the evidence currently available concerns younger women with a good prognosis.

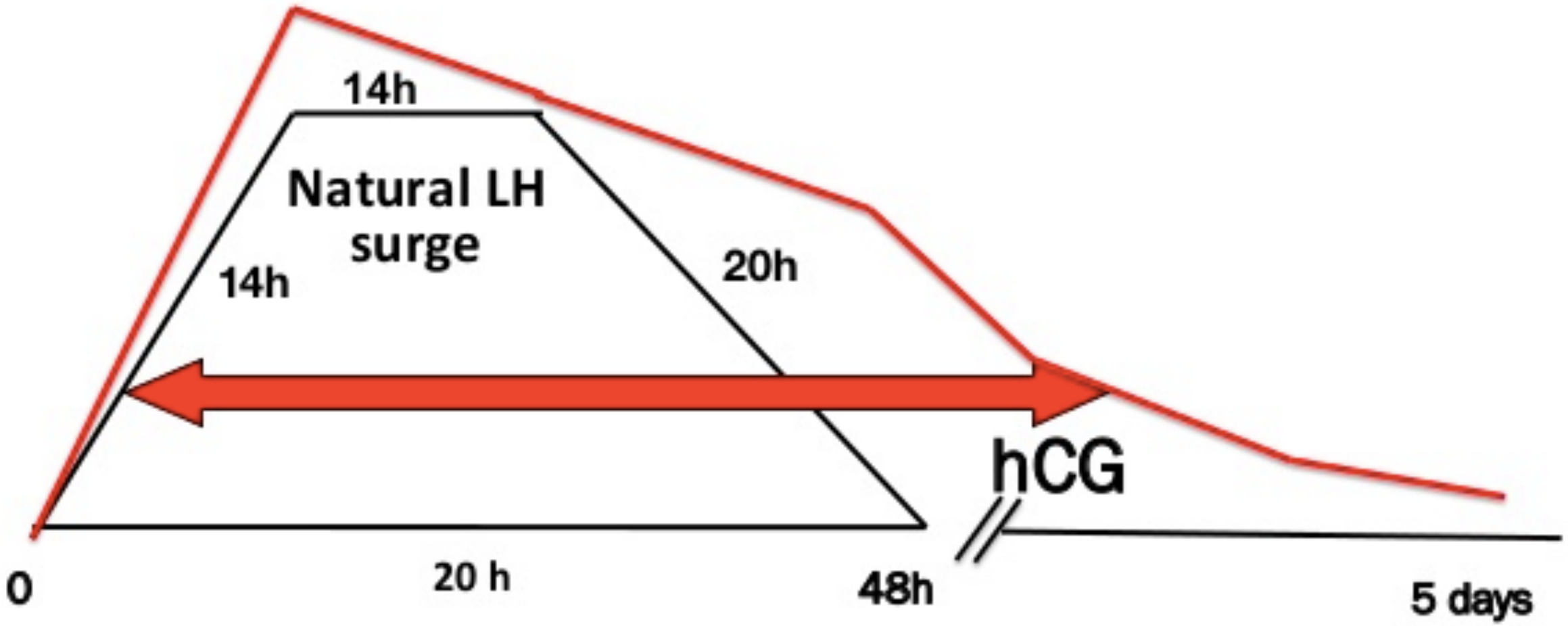
Luteāla fāze stimulētajā IVF/ ICSI ciklā

- multifolikulāra ovulācija - “multilutelas" olnīcas
- suprafizioloģiskā progesterona un estrogēna koncentrācija
- LH sekrēcijas inhibēšana Humaidan P, Papanikolaou EG, Kyrou D, Alsbjerg B, Polyzos NP, Devroey P, et al. The luteal phase after GnRH-agonist triggering of ovulation: present and future perspectives. Reprod Biomed Online. 2012;24(2):134–141.
- luteāla nepietiekamība - priekšlaicīga luteolīze
- neizdevusies implantācija
- agrīna grūtniecības pārtraukšana Fatemi HM. The luteal phase after 3 decades of IVF: what do we know? Reprod Biomed Online. 2009;19(Suppl 4):4331–4331

LH/hCG receptors







Adapted from Chan et al. *Hum Reprod.* 2003;18:2294-7

Luteāla fāze pēc hCG trigera

- hCG v.s. LH - garāks pussabrukšanas periods (>24 stundas)
- hCG trigers atbalsta dzelteno ķermeni 7-10 dienas
- embrija hCG sekrēcija mātes serumā ir limitēta
- endogēnais LH inhibēts (KOS)
- dzeltenā ķermeņa disfunkcija agrīnajā un vidējā luteālajā fāzē
- OHSS risks

OHSS

- biežāka KOS komplikācija
- 3-8% no IVF/ICSI cikliem
- hCG inducēts E2 pīķis - VEGF
- palielināta asins kapilāru caurlaidība
- cirkulējoša šķidruma pārēja no kapilāriem trešajā telpā

Tang H, Hunter T, Hu Y, Zhai SD, Sheng X, Hart RJ. Cabergoline for preventing ovarian hyperstimulation syndrome. Cochrane Database Syst Rev. 2012;2:CD00860

OHSS sekas

- hemokoncentrācija
- hipoperfūzija
- trombembolijas risks
- neizdevusies implantācija
- agrīna grūtniecības pārtraukšanās

Mozes M, Bogokowsky H, Antebi E, et al. Thromboembolic phenomena after ovarian stimulation with human gonadotrophins. Lancet. 1965;2(7424):1213–1215

OHSS vēlīnas sekas

- dzemdības <37 gest. ned.
- SGL
- GD, hipertensija, IUGR - atšķirības nav
- DAG iznākumi neatšķiras

Haas J, Baum M, Meridor K, Hershko-Klement A, Elizur S, Hourvitz A, Orvieto R, Yinon Y. Is severe OHSS associated with adverse pregnancy outcomes? Evidence from a case-control study. Reprod Biomed Online. 2014 Aug;29(2):216-21

Trombozes risks

- asociējas ar OHSS un grūtniecību
- KOS protokoli, kas samazina OHSS risku
- profilakse pacientēm ar papildus RF

Risk of thrombosis in women with malignancies undergoing ovarian stimulation for fertility preservation

Edgardo Somigliana[1,*], Fedro Alessandro Peccatori[2], Francesca Filippi[1], Fabio Martinelli[3], Francesco Raspagliesi[3] and Ida Martinelli[4]

OXFORD JOURNALS

Human Reproduction Update

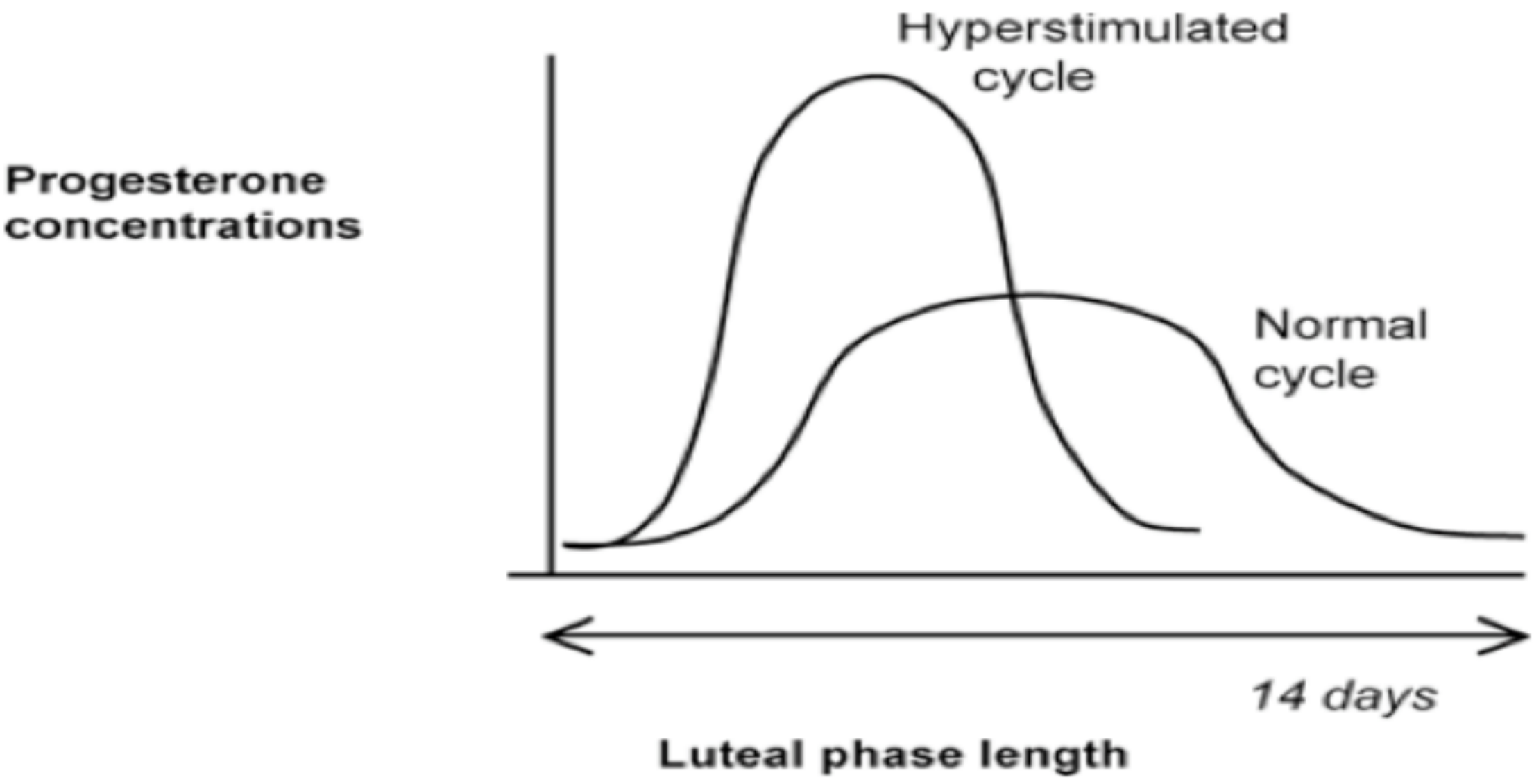
human reproduction update

Impact Factor: 8.657

Luteāla faze pēc GnRHa trigera

- GnRHa pussabrukšanas periods - 60 min
- LH pīķis 24-36 stundas v.s. 48 stundas NC
- estrogēni progresīvi samazinās
- progesterons samazinās, tad pieaug pēc OPU
- FSH pieaugums (līdzīgs NC)
- Retāk OHSS Humaidan P, Papanikolaou EG, Kyrou D, Alsbjerg B, Polyzos NP, Devroey P, et al. The luteal phase after GnRH-agonist triggering of ovulation: present and future perspectives. Reprod Biomed Online. 2012;24(2):134–141
- lielāks nobriedušo oocītu daudzums? Humaidan P, Kol S, Papanikolaou EG. GnRH agonist for triggering of final oocyte maturation: time for a change of practice? Hum Reprod Update. 2011;17(4):510–524.

Luteālas fāzes defekts KOS ciklā



adaptēts no Macklon et al., 2006

Luteālas fāzes atbalsts

- Estradiols - nav efektīvs Huang N, Situ B, Chen X, Liu J, Yan P, Kang X, Kong S, Huang M. Meta-analysis of estradiol for luteal phase support in in vitro fertilization/intracytoplasmic sperm injection. Fertil Steril. 2014 Dec 6. pii: S0015-0282(14)02289-4

- Progesterons - uzlabo dzimstību, klīniskas grūtniecības un progresējošas grūtniecības iespejamību van der Linden M, Buckingham K, Farquhar C, Kremer JA, Metwally M. Lutealphase support for assisted reproduction cycles. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD009154.

J Assist Reprod Genet. 2014 Jan;31(1):89-100. doi: 10.1007/s10815-013-0127-6. Epub 2013 Nov 6.

Efficacy of luteal phase support with vaginal progesterone in intrauterine insemination: a systematic review and meta-analysis.

Miralpeix E[1], González-Comadran M, Solà I, Manau D, Carreras R, Checa MA.

Author information

Abstract

PURPOSE: To evaluate the efficacy of luteal phase support with vaginal progesterone in women undergoing intrauterine insemination (IUI).

METHODS: Systematic review and meta-analysis. Randomized controlled trials (RCT) comparing supplementation of luteal phase with vaginal progesterone among women undergoing IUI versus a control group were included. The main outcome assessed was live birth rate.

RESULTS: Five RCT met the inclusion criteria. In all 1,271 patients were included (951 IUI cycles in the progesterone group, 935 in the control group). Women treated with vaginal progesterone achieved significantly higher live birth rate (risk ratio [RR] 1.94, 95 % confidence interval [CI] 1.36 to 2.77,), and clinical pregnancy rate (RR 1.41, 95 % CI 1.14 to 1.76) as compared with controls. In the subgroup analysis per stimulation protocol, this beneficial effect of receiving progesterone was only observed in the group stimulated with gonadotropins (RR 2.28, 95 % CI 1.49 to 3.51), compared to the group stimulated with clomiphene citrate (CC) (RR 1.30, 95 % CI 0.68 to 2.50). No differences were observed in the miscarriage and multiple pregnancy rates.

CONCLUSIONS: The supplementation of luteal phase with vaginal progesterone significantly increases live birth among women undergoing IUI when receiving gonadotropins for ovulation induction. Women receiving CC to induce ovulation do not seem to benefit from this treatment.

Treatment of luteal phase defects in assisted reproduction.

Muñoz E[1], Taboas E, Portela S, Aguilar J, Fernandez I, Muñoz L, Bosch E.

Author information

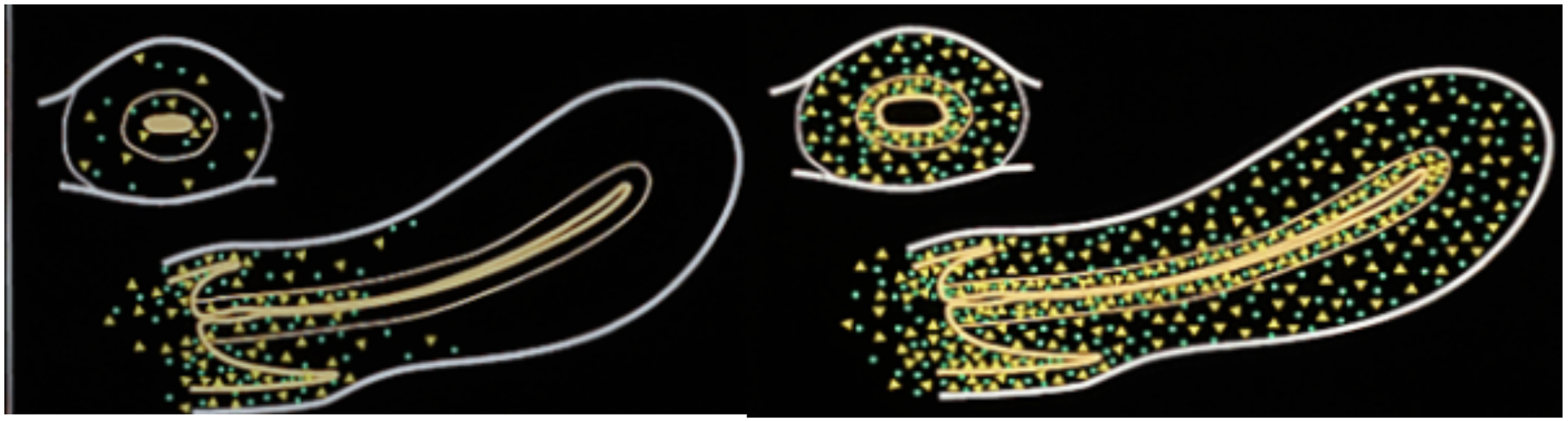
Abstract

Abnormal luteal function is a common issue in assisted reproduction techniques associated with ovarian stimulation probably due to low levels of LH in the middle and in the late luteal phase. This defect seems to be associated with supraphysiological steroid levels at the end of follicular phase. The luteal phase insufficiency has not got a diagnostic test which has proven reliable in a clinical setting. Luteal phase after ovarian stimulation becomes shorter and insufficient, resulting in lower pregnancy rates. Luteal phase support with progesterone or hCG improves pregnancy outcomes and no differences are found among different routes of administration. However, hCG increases the risk of ovarian hyperstimulation syndrome. In relation to the length of luteal support, the day of starting it remains controversial and it does not seem necessary to continue once a pregnancy has been established. After GnRHa triggering ovulation, intensive luteal support or hCG bolus can overcome the defect in luteal phase, but more studies are needed to show the LH utility as support.

Kā?

Pēc stundas

Pēc 4 stundām



Bulletti et al. Hum Reprod. 1997;12:1073-9

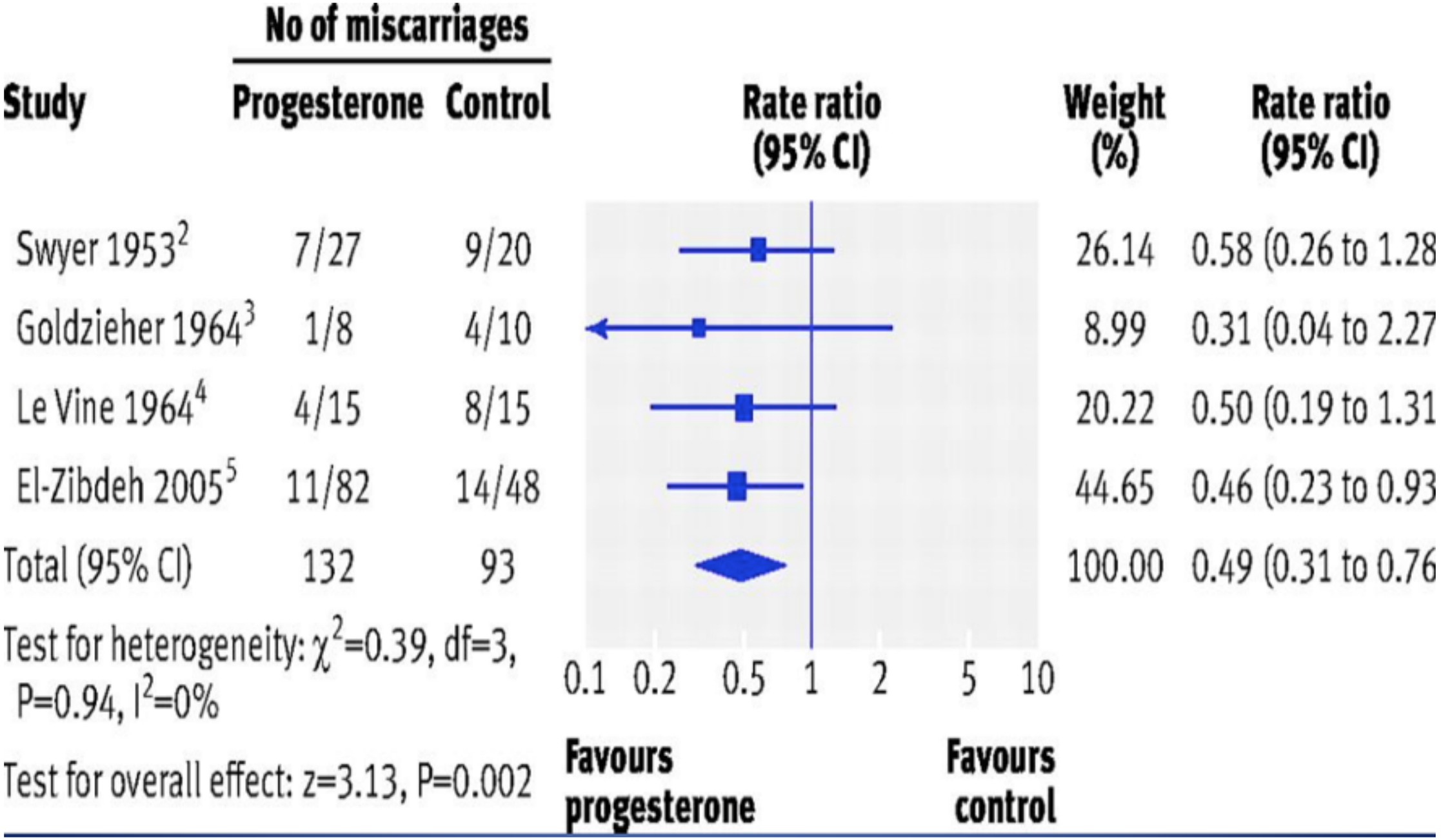
- IM/PV nav atšķirības klīniskas grūtniecības un AGP
  Mitwally et al., Fertil Steril, 2010

- PO var būt neefektīvs Penzias, 2002; Bourgain, 1990; Devroey, 1988

Cik?

- Mikronizētais progesterons 200mg PV 3 reizes dienā
- Progesterona gēls 8% 90mg reizi dienā
- Pozitīvs HCG? Andersen et al., 2002
- STOP??? - 6/7-10-12 nedēļai

Vai turpināt pacientēm ar NI un AGN ?



Coomarasamy A et al. BMJ 2011;342:bmj.d1914

Hum Reprod. 2014 May;29(5):931-7. doi: 10.1093/humrep/deu042. Epub 2014 Mar 6.

Non-visualized pregnancy losses are prognostically important for unexplained recurrent miscarriage.

Kolte AM[1], van Oppenraaij RH, Quenby S, Farquharson RG, Stephenson M, Goddijn M, Christiansen OB; ESHRE Special Interest Group Early Pregnancy.

STUDY QUESTION: Are non-visualized pregnancy losses (biochemical pregnancy loss and failed pregnancy of unknown location combined) in the reproductive history of women with unexplained recurrent miscarriage (RM) negatively associated with the chance of live birth in a subsequent pregnancy?

SUMMARY ANSWER: Non-visualized pregnancy losses contribute negatively to the chance for live birth: each non-visualized pregnancy loss confe a relative risk (RR) for live birth of 0.90 (95% CI 0.83; 0.97), equivalent to the RR conferred by each additional clinical miscarriage.

WHAT IS KNOWN ALREADY: The number of clinical miscarriages prior to referral is an important determinant for live birth in women with RM, whereas the significance of non-visualized pregnancy losses is unknown.

STUDY DESIGN, SIZE, DURATION: A retrospective cohort study comprising 587 women with RM seen in a tertiary RM unit 2000-2010. Data on th outcome of the first pregnancy after referral were analysed for 499 women.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The study was conducted in the RM Unit at Rigshospitalet, Copenhagen, Denmark. We included all women with unexplained RM, defined as ≥3 consecutive clinical miscarriages or non-visualized pregnancy losses following spontaneous

Progestogen for treating threatened miscarriage (Review)

Wahabi HA, Fayed AA, Esmaeil SA, Al Zeidan RA

Authors' conclusions

The data from this review suggest that the use of progestogens is effective in the treatment of threatened miscarriage with no evidence of increased rates of pregnancy-induced hypertension or antepartum haemorrhage as harmful effects to the mother, nor increased occurrence of congenital abnormalities on the newborn. However, the analysis was limited by the small number and the poor methodological quality of eligible studies (four studies) and the small number of the participants (421), which limit the power of the meta-analysis and hence of this conclusion.

Pirmais trimestris

Grūtniecības laika noteikšana

- embrija vecums ET dienā
- ET3 - 16. gest diena s. 2n2d
- ET5 - 18. gest. diena s. 2n4d
- zemāka perinatāla M&M 39.-40.$^{0+6}$gest. ned

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

aium
The association for medical ultrasound
AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE

Society for Maternal-Fetal Medicine

COMMITTEE OPINION

Number 611 • October 2014

(See also Committee Opinion No. 579)

Committee on Obstetric Practice
American Institute of Ultrasound in Medicine
Society for Maternal-Fetal Medicine

Method for Estimating Due Date

- Ultrasound measurement of the embryo or fetus in the first trimester (up to and including 13 6/7 weeks of gestation) is the most accurate method to establish or confirm gestational age.
- If pregnancy resulted from assisted reproductive technology (ART), the ART-derived gestational age should be used to assign the estimated due date (EDD). For instance, the EDD for a pregnancy resulting from in vitro fertilization should be established using the age of the embryo and the date of transfer.
- As soon as data from the last menstrual period (LMP), the first accurate ultrasound examination, or both are obtained, the gestational age and the EDD should be determined, discussed with the patient, and documented clearly in the medical record. Subsequent changes to the EDD should be reserved for rare circumstances, discussed with the patient, and documented clearly in the medical record.

Table 1. Guidelines for Redating Based on Ultrasonography

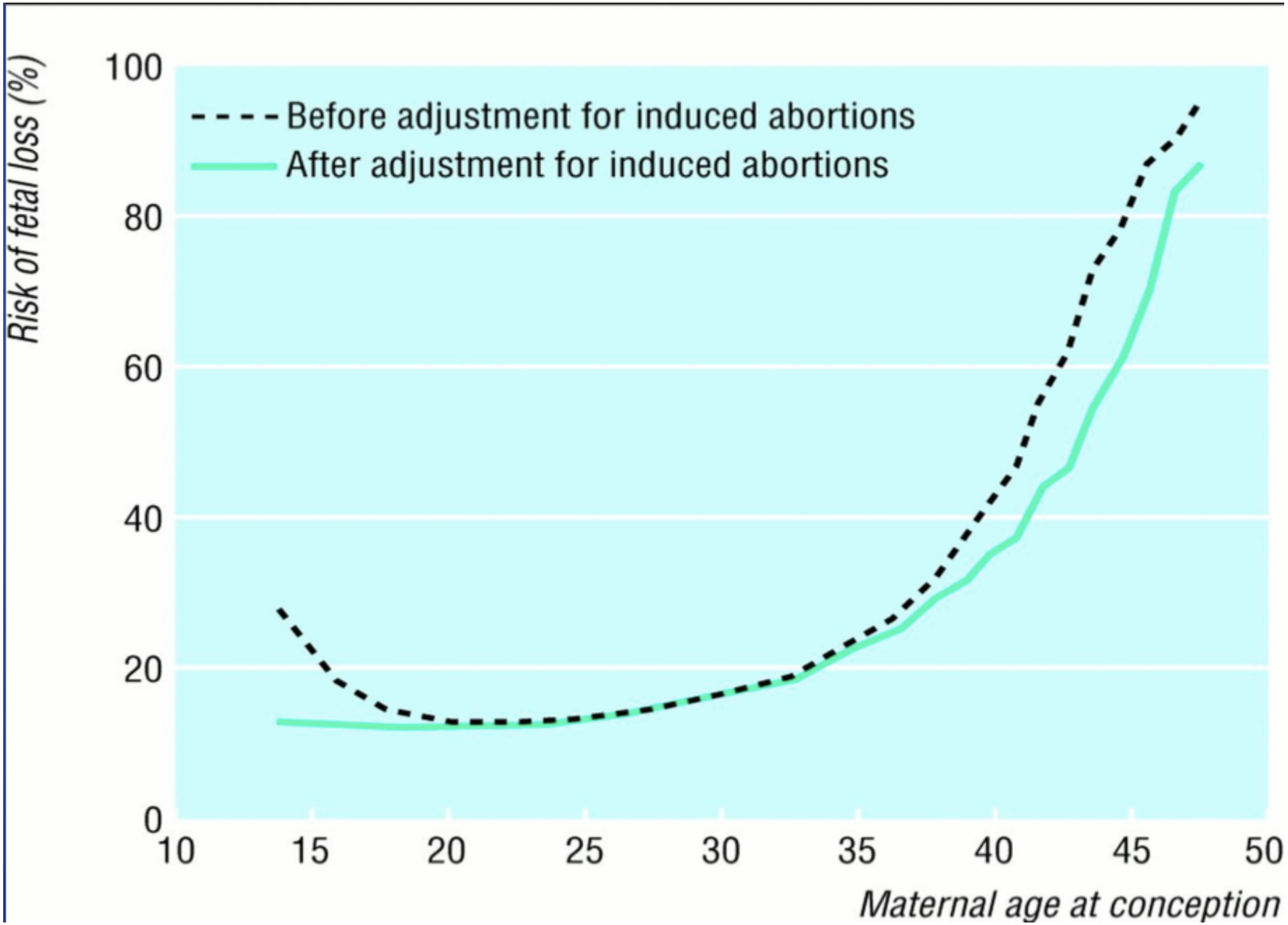
Gestational Age Range*	Method of Measurement	Discrepancy Between Ultrasound Dating and LMP Dating That Supports Redating
≤ 13 6/7 wk	CRL	
• ≤ 8 6/7 wk		More than 5 d
• 9 0/7 wk to 13 6/7 wk		More than 7 d
14 0/7 wk to 15 6/7 wk	BPD, HC, AC, FL	More than 7 d
16 0/7 wk to 21 6/7 wk	BPD, HC, AC, FL	More than 10 d
22 0/7 wk to 27 6/7 wk	BPD, HC, AC, FL	More than 14 d
†28 0/7 wk and beyond	BPD, HC, AC, FL	More than 21 d

Problēmas

- AGN
- grūtniecības pārtraukšanās draudi
- pirmā trimestra ģenētiskais skrīnings
- invazīvā prenatālā diagnostika

Mātes vecums

- grūtniecības inducēta hipertensija
- hroniskas saslimšanas: hipertensija, sirds saslimšanas, diabēts
- mātes saslimstība un mirstība
- IUAN
- ektopiska grūtniecība
- ĀGN
- >45 gadiem S.C. 50%, >50% S.C. ap 100%



Andersen A N et al. BMJ 2000;320:1708-1712

NATURAL CONCEPTION

LIVE BIRTH

~ 50%

CLINICAL PREGNANCY

miscarriage ~ 7%

AMENORRHEA

biochemical loss ~ 6%

pre-clinical loss ~ 7%

IMPLANTATION

~37%

(pre- implantation loss ~30%)

(CONCEPTION)

75% non implantation cycle

(non conceptive cycle)

NATURAL CYCLE

IVF CONCEPTION

LIVE BIRTH

30%

miscarriage 6%

biochemical loss 7%

non-visualised pregnancy loss

(pre-clinical loss ~23%)

(IMPLANTATION)

56%

(pre-implantation loss ~34%)

CONCEPTION: ET

IVF CYCLE

adaptēts no Visiting the “black box” of early pregnancy loss. Yvonne Koot ESHRE early pregnancy work group 11-12.12.2014

adaptēts no Visiting the “black box” of early pregnancy loss. Yvonne Koot ESHRE early pregnancy work group 11-12.12.2014

Asistētas ĀGN riska faktori

Riska faktors	Publikācija
Mātes vecums >35 gadiem	Maconochie et al., 2007, Nybo Andersen et al., 2000)
Tēva vecums >40 gadiem	Belloc et al., 2008, de la Rochebrochard and Thonneau, 2002)
Smags OHSS	Raziel et al. (2002))
Aptaukošanas ar/bez PCOS	Aviram et al., 2011, Boots and Stephenson, 2011, Purcell and Moley, 2011)
Olvadu patoloģija	Laisk et al., 2011, Stephens et al., 2011)
IUI	Bettio et al., 2008, Maconochie et al., 2007)
ICSI ar TESA	Bettio et al. (2008))
Olšūnas nobriešana in vitro	Buckett et al. (2008))
FET	Brandes et al. (2011))

70% ir saistīti ar aneipoidīju

Werner, M., Reh, A., Grifo, J., and Perle, M.A. **Characteristics of chromosomal abnormalities diagnosed after spontaneous abortions in an infertile population.** *J. Assist. Reprod. Genet.* 2012; (Epub ahead of print)

Progestogen for treating threatened miscarriage (Review)

Wahabi HA, Fayed AA, Esmaeil SA, Al Zeidan RA

Authors' conclusions

The data from this review suggest that the use of progestogens is effective in the treatment of threatened miscarriage with no evidence of increased rates of pregnancy-induced hypertension or antepartum haemorrhage as harmful effects to the mother, nor increased occurrence of congenital abnormalities on the newborn. However, the analysis was limited by the small number and the poor methodological quality of eligible studies (four studies) and the small number of the participants (421), which limit the power of the meta-analysis and hence of this conclusion.

Kas ir “evidence based”

- vecāku hromosomāla patoloģija - PGS/PGD
- antifosfolipīdu sindroms - antokoagulanti

Klīniskie pētījumi

- PROMISE - gaidām rezultātus
- ALIFE un ALIFE2 - trombofīlijas pacientēm aspirīns un heparīns
- T4LIFE - TPO antivielas
- TRUST - dzemdes starpsienas
- Primarāis iznākums - dzīvi dzimušo skaits

Dzīves veids

- ĶMI>25 Fedorcsak, 2000; Winter, 2002
- Smēķēšana: vīriešu Venners, 2004, sieviešu Winter, 2002
- vides toksicitāte
- stress - kortizols Nepomnanschy, 2006
- gadalaiki - cirkadiānie ritmi? Weinberg, 1994

PRENATAL PARANOIA.

Otrais trimestris

Problēmas

- istmiko-cervikāla nepietiekamība
- priekšlaicīgo dzemdību draudi - slikta prognoze
- otra trimestra USG skrīnings
- otra trimestra ģenētiskais skrīnings
- invazīvas prenatālas diagnostikas metodes
- grūtniecības inducēta hipertenzija
- gestācijas diabēts

Preeklampsija

- azoospermija/oligospermija - lielāks risks Ulkumen B, Silfeler D, Sofuoglu K, Silfeler I, Dayicioglu V. The incidence of preeclampsia in ICSI pregnancies. Pak J Med Sci. 2014 Jan;30(1):101-5

- ART - lielāks risks

- DAG proteinūrija ir biežāk un lielāk nekā VAG Smith NA, Lyons JG, McElrath TF. Protein:creatinine ratio in uncomplicated twin pregnancy. Am J Obstet Gynecol. 2010 Oct;203(4):381

- Riska noteikšana

- Aspirīns profilaktiski pēc pamošanās vai pirms gulētiešanas Ayala et al., 2013

Gestācijas diabēts

- VAG 2x lielāks risks Ashrafi M, Gosili R, Hosseini R, Arabipoor A, Ahmadi J, Chehrazi M. Risk of gestational diabetes mellitus in patients undergoing assisted reproductivetechniques. Eur J Obstet Gynecol Reprod Biol. 2014 May;176:149-52

- DAG nav biežāk un sliktāk, nekā VAG Lai FY, Johnson JA, Dover D, Kaul P. Outcomes of singleton and twin pregnancies complicated by preexisting diabetes and gestational diabetes: apopulation-based study in Alberta, Canada, 2005-2011

- Progesterons?

Trešais trimestris

Problēmas

- priekšlaicīgas dzemdības
- grūtniecības inducēta hipertenzija
- gestācijas diabēts
- placenta praevia
- dzemdības

Placentas un nabassaites patoloģija

- Placenta praevia - 1.6% asistētai vienaugļa grūtniecībai un 0.8% asistētai dviņu grūtniecībai v.s. 0.2% spontānai grūtniecībai Romundstad, L.B., Romundstad, P.R., and Sunde, A. VonDuring V, Skjaerven R, Vatten LJ. Increased risk of placenta previa in pregnancies following IVF/ICSI; a comparison of ART and non-ART pregnancies in the same mother. *Hum. Reprod.* 2006; 21: 2353–2358

- Nabas saite apvalkos līdz 10% un vasa praevia Gavriil, P., Jauniaux, E., and Leroy, F. Pathologic examination of placentas from singleton and twin pregnancies obtained after in vitro fertilization and embryo transfer. *Pediatr. Pathol.* 1993; 13: 453–462

Viena augļa grūtniecība

SET

- vienaugļa grūtniecība
- Dzīvi dzimušie dvīņi 2.3% (109/4701)
- MHBA (65/109)
- BHBA (45/109)
- MHMA (2/109)
- 12/109 bija atšķirīgs dzimums - 1 no 5 var būt pēc konkurentas SC

Osianlis T, Rombauts L, Gabbe M, Motteram C, Vollenhoven V. Incidence and zygosity of twin births following transfers using a single fresh or frozen embryo. Hum Reprod. 2014 Jul;29(7): 1438-43

Increased risk of preterm birth in singleton pregnancies after blastocyst versus Day 3 embryo transfer: Canadian ART Register (CARTR) analysis

Table II
Adjusted risks for adverse outcomes in singleton births from IVF/ICSI in Canada, 2001–2009, after transfer on Day 3 (reference) or Day 5/6.

Outcome	OR (95% CI) Day 5/6 versus Day 3[a]
All preterm births (<37 weeks)	**1.32 (1.17–1.49)**
Early preterm births (<32 weeks)	1.09 (0.84–1.42)
Low birthweight (<2500 g)	0.99 (0.85–1.15)
Very low birthweight (<1500 g)	0.93 (0.66–1.32)
Congenital anomalies	1.13 (0.85–1.50)

[a]Adjusted for the year of treatment, maternal age, parity, infertility diagnosis category, number of oocytes retrieved, insemination method, number of embryos transferred and the presence of a vanishing twin.

Bold indicates the main findings.

ART un priekšlaicīgas dzemdības

- Subfertilitāte
- Kontrolēta olnīcu stimulācija (OHHS)
- IVF laboratorijas vide
- Embriju skaits uz transfēru (viena embrija boja eja)

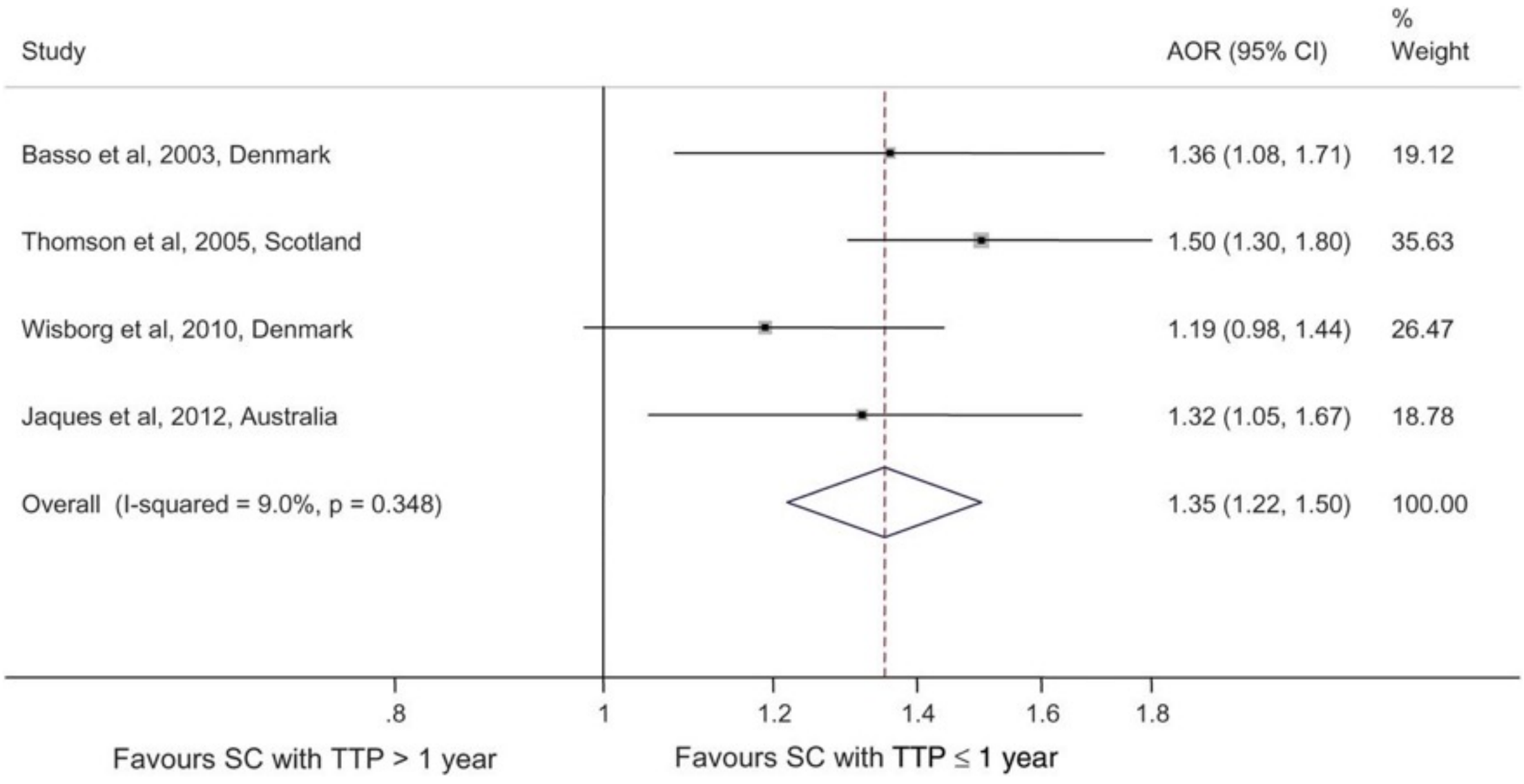
ART un priekšlaicīgas dzemdības

- Priekšlaicīgo dzemdību RF: subfertilitāte; IVF/ICSI; OI/IUI

- Priekšlaicīgo dzemdību risks samazinās: ICSI vs IVF; FET vs ET

Pinborg A, Wennerholm UB, Romundstad LB, Loft A, Aittomaki K,Söderström-Anttila V, Nygren KG, Hazekamp J, Bergh C. Why do singletons conceivedafter assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis. Hum Reprod Update. 2013 Mar-Apr;19(2):87-104

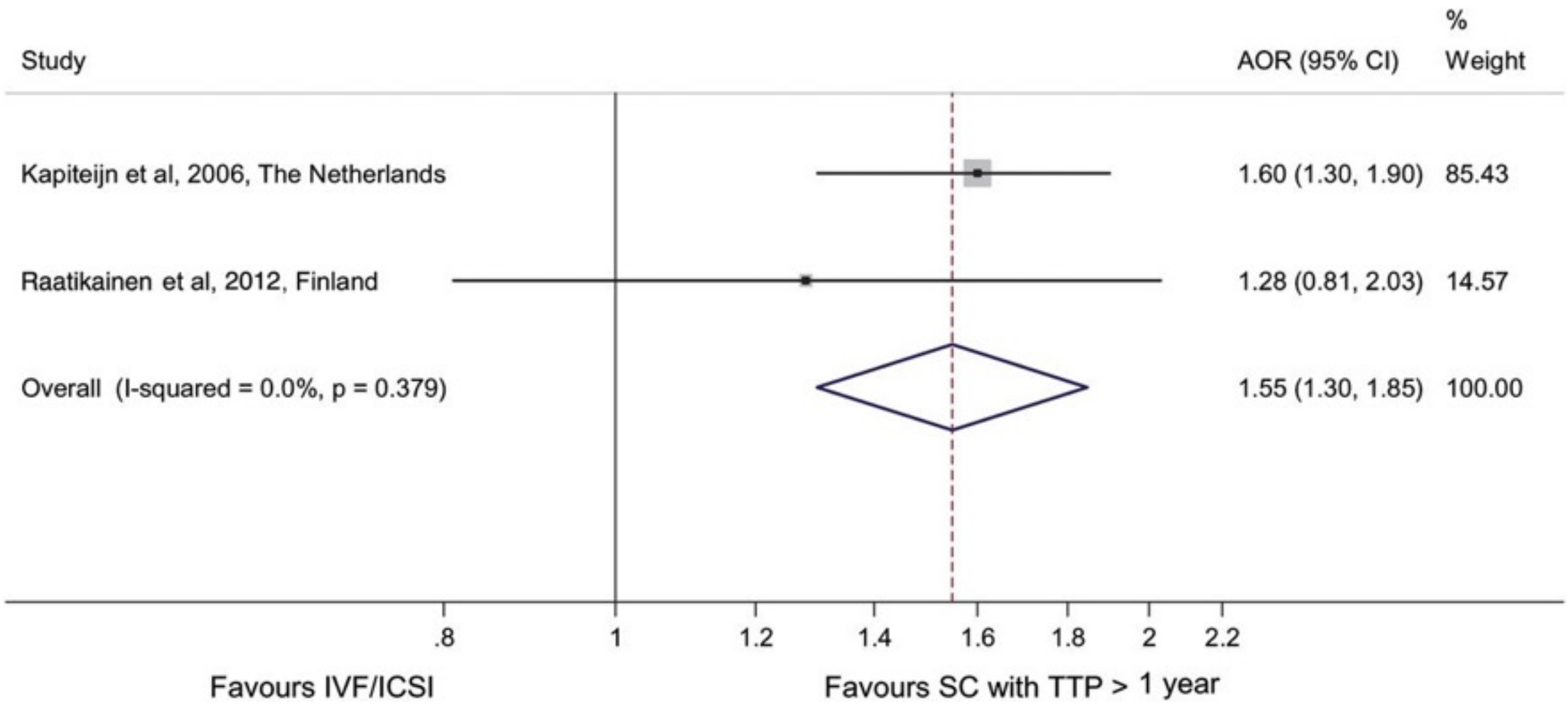
Pooled estimate on the risk of PTB in SC singletons of subfertile women with TTP > 1 year versus SC singletons of fertile women with TTP ≤ 1 year. τ2 = 0.0010.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

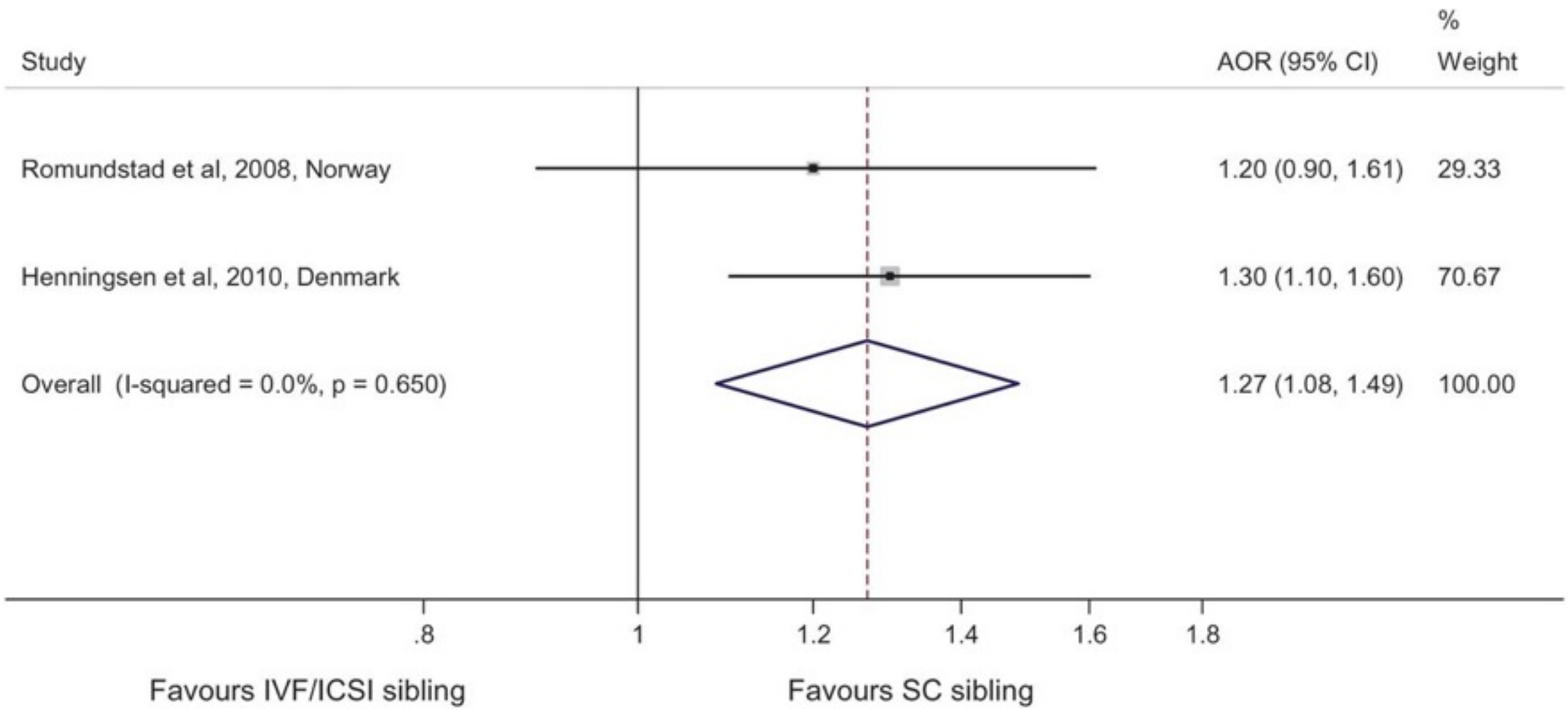
Pooled estimate on the risk of PTB in singletons born after IVF/ICSI versus SC singletons of subfertile women (TTP > 1 year). τ2 = 0.0000.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

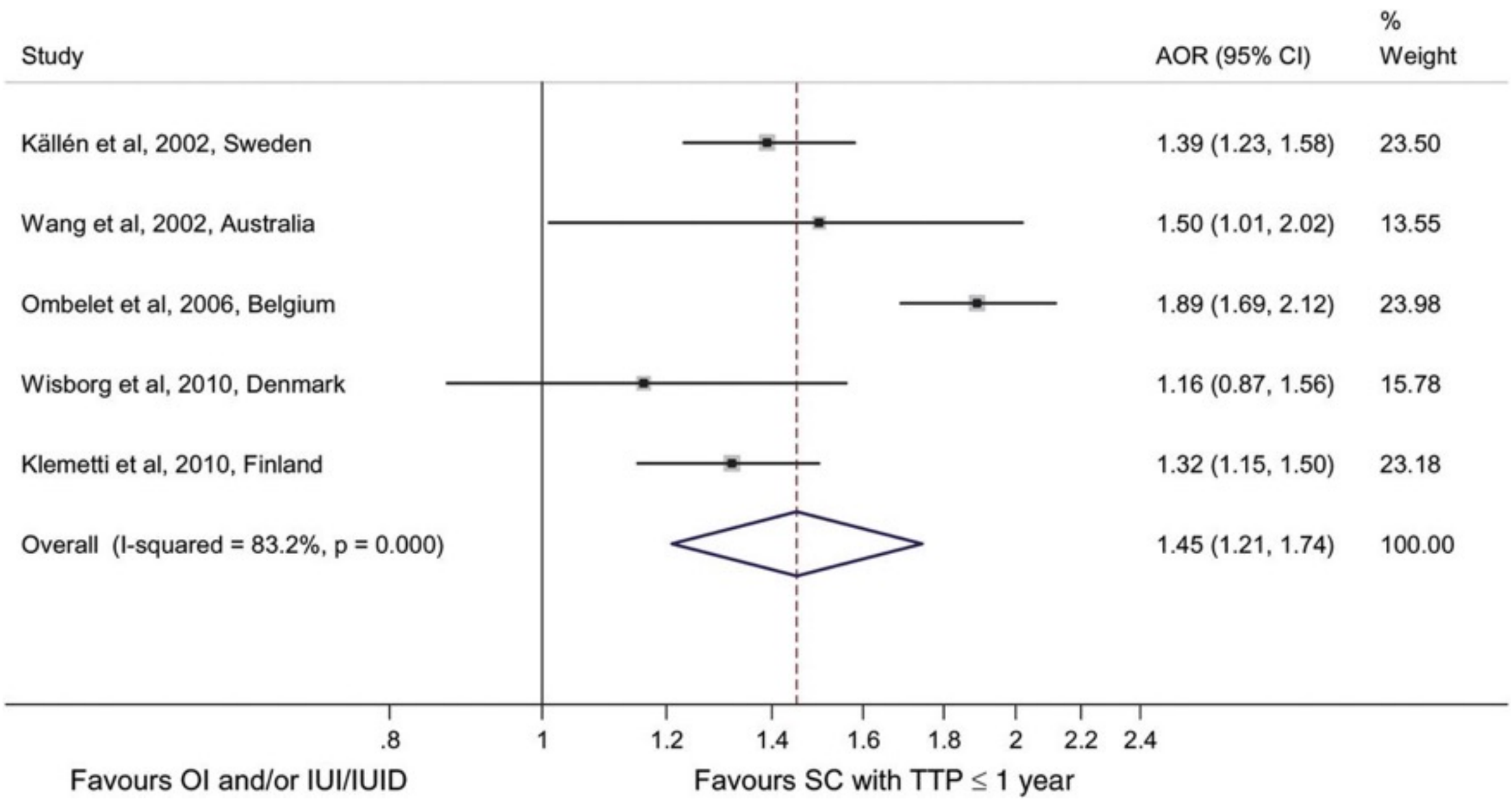
Pooled estimate on the risk of PTB in sibling studies of mothers to consecutive-singleton siblings of an IVF/ICSI child and an SC child. τ2 = 0.0000.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

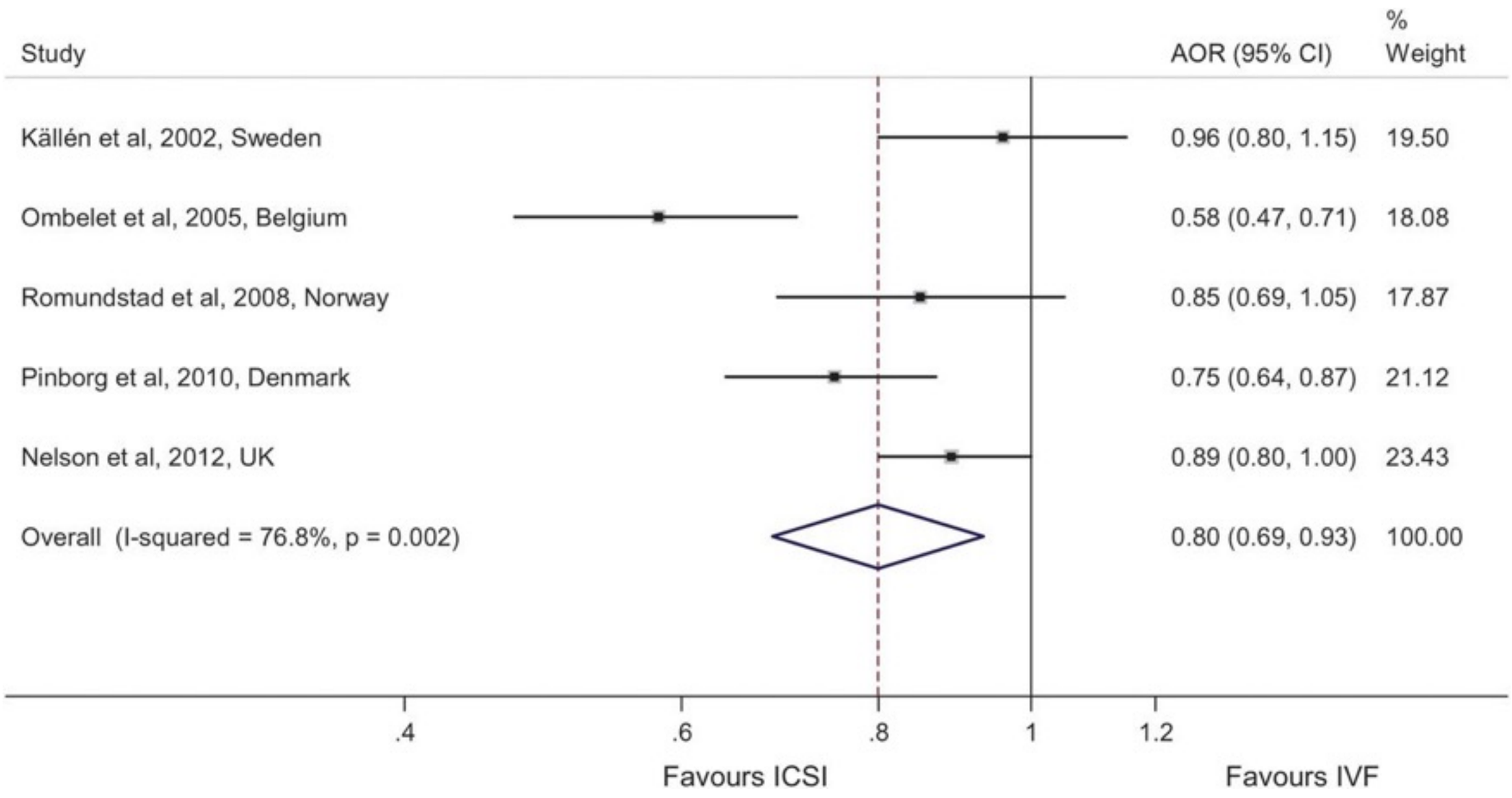
Pooled estimate on the risk of PTB in singletons born after OI and/or intrauterine insemination/ donor (IUI/IUID) versus SC singletons of fertile women with TTP ≤ 1 year. τ2 = 0.0329.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

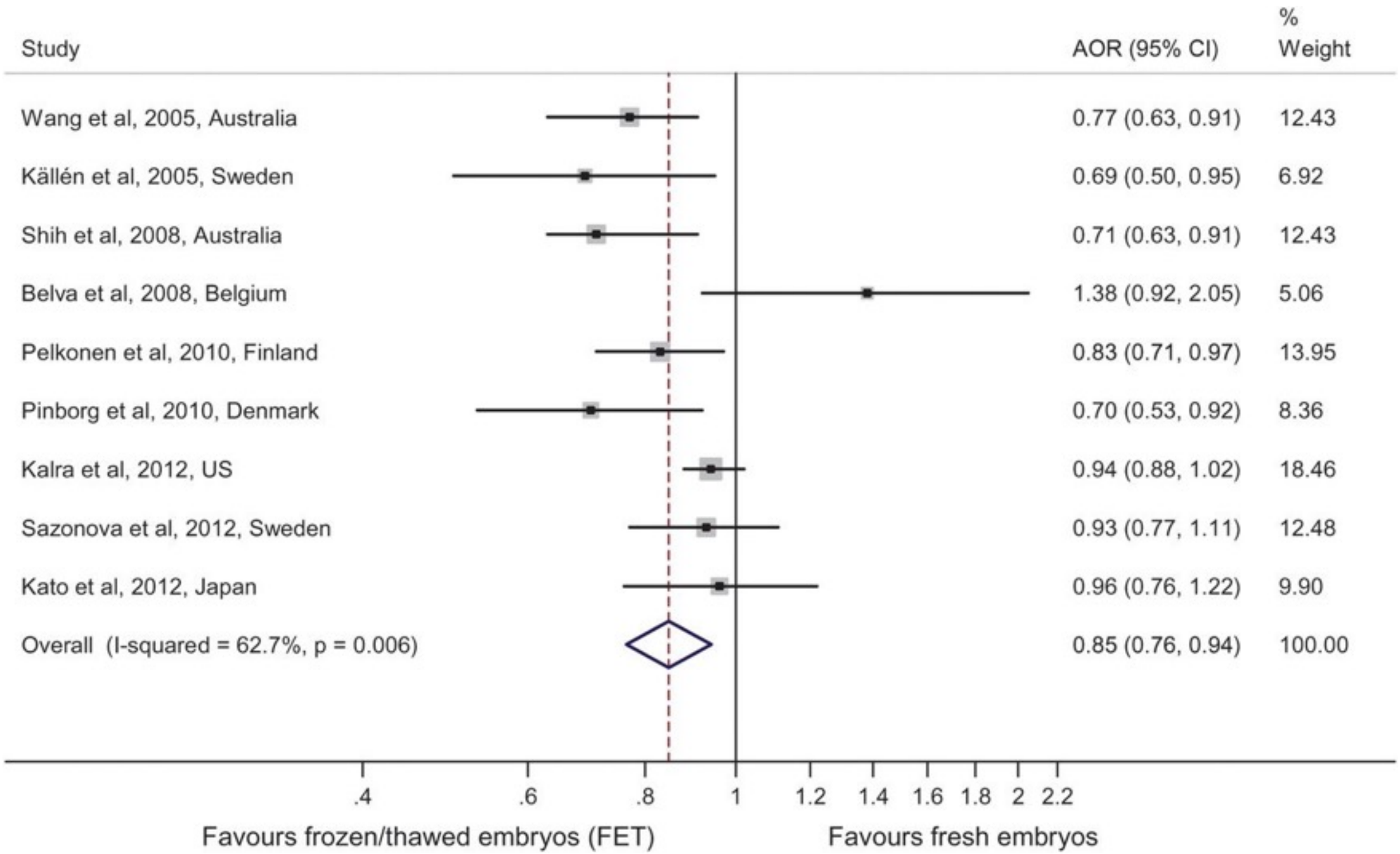
Pooled estimate on the risk of PTB singletons born after ICSI (fresh and frozen/thawed) cycles versus singletons born after IVF (fresh and frozen/thawed) cycles. τ2 = 0.0232.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

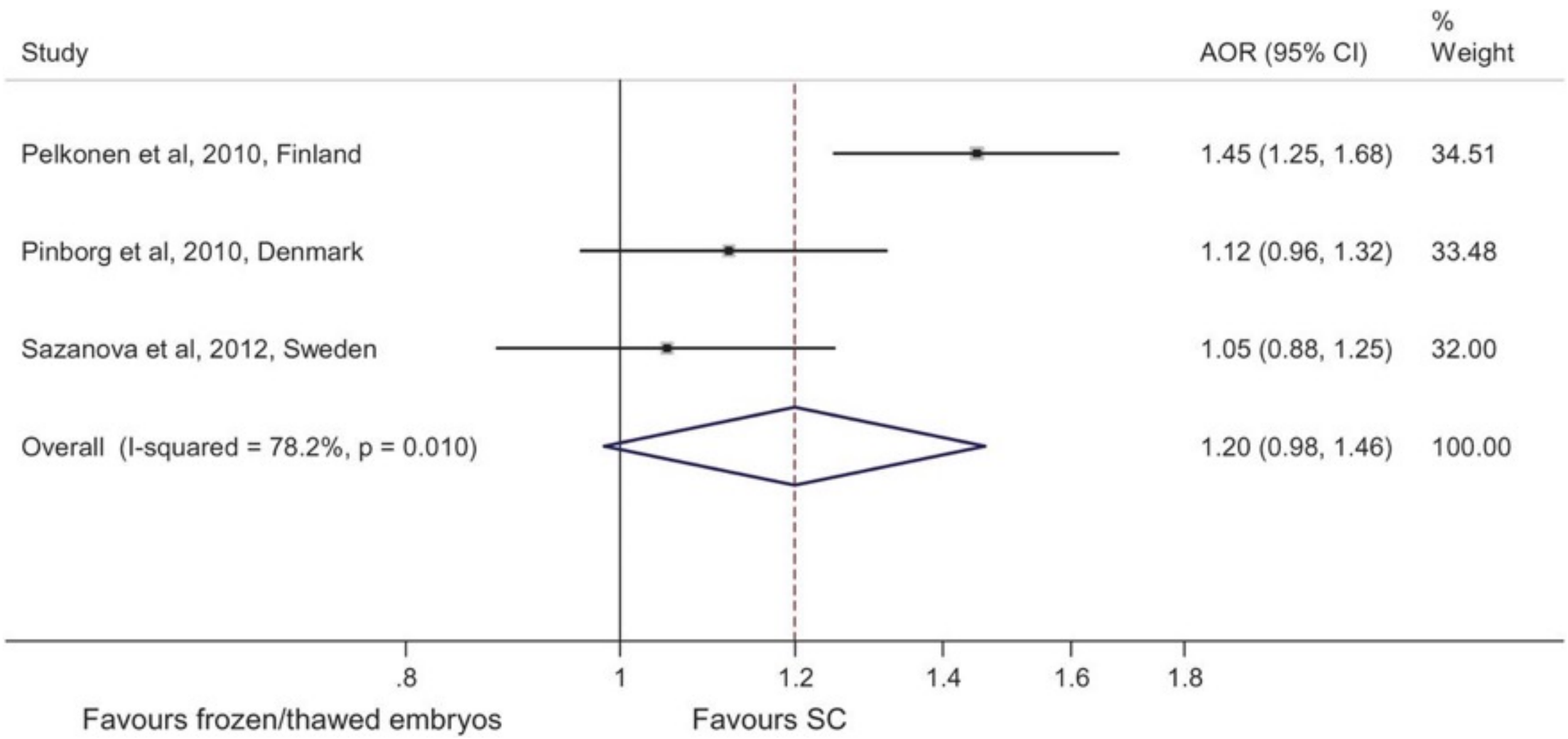
Pooled estimate on the risk of PTB in singletons born after IVF/ICSI in frozen/thawed cycles versus singletons born after IVF/ICSI in fresh cycles. τ2 = 0.0138.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

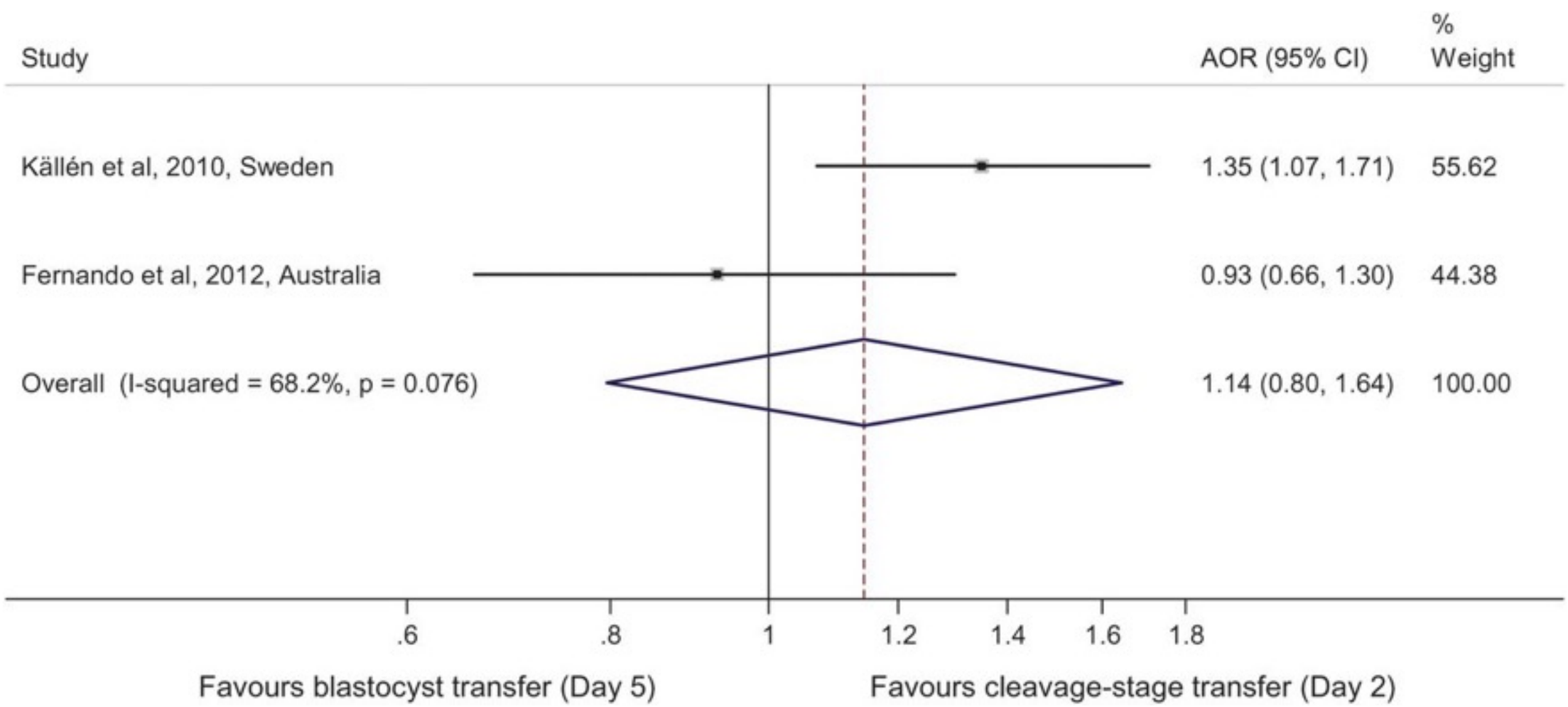
Pooled estimate on the risk of PTB in singletons born after IVF/ICSI in frozen/thawed cycles versus SC singletons in the general population. τ2 = 0.0240.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

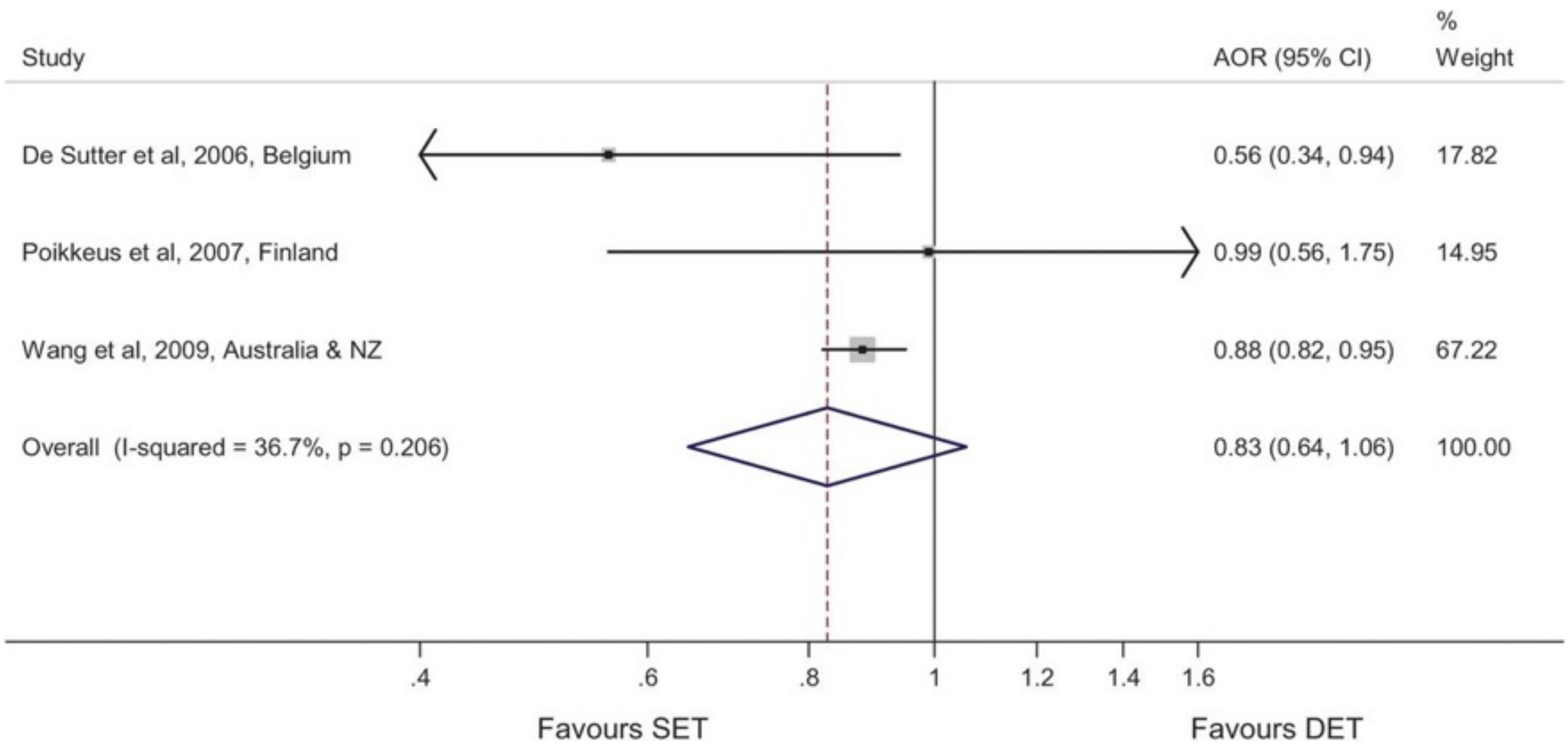
Pooled estimate on the risk of PTB in IVF/ICSI singletons born after blastocyst transfer versus IVF/ICSI singletons born after cleavage-stage transfer (Day 5 versus Day 2 culture). τ2 = 0.0473.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

Pooled estimate on the risk of PTB in singletons born after SET in fresh and frozen/thawed (FET) cycles versus singletons born after DET in fresh and FET cycles. τ2 = 0.0224.



Pinborg A et al. Hum. Reprod. Update 2013;19:87-104

human reproduction update

Priekšlaicīgas dzemdības

Hum Reprod. 2013 Apr;28(4):924-8. doi: 10.1093/humrep/des448. Epub 2013 Jan 24.

Increased risk of preterm birth in singleton pregnancies after blastocyst versus Day 3 embryo transfer: Canadian ART Register (CARTR) analysis.

Dar S[1], Librach CL, Gunby J, Bissonnette F, Gowan L, IVF Directors Group of Canadian Fertility and Andrology Society.

CI 0.73-1.38). CONCLUSIONS: Risk of PTB in IVF singleton pregnancies is significantly higher following blastocyst transfer compared with cleavage stage transfer. Risk of congenital anomalies may also be higher but further studies are needed to confirm this finding and to identify reasons for such outcomes.

Fertil Steril. 2010 Oct;94(5):1680-3. doi: 10.1016/j.fertnstert.2009.12.027. Epub 2010 Feb 4.

Blastocyst versus cleavage stage transfer in in vitro fertilization: differences in neonatal outcome?

Källén B[1], Finnström O, Lindam A, Nilsson E, Nygren KG, Olausson PO.

CONCLUSION(S): The results indicate a small increase in risk associated with blastocyst transfer, perhaps owing to the longer period of in vitro culture. There is a possibility that this effect is due, at least in part, to a selection of women for blastocyst transfers. Further studies are needed either to verify or to refute the found associations.

Obstet Gynecol. 2012 Jul;120(1):69-75. doi: 10.1097/AOG.0b013e31825b88fc.

Extended embryo culture and an increased risk of preterm delivery.

Kalra SK[1], Ratcliffe SJ, Barnhart KT, Coutifaris C.

CONCLUSION: Extended culture of embryos from cleavage stage to blastocyst stage increases the risk of preterm delivery. Unless blastocyst transfer results in a reduction in multiple births, it may be contributing to the perinatal morbidity associated with IVF-assisted conception.

Hum Reprod Update. 2014 May-Jun;20(3):439-48. doi: 10.1093/humupd/dmu001. Epub 2014 Jan 30.

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

Dar S[1], Lazer T, Shah PS, Librach CL.

WIDER IMPLICATIONS OF THE FINDINGS: We found a significantly higher risk of preterm birth (<37 weeks) in singletons after extended embryo culture (Day 5/6) compared with cleavage stage (Day 3) transfer, even when adjusting for confounding factors. Our findings are in agreement with the previous two studies; however, we did not show a difference in the very preterm deliveries (unlike the US study) or in fetal malformations (as in the Swedish study). We hypothesize that there may be a deleterious effect of prolonged in vitro embryo culture on subsequent placentation. Longer term follow-up studies will be required to determine if prolonged in vitro culture to the blastocyst stage has an adverse effect on the long-term health of offspring when compared with shorter cleavage stage culture.

Outcomes of singleton births after blastocyst versus nonblastocyst transfer in assisted reproductive technology

Dhanushi Fernando, B.Med.Sci., Jane L. Halliday, Ph.D., Susan Breheny, B.S., David Lindsay Healy, B.Med.Sci., M.B.B.S., Ph.D.

Patient(s)

4,202 women who conceived using in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) between 2004 and 2009.

Conclusion(s)

Obstetric and perinatal outcomes after blastocyst transfer on days 5 to 6 are similar when compared with embryo cleavage-stage transfers on days 2 to 4.

Fertility and Sterility®

Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth (Review)

Dodd JM, Jones L, Flenady V, Cincotta R, Crowther CA

Authors' conclusions

The use of progesterone is associated with benefits in infant health following administration in women considered to be at increased risk of preterm birth due either to a prior preterm birth or where a short cervix has been identified on ultrasound examination. However, there is limited information available relating to longer-term infant and childhood outcomes, the assessment of which remains a priority.

Dvīņi pēc ART

Biežāka ART komplikācija

26%

Dvīni pēc ART

- priekšlaicīgo dzemdību risks lielāks?
- SET ir DG samazināšanas stratēģija
- Pazudušais dvīnis - MGL, zems dzimšanas svars, priekšlaicīgas dzemdības
- Nav atšķirību mātes un perinatālajā S&M starp ART dvīņiem un SK
- Progresējoša dzemdes kakla saīsināšanās ir potenciāla problēma

Daudzaugļu grūtniecība

- mātes saslimstība un mirstība: hipertensija, preeklampsija/ eklampsija, gestācijas diabēts, placenta praevia, S.C. Sultana, R., Chen, X.K., Lee, C., and Hader, J. Outcomes in multiple gestation pregnancies among Canadian women age 35 years and older. *Healthc. Q.* 2011; 14: 22–24

- perinatāla saslimstība un mirstība

- priekšlaicīgas dzemdības

- samazināts dzimšanas svars

- attālināto veselības problēmu risks

- BCT 4x Joyce A. Martin JA, Brady E. Hamilton, Osterman MJ.K, Three Decades of Twin Births in the United States, 1980–2009. CCD 2012

“Dvīņu grūtniecība asociējas ar lielāku mātes un perinatālas saslimstības un mirstības risku neatkarīgi no mātes vecuma”

–ESHRE Capri Workshop Group, 2000, Mullins and Kumar, 2012

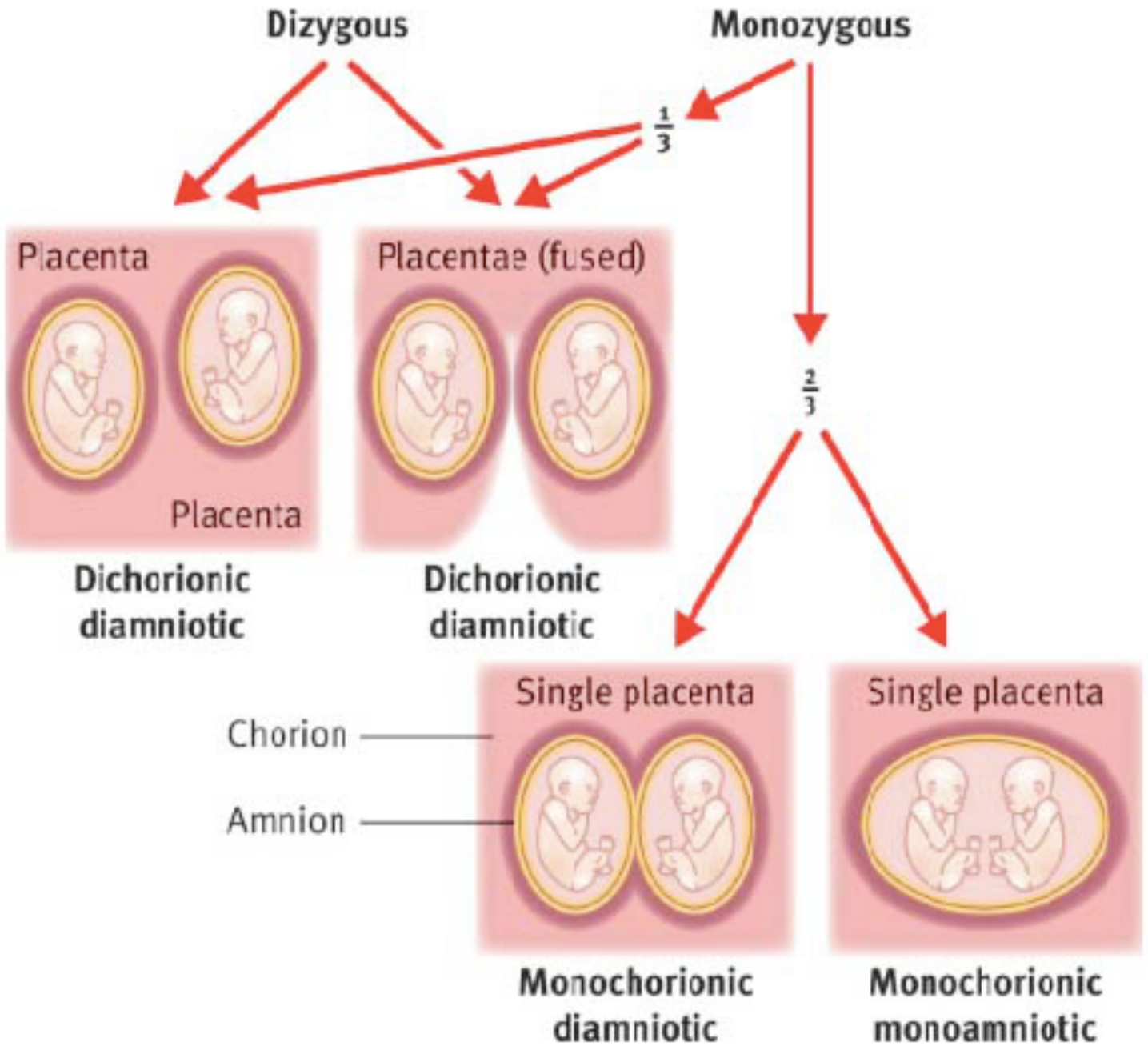
“Hipertensijai, kas asociējas ar hemokoncentrāciju un proteinūriju, vai preeklampsijai ir sliktāka prognoze dvīņu grūtniecības gadījumā. Kā arī daudzaugļu grūtniecība neitralizē protektīvo paritātes efektu uz preeklampsijas risku sekojošas veiksmīgas vienaugļu grūtniecības gadījumā.

– ESHRE Capri Workshop Group, 2000

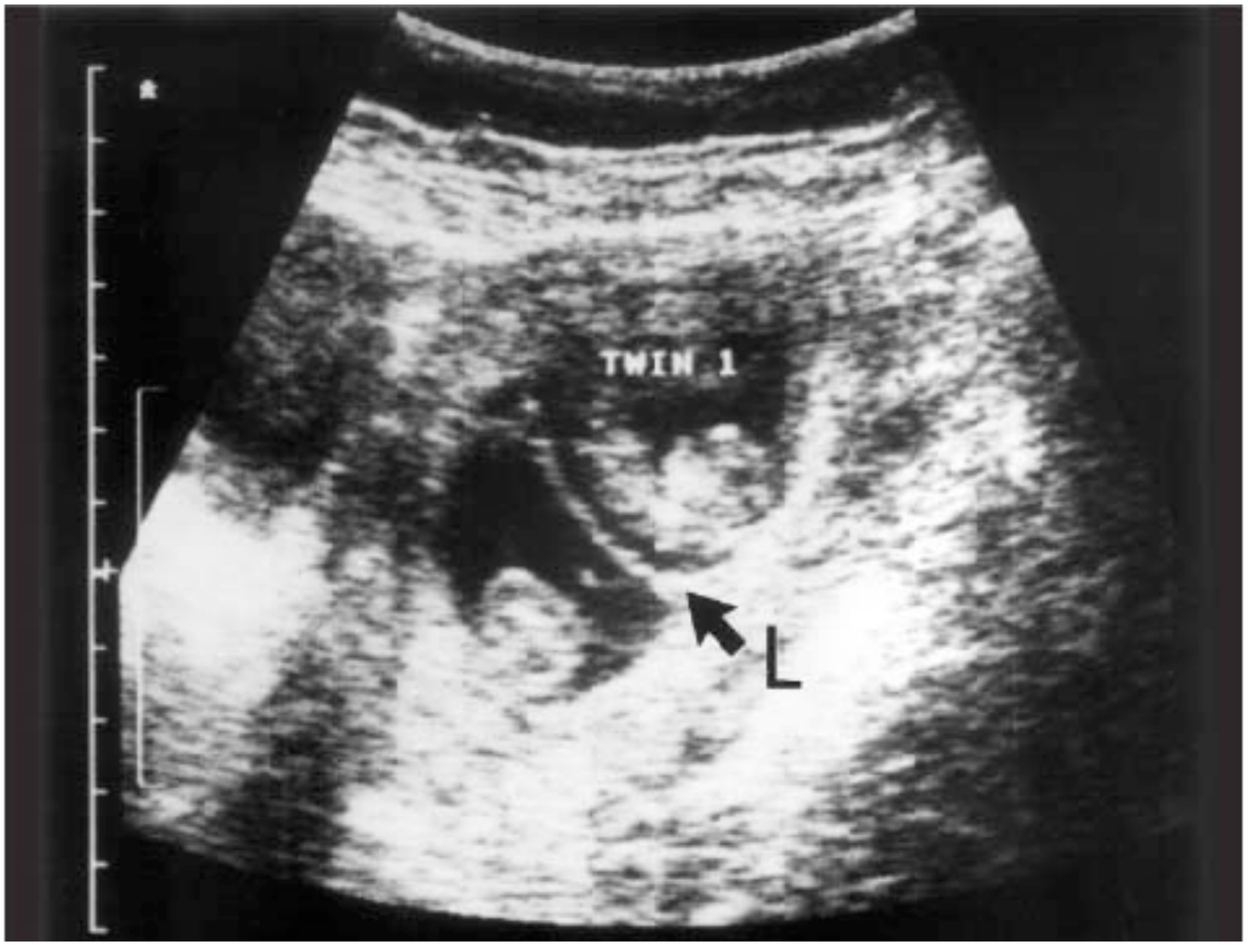
DET

- Vienaugļa grūtniecība
- Dvīņi BHBM - zemāks attīstības anomāliju risks Westergaard HB, Johansen AM, Erb K, Andersen AN. Danish National In-Vi- tro Fertilization Registry 1994 and 1995: a controlled study of births, malforma- tions and cytogenetic findings. Hum Re- prod 1999;14:1896-902. Davies M, Norman R. Neurological sequelae in in-vitro fertilisation babies. Lancet 2002;360:718-9.
- Dvīņi MHBA
- Dvīņi MHMA
- Pazudušais dvīnis
- Trīs augļu grūtniecība - MHBA/MHMA

MH vai BH

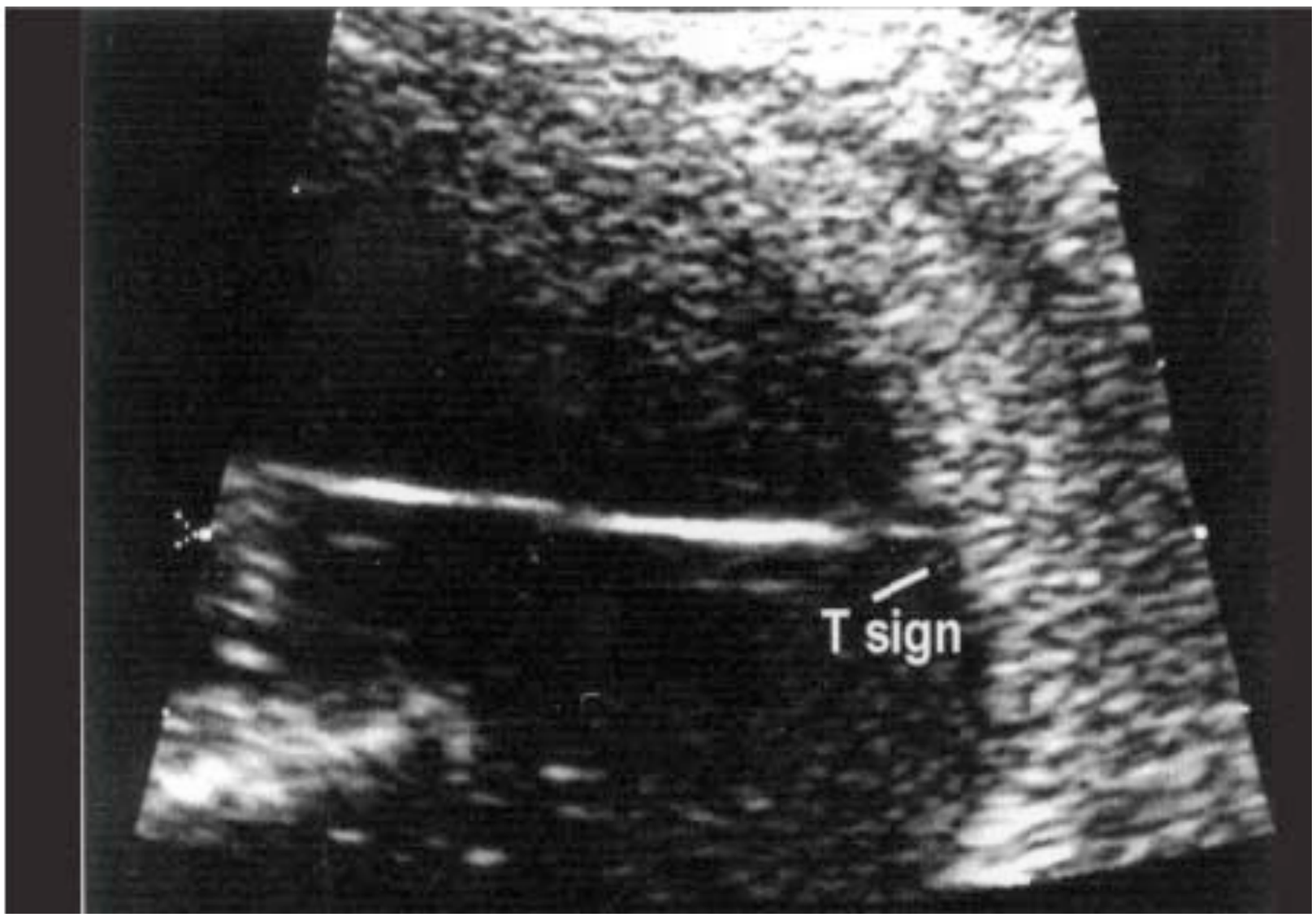

Dizygous
Monozygous
1/3
2/3
Placenta
Placentae (fused)
Placenta
Dichorionic diamniotic
Dichorionic diamniotic
Single placenta
Single placenta
Chorion
Amnion
Monochorionic diamniotic
Monochorionic monoamniotic

Lambda pazīme - BH



8.-10. gest. ned.

T - pazīme



8.-10. gest. ned.

ĀGN pēc DET

- 2-5 zemāks AGN risks nekā SET (La Sala et al., 2005; Miró et al., 2012; Tummers et al., 2003; Matias et al., 2007)

- palielinās pēc 34. g.v. Miró, F., Vidal, E., and Balasch, J. Increased live birth rate in twin pregnancies resulting from embryo assistance. *Obstet. Gynecol.* 2012; 119: 44–49

Pazudušais dvīnis

- spontānai grūtniecībai 20-40% Dickey, R.P., Taylor, S.N., Lu, P.Y., Sartor, B.M., Storment, J.M., Rye, P.H., Pelletier, W.D., Zender, J.L., and Matulich, E.M. Spontaneous reduction of multiple pregnancy: incidence and effect on outcome. *Am. J. Obstet. Gynecol.* 2002; 186: 77–83

- Priekšlaicīgas dzemdības, zems dzimšanas svars, persistējoša trofoblastiska slimība, cerebrāla trieka?

- Nelabvēlīgais iznākums pieaug līdz ar gestācijas laiku

- pēc DET - 10% Poikkeus, P., Gissler, M., Unkila-Kallio, L., Hyden-Granskog, C., and Tiitinen, A. Obstetric and neonatal outcome after single embryo transfer. *Hum Reprod*. 2007; 22: 1073–1079

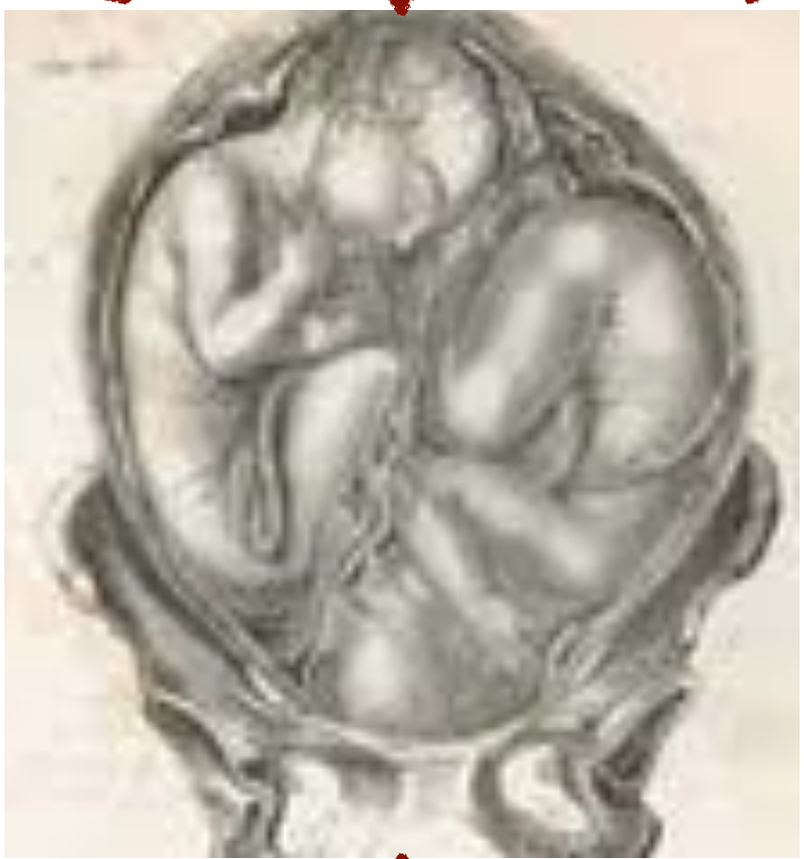
Priekšlaicīgas dzemdības

Dzemdes pārstiepšana

Dzemdes kakla saslimšana

Progesterona trūkums

Barības vielas



Imūnoloģija

Vaskulāras problēmas

Alerģija

Stress

?

Infekcija

Romero et at., 2013

Dvīņi un priekšlaicīgas dzemdības

- 15% no visiem priekšlaicīgi dzimušajiem
- <37 gest. ned. 5x biežāk nekā vienaugļa (60%)
- <32 gest. ned. 8x biežāk nekā vienaugļa (11%) Joyce A. Martin JA, Brady E. Hamilton, Osterman MJ.K, Three Decades of Twin Births in the United States, 1980–2009. CCD 2012

Ko darīt?

- Dzemdes kakla saīsināšanās monitorēšana
- Cerklāža
- Progesterons
- Cervikālie pessāriji

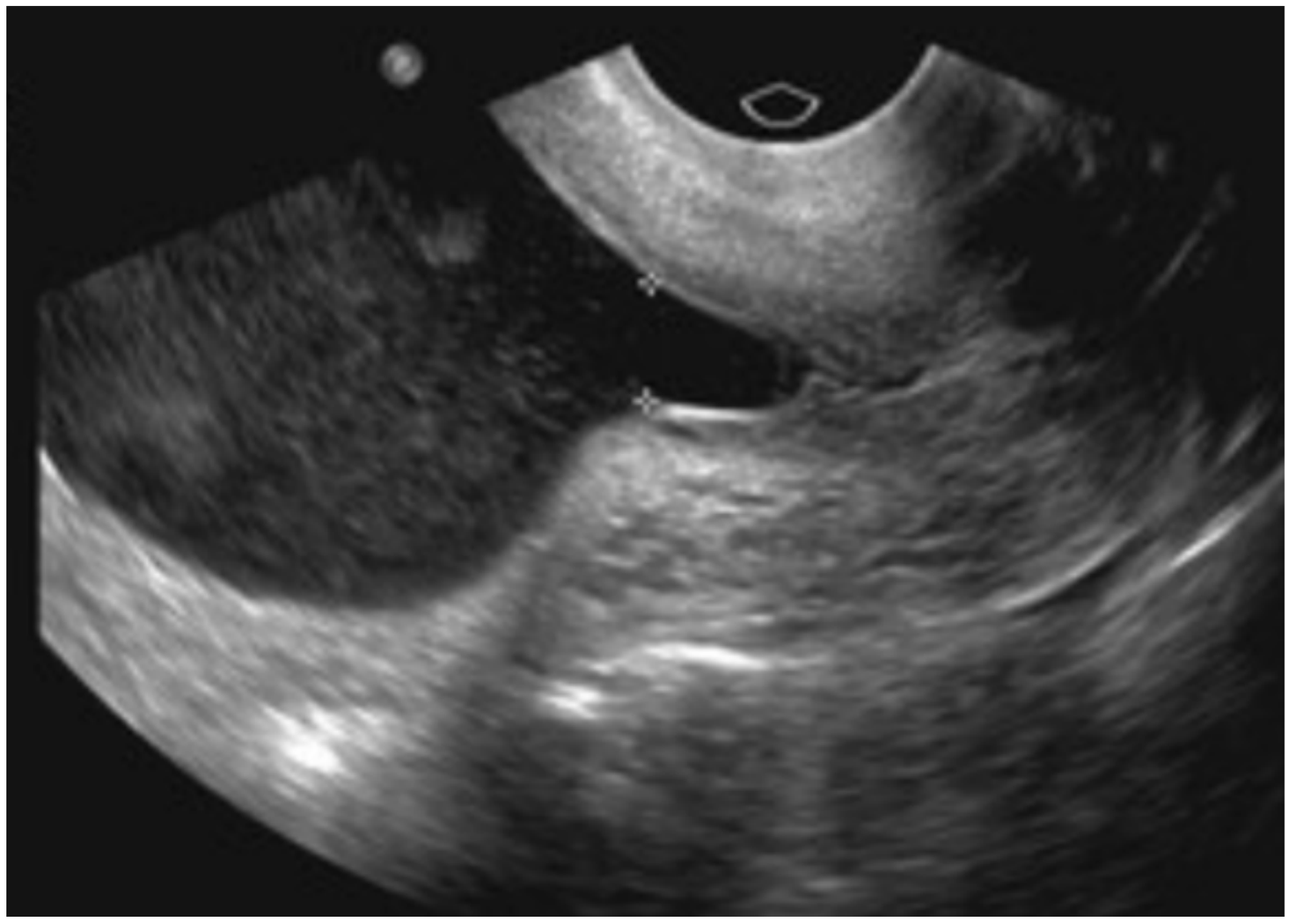
Saīsināts kakls - labākais prediktors

- zema riska asimptomātiskas pacientes
- augsta riska VAG
- DAG
- PD riska pacientes
- <25mm - 50%<34 gest. ned.
- <15mm - 50% <32 gest.ned.

Saīsināts dzemdes kakls

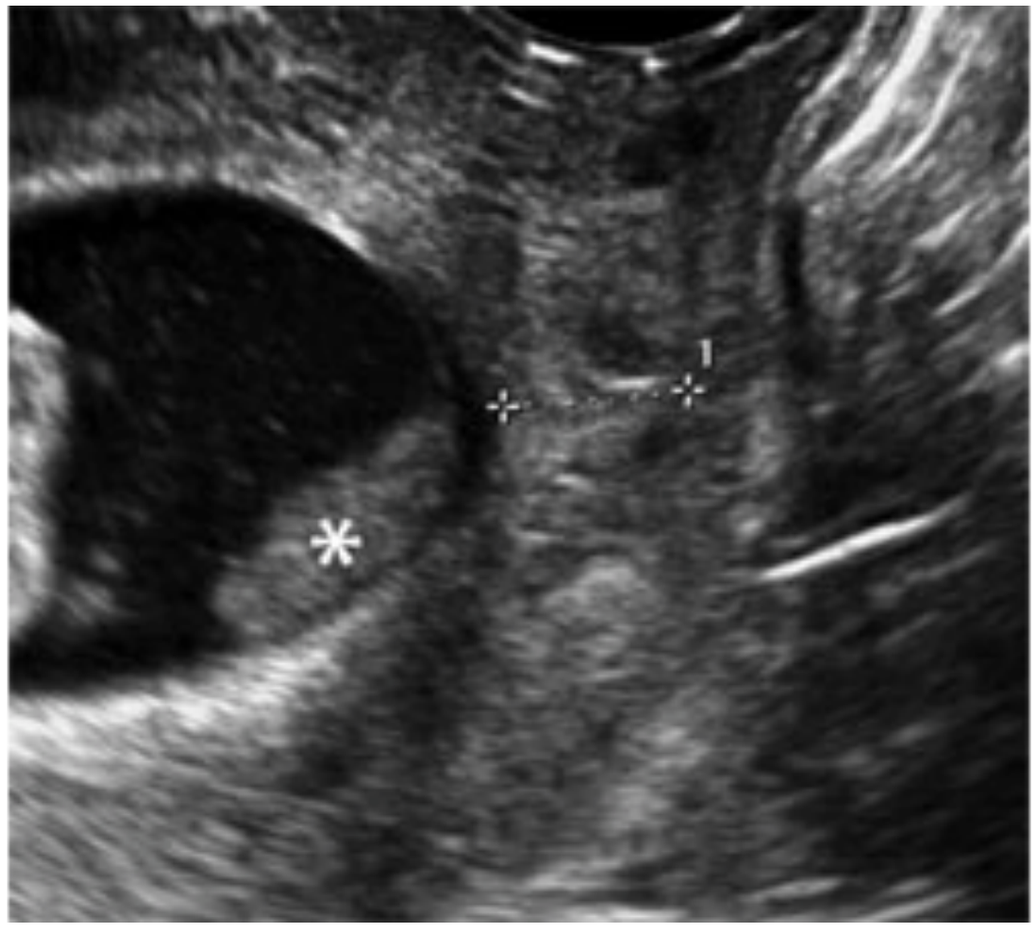
- TVUS 20-24 grūtniecības laikā asimptomatiskām sievietēm ar DG
- <20mm PD risks <32-34 gest. ned.
- <25mm PD risks <28 gest, ned. Conde-Agudelo A, Romero R, Hassan SS, Yeo L. Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: a systematic review and metaanalysis. Am J Obstet Gynecol. 2010
- saīsināšanās >2mm/nedēļā? Hofmeister C, Brizot Mde L, Liao A, Francisco RP, Zugaib M. Two-stagetransvaginal cervical length screening for preterm birth in twin pregnancies. JPerinat Med. 2010 Sep;38(5):479-84
- simptomātiskas pacientes?
- >24 gest. ned.?

Cervikāla piltuvīte



Augļa ūdeņu nogulsnes s. amniotic fluide sludge

- priekšlaicīgas dzemdības
- histoloģiski pierādītais horionamnionīts
- funizīts
- perinatāla nāve



Boyer A, Cameron L, Munoz-Maldonado Y, Bronsteen R, Comstock CH, Lee W,Goncalves LF. Clinical significance of amniotic fluid sludge in twin pregnancies with a short cervical length. Am J Obstet Gynecol. 2014 Nov;211(5):506.e1-9

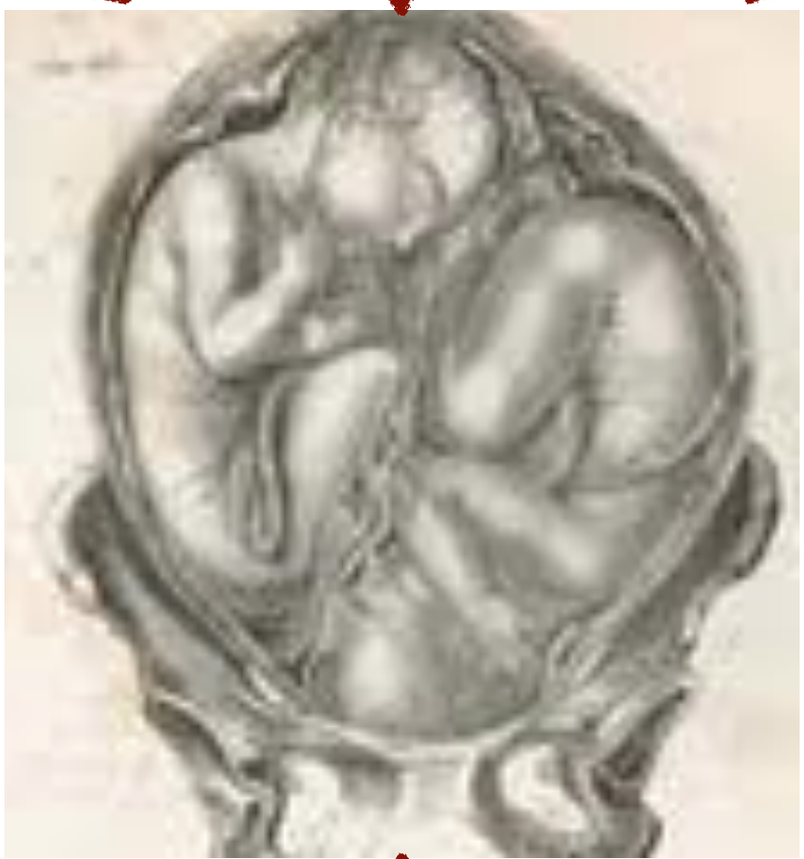
Priekšlaicīgas dzemdības

Dzemdes pārstiepšana

Dzemdes kakla saslimšana

Progesterona trūkums

Barības vielas



Imunoloģija

Vaskulāras problēmas

Alerģija

Stress

?

Infekcija

Romero et at., 2013

Cervical stitch (cerclage) for preventing preterm birth in multiple pregnancy (Review)

Rafael TJ, Berghella V, Alfirevic Z

Authors' conclusions

This review is based on limited data from five small studies of average to above average quality. For multiple gestations, there is no evidence that cerclage is an effective intervention for preventing preterm births and reducing perinatal deaths or neonatal morbidity.

Cerklāža

- nav ieteicama dvīņu grūtniecības gadījumā priekšlaicīgo dzemdību riska samazināšanai

Progestrerons

- mikronizētais progesterons p/v - var būt efektīvs arī dvīņiem, atslābina miometriju - klīniskie pētījumi

- progesterons i/m - nav efektīvs, var palielināt GD risku

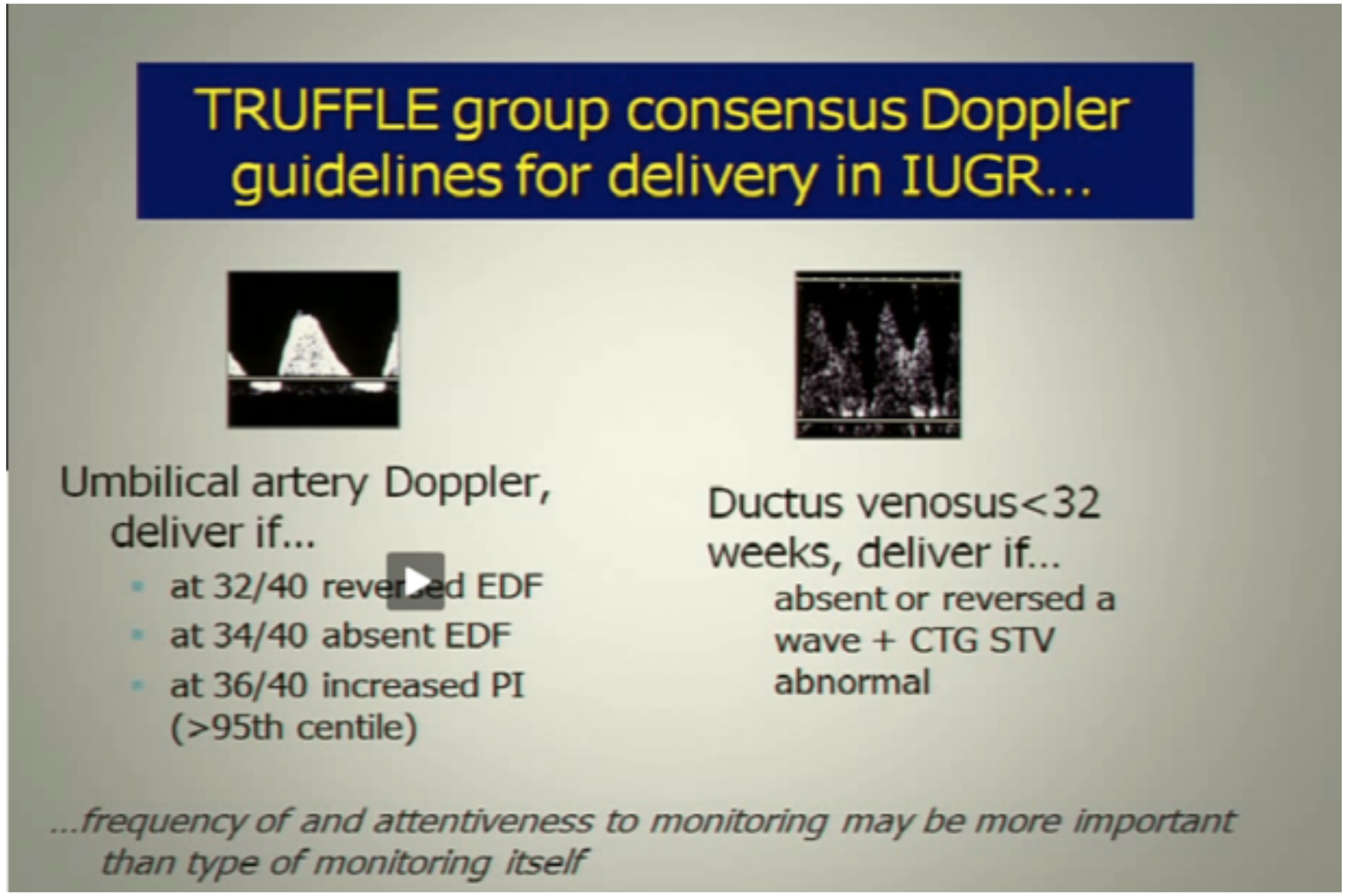
Cerklāžas pesāriji

Taktika

- dzemdes kakla garuma monitorēšana
- antenatālie kortikosteroīdi
- in utero transportēšana uz perinatālo centru
- tokolīze
- neiroprotekcija?

US eksperta kompetence

- Dikonkordanta dvīņu augšana
- sIUGR
- TTTS



Monozigotiskie dvīņi

- Perinatāla mirstība - 3x v.s. DZ Hillman, S.C., Morris, R.K., and Kilby, M.D. Co-twin prognosis after single fetal death: a systematic review and meta-analysis. *Obstet. Gynecol.* 2011; 118: 928–940
- Prenatāls neiroloģisks bojājums - 10X v.s. DZ
- Perinatāla mirstība 11% v.s. 5% DZ
- Attīstības anomālijas 2-3x biežāk nekā DZ
- TTTS 15-20% (neārstējot mirstība 90%) Huber, A. and Hecher, K. How can we diagnose and manage twin–twin transfusion syndrome. *Best. Pract. Res. Clin. Obstet. Gynecol.* 2004; 18: 543–556
- MHMA - nabassaites satīšanas
- Augsta perinatāla mirstība pēc 32. gest. ned.
- Viena dvīņa IUAN gadījumā - 4.81x cerebrāla trieka izdzīvojušam

MZ pēc ART

- pēc ART daudz retāk nekā SK (2-3% v.s. 26%)
- pēc KOS risks dubultojas (1-5%) v.s. 0.4% SK
- ovulācijas indukcija
- ICSI Haimov-Kochman, R., Daum, H., Lossos, F., Aizenman, E., Werner, M., Yagel, S., Laufer, N., Simon, A., and Hurwitz, A. Monozygotic multiple gestation after intracytoplasmic sperm injection and preimplantation genetic diagnosis. *Fertil. Steril.* 2009; 92: 44 (2037.e11–17)
- asistētais hatčings Sills, E.S., Moomjy, M., Zaninovic, N., Veeck, L.L., McGee, M., Palermo, G.D., and Rosenwaks, Z. Human zonapellucida micromanipulation and monozygotic twinning frequency after IVF. *Hum. Reprod.* 2000; 15: 890–895
- kultivēšana līdz 5/6 dienai
- PGS Haimov-Kochman, R., Daum, H., Lossos, F., Aizenman, E., Werner, M., Yagel, S., Laufer, N., Simon, A., and Hurwitz, A. Monozygotic multiple gestation after intracytoplasmic sperm injection and preimplantation genetic diagnosis. *Fertil. Steril.* 2009; 92: 44 (2037.e11–17)
- mātes vecums Pinborg, A. IVF/ICSI twin pregnancies: risks and prevention. *Hum. Reprod. Update.* 2005; 11: 575–593

“IUAN parasti notiek pirms 24. grūtniecības nedēļas. Pēc 24. grūtniecības nedēļas varbūtība, kā sievietei 1 mēnesi pēc MZ dzemdībām mājas būs divi dzīvie bērni ir vienāda kā pēc DZ grūtniecības.”

–Oldenburg, A., Rode, L., Bødker, B., Ersbak, V., Holmskov, A., Jørgensen, F.S., Larsen, H., Larsen, T., Laursen, L., and Mogensen, H. Influence of chorionicity on perinatal outcome in a large cohort of Danish twin pregnancies. *Ultrasound Obstet. Gynecol.* 2012; 39: 69–74

BCT - RF dvīņiem

- Priekšlaicīgas dzemdības
- IUAA
- Komplicētas dzemdības
- BCT 5x dvīniem vs. vienaugļa
- BCT 20x trīņiem vs. vienaugļa

Fetoredukcīja

Fertil Steril. 2014 Nov 20. pii: S0015-0282(14)02287-0. doi: 10.1016/j.fertnstert.2014.10.027. [Epub ahead of print]

Perinatal outcome after fetal reduction from twin to singleton: To reduce or not to reduce?

Haas J[1], Mohr Sasson A[2], Barzilay E[2], Mazaki-Tovi S[2], ...

CONCLUSION(S): Fetal reduction of twins to singleton is associated with a lower risk of prematurity and superior perinatal outcome compared with nonreduced twins. Therefore, the option of fetal reduction should be considered in certain cases of twin pregnancies, where the risk for adverse outcome seems exceptionally high.

- Tripet uz gemelli prolongē grūtniecību par 2-3 nedēļām

- nav optimāls risinājums

Fertility and Sterility®

Grūtniecības atrisināšanas veids

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 3, 2013 VOL. 369 NO. 14

A Randomized Trial of Planned Cesarean or Vaginal Delivery for Twin Pregnancy

Jon F.R. Barrett, M.B., B.Ch., M.D., Mary E. Hannah, M.D.C.M., Eileen K. Hutton, Ph.D., Andrew R. Willan, Ph.D., Alexander C. Allen, M.D.C.M., B. Anthony Armson, M.D., Amiram Gafni, D.Sc., K.S. Joseph, M.D., Ph.D., Dalah Mason, M.P.H., Arne Ohlsson, M.D., Susan Ross, Ph.D., J. Johanna Sanchez, M.I.P.H., and Elizabeth V. Asztalos, M.D., for the Twin Birth Study Collaborative Group*

CONCLUSIONS

In twin pregnancy between 32 weeks 0 days and 38 weeks 6 days of gestation, with the first twin in the cephalic presentation, planned cesarean delivery did not significantly decrease or increase the risk of fetal or neonatal death or serious neonatal morbidity, as compared with planned vaginal delivery. (Funded by the Canadian Institutes of Health Research; ClinicalTrials.gov number, NCT00187369; Current Controlled Trials number, ISRCTN74420086.)

"*Per vias naturales*"- labvēlīga iznākuma prediktori

- atkārtota dzemdētāja
- spontāns dzemdību sākums
- otrais auglis pakauša priekšguļā
- grūtniecības laiks 37^{0+6}

Otrais auglis

- >20 minūtes pieaug F2 perinatāla mirstība

- >15 minūtes pieaug F2 SC

Grūtniecības atrisināšanas laiks

- BHBA 37^{0+6}
- >38 gest. ned. IUAN risks pieaug
- neonatālie sarežģījumi >38. gr. nedēļas 3,5x vairāk
- MHBA 36^{0+6}
- MHMA 32^{0+6} - monitorēšana nevar uzlabot nelabvēlīgo iznākumu

Elective birth at 37 weeks' gestation for women with an uncomplicated twin pregnancy (Review)

Dodd JM, Deussen AR, Grivell RM, Crowther CA

Authors' conclusions

Early birth at 37 weeks' gestation compared with ongoing expectant management for women with an uncomplicated twin pregnancy does not appear to be associated with an increased risk of harms, findings which are consistent with the United Kingdom's National Institute for Health and Care Excellence (NICE) recommendations which advocate birth for women with a dichorionic twin pregnancy at 37 + 0 weeks' gestation. It is unlikely that sufficient clinical equipoise exists to allow for the randomisation of women to a later gestational age at birth.

Attīstības anomālijas pēc ART

- IVF/ICSI - hipospādijas, kardiovaskulāra, muskuloskeletāla, gastrointestināla sistēma (Ericson and Källén, 2001, Hansen et al., 2002, Olson et al., 2005, Pinborg et al., 2004, Zhu et al., 2006).

- vieaugļu grūtniecībai biežāk Reefhuis J, Honein MA, Schieve LA, Correa A, Hobbs CA, Rasmussen SA. As- sisted reproductive technology and major structural birth defects in the United States. Hum Reprod 2009;24:360-6

- IVF - pēc vecāku RF izslēgšanas - neatšķiras no spontānas grūtniecības

- ICSI - pēc vecāku RF izslēgšanas - augstāk nekā spontānai grūtniecībai

- BCT

- imprintiga saslimšanas: Angelmana/Prādera-Vilija sindromi (Le Bouc et al., 2010, Odom and Segars, 2010)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Reproductive Technologies and the Risk of Birth Defects

Michael J. Davies, M.P.H., Ph.D., Vivienne M. Moore, M.P.H., Ph.D., Kristyn J. Willson, B.Sc., Phillipa Van Essen, M.P.H., Kevin Priest, B.Sc., Heather Scott, B.Mgmt., Eric A. Haan, M.B., B.S., and Annabelle Chan, M.B., B.S, D.P.H.

N Engl J Med 2012;366:1803-13.

Table 1. Characteristics of Births and Terminations of Pregnancy According to Mode of Conception.

Characteristic	Assisted Conception (N=6163)	Spontaneous Conception (N=302,811)	P Value
	no. of births (%)		
Age			<0.001
20–24 yr	133 (2.2)	62,981 (20.8)	
25–29 yr	1367 (22.2)	114,074 (37.7)	
30–34 yr	2736 (44.4)	88,924 (29.4)	
35–39 yr	1612 (26.2)	31,728 (10.5)	
≥40 yr	315 (5.1)	5,104 (1.7)	
Socioeconomic status: lowest quartile*	1621 (26.3)	104,267 (34.4)	<0.001
White race†	5968 (96.8)	283,169 (93.5)	<0.001
Nulliparous	4023 (65.3)	113,489 (37.5)	<0.001
Paternal occupation: manager or professional‡	2374 (38.5)	82,217 (27.2)	<0.001
Smoked during pregnancy§	1021 (18.1)	29,727 (26.5)	<0.001
Singleton birth	4333 (70.3)	295,220 (97.5)	<0.001
Baby's sex¶			0.03
Male	3104 (50.4)	155,723 (51.4)	
Female	3052 (49.5)	146,803 (48.5)	
Diseases in pregnancy‖			
Any diabetes**	364 (5.9)	9,140 (3.0)	<0.001
Hypertension	96 (1.6)	3,410 (1.1)	0.01
Pregnancy-induced hypertension	770 (12.5)	26,496 (8.8)	<0.001
Urinary tract infection	344 (5.6)	14,940 (4.9)	0.08
Asthma	257 (4.2)	12,771 (4.2)	0.98
Epilepsy	41 (0.7)	1,604 (0.5)	0.13
Anemia	795 (12.9)	18,257 (6.0)	<0.001

Table 2. Characteristics of Births after Assisted Conception or Spontaneous Conception, According to Multiplicity.

Birth Characteristic	Assisted Conception			Spontaneous Conception		
	Singleton Births (N=4333)	Multiple Births (N=1830)	All Births (N=6163)	Singleton Births (N=295,220)	Multiple Births (N=7591)	All Births (N=302,811)
Pregnancy terminated because of defect — no. (%)	29 (0.7)	4 (0.2)	33 (0.5)	1,492 (0.5)	21 (0.3)	1,513 (0.5)
Stillborn — no. of births (%)	45 (1.0)*	44 (2.4)	89 (1.4)*	1,549 (0.5)	154 (2.0)	1,703 (0.6)
Liveborn — no. of births (%)†	4259 (98.3)	1782 (97.4)	6041 (98.0)	292,179 (99.0)	7416 (97.7)	299,595 (98.9)
Mode of delivery — no. of births (%)‡						
Vaginal	2709 (63.6)	626 (35.1)	3335 (55.2)	225,277 (77.1)	3683 (49.7)	228,960 (76.4)
Cesarean	1550 (36.4)*	1156 (64.9)	2706 (44.8)*	66,900 (22.9)	3733 (50.3)	70,633 (23.6)
Child's sex — no. of births (%)§						
Male	2123 (49.8)¶	923 (51.8)	3046 (50.4)	150,580 (51.5)	3642 (49.1)	154,222 (51.5)
Female	2136 (50.2)	859 (48.2)	2995 (49.6)	141,595 (48.5)	3773 (50.9)	145,368 (48.5)
Birth weight — g**	3259±641*	2240±661*	2958±796*	3,399±553	2407±620	3,375±576
Gestation — no. of births (%)*						
<32 wk	86 (2.0)	253 (14.2)	339 (5.6)	2,495 (0.9)	654 (8.8)	3,149 (1.1)
32–36 wk	337 (7.9)	813 (45.6)	1150 (19.0)	13,577 (4.6)	2999 (40.4)	16,576 (5.5)
37–40 wk	3402 (79.9)	714 (40.1)	4116 (68.1)	236,526 (81.0)	3759 (50.7)	240,285 (80.2)
>40 wk	434 (10.2)	2 (0.1)	436 (7.2)	39,581 (13.5)	4 (0.1)	39,585 (13.2)

Table 4. Odds Ratio for Any Birth Defects According to Type of Assisted Conception and Multiplicity.*

Type of Assisted Conception	Singleton Births			All Births		
	Defect	Unadjusted Odds Ratio	Adjusted Odds Ratio†	Defect	Unadjusted Odds Ratio	Adjusted Odds Ratio†
	no. of births with defect/ total no. of births			*ths with defect/ no. of births*		
Any	361/4333	1.45 (1.30–1.63)	1.28 (1.14–1.43)	13/6163	1.45 (1.32–1.60)	1.26 (1.14–1.40)
IVF						
Fresh- or frozen-embryo cycles	105/1484	1.25 (1.02–1.52)	1.06 (0.87–1.30)	65/2301	1.26 (1.07–1.48)	1.07 (0.90–1.26)
Fresh-embryo cycles	71/1005	1.25 (0.98–1.59)	1.05 (0.82–1.35)	21/1647	1.29 (1.06–1.57)	1.09 (0.89–1.33)
Frozen-embryo cycles	34/479	1.24 (0.88–1.76)	1.08 (0.76–1.53)	44/654	1.17 (0.87–1.59)	1.02 (0.75–1.39)
ICSI						
Fresh- or frozen-embryo cycles	91/939	1.72 (1.38–2.15)	1.55 (1.24–1.94)	39/1407	1.77 (1.47–2.12)	1.57 (1.30–1.90)
Fresh-embryo cycles	76/713	1.95 (1.53–2.48)	1.73 (1.35–2.21)	16/1111	1.89 (1.54–2.3)	1.66 (1.35–2.04)
Frozen-embryo cycles	15/226	1.17 (0.70–1.97)	1.10 (0.65–1.85)	23/296	1.37 (0.89–2.1)	1.28 (0.83–1.99)
GIFT	34/319	1.98 (1.40–2.80)	1.73 (1.21–2.47)	59/590	1.81 (1.37–2.41)	1.55 (1.16–2.07)
Intrauterine insemination	54/580	1.67 (1.25–2.23)	1.46 (1.09–1.95)	63/732	1.53 (1.18–1.99)	1.32 (1.01–1.73)
Donor insemination	36/428	1.51 (1.08–2.11)	1.37 (0.98–1.92)	36/468	1.37 (0.98–1.91)	1.24 (0.89–1.73)
Ovulation induction	19/306	1.08 (0.68–1.74)	0.99 (0.62–1.59)	27/374	1.27 (0.83–1.93)	1.16 (0.76–1.75)
Clomiphene citrate at home	7/36	3.87 (1.58–9.51)	3.19 (1.32–7.69)	9/46	3.92 (1.84–8.38)	3.39 (1.61–7.13)
Other	15/241	1.07 (0.63–1.82)	0.96 (0.56–1.63)	15/245	1.04 (0.61–1.78)	0.92 (0.54–1.58)
Spontaneous conception after previous birth from assisted reproductive technology	96/1306	1.27 (1.02–1.59)	1.26 (1.01–1.57)	99/1342	1.27 (1.02–1.58)	1.25 (1.01–1.56)
Infertile but no history of treatment with assisted reproductive technology	52/600	1.54 (1.15–2.05)	1.37 (1.02–1.83)	67/807	1.47 (1.13–1.90)	1.29 (0.99–1.68)
No use of assisted reproductive technology and fertile	16,841/293,314	1.00	1.00	80/300,662	1.00	1.00

VECUMS

“Aneiploidīju skaitu ART neietekmē.”

–Davies et al., 2012

PGS

“Neauglīgai populācijai ir a-priori attīstības anomāliju risks”

–Farhi and Fisch, 2007, Zhu et al., 2006

Vai cita grūtniece?

- priekšlaicīgas dzemdības
- zems jaundzimušā svars
- preeklampsija/eklampsija
- dvīņi
- perinatāla mirstība
- ķeizargrieziens
- placenta praevia/accreta
- cerebrāla trieka
- attīstības anomālijas?

IR CITA GRŪTNIECE

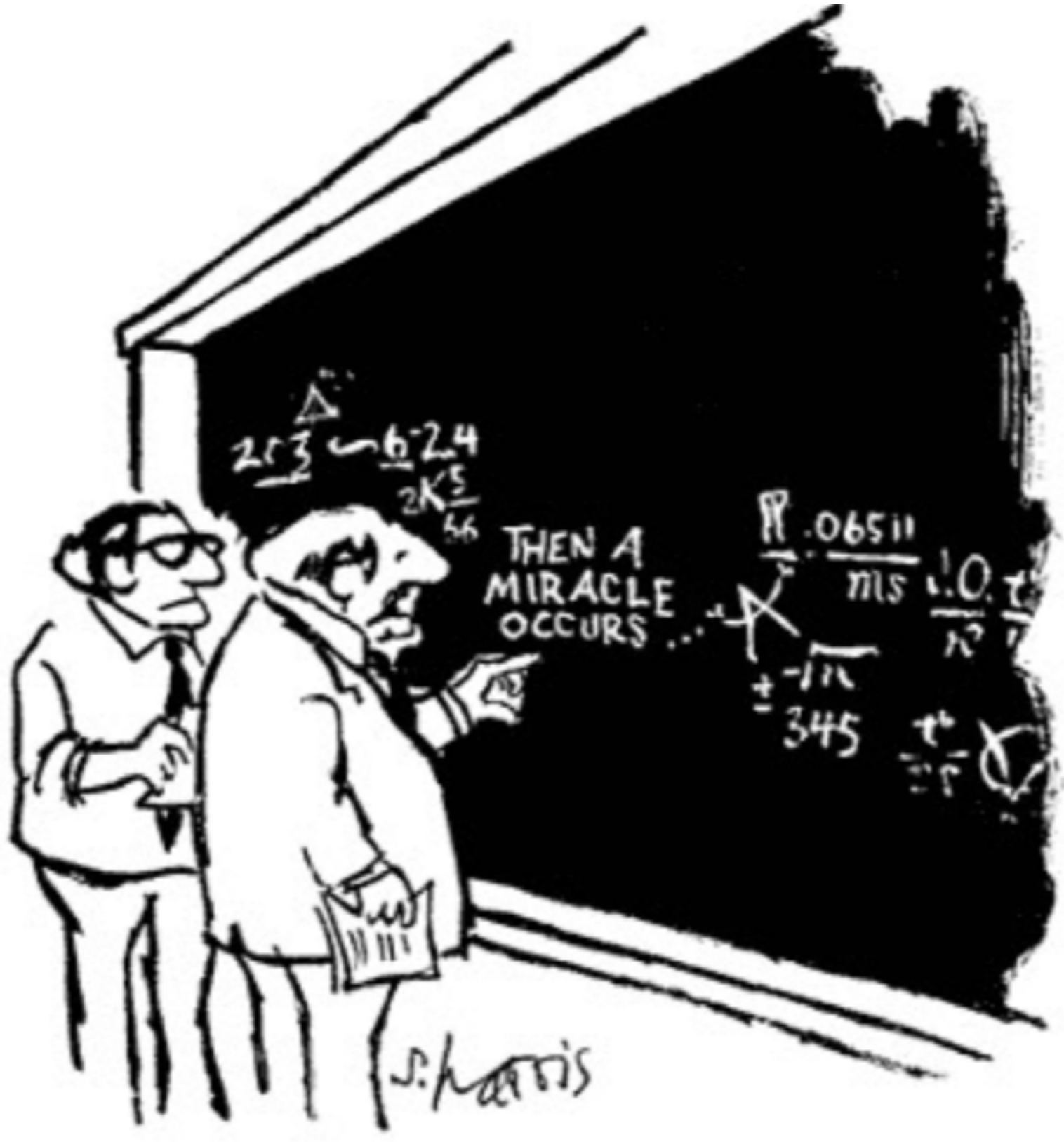
Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Obstetric andperinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematicreview and meta-analysis. Hum Reprod Update.
Farhi A, Reichman B, Boyko V, Hourvitz A, Ron-El R, Lerner-Geva L. Maternaland neonatal health outcomes following assisted reproduction. Reprod BiomedOnline. 2013 May;26(5):454-61
Stojnic J, Radunovic N, Jeremic K, Kotlica BK, Mitrovic M, Tulic I. Perinatal outcome of singleton pregnancies following in vitro fertilization. Clin ExpObstet Gynecol. 2013;40(2):277-83

Kāpēc nepieciešama specifiskā antenatāla aprūpe?

- Preeklampsija
- Priekšlaicīgas dzemdības
- IUAA
- Placenta praevia
- Augļa strukturālas anomālijas

Taktika

- Luteālas fāzes atbalsts
- ĀGN “profilakse”?
- Endokrīnas/koagulācijas problēmu korekcija
- Ģenētiskais skrīnings
- Strukturālo anomāliju skrīnings
- Priekšlaicīgo dzemdību riska izvērtēšana, monitorēšana, ārstēšana
- GD skrīnings
- Dzemdību datums un plāns



"I think you should be more explicit here in step two."