Paternal factors and ICSI children: does it matters?

FERTILITY

Agenda

- Semen quality decline
- Perinatal outcomes
- Birth defects
- Sperm quality: consequences on offspring

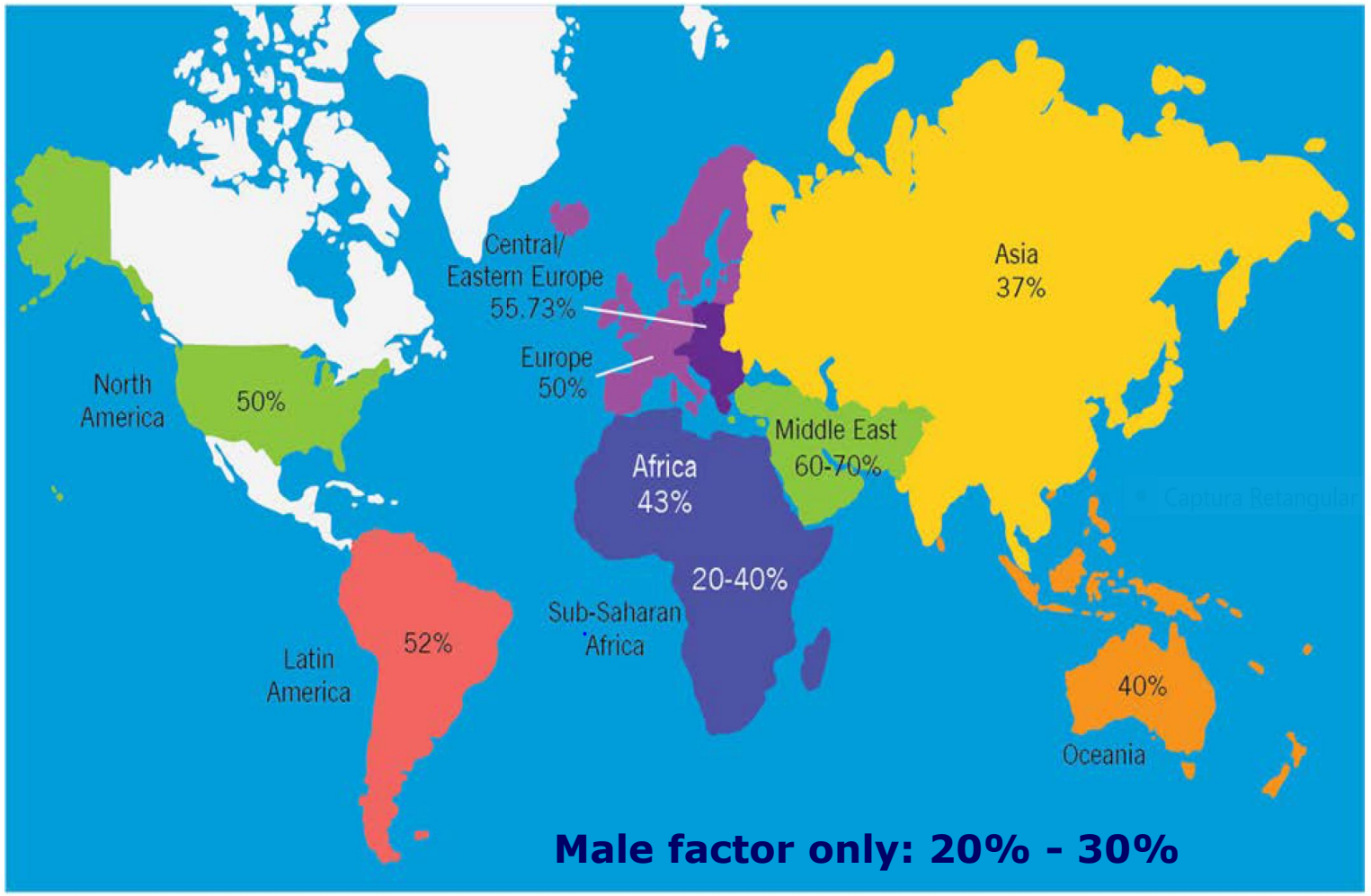


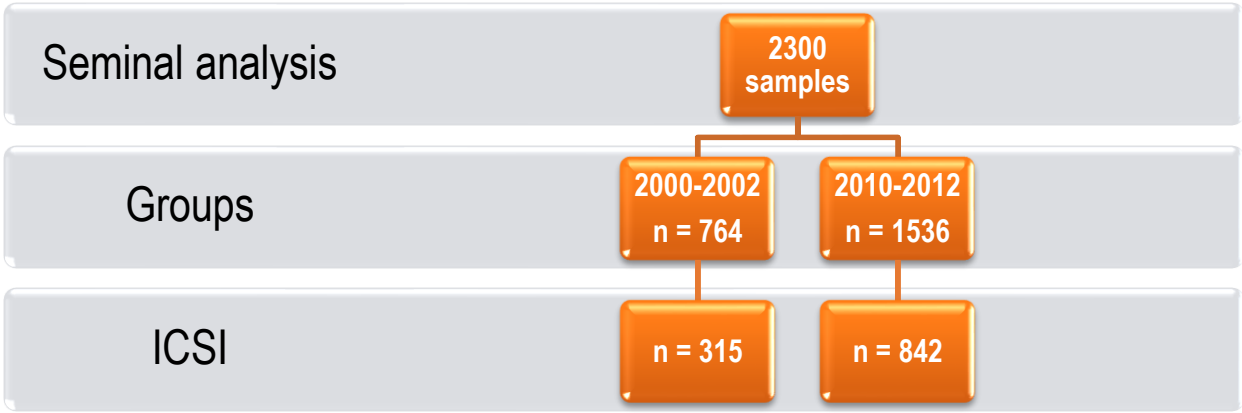
Figure 2 World map containing percentages of infertility cases per region that are due to male factor. This figure demonstrates rates of infertility cases in each region studied (North America, Latin America, Africa, Europe, Central/Eastern Europe, Middle East, Asia, and Oceania) due to male factor involvement.

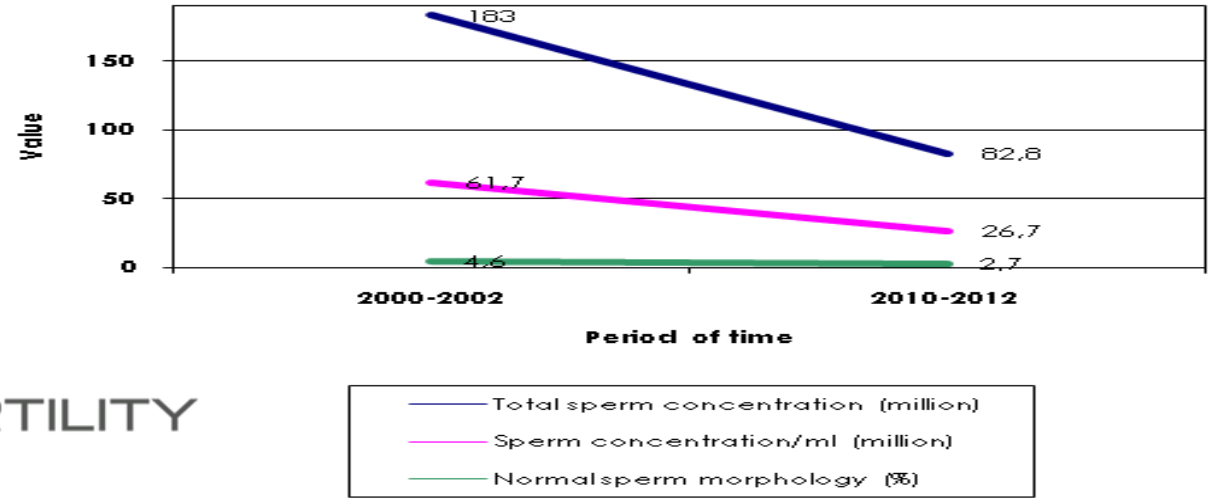
ORIGINAL ARTICLE

Vol. 41 (4): 757-763, July - August, 2015
doi: 10.1590/S1677-5538.IBJU.2014.0186

Decline in semen quality among infertile men in Brazil during the past 10 years

Edson Borges Jr. [1,2], Amanda Souza Setti [1,2], Daniela Paes de Almeida Ferreira Braga [1,2], Rita de Cassia Savio Figueira [1], Assumpto Iaconelli Jr. [1,2]





FERTILITY

Variable	2000-2002 (n=764)	2010-2012 (n=1536)	*p*
Male age (years)	35.0 ± 8.6	35.3 ± 8.1	0.318
Days of ejaculatory abstinence	4.2 ± 3.1	4.2 ± 2.7	0.777
Volumen (ml)	3.4 ± 1.8	3.3 ± 1.6	0.473
Concentretion/ml (million)	61.7 ± 69.4	26.7 ± 27.3	**<0.001**
Total Concentartion (million)	183.0 ± 197.0	82.8 ± 89.5	**<0.001**
Progressive motility(%)	36.4 ± 18.3	36.5 ± 19.2	0.812
Normal Morphology(%)	4.6	2.7	**<0.001**
Azoospermia (%)	38/764 (4.9)	131/1536 (8.5)	**<0.001**
Severe oligozoospermia(%)	114/726 (15.7)	426/1405 (30.3)	**<0.001**

Fertilização	2000-2002 (n=315)	2010-2012 (n=842)	*p*
Taxa de fertilização total (%)	82.5	81.3	0.619
Taxa de fertilização anormal (1PN + 3PN) (%)	12.2	7.8	**<0.001**

Article

Human and Experimental Toxicology
1–9

DOI: 10.1177/0960327117703690
journals.sagepub.com/home/het

Decline in sperm count in European men during the past 50 years

P Sengupta[1,2], E Borges Jr[3], S Dutta[4] and E Krajewska-Kulak[2]

Purpose: To investigate whether the sperm concentration of European men is deteriorating over the past 50 years of time.
Materials and Methods: We analysed the data published in English language articles in the past 50 years in altering sperm concentration in European men.

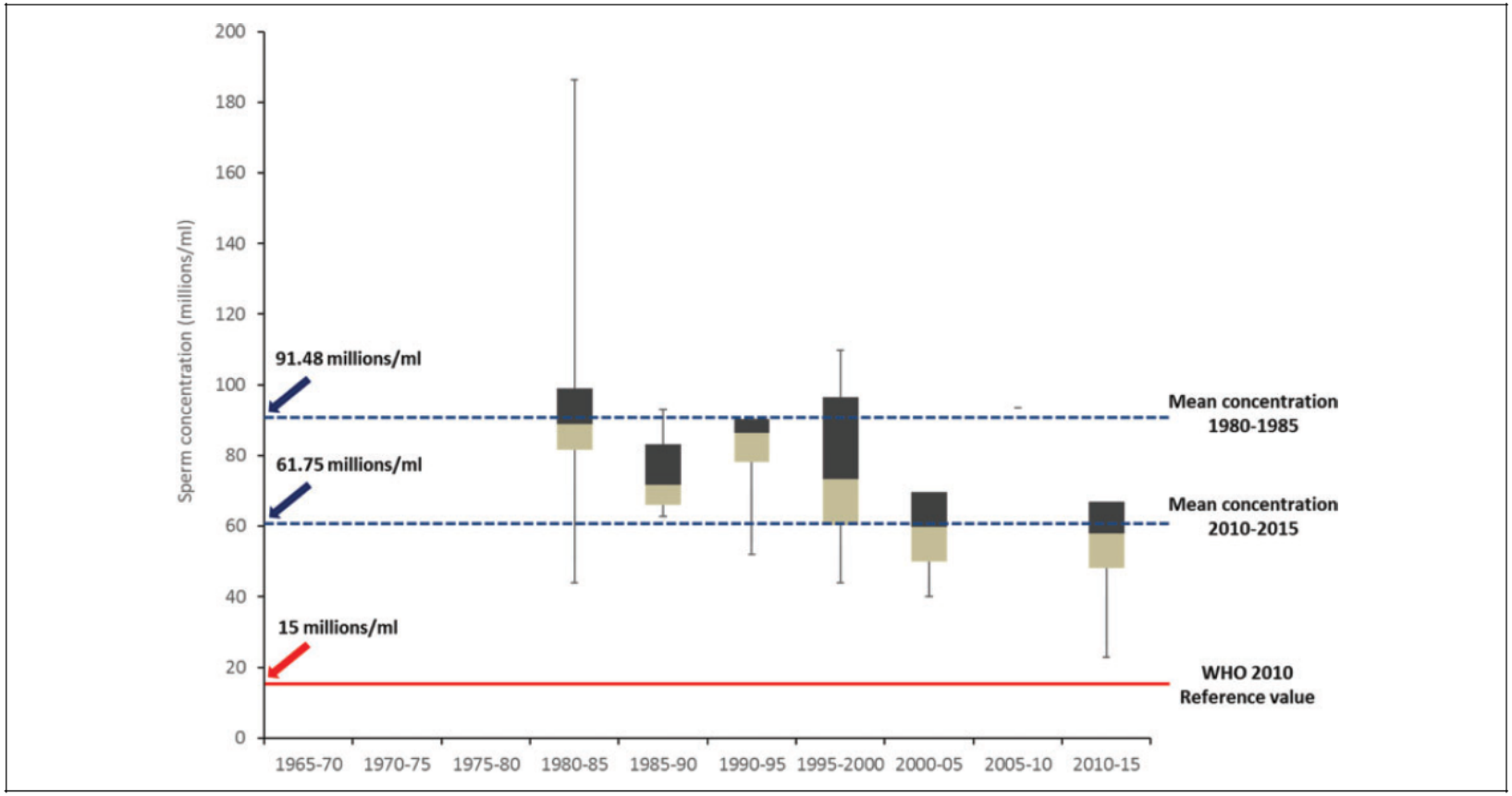


Figure 2. Box and whisker plot of sperm concentration data of European men of the past 50 years.

Time-dependent decline in observed spermatic concentration from 1965 to 2015

(r= -0.307, p<0.02; decrease: 32.5%)

FERTILITY

Perinatal outcomes

FERTILITY

Human Reproduction Update, Vol.18, No.5 pp. 485–503, 2012
Advanced Access publication on May 19, 2012 doi:10.1093/humupd/dms018

human reproduction update

Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis

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

[1]Assisted Reproduction Unit, Aberdeen Maternity Hospital, Aberdeen AB25 2ZL, UK [2]Aberdeen Maternity Hospital, Aberdeen AB25 2ZL, UK [3]Division of Applied Health Sciences, University of Aberdeen, Aberdeen Maternity Hospital, Aberdeen AB25 2ZL, UK

FERTILITY

ART: obstetric and perinatal outcomes

Outcome	Overal effect: RR (IC-95%)
Antipartum hemorrhage	2,49 (2,30 a 2,69)
Congenital anomalies	1,67 (1,33 a 2,09)
Hypertension	1,49 (1,39 a 1,59)
Premature rupture of membranes	1,16 (1,07 a 1,26)
Caesarean Section	1,56 (1,51 a 1,60)
Birth weight< 2.500 g	1,65 (1,56 a 1,75)
Birth weight < 1.500 g	1,93 (1,72 a 2,17)
Perinatal mortality	1,87 (1,49 a 2,37)
Delivery at 37 weeks	1,54 (1,47 a 1,62)
Delivery at 32 weeks	1,68 (1,48 a 1,91)
Transfer to NICU	1,58 (1,42 a 1,77)
Gestacional diabetes	1,48 (1,33 a 1,66)
Induction of labour	1,18 (1,10 a 1,28)
Small for gestacional age	1,39 (1,27 a 1,53)

FERTILITY Pandey S, *et al. Hum Reprod Update*. 2012 Sep-Oct;18(5):485-503.

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[1,*], U.B. Wennerholm[2], L.B. Romundstad[3], A. Loft[1], K. Aittomaki[4], V. Söderström-Anttila[5], K.G. Nygren[6], J. Hazekamp[7], and C. Bergh[8]

Birth criteria – Preterm (PT)

1982 – 2012, PUBMED, Cochrane, 65 studies

- Fertile x Subfertile *(AOR= 1,35)*
- FIV/ICSI x Subfertile *(AOR= 1,55)*

FERTILITY

Perinatal outcomes associated with assisted reproductive technology: the Massachusetts Outcomes Study of Assisted Reproductive Technologies (MOSART)

Fertility and Sterility® Vol. 103, No. 4, April 2015

Eugene Declercq, Ph.D.,[a] Barbara Luke, Sc.D., M.P.H.,[b] Candice Belanoff, Sc.D.,[a] Howard Cabral, Ph.D.,[a] Hafsatou Diop, M.D.,[c] Daksha Gopal, M.P.H.,[a] Lan Hoang, M.P.H.,[a] Milton Kotelchuck, Ph.D.,[d] Judy E. Stern, Ph.D.,[e] and Mark D. Hornstein, M.D.[f]

- *334.628 birth and fetal death, 2004-2008*
- 3 groups:
  - *ART: 11.271, subfertile: 6.609, fertile: 316.748*

FERTILITY

Perinatal outcomes associated with assisted reproductive technology: the Massachusetts Outcomes Study of Assisted Reproductive Technologies (MOSART)

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Eugene Declercq, Ph.D.,[a] Barbara Luke, Sc.D., M.P.H.,[b] Candice Belanoff, Sc.D.,[a] Howard Cabral, Ph.D.,[a] Hafsatou Diop, M.D.,[c] Daksha Gopal, M.P.H.,[a] Lan Hoang, M.P.H.,[a] Milton Kotelchuck, Ph.D.,[d] Judy E. Stern, Ph.D.,[e] and Mark D. Hornstein, M.D.[f]

- ART singleton x subfertile: > preterm and low birth weight

  (AOR=1,23 – 1,26, respectively)

- ART and subferile x fertile: > preterm and low birth weight

  (OR= 1,3)

FERTILITY

Perinatal outcome of singleton siblings born after assisted reproductive technology and spontaneous conception: Danish national sibling-cohort study

Fertility and Sterility® Vol. 95, No. 3, March 1, 2011 959

Anna-Karina Aaris Henningsen, M.D.,[a] *Anja Pinborg, M.D.Sc.,*[a] *Øjvind Lidegaard, M.D.Sc.,*[b] *Christina Vestergaard, M.P.H.,*[b] *Julie Lyng Forman, M.Sc., Ph.D.,*[c] *and Anders Nyboe Andersen, M.D.Sc.*[a]

Setting: Denmark, from 1994 to 2008.

Patient(s): Pairs of siblings (13,692 pairs; n = 27,384 children) conceived after IVF, intracytoplasmatic sperm injection (ICSI), frozen embryo replacement (FER), or spontaneous conception subcategorized into five groups according to succession: [1] IVF-ICSI vs. spontaneous conception (n = 7,758), [2] IVF-ICSI vs. FER (n = 716), [3] FER vs. FER (n = 34), [4] IVF-ICSI vs. IVF-ICSI (n = 2,876), and [5] spontaneous conception vs. spontaneous conception (n = 16,000).

- ART children (all treatments) 65 g lighter *x* Natural Conceived pars
- ICSI/FIV *x* Natural Conceive: > risk lower birth weight (OR= 1,4) and preterm delivery (OR= 1,3)

FERTILITY

Assisted reproductive technology and perinatal outcomes: conventional versus discordant-sibling design

Nafeesa N. Dhalwani, Ph.D.,[a,b,c] Sheree L. Boulet, Dr.P.H.,[a] Dmitry M. Kissin, M.D.,[a] Yujia Zhang, Ph.D.,[a] Patricia McKane, M.P.H.,[d] Marie A. Bailey, M.S.W.,[e] Maria-Elena Hood, M.P.H.,[f] and Laila J. Tata, Ph.D.[b]

Fertility and Sterility® Vol. 106, No. 3, September 1, 2016

TABLE 4

Association among ART and low birth weight, preterm birth, low Apgar score, and SGA.

Type of analysis	ART group, n (%)	Non-ART group, n (%)	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Conventional analysis	**n = 32,762**	**n = 3,863,480**				
Low birth weight	2,762 (8.4)	230,048 (6.0)	1.46 (1.40, 1.51)	<.001	1.38 (1.32, 1.43)	<.001[a]
Preterm birth	3,813 (11.6)	307,327 (8.0)	1.52 (1.47, 1.58)	<.001	1.51 (1.46, 1.56)	<.001[b]
Low Apgar (<7)	424 (1.3)	45,599 (1.2)	1.09 (0.99, 1.21)	.059	0.99 (0.90, 1.09)	.888[c]
SGA[d]	593 (1.8)	67,350 (1.7)	1.04 (0.96, 1.13)	.316	1.11 (1.03, 1.21)	.01[b]
Discordant-sibling pair analysis[e]	**n = 6,458**	**n = 6,458**				
Low birth weight	436 (6.8)	314 (4.9)	1.41 (1.24,1.62)	<.001	1.33 (1.13,1.56)	<.001[a]
Preterm birth	627 (9.7)	516 (7.9)	1.24 (1.11,1.38)	.001	1.20 (1.07,1.34)	.002[b]
Low Apgar (<7)	64 (1.0)	84 (1.3)	0.76 (0.55,1.06)	.101	0.75 (0.54,1.05)	.096[c]
SGA[d]	94 (1.4)	75 (1.2)	1.25 (0.93,1.69)	.132	1.22 (0.88,1.68)	.237[b]

[a] Adjusted for maternal age, year of birth, parity, infant's sex, gestational age, and time since last recorded delivery.
[b] Adjusted for maternal age, year of birth, parity, infant's sex, nd time since last recorded delivery.
[c] Adjusted for maternal age, year of birth, parity, infant's sex, gestational age, delivery type, and time since last recorded delivery.
[d] 2 SD lower than the mean birth weight for gestational age and sex.
[e] One sibling was conceived naturally, and the other one was conceived through ART.

Dhalwani. ART and perinatal outcomes. Fertil Steril 2016.

Birth Defects

FERTILITY

Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis

Fertility and Sterility® Vol. 97, No. 6, June 2012

Juan Wen, B.S.,[a,b] Jie Jiang, B.S.,[a,b] Chenyue Ding, B.S.,[d] Juncheng Dai, M.D.,[b] Yao Liu, B.S.,[b] Yankai Xia, M.D., Ph.D.,[a,c] Jiayin Liu, M.D., Ph.D.,[a,d] and Zhibin Hu, M.D., Ph.D.[a,b]

- 124.468 children: FIV/ICSI compared with Natural Conceived
- RR Congenital anomalies: ***1,37*** (95%; CI: 1,26-1,48)
- FIV (46.890) x ICSI (27.754): ***no difference***
  (RR: 1,05, 95%; CI: 0,91-1,02)

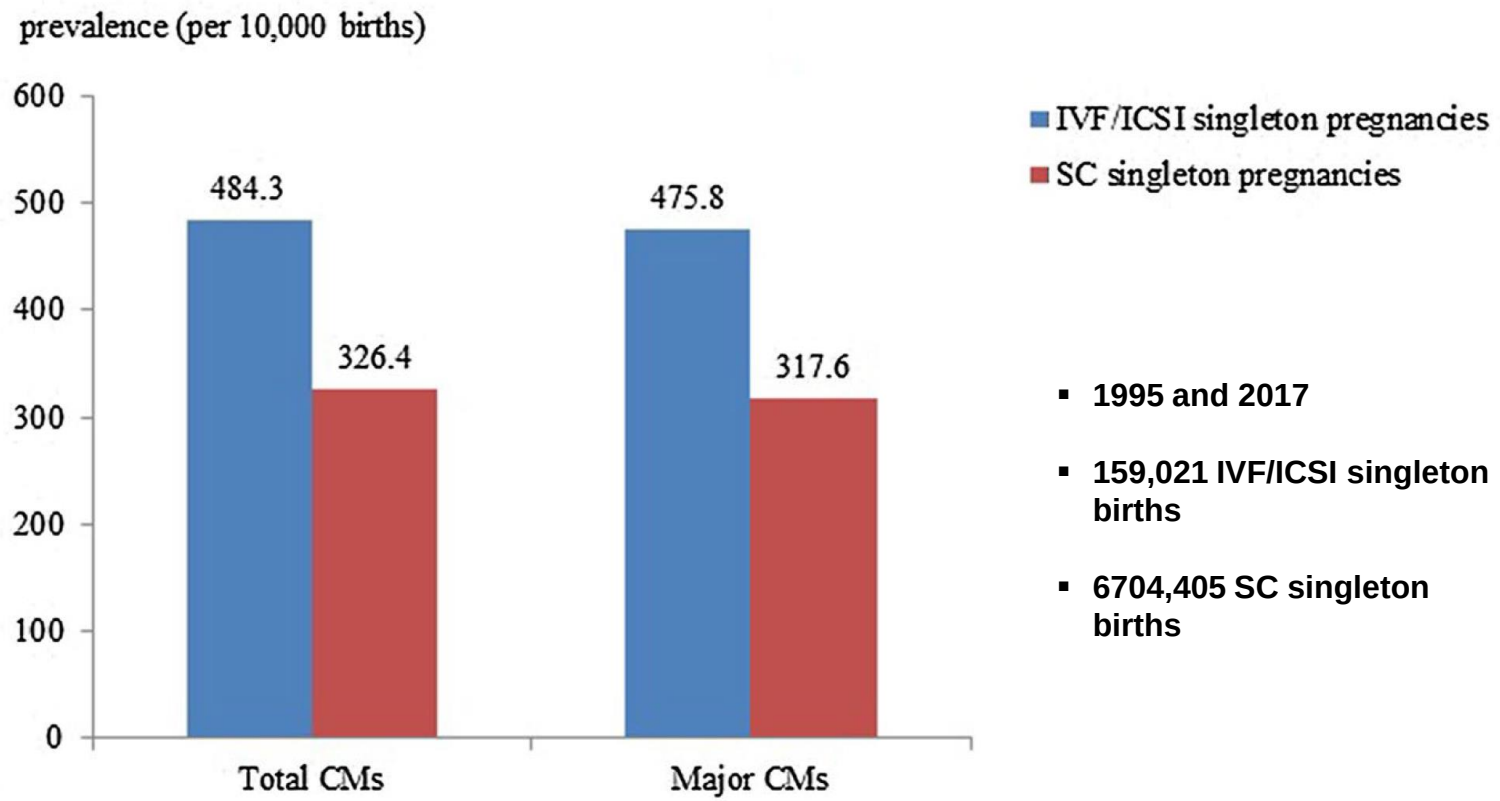
FERTILITY

Archives of Gynecology and Obstetrics (2018) 297:1115–1130
https://doi.org/10.1007/s00404-018-4712-x

REVIEW

Birth prevalence of congenital malformations in singleton pregnancies resulting from in vitro fertilization/intracytoplasmic sperm injection worldwide: a systematic review and meta-analysis

Letao Chen[1] · Tubao Yang[1] · Zan Zheng[1] · Hong Yu[2] · Hua Wang[2] · Jiabi Qin[1]



- 1995 and 2017
- 159,021 IVF/ICSI singleton births
- 6704,405 SC singleton births

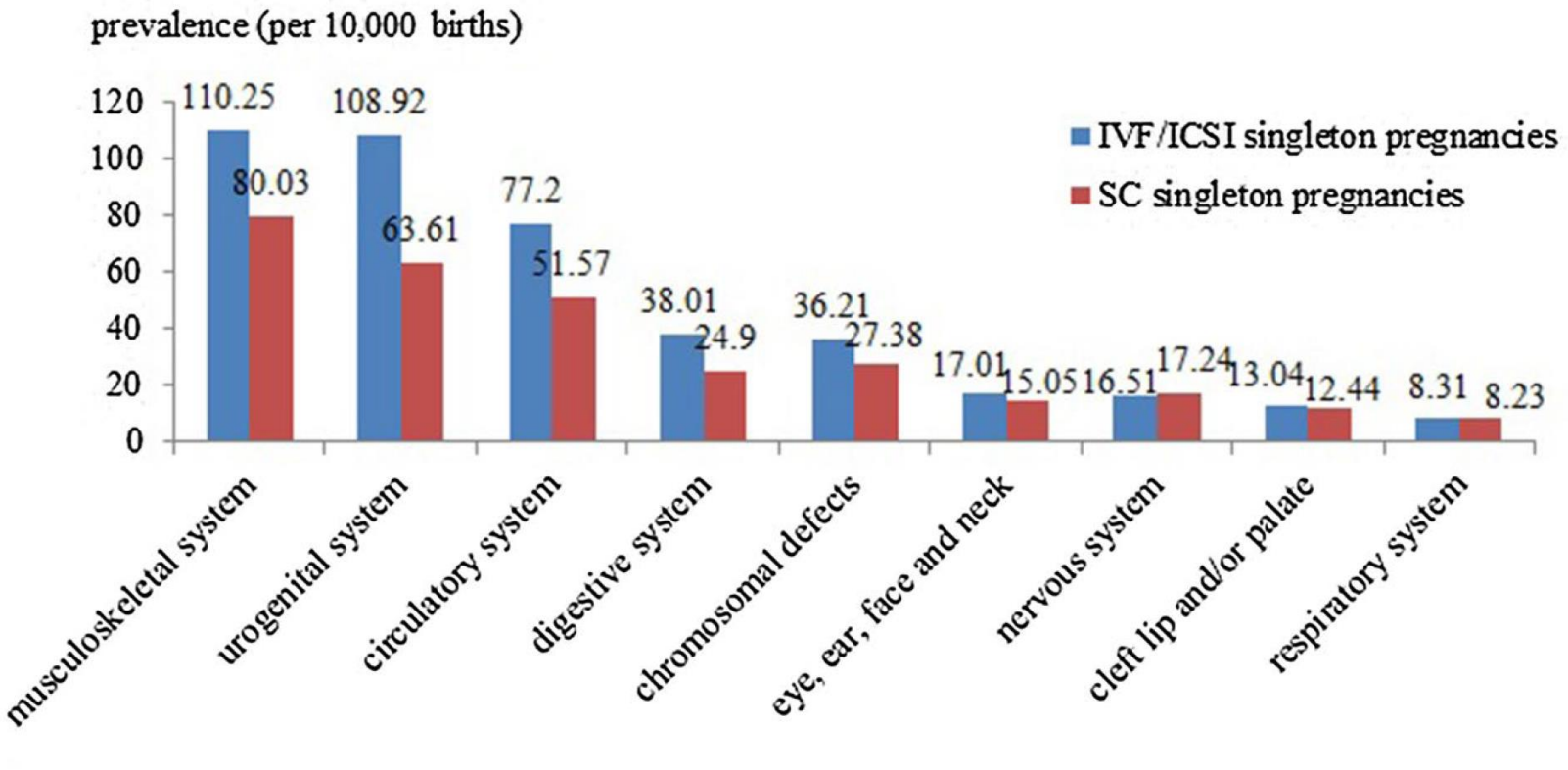
FERTILITY

Archives of Gynecology and Obstetrics (2018) 297:1115–1130
https://doi.org/10.1007/s00404-018-4712-x

REVIEW

Birth prevalence of congenital malformations in singleton pregnancies resulting from in vitro fertilization/intracytoplasmic sperm injection worldwide: a systematic review and meta-analysis

Letao Chen[1] · Tubao Yang[1] · Zan Zheng[1] · Hong Yu[2] · Hua Wang[2] · Jiabi Qin[1]



Sperm quality
Consequences on offspring

FERTILITY

ANDROLOGY

ISSN: 2047-2919 *Andrology*, 2018, 6, 635–653 ANDROLOGY

REVIEW ARTICLE

Correspondence:
Sarah R. Catford, Hudson Institute of Medical Research, 27-31 Wright St, Clayton, VIC 3168, Australia.
E-mail: sarah.catford@monashhealth.org

Keywords:
children, follow-up, ICSI, intracytoplasmic sperm injection, offspring

Received: 4-Jun-2017
Revised: 13-Jun-2018
Accepted: 19-Jun-2018

doi: 10.1111/andr.12526

Long-term follow-up of ICSI-conceived offspring compared with spontaneously conceived offspring: a systematic review of health outcomes beyond the neonatal period

[1,2,3]S. R. Catford, [1,2]R. I. McLachlan, [4]M. K. O'Bryan and [3,5]J. L. Halliday

[1]Hudson Institute of Medical Research, Clayton, VIC, Australia, [2]Department of Obstetrics and Gynecology, Monash University, Clayton, VIC, Australia, [3]Public Health Genetics, Murdoch Childrens Research Institute, Parkville, VIC, Australia, [4]The School of Biological Sciences, Monash University, Clayton, VIC, Australia, [5]Department of Paediatrics, University of Melbourne, Parkville, VIC, Australia

CONCLUSION: Whilst neurodevelopment, growth, vision, and hearing appear similar between ICSI and SC children, evidence suggests differences in general physical health, and metabolic and reproductive endpoints

FERTILITY

Long-term follow-up of ICSI-conceived offspring compared with spontaneously conceived offspring: a systematic review of health outcomes beyond the neonatal period

[1,2,3]S. R. Catford, [1,2]R. I. McLachlan, [4]M. K. O'Bryan and [3,5]J. L. Halliday

Andrology, 2018, 6, 635–653

Impaired spermatogenesis in ICSI-conceived young adult males, as indicated by reduced semen quality, and possibly higher FSH and lower inhibin B levels, compared to their SC peers

Human Reproduction, Vol.32, No.2 pp. 439–446, 2017
Advanced Access publication on December 22, 2016 doi:10.1093/humrep/dew324

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Reproductive hormones of ICSI-conceived young adult men: the first results

Florence Belva[1,*], Mathieu Roelants[2], Jean De Schepper[3], André Van Steirteghem[4], Herman Tournaye[4], and Maryse Bonduelle[1]

ICSI-conceived men were more likely to have low inhibin B (<10th percentile) and high FSH (>90th percentile) levels.

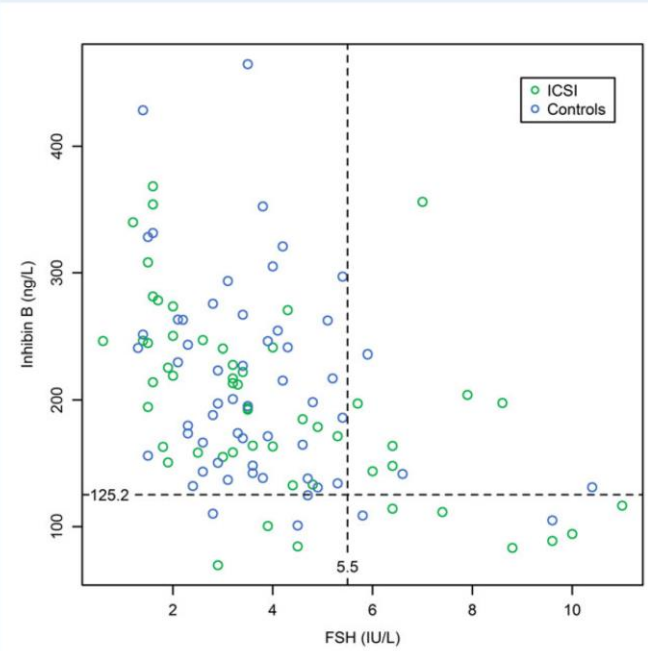


Figure 1 Serum inhibin B and FSH levels in ICSI and control men.

FERTILITY

Human Reproduction, Vol.32, No.2 pp. 439–446, 2017
Advanced Access publication on December 22, 2016 doi:10.1093/humrep/dew324

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Reproductive hormones of ICSI-conceived young adult men: the first results

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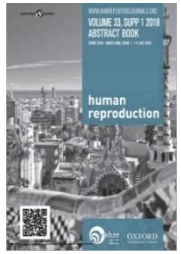
Table III Correlations between reproductive hormone levels and semen parameters and testis volume.

	FSH		Testosterone		LH		Inhibin B	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value	*r*	*P*-value
Sperm concentration	−0.3	0.001	0.1	0.30	−0.2	0.01	0.2	0.02
Total sperm count	−0.3	0.001	0.1	0.62	−0.2	0.02	0.2	0.01
Total motile count	−0.4	0.01	0.1	0.31	−0.2	0.06	0.2	0.01
Sperm morphology	−0.2	0.03	0.1	0.23	−0.1	0.1	−0.1	0.84
Testis volume	−0.2	0.05	0.2	0.04	−0.1	0.6	0.4	<0.01

INVITED SESSION

SESSION 01: KEYNOTE SESSION

Monday 2 July 2018 Forum (Auditorium) 08:30–09:30



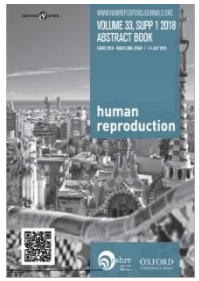
O-001 Human Reproduction Keynote Lecture - Semen quality of young adult ICSI offspring: The first results

F. Belva[1], M. Bonduelle[1], M. Roelants[2], D. Michielsen[3], A. Van Steirteghem[4], G. Verheyen[4], H. Tournaye[4]

- UZ Brussel, 03/2013 – 04/2016, 54 young males
- Reproductive and metabolic health of young males 18-22 years old, born of ICSI with ejaculated spermatozoa x natural conception (NC)

O-001 Human Reproduction Keynote Lecture - Semen quality of young adult ICSI offspring: The first results

F. Belva[1], M. Bonduelle[1], M. Roelants[2], D. Michielsen[3], A. Van Steirteghem[4], G. Verheyen[4], H. Tournaye[4]



ICSI: lower conc/mL, total, TMSC (17,7 mil/ml, 31,9 mil e 12,7 mil) compared ***NC*** (37 mil/mL; 86.8 mil; 38.6 mil)

- ***NC:*** almost doubled sperm concentration/mL (*ratio 1.9*, 95% CI 1.1-3.2)
- ***ICSI:*** two-fold lower total sperm count (*ratio 2.3*, 95% CI 1.3-4.1) and TMSC (*ratio 2.1*, 95% CI 1.2-3.6)

ICSI:

- three times more likely to have sperm concentrations below the WHO reference value of 15 million/ml (*AOR 2.7*; 95% CI 1.1–6.7)
- four times more likely to have total sperm counts below 39 million (*AOR 4.3*; 95% CI 1.7-11.3)

Human Reproduction Update, Vol.24, No.3 pp. 320–389, 2018
Advanced Access publication on February 15, 2018 doi:10.1093/humupd/dmy005

human reproduction update

The effect of paternal factors on perinatal and paediatric outcomes: a systematic review and meta-analysis

Nan B. Oldereid [1,*], Ulla-Britt Wennerholm[2], Anja Pinborg[3], Anne Loft[4], Hannele Laivuori[5,6,7,8], Max Petzold[9], Liv Bente Romundstad[10,11], Viveca Söderström-Anttila[12], and Christina Bergh[13]

[1]Livio IVF-klinikken Oslo, Sørkedalsveien 10A, 0369 Oslo, Norway [2]Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Sahlgrenska University Hospital East, SE 416 85 Gothenburg, Sweden [3]Department of Obstetrics and Gynecology, Hvidovre Hospital, Institute of Clinical Medicine, Copenhagen University Hospital, Copenhagen, Denmark [4]Fertility Clinic, Section 4071, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK–2100 Copenhagen, Denmark [5]Department of Obstetrics and Gynecology, Tampere University Hospital, Teiskontie 35, FI-33521 Tampere, Finland [6]Faculty of Medicine and Life Sciences, University of Tampere, Arvo Ylpön katu 34, FI-33520 Tampere, Finland [7]Medical and Clinical Genetics, University of Helsinki and Helsinki University Hospital, Haartmaninkatu 8, FI-00290 Helsinki, Finland [8]Institute for Molecular Medicine Finland, Helsinki Institute of Life Science, University of Helsinki, Tukhomankatu 8, FI-00290 Helsinki, Finland [9]Swedish National Data Service and Health Metrics Unit, University of Gothenburg, 405 30 Gothenburg, Sweden [10]Spiren Fertility Clinic, Norwegian University of Science and Technology, Trondheim NO-7010, Norway [11]Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway [12]Mehiläinen Felicitas, Mannerheimintie 20A, 00100 Helsinki, Finland [13]Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Reproductive Medicine, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden

- 14.371 articles, 238 included, 81 metanalisys
- Age, lifestyle, weight, height, body fat, cigarette

FERTILITY

Table XI Summary results of the meta-analyses of the association between paternal factors and perinatal and paediatric outcomes.

Exposure	Outcome	Pooled estimate (with 95% CI)	Certainty of evidence GRADE
Paternal age	PTB	1.02 (1.00–1.05)	⊕⊕◯◯
	Low BW	1.00 (0.97–1.03)	⊕⊕◯◯
	Stillbirth	1.19 (1.10–1.30)	⊕⊕◯◯
★	Children with any birth defects	1.05 (1.02–1.07)	⊕⊕⊕◯
★	CHDs	1.03 (0.99–1.06)	⊕⊕⊕◯
	Orofacial clefts	0.99 (0.95–1.04) 1.14 (1.02–1.29)*	⊕⊕◯◯
★	Gastroschisis	0.88 (0.78–1.00)	⊕⊕⊕◯
★	Spina bifida	0.97 (0.90–1.04)	⊕⊕⊕◯
★	Trisomy 21	1.13 (1.05–1.23)	⊕⊕⊕◯
★	Acute lymphoblastic leukaemia	1.08 (0.96–1.21)	⊕⊕⊕◯
★	Autism and ASDs	1.25 (1.20–1.30)	⊕⊕⊕◯
★	Schizophrenia	1.31 (1.23–1.38)	⊕⊕⊕◯
Paternal BMI	No meta-analysis		
Paternal smoking	PTB	1.16 (1.00–1.35)	⊕⊕◯◯
	Low BW	1.10 (1.00–1.21)	⊕⊕◯◯
	SGA	1.22 (1.03–1.44)	⊕⊕◯◯
	CHDs	1.75 (1.25–2.44)	⊕⊕◯◯
	Orofacial clefts	1.51 (1.16–1.97)	⊕⊕◯◯
	Brain tumours	1.12 (1.03–1.22)	⊕⊕◯◯

*Exposure: Paternal age >45 years.

Human Reproduction, pp. 1–11, 2019
doi:10.1093/humrep/dey394

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Risk of cancer in children and young adults conceived by assisted reproductive technology

Mandy Spaan[1], Alexandra W. van den Belt-Dusebout[1], Marry M. van den Heuvel-Eibrink[2], Michael Hauptmann[1], Cornelis B. Lambalk[3], Curt W. Burger[4], and Flora E. van Leeuwen[1,*], on behalf of the OMEGA-steering group[†]

STUDY DESIGN, SIZE, DURATION: A nationwide historical cohort study with ***prospective follow-up (median 21 years)***, including all live-born offspring from women treated with subfertility treatments between 1980 and 2001.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Of 47 690 live-born children, 24 269 were ART-conceived, 13 761 naturally conceived and 9660 were conceived naturally or through fertility drugs, but not by ART

SUMMARY ANSWER:

ART-conceived children do not appear to have an increased risk of cancer.

FERTILITY

Childhood Cancer Risk in the Siblings and Cousins of Men with Poor Semen Quality

Ross E. Anderson,* Heidi A. Hanson, William T. Lowrance, Jeffrey Redshaw, Siam Oottamasathien, Anthony Schaeffer, Erica Johnstone, Kenneth I. Aston, Douglas T. Carrell, Patrick Cartwright, Ken R. Smith and James M. Hotaling

THE JOURNAL OF UROLOGY® Vol. 197, 898-905, March 2017

- The 3 most common cancers diagnosed in siblings were acute lymphoblastic leukemia, brain cancer and Hodgkin lymphoma

- Oligozoospermia was associated with a ***twofold increased risk of any childhood cancer and a threefold increased risk of acute lymphoblastic leukemia*** in the siblings of subfertile men compared to fertile controls (HR 2.09, 95% CI 1.18e3.69 vs HR 3.07, 95% CI 1.11e8.46).

Male infertility: a biomarker of individual and familial cancer risk

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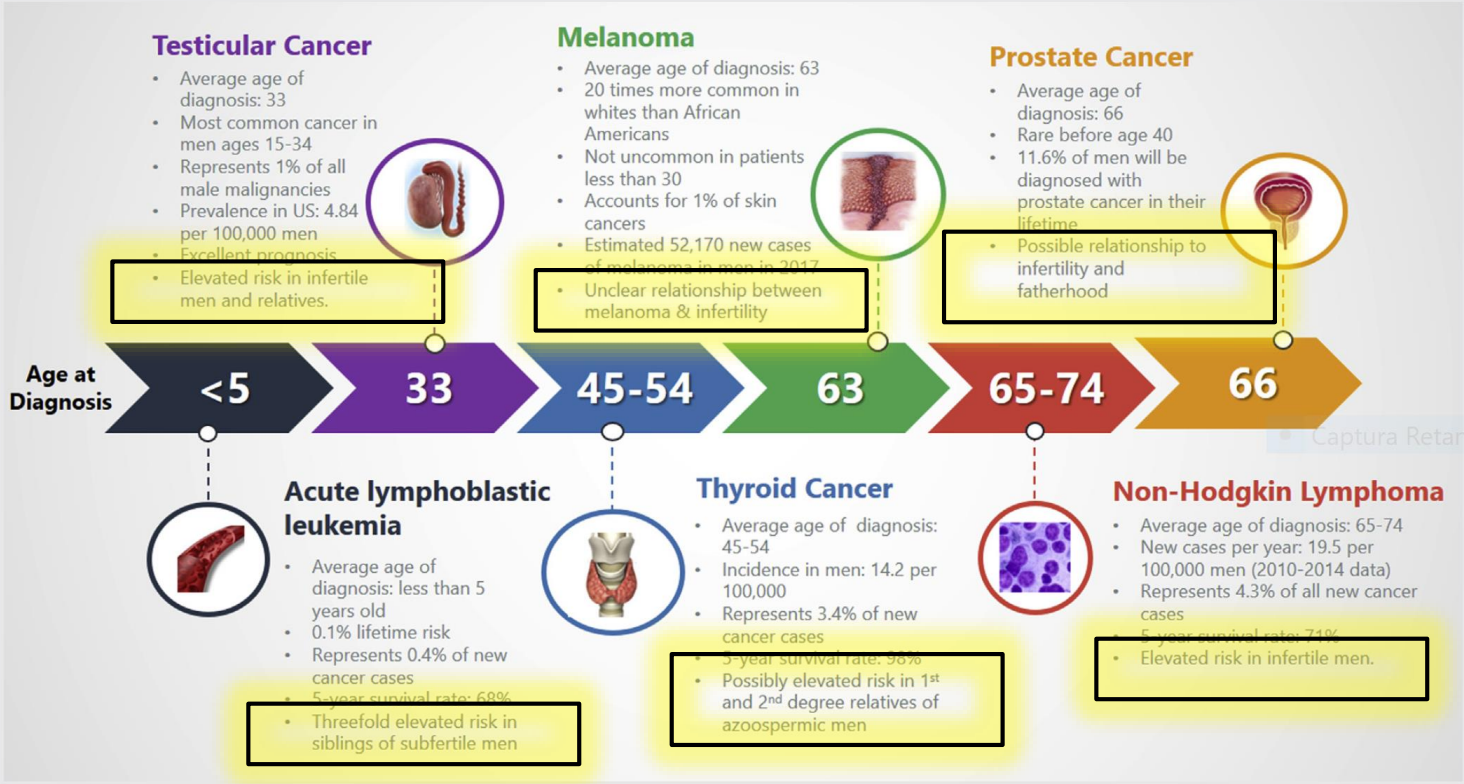
Fertility and Sterility® Vol. 109, No. 1, January 2018



Specific malignancies associated with infertile men and their family members by average age at diagnosis.

Hanson. Male infertility and cancer risk. Fertil Steril 2017.

Human Reproduction, Vol.32, No.1 pp. 239–247, 2017
Advanced Access publication on December 6, 2016 doi:10.1093/humrep/dew289

human reproduction ORIGINAL ARTICLE *Reproductive epidemiology*

Risk of childhood mortality in family members of men with poor semen quality

Heidi A. Hanson[1,2,*], Erik N. Mayer[3], Ross E. Anderson[3], Kenneth I. Aston[3,4,5], Douglas T. Carrell[3,5], Justin Berger[2], William T. Lowrance[3], Ken R. Smith[2,6], and James M. Hotaling[3,4]

- Relationship between Fertility and Congenital Malformations
- The increased risk of congenital birth defects may not be due to the ART, but rather genetic or environmental factors that link the two outcomes
- ***An increased risk of death due to Congenital Malformations (CM) in First Degree Relatives (FDR), of men with lower semen parameters***

O-91 Tuesday, October 9, 2018 10:45 AM

MALE FACTOR INFERTILITY AND RISK OF MORTALITY: A REGISTER BASED COHORT STUDY.

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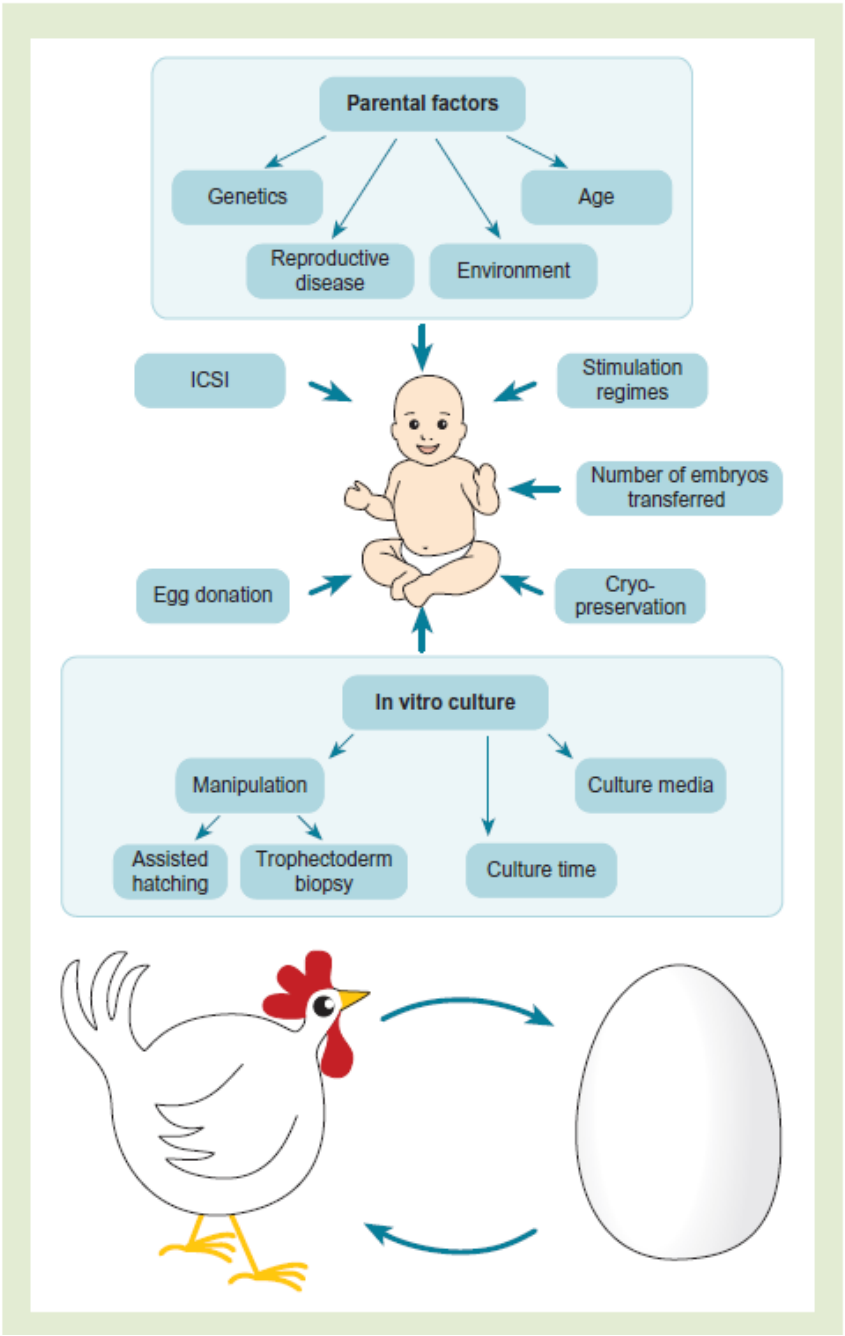
- All men whose partner had undergone fertility treatment in all public and private fertility clinics in Denmark (n=51,289)
- Men with **azoospermia** (n=1,722) had a **two-fold increased mortality risk** [OR 2.1, 95% CI 1.3-3.4]


Parental factors
Genetics
Age
Reproductive disease
Environment
ICSI
Stimulation regimes
Number of embryos transferred
Egg donation
Cryo-preservation
In vitro culture
Manipulation
Culture media
Assisted hatching
Trophectoderm biopsy
Culture time

FERTILITY

Messages

- Worse obstetric and perinatal outcomes in children conceived after ART
- Increase preterm delivery and low birth weight comparing ART x subfertile x fertile children
- Increase birth defects in ART children
- Impaired spermatogenesis in ICSI-conceived young adult males
- Increased risk of worse seminal quality in ICSI/IVF children

Messages

- Paternal age related to birth defects, CHDs ...sis, spina bifida, trissomy 21, acute lymphoblastic le...
- Increased risk of childhood and fa...er
- Increased risk of death due ...ital Malformations (CM) in First Degree Relatives (F...n with lower semen parameters
- Increased risk of ...g and Epigenetic Inheritance Disorders in ICSI/IVF c...ated to compromised spermatogenesis

Male infertility as a window to health

FERTILITY