V SIMPÓSIO INTERNACIONAL DE
REPRODUÇÃO HUMANA
E GENÉTICA

Idade paterna avançada: Devemos nos preocupar?

FERTILITY
MEDICAL GROUP

Edson Borges Jr.

Declaro:

Ausência de Conflito de Interesse

Resolução do Conselho Federal de Medicina nº 1.595/2.000

FERTILITY

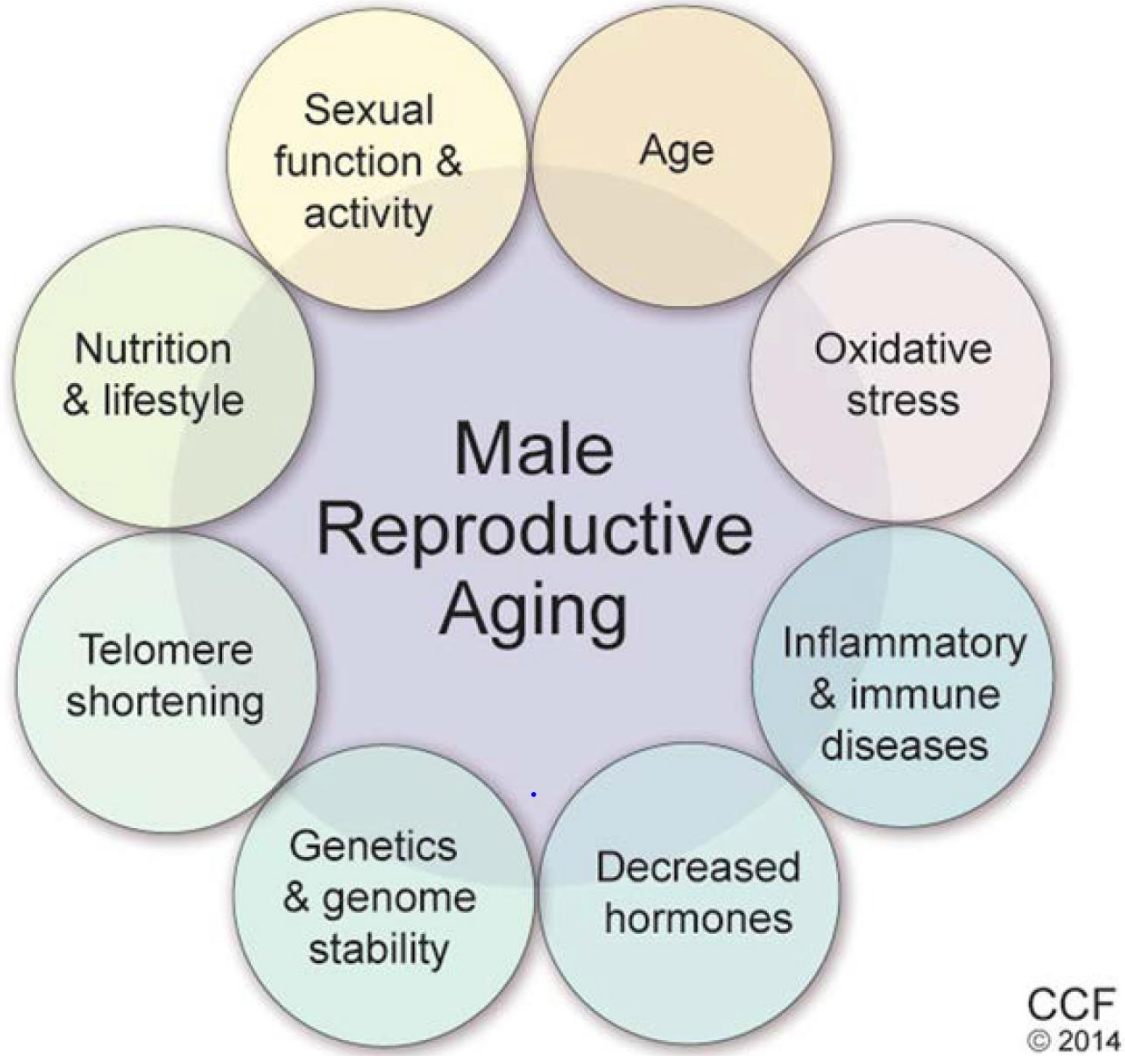
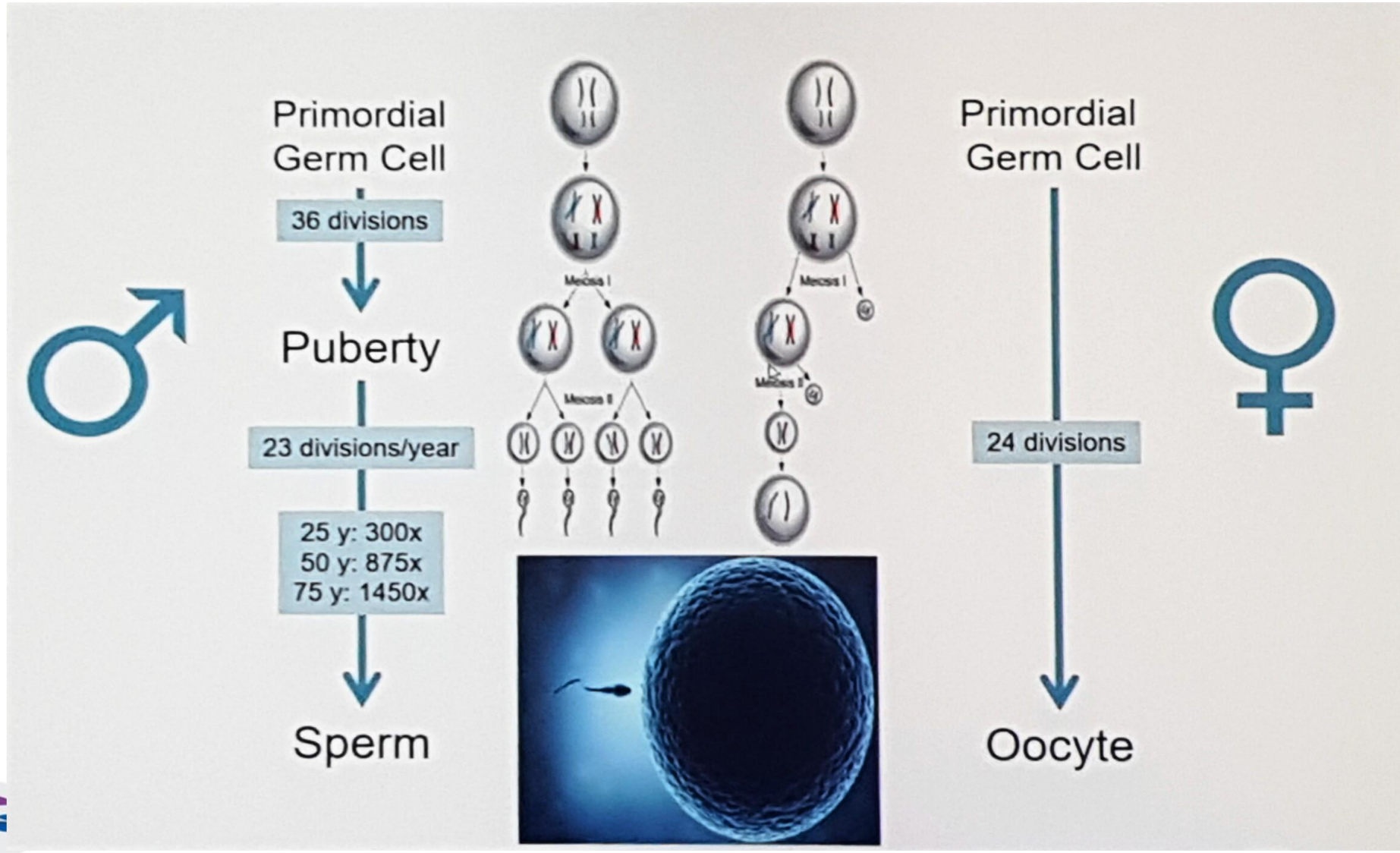
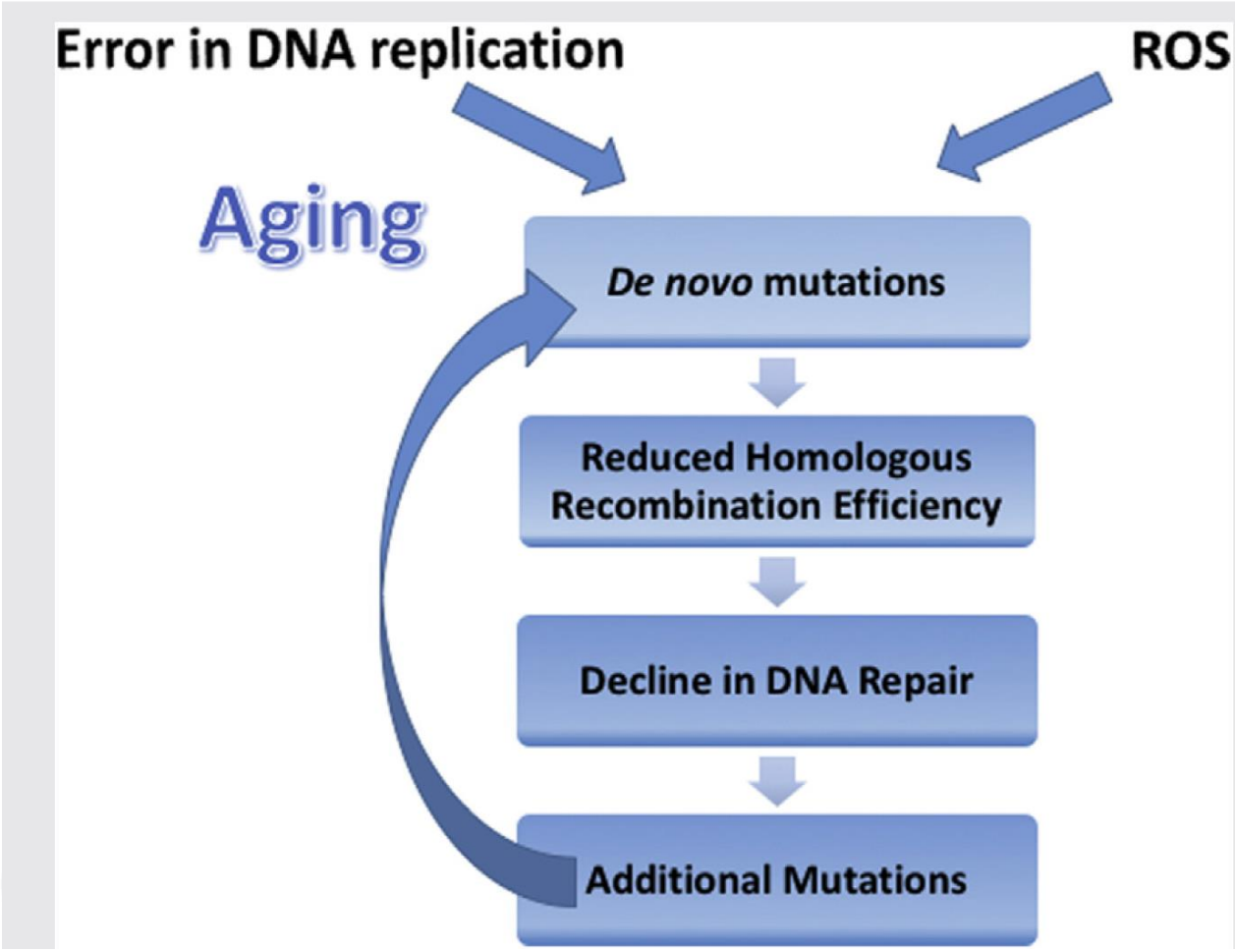


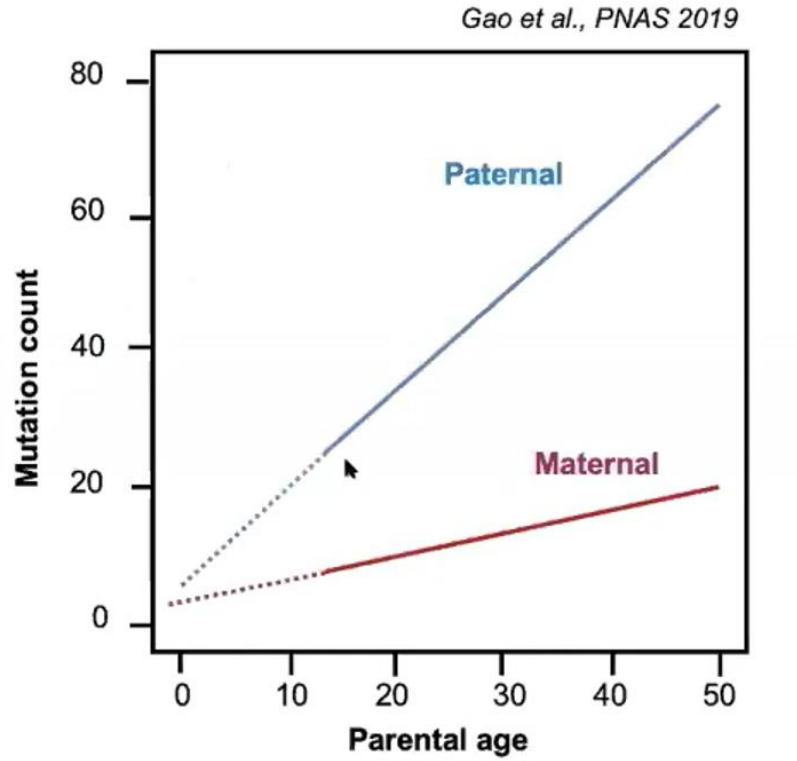
Figure 1 Main factors involved in impaired male infertility due to reproductive aging.

Diffferences in gametogenesis



Replications erros and de novo mutations





AGENDA

- Fertilidade masculina – efeito temporal
- Nos resultados de RA
- Nas chances de gestação, nascimento e aborto
- Nos desfechos perinatias
- Na prole

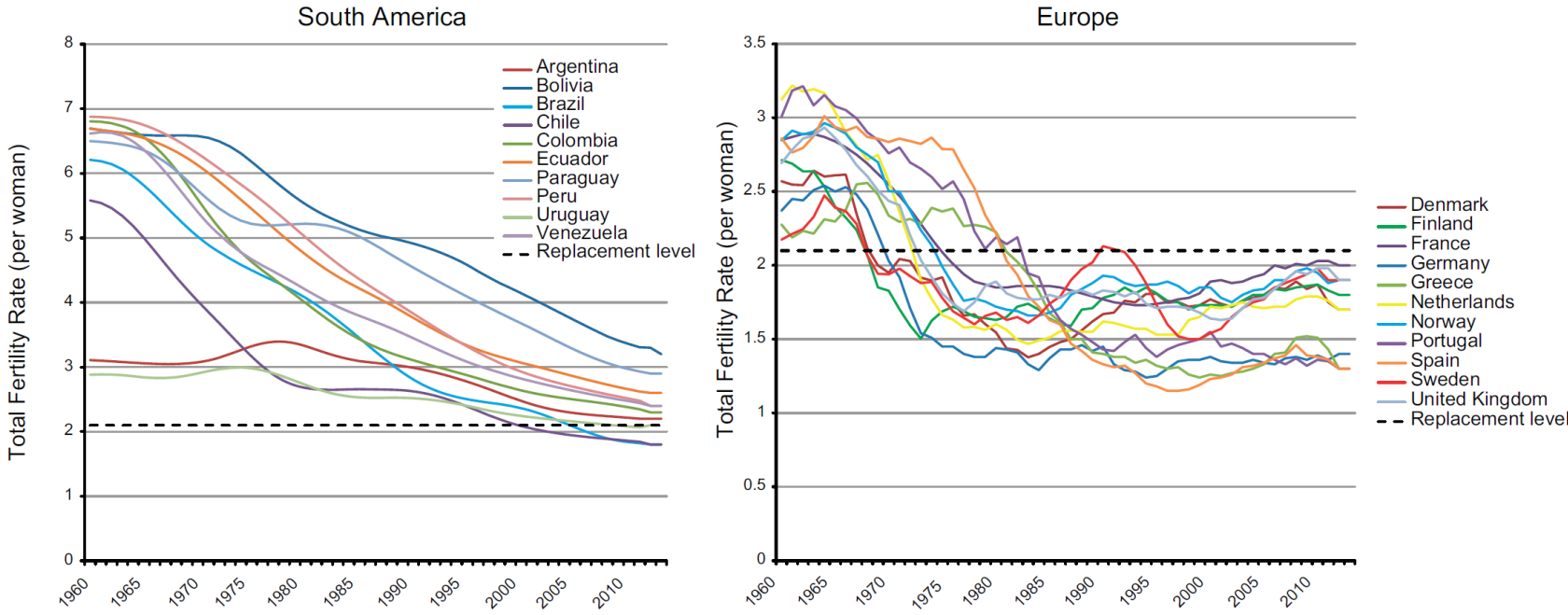
FERTILITY

Physiol Rev 96: 55–97, 2016
Published November 18, 2015; doi:10.1152/physrev.00017.2015

MALE REPRODUCTIVE DISORDERS AND FERTILITY TRENDS: INFLUENCES OF ENVIRONMENT AND GENETIC SUSCEPTIBILITY

Niels E. Skakkebaek, Ewa Rajpert-De Meyts, Germaine M. Buck Louis, Jorma Toppari, Anna-Maria Andersson, Michael L. Eisenberg, Tina Kold Jensen, Niels Jørgensen, Shanna H. Swan, Katherine J. Sapra, Søren Ziebe, Lærke Priskorn, and Anders Juul

Taxa de Fecundidade



FERTILITY

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Incidência de Criptorquidia

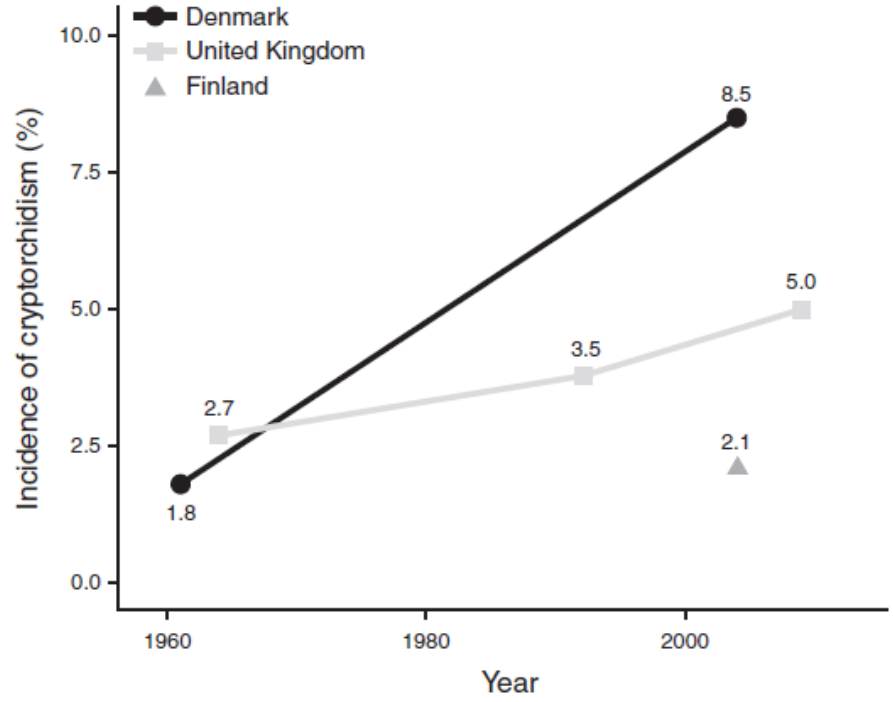

FIGURE 7. Incidence of cryptorchidism at birth on the basis of prospective clinical studies from the 1950s to the 2000s in Denmark, Finland, and United Kingdom. The data points are marked on the year of the publication of the study which represents the preceding incidence rate (3, 47, 61, 184, 377).

FERTILITY

Physiol Rev 96: 55–97, 2016
Published November 18, 2015; doi:10.1152/physrev.00017.2015

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Incidência de Câncer de Testículo

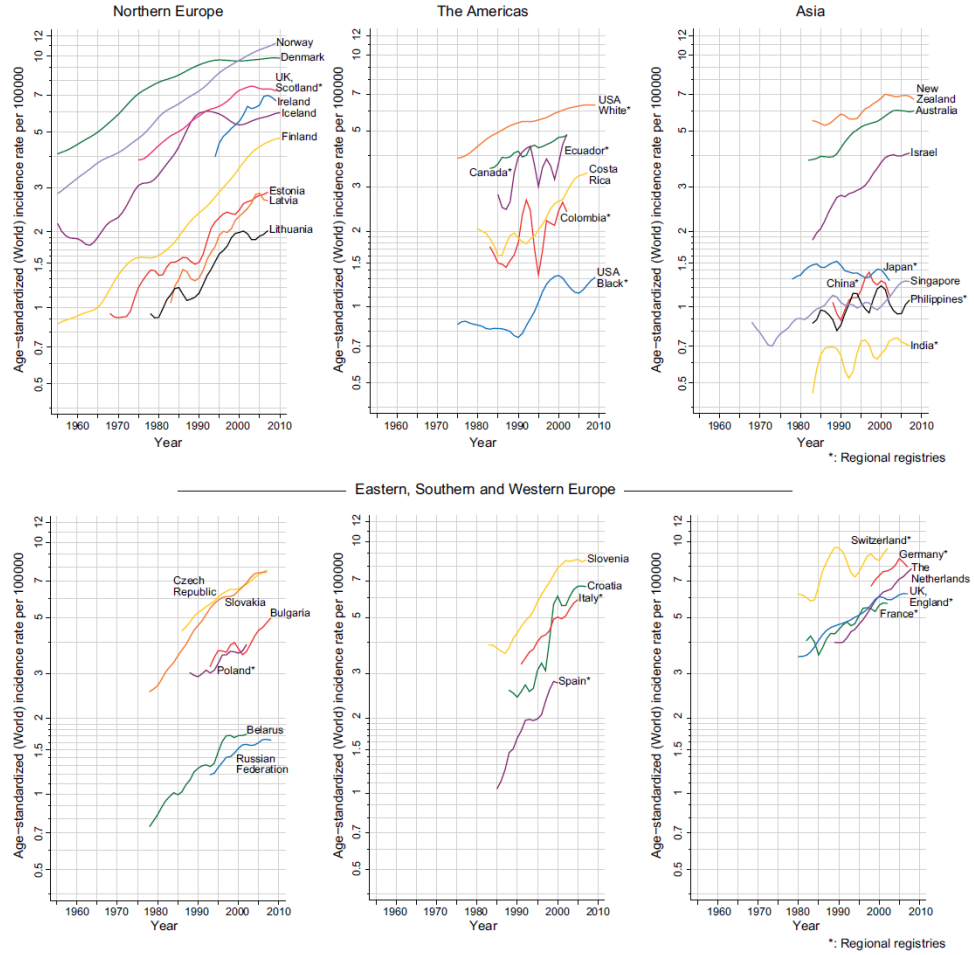

FIGURE 4. Trends in testicular cancer; age-standardized (world) incidence (regional or national), all ages. [Modified from Znaor et al. (481). Courtesy of Dr. Arinana Znaor and statistician Mathieu Laversanne, M.Sc., WHO, International Agency for Research in Cancer (IARC), Lyon, France.]

FERTILI

Physiol Rev 96: 55-97, 2016
Published November 18, 2015; doi:10.1152/physrev.00017.2015

MALE REPRODUCTIVE DISORDERS AND FERTILITY TRENDS: INFLUENCES OF ENVIRONMENT AND GENETIC SUSCEPTIBILITY

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Idade da Puberdade

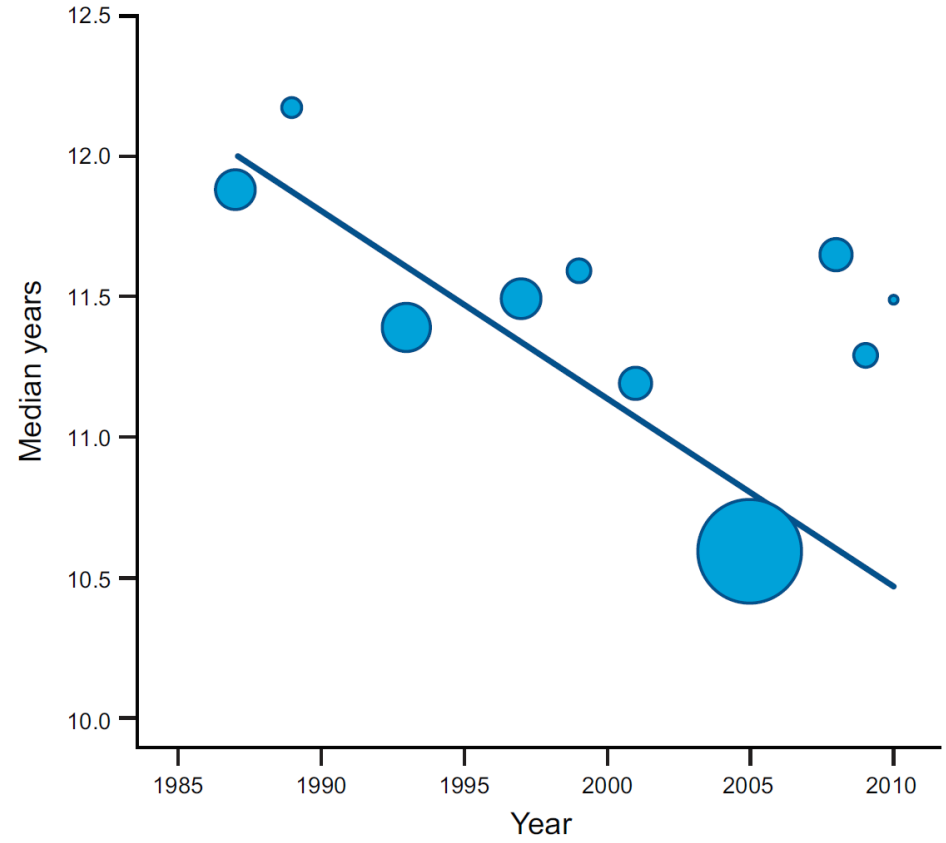


FIGURE 8. Recent changes in male pubertal timing. Testicular volume was >3 ml. [From Mouritsen et al. (293).]

FERTILITY

Article

HET

Human and Experimental Toxicology
1–9

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

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]

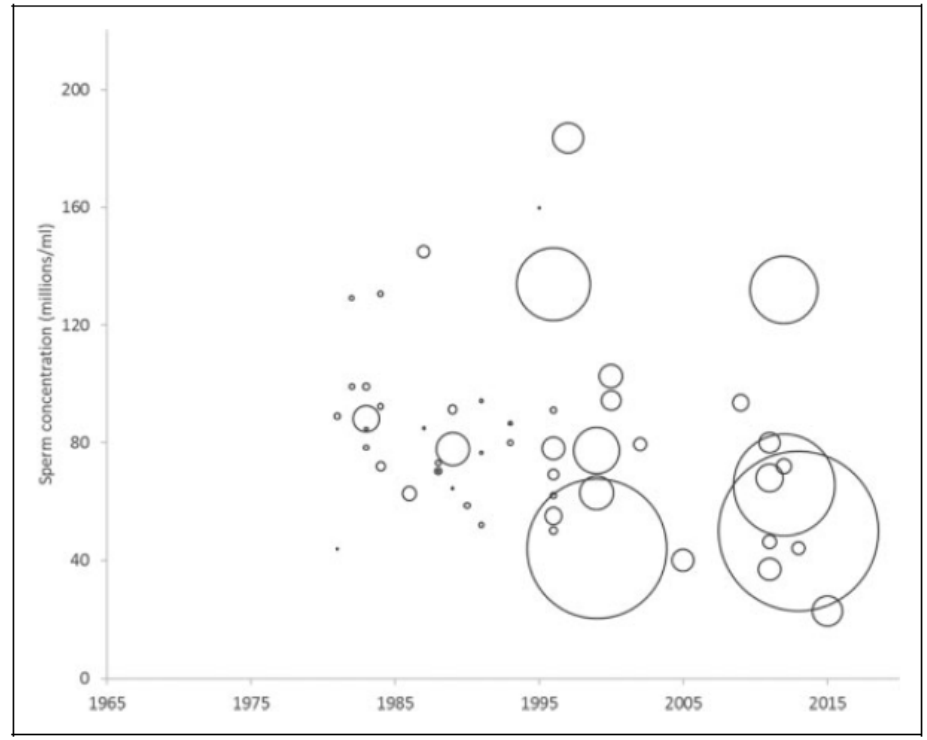


Figure 1. Temporal decline in sperm concentration ($\times 10^6$/ml) from 1965 to 2015, bubble size corresponds to the number of men in the study.

A time dependent decline in sperm concentration was observed from 1965 to 2015 (r=0.307, p=0.02)

An overall 32.5%decrease in mean sperm concentration

FERTILITY

MALE FACTOR

1870 Fertility and Sterility® Vol. 93, No. 6, April 2010

Negative influence of paternal age on clinical intracytoplasmic sperm injection cycle outcomes in oligozoospermic patients

Renata Cristina Ferreira, M.S.,[a,b] *Daniela Paes de Almeida Ferreira Braga, D.V.M., M.S.,*[a,b] *Tatiana Carvalho de Souza Bonetti, M.S.,*[a,b] *Fabio Firmbach Pasqualotto, M.D., Ph.D.,*[c] *Assumpto Iaconelli, Jr., M.D.,*[a,b] *and Edson Borges, Jr., M.D., Ph.D.*[a,b]

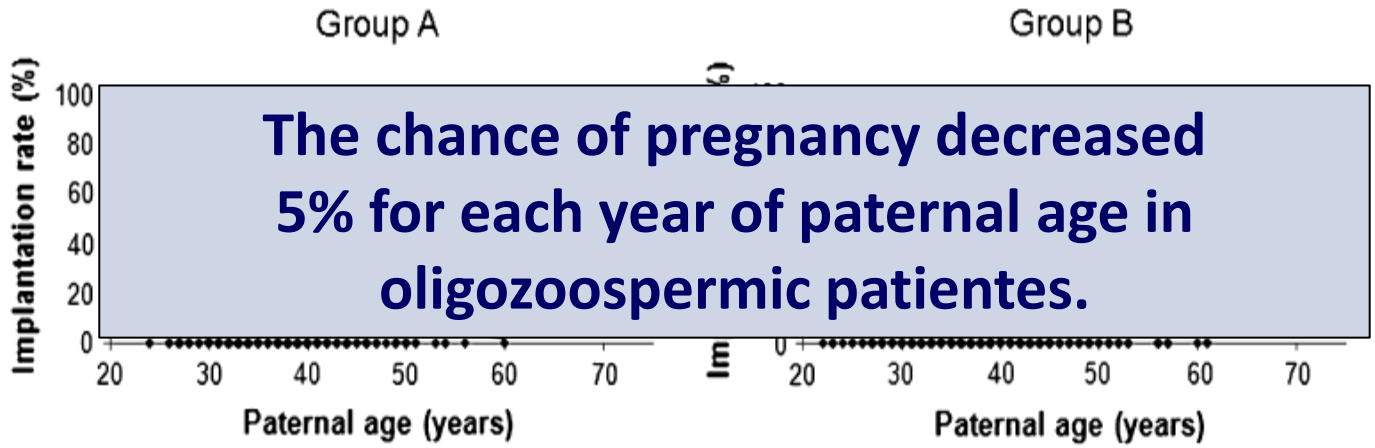
Patient(s): The study included 1,024 couples undergoing ICSI cycles with fresh spermatozoa.

Intervention(s): The influence of paternal age on ICSI outcomes of oligozoospermic and normozoospermic patients was evaluated.

Main Outcome Measure(s): Rates of high-quality embryos, pregnancy, implantation, and miscarriage were evaluated through linear logistic regression analyses.

FIGURE 2

Influence of paternal age on implantation rate. Multiple linear regression was performed and was adjusted for maternal age, numbers of oocytes retrieved, sperm concentration, and fertilization rate. Group A (oligozoospermic patients): $P=.008$, RC = −0.7009 (implantation rate regression equation: in implantation rate = 48.2 − 0.701 paternal age − 0.177 maternal age − 0.220 number of oocyte retrieved − 0.092 sperm concentration + 0.082 fertilization rate); group B (normozoospermic patients): $P=.752$, RC = 0.0566 (implantation rate regression equation: in implantation rate = 32.1 + 0.057 paternal age − 0.758 maternal age + 0.426 number of oocyte retrieved − 0.024 sperm concentration + 0.0542 fertilization rate).



The chance of pregnancy decreased 5% for each year of paternal age in oligozoospermic patientes.

Ferreira. Paternal age and ICSI outcomes. Fertil Steril 2009.

Received: 31 March 2021 | Revised: 29 July 2021 | Accepted: 30 July 2021

DOI: 10.1111/and.14211

ORIGINAL ARTICLE

First International Journal of Andrology
ANDROLOGIA
WILEY

Early and late paternal contribution to cell division of embryos in a time-lapse imaging incubation system

Amanda Souza Setti[1,2] | Daniela Paes de Almeida Ferreira Braga[1,2] | Livia Vingris[3] | Assumpto Iaconelli Jr.[2,4] | Edson Borges Jr.[2,4]

FERTILITY

RESULTS

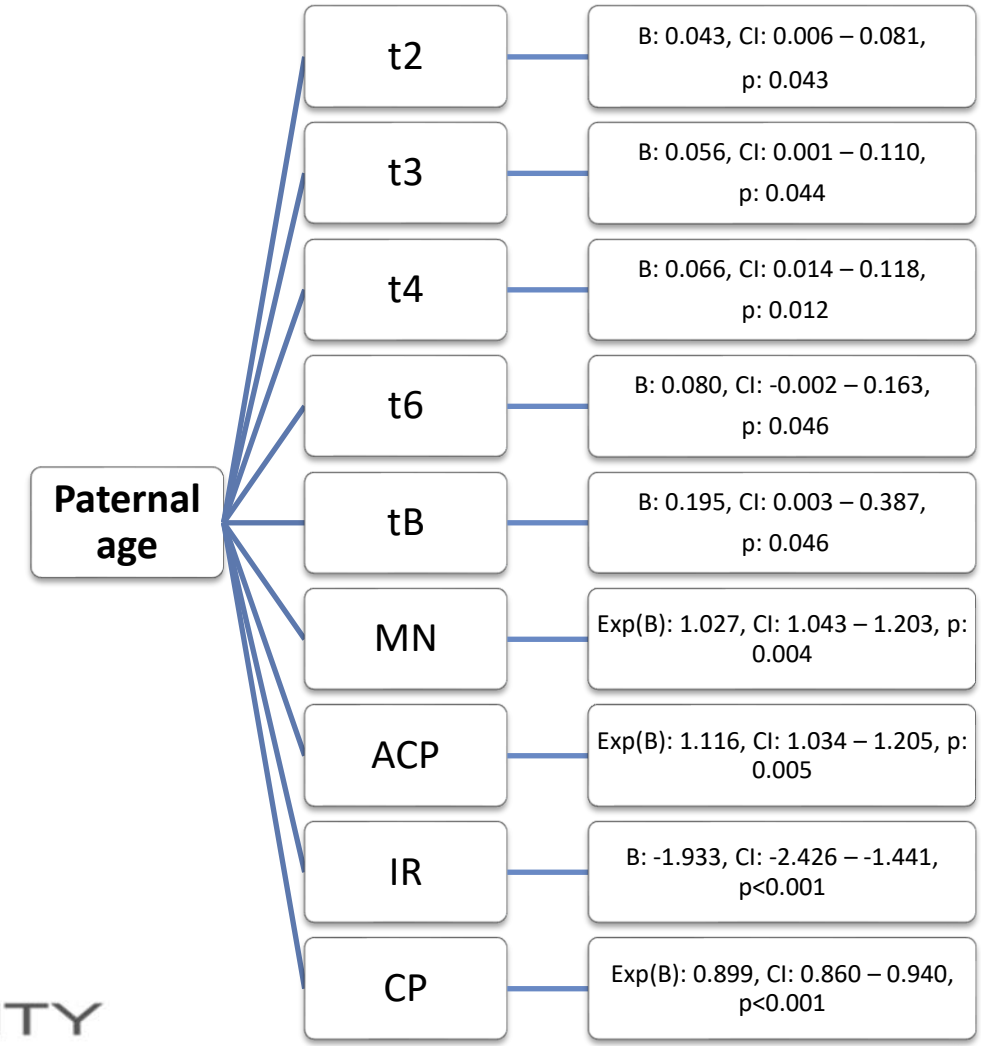
First International Journal of Andrology
aNDROLOGIa
Early and late paternal contribution to cell division of embryos in a time-lapse imaging incubation system

Variable	Mean ± SD
Semen analysis	
Male age (years)	41.3 ± 6.8
Ejaculatory abstinence length (days)	3.2 ± 2.5

FERTILITY

RESULTS

First International Journal of Andrology
aNDROLOGIa
Early and late paternal contribution to cell division of embryos in a time-lapse imaging incubation system



FERTILITY

Received: 14 February 2022 | Revised: 20 April 2022 | Accepted: 9 May 2022

DOI: 10.1111/and.14485

ORIGINAL ARTICLE

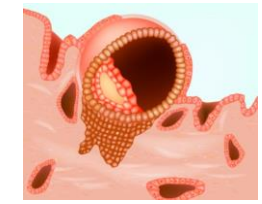
First International Journal of Andrology
ANDROLOGIA
WILEY

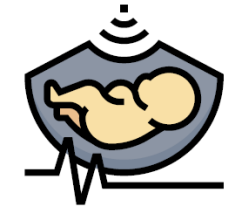
Paternal ageing impacts blastulation and the outcomes of pregnancy at different levels of maternal age: A clustering analysis of 21,960 oocytes and 3837 ICSI cycles

Amanda Souza Setti[1,2] | Daniela Paes de Almeida Ferreira Braga[1,2] | Patricia Guilherme[1] | Livia Vingris[1] | Assumpto Iaconelli Jr[1,2] | Edson Borges Jr[1,2]

FERTILITY

Variable	Value (n=3837)
Female age (y-old)	35.3 ± 4.5
Female BMI	24.2 ± 3.9
Male age (y-old)	38.0 ± 6.4

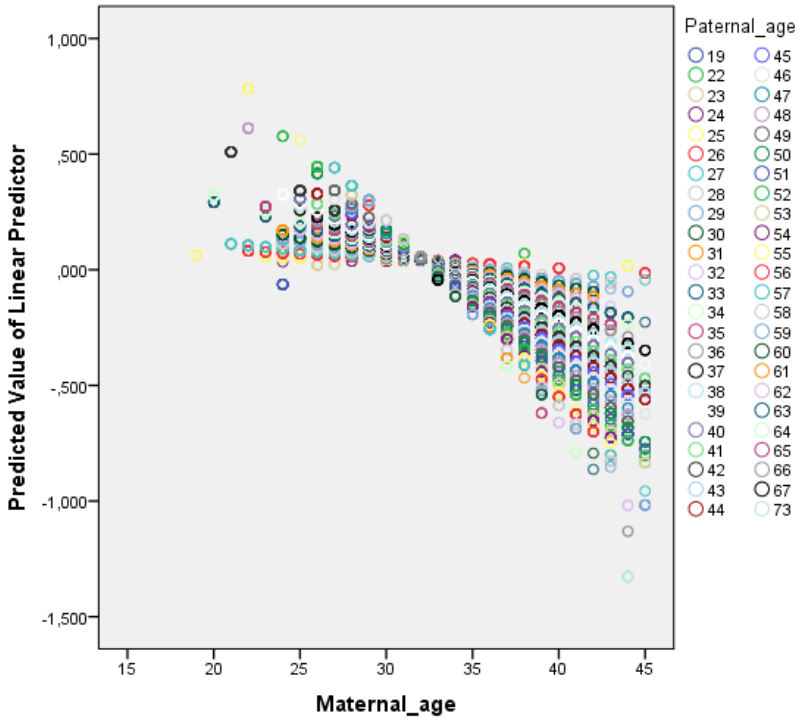




FERTILITY

Andrologia. 2022;e14485.
https://doi.org/10.1111/and.14485

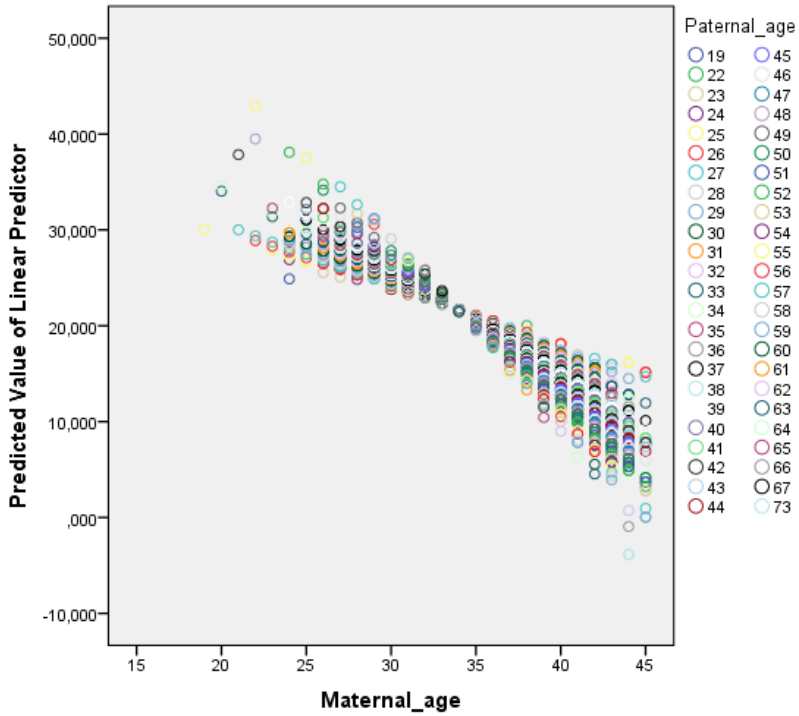
Dependent variable	B	OR	CI	p-value
Blastocyst development	- 0.005	0.995	0.994 – 0.996	< 0.001



FERTILITY

Andrologia. 2022;e14485.
https://doi.org/10.1111/and.14485

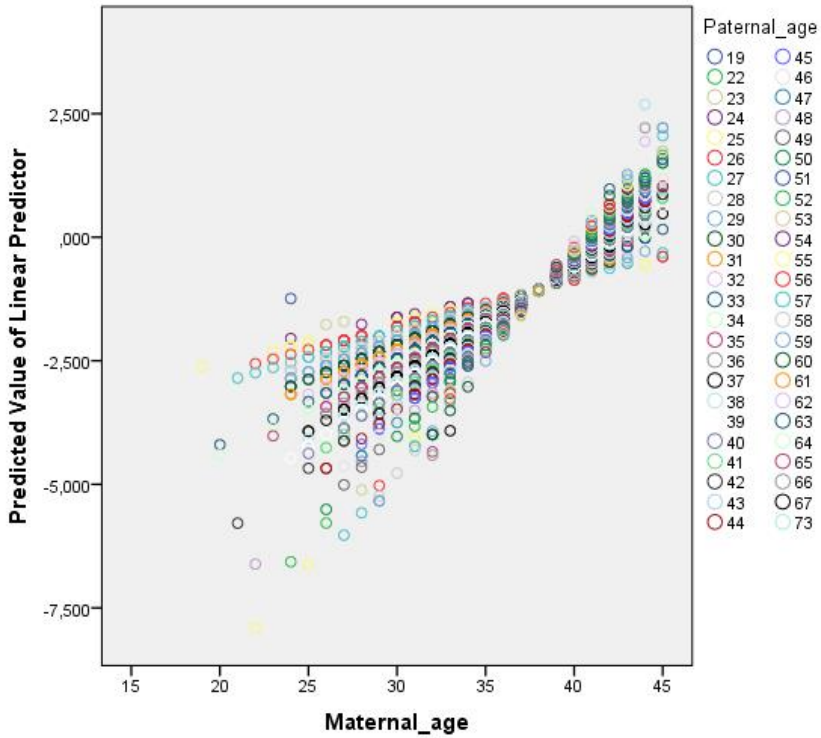
Dependent variable	B	OR	CI	p-value
Implantation rate	- 0.041	0.960	0.947 – 0.973	< 0.001



FERTILITY

Andrologia. 2022;e14485.
https://doi.org/10.1111/and.14485

Dependent variable	B	OR	CI	p-value
Miscarriage rate	0.011	1.012	1.005 – 1.018	0.001



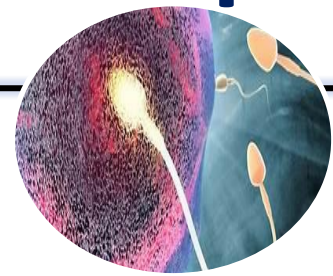
FERTILITY

Andrologia. 2022;e14485.
https://doi.org/10.1111/and.14485

For every ***1-year increase in paternal age***, the odds ratio of live-birth reduces by:

- **1%** in females aged 37 years,
- **1.6%** in those aged 38 years,
- **2.4%** in 39-year-old females,
- **5%** in 42-year-old females and so on.

✘ Misleading concept



FERTILITY

Andrologia. 2022;e14485.
https://doi.org/10.1111/and.14485

Effect of paternal age on outcomes in assisted reproductive technology cycles: systematic review and meta-analysis

Guy Morris, M.B.Ch.B. (Honours), M.R.C.O.G.,[a,b] Dimitrios Mavrelos, M.D., M.R.C.O.G.,[a,b] Efstathios Theodorou, M.R.C.O.G.,[a] Mia Campbell-Forde, B.Sc., M.Sc.,[a] David Cansfield, B.Sc. (Hons), M.Res.,[a] Ephia Yasmin, M.D., M.R.C.O.G.,[a,b] Philippa Sangster, M.Sc., F.R.C.S. (Urol),[a,b] Wael Saab, M.D., M.R.C.O.G.,[a] Paul Serhal, F.R.C.O.G.,[a] and Srividya Seshadri, M.D., M.Sc., M.R.C.O.G.[a]

[a] Centre for Reproductive and Genetic Health, London, United Kingdom; and [b] Reproductive Medicine Unit, University College London Hospitals National Health Service Foundation Trust, London, United Kingdom

Fertil Steril Rev 2020;1:16–34. 2020

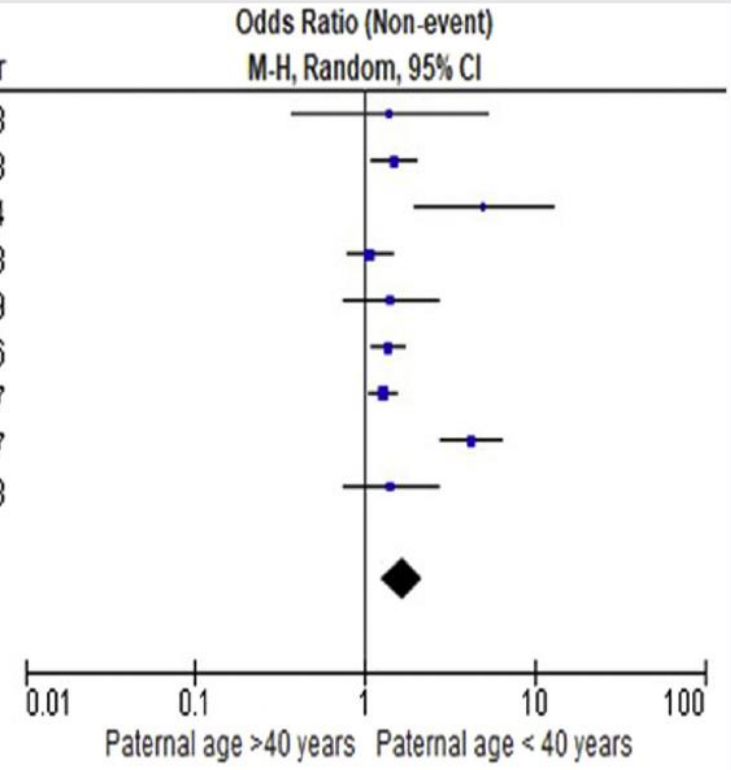
- Live birth rate was reported in three autologous oocyte studies (2,926 cycles) and five donor oocyte studies (7,648 cycles).

FERTILITY

Study or Subgroup	Paternal Age > 40 Events	Total	Paternal age <40 Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI	Year
Spandofer 1998	4	9	205	389	3.6%	1.39 [0.37, 5.26]	1998
Kumtepe 2003	90	241	317	678	14.3%	1.47 [1.09, 1.99]	2003
Klonoff-Cohen 2004	6	46	47	110	5.9%	4.97 [1.95, 12.70]	2004
Bellver 2008	99	193	577	1093	14.3%	1.06 [0.78, 1.44]	2008
Nijs 2009	18	47	108	231	9.1%	1.41 [0.74, 2.69]	2009
Wu 2016	135	324	1139	2303	15.3%	1.37 [1.08, 1.73]	2016
Chapuis 2017	230	678	720	1813	16.0%	1.28 [1.07, 1.54]	2017
McPherson 2017	25	227	804	2344	12.4%	4.22 [2.76, 6.45]	2017
Kaarouch 2018	18	47	108	231	9.1%	1.41 [0.74, 2.69]	2018
Total (95% CI)		**1812**		**9192**	**100.0%**	**1.65 [1.24, 2.19]**	
Total events	625		4025				

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 37.37$, $df = 8$ ($P < 0.00001$); $I^2 = 79\%$

Test for overall effect: $Z = 3.47$ ($P = 0.0005$)



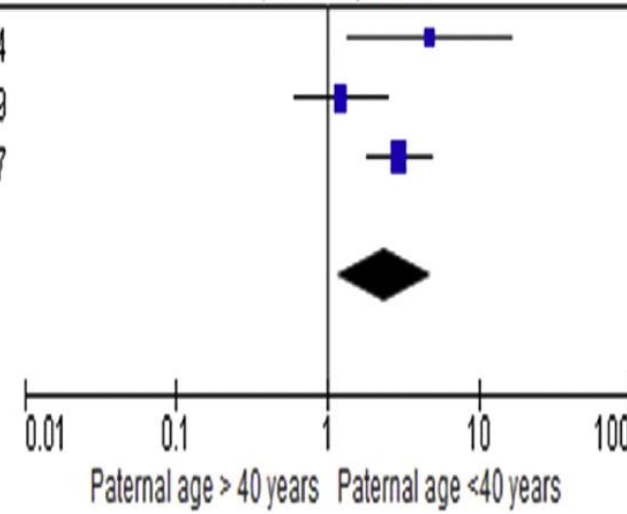
Effect of paternal age on clinical pregnancy rate (CPR). Autologous oocytes. CI = confidence interval; M-H = Mantel-Haenszel.

Morris. Paternal age and ART: is there an effect? Fertil Steril Rev 2020.

Study or Subgroup	Paternal Age > 40 Events	Total	Paternal age < 40 Events	Total	Weight	Odds Ratio (Non-event) M-H, Random, 95% CI	Year
Klonoff-Cohen 2004	3	44	27	105	20.6%	4.73 [1.35, 16.53]	2004
Nijs 2009	12	47	68	231	35.7%	1.22 [0.60, 2.49]	2009
McPherson 2017	18	155	653	2344	43.6%	2.94 [1.78, 4.84]	2017
Total (95% CI)		**246**		**2680**	**100.0%**	**2.37 [1.15, 4.85]**	
Total events	33		748				

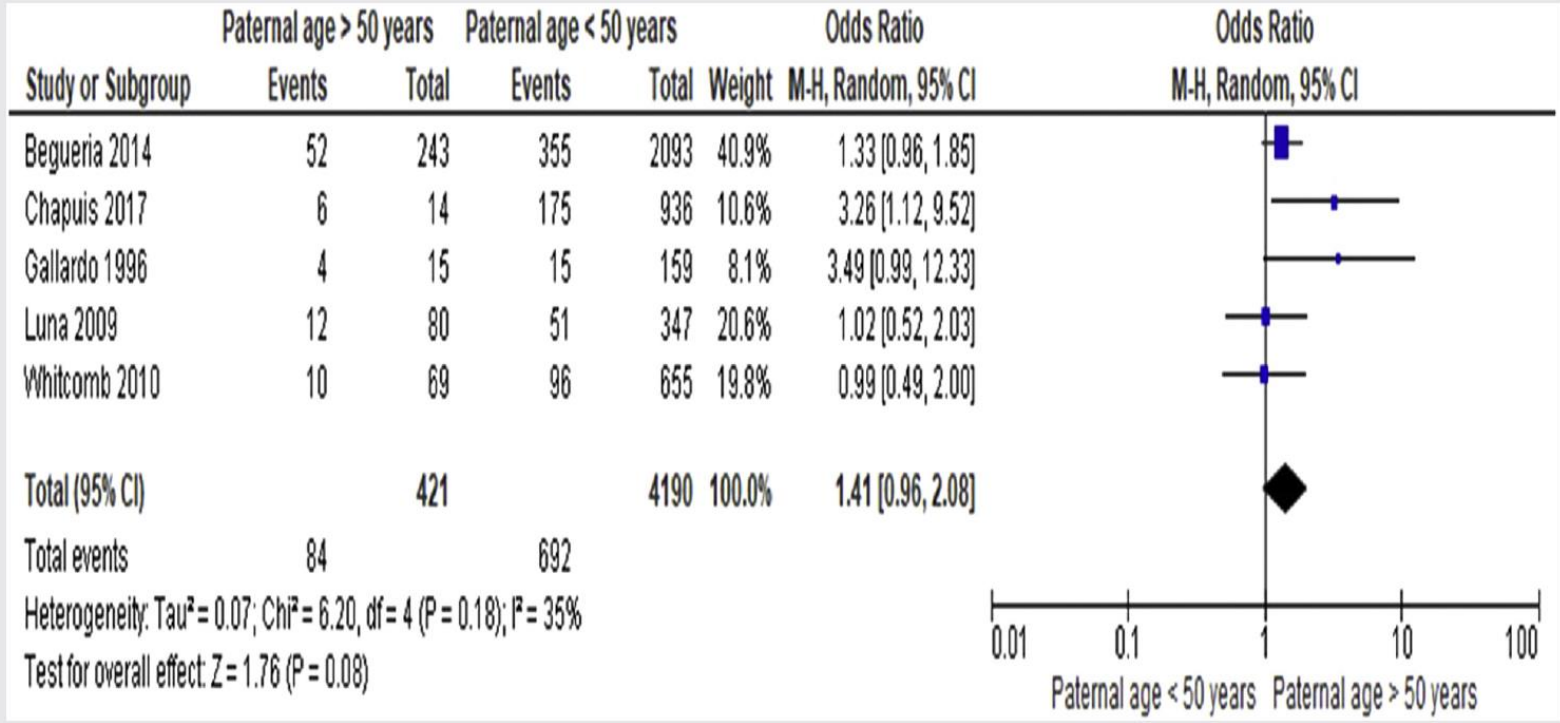
Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 5.30$, $df = 2$ ($P = 0.07$); $I^2 = 62\%$

Test for overall effect: $Z = 2.35$ ($P = 0.02$)



Effect of paternal age on live birth rate (LBR). Autologous oocytes. CI = confidence interval; M-H = Mantel-Haenszel.

Morris. Paternal age and ART: is there an effect? Fertil Steril Rev 2020.



Effect of paternal age >50 years on miscarriage rate (MR). Donor oocytes. CI = confidence interval; M-H = Mantel-Haenszel.

Morris. Paternal age and ART: is there an effect? Fertil Steril Rev 2020.

- 1188 ciclos ICSI
- mulheres de até 35 anos
- boa reserva ovariana e sem fator uterino
- concentração espermática > 1 milhão/ml

Tabela 2. Taxas de nascidos vivos e valor de p da comparação entre os grupos

Grupos	Taxa de nascidos vivos	p
<35	55,71%	
36-40	50,92%	0.41
41-45	59,78%	0.69
46-50	50,00%	0.72
>51	52,94%	0.90

Received: 6 September 2019 | Revised: 19 November 2019 | Accepted: 19 November 2019

DOI: 10.1111/andr.12737

ORIGINAL ARTICLE

ANDROLOGY WILEY

Increasing paternal age and ejaculatory abstinence length negatively influence the intracytoplasmic sperm injection outcomes from egg-sharing donation cycles

Amanda S. Setti[1,2] | Daniela Paes Almeida Ferreira Braga[1,2] |
Assumpto Iaconelli Junior[1,2] | Edson Borges Junior[1,2]

Paternal variable	Fertilization (%)	D3 high-quality embryos (%)	D3 normal embryo development (%)	Blastocyst development (%)	High-quality blastocysts (%)	Implantation (%)	Pregnancy chance	Miscarriage chance	Live birth chance
Age									
B	−0.276	−0.040	−2.750	−0.070	−44.058	−0.060	Exp(B) 0.664	Exp(B) 1.019	Exp(B) 0.812
SE	0.085	0.017	0.8625	0.035	20.248	0.007	0.187	0.052	0.100
CI	−0.44 to −0.11	−0.07 to −0.01	−4.44 to −1.06	−0.14 to −0.002	−84.07 to −4.05	−0.08 to −0.05	0.457 to 0.967	0.918 to 1.131	0.665 to 0.991
P	.001	.021	.001	.043	.031	<.001	.033	.718	.041
EA									
B	−0.083	−0.003	−0.300	−0.589	13.8125	−0.012	Exp(B) 0.051	Exp(B) 0.861	Exp(B) 0.169
SE	0.847	0.015	0.014	0.243	88.143	0.003	1.803	0.190	1.195
CI	−0.44 to −0.11	−0.01 to −0.001	−0.06 to −0.02	−1.07 to −0.11	−160.34 to 187.97	−0.20 to −0.35	0.001 to 1.870	0.589 to 1.258	0.015 to 1.851
P	.765	.028	.036	.016	.876	<.001	.103	.435	.142

FERTILITY

Is increasing paternal age negatively associated with donor oocyte recipient success? A paired analysis using sibling oocytes

Kelly McCarter, M.D.,[a] Robert Setton, M.D.,[b] Alice Chung, B.A.,[b] Anjile An, M.P.H.,[c] Zev Rosenwaks, M.D.,[b] and Steven Spandorfer, M.D.[b]

Fertil Steril 2021;116:373–9. 2021

Supplemental Table 1. Odds ratio and 95% confidence interval for pregnancy

	OR	95% CI	p-value
Partner Age Group			
< 45	—	—	
>= 45	0.35	0.13, 0.95	**0.04**
Parous			
Yes	—	—	
No	4.59	1.47, 14.4	**0.009**
Sperm			
Fresh	—	—	
Frozen	10.4	0.43, 251	0.15

Influence of paternal age on assisted reproductive technology cycles and perinatal outcomes

Audrey M. Marsidi, M.D.,[a] Lauren M. Kipling, M.P.H.,[b] Jennifer F. Kawwass, M.D.,[a] and Akanksha Mehta, M.D.[c]

[a] Division of Reproductive Endocrinology and Infertility, Department of Gynecology and Obstetrics, Emory Reproductive Center, Atlanta, Georgia; [b] Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, Georgia; and [c] Department of Urology, Emory University School of Medicine, Atlanta, Georgia

Fertil Steril 2021;116:380-7

- 77,209 fresh nondonor cycles
- Compared with paternal age ≤ 45 years, paternal age ≥ 46 years was associated with:
  - **a lower likelihood of pregnancy per cycle** (adjusted risk ratio [aRR] 0.81; 95% confidence interval [CI] 0.76–0.87) and per transfer (aRR 0.85; 95% CI 0.81–0.90);
  - **a lower likelihood of live birth per cycle** (aRR 0.76; 95% CI 0.72–0.84) **and per transfer** (aRR 0.82; 95% CI 0.77–0.88),
    (after controlling for maternal age and other confounders).

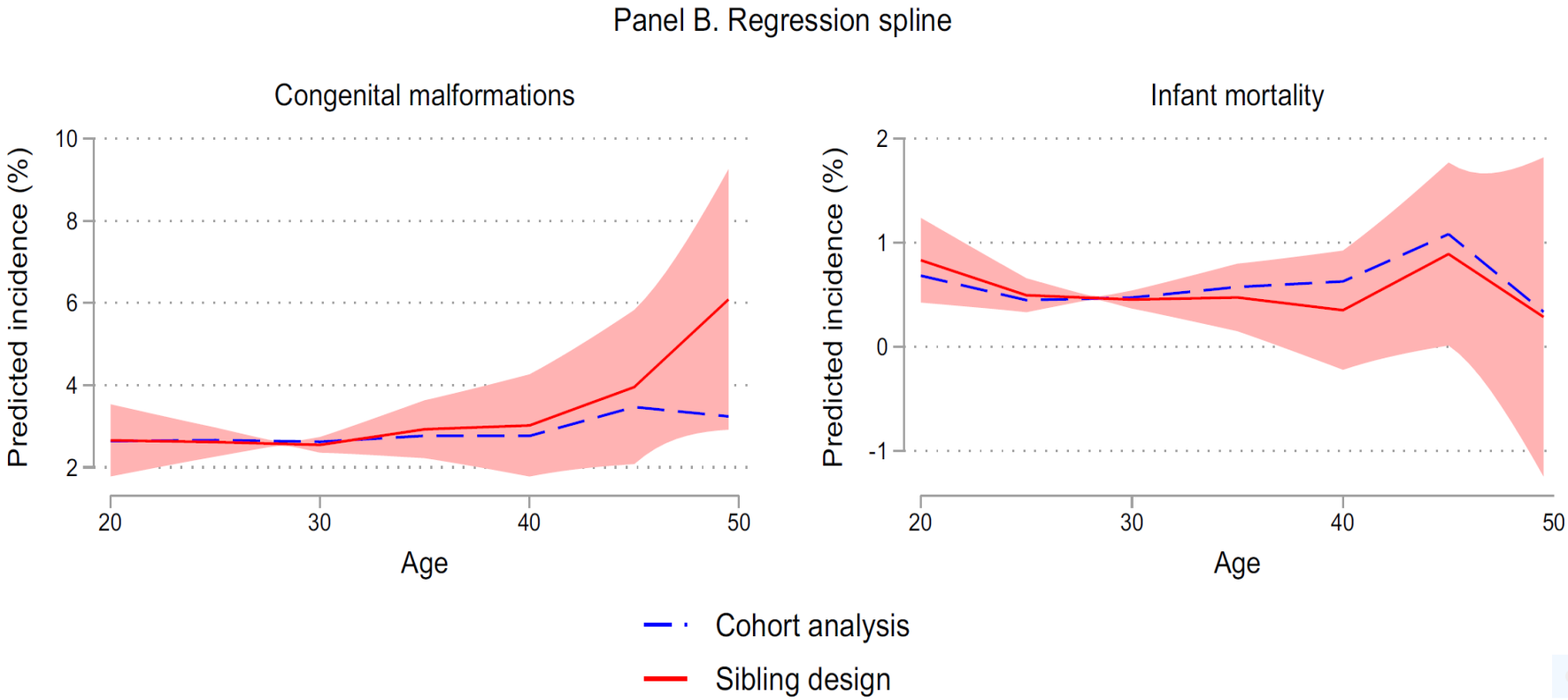
FERTILITY

European Journal of Epidemiology (2021) 36:849–860
https://doi.org/10.1007/s10654-021-00734-8

REPRODUCTIVE EPIDEMIOLOGY

Parental age and birth defects: a sibling study

Hans K. Hvide[1,2,3] · Julian Johnsen[4] · Kjell G. Salvanes[2,5,6,7,8]



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REPRODUCTIVE EPIDEMIOLOGY

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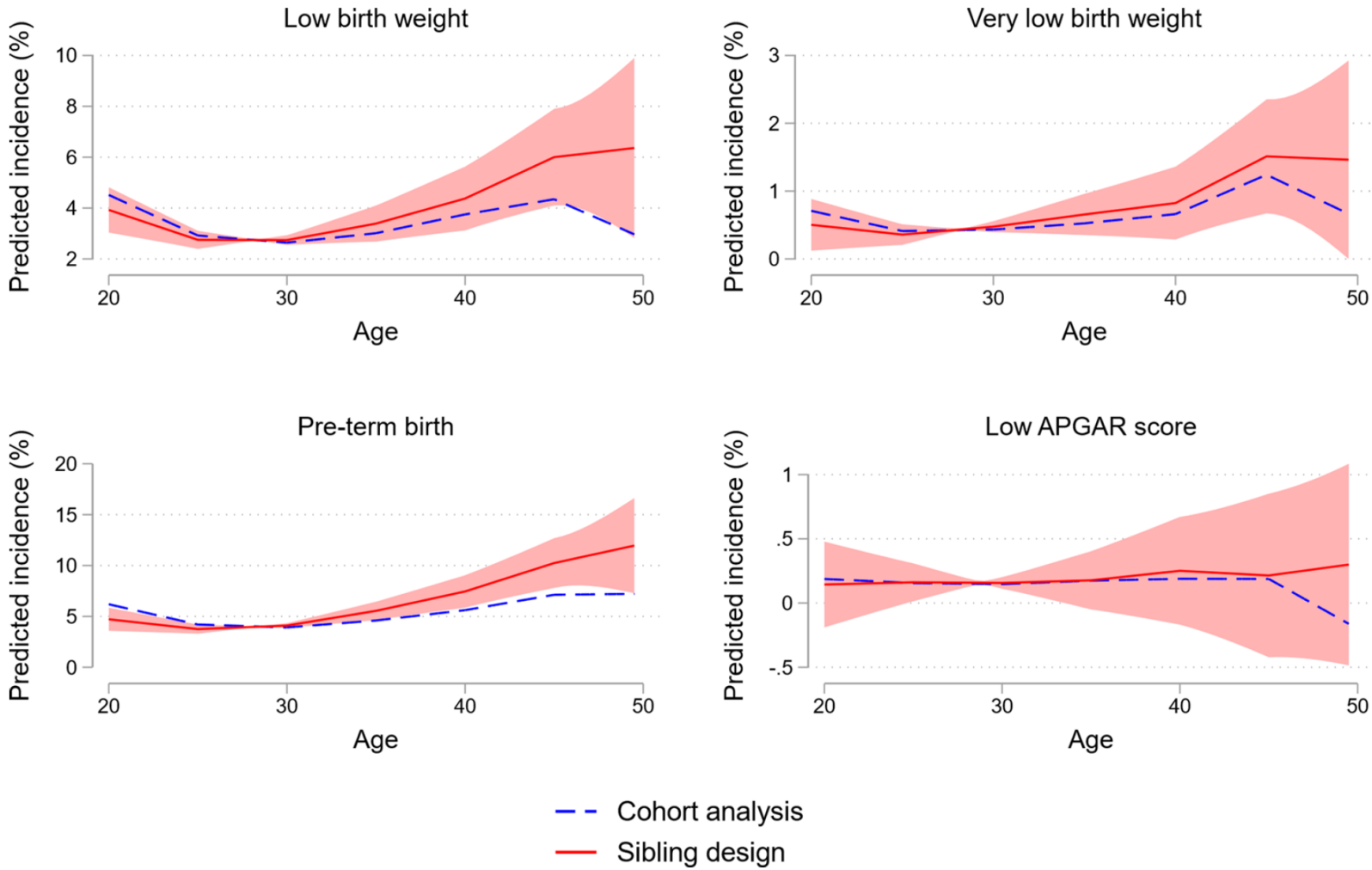

Human Reproduction Update, Vol.16, No.1 pp. 65–79, 2010
Advanced Access publication on August 20, 2009 doi:10.1093/humupd/dmp027

human reproduction update

Paternal age and reproduction

Gideon A. Sartorius[1,2] and Eberhard Nieschlag[1,3]

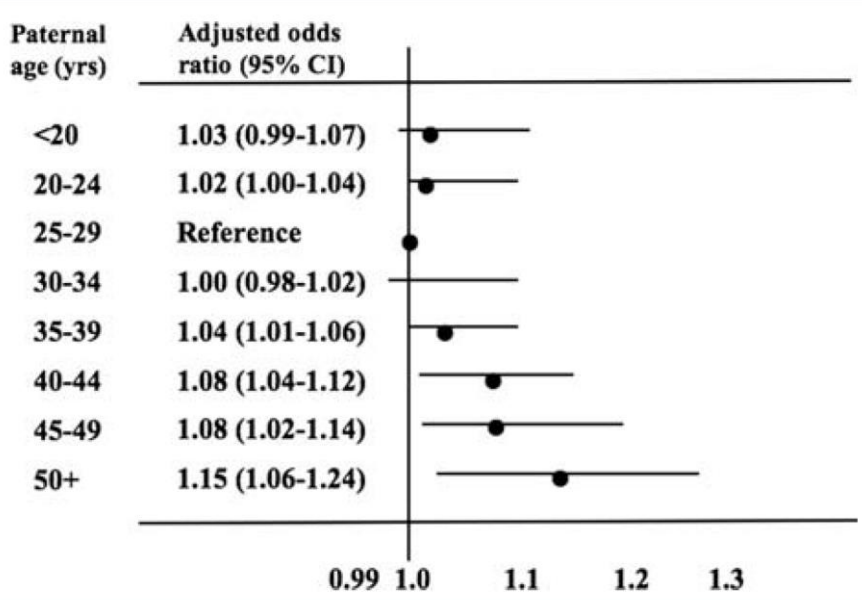

Figure 4 Relative risk of birth defects depending on paternal age.

Retrospective analysis of 5 213 248 subjects in the USA. Increased risk for heart defects, circulatory/respiratory defects, diaphragmatic hernia, tracheo-oesophageal fistulas, musculo-sceletal anomalies (data extracted from Yang *et al.*, 2007).

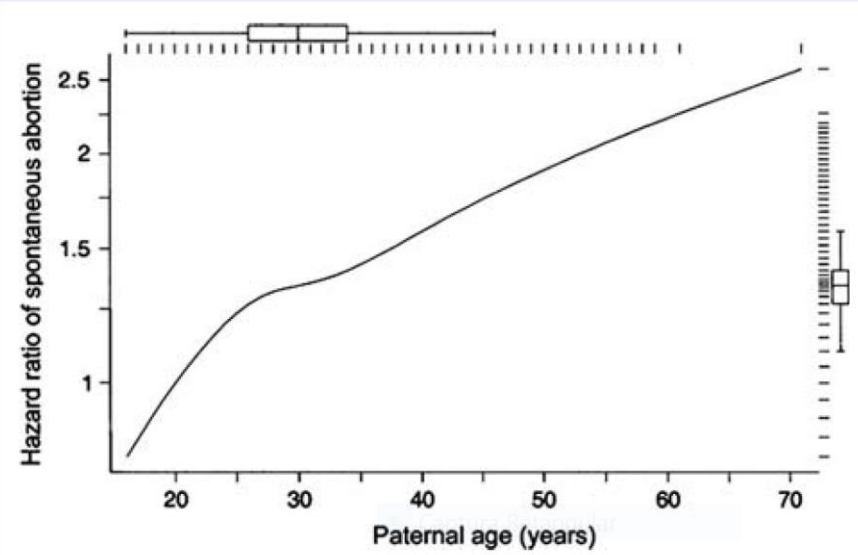

Figure 3 Hazard ratios of spontaneous miscarriages between 6 and 20 weeks according to paternal age adjusted for different confounders including maternal age (using prospective data from 5121 Californian women, men aged 20 years as referent).

Boxplots along the top and right side indicate data distribution according to each axis (with permission from Slama *et al.*, 2005).

Human Reproduction Update, Vol.26, No.5, pp. 650–669, 2020
Advance Access Publication on May 2, 2020 doi:10.1093/humupd/dmaa010

human reproduction update

Advanced paternal age is associated with an increased risk of spontaneous miscarriage: a systematic review and meta-analysis

Nadia A. du Fossé[1,*], Marie-Louise P. van der Hoorn[1], Jan M.M. van Lith[1], Saskia le Cessie[2,3], and Eileen E.L.O. Lashley[1]

Pooled risk estimates for miscarriage for age categories 30–34, 35–39, 40–44 and ≥45 years of age were:

- 1.04 (95% CI 0.90,1.21),
- 1.15 (0.92, 1.43),
- 1.23 (1.06, 1.43),
- 1.43 (1.13, 1.81) respectively (reference category 25–29 years)

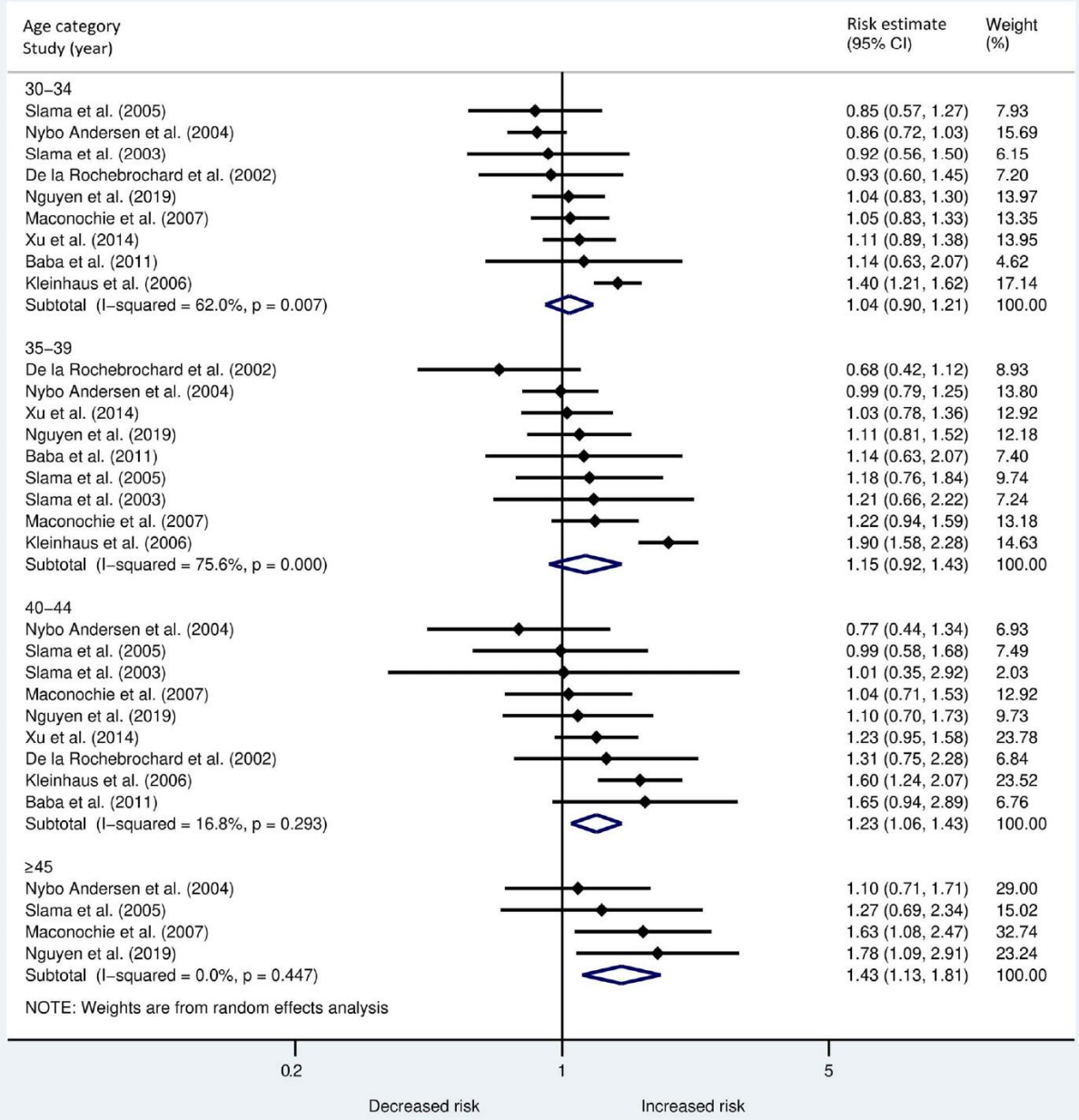

Figure 2 Forest plot describing the association between paternal age in different age categories and the risk of miscarriage <20 weeks.

FERTILITY

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 artigos, 238 incluídos, 81 para a meta-análise
- Idade, estilo de vida, peso, altura, gordura corporal, cigarro

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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.

FERTILITY

Is advanced paternal age a health risk for the offspring?

Anne-Marie Nybo Andersen, M.D., Ph.D. and Stine Kjaer Urhoj, M.Sc.
Department of Public Health, University of Copenhagen, Copenhagen, Denmark

Adverse health outcomes in offspring probably affected by advanced paternal age, their occurrence, and assessed evidence for the paternal age effect (strong/medium/weak).

Adverse health condition	Population-based prevalence/lifetime risk	Evidence for a paternal age effect
Fetal death[a]		
Miscarriage (early fetal death)	1,500/10,000 clinically recognized pregnancies	Weak
Stillbirth (late fetal death)	0.4/10,000 births	Medium
Congenital syndromes and anomalies[b]		
Achondroplasia	<1/10,000 births	Strong
Thanatophoric dysplasia	<1/10,000 births	Strong
Osteogenesis imperfecta	<1/10,000 births	Strong
Apert syndrome	<1/10,000 births	Strong
Pfeiffer's syndrome	<1/10,000 births	Strong
Crouzon's syndrome	<1/10,000 births	Strong
Marfan syndrome	2/10,000 births	Strong
Neurofibromatosis (NF-1)	3/10,000 births	Strong
Syndactyly	5/10.000 births	Medium
Cleft palate	15/10,000 births	Strong
Patent ductus arteriosus	5/10,000 births (term babies)	Medium-weak
Down syndrome	5/10.000 births[c]	Weak
Club foot	15/10.000 births	Weak
Other perinatal conditions[a]		
Preterm birth	700/10,000 births	Medium
Preeclampsia	300/10,000 births	Weak
Childhood cancers[a]		
Retinoblastoma	0.6/10,000 individuals	Medium
Acute lymphatic leukemia	12/10.000 individuals	Strong
Neurodevelopmental outcomes[d]		
Autism spectrum disorders	93/10,000 individuals	Strong
Schizophrenia/psychosis	367/10.000 individuals	Strong
Attention deficit-hyperactivity disorder	192/10,000 individuals	Weak
Bipolar disorder	184/10,000 individuals	Weak

[a] If the occurrences vary substantially between countries, we have given population-based occurrence measures from Denmark, 2000–2010.
[b] Prevalence according to www.orpha.net.
[c] Prevalence among births in a population with prenatal screening and termination of pregnancy on demand. The prevalence is approximately 130/10,000 in an unscreened population, depending on parental age distribution.
[d] Lifetime prevalence according to Pedersen et al. (68).

Nybo Andersen. Health in offspring of older fathers. Fertil Steril 2016.

Age-related alterations in the genetics and genomics of the male germ line

Amin S. Herati, M.D.,[a,b] Boryana H. Zhelyazkova, B.A.,[c] Peter R. Butler, B.A.,[a,b] and Dolores J. Lamb, Ph.D.[a,b,c]

Fertility and Sterility® Vol. 107, No. 2, February 2017

Offspring genetic conditions associated with advanced paternal age.

Condition	Paternal age (y)	Relative risk	Population risk	Adjusted risk
Achondroplasia	>50	7.8	1/15,000	1/1,923
Apert syndrome	>50	9.5	1/50,000	1/5,263
Pfeiffer syndrome	>50	6	1/100,000	1/16,666
Crouzon syndrome	>50	8	1/50,000	1/6,250
Neurofibromatosis I	>50	3.7	1/3,000–1/4,000	[illegible]
Retinoblastoma	>45	3	1/15,000–1/20,000	[illegible]
Down syndrome	40–44	1.37	1/1,200[a]	1/876[a]
Epilepsy	40–45	1.3	1/100	1/77.0
Breast cancer	>40	1.6	1/8.5	1/5.3
Childhood leukemia	>40	1.14	1/25,000	1/21,930
Childhood central nervous system tumor	>40	1.69	1/36,000	1/21,302

Note: Adapted with permission from Ramasamy et al. (10).
[a] Maternal age 20–29 years.

Herati. Paternal aging and the male germ line. Fertil Steril 2017.

[a] Maternal age 20–29 years.

FERTILITY

Old, older and too old: age limits for medically assisted fatherhood?

Andrea Mechanick Braverman, Ph.D.

Department of Obstetrics and Gynecology, Thomas Jefferson University, Philadelphia, Pennsylvania

Fertil Steril 2017;107:329–33

Child's age at time of father's death.

Father's age at child's birth (y)	Father's expected age of death at time of child's birth (y)	Child's expected age at time of father's death (y)	Probability of father's death by child's age 5 (%)	Probability of father's death by child's age 10 (%)	Probability of father's death by child's age 15 (%)	Probability of father's death by child's age 20 (%)
20	76	56	0.74	1.45	2.19	3.10
25	77	52	0.71	1.46	2.38	3.77
30	77	47	0.75	1.69	3.08	5.17
35	77	42	0.94	2.34	4.45	7.56
40	78	38	1.42	3.54	6.69	10.91
45	78	33	2.16	5.34	9.63	15.69
50	79	29	3.26	7.63	13.83	22.19
55	80	25	4.52	10.93	19.57	31.46
60	81	21	6.71	15.76	28.21	44.91
65	82	17	9.7	23.05	40.94	61.72
70	84	14	14.79	34.60	57.61	79.02
75	85	10	23.25	50.26	75.38	91.98

Note: Source: Zweifel 2015 (6).

Braverman. Age limits for fatherhood. Fertil Steril 2016.

FERTILITY

SCIENTIFIC REPORTS
nature research

OPEN

Associations of parental age with offspring all-cause and cause-specific adult mortality

David Carslake[1,2*], Per Tynelius[3], Gerard J. van den Berg[4] & George Davey Smith[1,2]

Swedish registry data to examine all-cause and cause specific adult mortality (293,470 deaths among 5,204,433 people, followed up to a maximum of 80 years old) in relation to parental age.

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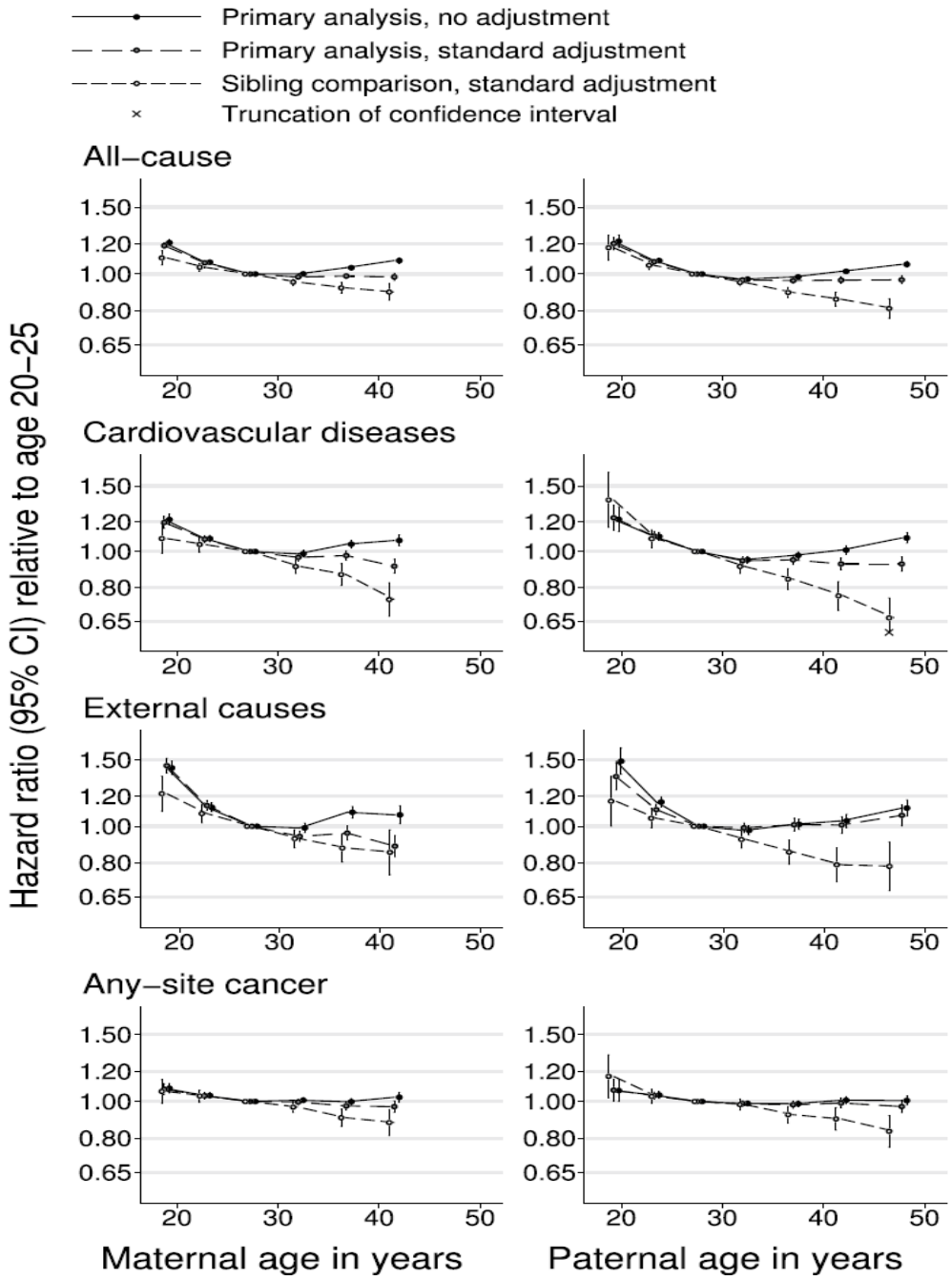

Para as causas mais comuns de morte, a sobrevivência adulta foi melhorada na prole de pais mais velhos!!

Idade paterna avançada:
Devemos nos preocupar?

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http://fertility.com.br/aulas -ministradas/

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Obrigado!

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