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The sperm as harbinger of overall male health

3rd INTERNATIONAL MEETING
"THE FUTURE OF A.R.T."

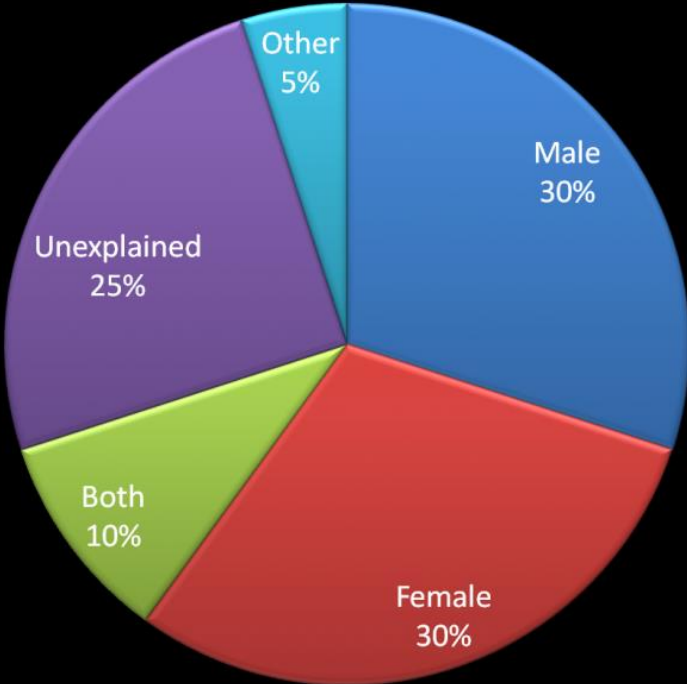
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13th March 2026

Disclosures

- Parts of my research has been funded by ReproUnion (www.reprounion.eu). ReproUnion has an unrestricted grant from Ferring Pharmaceuticals since 2015.

Infertility Causes



- Male
- Female
- Both
- Unexplained
- Other



Most fertility treatments are conducted by experts in female reproductive function

Today's ART paradigm

Male partner

- Ejaculate
- Testicular sperm (PESA/TESE/TESA)

Female partner

Investigations

- Hormone profile, AMH, antral follicle count
- Ultrasound monitoring
- Infection screen & general health

Controlled ovarian stimulation

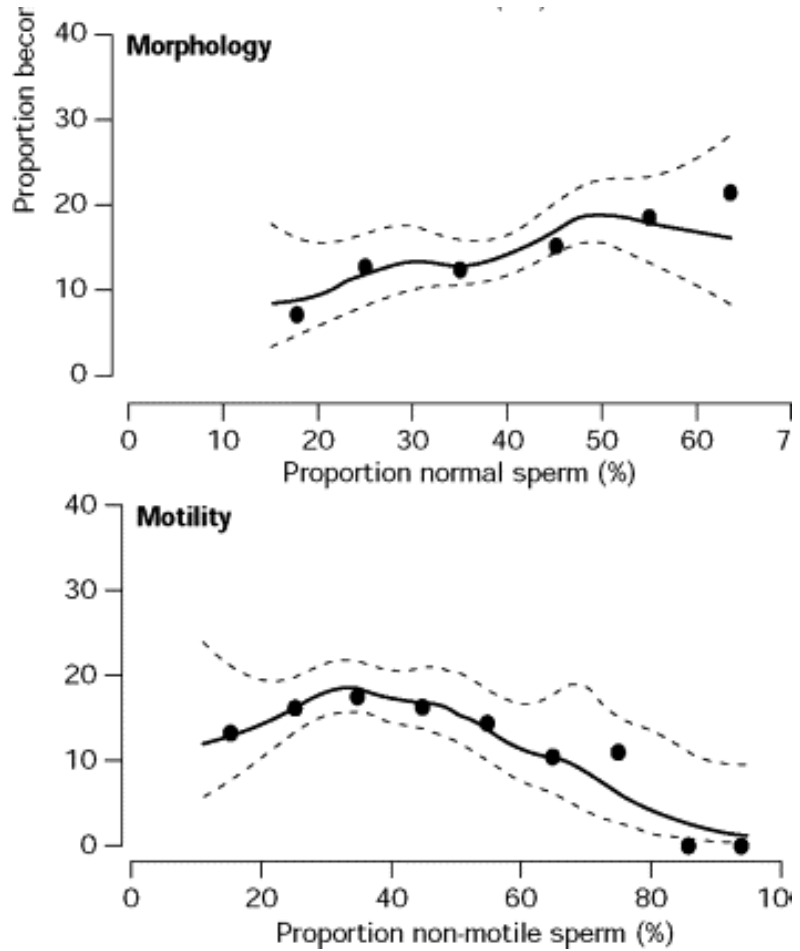
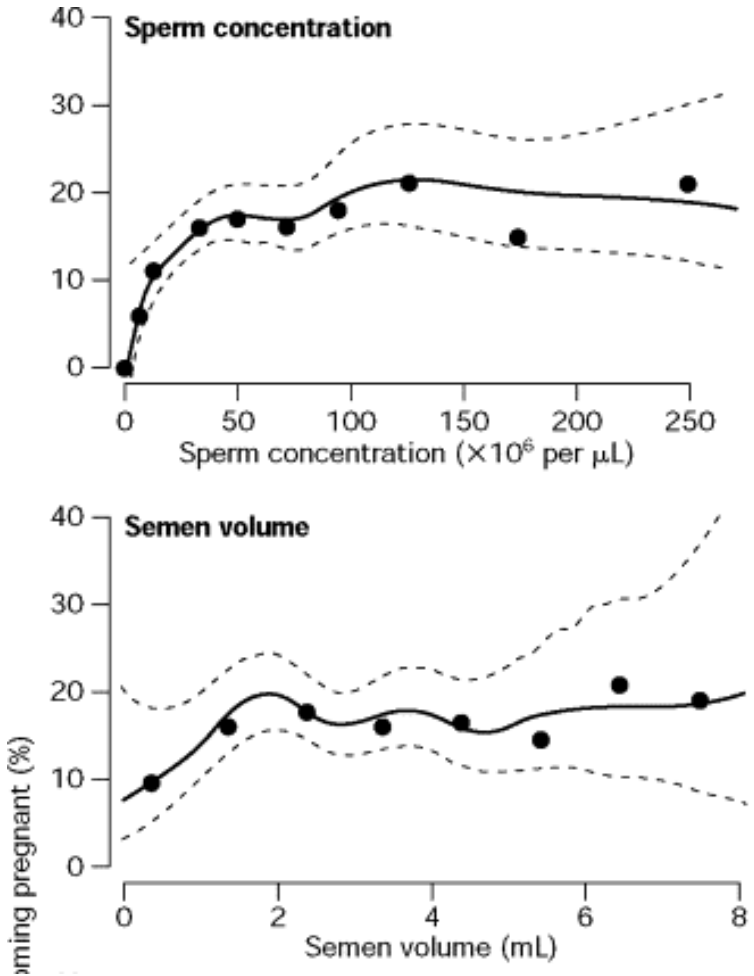
- Potent gonadotropins (FSH/hCG)
- GnRH analogues
- Frequent injections & monitoring

Oocyte retrieval (anesthesia)
Fertilization in lab (IVF/ICSI)

Potential maternal risks

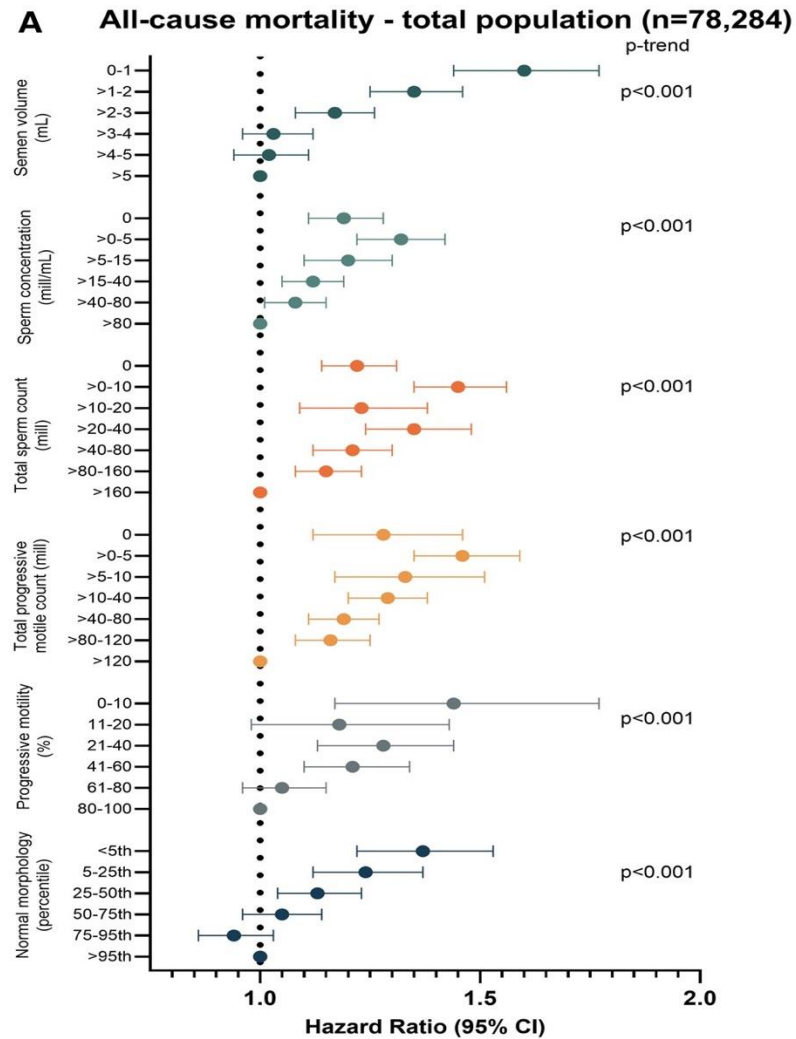
- OHSS, thromboembolism (rare with modern protocols but relevant)
- Discomfort, time off work, mental load

Standard semen parameters and chance of spontaneous pregnancy

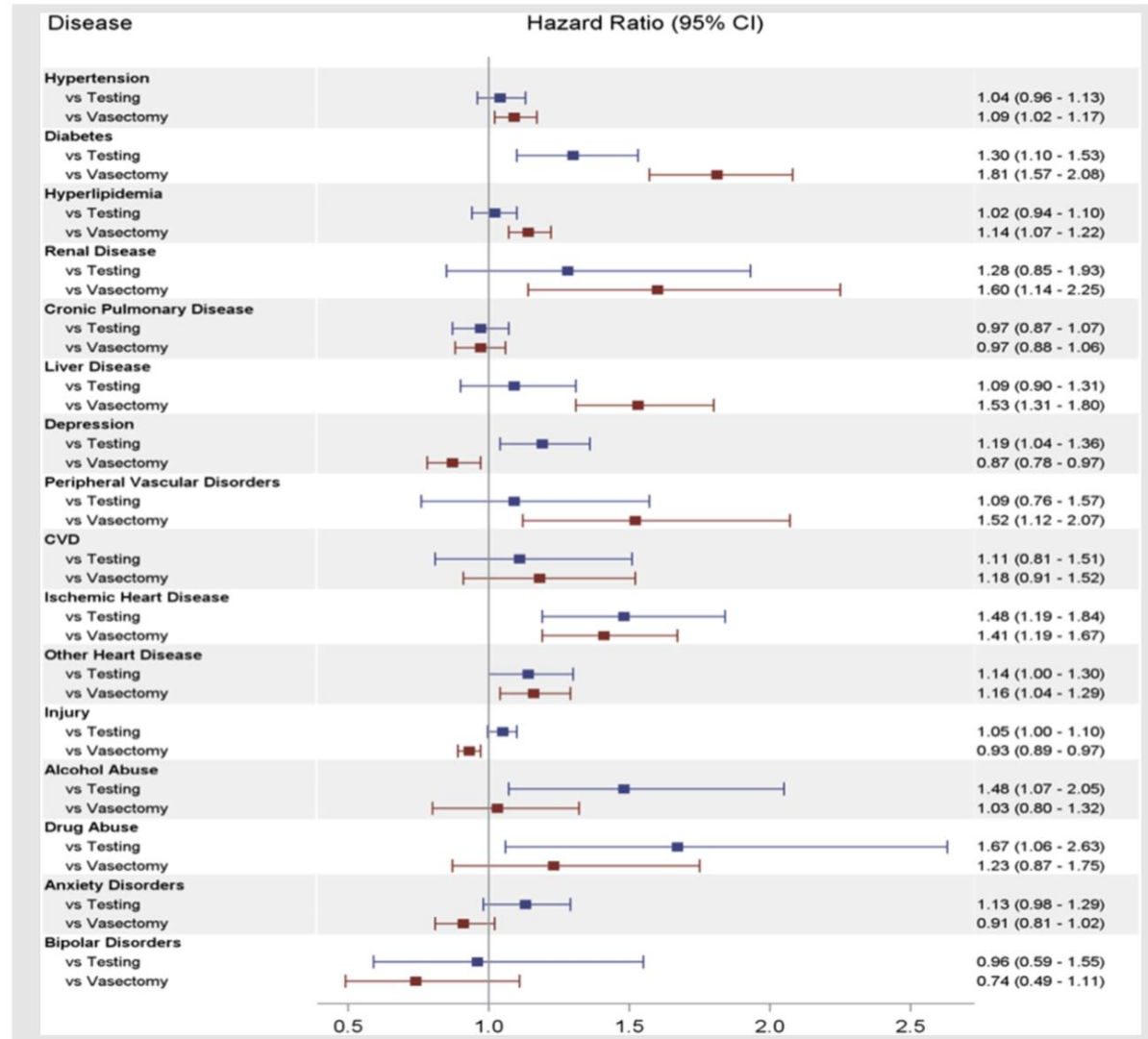


Bonde *et al.* Lancet 1998

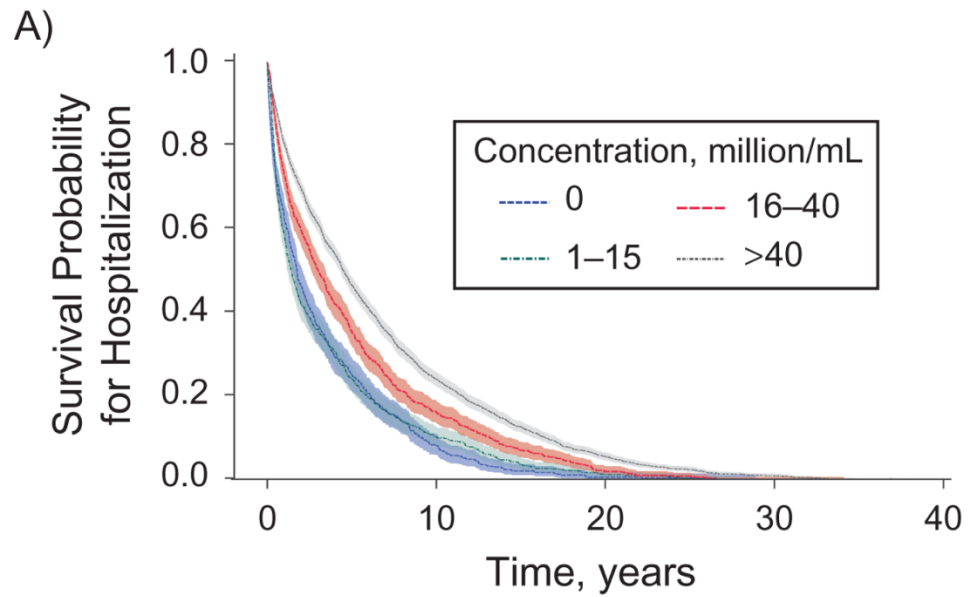
Semen quality vs. all-cause mortality



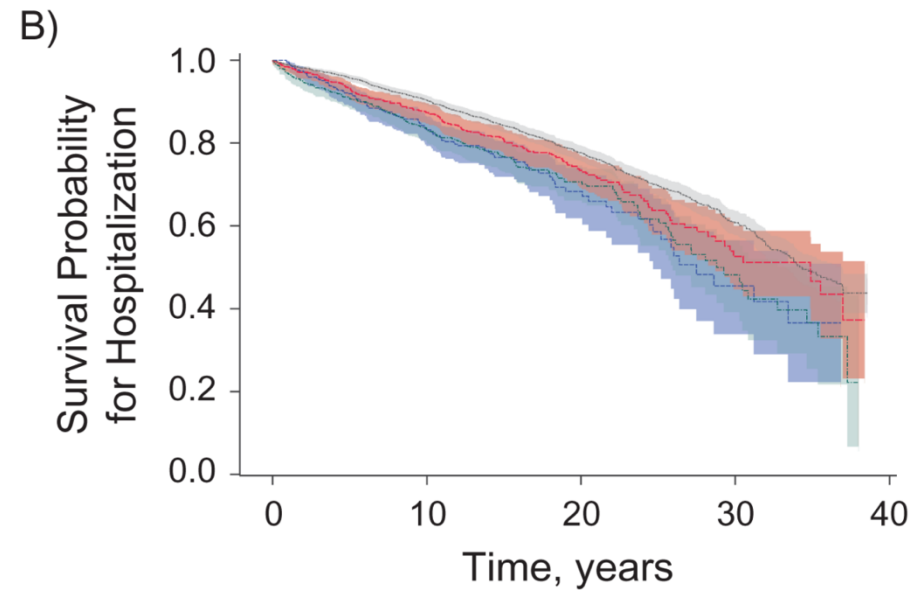
No specific infertility-related diseases



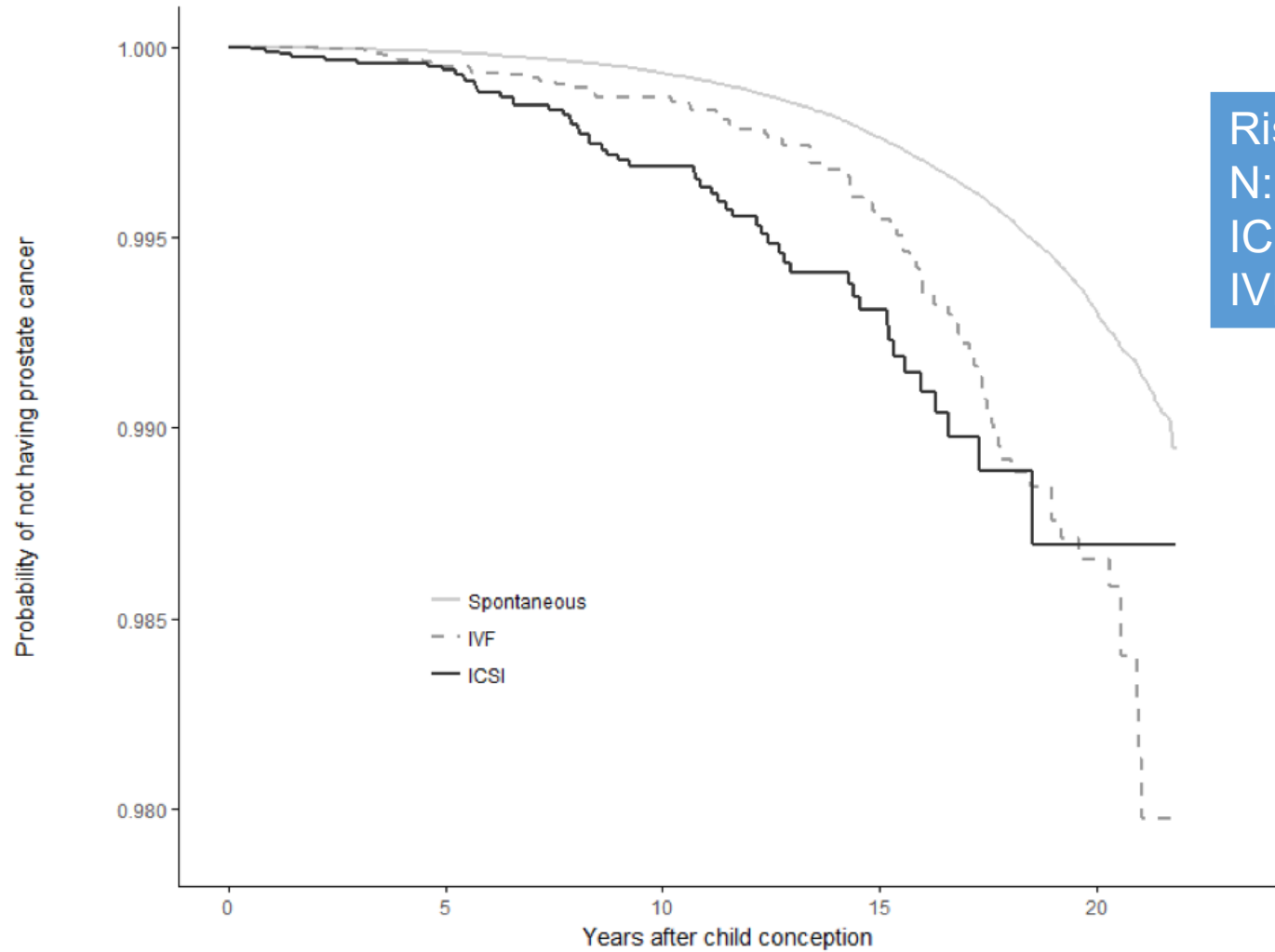
Cardiovascular disease



Diabetes

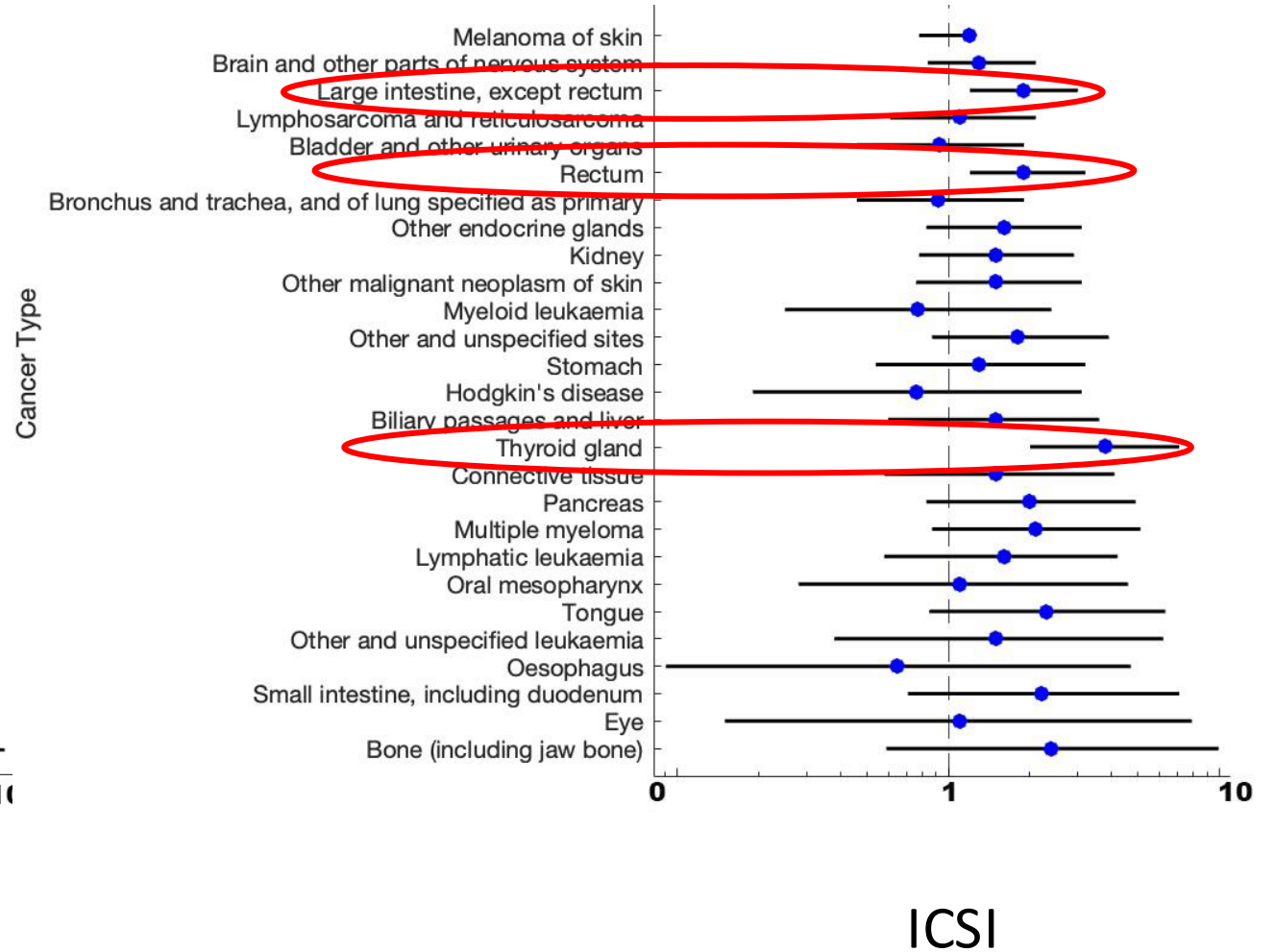
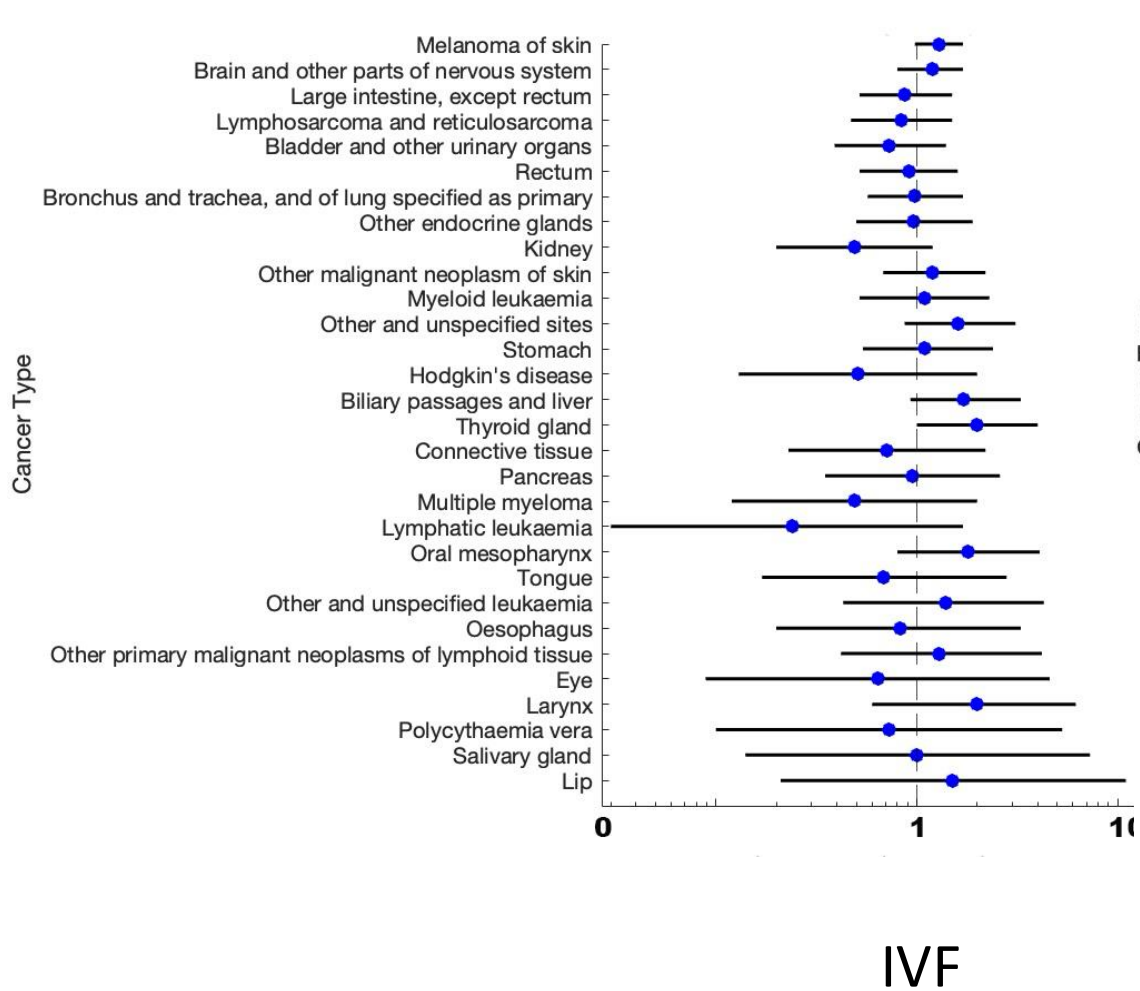


Cohort study on 4,712 men with long-term follow-up

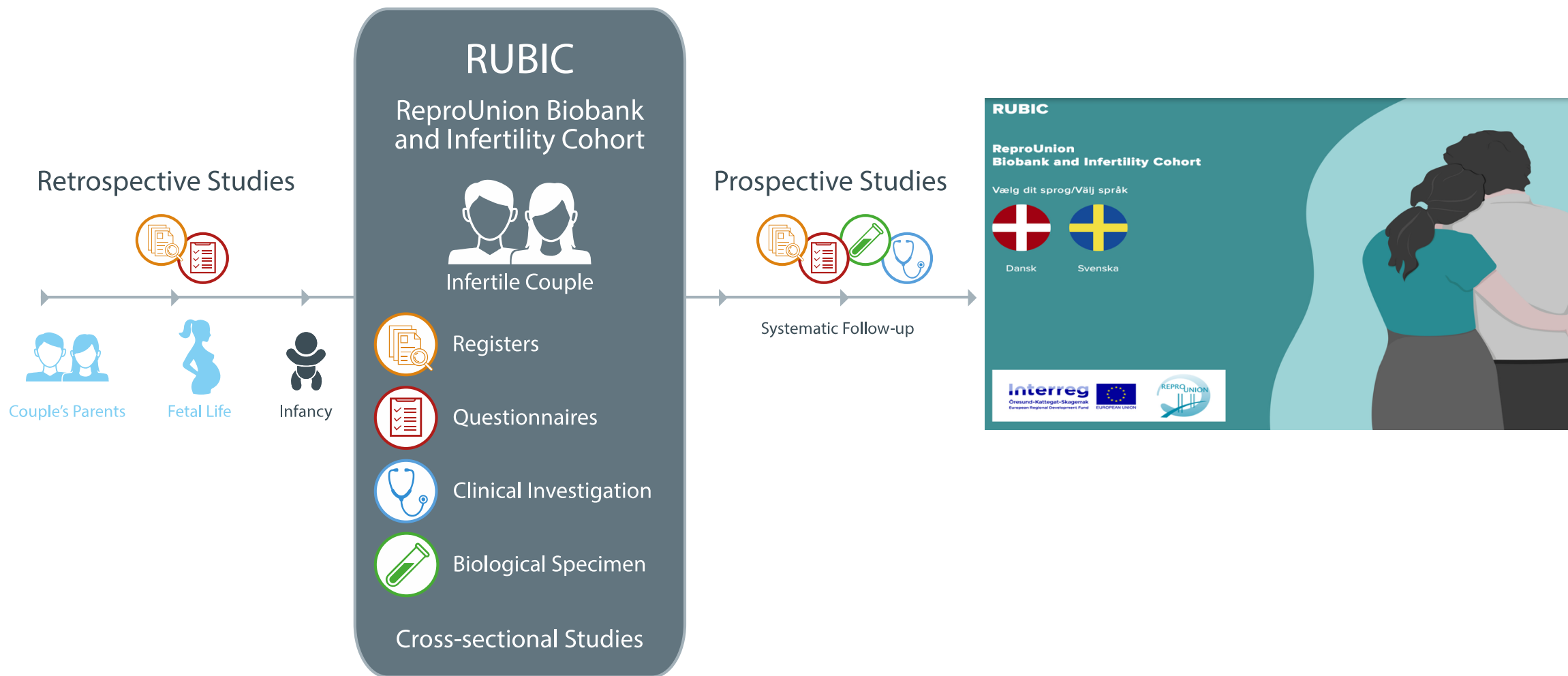


Risk of early onset PCa (<55 år EAU)
 N: 1 181 490 first time fathers
 ICSI: HR=1.86, 95% CI=1.25 - 2.77
 IVF: HR=1.51, 95% CI=1.09 - 2.08

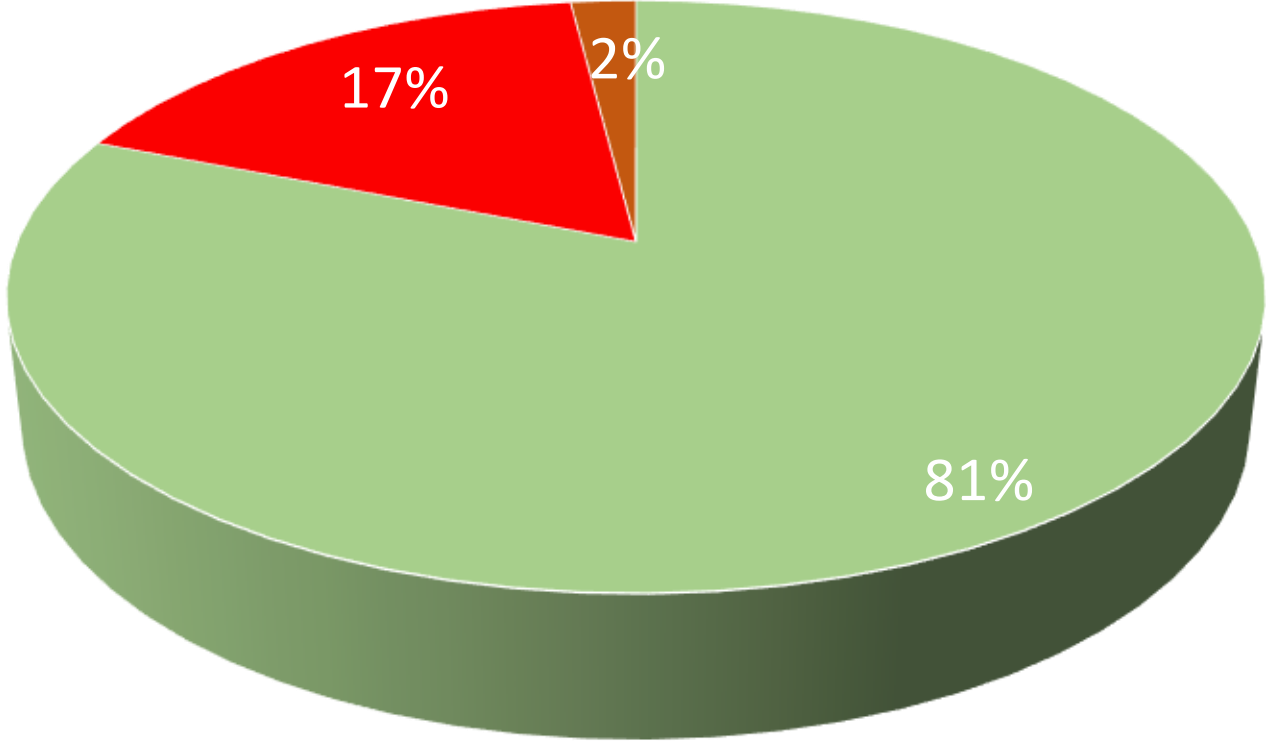
Risk of non-reproductive cancers



RUBIC – ReproUnion Biobank and Infertility Cohort



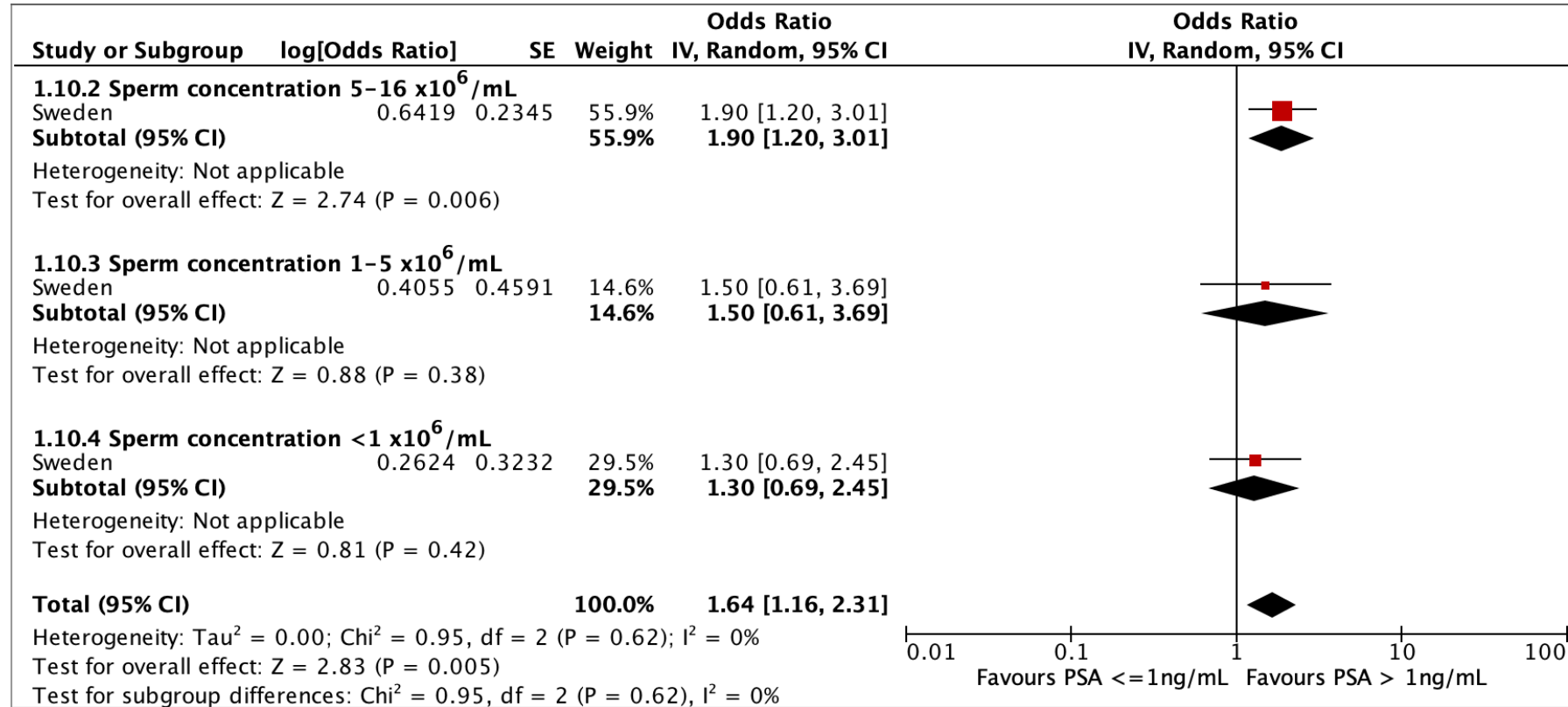
Risk of Metabolic Syndrome among men from infertile couples



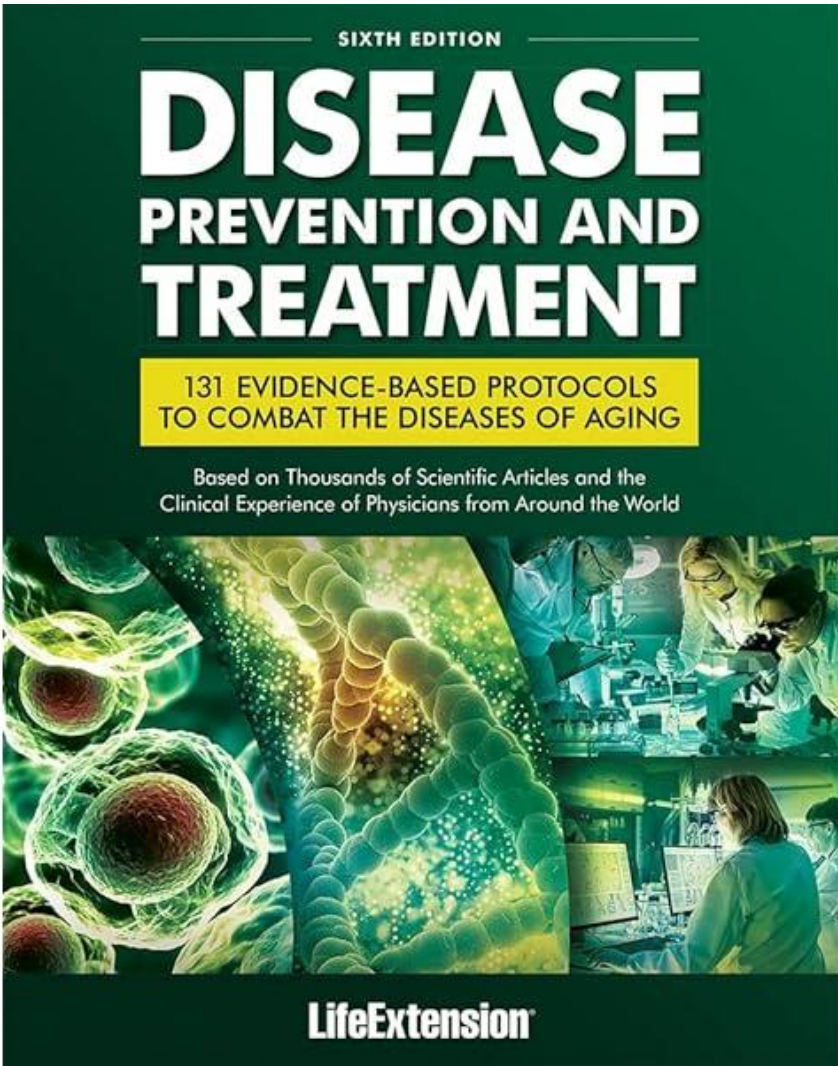
■ NO MetS ■ Undiagnosed MetS ■ Diagnosed MetS

Dahlberg *et al.* unpublished

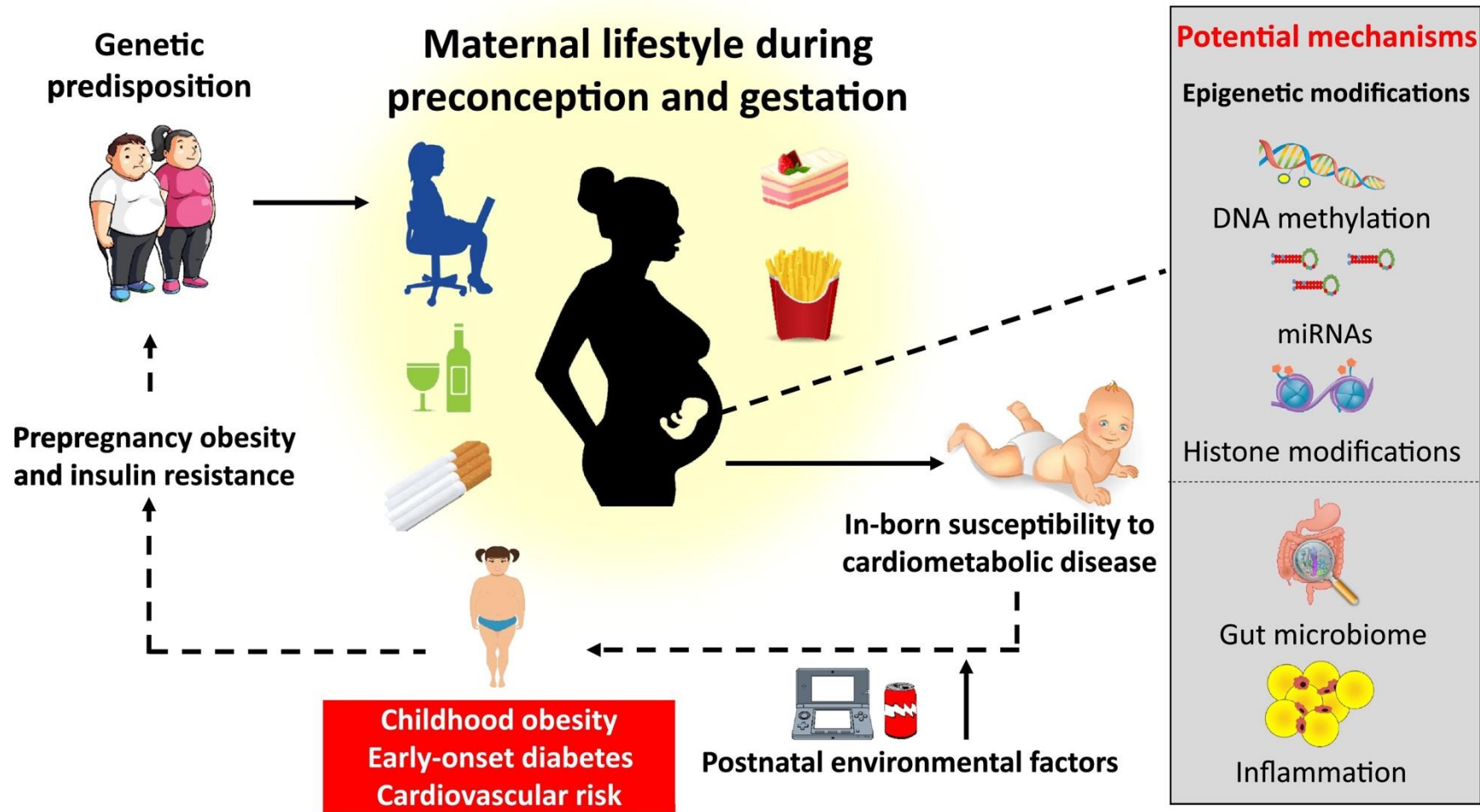
Risk of high PSA (>1 ng/mL)



Preconception health check of the male partner may help in identifying those being at high risk of developing life-threatening diseases



Routines for maternal preconception and antenatal health care



Paternal health plays a role not just for him



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Gynecology MFM

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Human Reproduction, Vol.36, No.3, pp. 785–793, 2021
Advance Access Publication on December 18, 2020 doi:10.1093/humrep/deaa332

human
reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

Original Research

Association of preconception paternal health and adverse maternal outcomes among healthy mothers

Gayathree Murugappan MD¹ , Shufeng Li MS³, Stephanie A. Leonard PhD², Virginia D. Winn MD, PhD², Maurice L. Druzin MD², Michael L. Eisenberg MD³

Show more

Association between preconception paternal health and pregnancy loss in the USA: an analysis of US claims data

Alex M. Kasman¹, Chiyuan A. Zhang¹, Shufeng Li¹, Ying Lu², Ruth B. Lathi³, David K. Stevenson³, Gary M. Shaw³, and Michael L. Eisenberg^{1,4,*}

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Original article

Association of preconception paternal health on perinatal outcomes: analysis of U.S. claims data

Alex M. Kasman M.D., M.S. ^a , Chiyuan A. Zhang M.P.H. ^a, Shufeng Li M.S. ^a, David K. Stevenson M.D. ^b, Gary M. Shaw Dr.P.H. ^b, Michael L. Eisenberg M.D. ^{a, c}

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Adverse outcomes associated with poor paternal health

Female

- Miscarriage
- Pre-eclampsia
- Gestational diabetes

Child

- Congenital malformations
- Low birth weight
- Cancer
- Impaired semen quality



Andrology: Volume 13, Issue 1
Special Issue: Periconceptional Paternal Exposures, Pregnancy Outcomes and Health of the Offspring

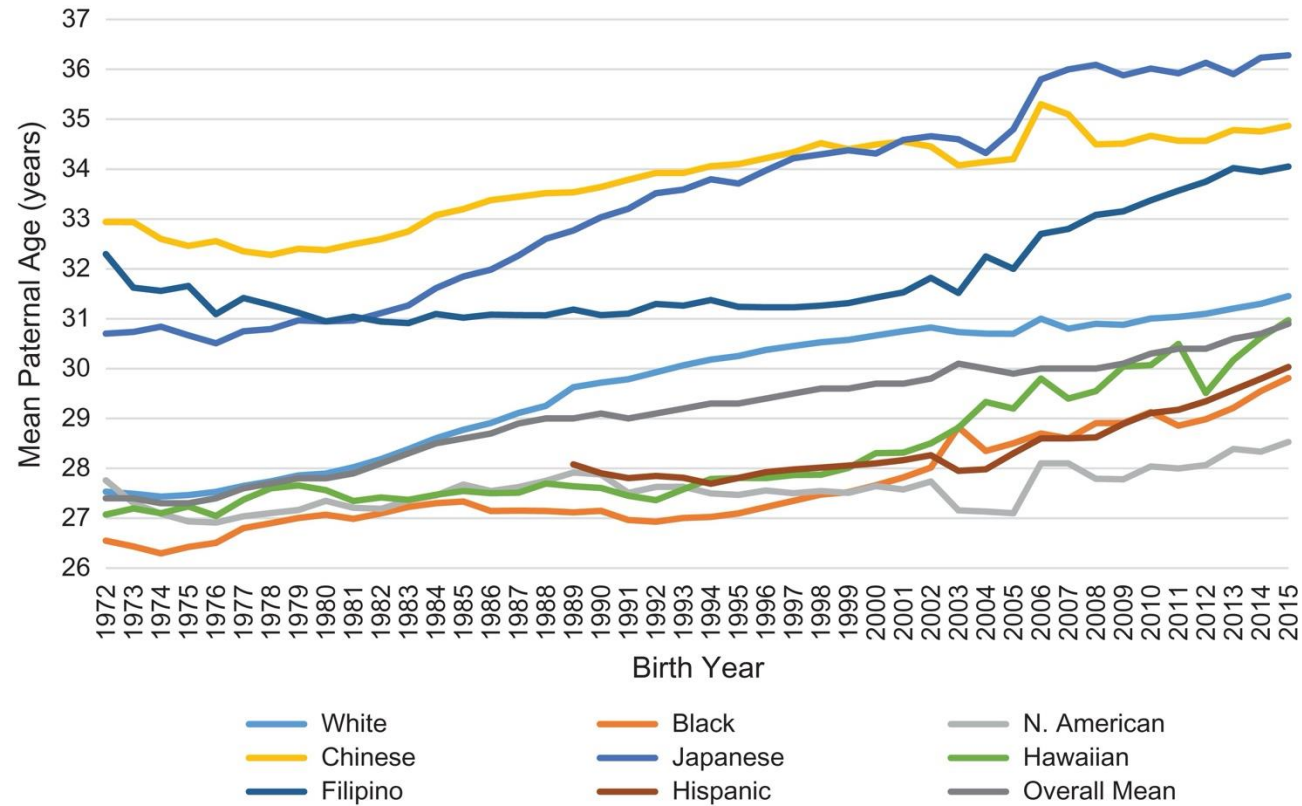
Pages: 1-168
January 2025

Guest Editor(s):

Sandra Søgaard Tøttenborg

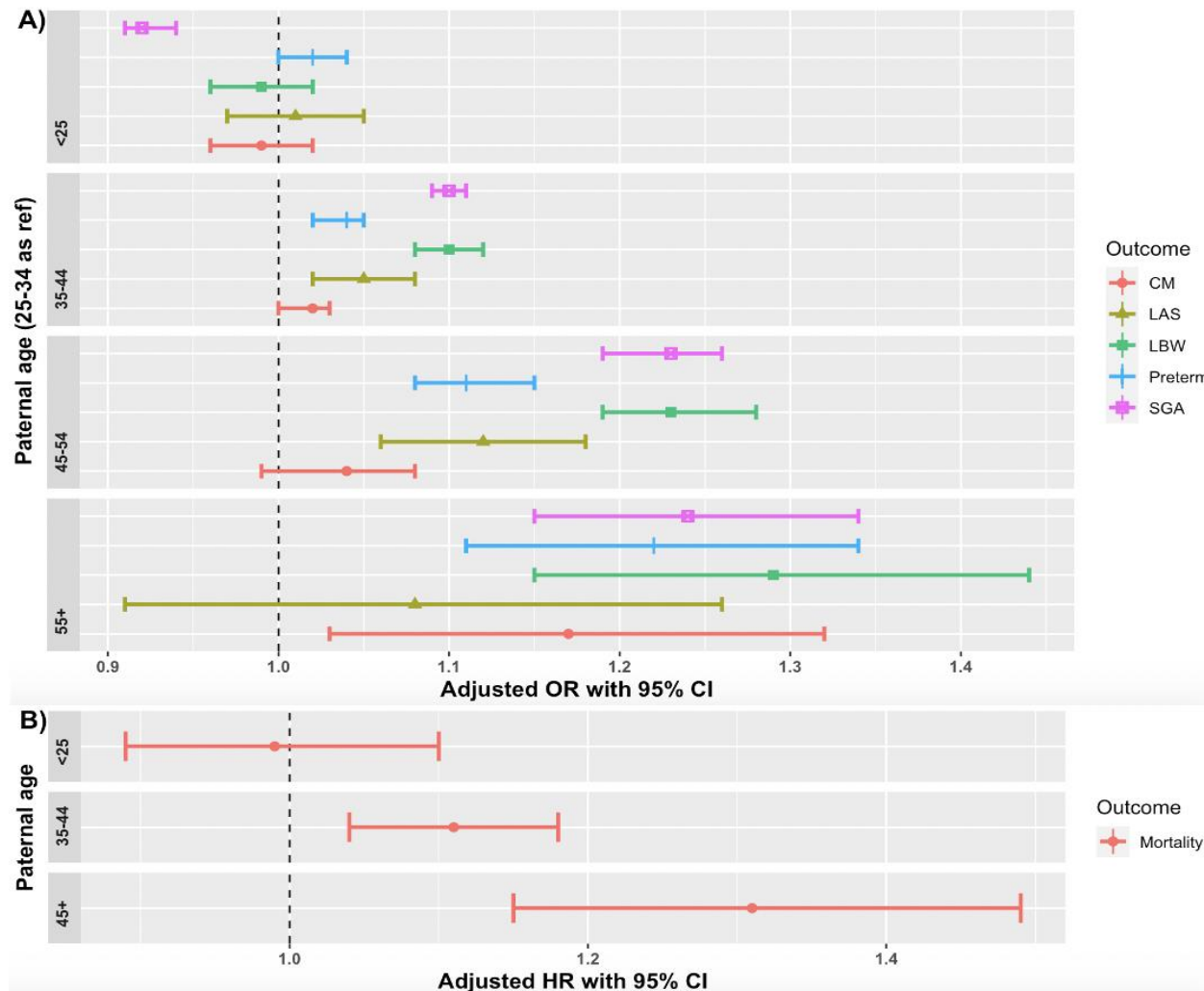
Michael Eisenberg

Increasing paternal age - more health issues



Khandwala *et al.* Human Reprod 2007.

Paternal age and health of the children



Adverse perinatal characteristics and infantile mortality in children of 45+ years old fathers

RESEARCH

OPEN ACCESS

Check for updates

Association of paternal age with perinatal outcomes between 2007 and 2016 in the United States: population based cohort study

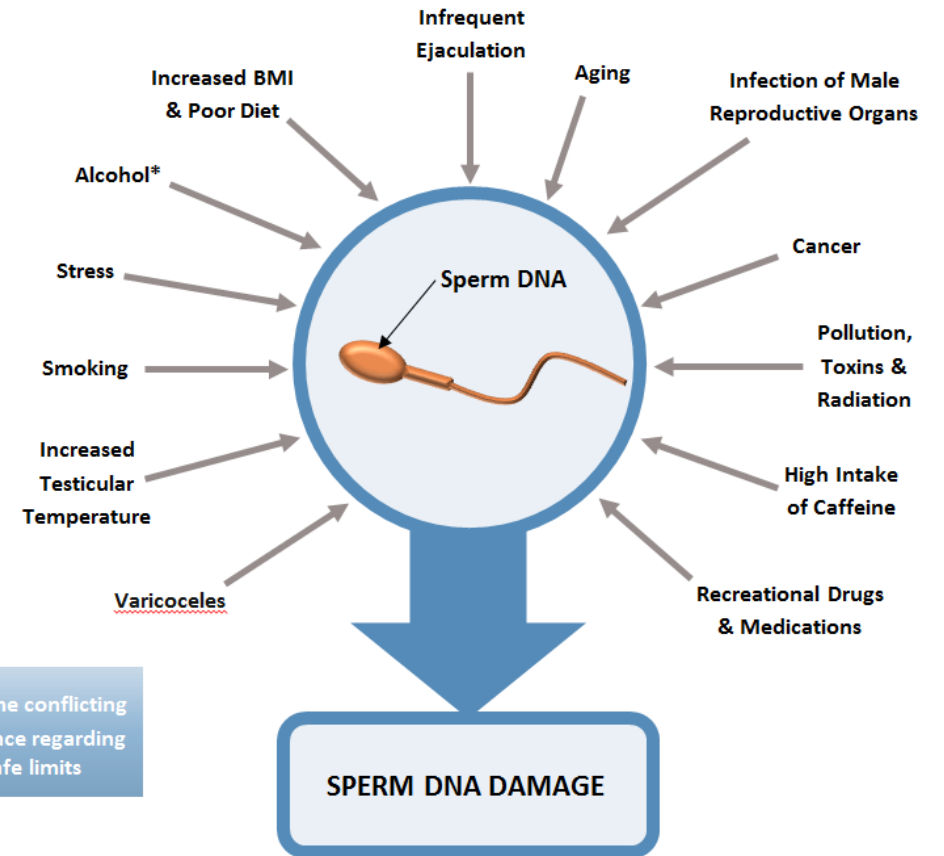
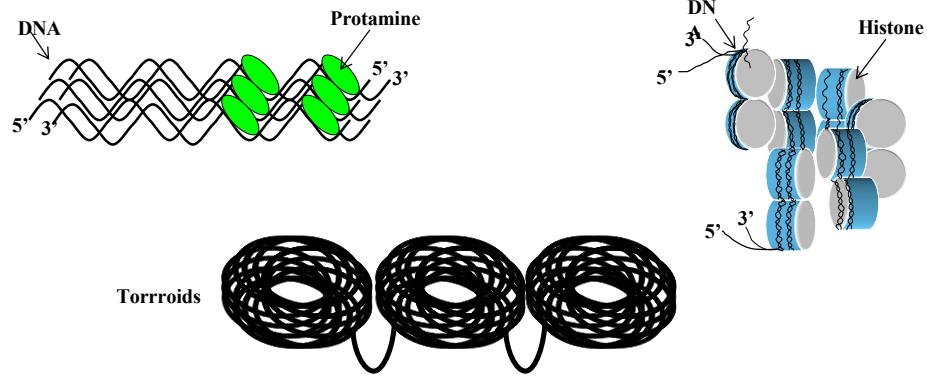
Yash S Khandwala,¹ Valerie L Baker,² Gary M Shaw,³ David K Stevenson,³ Ying Lu,⁴ Michael L Eisenberg^{1,2}

Looking for



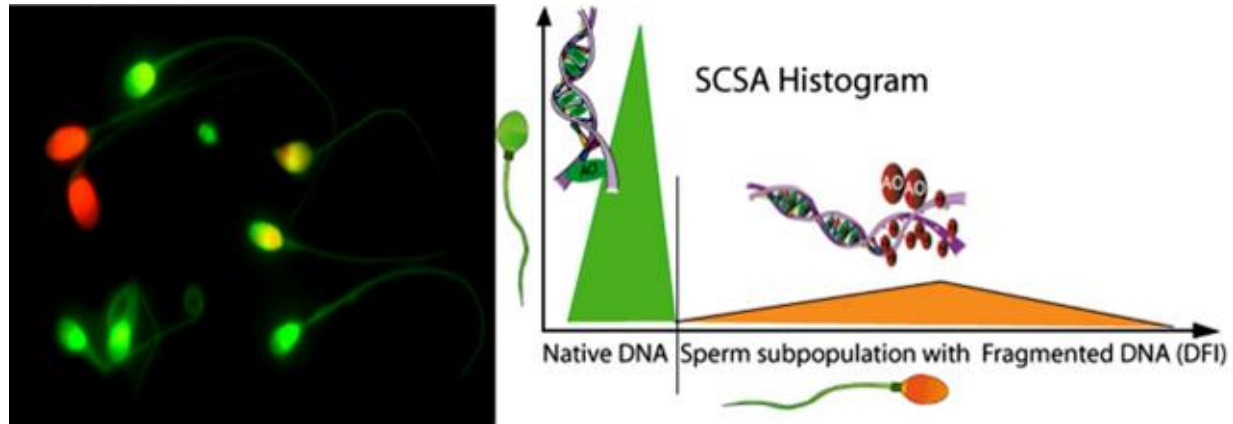
Sperm DNA Fragmentation Index (DFI)?

Sperm chromatin



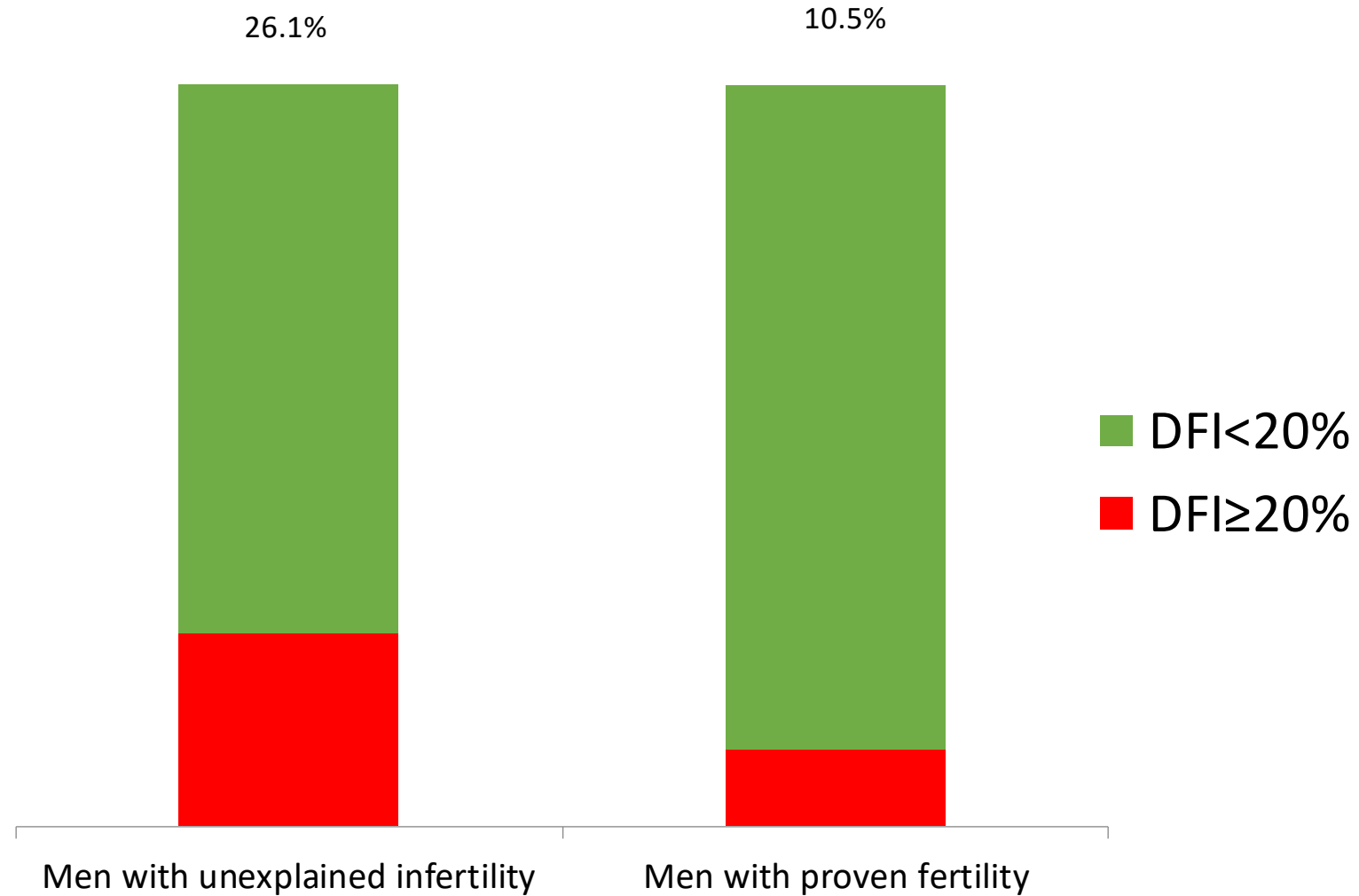
* Some conflicting evidence regarding safe limits

Assessment of sperm DNA Fragmentation Index



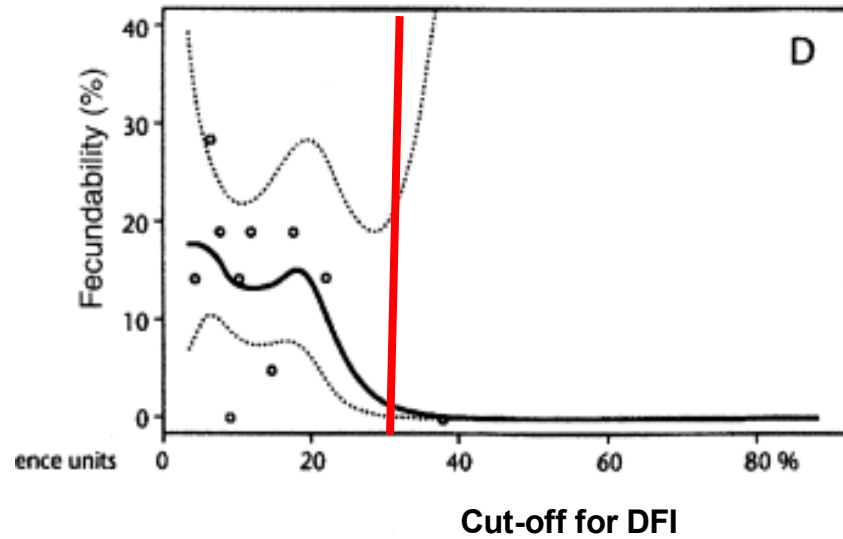
**Sperm Chromatin
Structure Assay (SCSA®
and SDFA) Evenson et al.
1980.**

DFI > 20% in 25% men with normal standard semen parameters



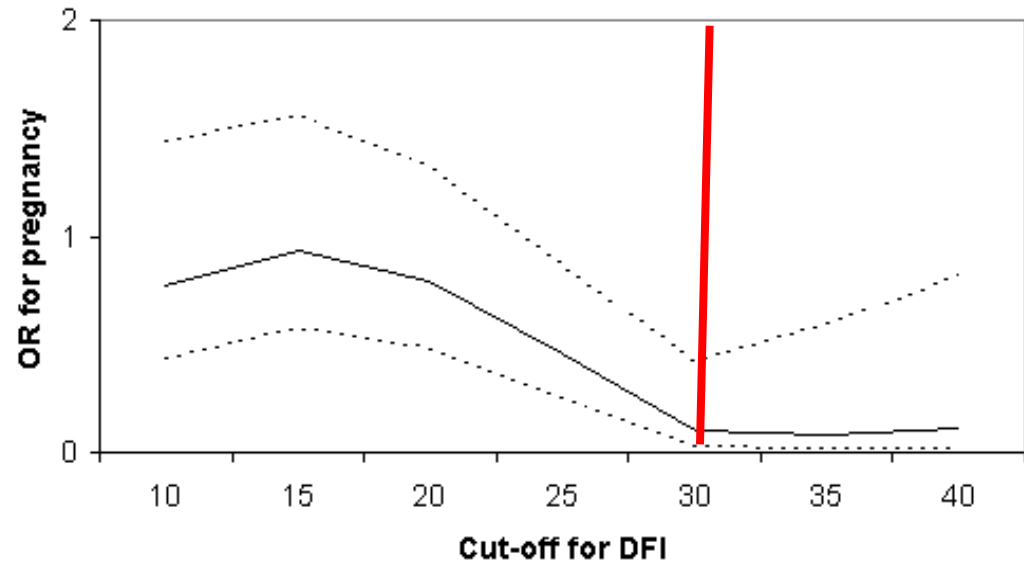
High DFI and chance of pregnancy *in vivo*

Spontaneous pregnancy



Spanò *et al.* Fertil Steril 2000

Intratutering insemination

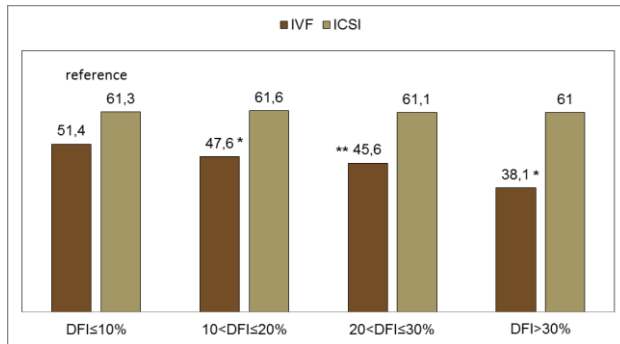


Bungum *et al.* Hum Reprod, 2007

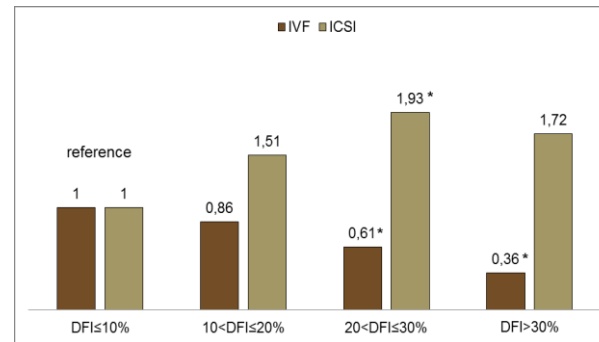
Millions of IUI treatments and hormone stimulations can be avoided

DFI>20% i the first treatment cycle (1633 cycles): IVF vs. ICSI

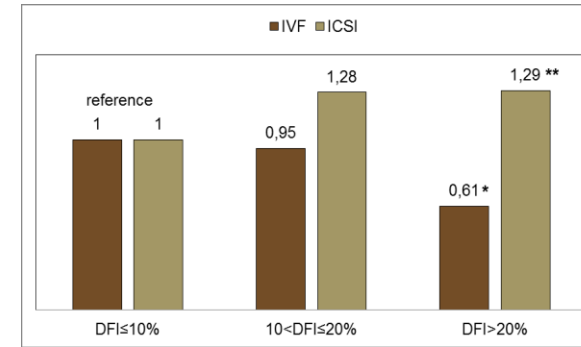
Fertilization Rate



GQE



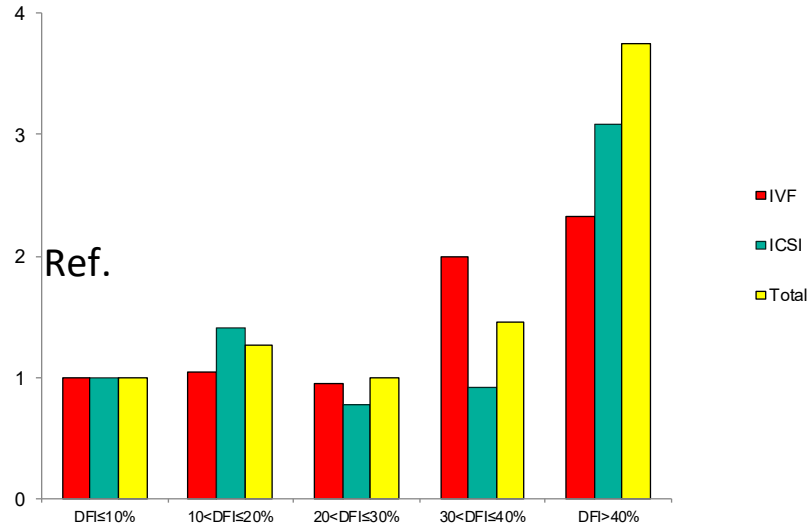
LBR



IVF but NOT ICSI: Less number Good Quality Embryos, lower fertilization rate, lower Live Birth Rate

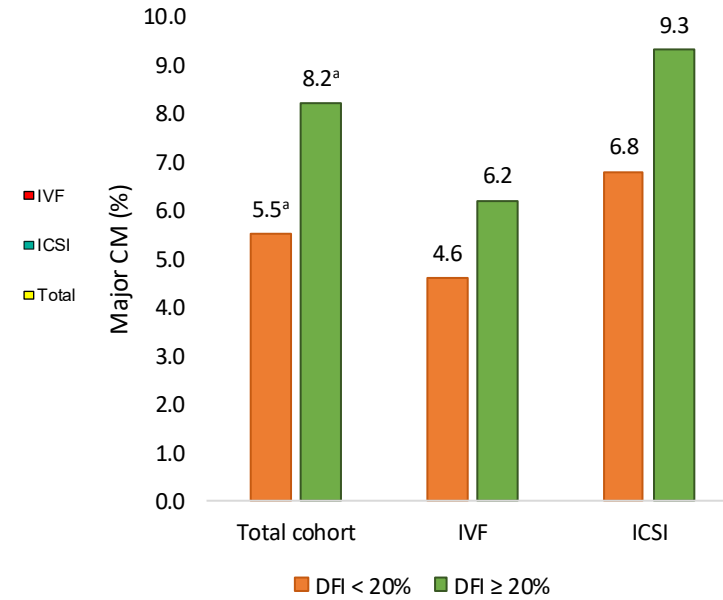
Negative pregnancy outcomes and high (>20%) DFI

Early miscarriage



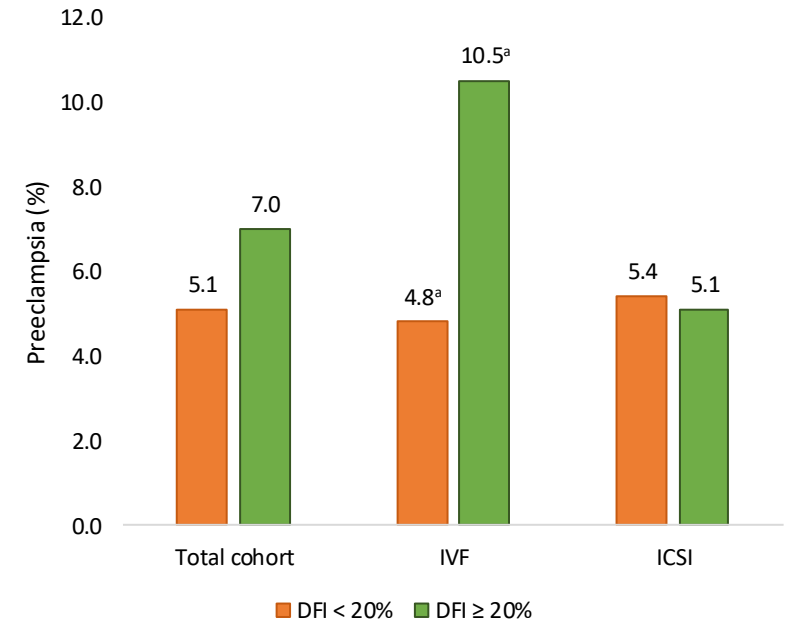
Oleszczuk *et al.* Andrology 2016

Congenital malformations



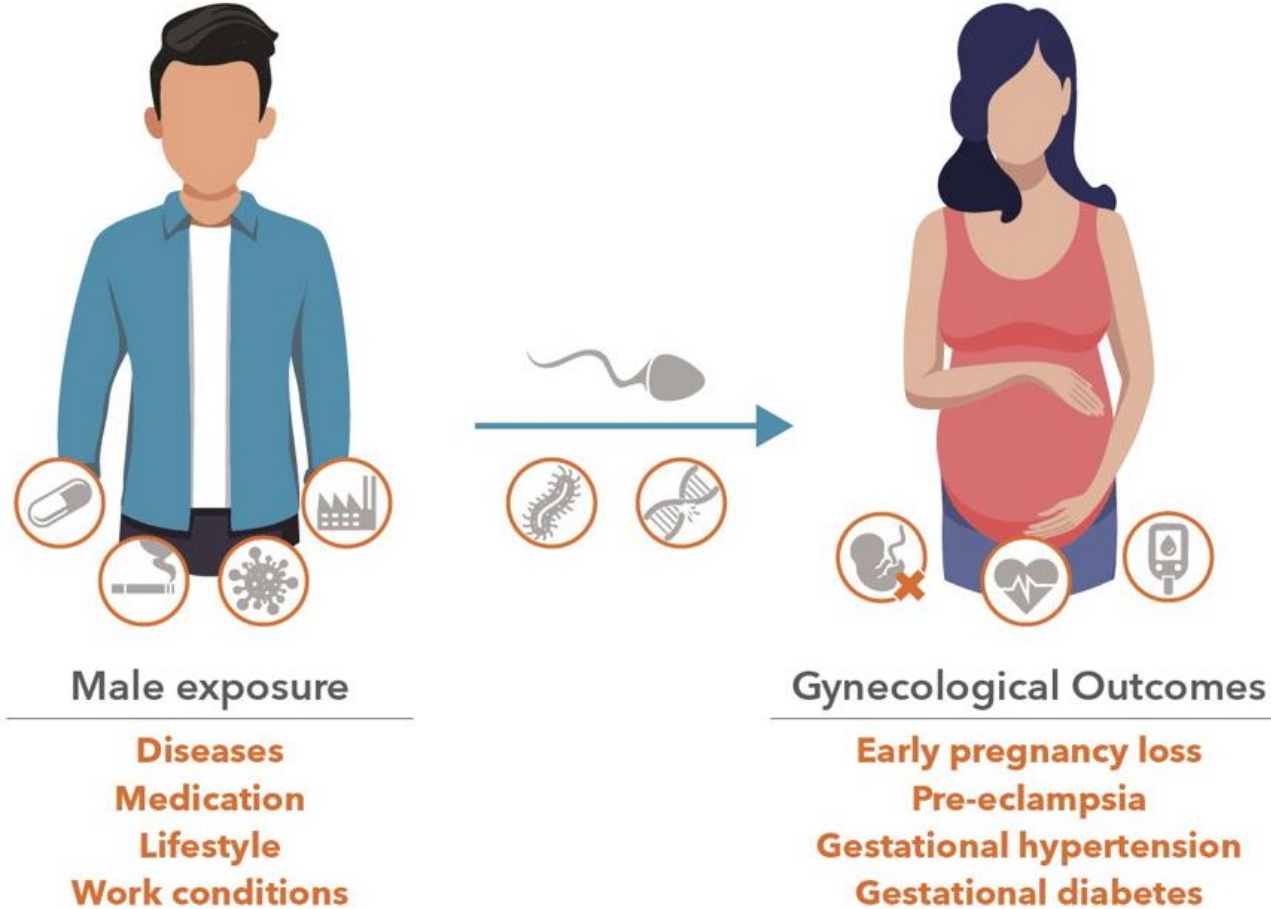
Stenqvist *et al.* unpublished

Pre-eclampsia



Stenqvist *et al.* Fertil Steril 2025

Impact of Male Preconception Health on Risk of Adverse Conditions in Pregnancy



Paradigm shift in managing male partner in infertile couple

Large and easily accessible group (in contact with health care system)

High-risk group for serious, preventable diseases

Saving female partner for unnecessary hormone treatments

Identify high-risk pregnancies for:

Adverse outcomes

Impaired child health

Future, couple-centric paradigm

Male partner proactive preconception care

- Screening: BP, HbA1c, lipids, PSA, hormones
- Lifestyle: weight, exercise, sleep, smoking
- Andrology: varicocele eval, meds review
- Targeted DFI testing)



Female partner lighter, safer pathway

Options prioritised:

- Expectant / timed intercourse when appropriate
- IUI or mild IVF before full stimulation
- IVF/ICSI only when indicated

If stimulation: lower doses, fewer scans, patient-centred protocols; lower OHSS risk

Expected benefits

- Fewer heavy ART cycles; faster time-to-pregnancy in some
- Reduced treatment burden for the woman
- Improved couple health behaviours

Acknowledgements

- Yvonne Lundberg Giwercman
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