



Increasing Trends in Male Reproductive Disorders, Environmental Exposures, and Implications for Human Health

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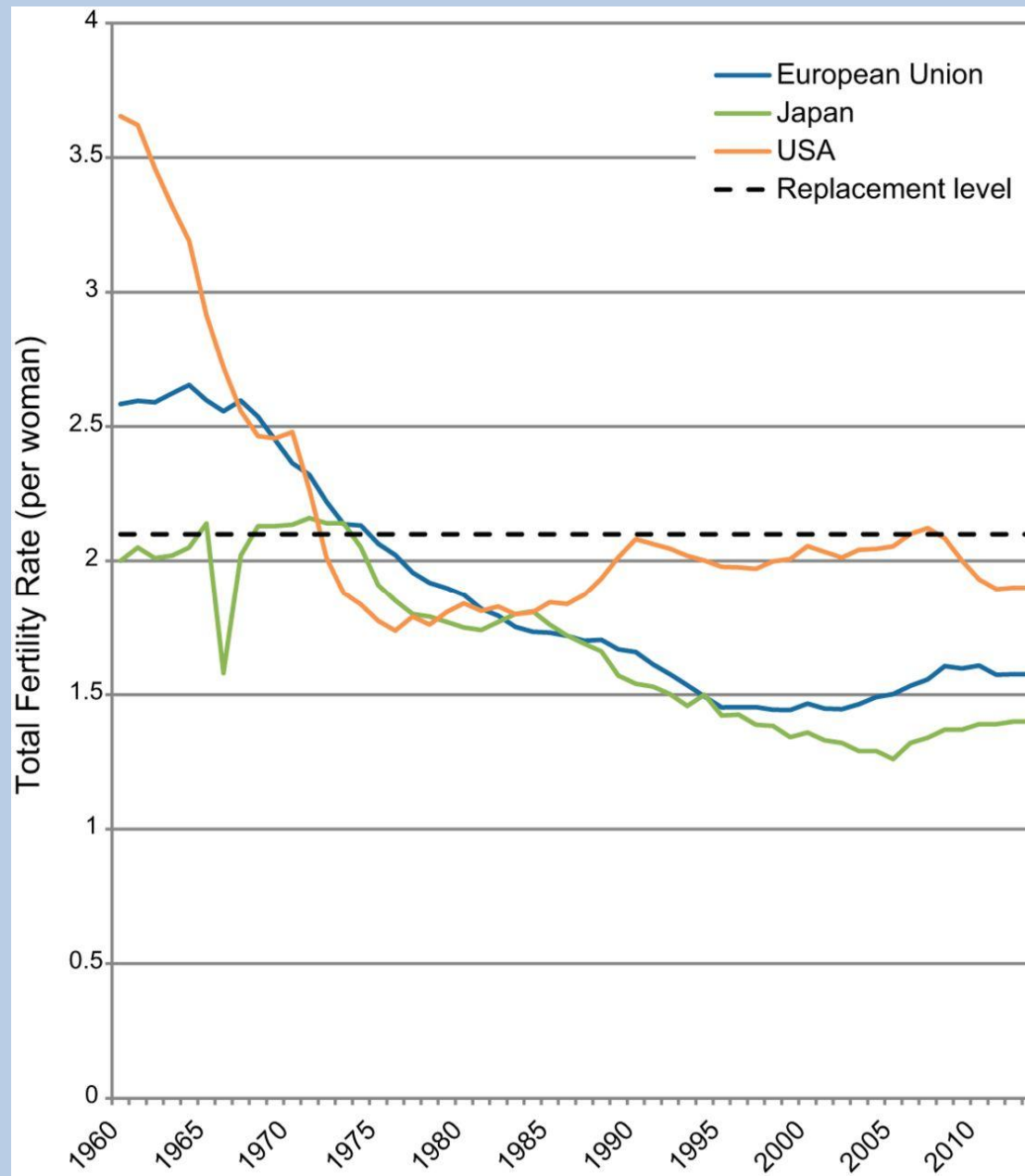
International Center for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Rigshospitalet, University of Copenhagen, Denmark

Teleconference 20 April, 2016

Nothing to declare



Total Fertility Rates (TFR), European Union, Japan and United States, 1960–2013



Skakkebaek et al. *Physiol Rev* 2016;96:55-97



Increasing political focus on low fertility

Falling Japanese population puts focus on low birth rate

Unless re-energised, demographics will erode Japan's superpower status

Wed, Dec 2, 2015, 01:00

David McNeill in Tokyo



Elderly people work out with dumb-bells by a temple in Tokyo recently. The estimated number of people aged 80 or older in Japan has topped 10 million for the first time. Photograph: Yoshikazu Tsuno/AFP

THE STRAITS TIMES. MICA (P) 108/11/2010 TUESDAY, JANUARY 18 2011 SINGAPORE PRESS HOLDINGS PUBLICATION ESTABLISHED 1845 90 CENTS

New year, new destinations LIFE! PAGES C4&5

Good start for art LIFE! PAGE C8

Caroline who? The identity crisis in women's tennis SPORT, PAGE B8

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INSIDE 72 PAGES IN FOUR PARTS

"Tax dodgers" exposed

Fertility figures hit all-time low

Shortage of babies a key hurdle to achieving a sustainable population

By LI XUEYING POLITICAL CORRESPONDENT

SINGAPORE'S baby shortfall worsened last year when the Total Fertility Rate...

Such a population, he said, has a strong citizen core, a stable ethnic mix...

For the foreseeable future, we will need to tap on immigration to augment our population, to support economic growth and to mitigate the impact of ageing," he added.

Last year also saw the effect of the Government's tightened Immigration framework of late 2009, designed to better manage the inflow and quality of new immigrants.

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Germany's birthrate is the lowest in Europe - and falling fast

50% fewer children and young people!

After generous parental allowances fail to reverse the trend, experts call for a different approach



The birthrate in Germany is falling. Many believe this is due to the problems of working women finding childcare. Photograph: Adam Gault / Alamy/Alamy

Most popular in US

Senate passes controversial cybersecurity bill Cisa 74 to 21

World Series 2015: Mets 4-5 Royals - as it happened

Health threat of sugar is vastly underestimated, study claims

Hitler comedy Look

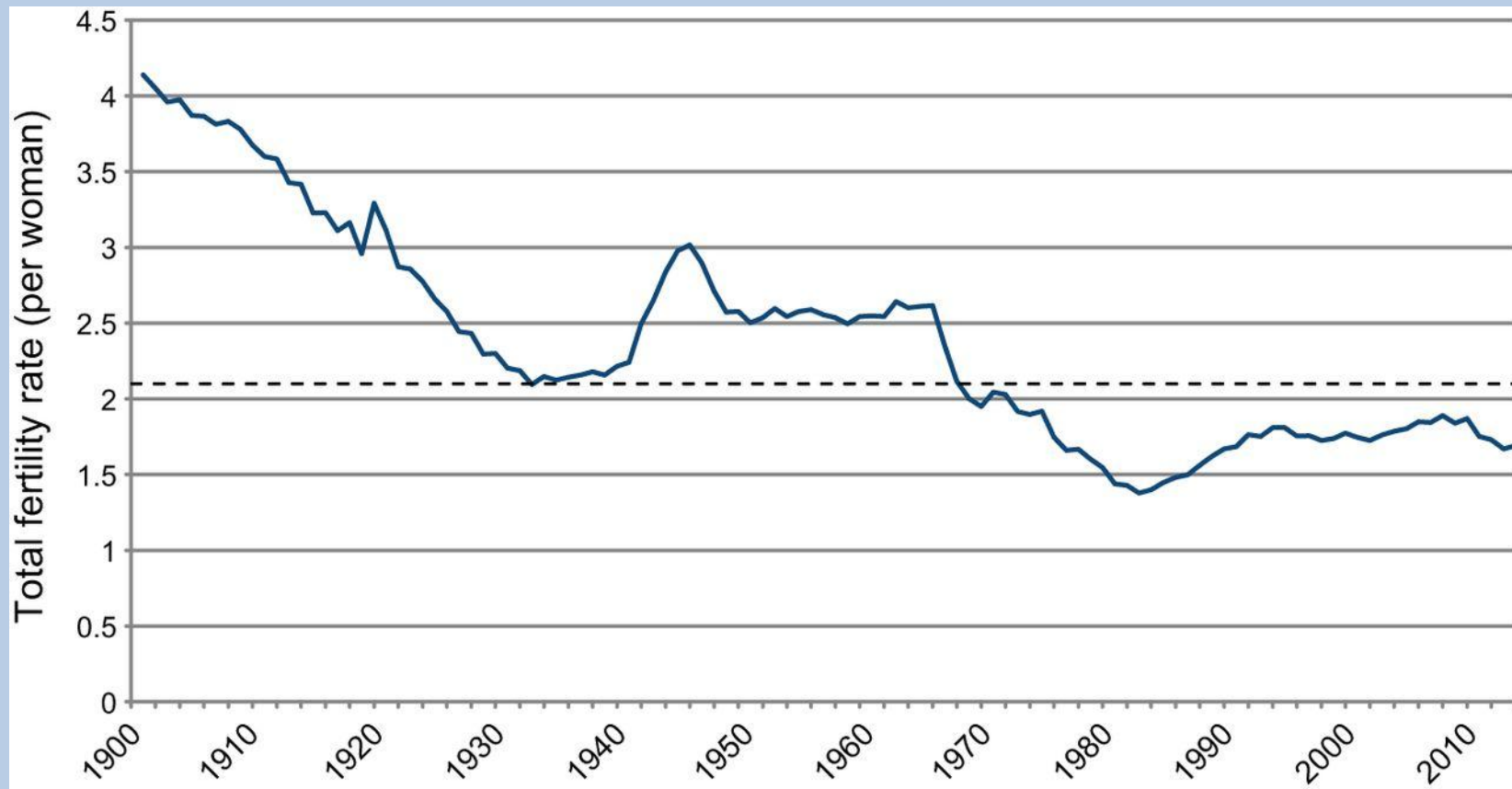
In all the data about Germany, it's the one statistic that bucks the trend. Its economy is strong, its cities are regularly cited as among the best in the world to live in – but Germany is a **shrinking** According to the national statistics office, **fewer babies were born in Germany last year than at any time in its history.** A total of 663,000 children were born, 15,000 fewer than in 2010 and in stark contrast to 1964 when German births (east and west) peaked at just under 1.4 million. The rate for younger women in particular fell last year,



Possible Reasons for Declining Fertility Rates

- Some social scientists and demographers:
 - a. people just plan to have fewer kids and
 - b. use of modern contraception and induced abortions

Total Fertility Rate (TFR), Denmark 1901–2014



Skakkebaek et al. *Physiol Rev* 2016, Blomberg Jensen et al *PLoS One*, 2015



45% Unintended Pregnancy Rate in USA

Finer & Zolna, NEJM, 2016

Pregnancy either

Mistimed -not wanted at the time that pregnancy occurred but at a later time

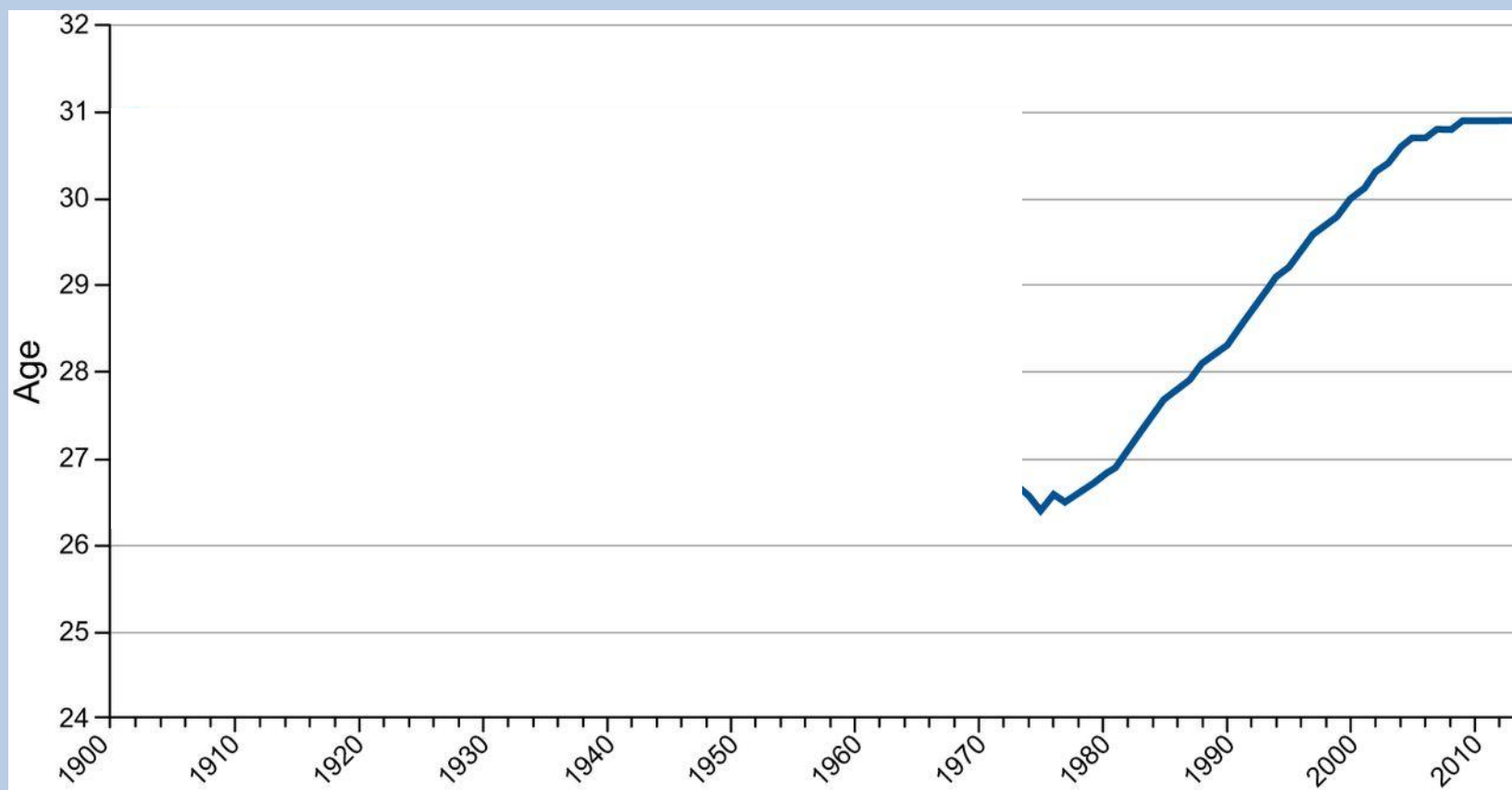
or

Unwanted – not wanted then or at any time in the future

Possible Reasons for Declining Fertility Rates

- Some social researchers (demographers):
 - a. people intend to have fewer kids and
 - b. use of modern contraception and induced abortion
- Gynecologists: Women are too old when they start trying to become pregnant

Mean ages of Danish women delivering from 1975–2014



Mean ages of Danish women delivering from 1901–2014.



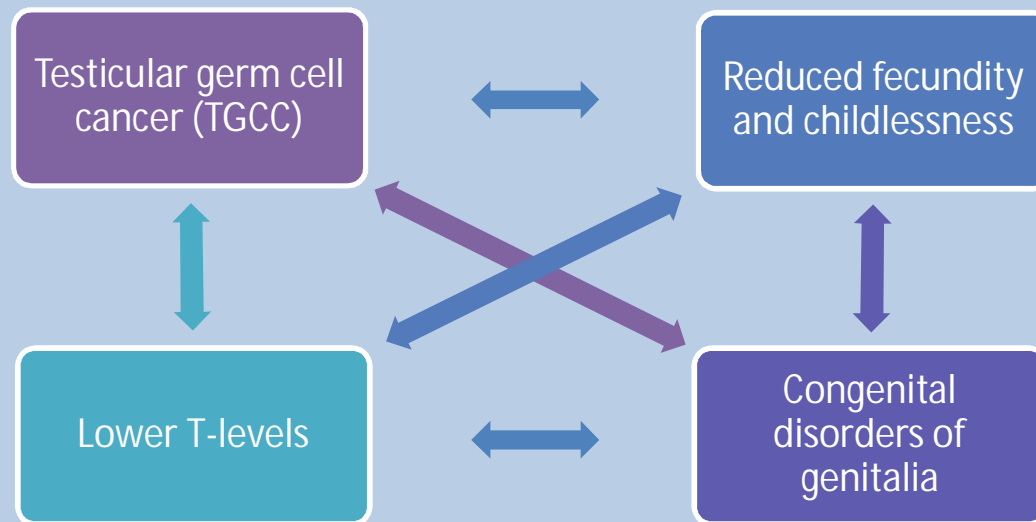
Possible Reasons for Declining Fertility Rates

- Social researchers (demographers):
 - a. people intend to have fewer kids and
 - b. use of modern contraception and induced abortion
- Gynecologists: Women are too old when they start trying to become pregnant
- Fecundity (ability to conceive) has declined, male or female, or both

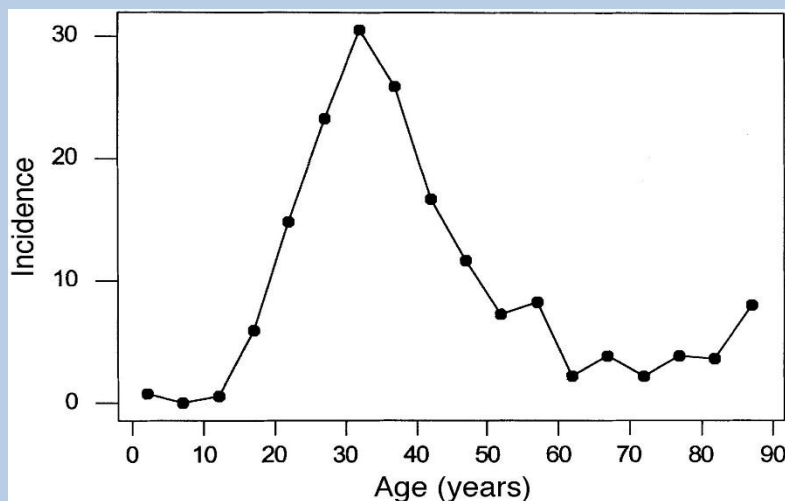
Fewer Unintended Pregnancies and Widespread Infertility

- 40-50% of children in US and Europe are born after sex where pregnancy was not planned.
- But previously a higher number.
- Hypothesis I will discuss is: Does a general decline in male reproductive health play a role for birth rates by causing a reduction in the number of unintended pregnancies and more infertility?

Links and Trends in Male Reproductive Disorders A Square

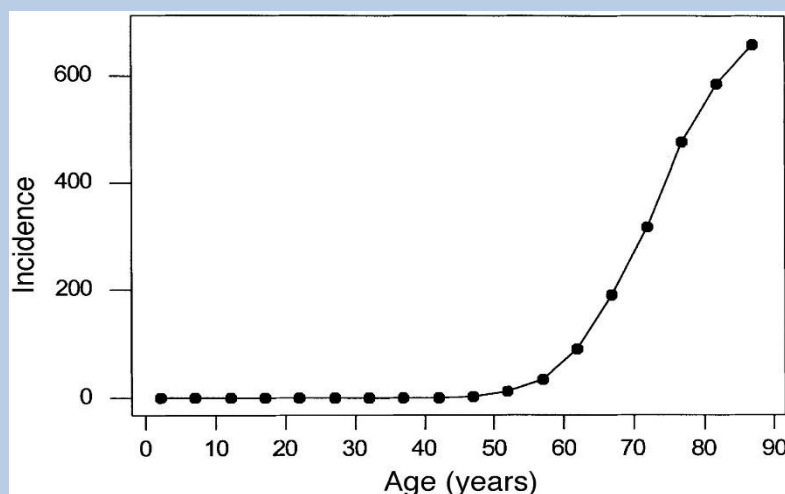


Age-standardized incidence in DK, around 1995



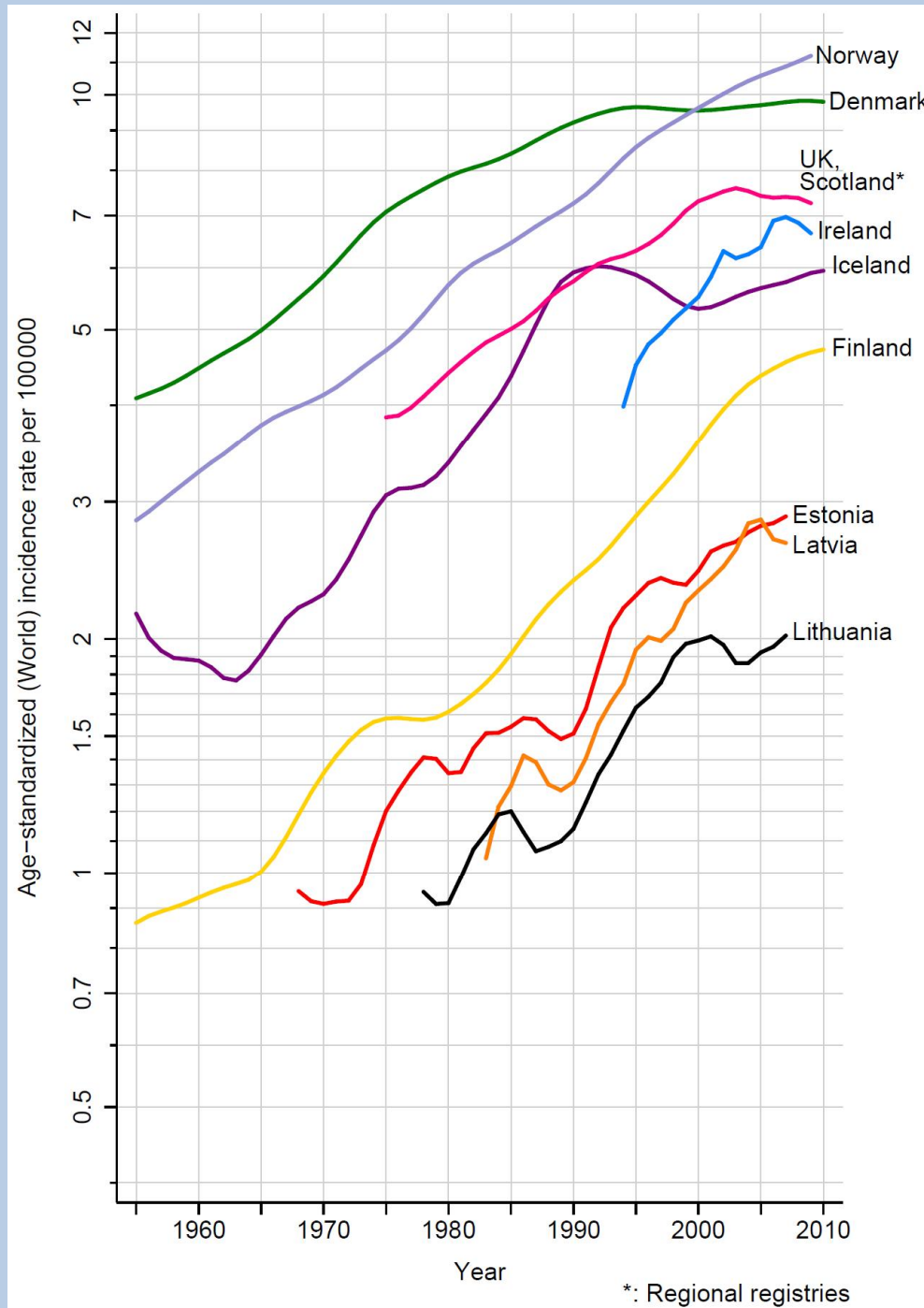
Testicular Cancer

Well diagnosed
and registration
close to complete



Prostate Cancer

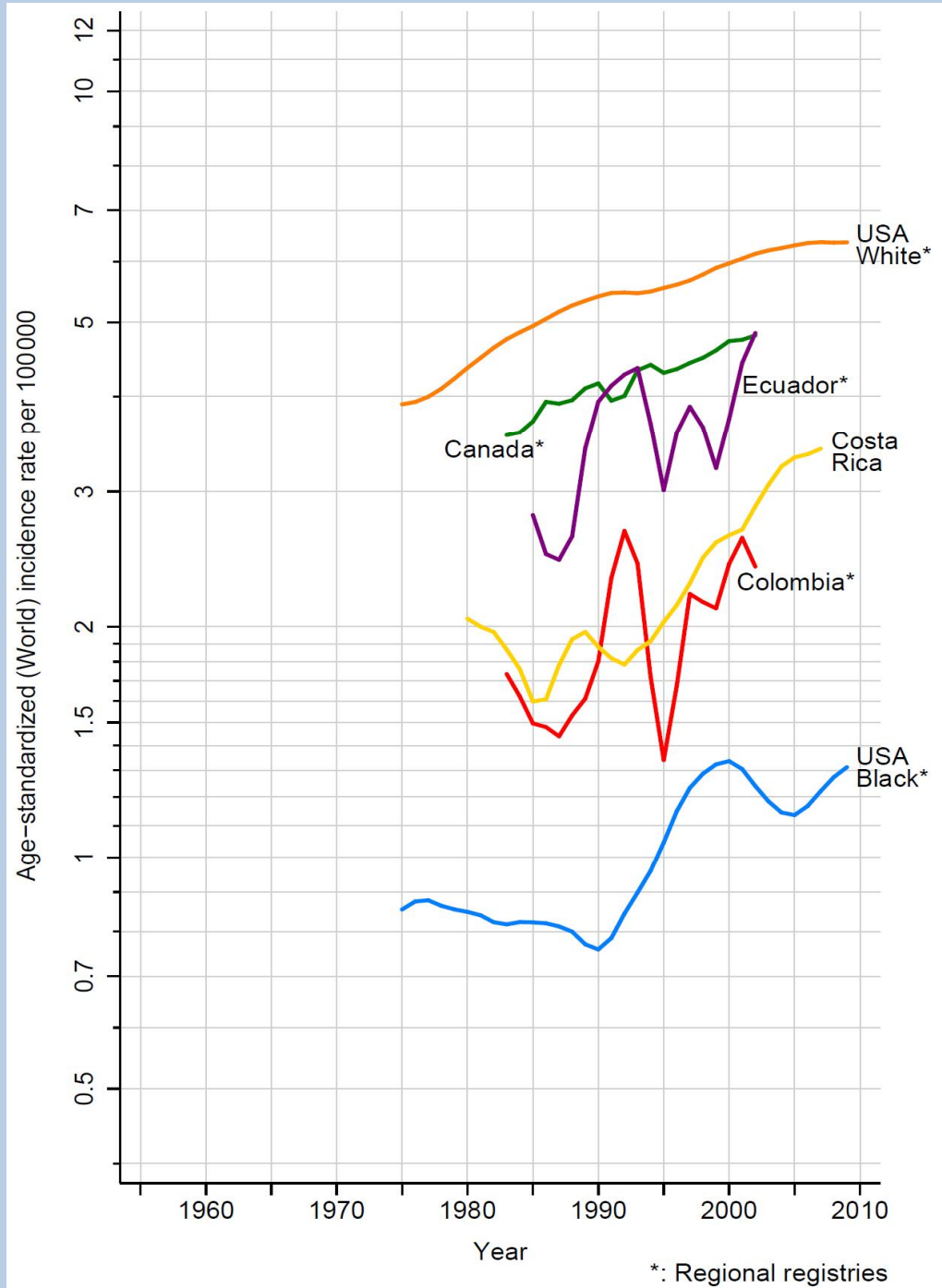
*From Møller, Hum Reprod
2001*



Trends in testicular germ cell cancer

Northern Europe

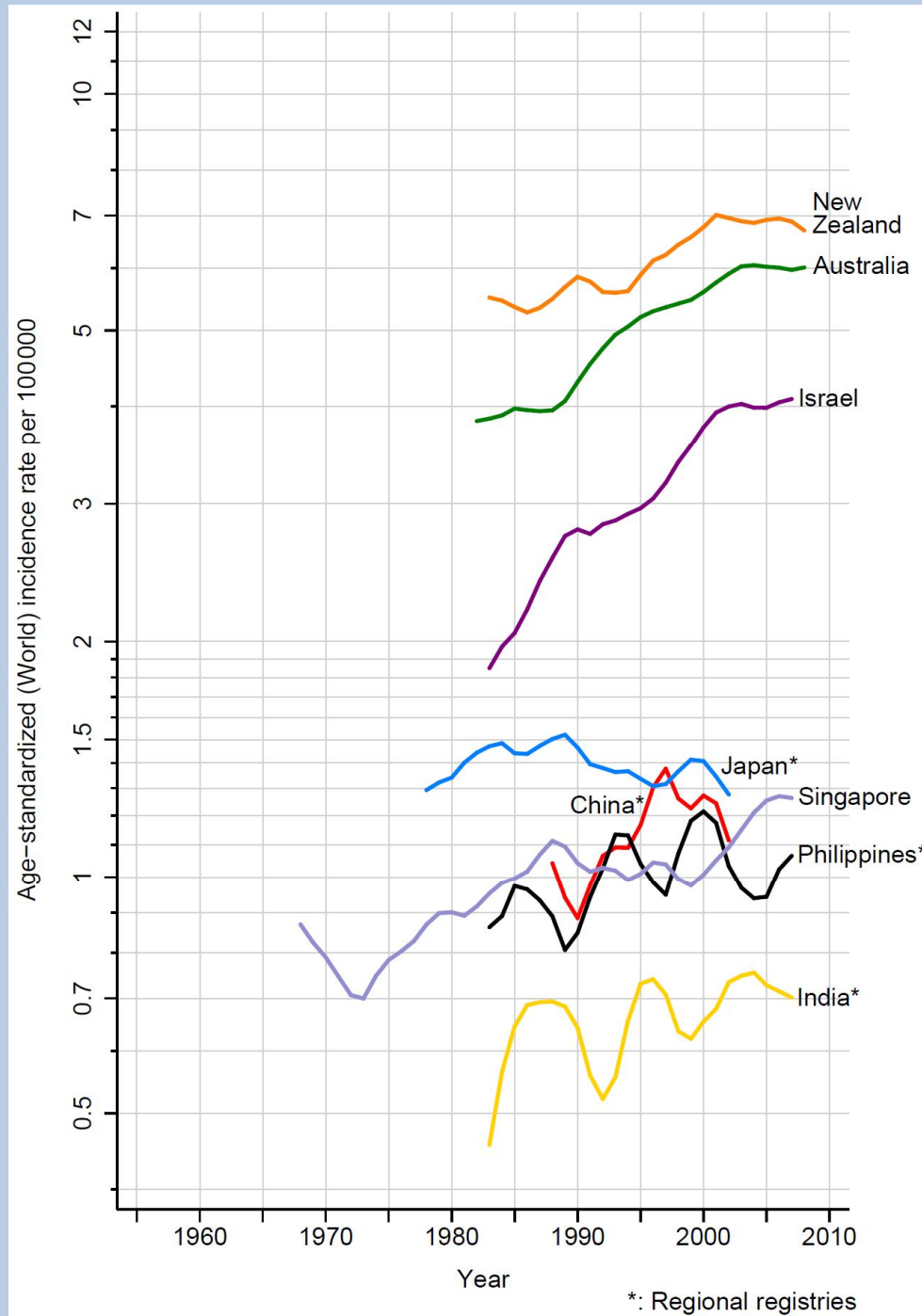
Modified from Znaor et al, European Urology, 2014



Trends in testicular germ cell cancer

The Americas

Modified from Znaor et al, European Urology, 2014

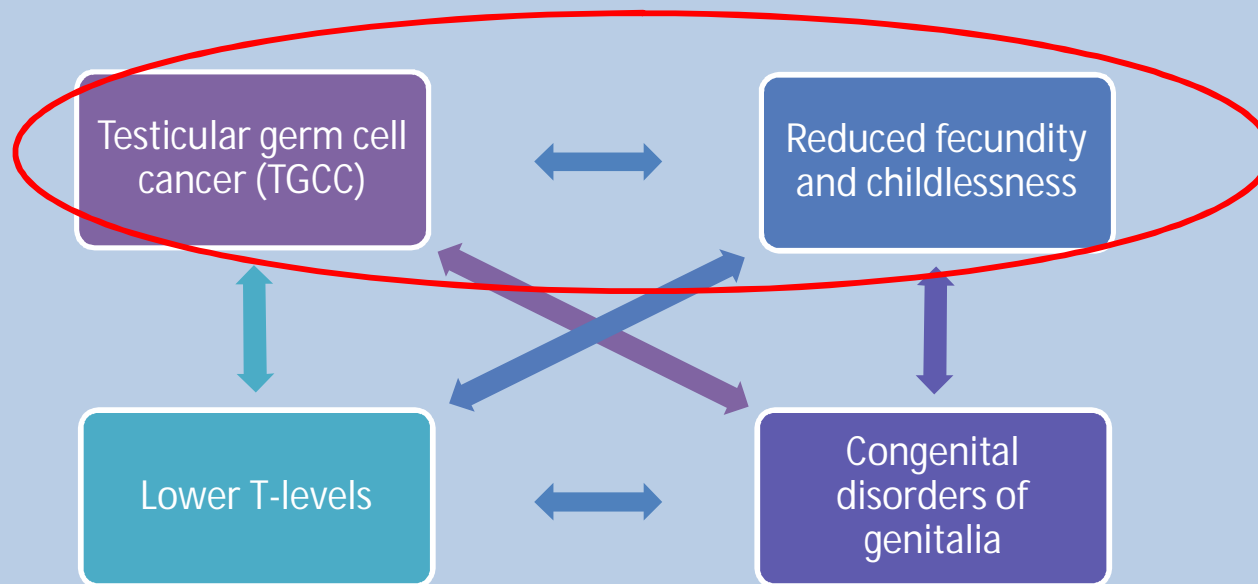


Trends in testicular germ cell cancer

Asia

Modified from Znaor et al, European Urology, 2014

Links and Trends in Male Reproductive Disorders A Square



Reprinted from THE LANCET, September 9, 1972, pp. 516-517

POSSIBLE CARCINOMA-IN-SITU OF THE TESTIS

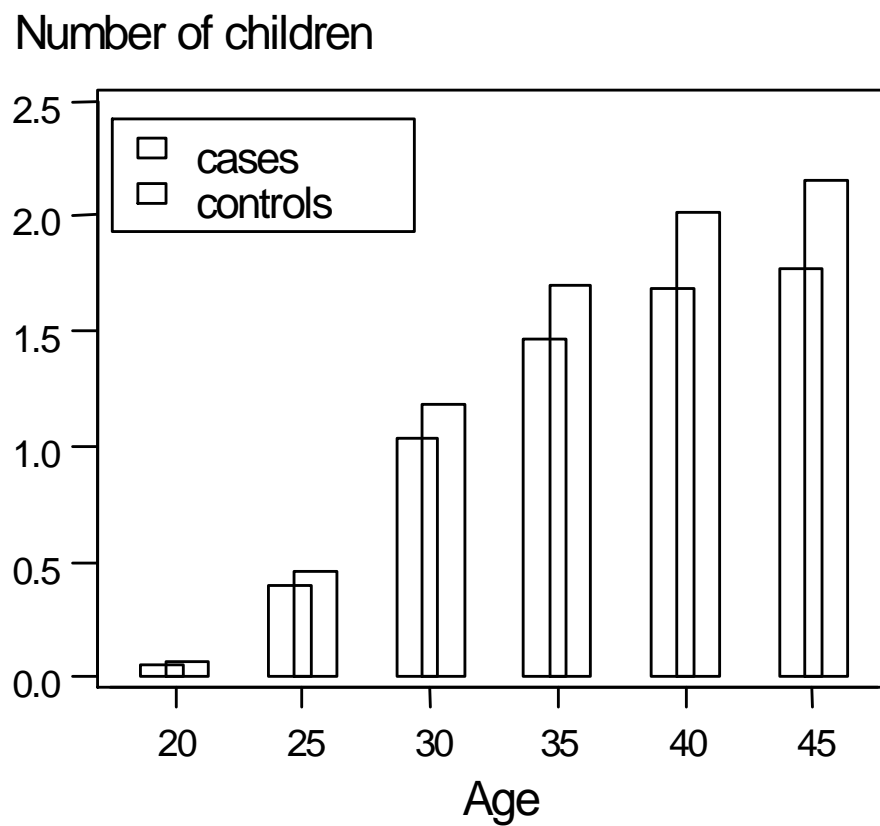
NIELS E. SKAKKEBÆK

*Chromosome Laboratory and Fertility Clinic,
Department of Obstetrics and Gynæcology, Rigshospitalet,
Copenhagen Ø, Denmark*

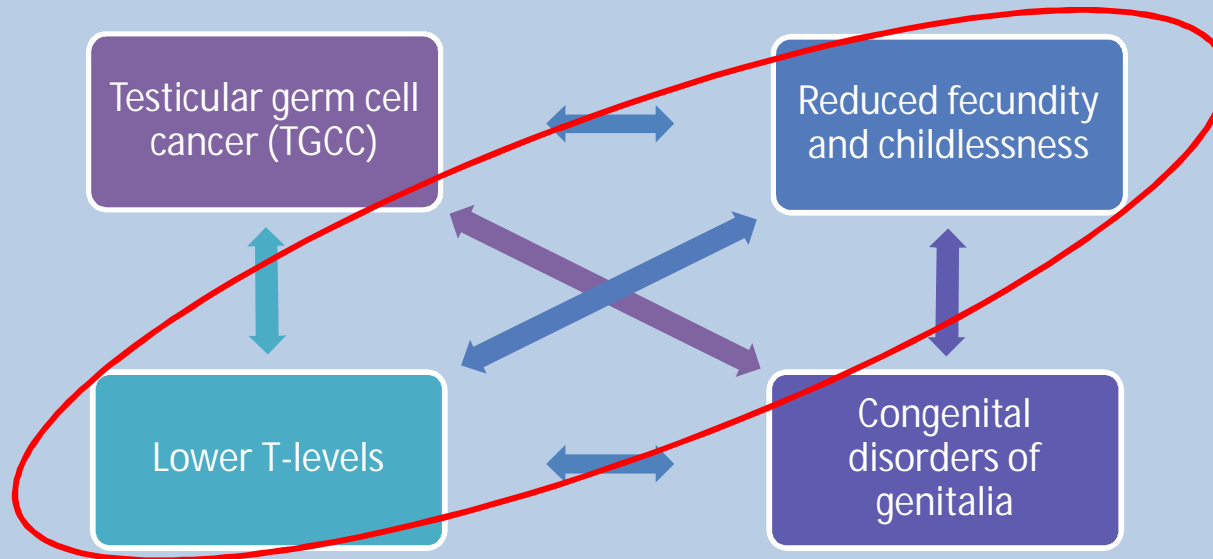
Summary Embryonal carcinoma of the testis was detected in two infertile men in whom testicular biopsies had revealed an abnormal seminiferous epithelium with atypical germ cells. The tumours occurred within $4\frac{1}{2}$ years of testicular biopsy. It is suggested that the atypical germ cells represented a carcinoma-in-situ.

Skakkebaek, Lancet , 1972

Evidence for decreased fertility in men prior to development of testicular cancer



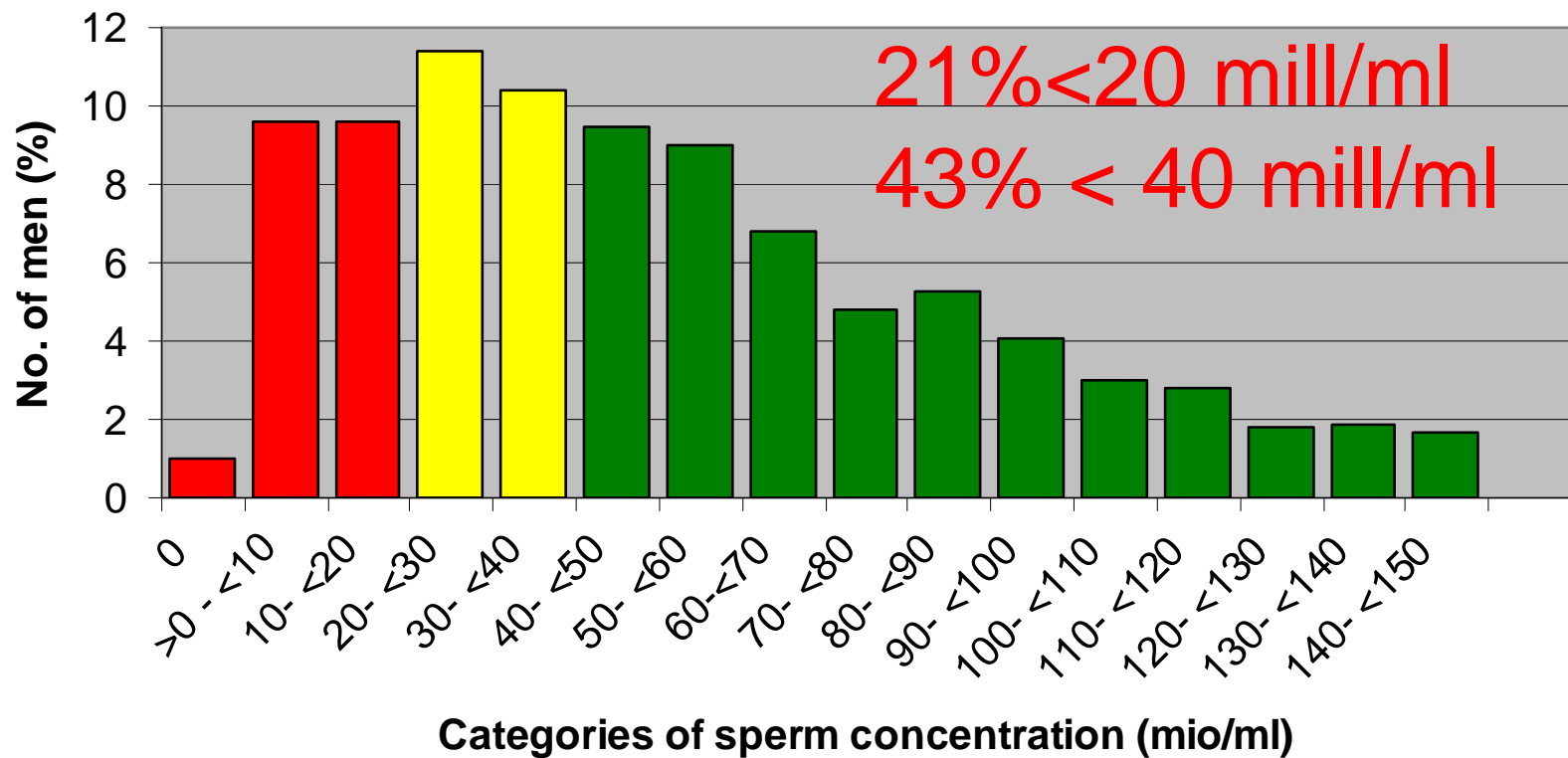
Links and Trends in Male Reproductive Disorders



Sperm count of 4867 young men from the general population

Jørgensen et al, BMJ Open, 2012

Sperm concentration, young Danish men



Adjusted for duration of ejaculation abstinence

Similar results from Finland, Germany, USA, Japan and Australia

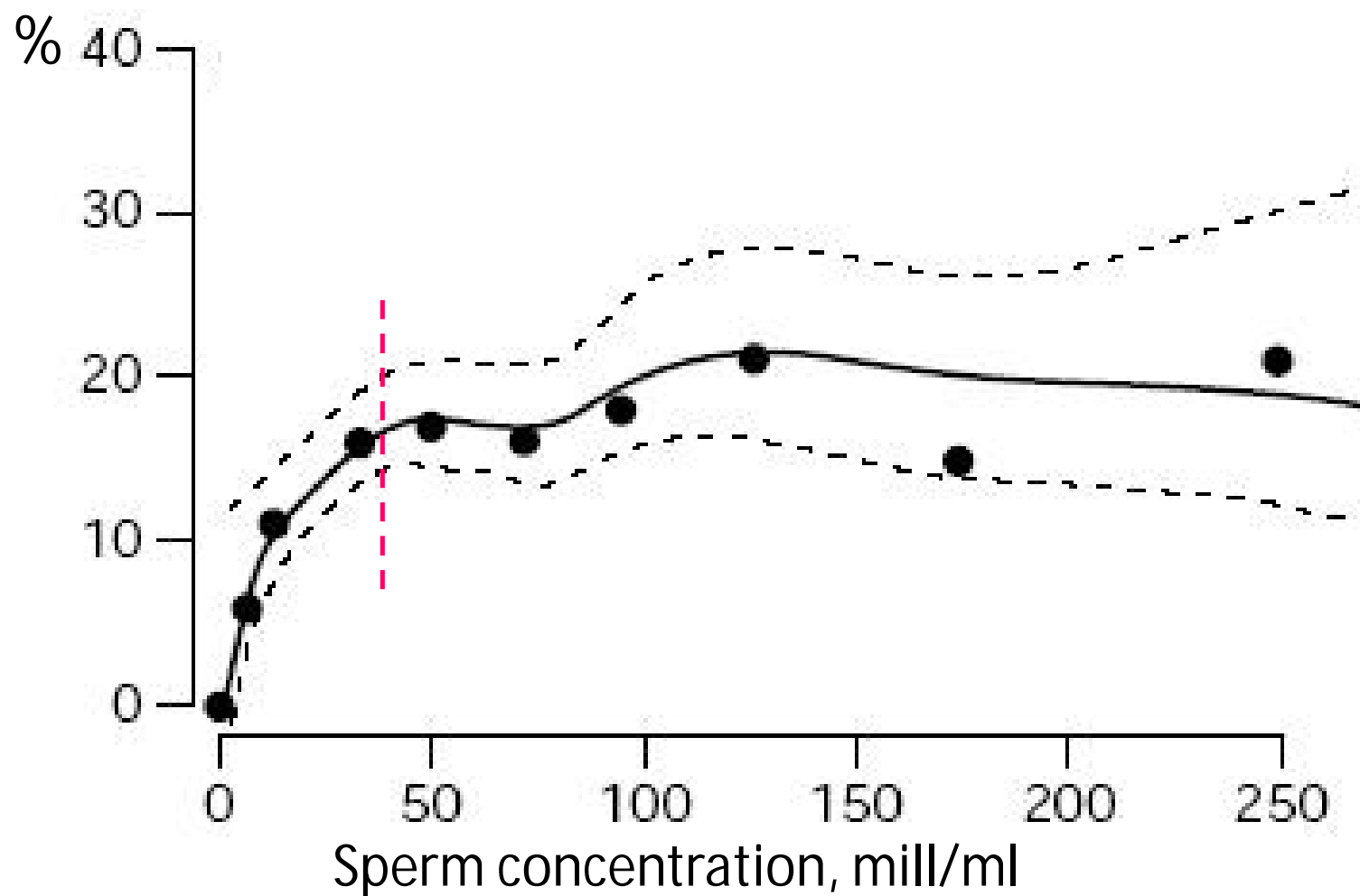


Should we be concerned about these publications on low sperm counts ?

Some people may think:

"after all, only one sperm is necessary for fertilization.... "

Probability of pregnancy within one menstrual cycle



Bonde et al.: Lancet, 1998

Increasing need for assisted reproduction

Most recent data (2015) from Danish Fertility Society shows that:

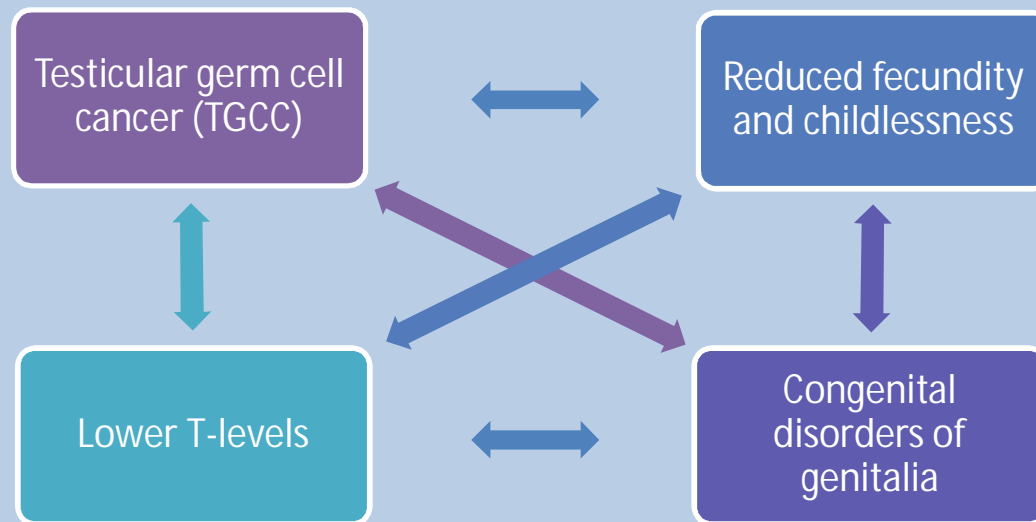
8 % of the 2012 national birth cohort conceived after assisted reproduction

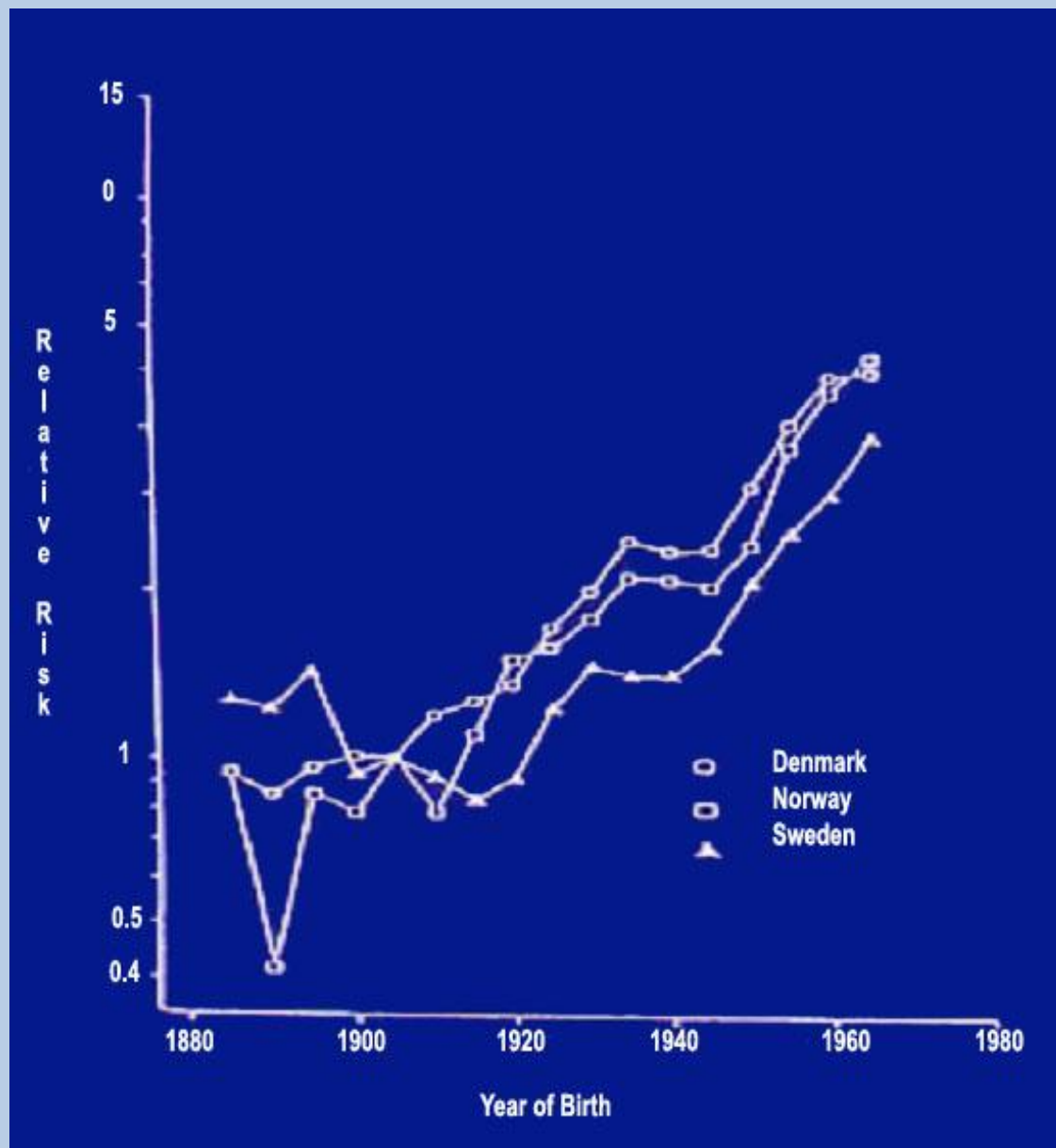
(IVF, ICSI, IUI-H or IUI-D)

<http://www.fertilitetsselskab.dk/>

In addition, almost 1% of children adopted

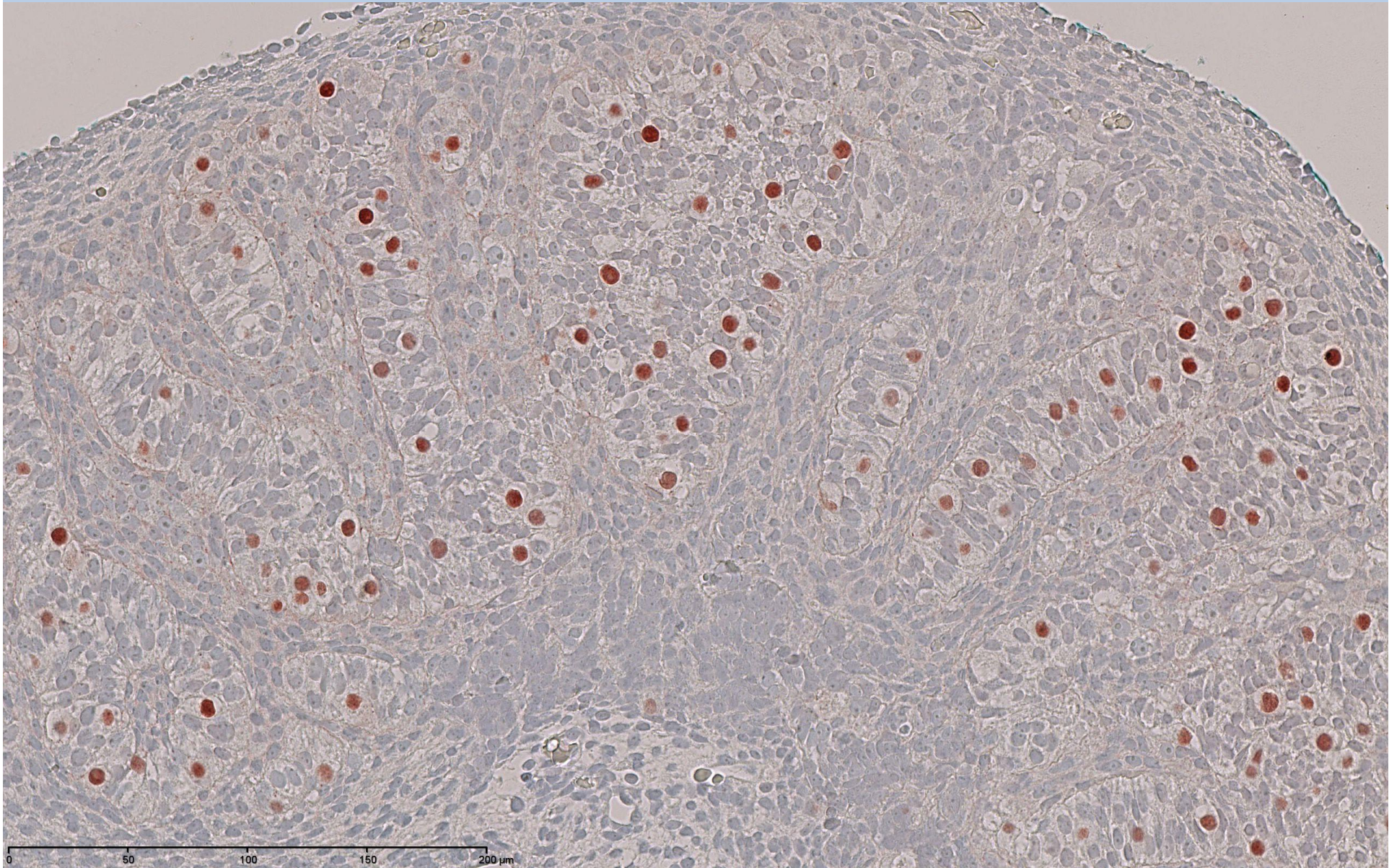
Links and Trends in Male Reproductive Disorders Roots in fetal development

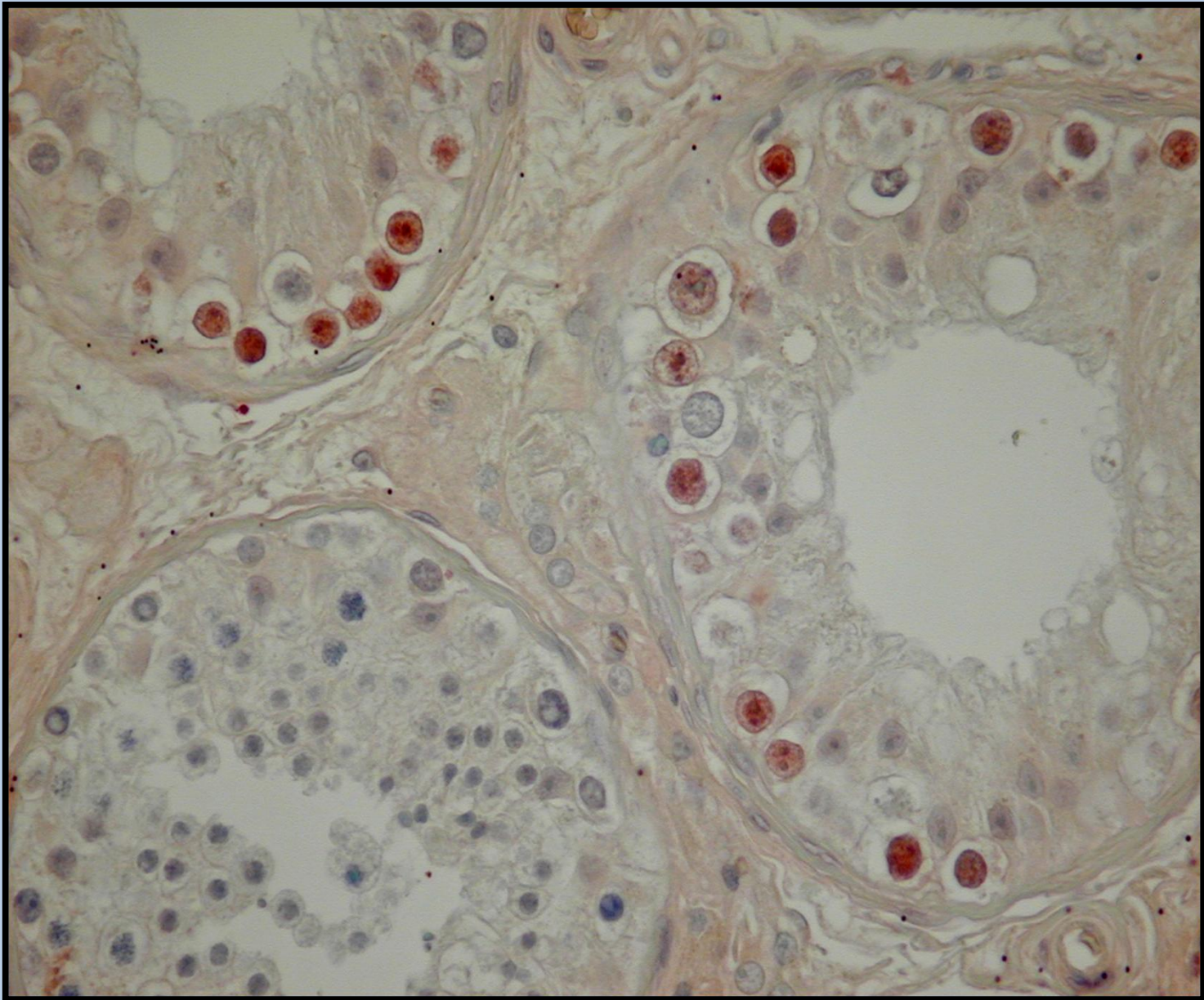




Bergström et al. J.N.C.L. 1988

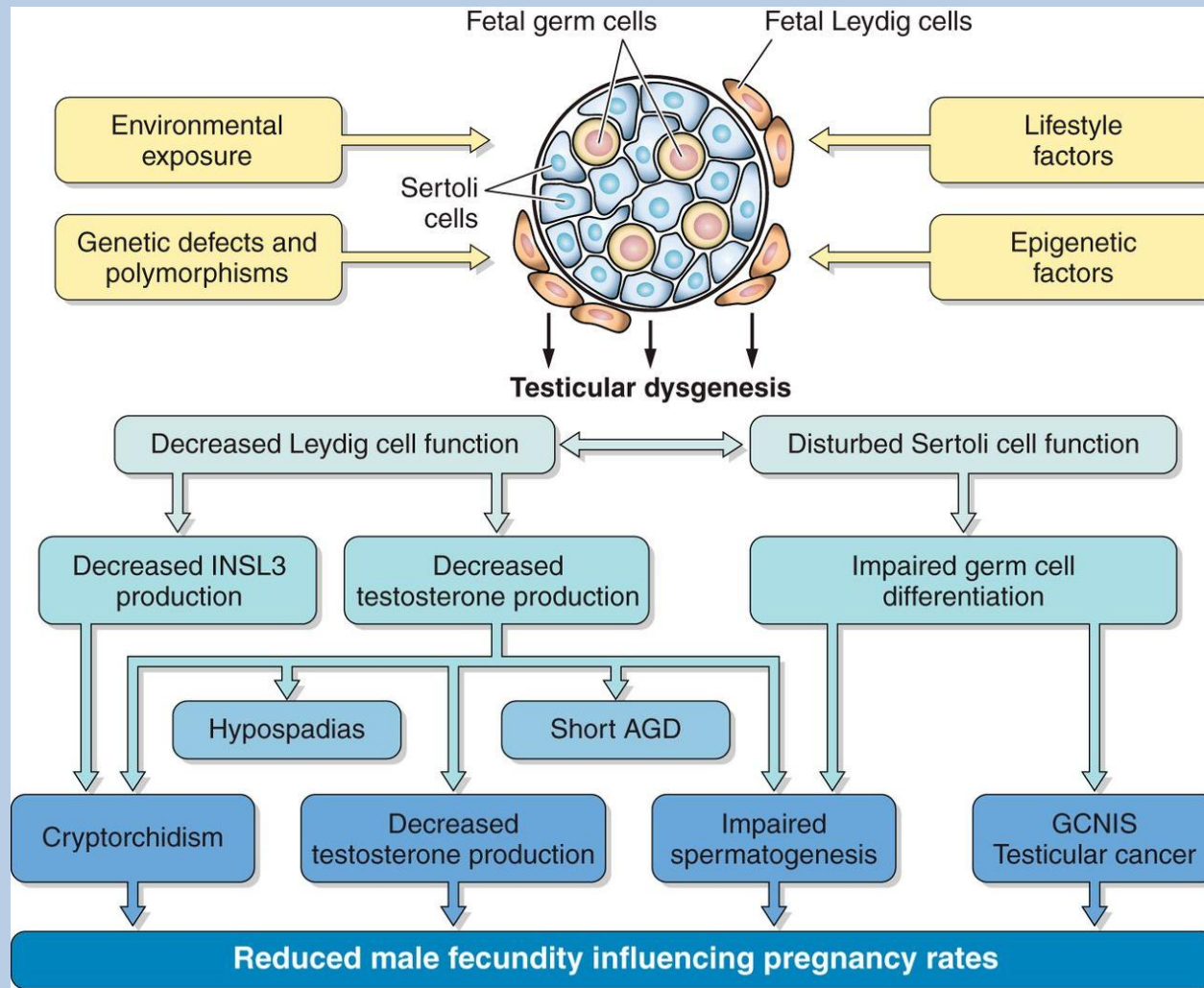
Gonocytes expressing OCT 4, gestational week 10





Oct-4 expression in GCNIS cells (adult, infertile male)

Testicular Dysgenesis Syndrome (TDS)



WHO-UNEP: Strong evidence that EDCs can have adverse effects on male reproduction at the level of the pituitary, the testicle and the gamete

- Effects in wild life
- Effects in experimental settings
- Potential effects in humans
- We are all exposed
- Possible transgenerational effects

Conclusions

- Testicular cancer is an important marker of endocrine disruption of the fetal human testis.
- Worldwide increases in testicular cancer incidence.
- Semen quality of young men now rarely meets all criteria of the WHO standard.
- Extremely low fertility rates below replacement levels have previously been seen as a result of womens choices.
- However, an increasing number of data suggest that male infertility also contributes to low birth rates.
- We and others are testing the hypothesis that environmental exposures contribute to the current epidemic of subfertility and infertility, which likely is associated with decreasing populations in many industrialized countries.
- Good news: Exposures can be reduced by better regulation of chemicals!



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