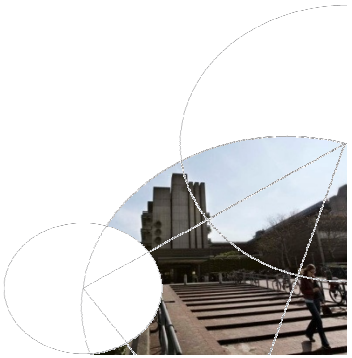
Lifestyle impact on gamete and embryo quality

Jens Peter Bonde

Department of Occupational and Environmental Medicin, Bispebjerg Hospital, University of Copenhagen

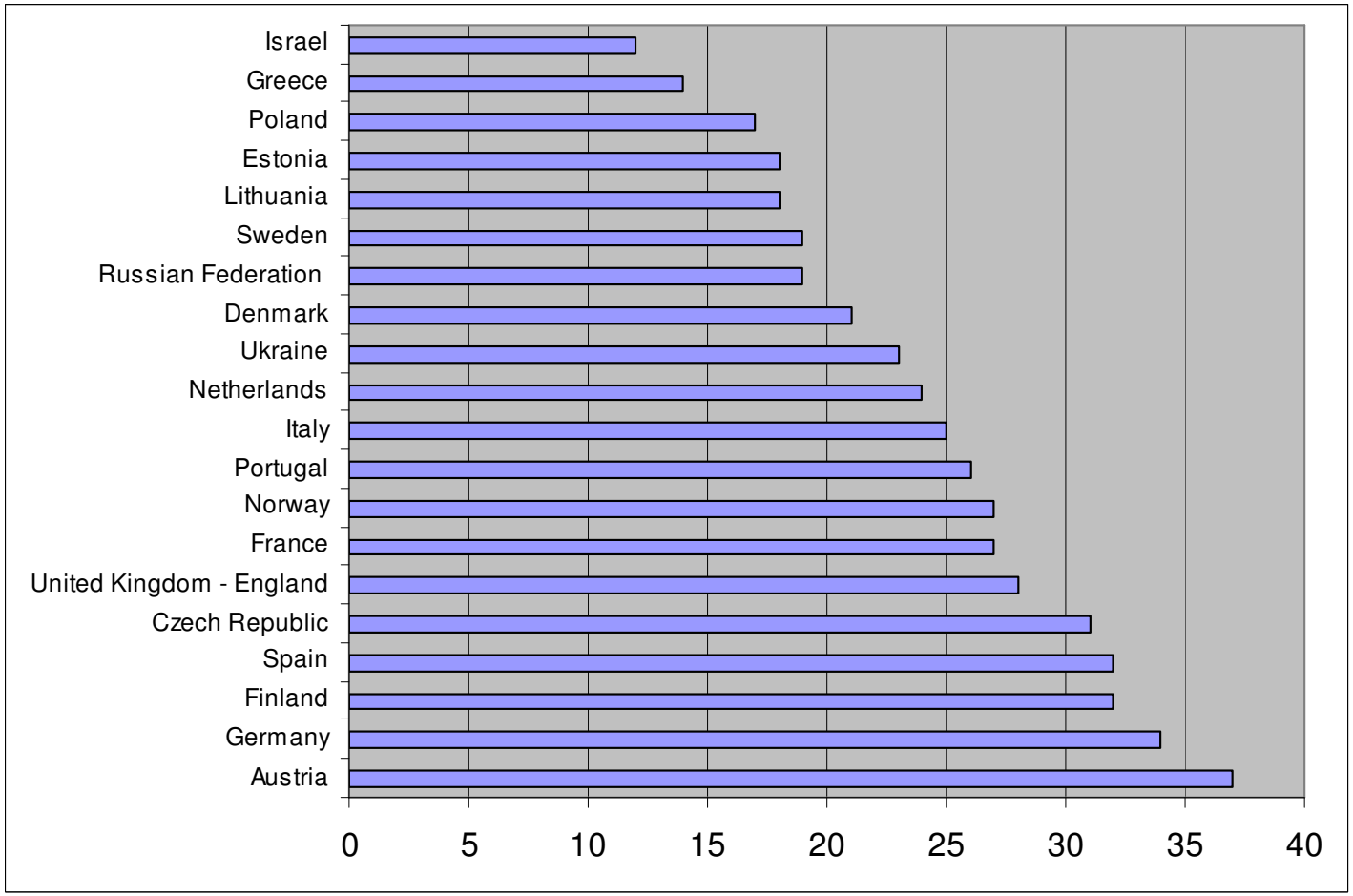
ESHRE CAMPUS WORKSHOP LISBON October 8-10 2010



Focus on

- Tobacco smoking
- Alcoholic beverages
- Caffeine
- Obesity
- (Psychosocial stressors)
- (xenobiotics in the diet)
- (Recreational drugs)

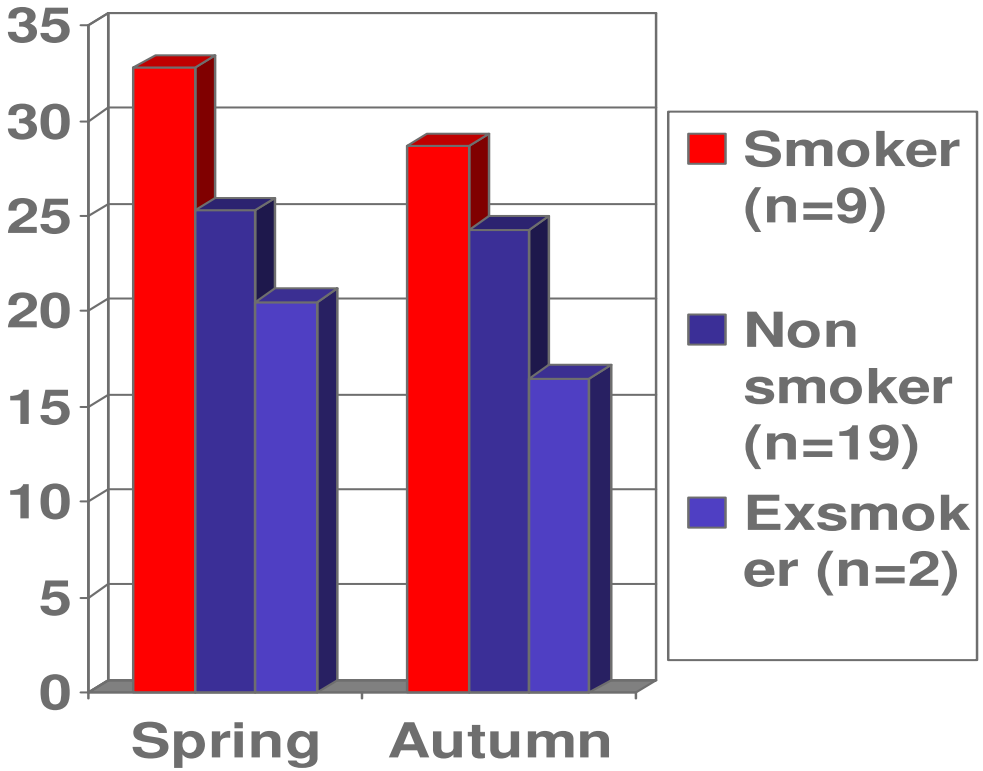
Smoking prevalence among women in Europe 2000-2001 (WHO 2002)



Reproductive toxicity of tobacco smoking in healthy adults

- **WOMEN:**
  - **Couple fecundability (probability of conception) reduced by 20-30% if the woman smoke (Bolumar et al Am J Epidemiol 1996)**
- **MEN:**
  - **No effect on fecundability (Bolumar)**
  - **Minor reduction of sperm counts (in average 10-20%), Vine et al Fertil Steril 1996)**

Average number of sperm cells with aneuploid chromosomes 1 and 7 (per 10.000 spermatozoa) in Danish Farmers



Harkonen et al 1999

- Other evidence:
  - Rubes 1998: disomy Y
  - Robbins 1997: XX18 aneuploidy
- Importance?
  - no selection against genetic abnormal sperm in mice

Effect of smoking on IVF endpoints: Comprehensive review by Klonoff-Cohen Hum Reprod Update 2005: 180-204

- **Smoking women have:**
  - Longer follicular phase
  - Fewer apsirated oocytes
  - Lower follicular levels of estradiol
  - Lower fertilization rate
  - Fewer embryos
  - Reduced pregnancy rate
  - Higher rate of fetal loss
  - Higher rate of low birth weight
- **Smoking men have:**
  - Reduced pregnancy rate?

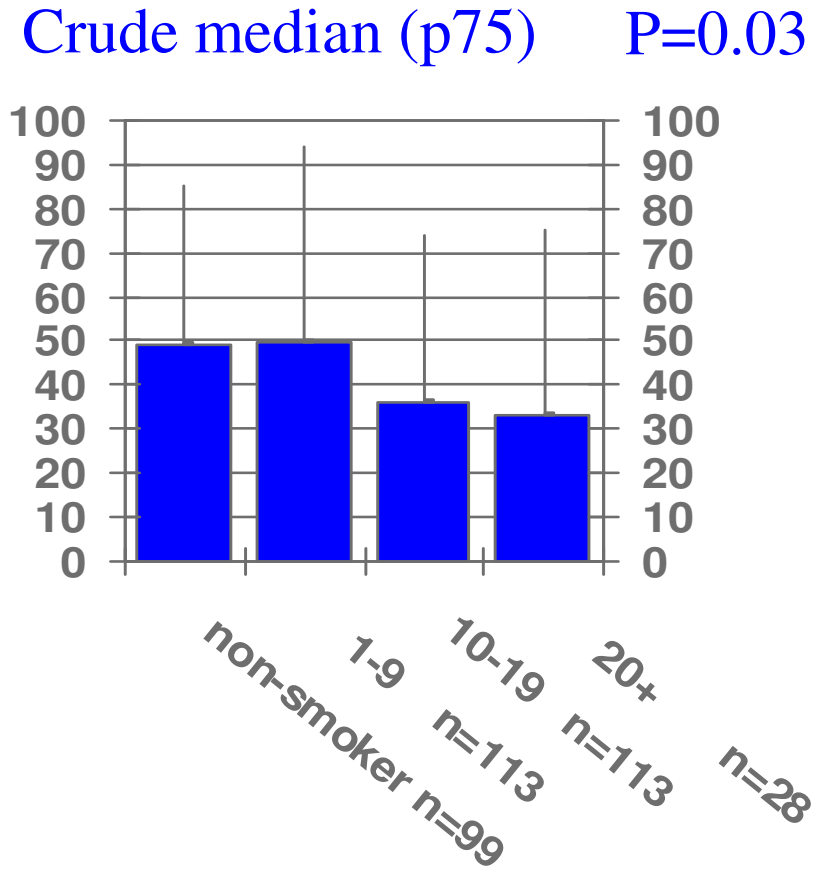
Studies on semen quality in sons of smoking mothers

Jennifer Ratcliffe et al 1992	semen quality, DES trial	–
Storgaard et al 2003	semen in twins	+
TK Jensen et al 2004	semen, military conscripts	+
MS Jensen et al 2005	semen, occupational studies	+

Design of the most recent study by Ramlau-Hansen et al

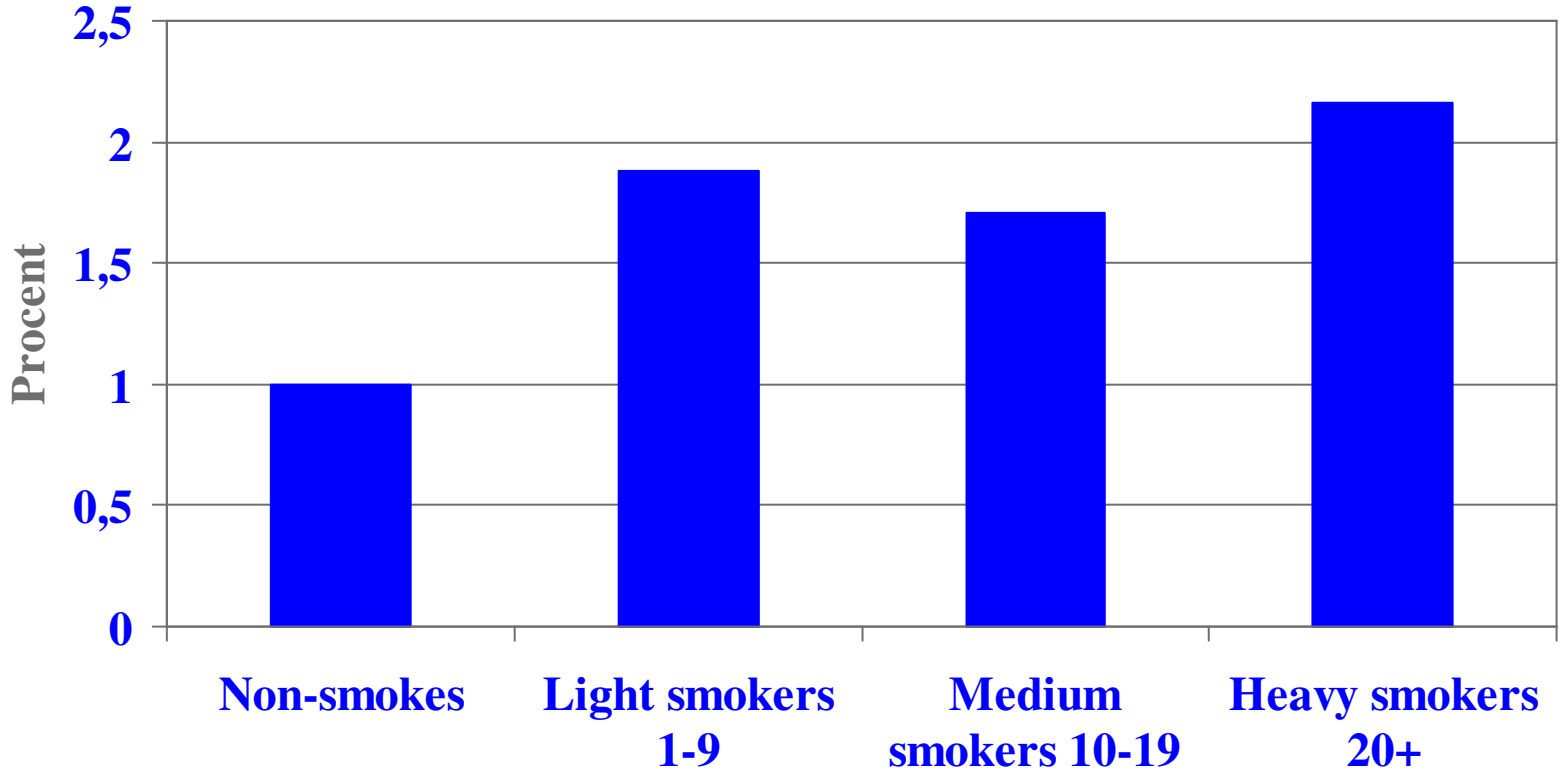
- Follow-up of 11,980 pregnant women enrolled 1984-87
- Sons were recruited to obtain a balanced distribution across maternal pregnancy smoking categories
- In all 347 sons among 716 invited were enrolled (49%)

Sperm concentration (mill/ml) in sons 18-20 years of age according to maternal smoking during pregnancy

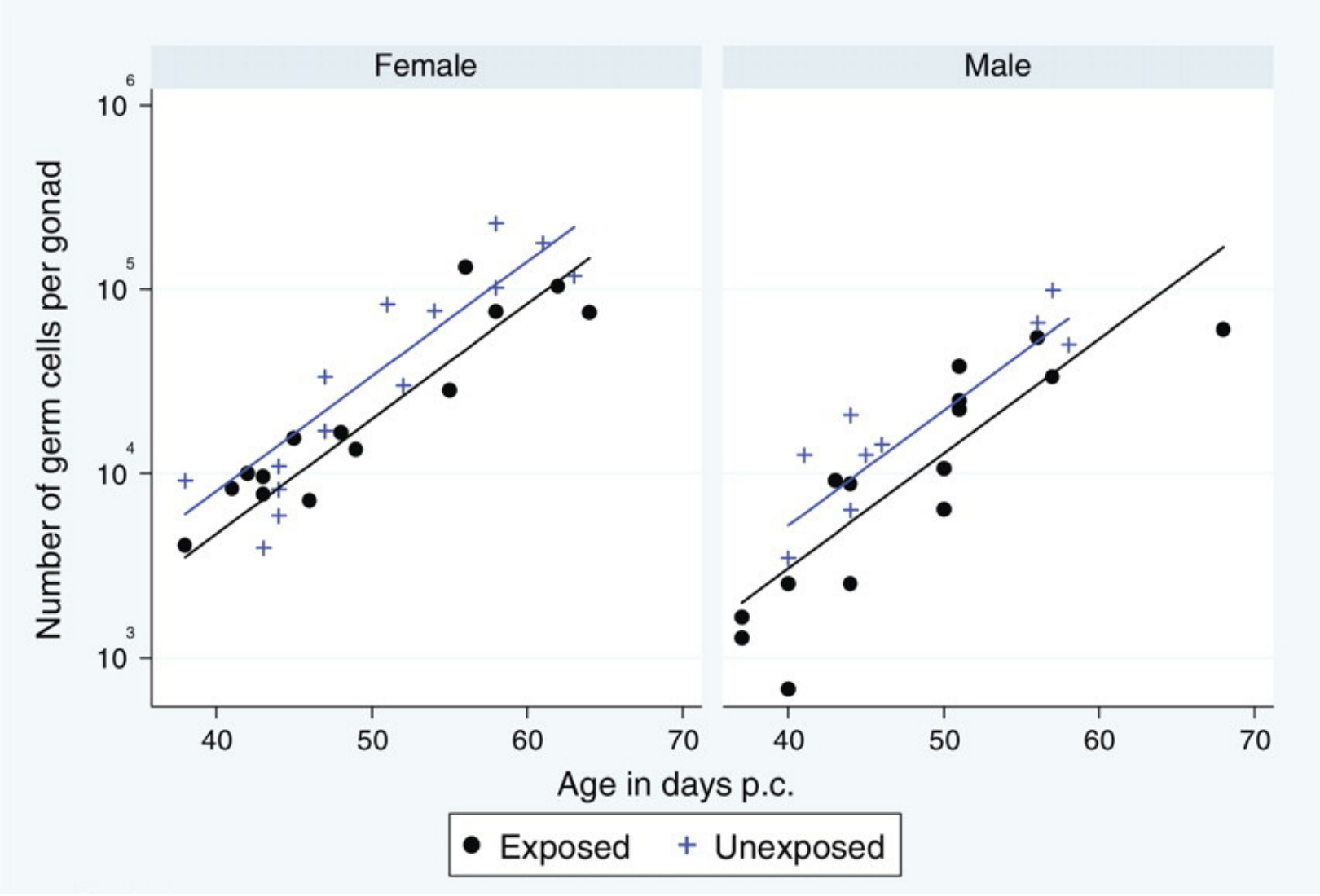


Ramlau-Hansen et al: Am J Epidemiol. 2007 65(12):1372-9.

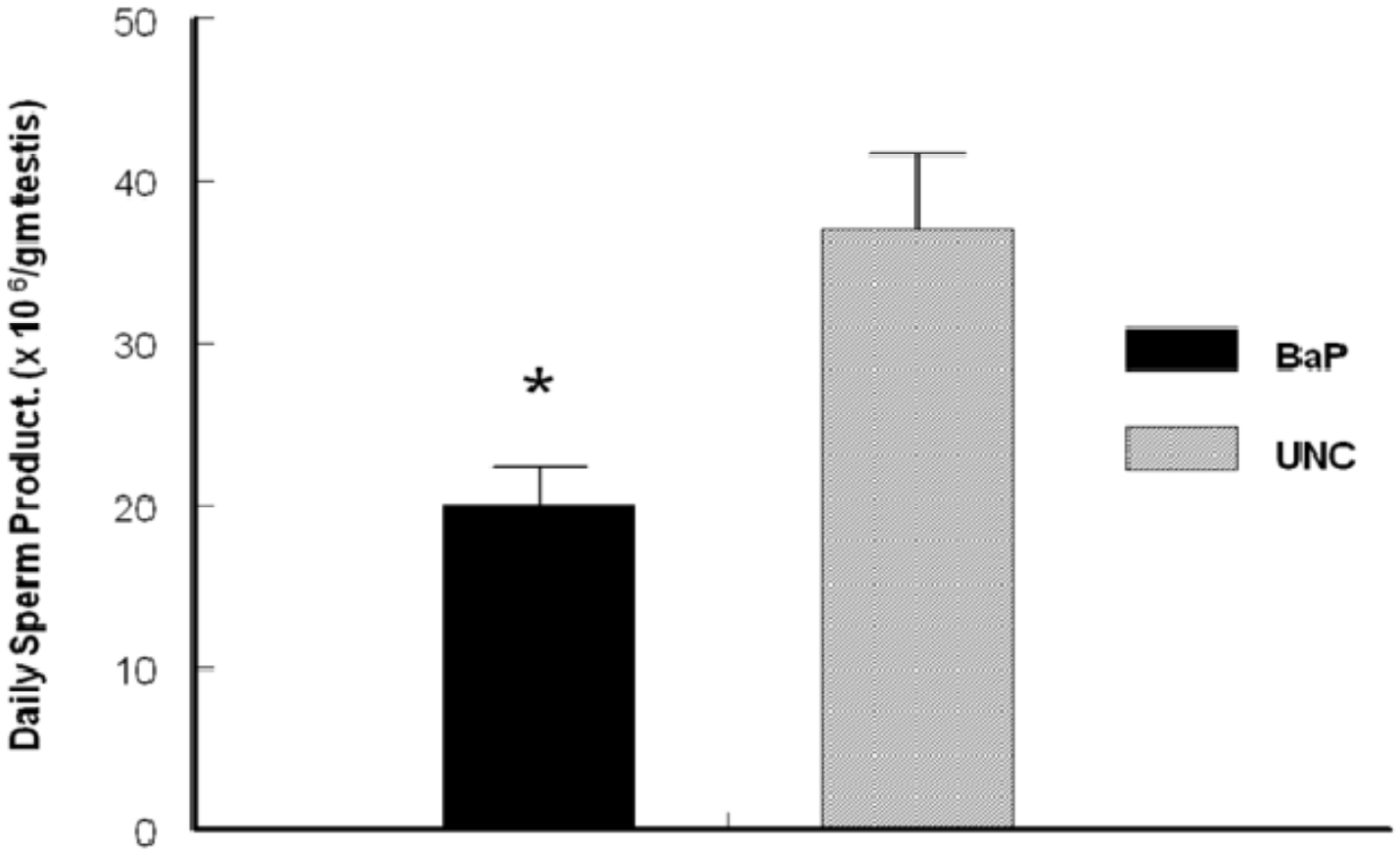
Odds risk ratio for oligospermia with non-smoking as reference



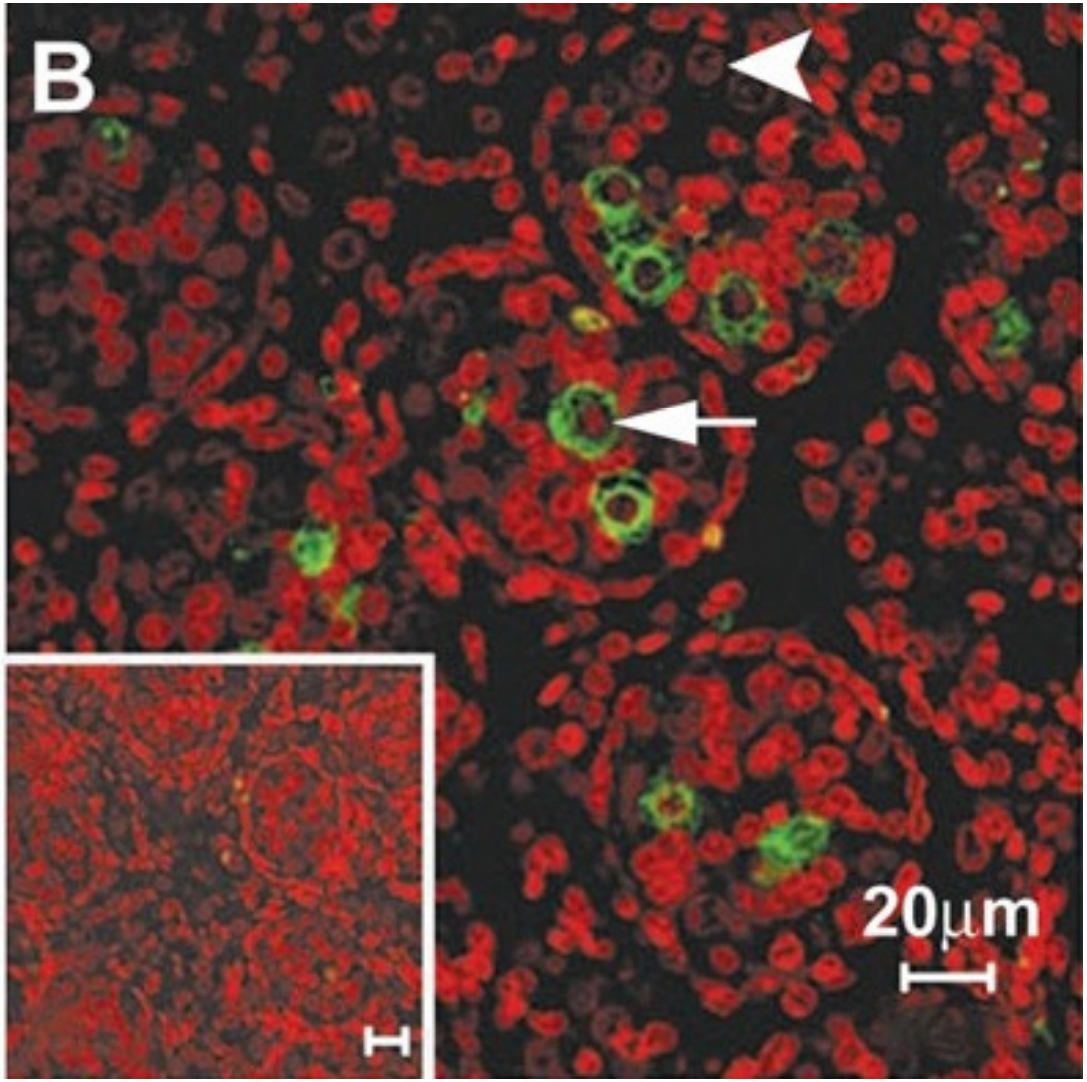
Cigarette smoking during early pregnancy reduces the number of embryonic germ and somatic cells. Mamsen LS et al Human Reprod 2010



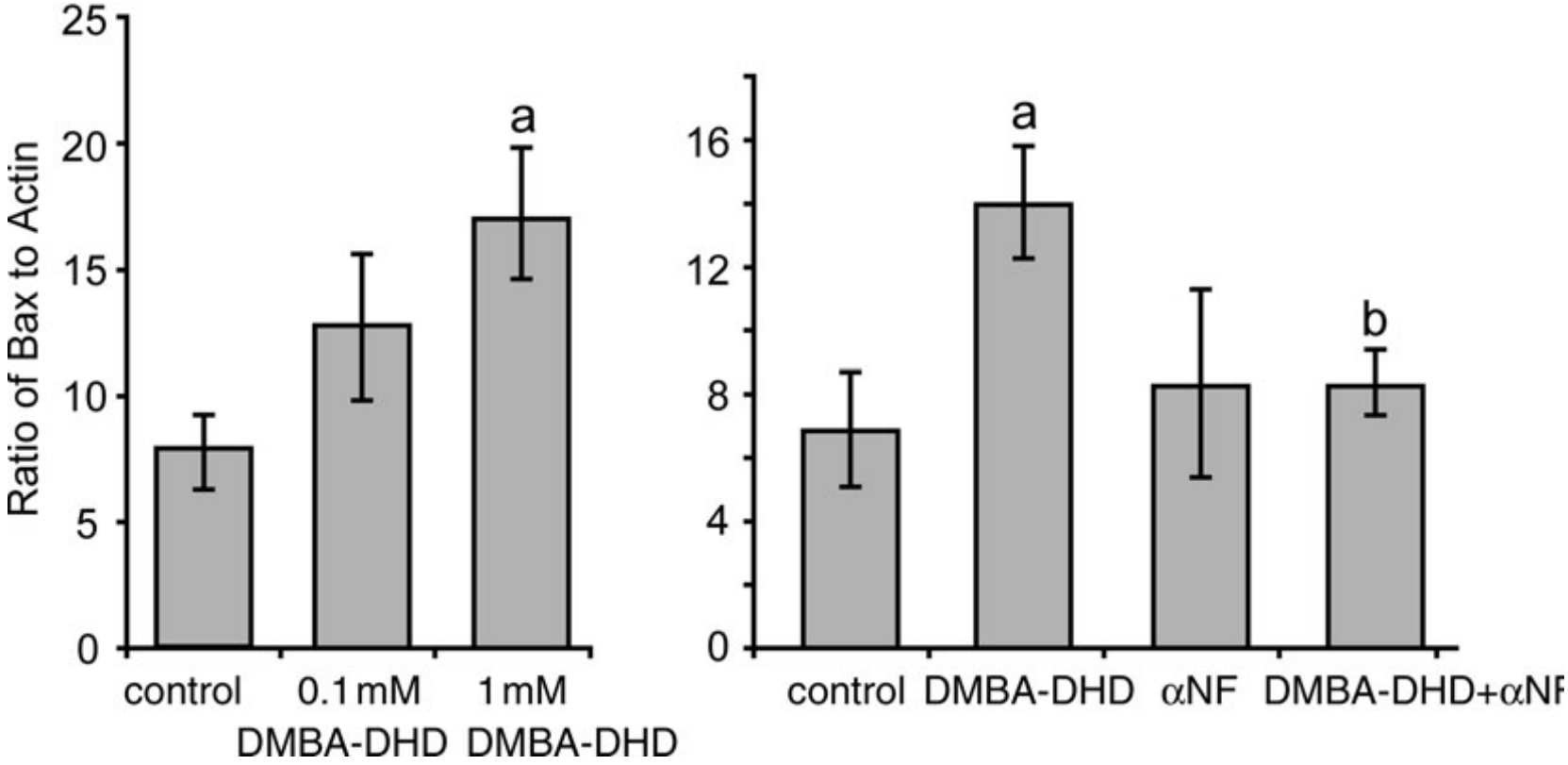
Effect of inhaled BaP on daily sperm production per gram of testis in F-344 male rats exposed to 75 µg BaP/m3 for 60 days. Ramesh A et al Exp Tox Pathol 2008 269-80



Expression of AhR in fetal germ cells. Coutts SM et all Human Reprod 2007



The AHR agonist DMBA-DHD increases expression of a pro-apoptotic marker as BAX. Coutts SM et al Hum Reprod 2007



Smoking

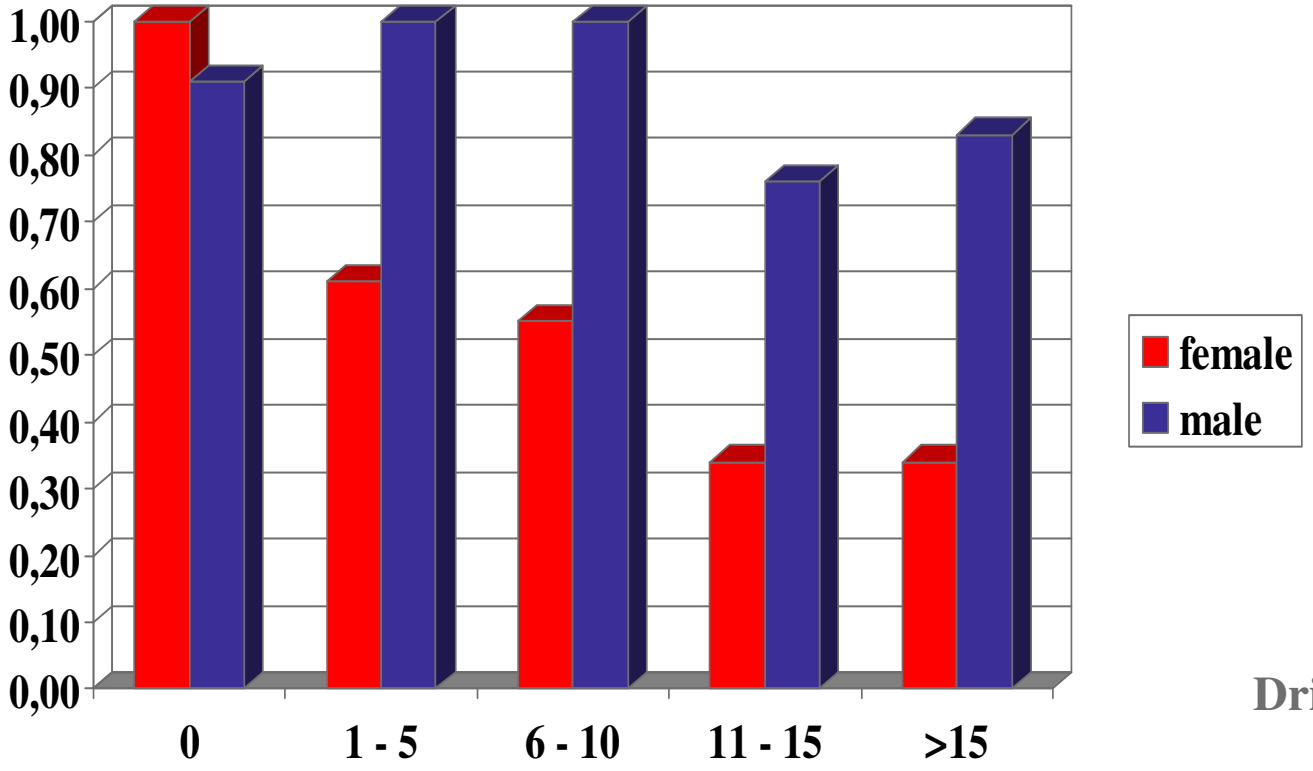
- Detrimental to IVF endpoints
- Consistent but limited epi-evidence that *in-utero* exposure is causing to reduced sperm counts in sons
- Is related to fewer germ cells in fetal gonads
- Mechanism: upregulation of AhR in fetal germ cells by PAH may increase cell loss by programmed cell death (apothosis)?

Effect of maternal ALCOHOL on IVF endpoints: Klonoff-Cohen et al Fertil Steril 2003

- Decreased oocyte retrieval
- Decreased pregnancy rate
- Increased risk of miscarriage

- **Insufficient evidence**
- **Spindle apparatus failure?**
- **Impaired implantation?**

Fecundability odds ratio according to intake of alcoholic beverages during mid menstrual cycle in a prospective study of first pregnancy planners



T Kold Jensen et al. BMJ 1998

Findings not corroborated:

Low intake of alcoholic beverages were not related to delayed time to conception in the Danish National Birth Cohort

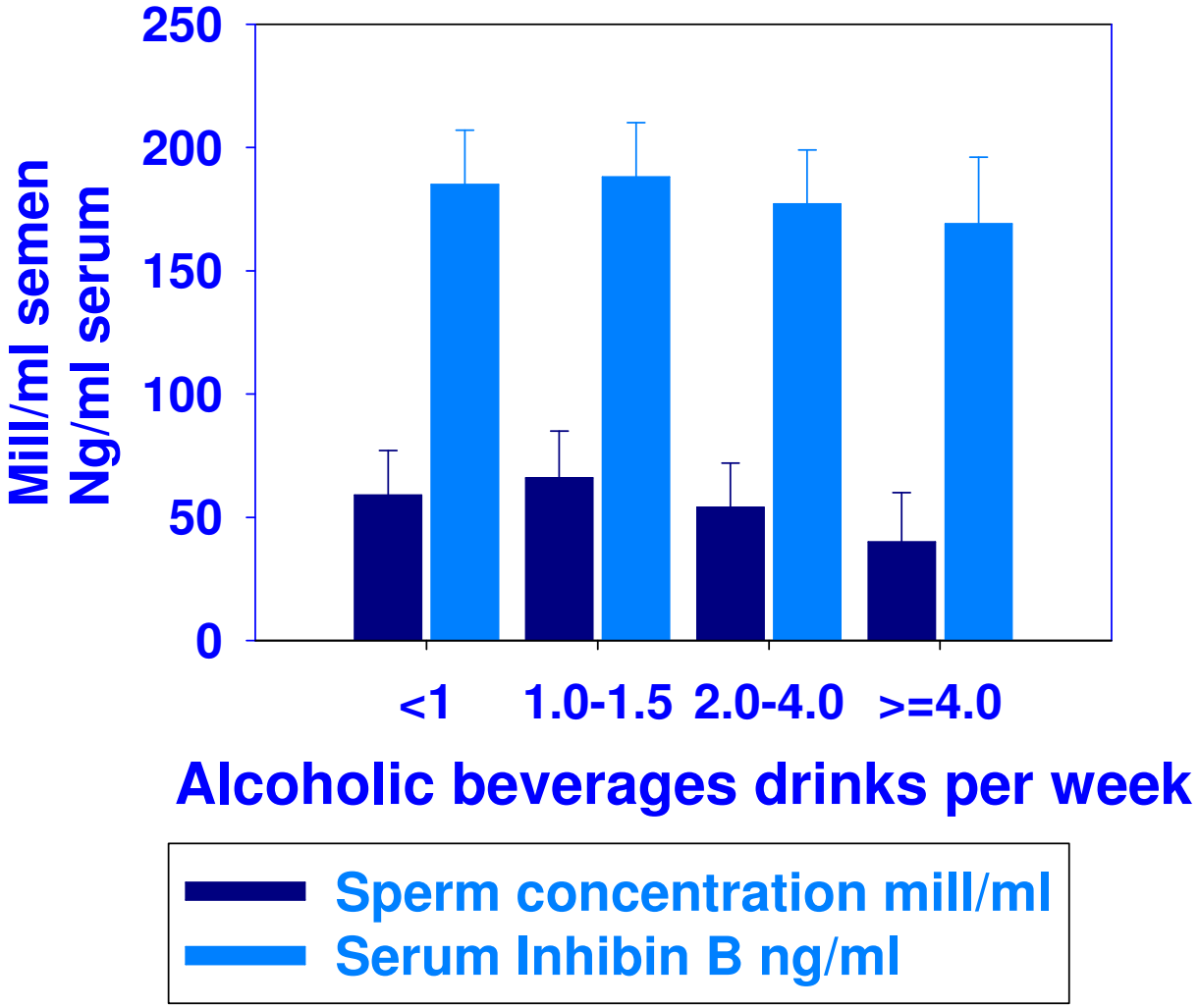
(Juhl M al Hum Reprod. 2001: 2705-9) :

n = 39612

inaccurate recall?

time specificity?

Male reproductive effects of maternal alcohol intake during pregnancy.
Ramlau-Hansen et al. Human Reproduction 2010: 1–6



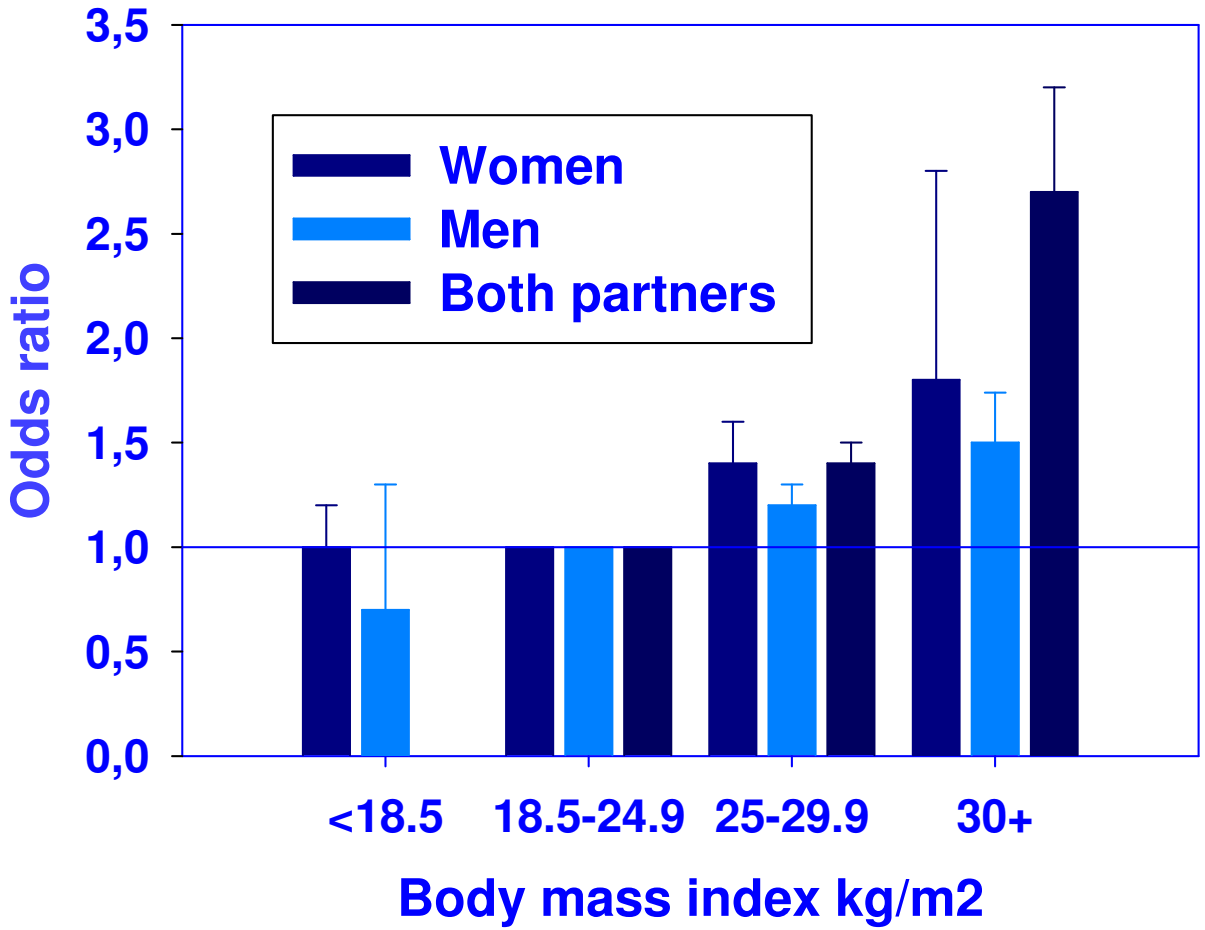
Effects of maternal CAFFEINE on IVF endpoints: Klonoff-Cohen et al Hum Reprod 2002

- Increased rate of miscarriage

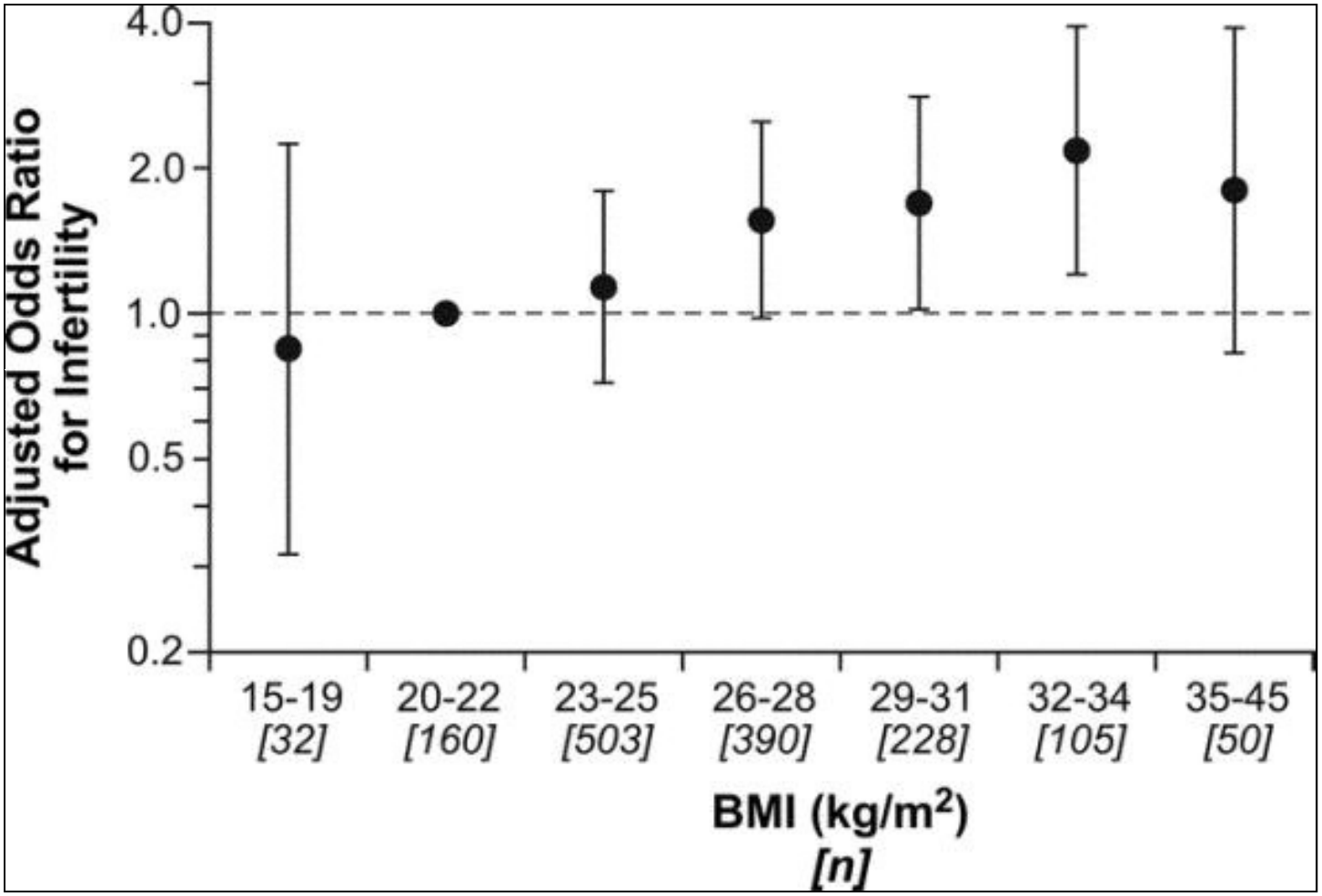
- **Insufficient evidence**
- **Hormonal disruption? (anti-estrogenic effetcs)**

Subfecundity in obese men and women.

Ramlau-Hansen et al.Human Reproduction 2007;22:1634–37



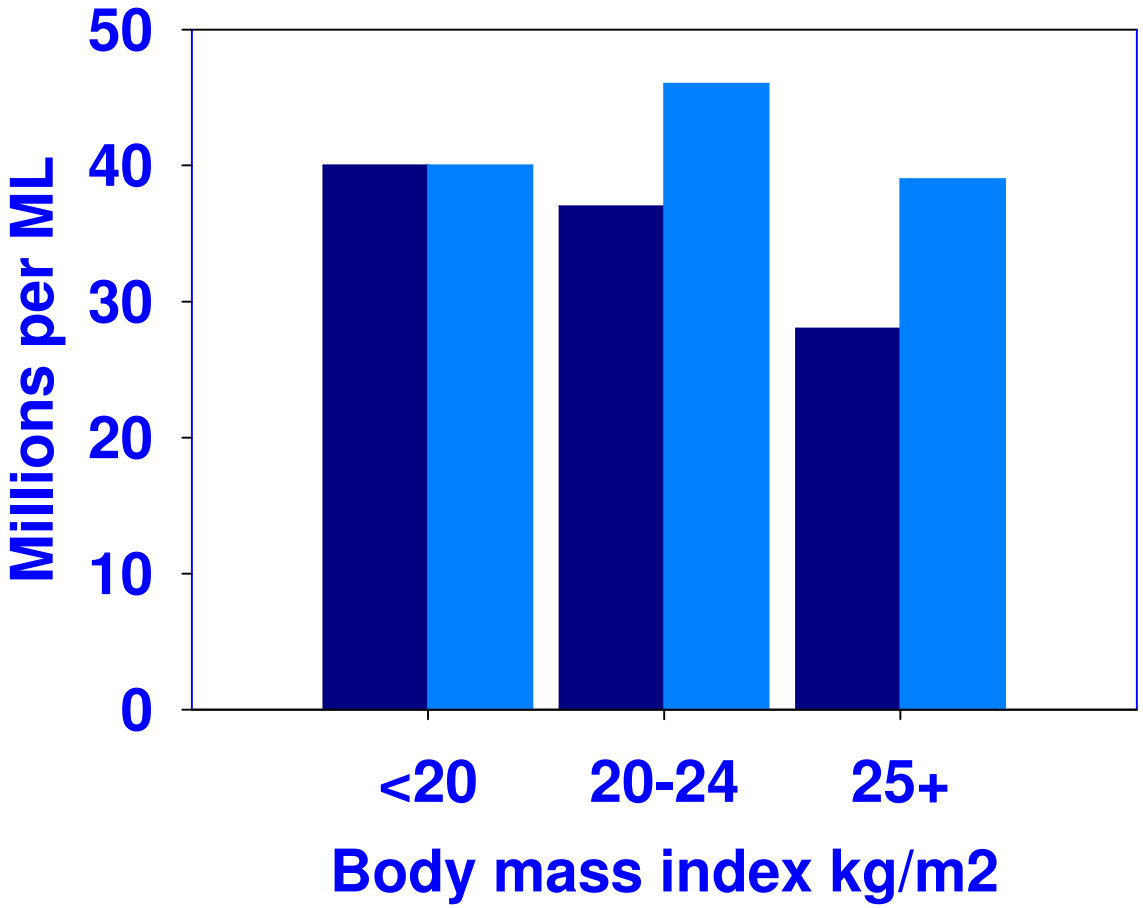
Reduced Fertility Among Overweight and Obese Men.
Sallmen M et al Epidemiology. 2006;17: 520-523.



Is body mass index related to reduced semen quality?

- Jensen TK et al, Fertil Steril 2004: 20-25% reduced sperm count in overweight obese army conscripts
- Macdonald AA et al, Hum Reprod Update 2010: no evidence of an association between increased BMI and semen characteristics based upon five pooled studies

Crude sperm concentration according to body mass index



Adults:
Jensen TK et al
Fertil Steril 2004
Prenatal:
Ramlau-Hansen et a
Hum reprod 2007

Conclusion

- Some advances in the understanding of reproductive effects of life style factors
- Healthy life-style may have bearings for prevention of infertility and improved results of IVF treatments

Thank you for your attention!