

Lifestyle and infertility

Age, smoking, caffeine, alcohol
and male fertility

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Lifestyle and infertility

- Some definitions
- How big is the problem?
- Age and fertility
- Smoking
- Alcohol
- Caffeine
- Male fertility

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Some definitions

- **Infertility:**
 - No pregnancy after one year attempt
- **Fecundity:**
 - The capability to become pregnant and deliver
- **Fecundability:**
 - Pregnancy chance per cycle (mean: 20%)
- **Fecundability ratio:**
 - Pregnancy chance among exposed compared with non exposed

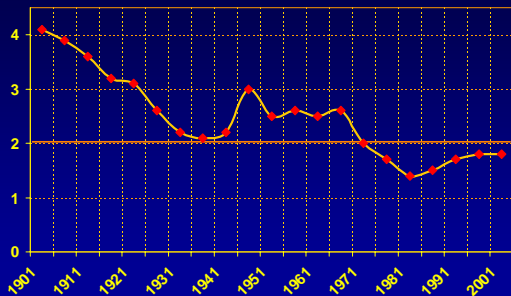
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Total fecundity rate in DK 1901-2001



Lisbeth B Knudsen, Fertility trends in DK in the 1980s
Danmarks Statistik online.

Li/03

Infertility: Prevalence

Infertility now: Women in fertile age: 10%

Infertility ever: Women in fertile age: 15%

Infertility life time risk: Couple: 25%

Seeking aid for infertility: 10%

No children despite wish at 50 years: 4%

Is the problem increasing? Yes. Because

- More infertile at a certain age
- Sooner seeking for aid among infertile
- Older age when pregnancy wish arises

Schmidt L. Hum reprod 1995; 10: 1407-18

Li/04

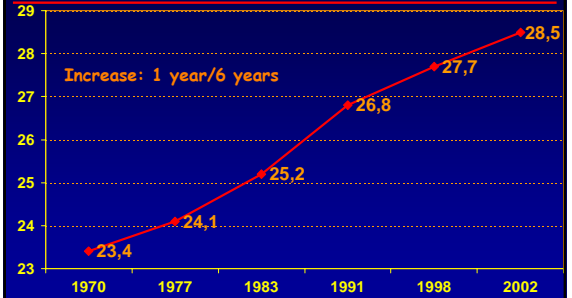
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Age at first birth Denmark 1970-2002



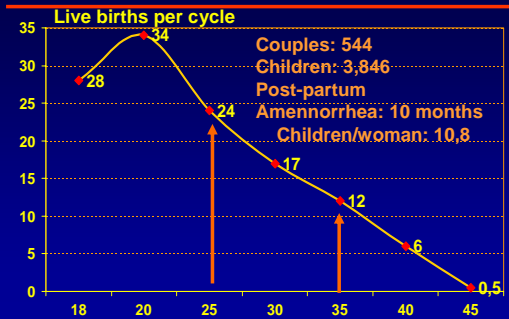
Knudsen LB. Fertility trends in DK in the 1980s og DK's Statistik Li/04

What is a woman, and what can you expect from her?

North & South Dakota to where the *Hutterites* immigrated at end of 19th century. Approx. 215 persons immigrated about 1870. In 1960 they were 5.450

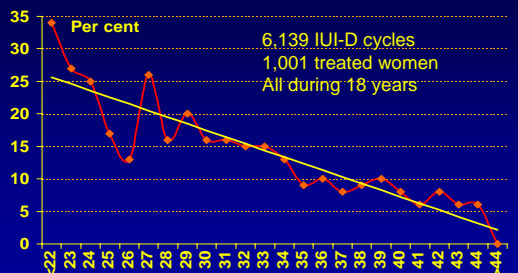
- No contraception allowed
- Children have high priority
- Socially comparable with other couples.
- Let's look at 544 couple, all married and all with at least one child to quantify womans fertility

Fecundity according to age



Larsen U et al. Social Biology 2000; 47: 34-50

Donor IUI. Pregnancies/100 cycles



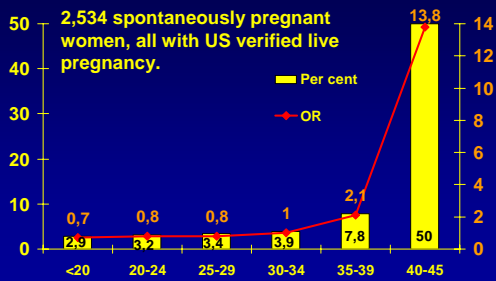
Botchan A et al. Hum Reprod 2001; 16: 2298-2304

Li/02

Why does fertility decrease by age?

- Egg's get older
- Increased risk of spontaneous abortion

Spontaneous fetal loss after living pregnancy week 12-24 (CH).



Hoesli et al. Am J Med Genet 2001; 100: 106-9 Li/02

Age and fertility: Conclusion

- The dramatic increase in age at first delivery through last three decades has increased the risk of infertility substantially
- This development is expected to continue over the next decades
- Age at first pregnancy wish is probably the most important life style factor in effect

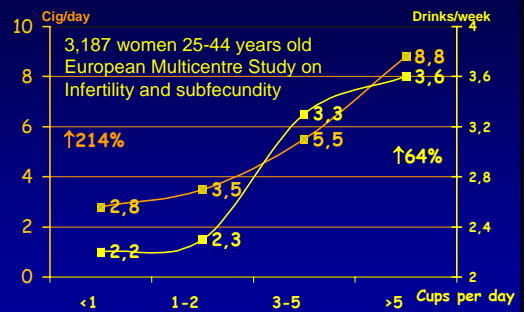
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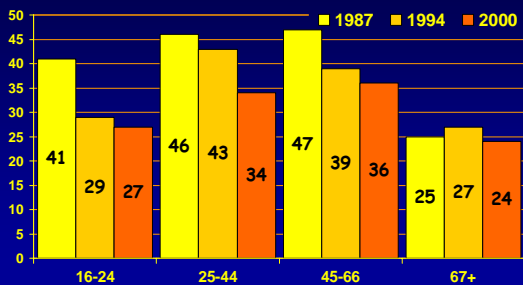
Naughty girls



Bolunar et al. Am J Epidemiology 1997; 145: 324-34. Li/04

Smoking in DK in 1987, 1994 & 2000

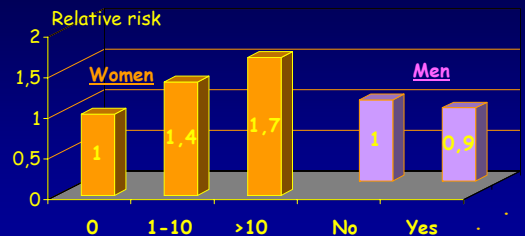
Women, N=8,494



Sundhed og Sygelighed i DK 2000. SIF 2002 Li/203

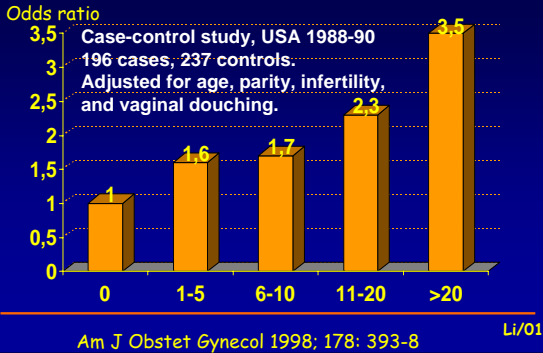
Fertility and smoking

Risk of waiting time >9,4 months



Bolunar et al. Am J Epidemiology 1996; 143: 578-87. Li/01
European multicenter study on infertility and subfecundity

Smoking and ectopic pregnancy



Smoking - IVF

	-smo	ex-smo	+smo
No	499	111	37
Ø2/FSU U	82	71	60
Oocytes	13.5	13.6	12.6
Fertilis. rate	54%	54%	50%
Embryos	8.0	8.2	6.6
Embr. transf	3.6	3.5	3.6
Implant. rate	16	16	6.7

Voorhis et al. Obstet Gynecol 1996; 8: 785-91

Li/01

IVF and smoking: Århus 2000-03

- Observational cohort study at Skejby
- Couples undergoing IVF or ICSI from January 2000 through December 2003
- **Confounders included:** Coffee, alcohol, BMI, length of infertility, previous pregn, cause of infertility
- **Outcomes:** oocytes retrieved, fertilisation rate, clinical pregnancy rate week 7 (US)

Rikke Krogh, Kesmodel & Ingerslev. Paper in preparation. Li/05

IVF and smoking: Results

OR (95% CI)	Oocytes retrieved	Fertilisation rate	Pregnancy rate
N=777			
Female			
- smoking	1	1	1
+ smoking	1.0 (0.7-1.5)	1.2 (0.8-1.7)	1.0 (0.7-1.4)
Male			
- smoking	1	1	1
+ smoking	1.0 (0.7-1.5)	1.0 (0.7-1.4)	1.2 (0.8-1.7)

Conclusion: No effect of smoking on IVF

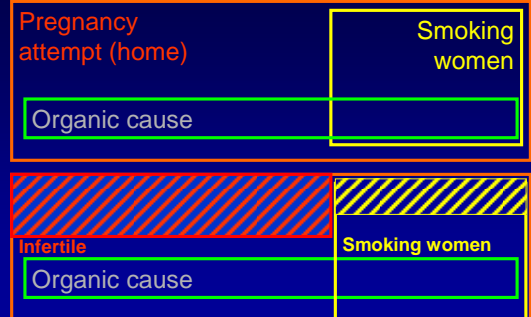
Rikke Krogh, Kesmodel & Ingerslev. Paper in preparation. Li/05

Smoking: Selection bias



Li/05

Smoking: Selection bias

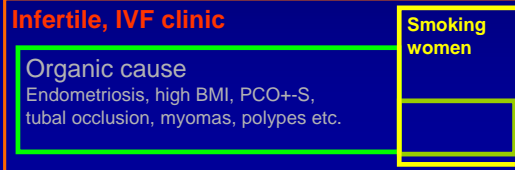


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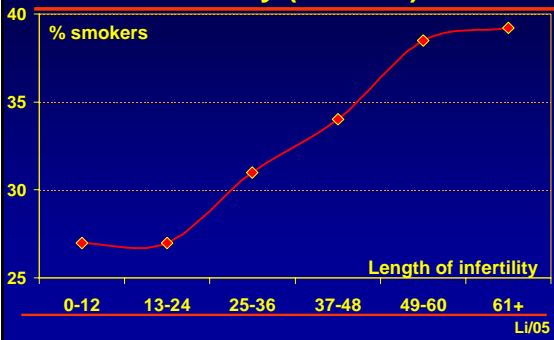
Smoking: Selection bias



Smoking: Selection bias



Smokers (%) according to length of infertility (months)



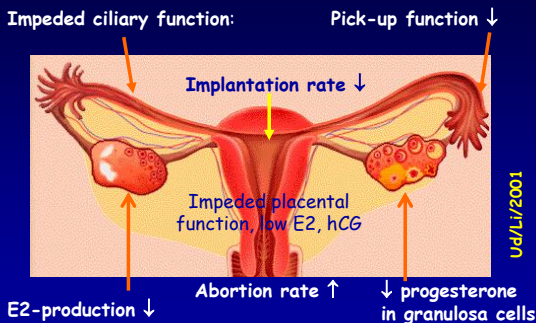
Smoking: Selection bias

Diagnosis	% smokers
All women (n=1,441)	32%
Anovulation	18%
Endometriosis	20%
Other	25%
Idiopathic	28%
Male factor	32%
Tubal factor (22%)	44%

Rikke Krogh, Kesmodel & Ingerslev. Paper in preparation.

Li/05

Smoking and fertility



Shiverick et al: Placenta, 1999; 20: 265-72

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Alcohol and fertility

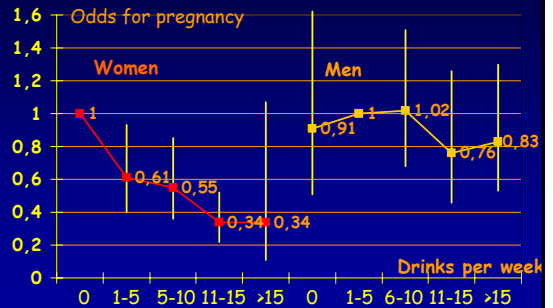
Does small amounts of alcohol have an impact on natural fertility?

- Only few studies
- Danish prospective study 1992-94 with 430 couples, 20-35 years, trying to become pregnant for the first time
- Alcohol intake was recorded in detail through 6 cycles
- Control for smoking, BMI, and semen count

Jensen et al. *BMJ* 1998; 317: 505-10

Fertility and alcohol

Fecundability odds, 95% CI



Jensen TK et al. *BMJ* 1998; 317: 505-10.

Alcohol and time to pregnancy

Cross sectional study DK 1997-2000 including 39,612 pregnant women (Danish birth cohort). 29,933 planned pregnancies included.

Included: 60% of invited = 1/3 of all pregnant.

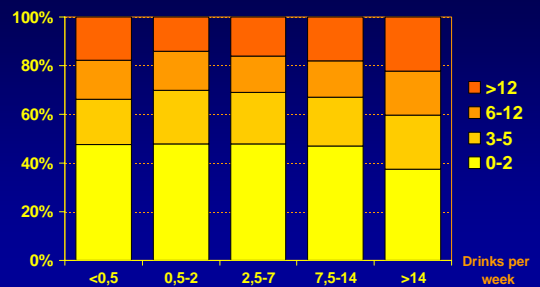
Asked about alcohol habits before pregnancy, which was correlated to time to pregnancy.

Included confounders: Smoking (in pregnancy), BMI, parity and age.

Outcome measure: Subfecundity odds ratio

Juhl M et al. *Human reprod* 2002; 16: 2705-9. Li/O2

Waiting time to pregnancy in months and drinks per week

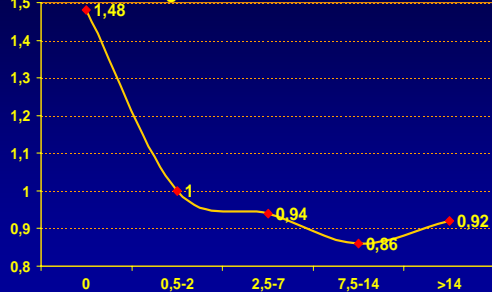


Confounders: Age, Smoking, BMI, parity

Li/O2

Subfecundity OR and drinks per week

Risk of waiting time >12 months

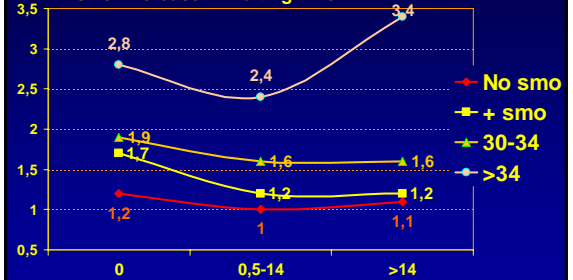


Juhl M, et al. *Human Reprod* 2002; 16: 2705-9

Li/O2

Time to pregnancy, age, alcohol & smoking

Risk of increase in waiting time



Li/O2

Alcohol and pregnancy

- The birth cohort of Århus, 1989-96 with 25.000 pregnant women and their deliveries demonstrates that 5 drinks per week as compared with no alcohol =>
- 2,5 x increased risk of stillbirth
- 3 x increased risk of abortion w 7-12
- Increased risk of premature birth
- Increased risk of low birth weight

Kesmodel U. Am J Epidemiol 2002; 155: 305-12
Kesmodel U. Alcohol Alcohol 2002; 37: 87-92

Li/03

Alcohol and fertility

Clinical recommendation:

Women who attempt pregnancy should reduce their alcohol intake to less than five drinks per week.

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Caffeine

Caffeine is found in

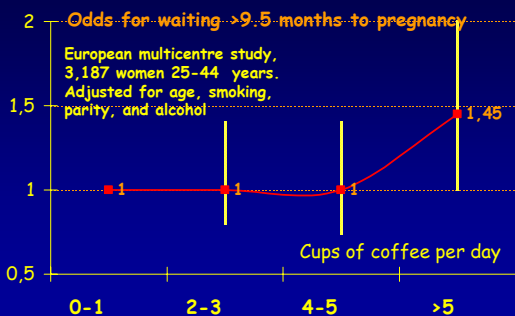
- 1 cup of coffee = 100 mg
- 1 cup of tee = 50 mg
- ½ litre cola = 50 mg
- 30 g chocolade = 10 mg
- 1 cup of cacao = 5 mg
- Caffeine passes all biological membranes incl. the placenta barrier

Jensen et al. BMJ; 1998: 505-10

Li/01

Fertility and coffee

Fecundability odds, 95% CI



Bolúmar et al. Am J Epidemiol 1997; 145: 324-34

Li/01

Caffeine and fertility: Conclusion

- Less than five cups of coffee per day has no influence on fertility
- Women attempting to be pregnant should drink less than five cups of coffee per day

Li/05

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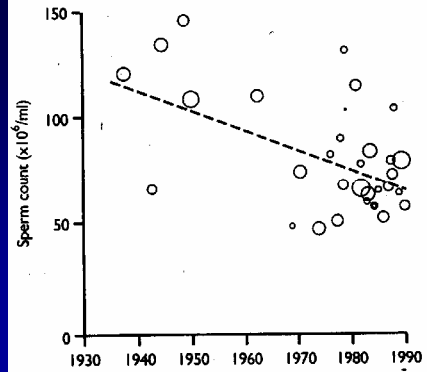
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Sperm count by time

61 papers
14,947 men

Carlsen et al. BMJ 1992; 305: 609-13



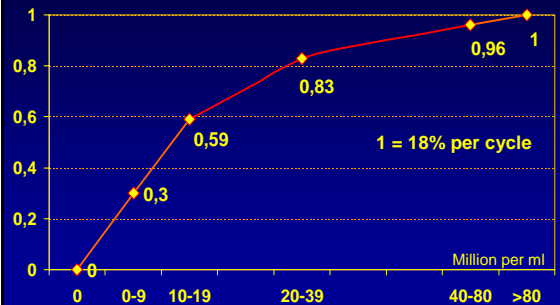
Sperm count and fecundity

- 430 couples with first pregnancy wish
- Followed through 6 menstrual cycles
- Delivering a sperm sample at enrolment
- Information about smoking habits, age of woman, occupation of women, urogenital disorders, BMI, and woman's smoking habits
- Outcome: pregnancy chance per cycle

Bonde JPE et al. Lancet 1998; 352: 1172-7.

Li/05

Sperm count and fecundity



Bonde et al. Lancet 1998; 352: 1172-7.

Li/05

Sperm count in Danish men

- 1.868 men, 18-22 years old, median 19 years
- Military session, 1996-2001
- Delivering a sperm sample
- Abstinence for 48 hours
- Median sperm count: 46 mio/ml (41-51)
- Sperm count **<40 mio/ml: 44% (-17%)**
- Sperm count **<20 mio/ml: 22% (-41%)**

Jørgensen et al. Månedsskr Prakt Lægegerm 2003; 81: 169-75

Sperm count in Nordic-Baltic area

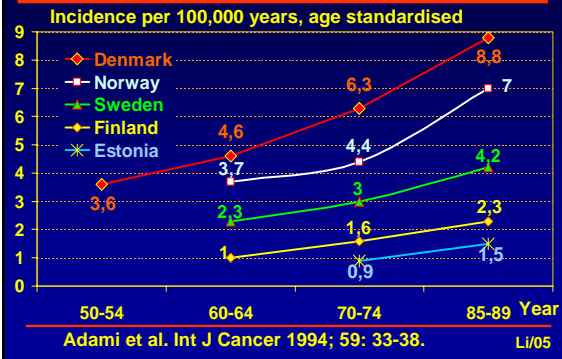
	Norway	Denm	Finland	Estonia
Particip.	240	300	324	104
Period	1998	97-99	98-00	97-99
Sperm count in mio/ml (median)				
All	41	41	54	57
Clean	42	45	53	63

West-east gradient

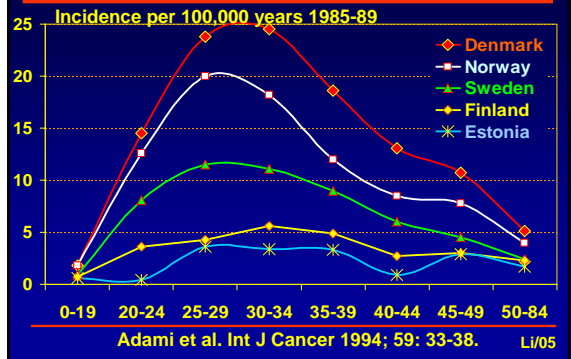
Jørgensen et al: Hum Reprod 2002; 8: 2199-2208

Li/05

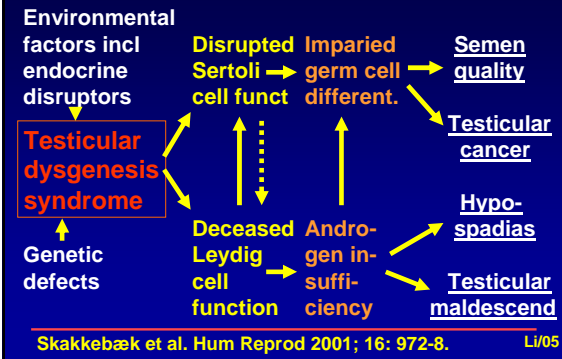
Testicular cancer: west-east gradient



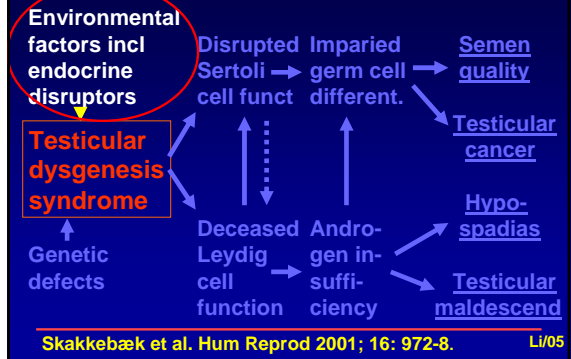
Testicular cancer according to age



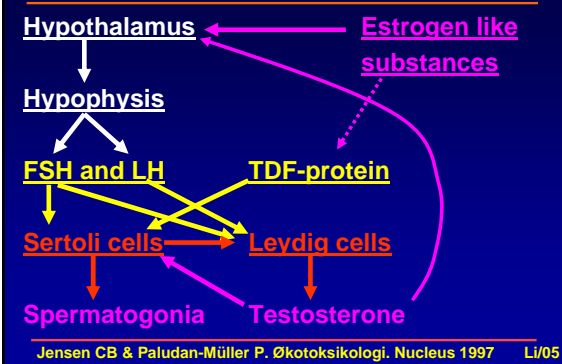
Testicular dysgenesis syndrome



Testicular dysgenesis syndrome



Male gonadogenesis



Male fertility

- Pregnant women are exposed to endocrine disruptors affecting the fertility of their male offspring lifelong.
- The most urgent task concerning infertility is to identify the environmental factors, responsible for the decreasing sperm count in men
- The west-east gradient in the Baltic area is a good starting point for this research