

Infertilitets epidemiologi

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U-kursus

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Infertilitet epidemiologi

- **Definitioner**
- **Problemetets størrelse**
- **Alder og fertilitet**
- **Rygning**
- **Alkohol**
- **Kaffe**
- **Overvægt**
- **Mandlig fertilitet**

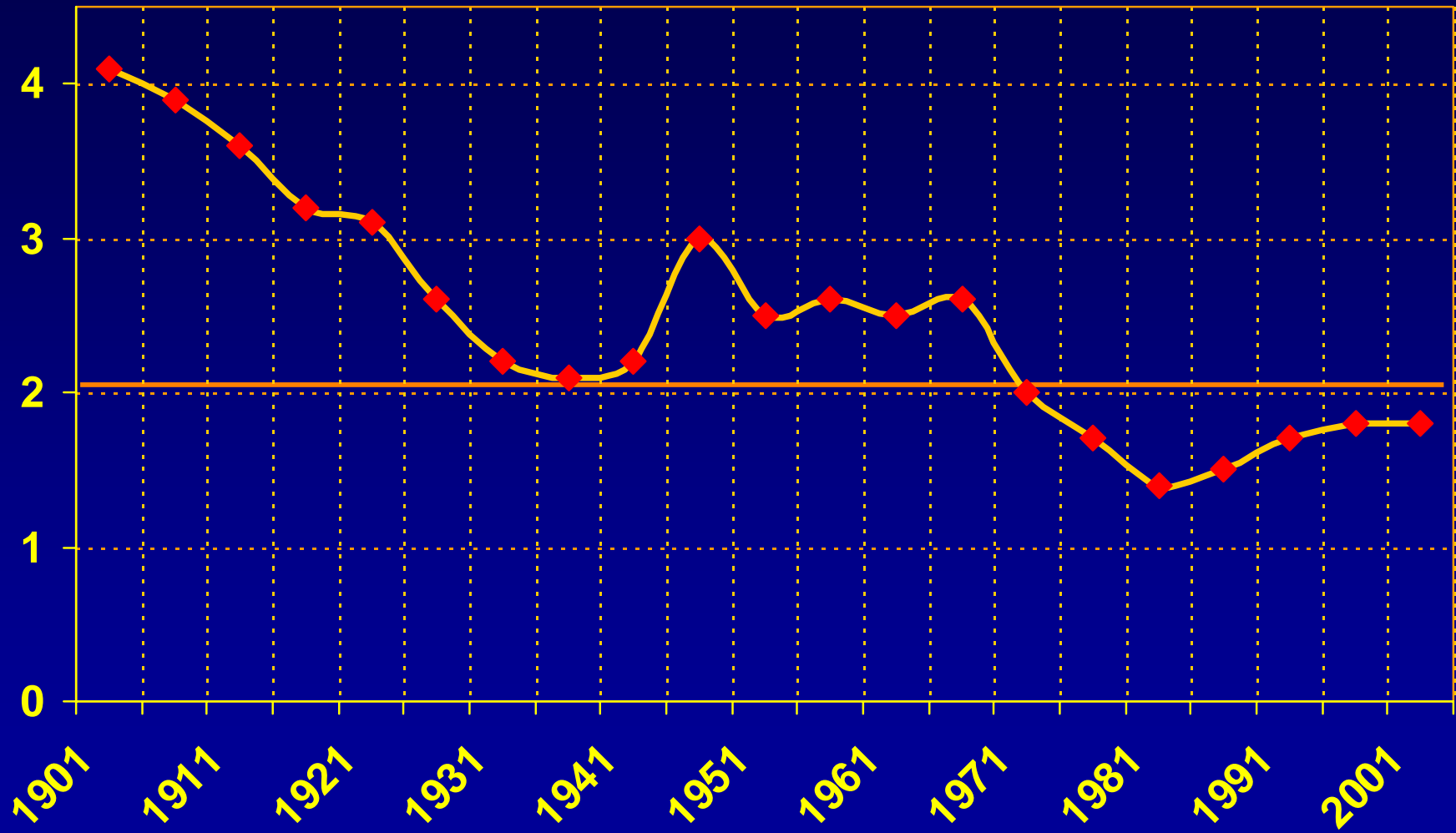
Nogle definitioner

- **Infertilitet:**
 - Ikke gravid efter 1 år (i DK 15%)
 - **Fecunditet:**
 - Evnen til at blive gravid og føde
 - **Fecundabilitet:**
 - Graviditeter pr. cyklus (raske 20%)
 - **Fecundabilitetsratio:**
 - Graviditetschance hos eksponerede i forhold til graviditetschance blandt ikke eksponerede
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Infertilitet epidemiologi

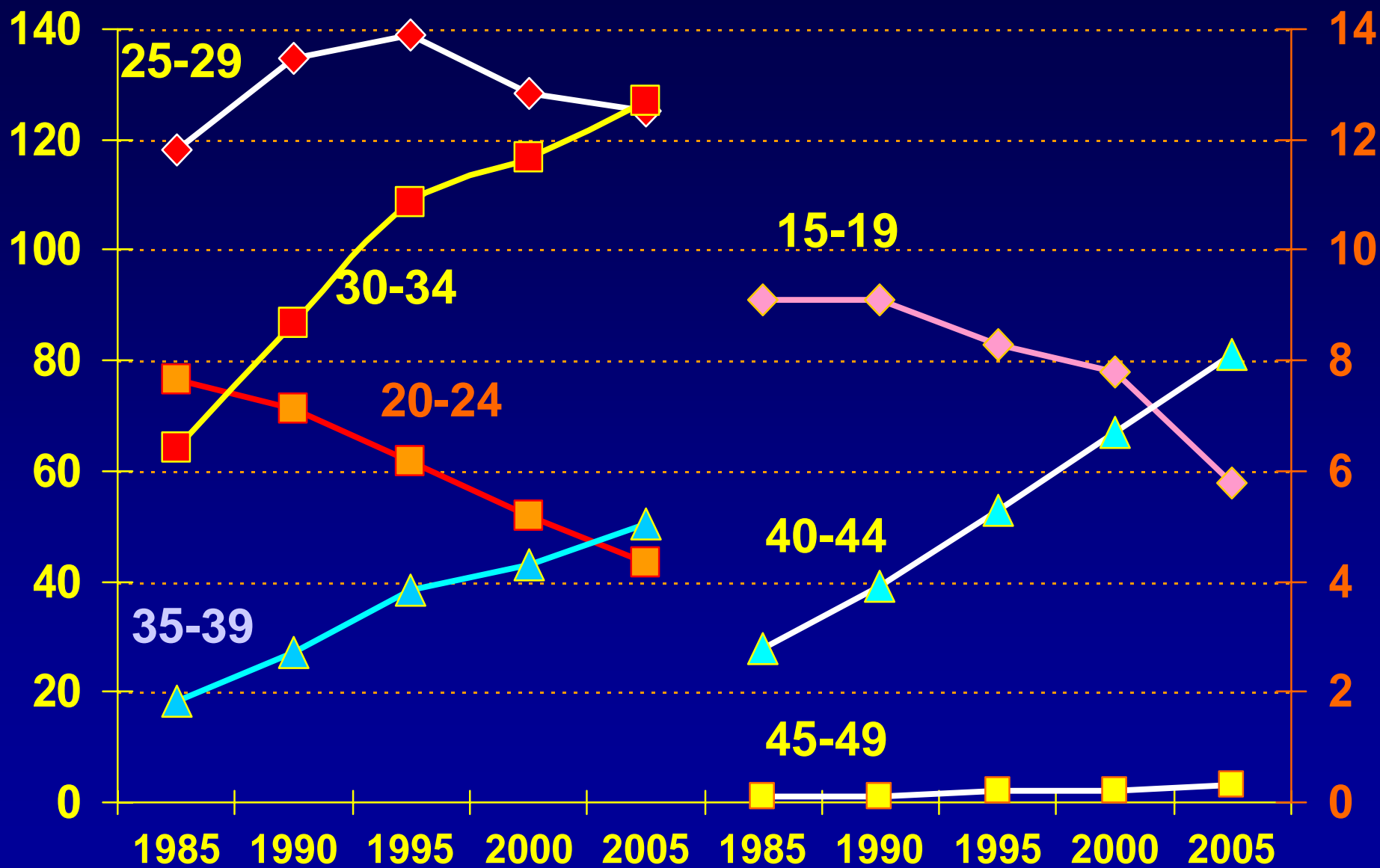
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Total fecundity rate in DK 1901-2007

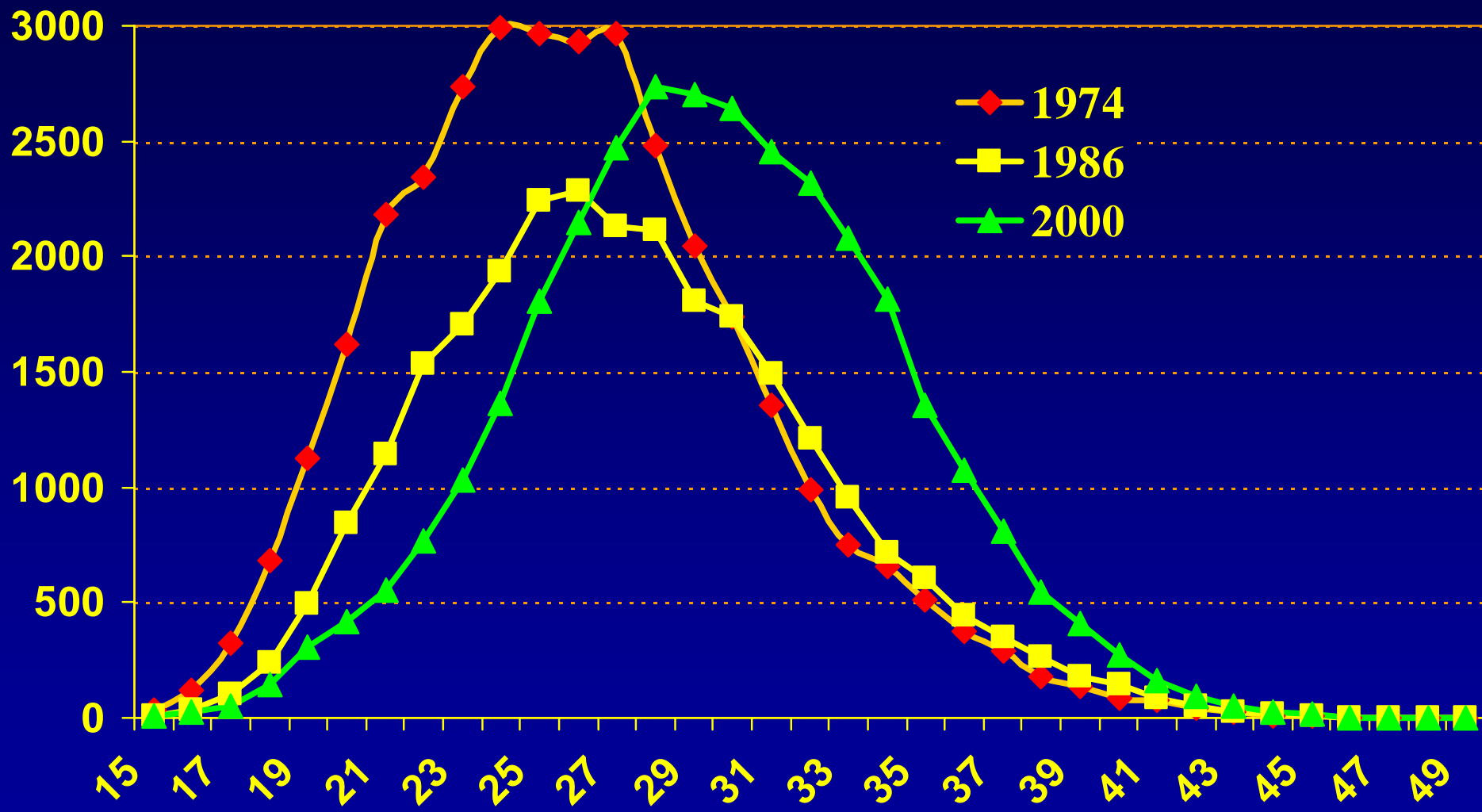


Lisbeth B Knudsen, Fertility trends in DK in the 1980s
Danmarks Statistik online: www.dst.dk

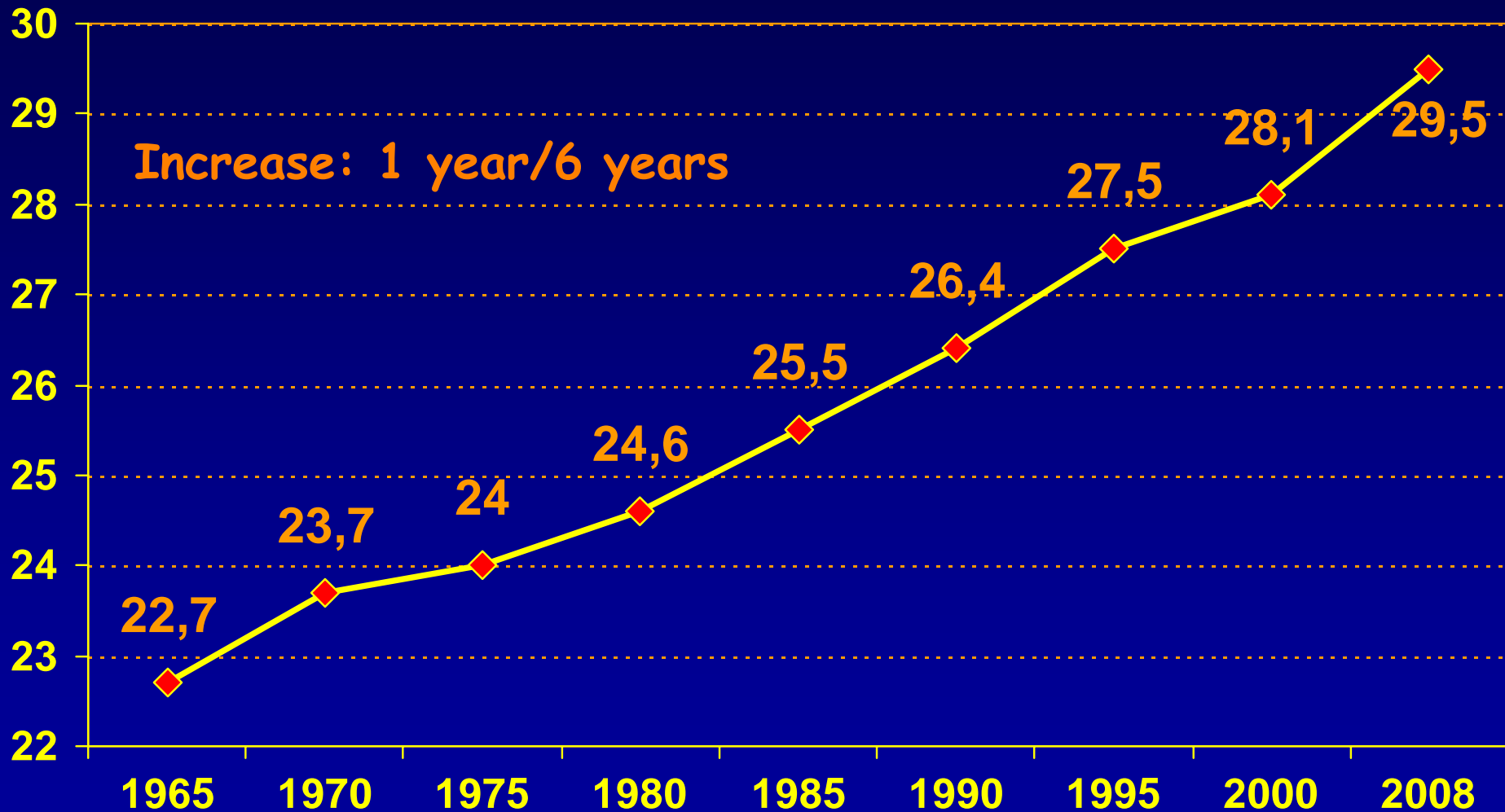
Fertility rates per 1,000 in DK 1985-2005



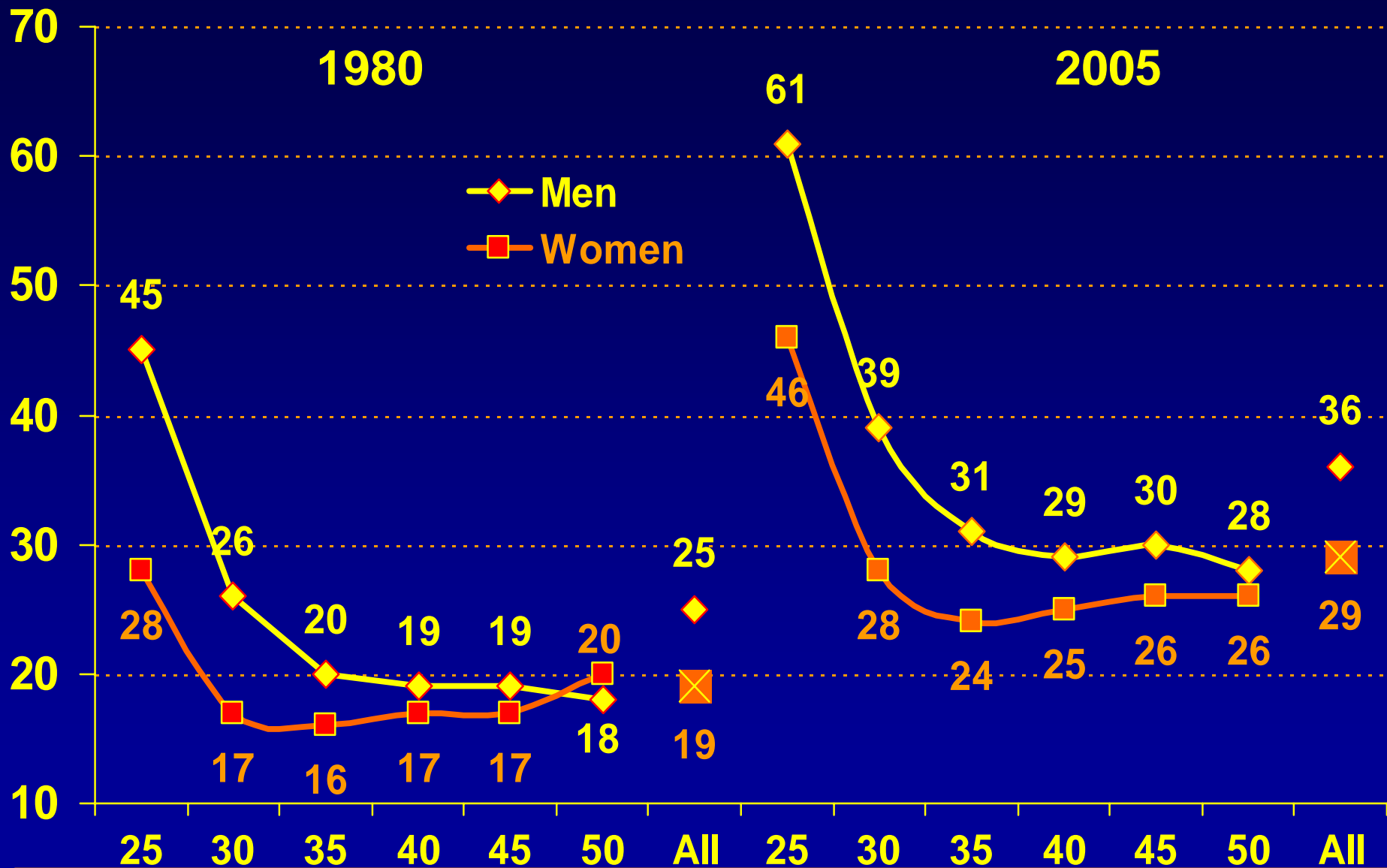
Levendedefødte i DK i 1974, 1986 og 2000



Age at first birth Denmark 1965-2007



Singles (%) in Denmark in 1980 and 2005



Infertilitet epidemiologi

Hvor stort er problemet i Danmark?

Infertilitets prævalens (nu): Kvinder i fertil alder: 6%

Intertilitets prævalens (ever): Kv i fertil alder: 15%

Infertilitets life time risk: Par: 25%

Anmodn. om lægehjælp for infertilitet: 10%

Ufrivillig barnløshed: 7%

Barnløse ved menopause: 12%

Er problemet stigende? Ja. Mulige årsager er

- Flere infertile i given alder
 - Større søgning om hjælp blandt infertile
 - Ændret fertilitet som følge af aldersforskydning
-

Infertilitet epidemiologi

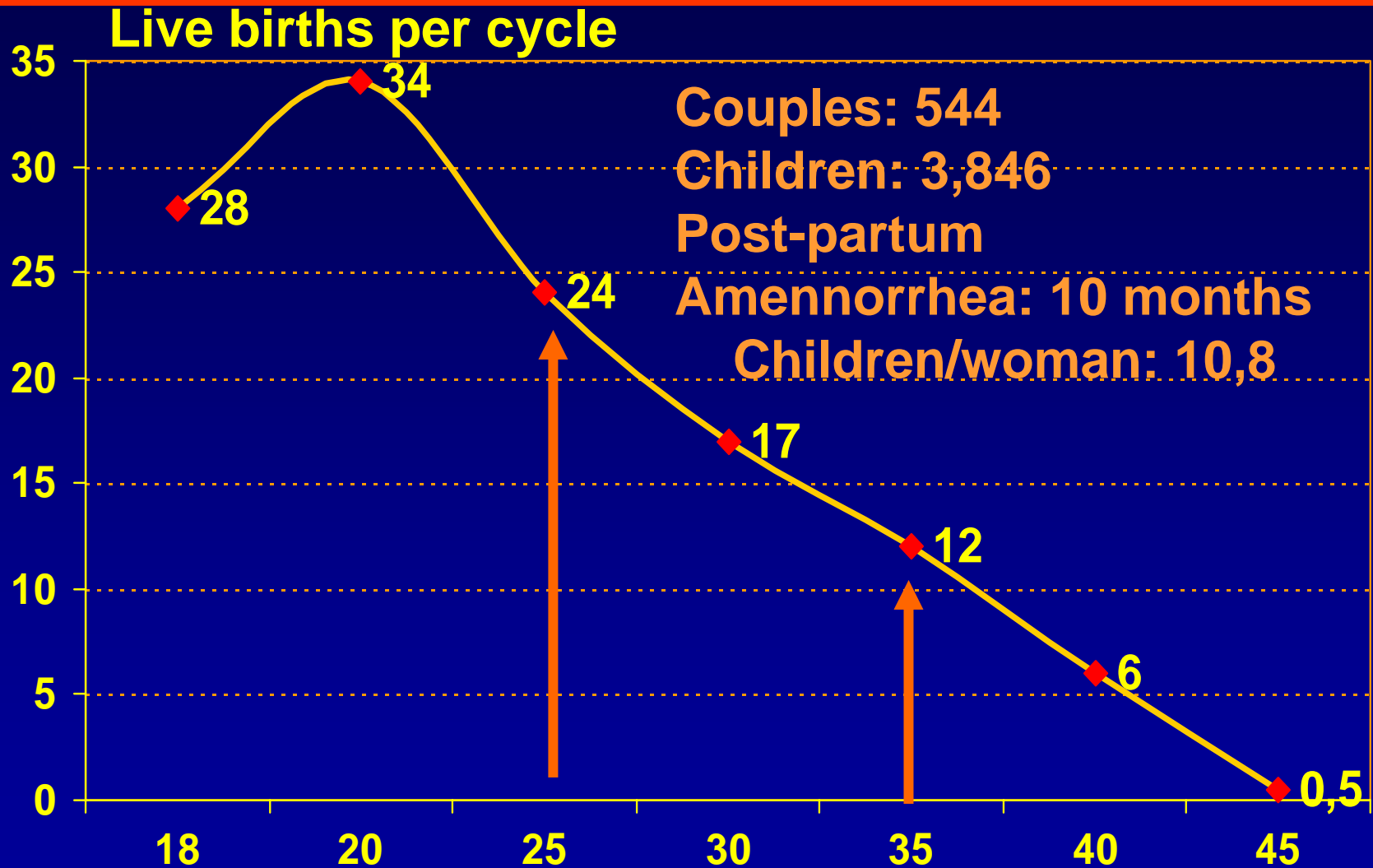
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Hvad er en kvinde, og hvad kan hun

Vi skal til North & South Dakota hvortil *Hutteritter* immigrerede i slutningen af det 19. århundrede. Der immigrerede 215 personer omkring 1870, i 1960 var de 5.450

- De må ikke anvende kontraception
 - Børn prioriteres højt, jo flere jo bedre
 - Socialt ligestillede med resten af befolkning.
 - Vi skal følge 544 par, alle gift, og alle med mindst et barn for at se hvad kvinderne kan
-

Fecundity rate among Hutterite women



Hvorfor falder fecunditeten med alderen?

Mulige mekanismer:

- Ovarie funktion
 - Tuba funktion
 - Ændringer i endometriet
 - Ændringer i hormoner
 - Ændringer i sædkvalitet
 - Ændringer i sexual vaner
 - Øget abort rate
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Hvorfor falder fecunditeten med alderen?

Mulige mekanismer:

1. Ovarie funktion

Tuba funktion

Ændringer i endometriet

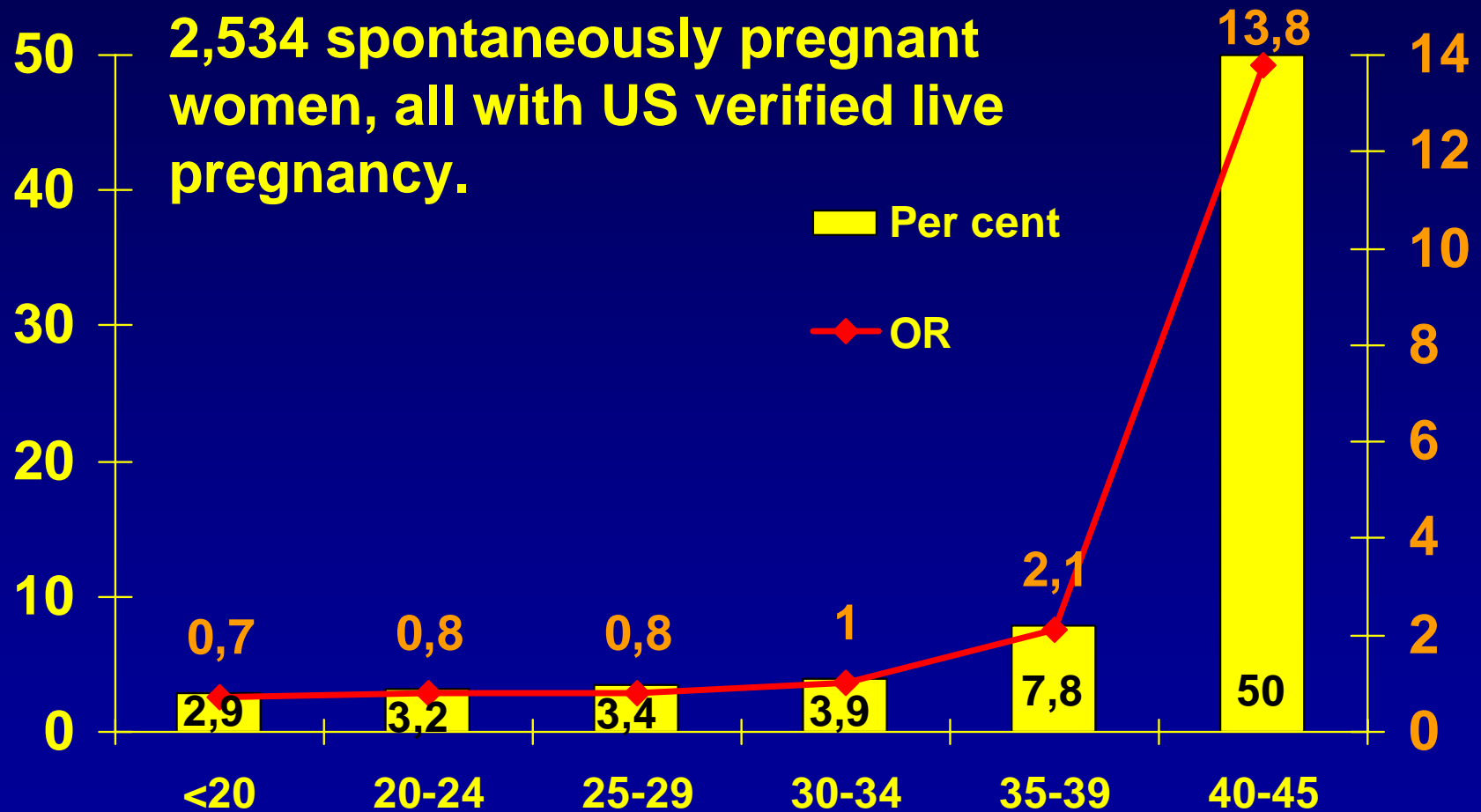
Ændringer i hormoner

Ændringer i sperm kvalitet

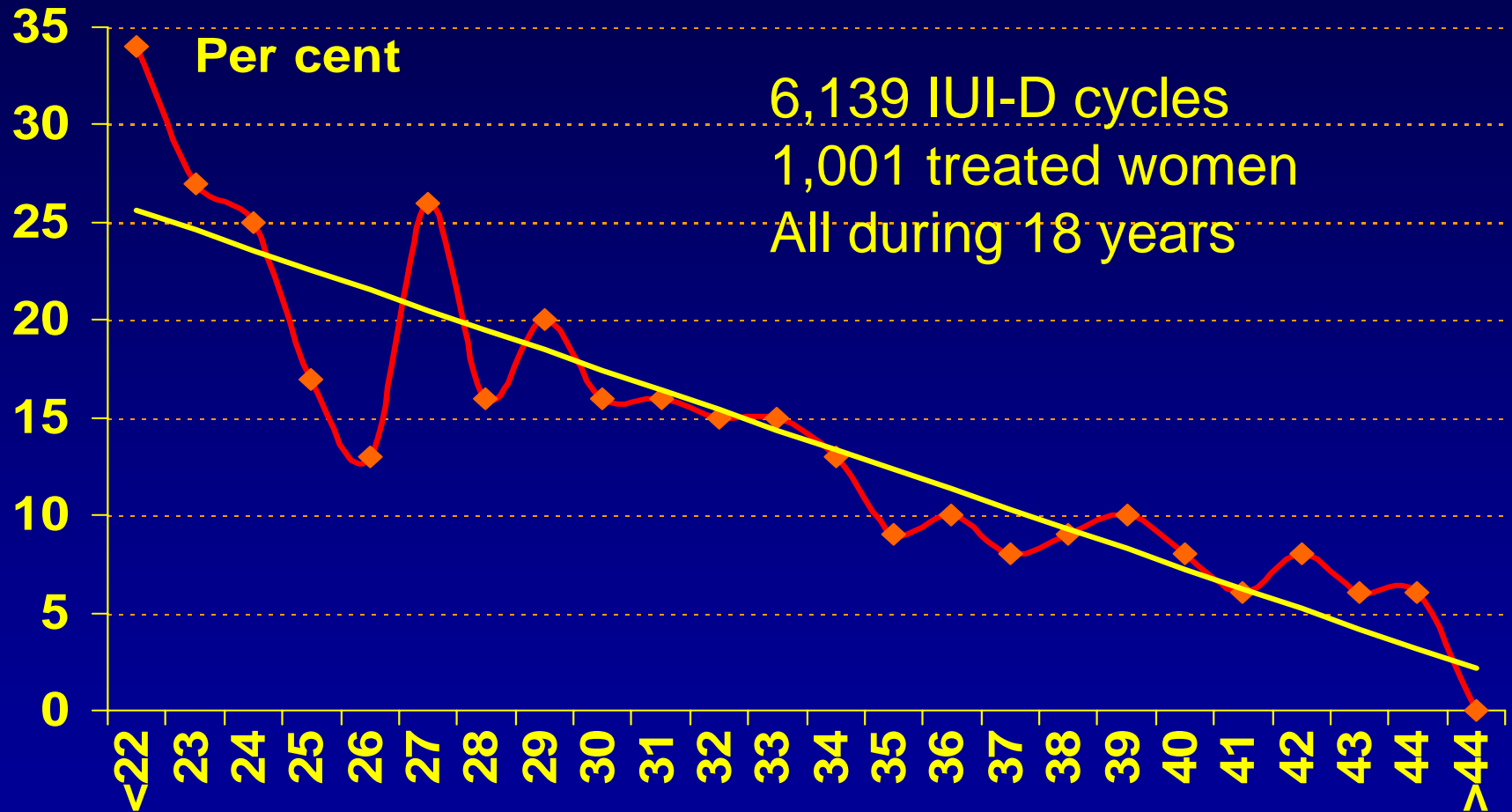
Ændringer i sexual vaner

2. Øget abort rate

Spontaneous fetal loss week 12-24 after early living pregnancy.



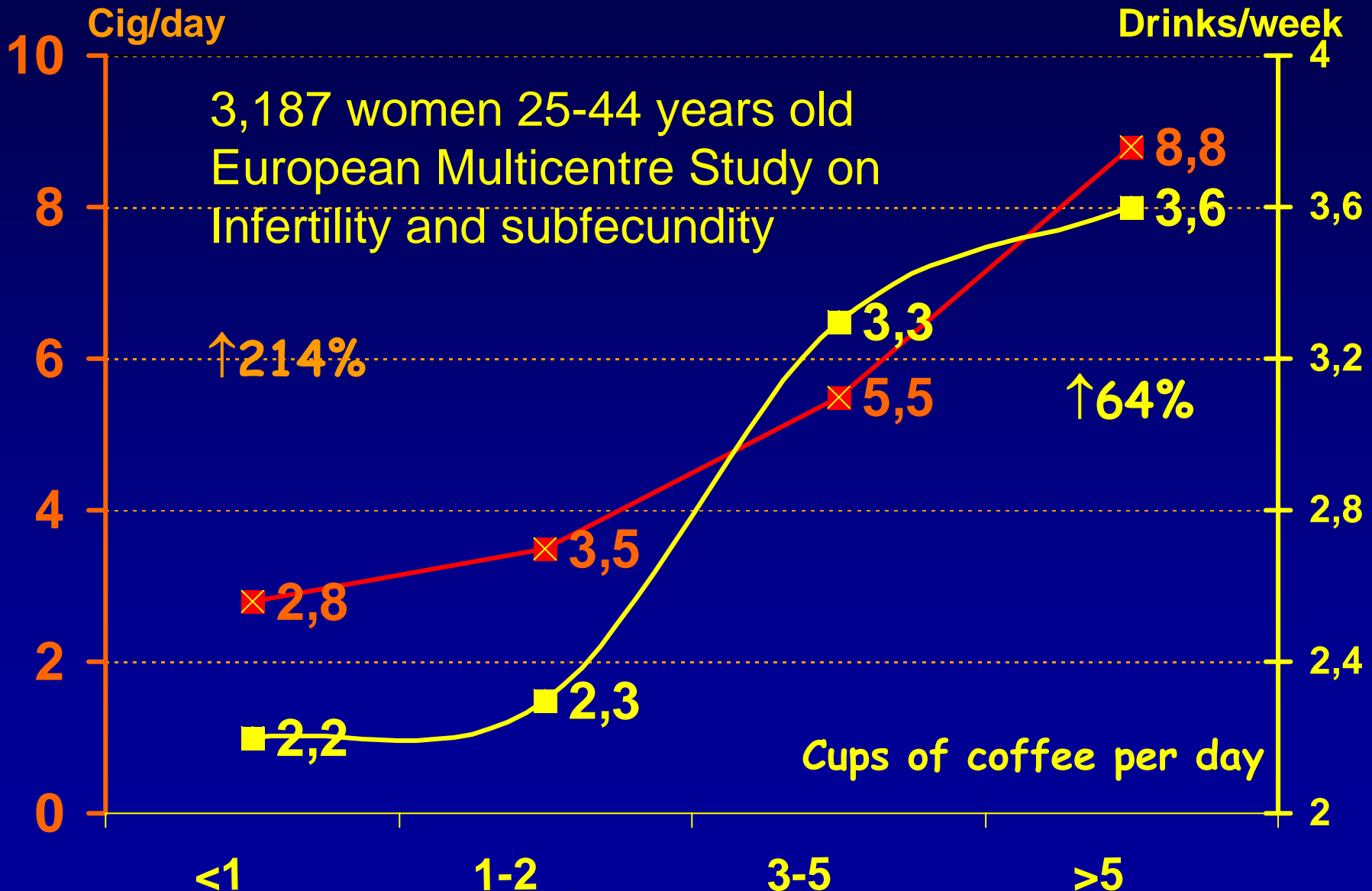
Donor IUI. Pregnancies/100 cycles



Infertilitet epidemiologi

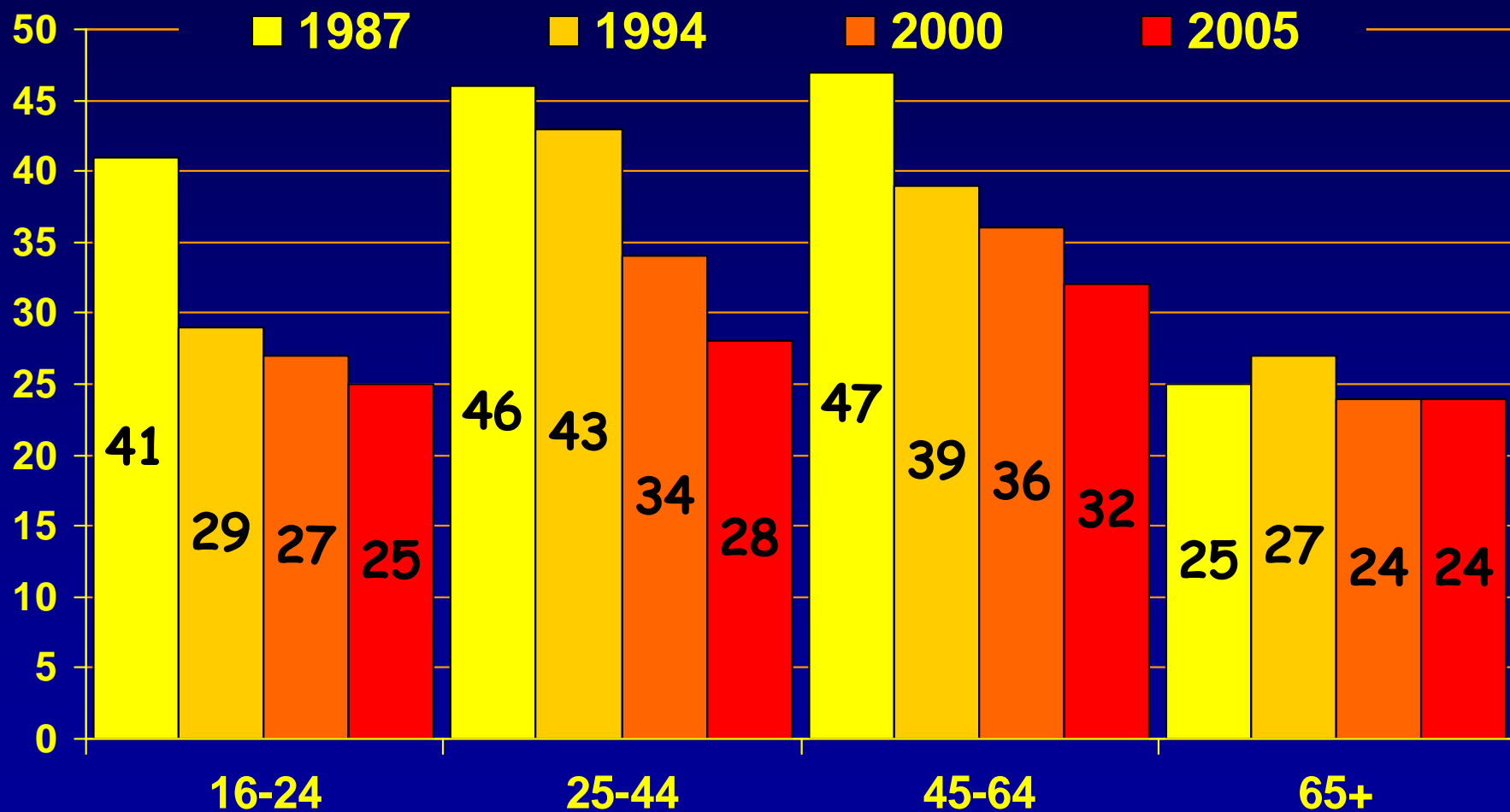
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Naughty girls



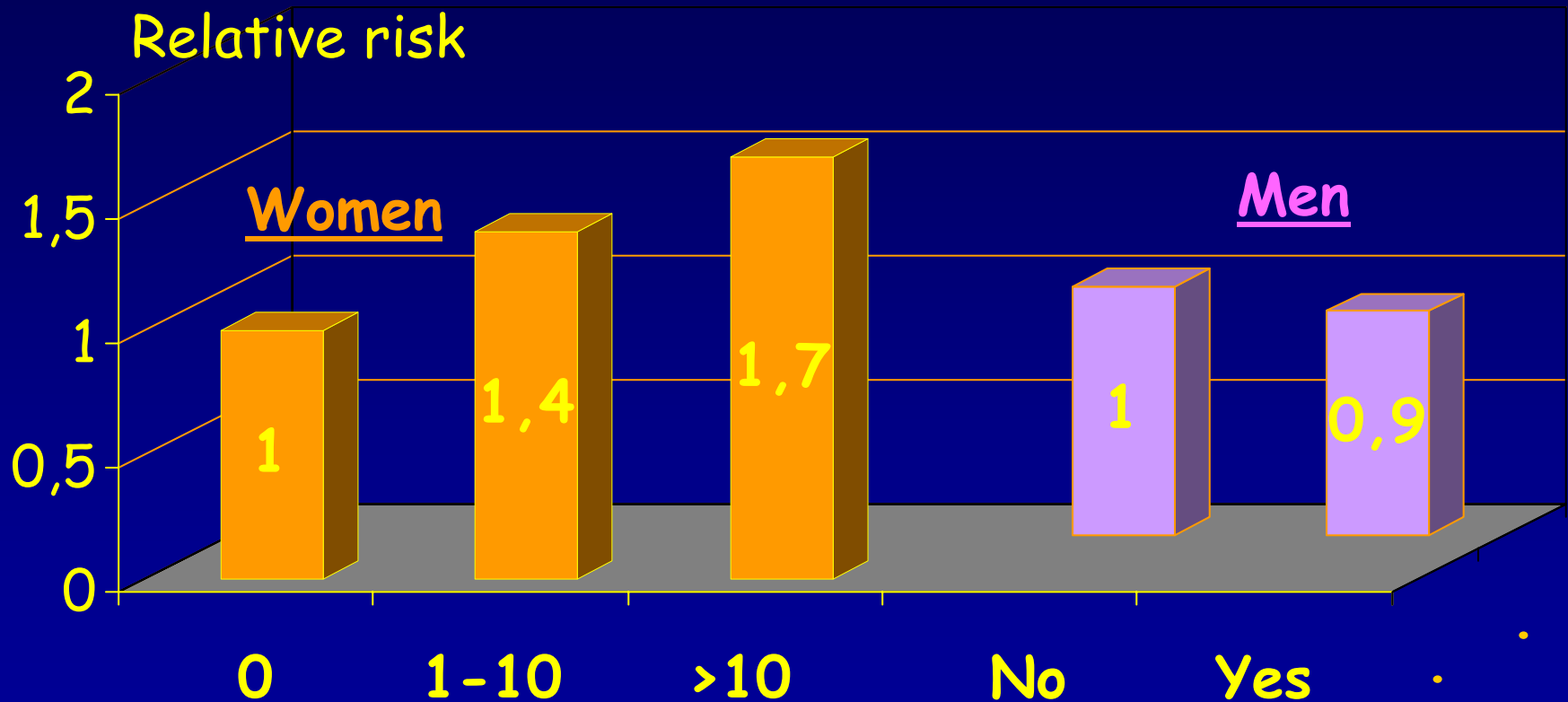
3,187 women 25-44 years old
European Multicentre Study on
Infertility and subfecundity

Smoking in women in DK in 1987, 1994, 2000 and 2005



Fertility and smoking

Risk of waiting time >9,4 months

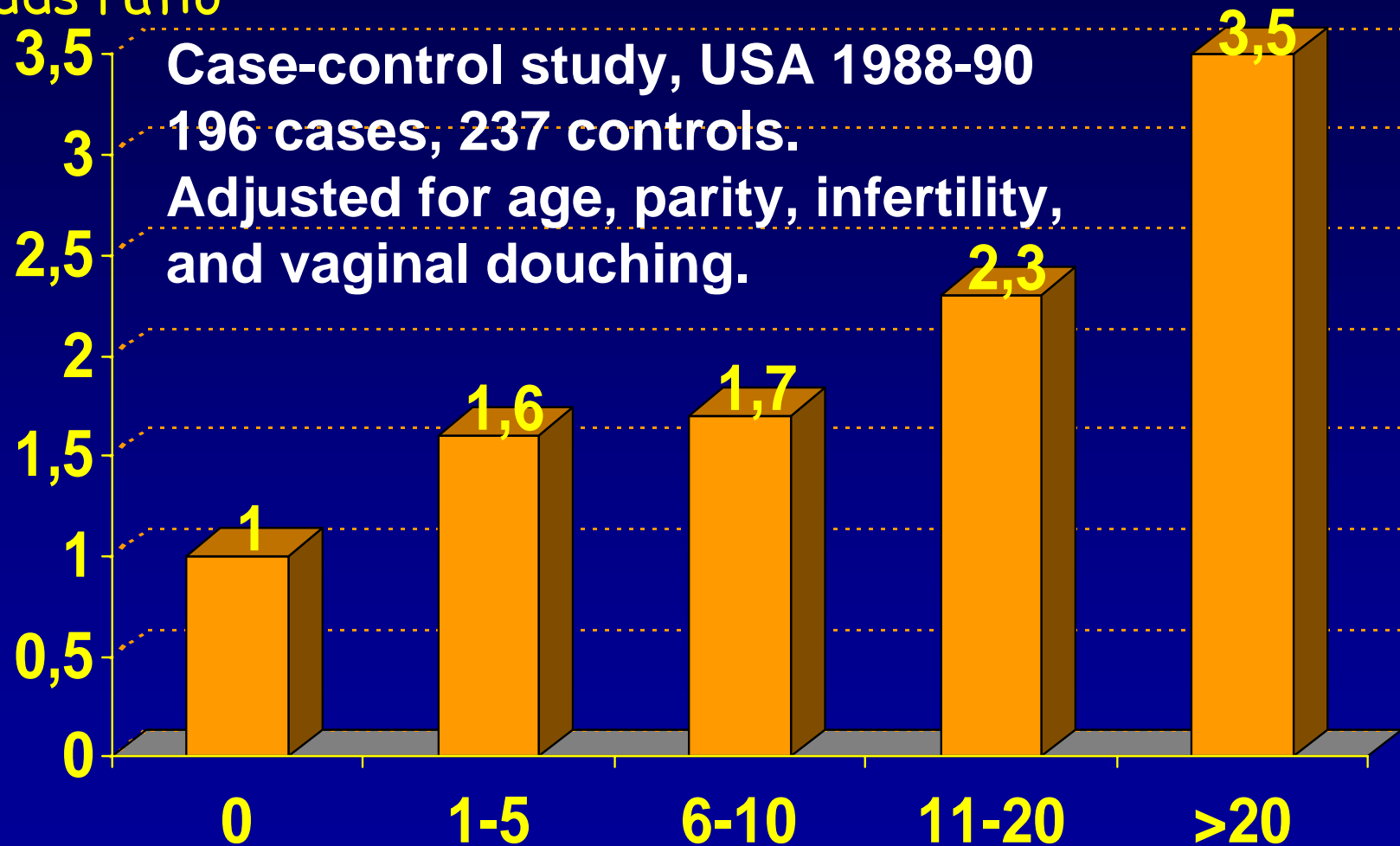


Bolumar et al. Am J Epidemiology 1996; 143: 578-87.
European multicenter study on infertility and subfecundity

Li/01

Smoking and ectopic pregnancy

Odds ratio



Smoking - IVF

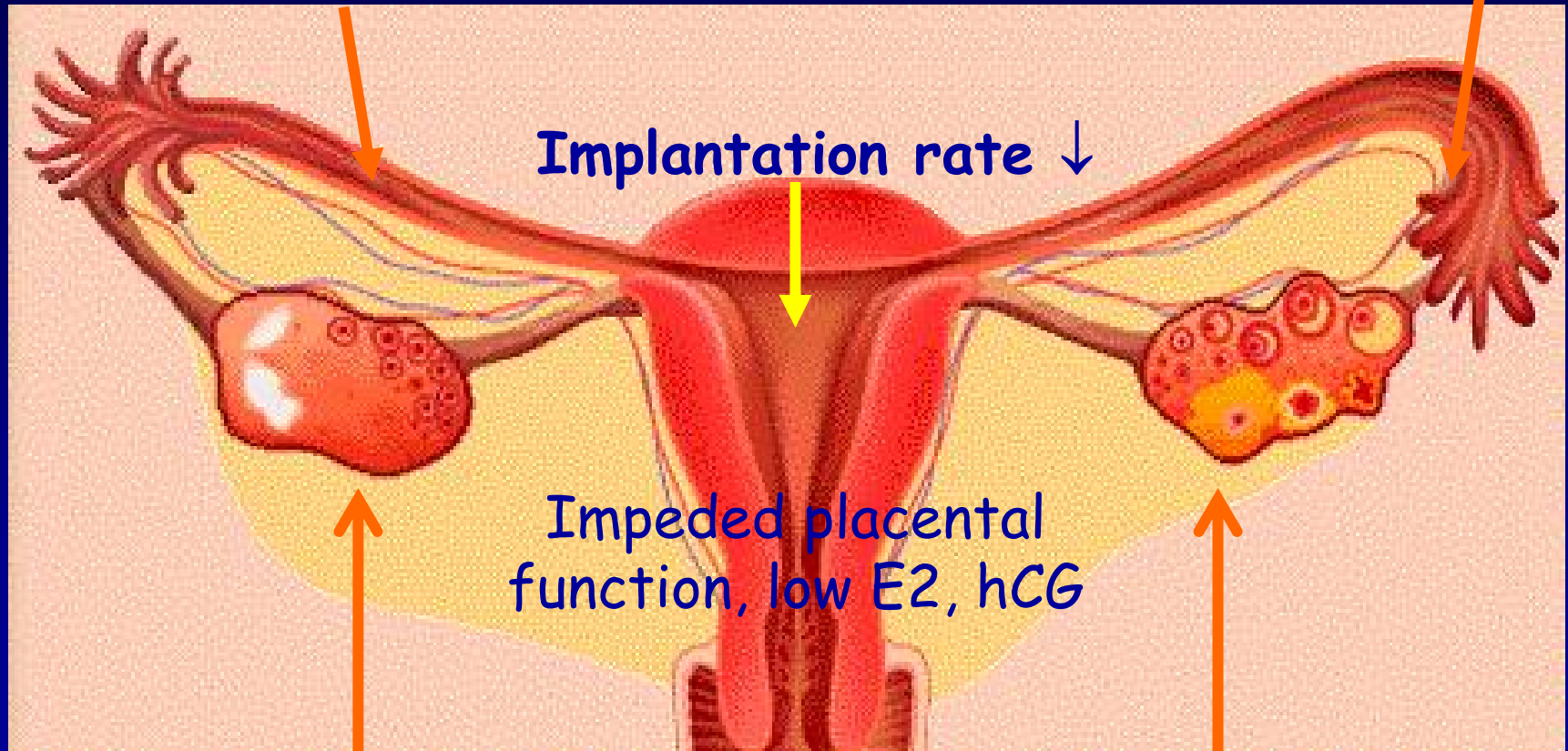
	-smo	ex-smo	+smo
No	499	351	111
Ø2/FSU U	82	71	60
Oocytes	13.5	13.6	12.6
Fertilis. rate	54%	54%	50%
Embryos	8.0	8.2	6.6
Embr. transf	3.6	3.5	3.6
Implant. rate	16%	16%	6.7%

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

Smoking and fertility

Impeded ciliary function:

Pick-up function ↓



E2-production ↓

Abortion rate ↑

↓ progesterone
in granulosa cells

Rygning hos mænd

- Mindsker sædkvaliteten lidt
Kun betydning ved excessiv rygning eller dårlig sædkvalitet
- Udsætter kvinden for passiv rygning
(Betydning aldrig dokumenteret)
- Mindsker chancen for at kvinden kan ophøre med at ryge
- Skaber et dårligt indeklima for et kommende barn

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Alkohol og fertilitet

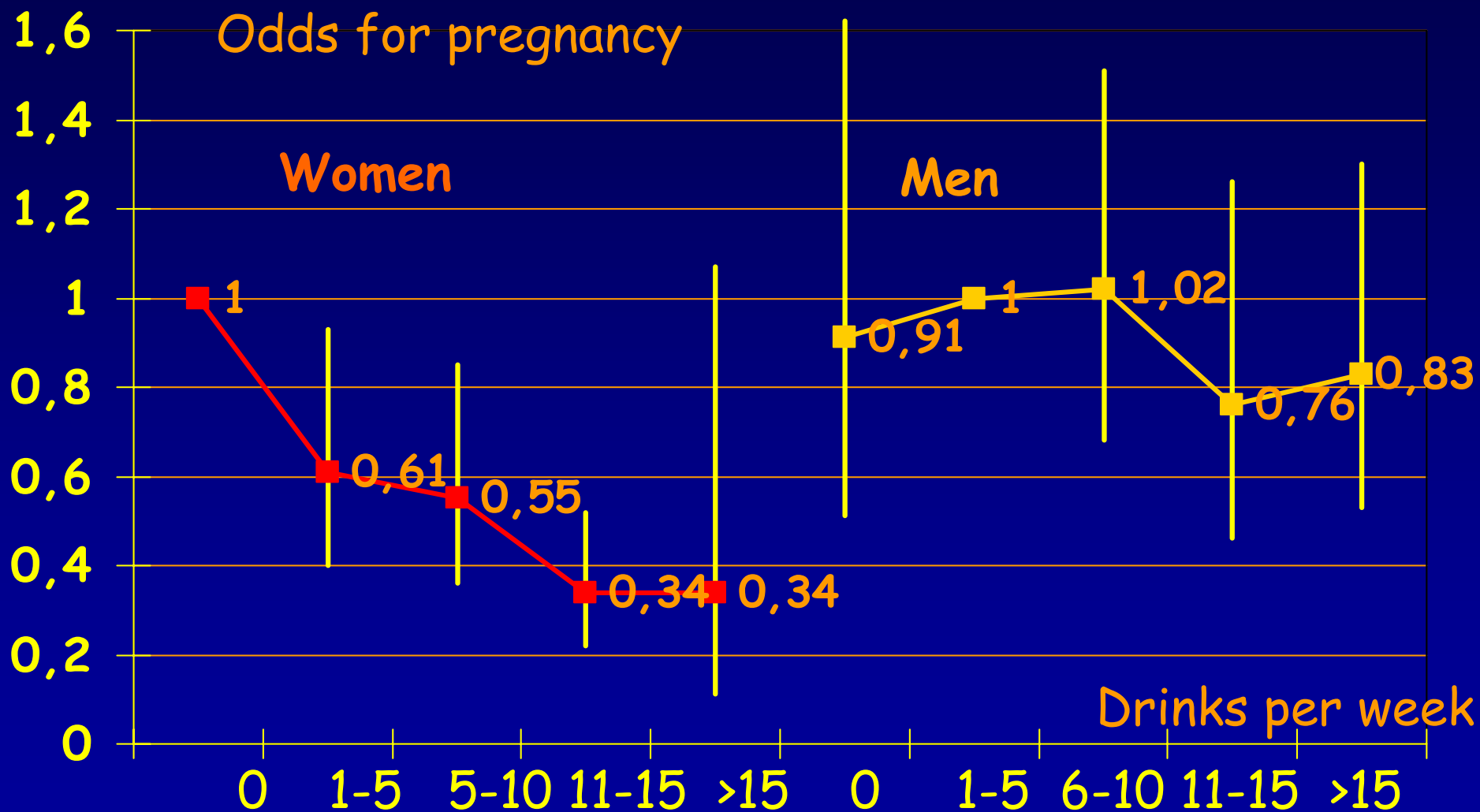
Nedsætter beskedne mængder alkohol fertiliteten?

- Kun få undersøgelser
 - Dansk prospektivt studie 1992-94 med 430 par, 20-35 år, som prøvede at opnå graviditet for første gang.
 - Alkohol indtag blev registreret tæt gennem 6 cykli
 - Kontrol for rygning, BMI, sædkvalitet, kaffe
-

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.

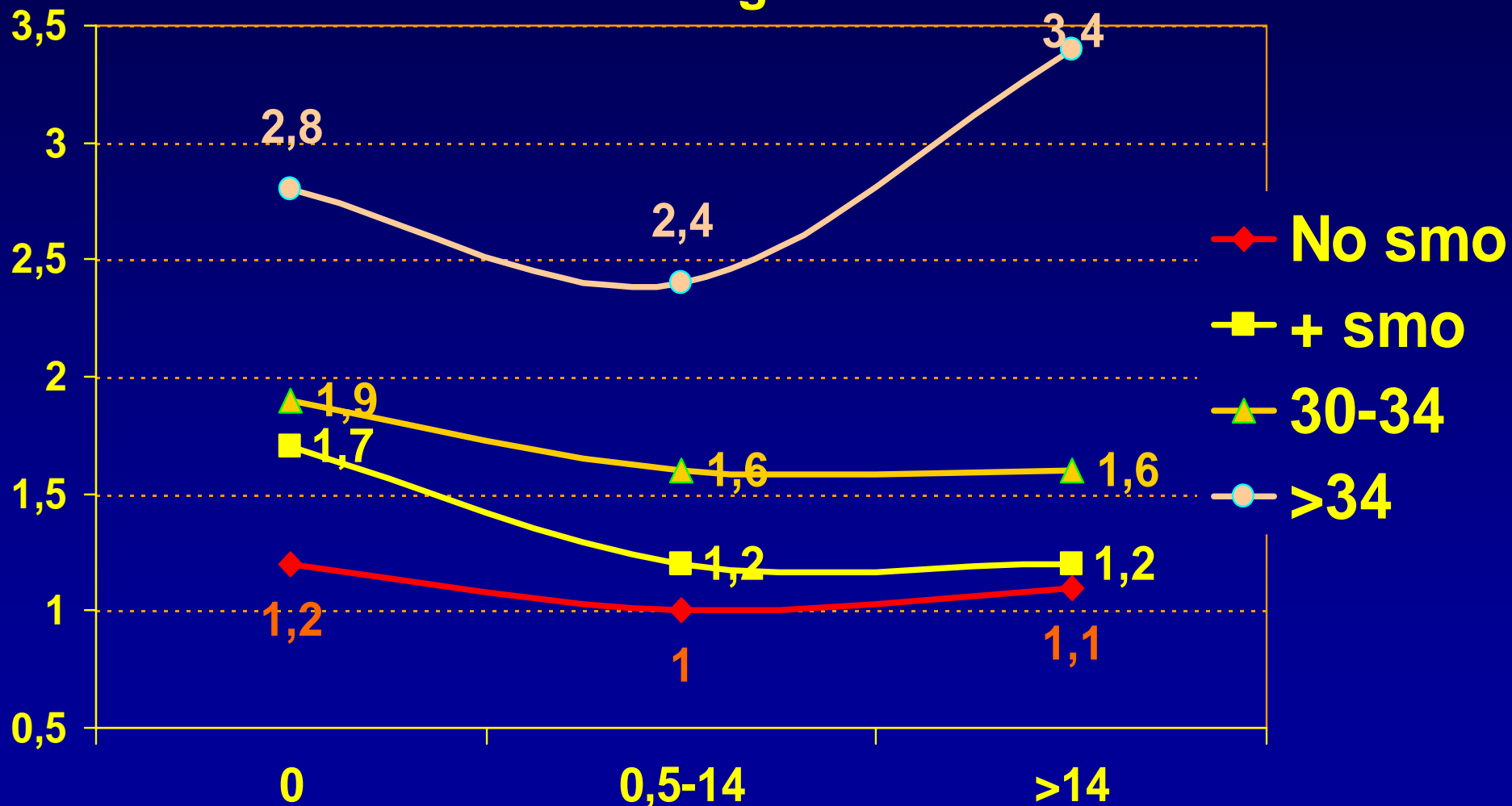
Outcome measure: Subfecundity odds ratio

Subfecundity OR and drinks per week



Time to pregnancy and alcohol, stratified according to age and smoking

Risk of increase in waiting time



Alkohol og graviditet

- Studie over "den århusianske fødselskohorte" 1989-96 med 25.000 gravide og disse fødsler dokumenterer at 5 genstande/uge =>
- 2,5 x risiko for dødfødsel
- 3 x øget risiko for abort i 7.-12. uge
- øget risiko for tidlig fødsel
- øget risiko for lav fødselsvægt

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

Alkohol hos mænd

- Mindre end 10 genstande om ugen betyder ingenting for
 - sædkvalitet
 - fertilitet
 - abortrisiko
 - misdannelser
- Mere end 10 genstande om ugen mindsker sædkvalitet lidt

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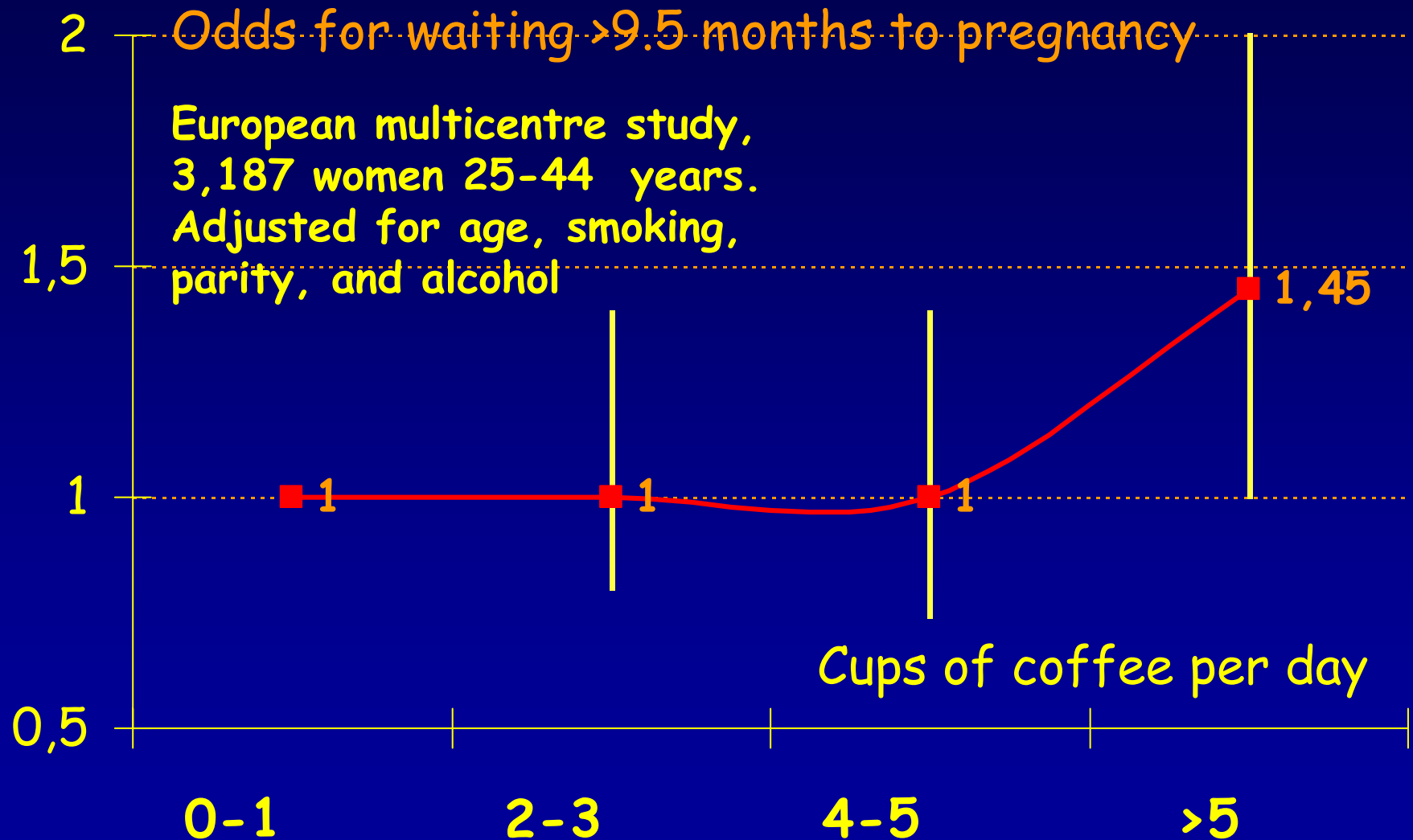
Koffein

Koffein findes i

- 1 kop kaffe = 100 mg
- 1 kop te = 50 mg
- ½ liter cola = 50 mg
- 30 g chokolade = 10 mg
- 1 kop kakao = 5 mg
- medicin.
- Koffein passerer alle biologiske membraner inkl.. placenta-barrieren
- Koffein findes i alle kropsvæsker kort efter indtag

Fertility and coffee

Fecundability odds, 95% CI



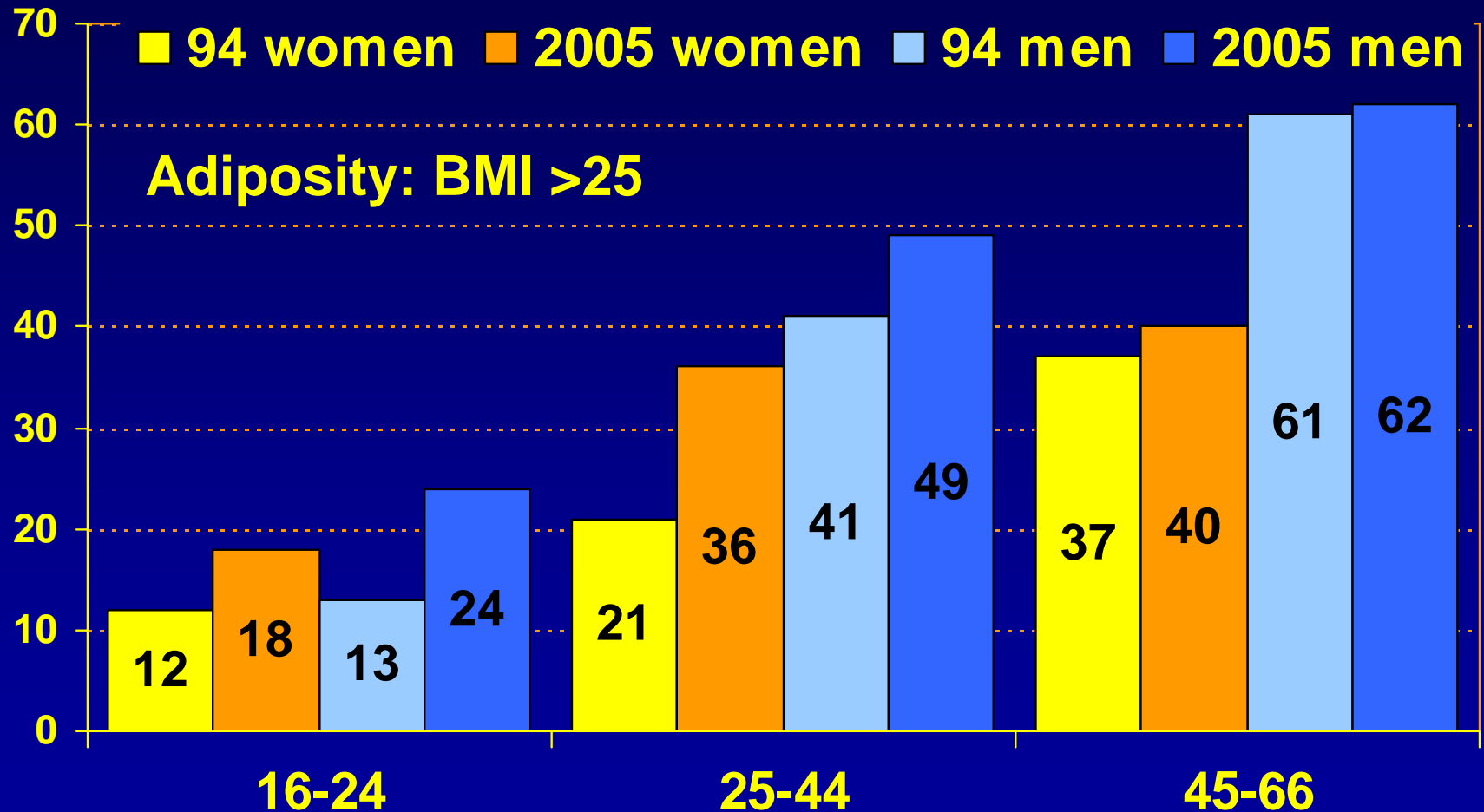
Kaffe og fertilitet: Konklusion

- Mindre end fem kopper kaffe om dagen påvirker ikke fertiliteten
- Mindre end fem kopper kaffe om dagen påvirker ikke risikoen for spontan abort
- Mere end fem kopper kaffe om dagen mindsker fertiliteten
- Mere end fem kopper kaffe om dagen øger risikoen for første trimester spontan abort (blandt ikke rygere)

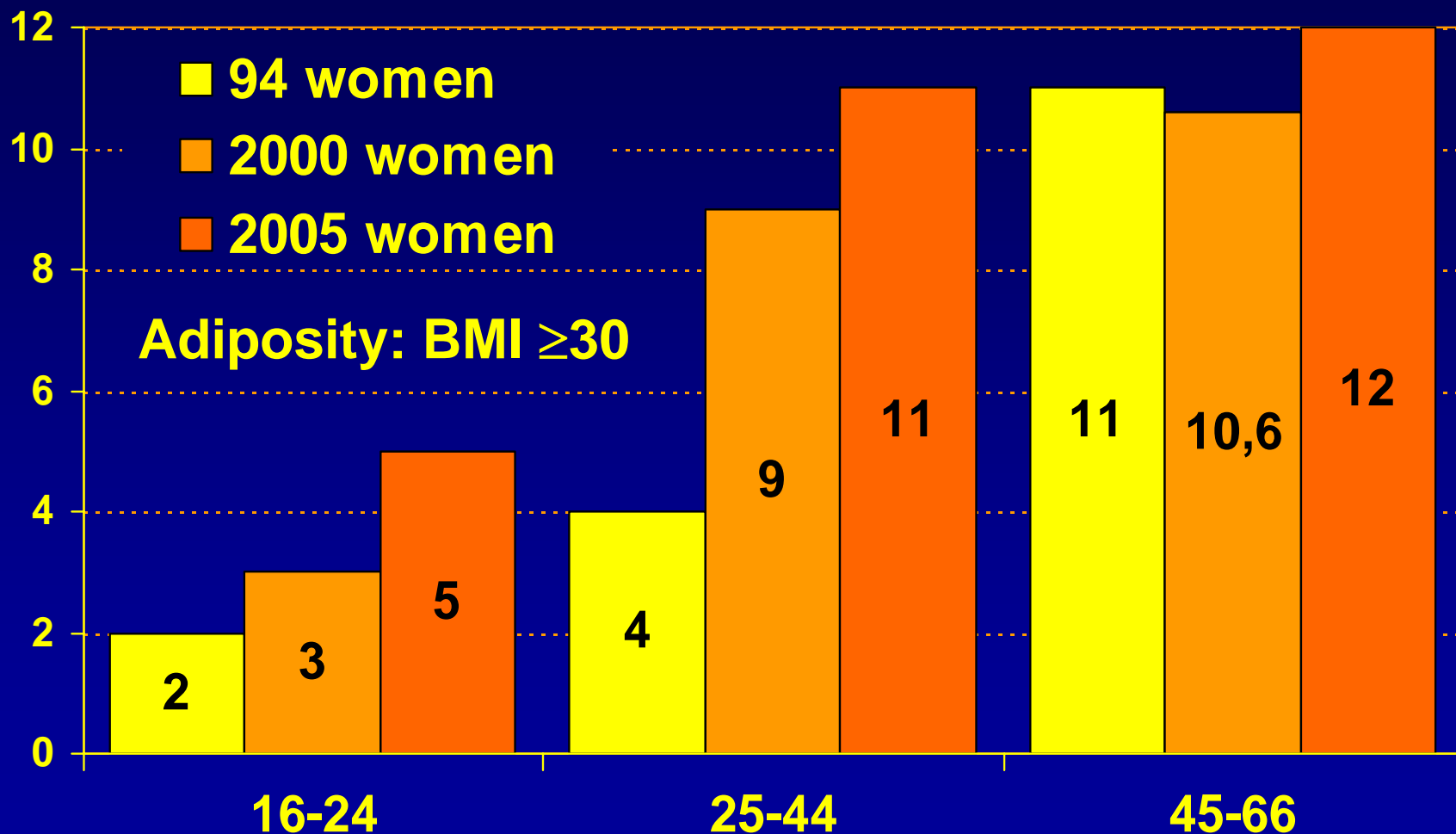
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Adiposity in Danish women and men in 1994 and 2005. N=16,000

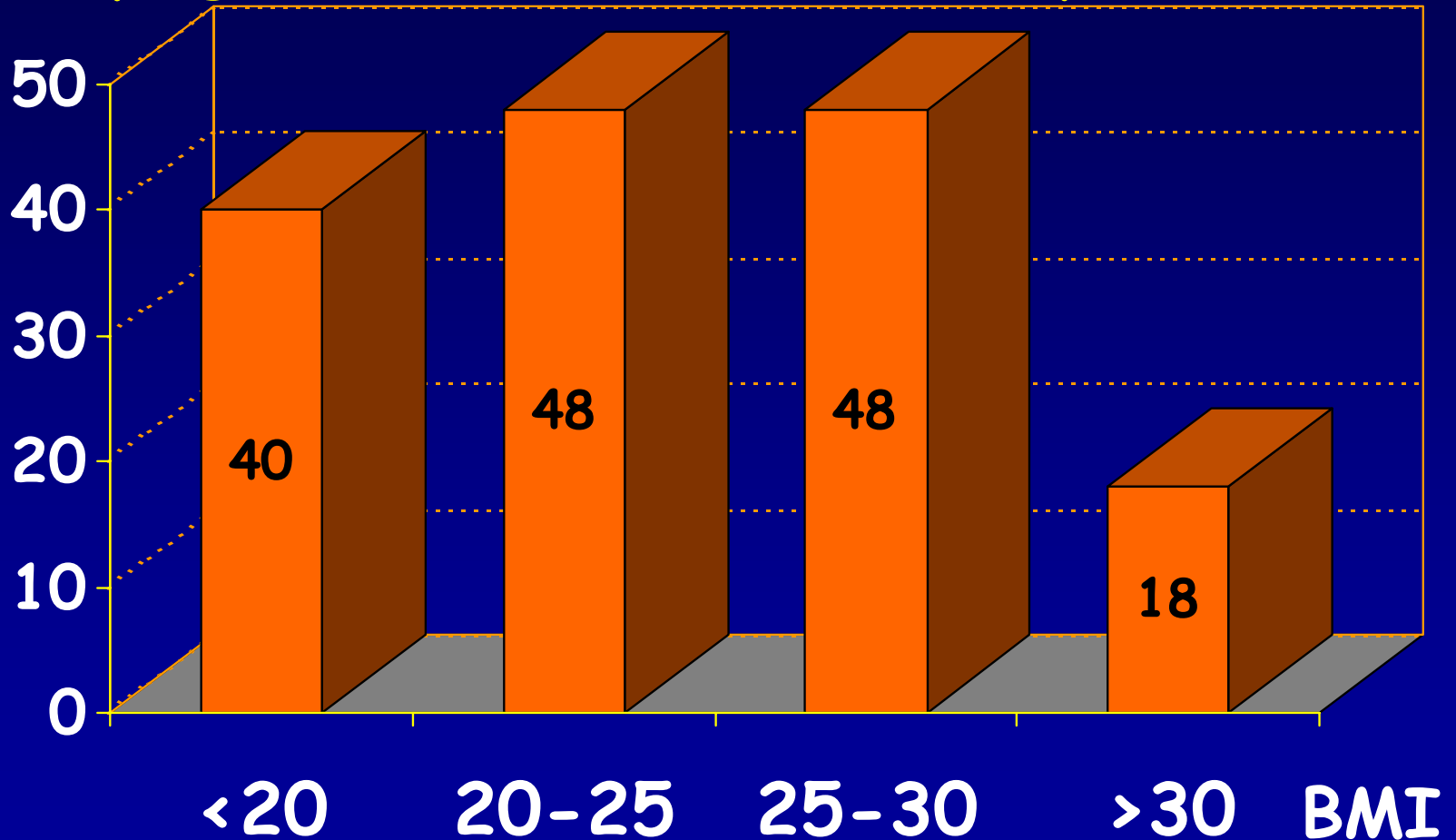


Severe adiposity in Danish women in 1994, 2000 and 2005



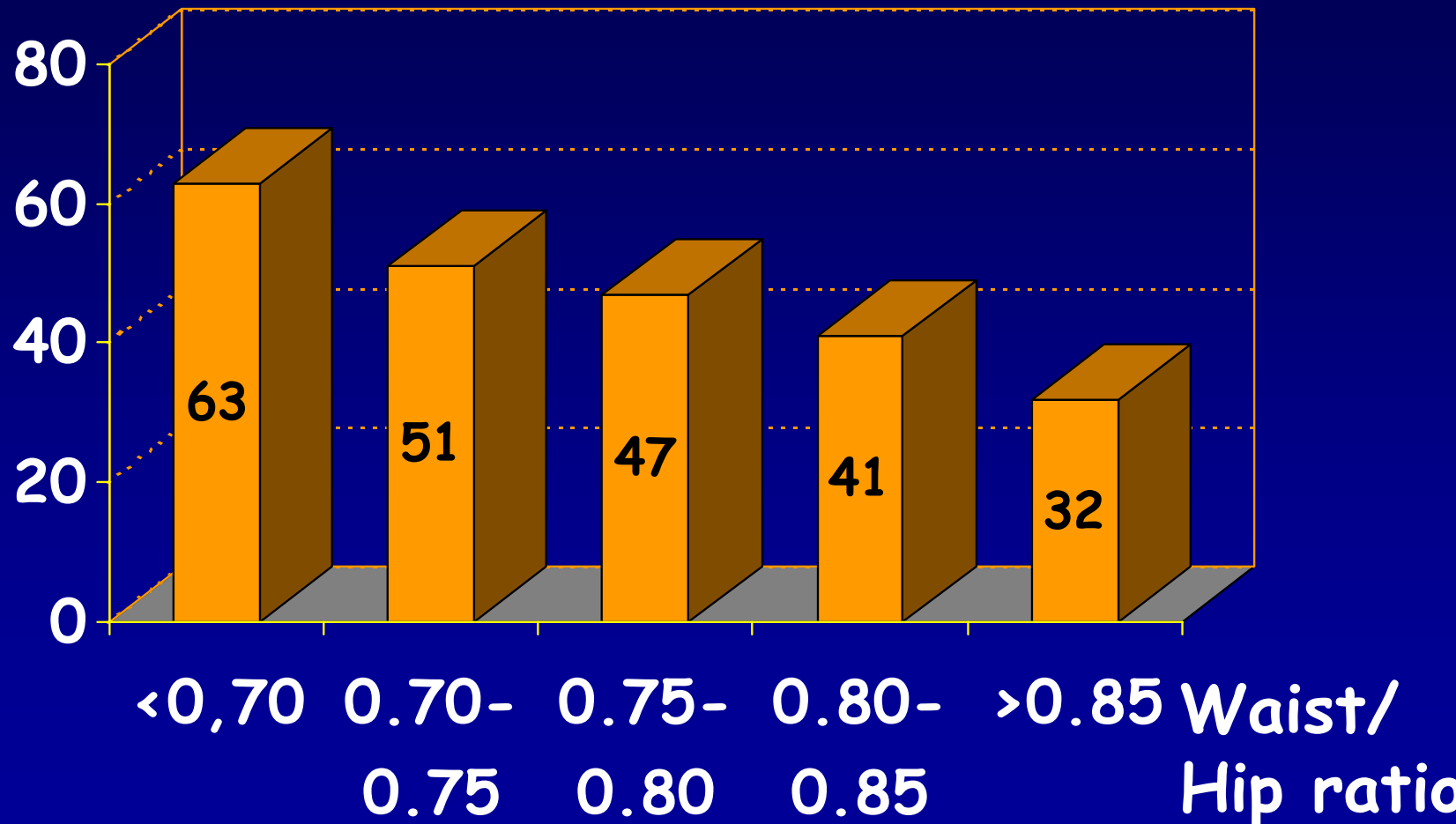
Fat and fecundity

% pregnant within 12 insemination cycles (n=489)

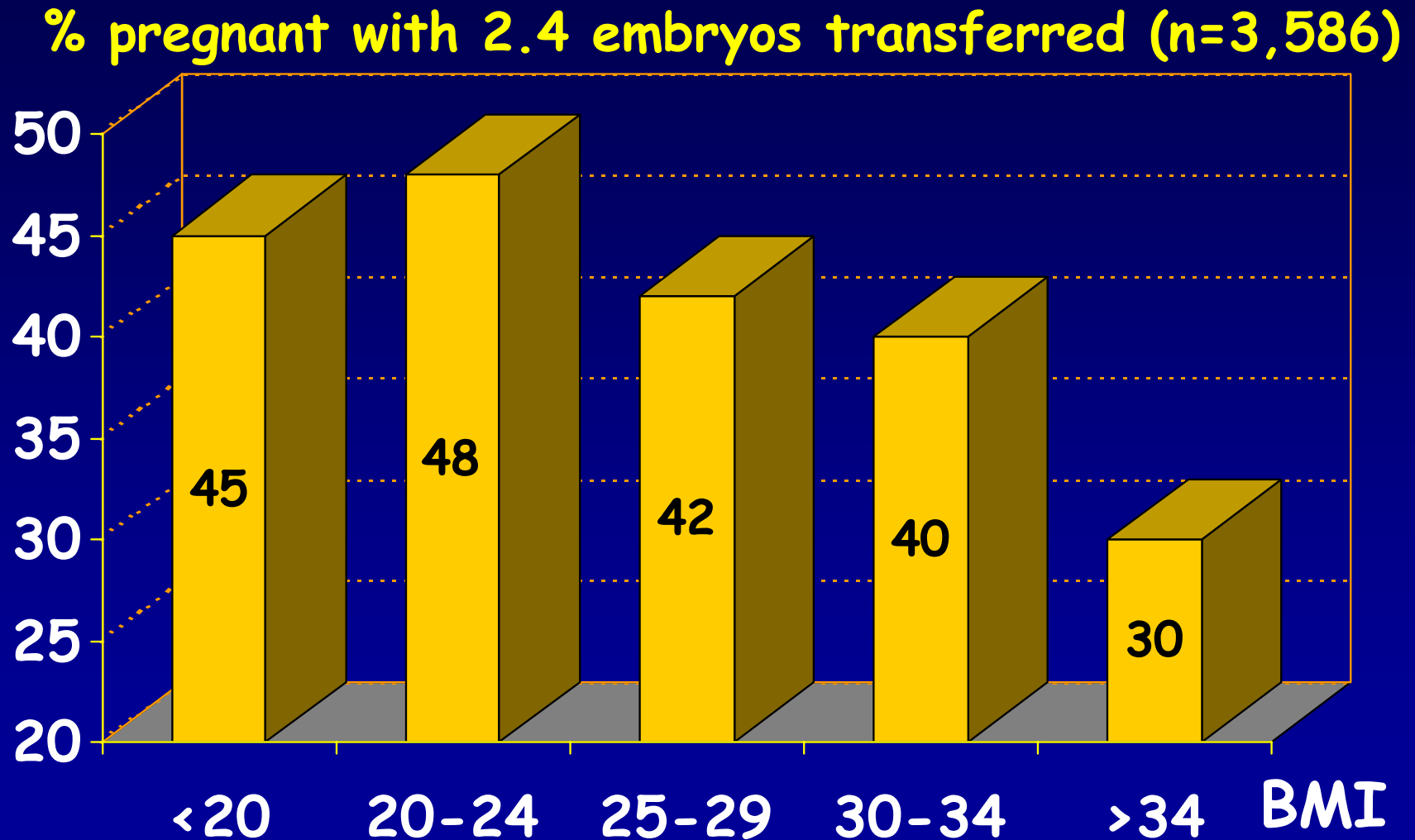


Fat and fecundity

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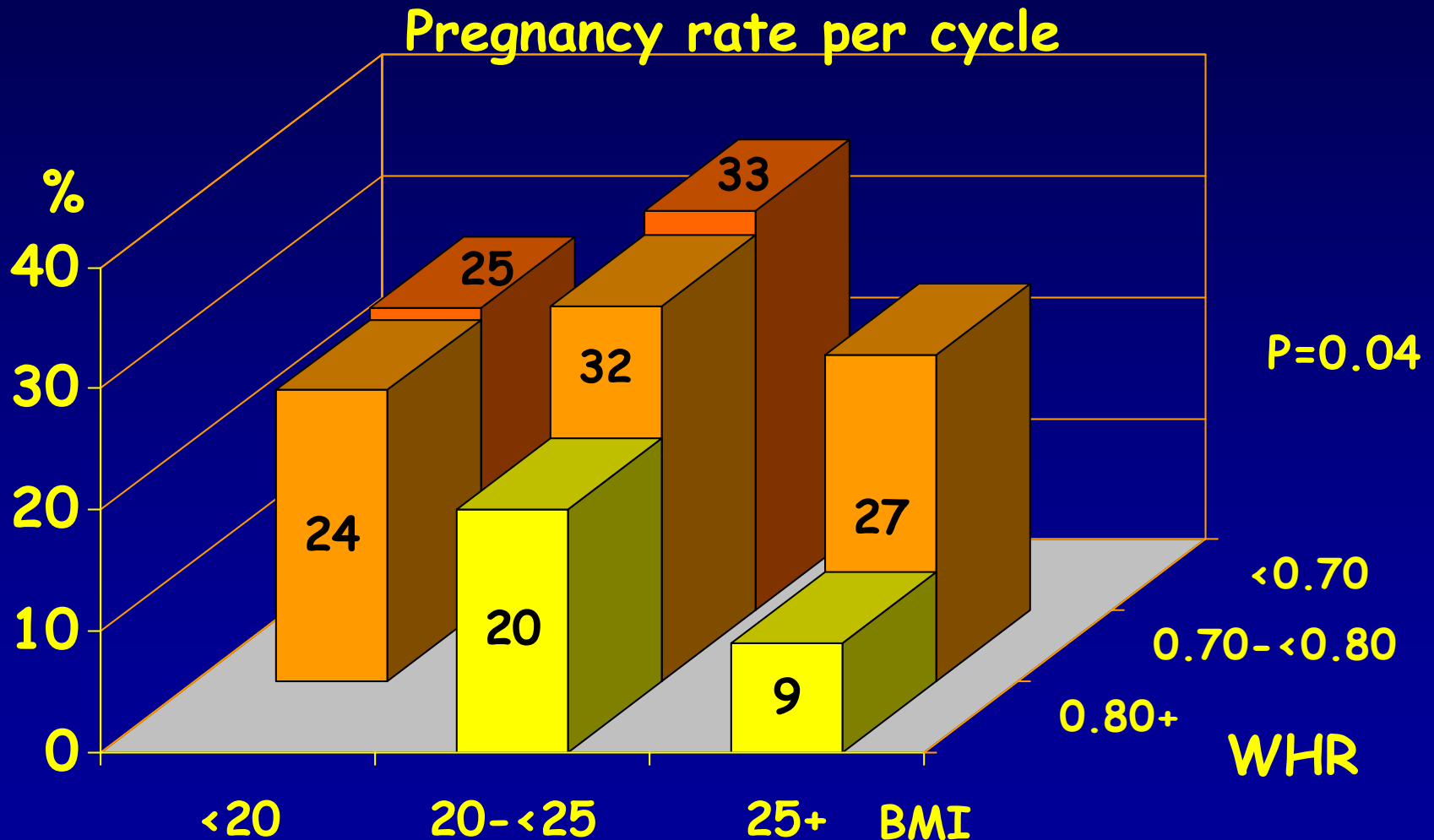


BMI & IVF: Clinical pregnancy rate



Fat and fecundity

Pregnancy rates in 220 IVF cycles



Pregnancy loss after IVF/ICSI

BMI	<25	≥25	p
Number	304	79	
Oocytes recovered	10	8	0.03
Fertilisation rate	79%	82%	ns
Live birth	75%	63%	0.04
Abortion <week 6	12%	22%	0.03
Abortion week 6-12	9%	13%	ns
Abortion >week 12	1.3%	1.3%	ns

Fedorcsák et al. Acta Obstet Gynecol
Scand 2000; 79: 43-48.

Li/00

Fedme og fertilitet: Konklusion

- Overvægt reducerer chancen for spontan graviditet ved især at påvirke ovariefunktionen
- Overvægt mindsker chancen for graviditet ved IUI og IVF behandling
- Overvægt øger risikoen for tidlig spontan abort
- Vægttab bedrer muligheden for spontan graviditet

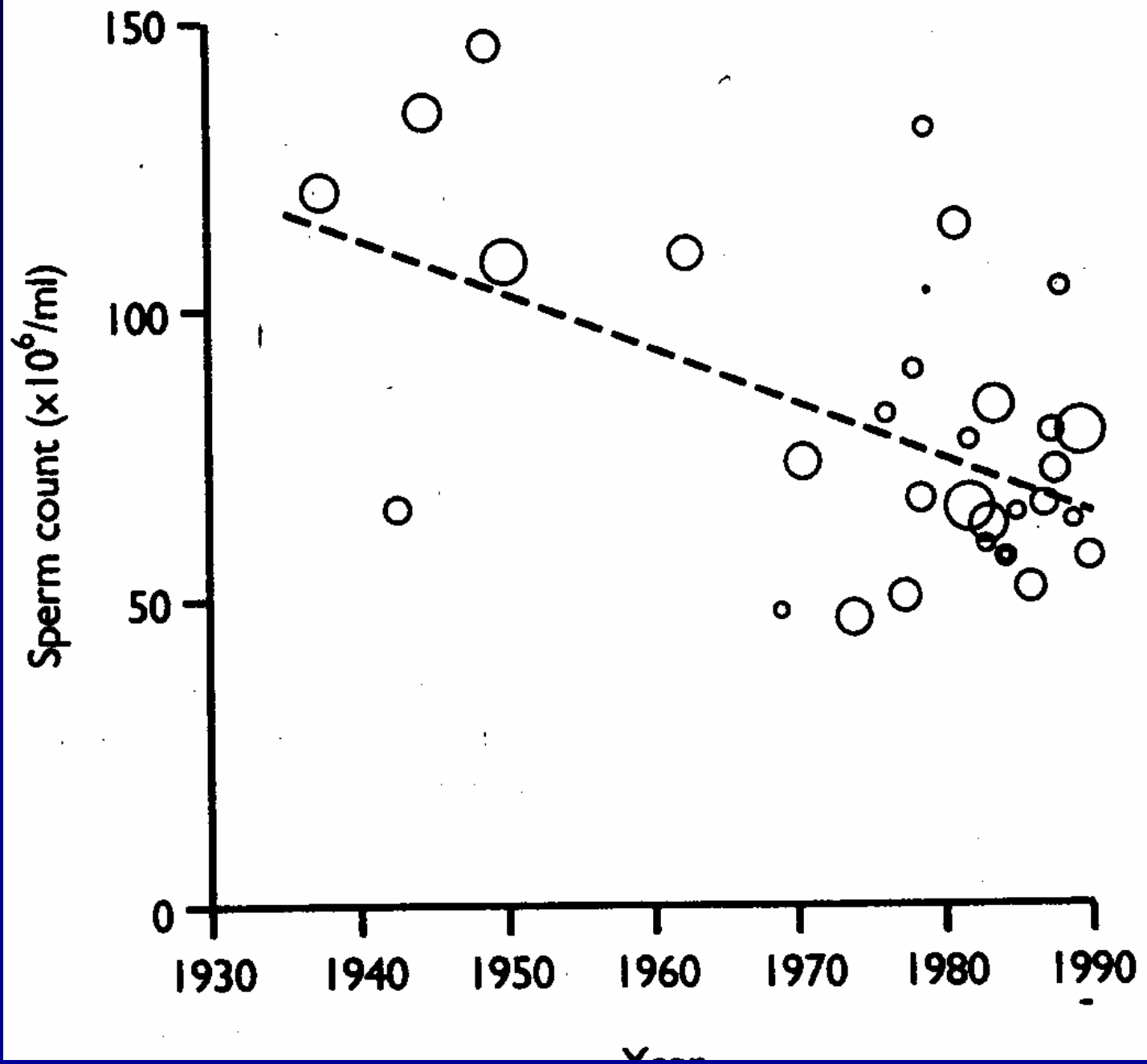
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Sperm count by time

61 papers
14,947 men

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

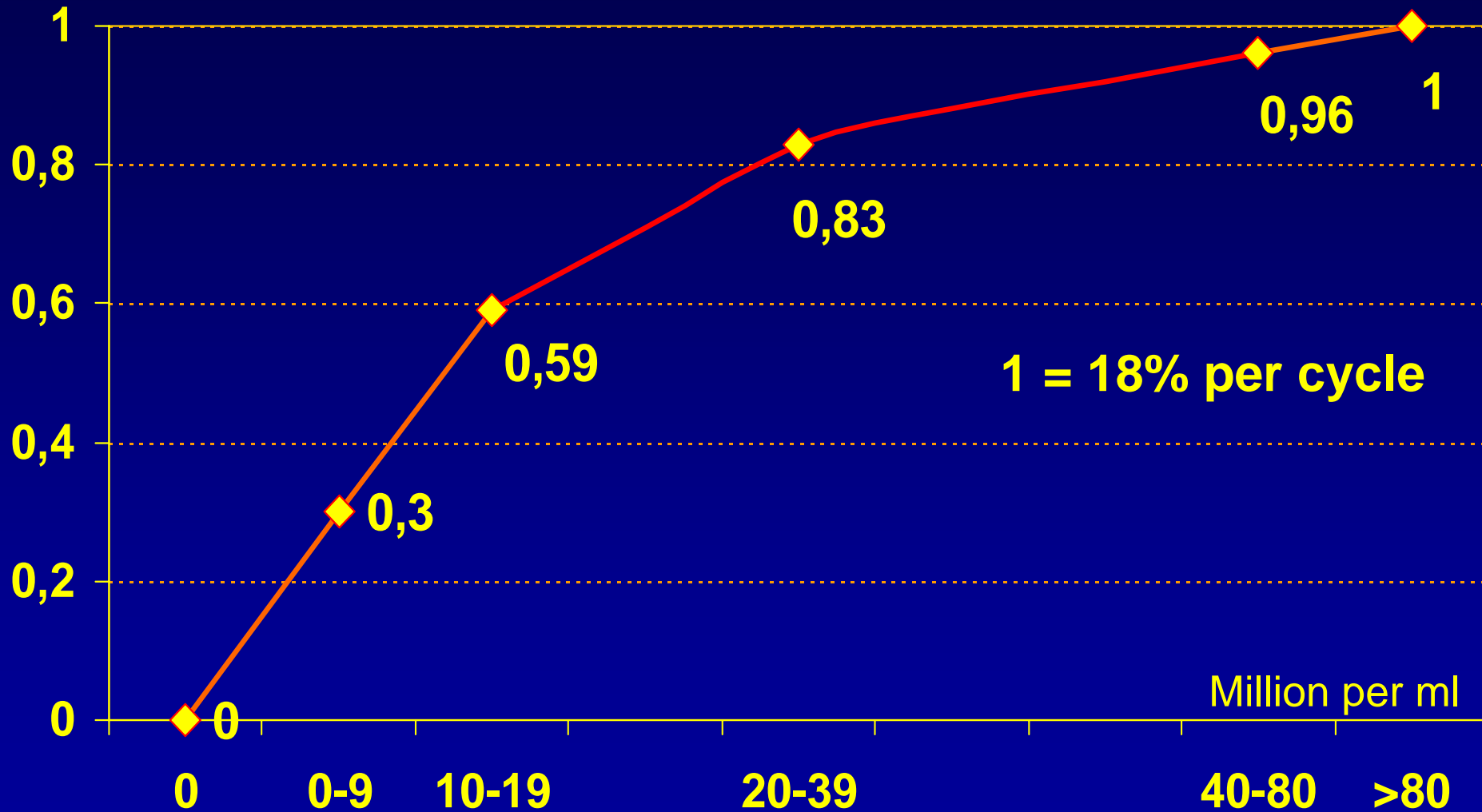


Sperm count and fecundity

- 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.

Sperm count and fecundity



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

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%)**

Sperm count in Nordic-Baltic area

Denmark **Norway** **Finland** **Estonia**

Particip.	300	240	324	104
Period	97-99	1998	98-00	97-99

Sperm count in mio/ml (median)

All	41	41	54	57
Clean	45	42	53	63

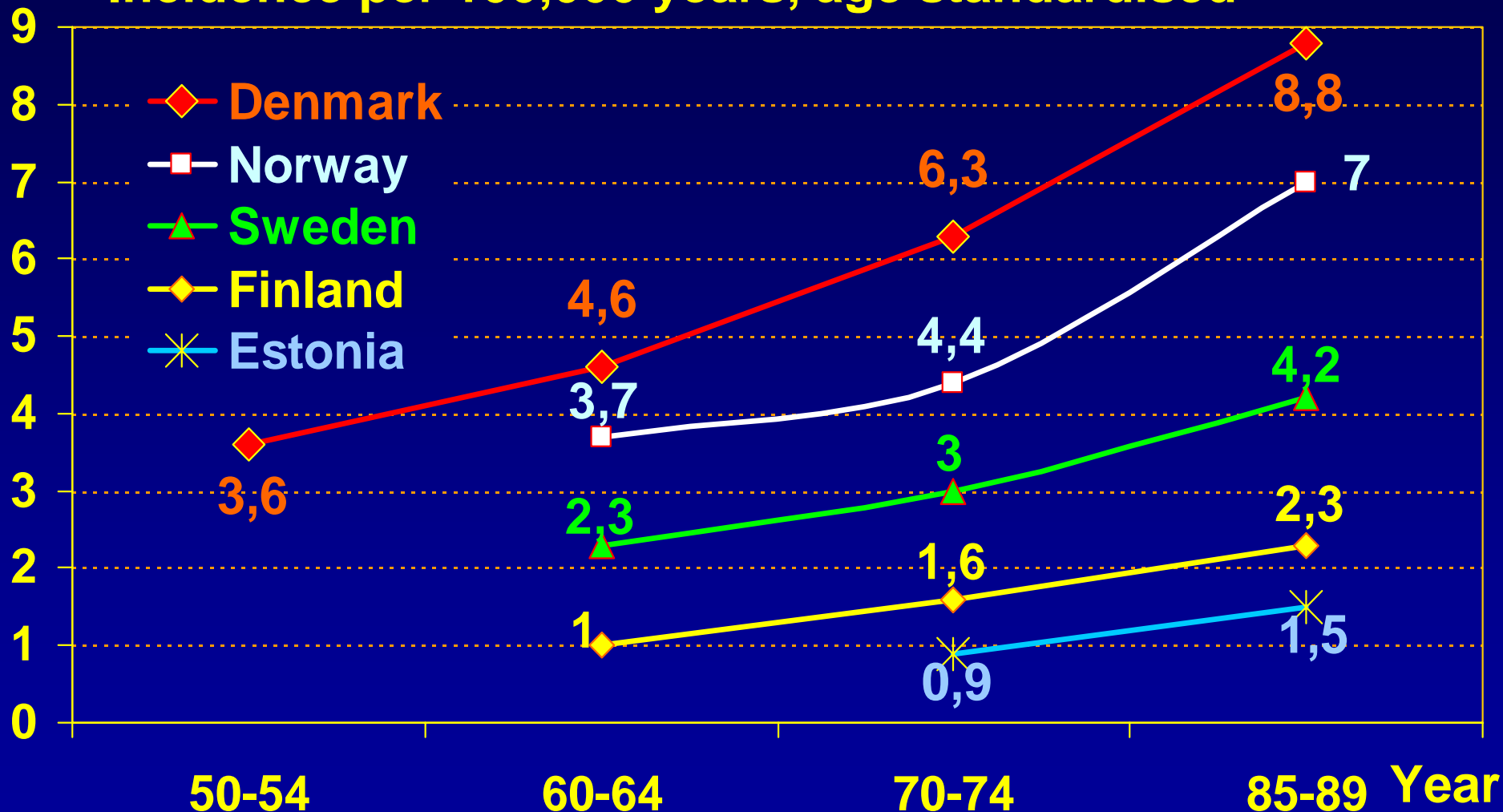
West-east gradient

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



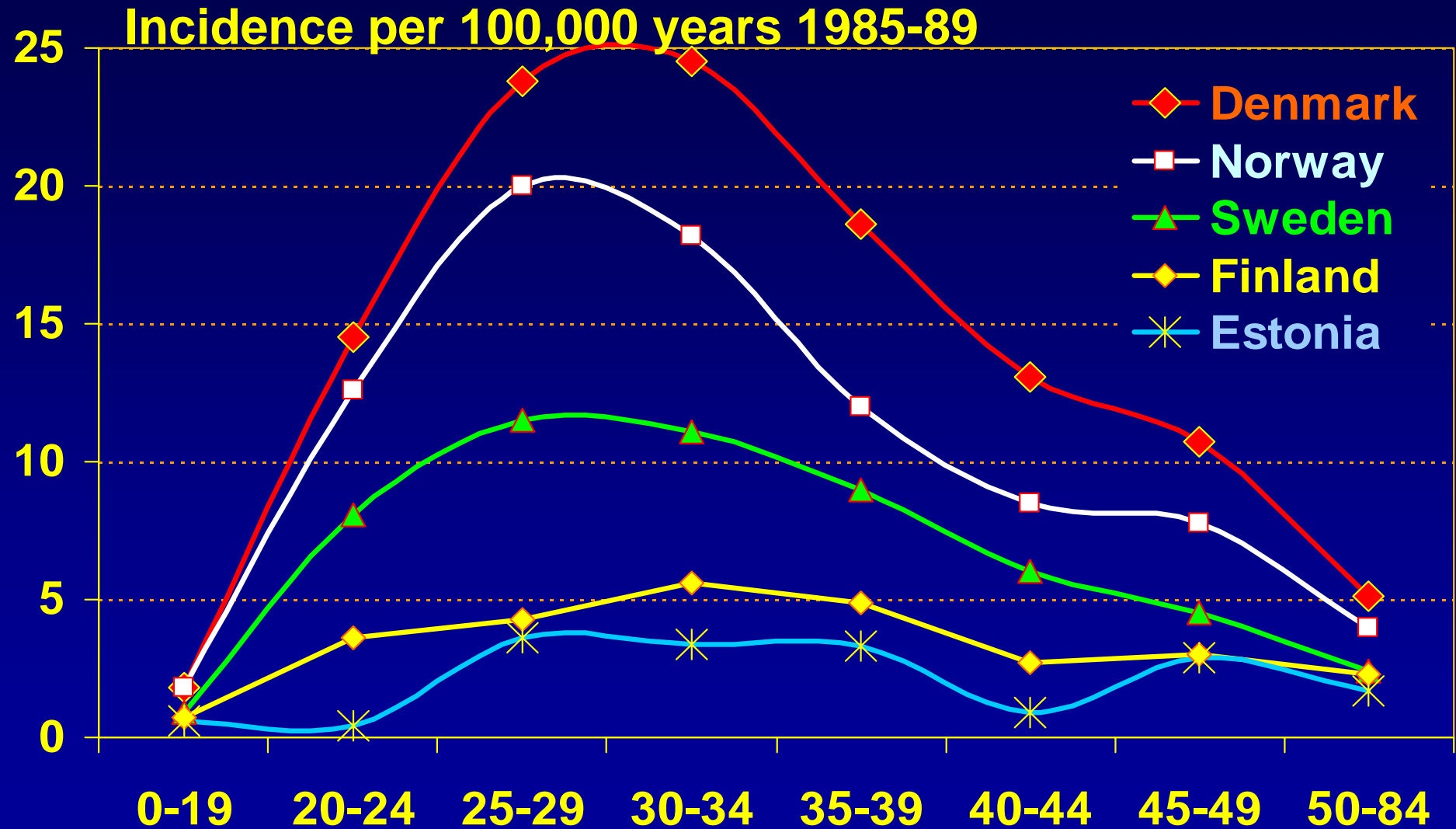
Testicular cancer: west-east gradient

Incidence per 100,000 years, age standardised

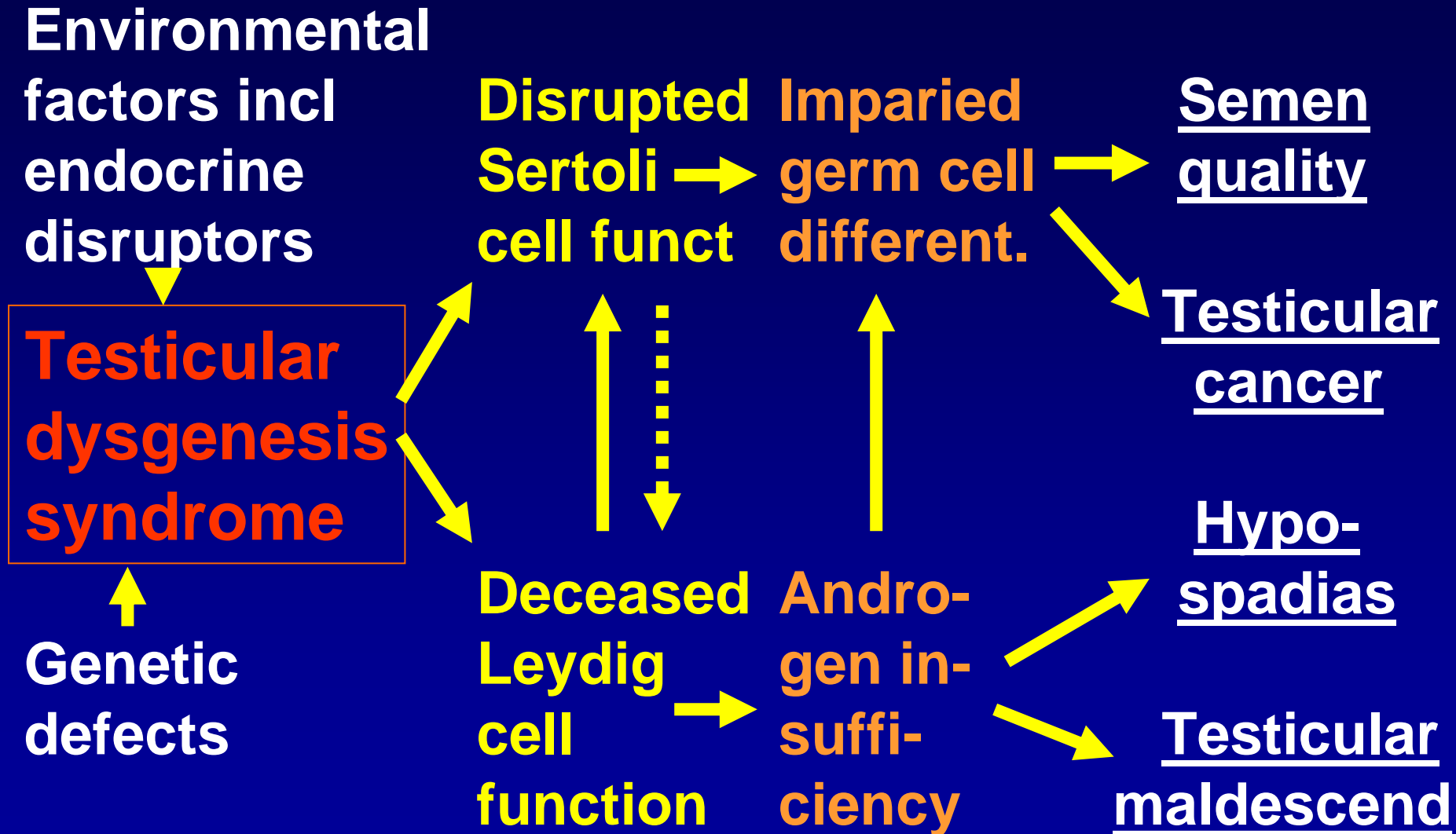


Adami et al. Int J Cancer 1994; 59: 33-38.

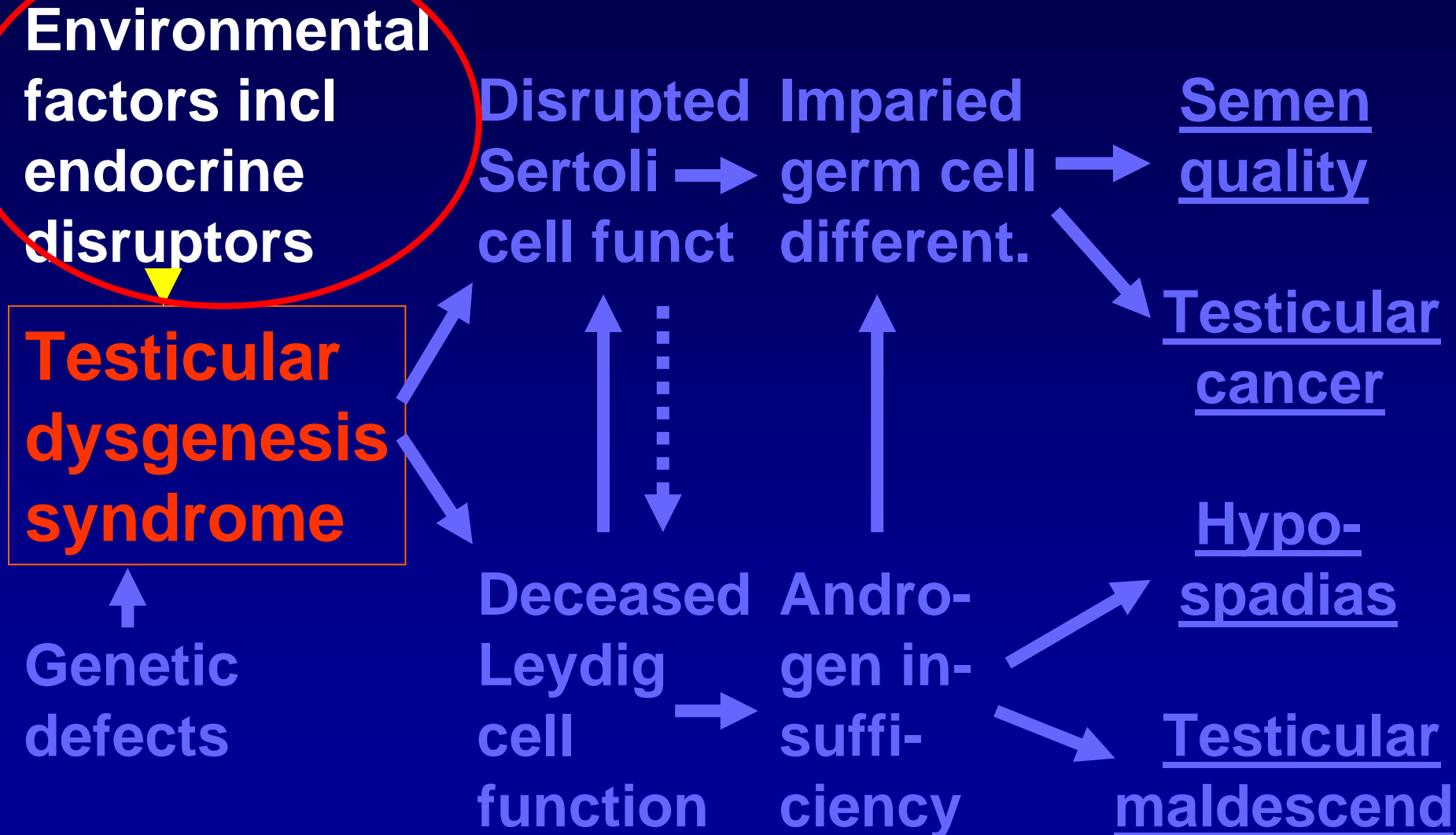
Testicular cancer according to age



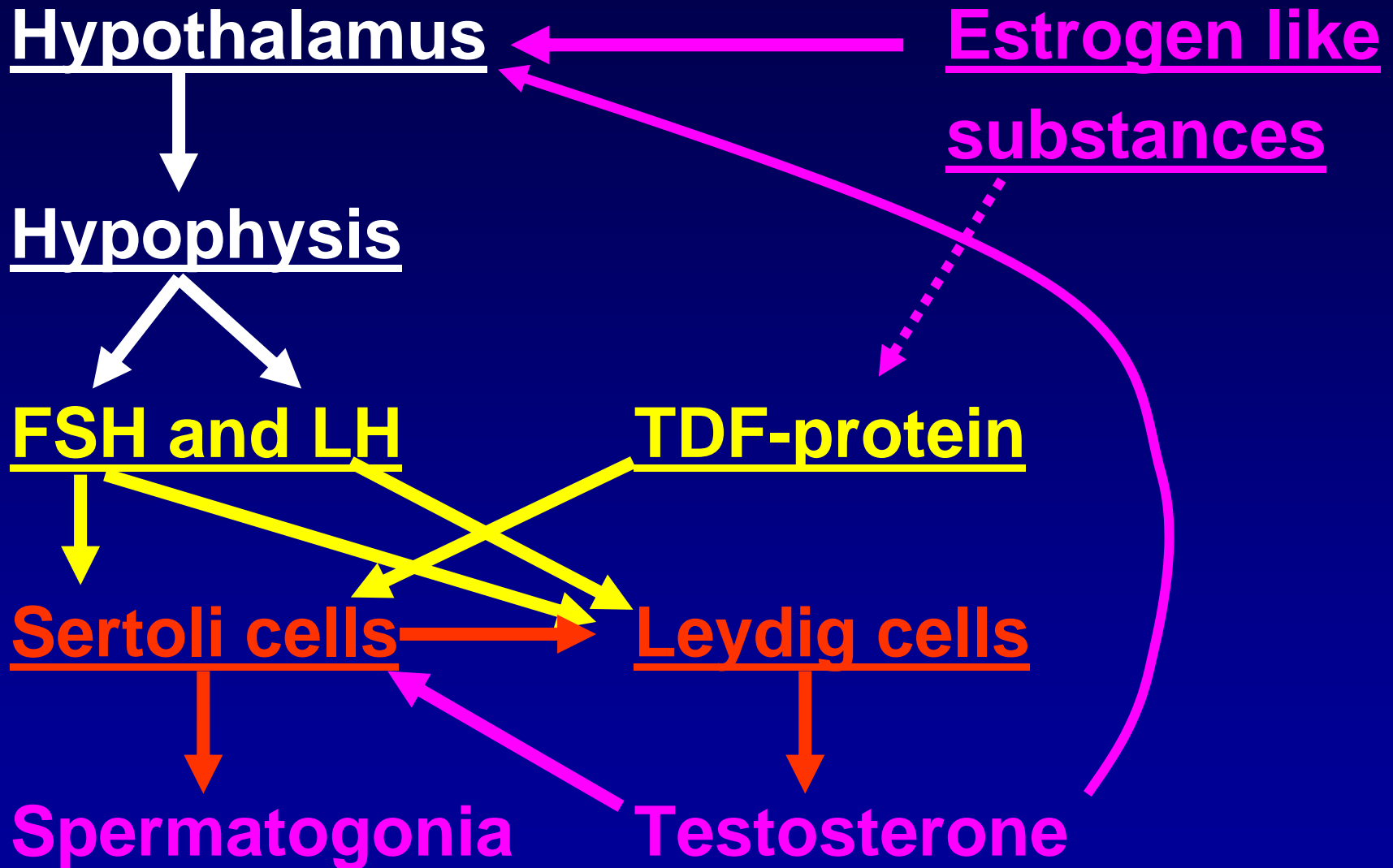
Testicular Dysgenesis Syndrome



Testicular dysgenesis syndrome



Male gonadogenesis



Phthalate exposure and anogenital distance (AGD) in male infants

- 134 boys 2-36 months
- Measure of AGD, weight and age.
- Anogenital index = AGD / weight mm/kg
- Measurement of urine phthalates during pregnancy.
- Correlation between ADI and phthalates
- Correlation AGD with penile volume and incomplete testicular descent

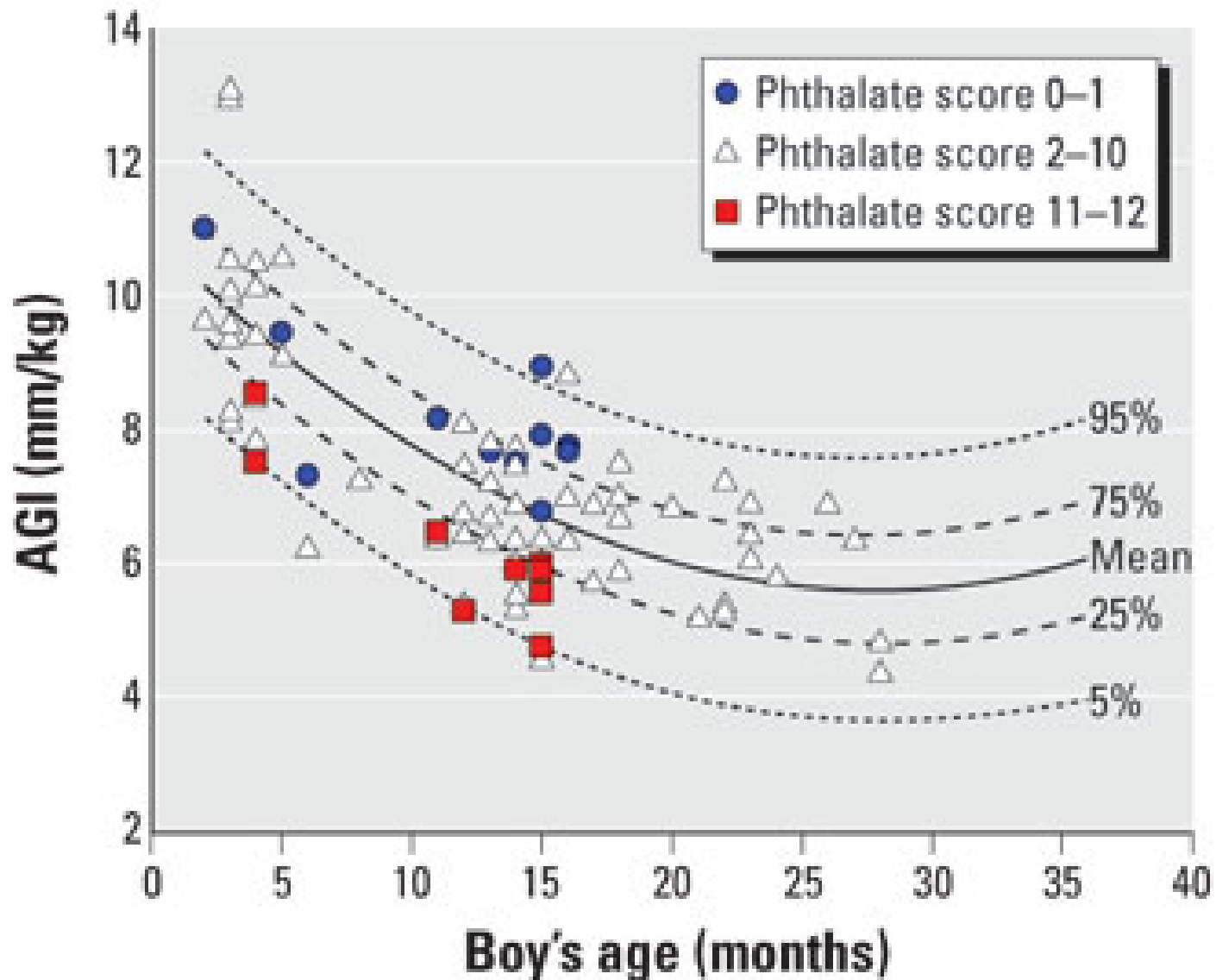


Figure 1. Mean AGI (mm/kg) in relation to boys' age at examination (months).

Phthalate exposure in rats

- Exposure of phthalates day 13-20 in 32 pregnant rats. Control group of 32 pregnant rats exposed to corn oil.
- Rats killed on day 15, 17, 19 and 21 of fetal life, and post partum at day 4, 25 and 90.
- Testes analysed immunohistochemistry
- Abnormal Leydig cell aggregation from fetal day 17. In addition dysgenetic tubules later Sertoli Cell only syndrome.

Male fertility

- Pregnant women are exposed to endocrine disruptors affecting the fertility of their male offspring lifelong.
- Phthalate exposure in rats causes TDS like changes in male rats.
- Phthalates are the most likely but probably not the only candidate for the responsibility of TDS in humans

Dansk Fertilitetselskab

www.fertilitetselskab.dk

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