Your environment: Your fertility

Strong Fertility Center Education Series
September 25, 2008

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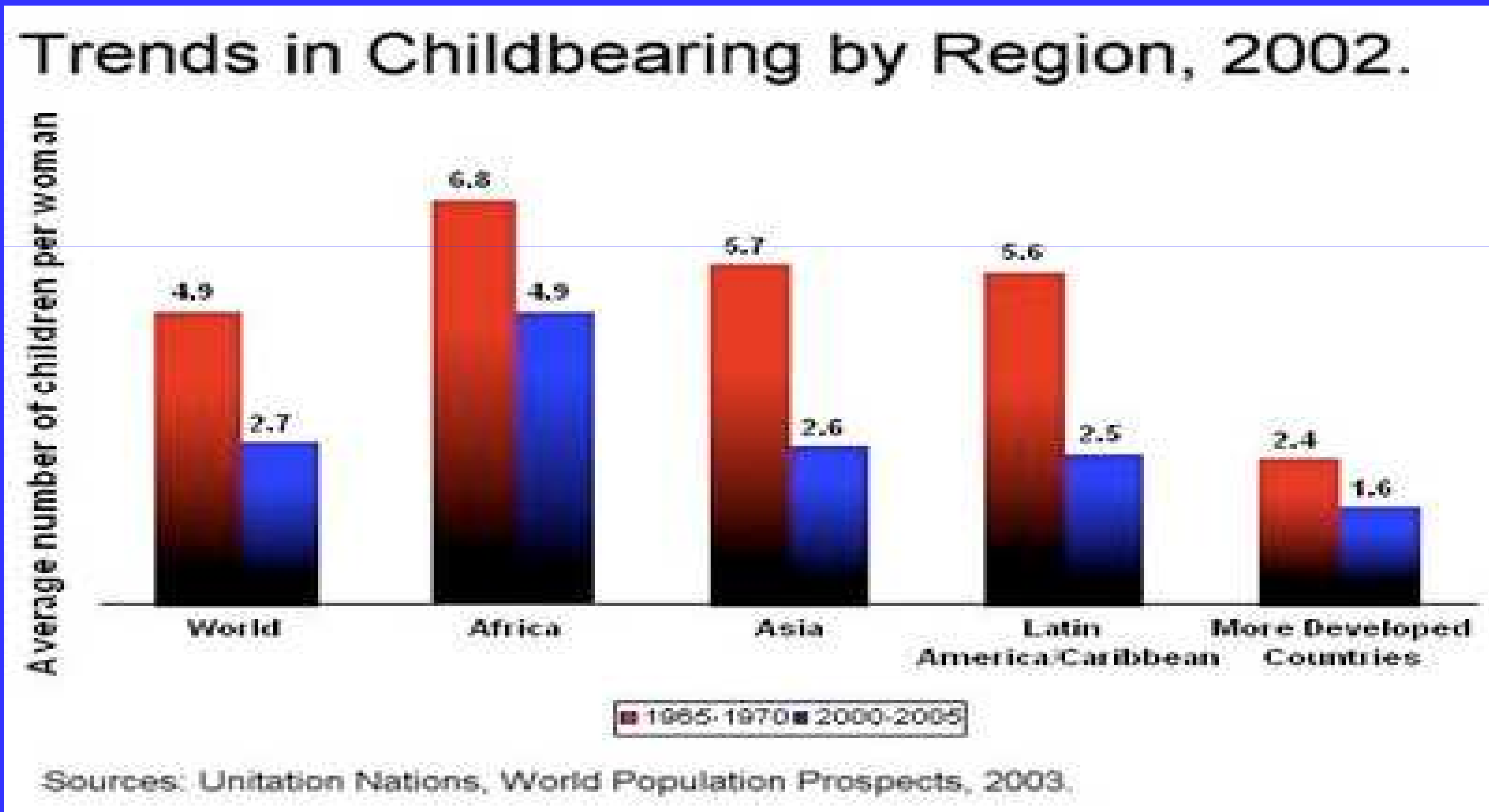
Has fertility declined?

The answer depends on the definition of fertility

Demographers' definition of fertility:

- Average number of children per woman
- By this measure *fertility has declined dramatically* worldwide since 1965



If you are not fertile are you infertile?

- **Not necessarily**
  - **You may have chosen**
    - **Not to have a child**
    - **To delay childbearing**
- **So, what defines infertility?**

Impaired fecundity

- A woman has ***"impaired fecundity*"** if:
  - It is difficult or physically impossible for her to conceive and bring a child to term *or*
  - Impossible for her husband to conceive a child *or*
  - She was continuously married or cohabiting and had not used contraception without conceiving for the prior 3 years.

By this measure, infertility is increasing

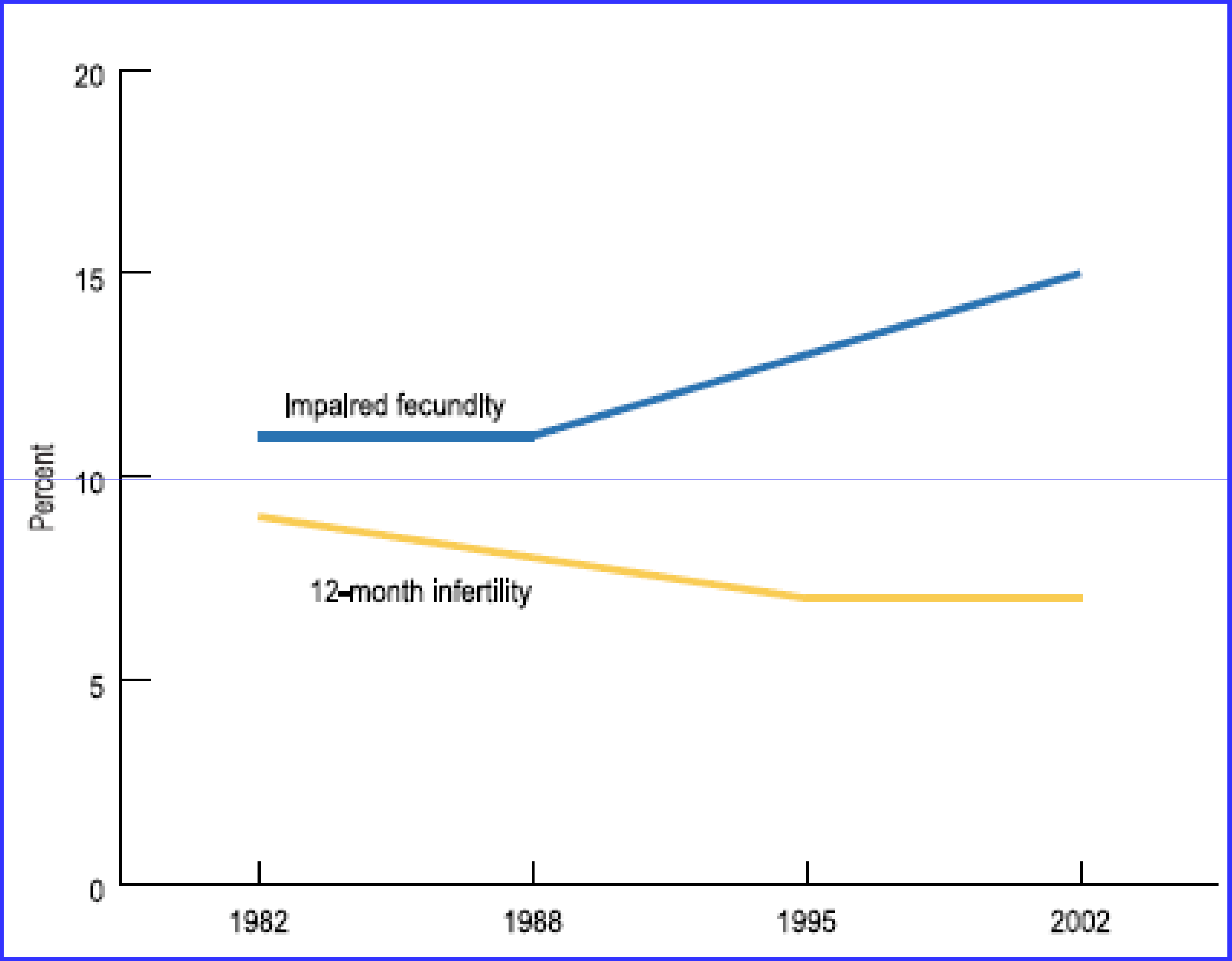
But, by another definition…

A woman has *12-month infertility* if she did not conceive (with or without treatment) *during the preceding 12 months, and was:*

- **15-44 and married**
- **Sexually active**
- **Not sterilized**
- **Not using any contraceptives**

By this measure, infertility is declining

Two measures of infertility: Two answers



Chandra et. al. NSFG 2002. Vital Health Stat 23(25), 2005

Time to Pregnancy (TTP)

TTP: number of months (cycles) of unprotected intercourse until conception

Strengths of TTP compared to other measures:

- More precisely defined
- More consistently used
- Most suitable for cross-study comparisons

(Joffe, 1996)

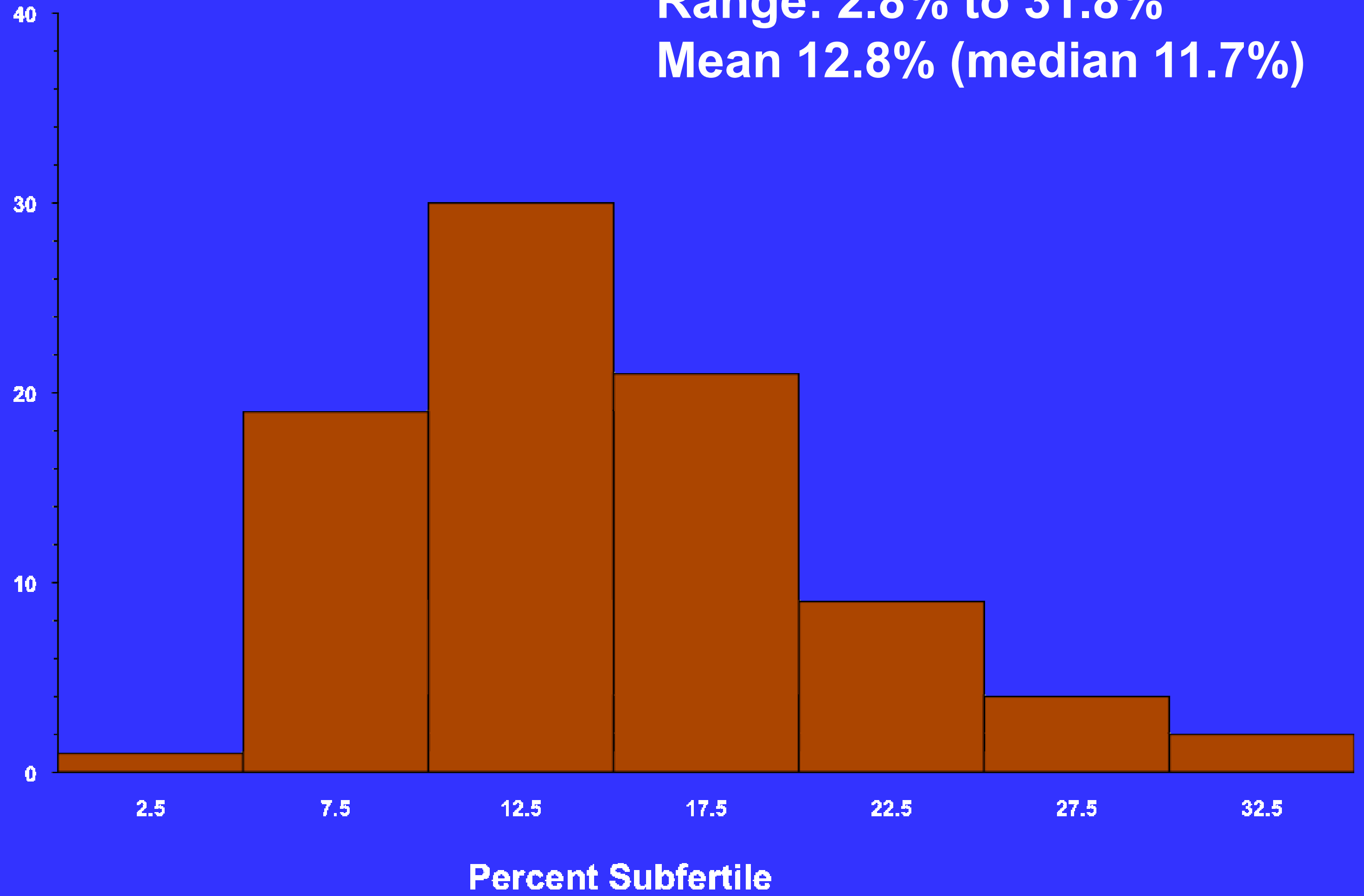
Planning or "wantedness" of pregnancy

- **TTP Most useful for couples planning pregnancy**
- **TTP poorly defined for *unplanned pregnancies***
- **But 49% of pregnancies in the US (not ending in miscarriage) in 1994 were unplanned (Henshaw 1998)**

All these factors make TTP very variable

Distribution of Percent Subfertile (TTP>=12 months)

Range: 2.8% to 31.8%
Mean 12.8% (median 11.7%)



Prospective studies of pregnancy planners

	UNITED STATES			EUROPE
Sample Size	611	221	200	430
Study Years	*1963-68*	*1983-85*	*1994*	1992-95
Study Area	United States	North Carolina	Washington, DC	Denmark
Rate of clinically-recognized pregnancy after:				
3 cycles	.60	.56	.51	.40
6 cycles	.76	.69	.71	.70
9 cycles	.83	.70	.78	N/A

Infertility

- Inability to become pregnant after 12 months of unprotected intercourse
  - Ovulation disorders 27%
  - Semen abnormality 25%
  - Tubal defect 22%
  - Unexplained 17%
  - Endometriosis 5%
  - Other 4%

Barbieri. In: Yen and Jaffe's Reproductive Endocrinology 2004

Infertility

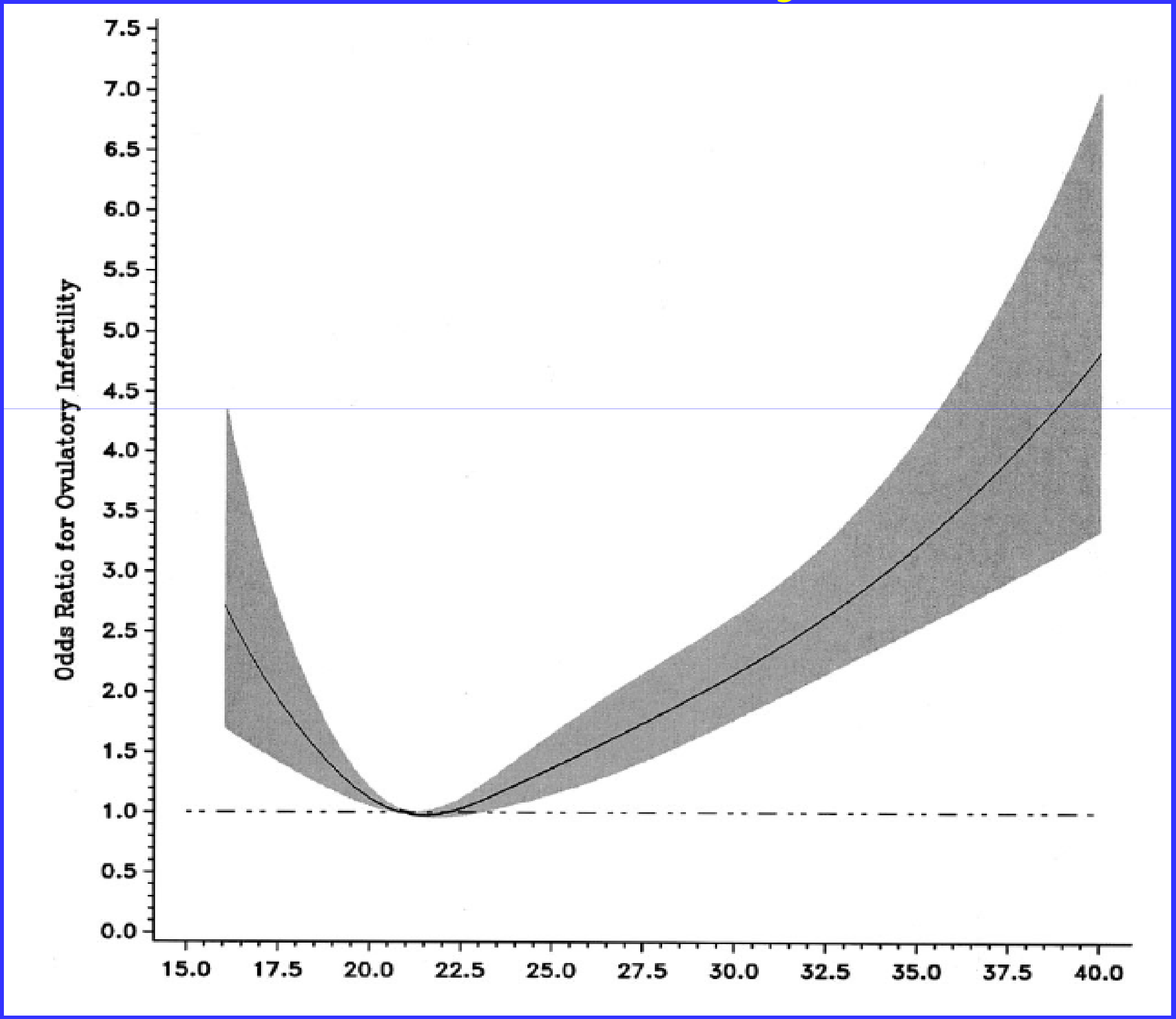
- 10 to 15% of couples trying meet definition
  - Over 7 million in the United States
- Frequency may increase with delayed childbearing
  - Mean age at 1st and 2nd pregnancy has increased by about 4 years over the past 3 decades.
- Few modifiable risk factors for infertility known

Possible environmental factors

- Environmental = non-genetic
- Includes:
  - Lifestyle factors (smoking, drinking, stress)
  - Diet, nutrition and exercise
  - Chemicals in our food, water air
    - At home, work and elsewhere

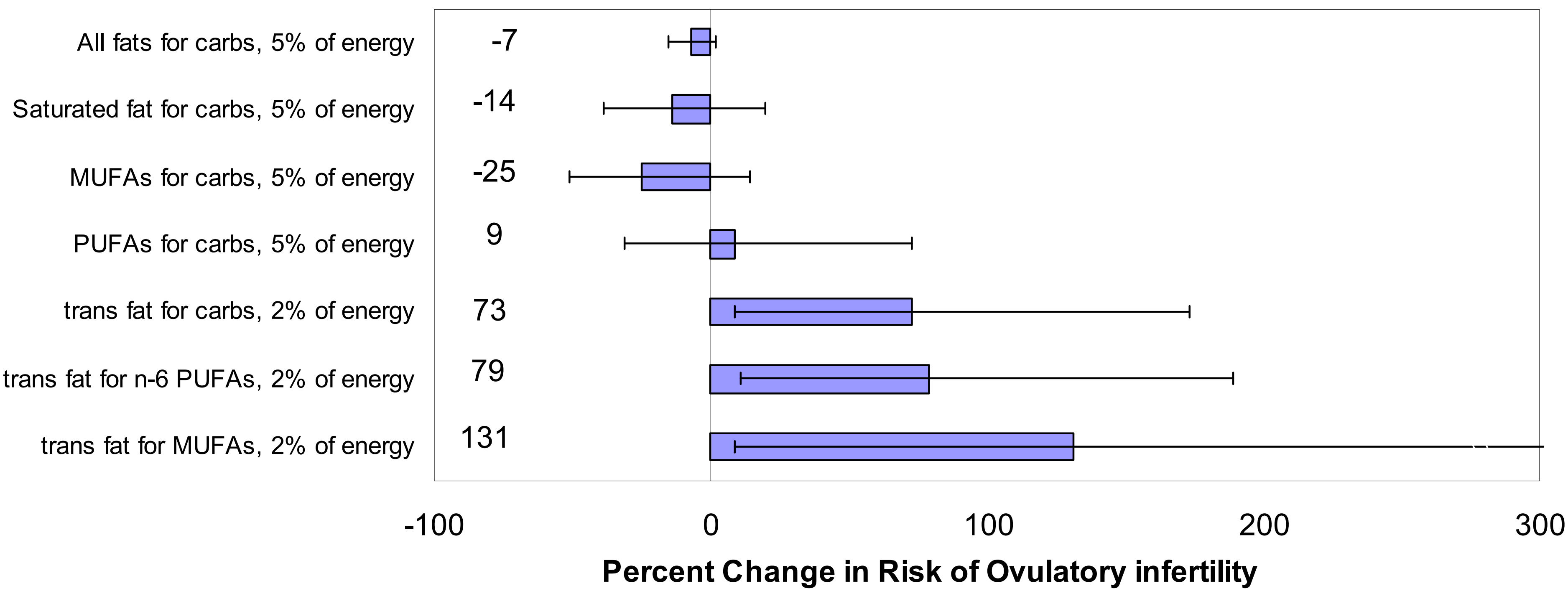
Nonchemical agents

BMI and ovulatory infertility



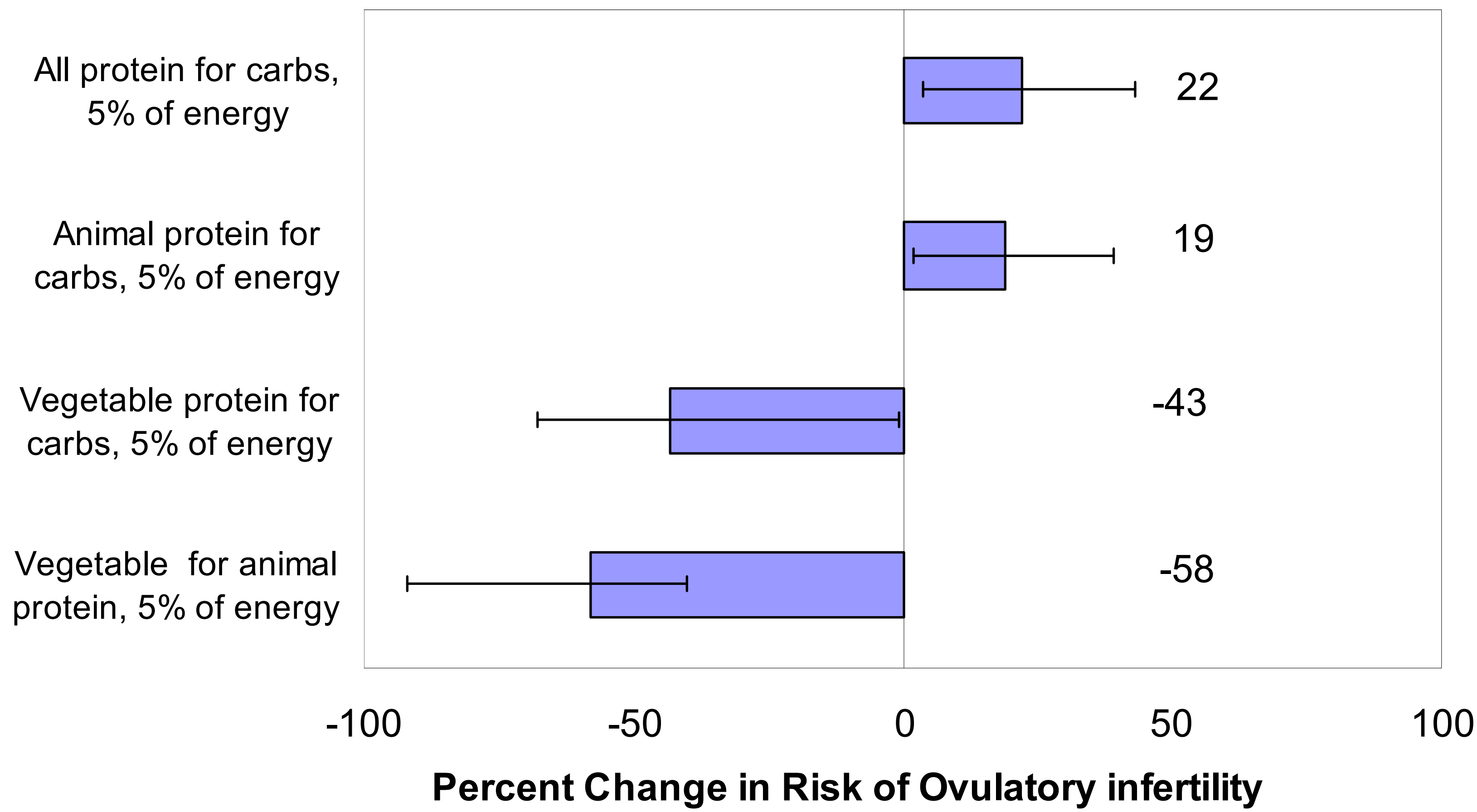
Rich-Edwards JW et al. Epidemiology 2002

Fatty acid intake



Chavarro et al. Am J Clin Nutr 2007

Protein intake



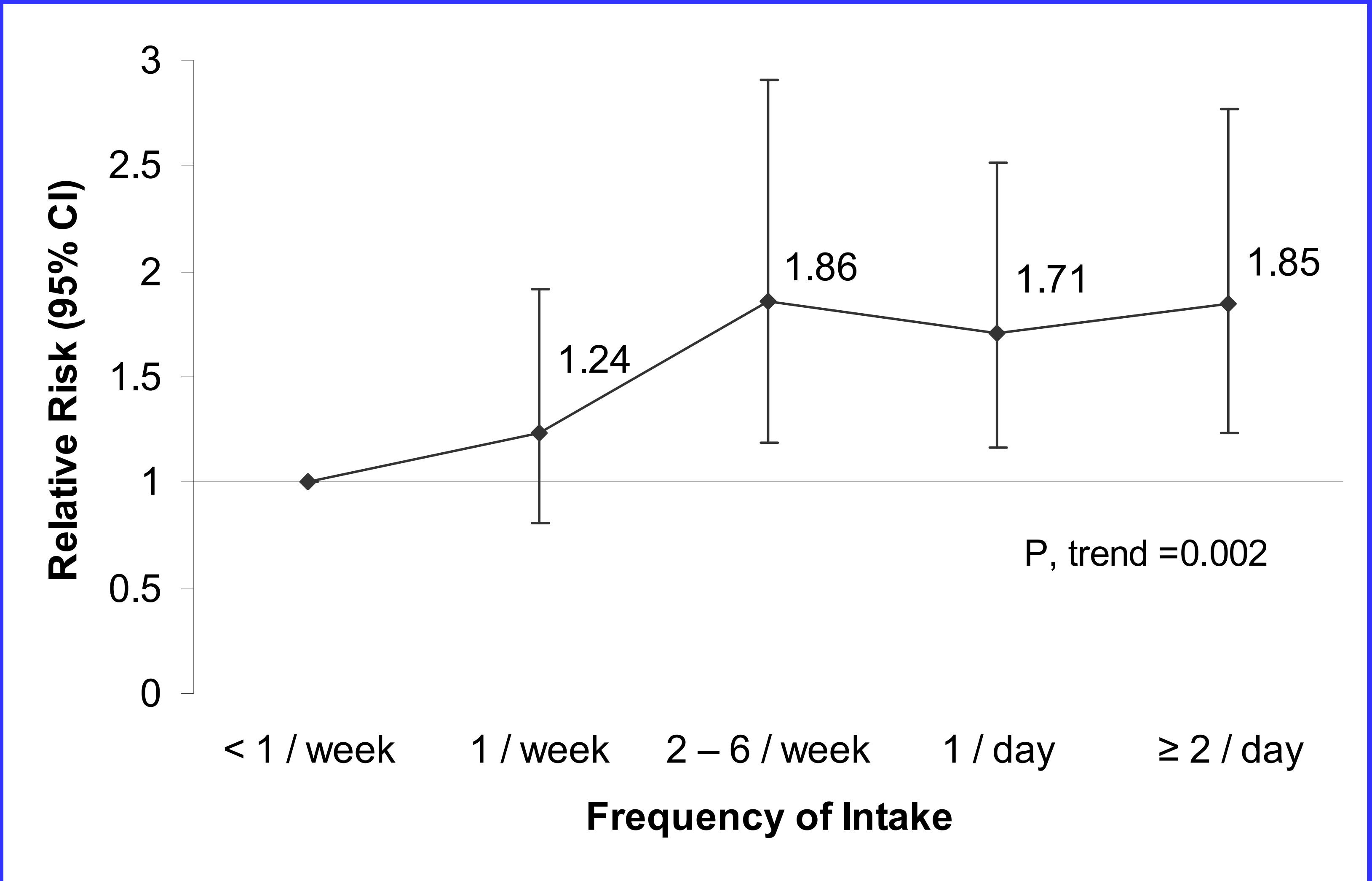
Chavarro et al. Am J Obstet Gynecol 2008

Frequency of multivitamin use

	Cases / Non-cases	Age-Adjusted RR (95% CI)	Multivariate-Adjusted RR (95% CI)
Multivitamin Use			
Non Users	224 / 10,926	1.00 (referent)	1.00 (referent)
Users	214 / 15,607	0.67 (0.55, 0.80)	0.65 (0.53, 0.80)
Frequency of use			
Non Users	224 / 10,926	1.00 (referent)	1.00 (referent)
≤ 2 tablets/wk	32 / 1,808	0.84 (0.58, 1.23)	0.88 (0.60, 1.28)
3 – 5 tablets/ wk	52 / 3,796	0.66 (0.49, 0.90)	0.69 (0.51, 0.95)
≥ 6 tablets/ wk	127 / 9,783	0.63 (0.51, 0.79)	0.59 (0.46, 0.75)
P trend		<0.001	<0.001

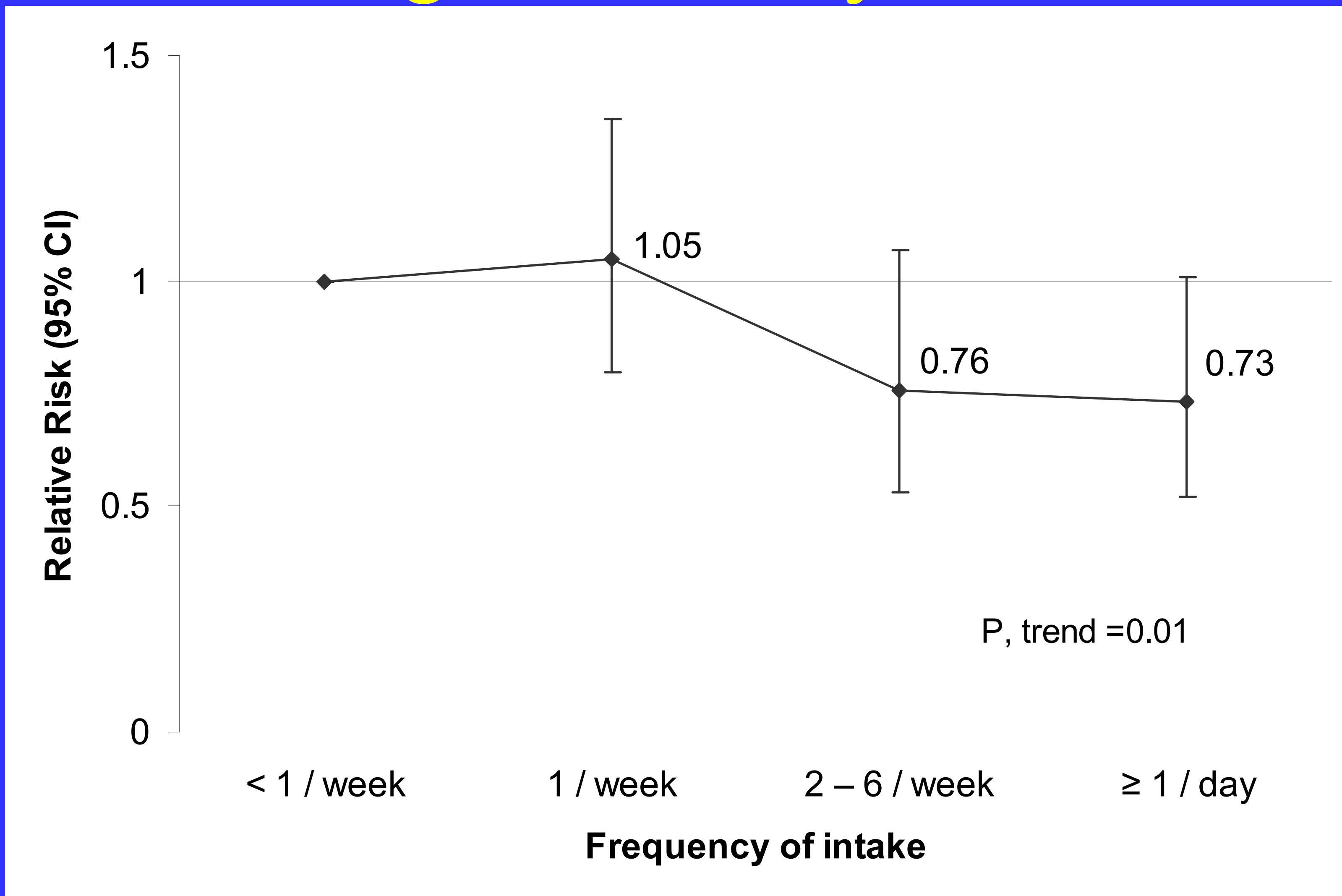
Chavarro et al. Fertil Steril 2007

Low-fat dairy foods



Chavarro et al. Hum Reprod 2007

High-fat dairy foods



Chavarro et al. Hum Reprod 2007

Lowest risk exposure levels

1. Vigorous physical activity: > 30 min/day
2. Body mass index: 20 – 24.9
3. Animal protein: < 10% of energy
4. Vegetable protein: >7% of energy
5. Blood sugar: bottom 10% of distribution
6. Iron: > 40 mg/day
7. Low fat dairy: < 1 serving/week
8. High fat dairy: ≥ 1 serving/day
9. Multivitamins: ≥ 6 tablets/week

Chavarro et al.

How much can be prevented

Characteristic	%	RR (95% CI)	PAR% (95% CI)
Physical activity > 30 min/day	14	0.78 (0.58 – 1.05)	21 (0 – 40)
BMI 20 – 24.9	54	0.64 (0.53 – 0.78)	21 (12 – 29)
Diet score Q5	19	0.48 (0.35 – 0.67)	46 (29 – 60)
4+ factors	14	0.40 (0.27 – 0.59)	55 (36 – 70)
5+ factors	4	0.31 (0.14 – 0.70)	66 (29 – 86)

Chavarro et al. Obstet Gynecol 2007

BMI and reproductive potential

BMI	Testis Size (mL)	Semen Volume (mL)	Sperm concentration (%)	Sperm count (%)
< 20	-2.0 *	- 0.24 *	-28.1 *	-36.4 *
20–24.9	Ref	Ref	Ref	Ref
≥ 25	0.1	-0.003	- 21.6 *	- 23.9 *

Jensen et al. Fertil Steril 2004


GUESS YOUR SPERM COUNT
WIN
WEYANT

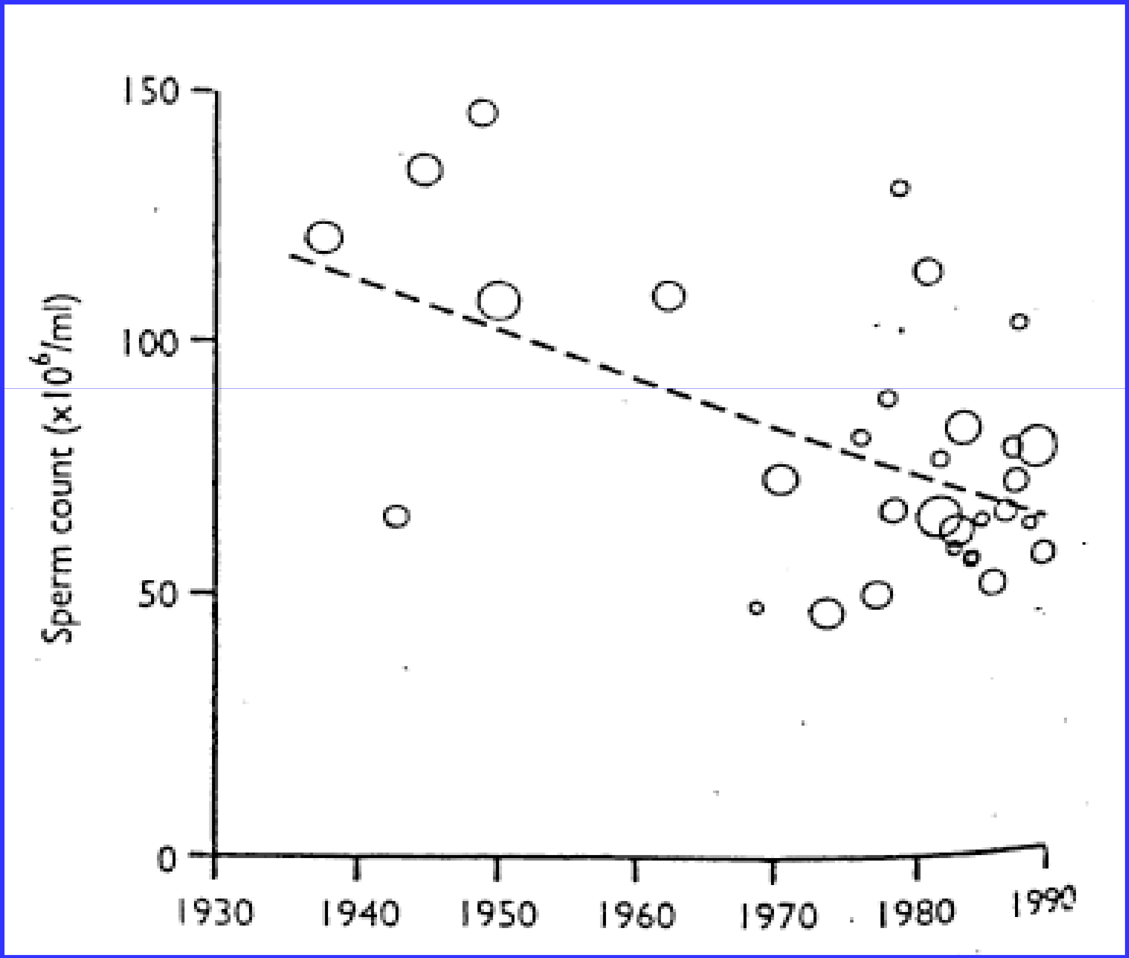
Chemicals in the Environment

Carlsen et. al. 1992

- Meta-analysis of 61 studies published 1938-1991(included 14,947 men)
- Found a significant decrease in sperm density:
  - ***1940: 113 x 10^6/mL***
  - ***1990: 66 x 10^6/mL***

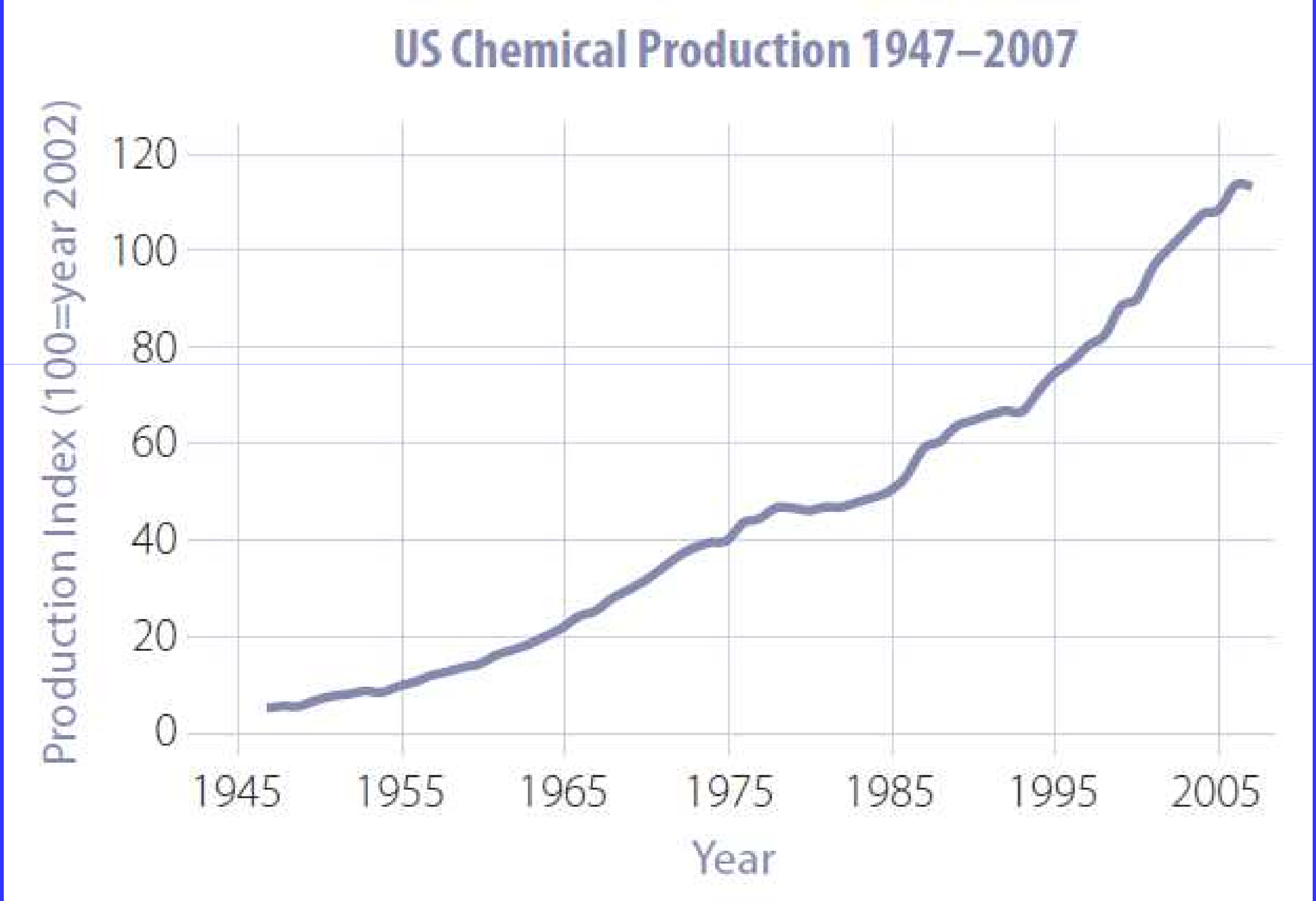
Average decline: 1%/yr (-0.93 x 10^6/mL)

Carlsen et al. 1992



Circles proportional to log sample size

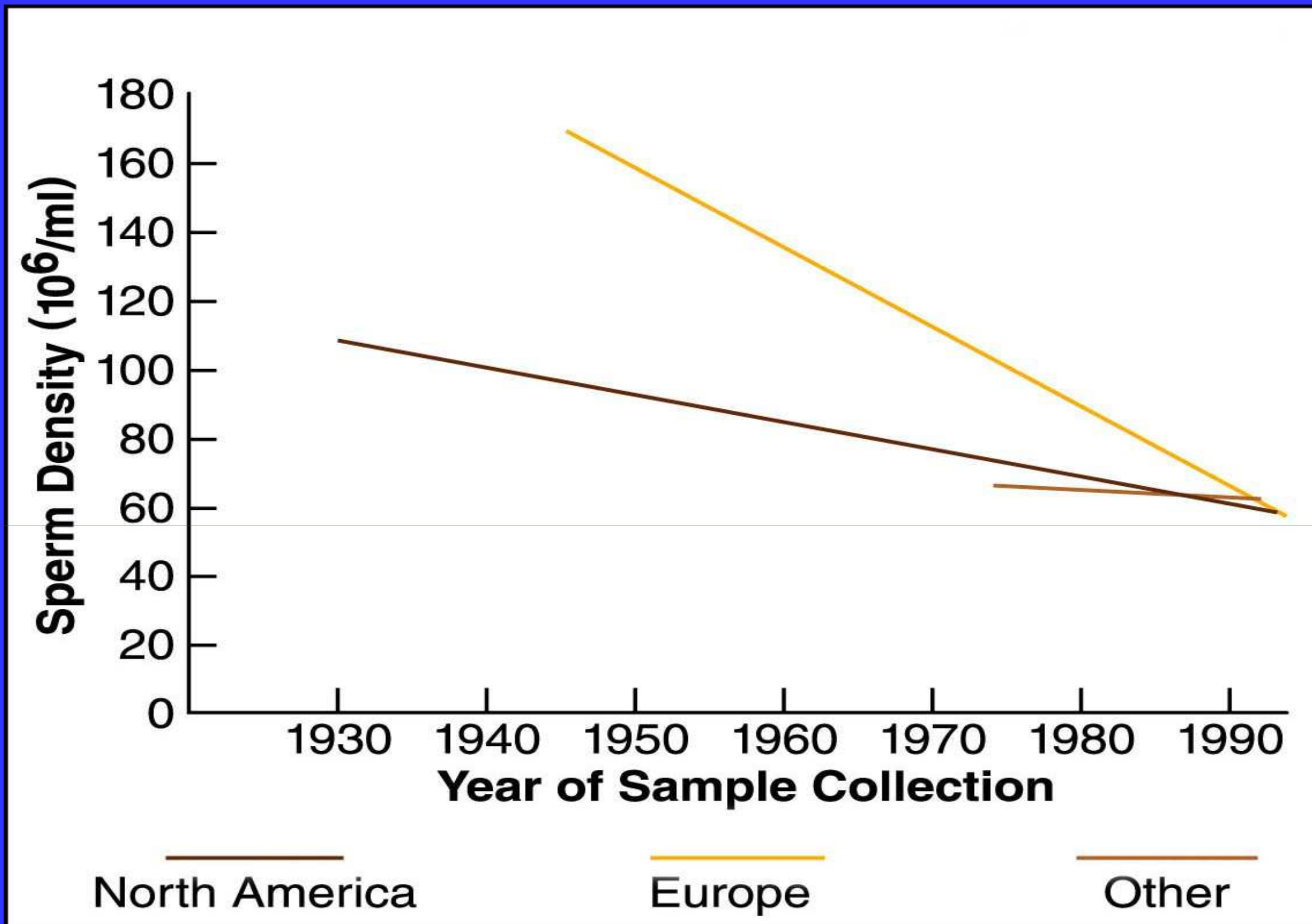
Chemicals in the environment



Swan et al. 2000

- New literature search: 1934-1996
- Analysis included 101 studies
- North America: 44
- Europe: 34
- Other: 23

Average decline: 1%/yr (-0.94 x 10^6/mL)



Swan et al. 2000

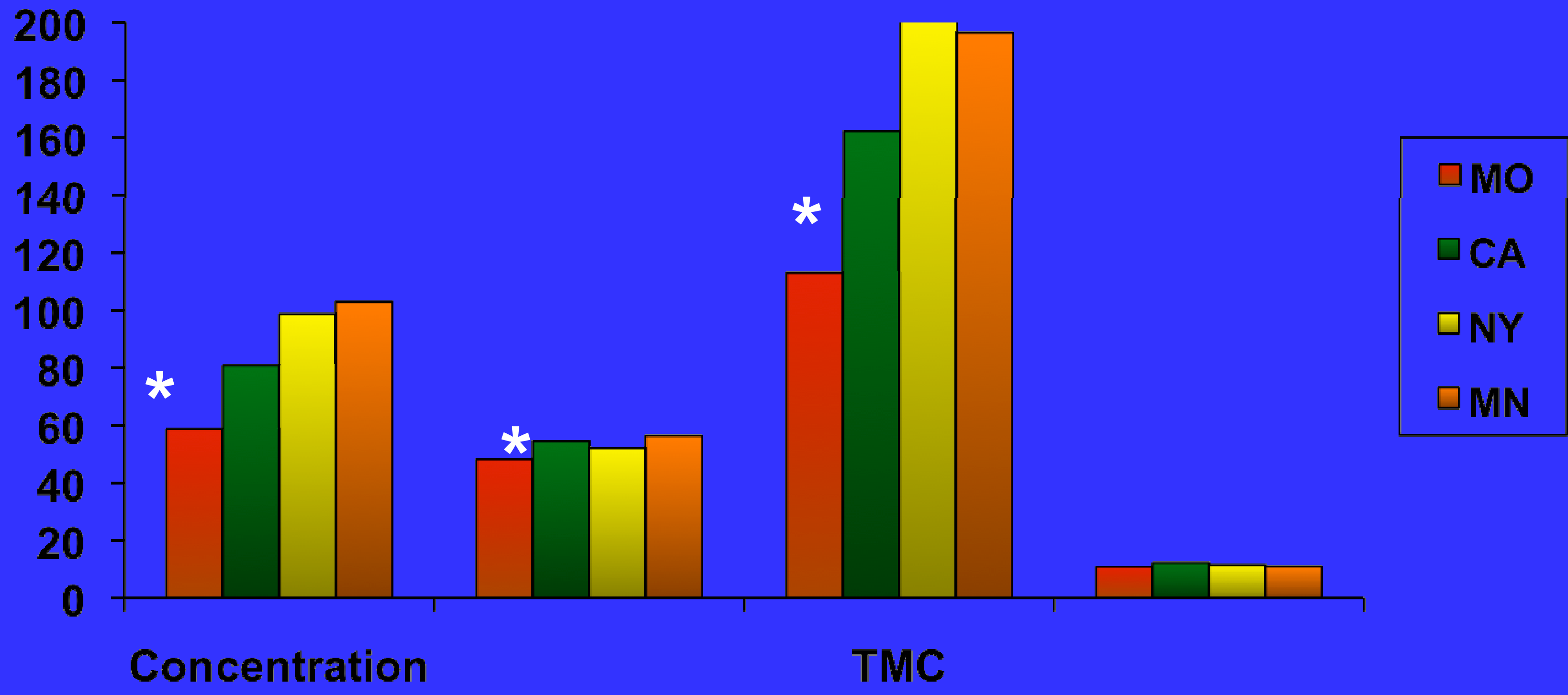
- ***Overall*** sperm density appears to have declined.
- Not explained by ***obvious confounders.***
- ***Rate*** of ***decline varies*** geographically.
- ***Mean density varies*** geographically.
- Though significant, decline was not convincing.

A new approach was needed

The Study for Future Families (SFF)

Designed to examine geographic variation in semen quality

Semen Quality by Center



Swan et al 2003

* P-Value for MO vs. all other centers <.001

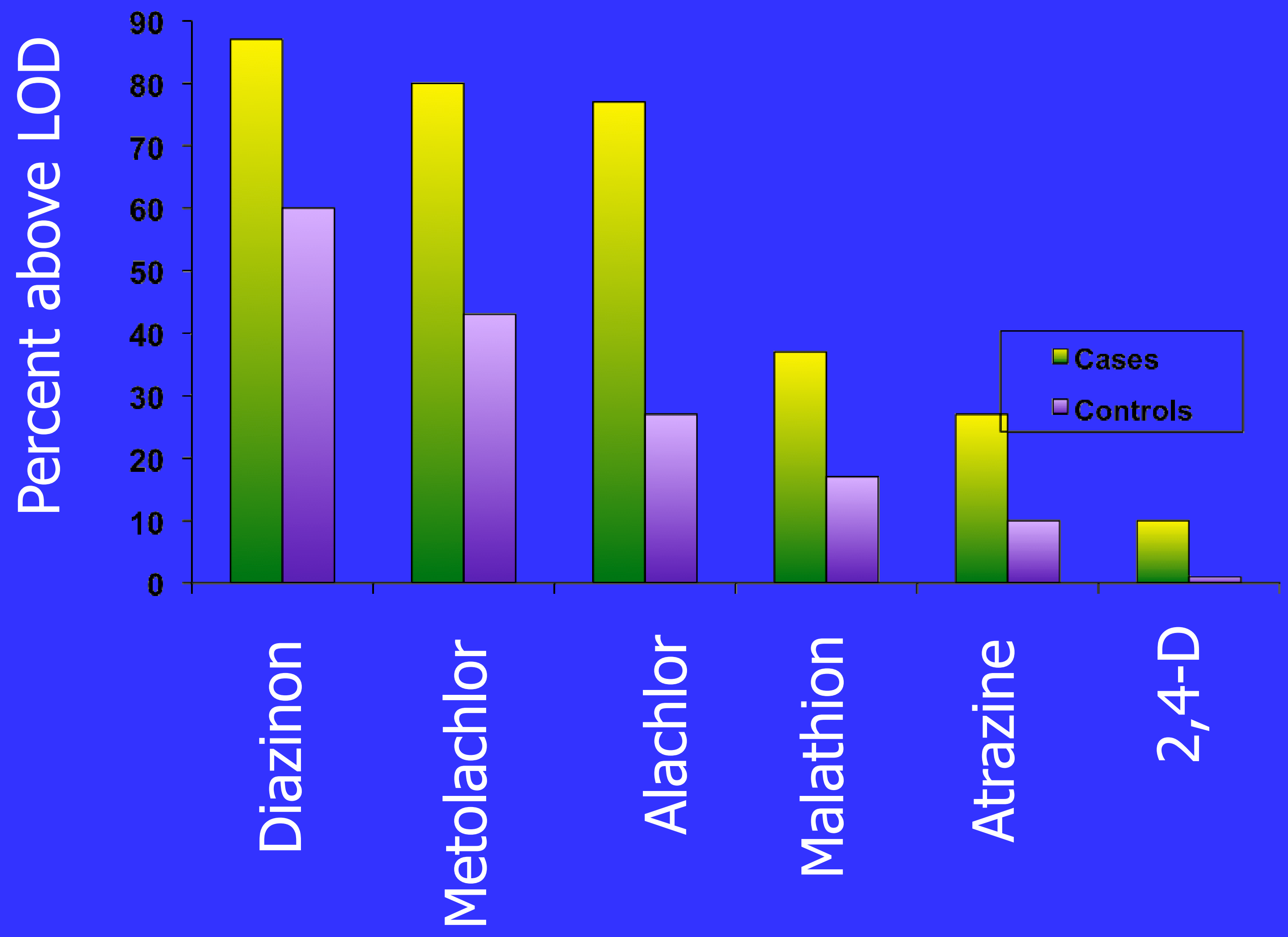
MO – 57%   MN – 19%

Nested Case-Control Study in Missouri

- ***Cases:*** Poor semen quality
  - – Mean concentration: 32.4 x 10^6/mL

- ***Controls***: Normal semen quality
  - – Mean concentration: 72.2 x 10^6/mL

Pesticides Detected More Often in Cases Than Controls



Chemicals and diet might act together

Xenoestrogens and sperm quality

- Maternal beef consumption

- Dairy foods

- Processed beef consumption

Swan et al. Hum Reprod 2007

Mendiola et al. Fertil Steril in press

Diet: Another possible source of geographic variation in semen quality

- Hypothesis: Mother's beef consumption during pregnancy can affect her son's semen quality

Background

- Diethylstilbestrol present in US beef from 1954-1979.
- Six hormones (anabolic steroids) used in production of US beef:
  - Natural steroids: estradiol, testosterone and progesterone
  - Synthetic hormones, zeranol (an estrogen), trenbolone acetate (a steroid with androgen action) and melengestrol acetate (a progestin)
- Since 1988 no hormone-treated beef sold in the EU

We examined this hypothesis in our study

- We looked at semen parameters in SFF men in relation to amount of beef their mothers ate while pregnant.
- Mothers' beef consumption was also analyzed in relation to her son's history of previous subfertility.
- Regression analyses controlled for son's age, abstinence time, and alcohol consumption.
- Definition:

Eating >1 beef meal a day = "High beef consumer"

Results (1)

- *Sperm concentration* was inversely related to mothers' beef meals per week (P = 0.041).
- Sons of *"high beef consumers"* vs. *others*:
  - Sperm concentration reduced 24.3% (P = 0.014)
  - 17% had sperm concentration < 20 x 10^6/ml compared to 5.7% of others (P = 0.002)

(Swan et al. 2007)

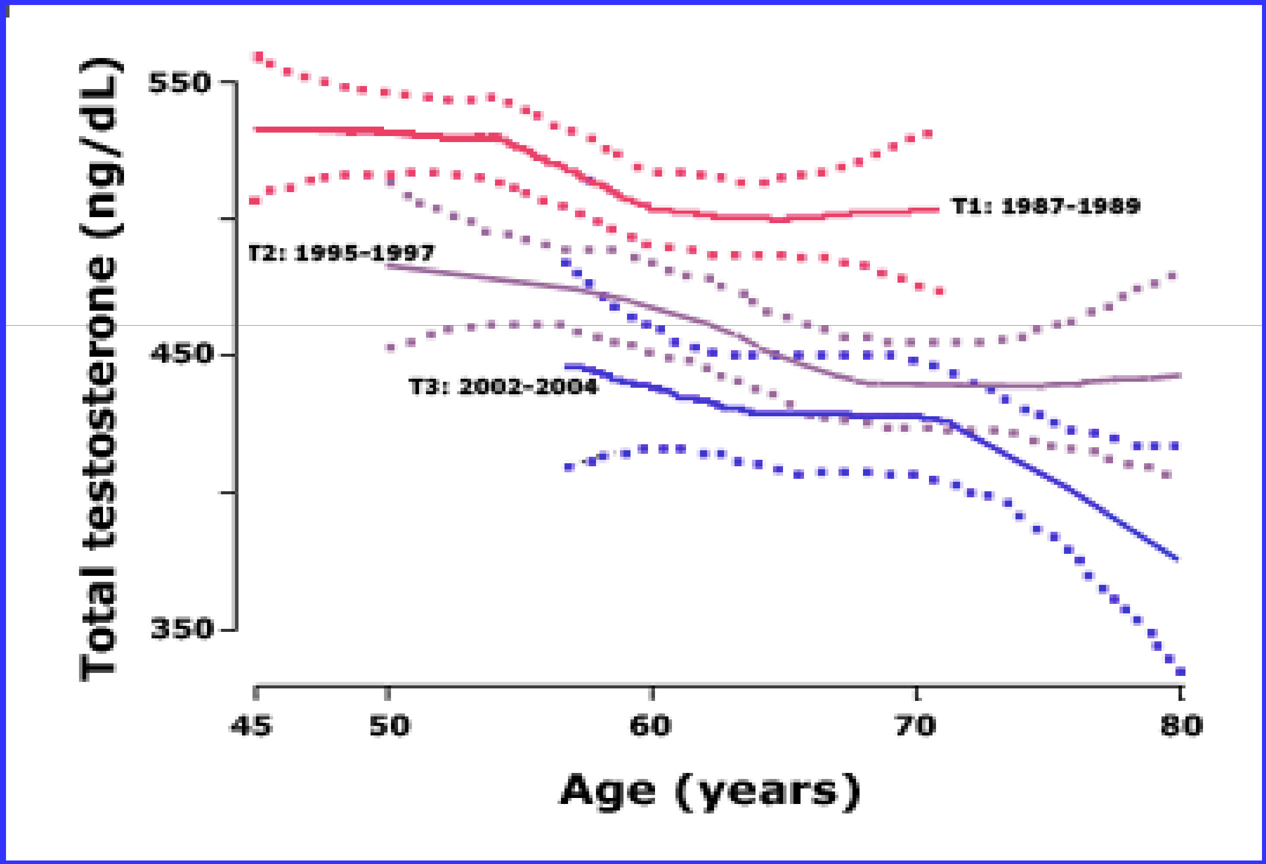
Results (2)

- History of previous subfertility twice as frequent among sons of high beef consumers frequency ($p = 0.016$).
- Sperm concentration was not significantly related to:
  - the mother’s consumption of other meat
  - the man’s consumption of any meat

Sperm Production Unlikely to be Effected in Isolation

- If sperm decline is real, we would expect trends in related parameters, such as steroid hormones.
- If geographic variability in semen quality is real, we would expect variability in other endpoints reflecting testicular development.

Total Testosterone: Declined 1.2% /yr (1980-2004)



Travison 2006

Conclusion (1)

- Sperm concentration shows significant declines in some areas of the world.
- Semen quality shows significant geographic variation.
- Environmental factors (such as pesticides and anabolic steroids) are suspect but not proven causes.

Conclusions (2)

Fertility can be influenced by a mixture of exposures at different developmental stages:

– ***In utero exposures*** including environmental endocrine disruptors (e.g. pesticides, hormones in beef)

– ***Early postnatal development*** (e.g. BPA in infant formula)

– ***Adult exposure*** (e.g. pesticides, phthalates)

Useful websites and groups to "Google"

- Shaping Our Legacy: Reproductive Health and the Environment (http://www.prhe.ucsf.edu/prhe/pubs/shapingourlegacy.html
- Our Stolen Future (http://www.environmentalhealthnews.org)
- Environmental Health News
- Environmental Working Group
- National Geographic Green Guide
- National Resources Defense Council

Final Slide

Thank you