

## Sekse en gender in hart-en vaatziekten:



Zijn het allemaal hormonen?

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# Sekse/Gender in hart-en vaatziekten: Zijn het allemaal hormonen?

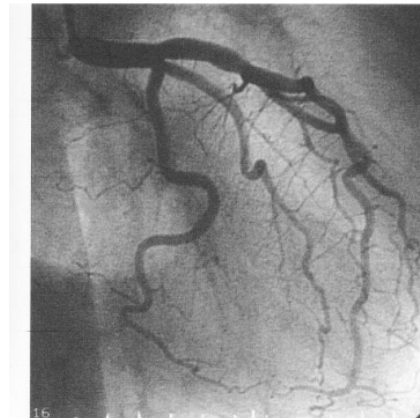
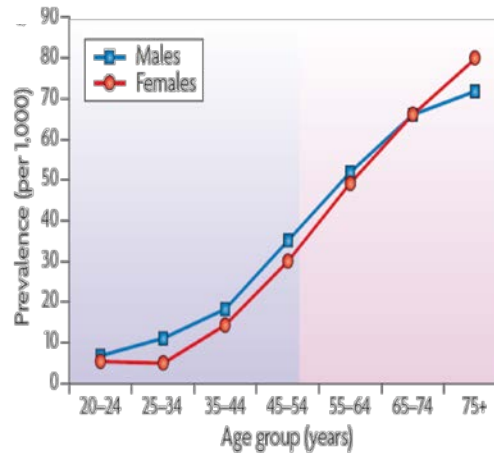
## Deze presentatie

- Sekse en gender verschillen hart- en vaatziekten
- Rol hormonen
- Menopauze en hart-en vaatziekten
- Hormoontherapie en hart-en vaatziekten
- Menstruele cyclus
- Take home messages

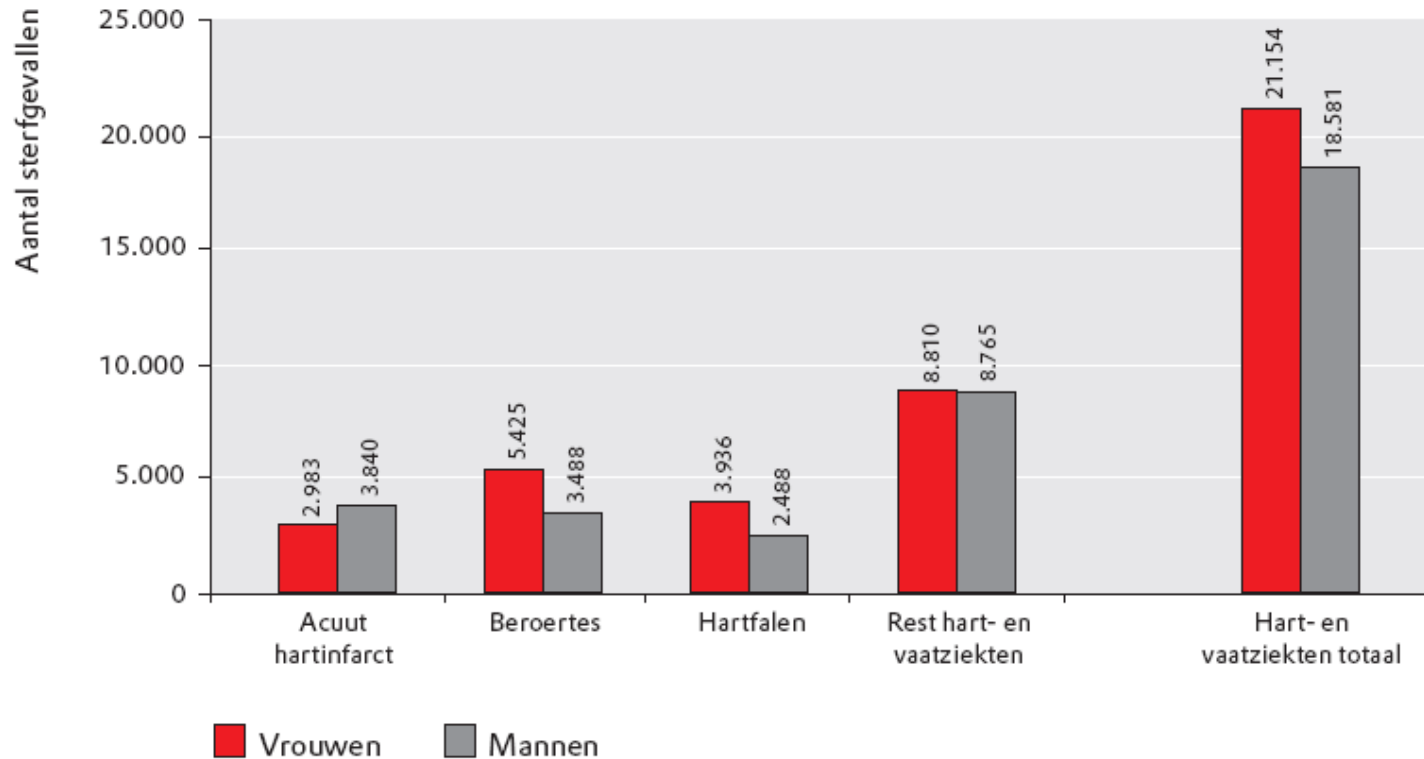
## Sekse/Gender verschillen in hart-en vaatziekten:

### *Verschillen mannen & vrouwen hart- en vaatziekten*

- **Epidemiologie**
  - Uiting HVZ
  - Betrokken vaatbed
  - Leeftijd HVZ
- **Klachten**
- **Ziekte**
- **Risico factoren**

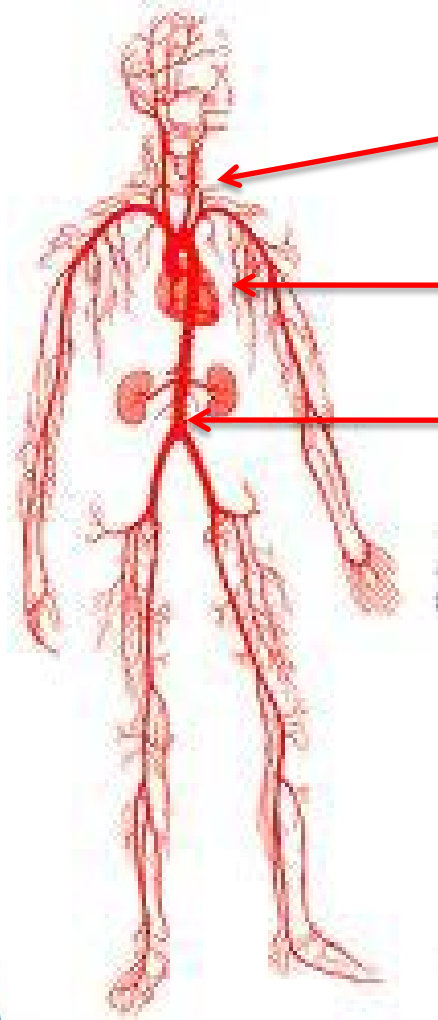


## Sekse/Gender verschillen in hart-en vaatziekten: Uiting HVZ



Sterfte hart m/v in NL 2010

## Sekse/Gender verschillen in hart-en vaatziekten: Vaatbed

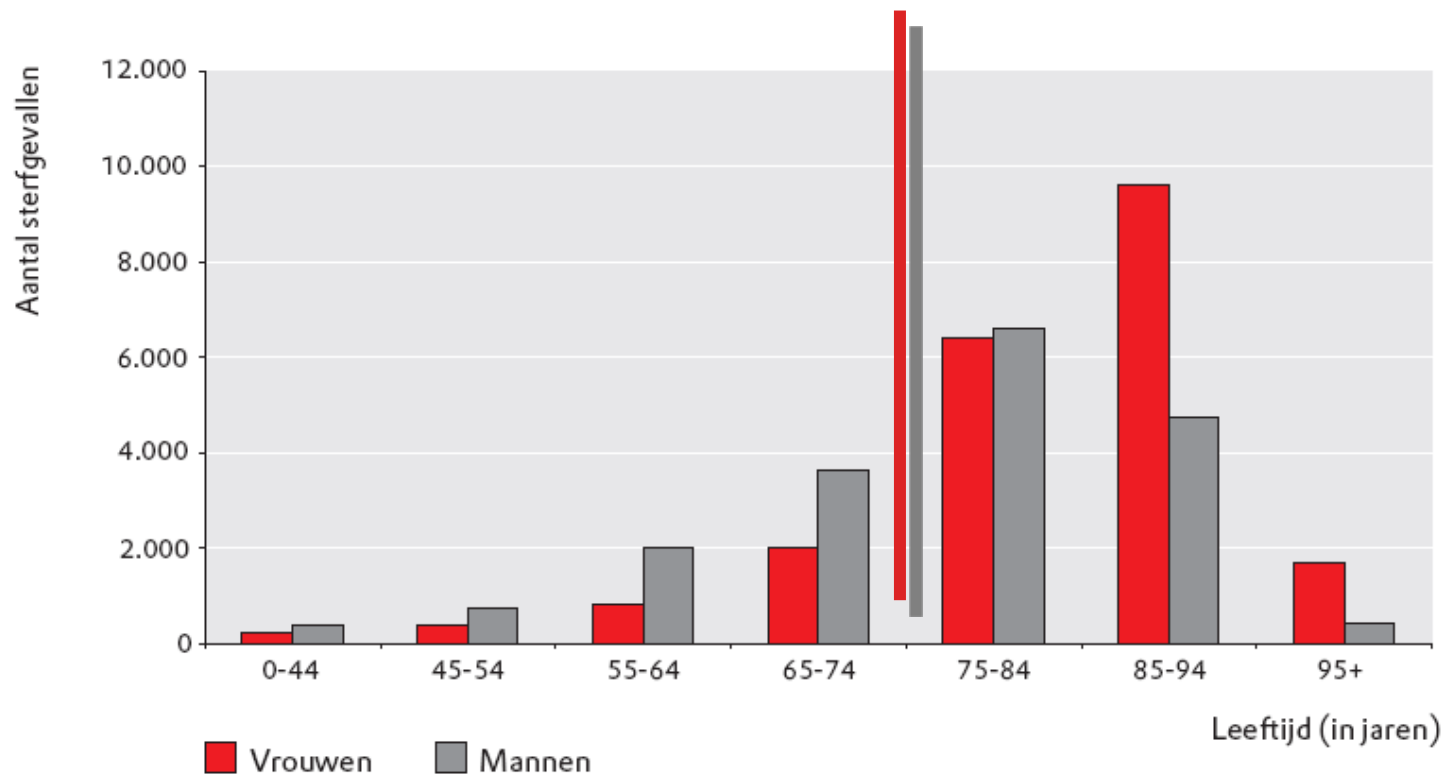


*Plaques carotiden* ♂:♀ = 2:1

*Coronaire calcificatie* ♂:♀ = 4:1

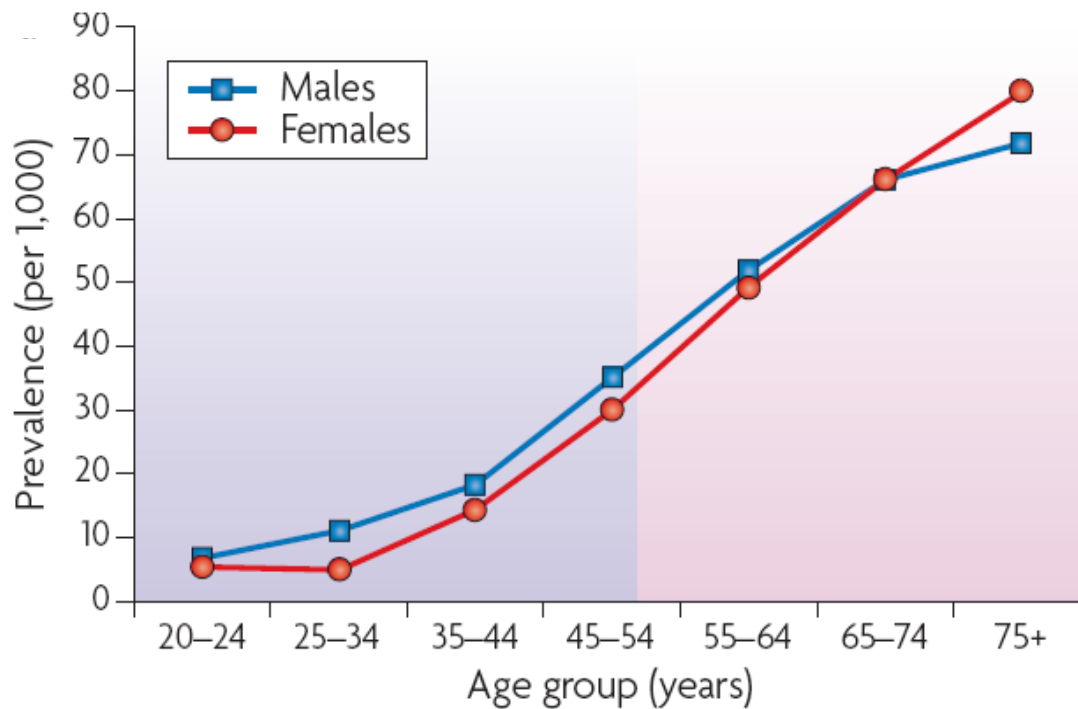
*Aorta calcificatie* ♂:♀ = 1:1

## Sekse/Gender verschillen in hart-en vaatziekten: Leeftijd sterte HVZ



Sterfte hart m/v in NL 2010

## Sekse/Gender verschillen in hart-en vaatziekten: Leeftijd HVZ



**Sekse/Gender verschillen in hart-en vaatziekten:**

Meest in oogspringende verschil

**Pre-menopauzale vrouwen**

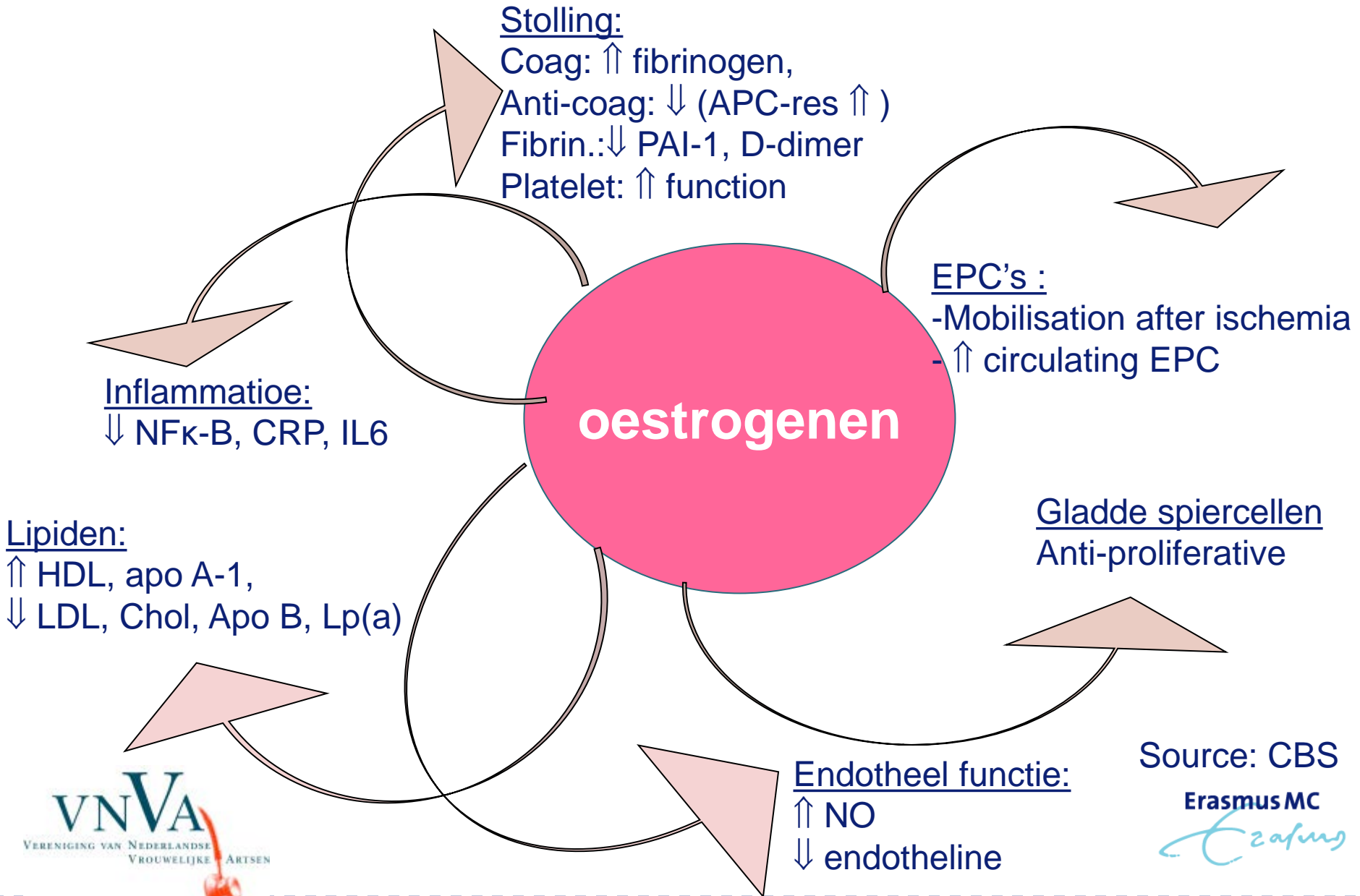
VS

**Mannen/ Postmenopauzale vrouwen**

**Vrouwelijke hormonen**



# Effecten oestrogenen op HVZ:



Source: CBS

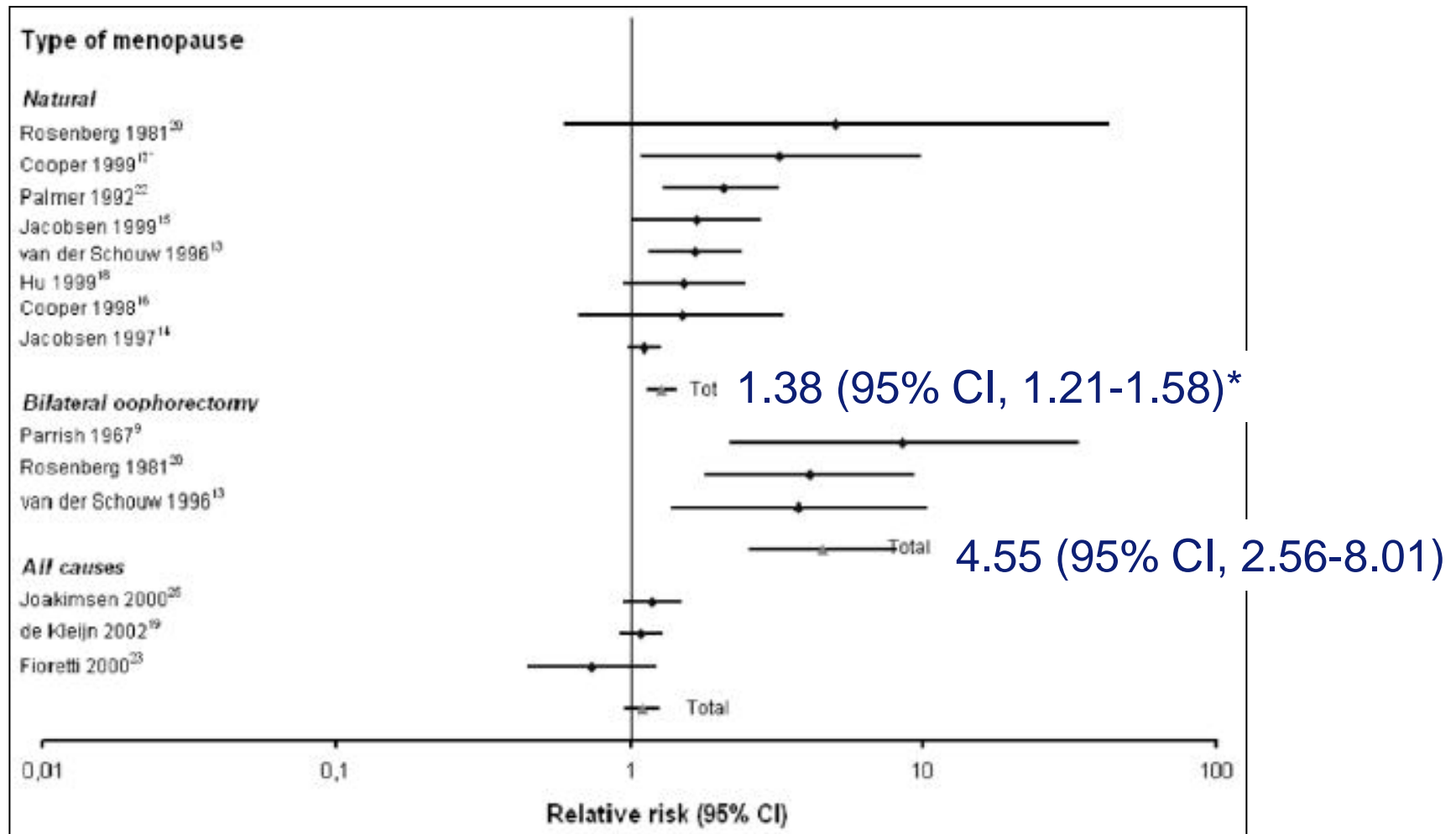
Erasmus MC

## Menopauze & HVZ:

	Hazard ratio (95% CI)
<b>Crude, adjusted only for biological age</b>	0.982 (0.968–0.996)
<b>Adjusted for all variables simultaneously</b>	0.983 (0.975–0.998)
<b>Adjusted for single variables</b>	
Year of birth	0.982 (0.968–0.996)
Natural menopause	0.981 (0.966–0.996)
Oral contraceptive use	0.983 (0.969–0.998)
Parity/age at first delivery	0.983 (0.969–0.998)
Body-mass index $\geq 30$ kg/m <sup>2</sup>	0.982 (0.968–0.997)
Upper-body fat distribution	0.982 (0.969–0.996)
Smoking	0.985 (0.971–0.999)
Hypertension	0.982 (0.968–0.996)
Diabetes	0.982 (0.968–0.996)
Previous cardiovascular disease	0.984 (0.969–0.998)

**Table 3: Hazard ratio of age at menopause and cardiovascular mortality adjusted for potential confounders**

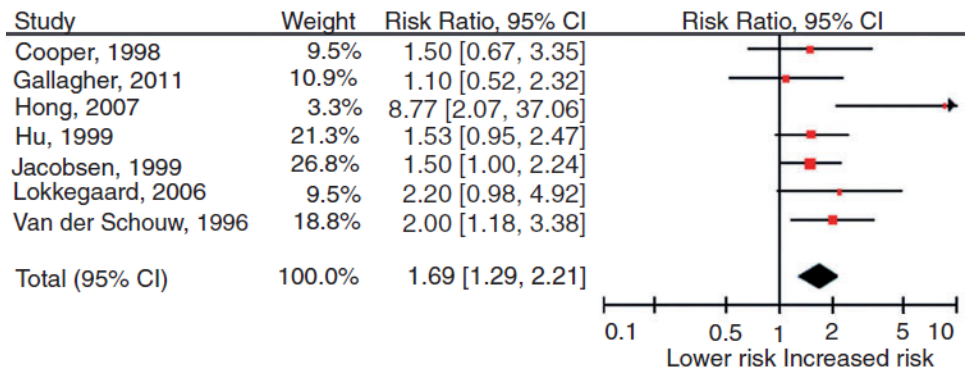
# “Abnormale” Menopauze & HVZ:Ovariectomie



\* Controlled for age and smoking

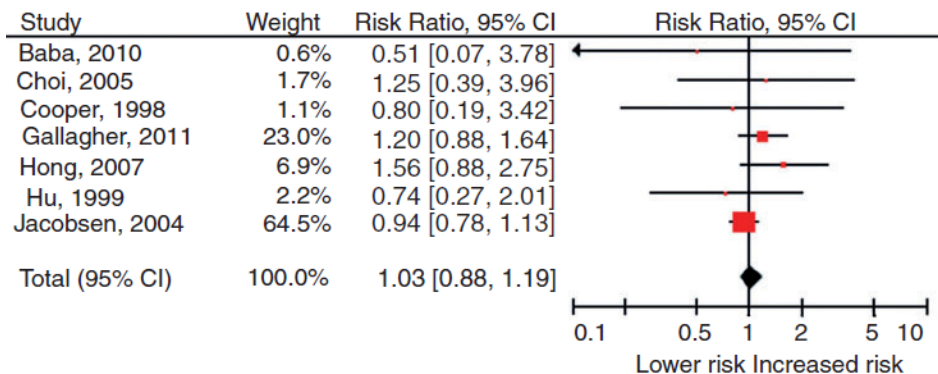
Atsma et al, Menopause 2006

# “Abnormale” Menopauze & HVZ: POI



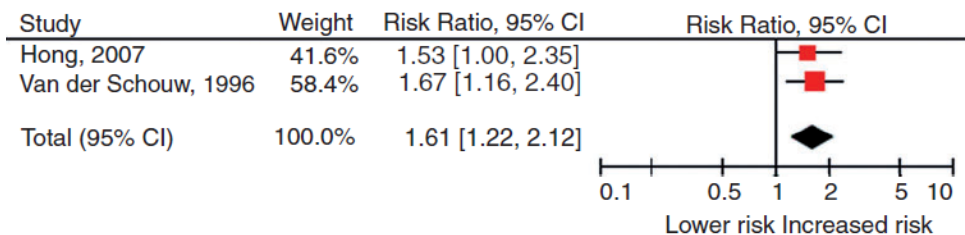
Fatal/nonfatal IHD

Heterogeneity:  $\tau^2 = 0.03$ ;  $\chi^2 = 7.66$ ,  $df = 6$  ( $P = 0.26$ );  $I^2 = 22\%$   
 Test for overall effect:  $Z = 3.83$  ( $P = 0.0001$ )



Fatal/nonfatal stroke

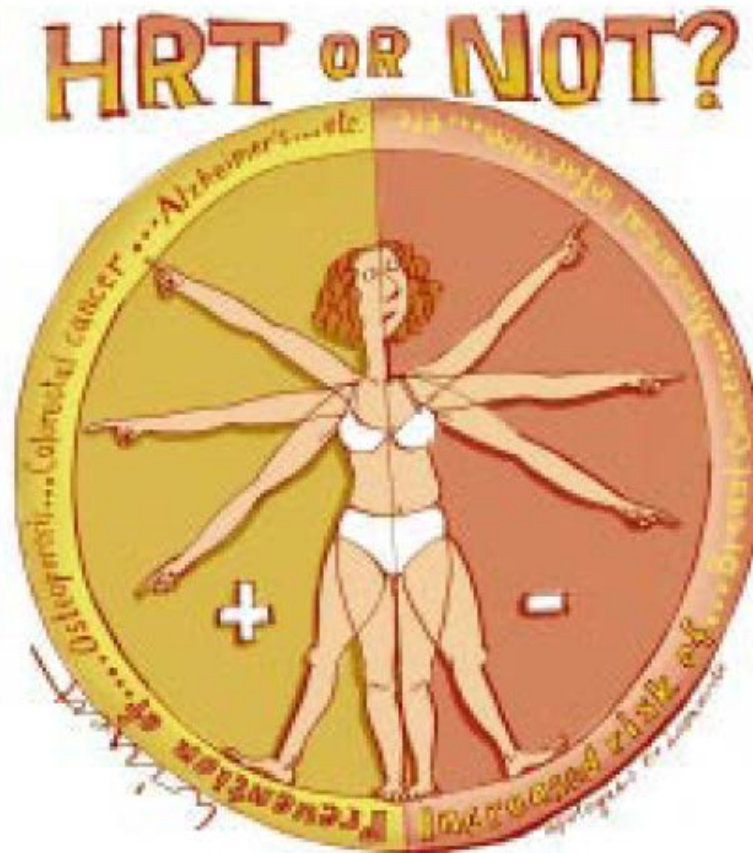
Heterogeneity:  $\tau^2 = 0.00$ ;  $\chi^2 = 4.96$ ,  $df = 6$  ( $P = 0.55$ );  $I^2 = 0\%$   
 Test for overall effect:  $Z = 0.33$  ( $P = 0.74$ )



Fatal/nonfatal total CVD

Heterogeneity:  $\tau^2 = 0.00$ ;  $\chi^2 = 0.09$ ,  $df = 1$  ( $P = 0.76$ );  $I^2 = 0\%$   
 Test for overall effect:  $Z = 3.37$  ( $P = 0.0007$ )

## Sekse/Gender verschillen in hart-en vaatziekten:



Source: CBS

Erasmus MC

## Sekse/Gender verschillen in hart-en vaatziekten: Oestrogenen en HVZ

# The Inhibition of Coronary Atherosclerosis by Estrogens in Cholesterol-Fed Chicks

By R. PICK, M.D., J. STAMLER, M.D., S. ROBBARD, M.D., Ph.D., AND L. N. KATZ, M.D.

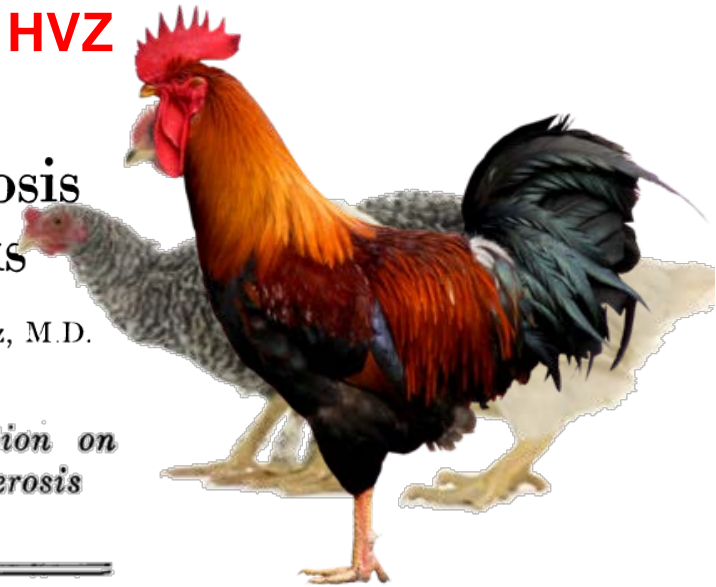


TABLE 1.—*Effects of Estrogen Administration on Plasma Lipids and on Coronary Atherosclerosis in Cholesterol-fed Chicks*

	No. of chicks*	Total cholesterol mg.%	Lipid Pt mg.%	C/P ratio‡	% Coronary lesions
Group 1: 2C-O§	13	895¶ 380–1800	17 8–25	47 32–77	100
Group 2: 2C-O + estrogen	12	742 129–1800	47 6–109	16 9–25	33

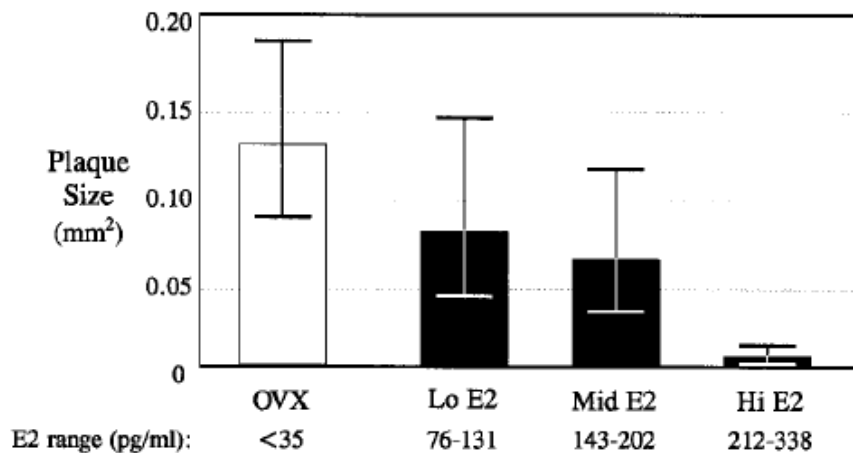
Source: CBS

Erasmus MC

The Erasmus MC logo, featuring a stylized signature in blue ink.

*Pick, circulation 1952*

# Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie



103 macacenen

1. Ovariectomie
2. Kort atherosclerotisch dieet
3. Randomisatie oestrogenen/placebo



# Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie

## Observationele studies:

“Estrogen is good for you”

Voorbeeld:

1945 blanke vrouwen NHANES  
HRT reduceert risico op HVZ  
Relative risk CVD 0.66 (CI 0,48-0,90)



Source: CBS

Erasmus MC

The logo for Erasmus MC, featuring the name 'Erasmus' in a stylized, cursive font.



# Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie- 1995



# Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie- 1995

## Estrogen and Coronary Heart Disease in Women

Elizabeth Barrett-Connor, MD, Trudy L. Bush, PhD, MHS

prevention. Until better data are available, in our opinion, the prescription of estrogen solely or primarily to prevent heart disease should be considered for women at high risk—particularly women who have high LDL cholesterol or low HDL cholesterol levels. In such

# Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie- 1995

*European Heart Journal* (1996) 17 (Supplement D), 9–14

## Evidence for primary and secondary prevention of coronary artery disease in women taking oestrogen replacement therapy

T. L. Bush

oestrogen/progestin interactions. The Heart and Oestrogen/Progestin Replacement (HERS) Study, currently underway, is a secondary prevention trial testing the protective effect of hormone therapy in women with documented CAD. This trial may definitively answer the question of whether hormones protect against CAD. After HERS, it may be unethical to continue conducting placebo-controlled trials in a therapy that has such documented cardioprotective benefit.

# Sekse/Gender verschillen in hart-en vaatziekten: Epidemioloaie

## VIEWPOINT

### Postmenopausal oestrogen and cardioprotection

JAN P. VANDENBROUCKE

It remains puzzling that in the first study all the effect on total mortality disappeared after correcting for diseases that were present at baseline, whereas in the other two the effect of oestrogens remained non-specific. In all observational studies of oestrogen substitution, it is still entirely possible that a woman who receives a prescription for hormone replacement is subtly healthier, or more determined to stay that way, than a woman who forgoes this therapy. Meta-analysis and cost-benefit analysis are unlikely to reveal the true benefit of oestrogen therapy if the increasing number of studies being pooled all have the same defect—ie, lack of comparability between users and non-users. Perhaps we should demand some colossal well-controlled trials before we let the genie of universal preventive prescription escape from the bottle.

## Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie

Study                      HERS                      WHI-I                      WHI-II                      RUTH

**GEEN VOORDEEL** Hart-en vaatziekten

**WEL NADEEL:**

Meer trombooses

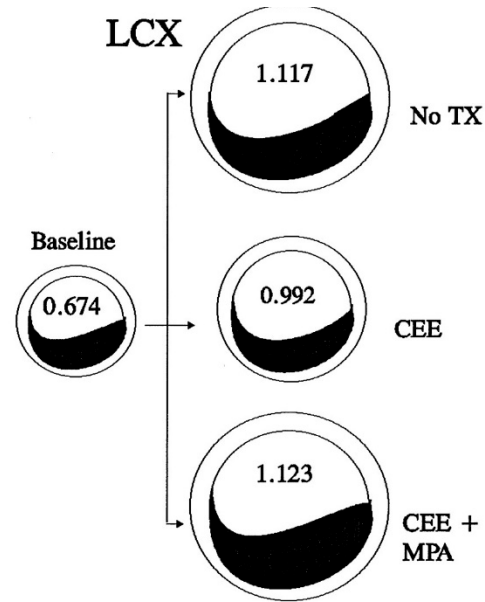
Mogelijk meer borstkanker

	HERS	WHI-I	WHI-II	RUTH
DVT/PE	U	U	U	U
Breastca	=	U	=	F
Fractures	=	F	F	F

## Sekse/Gender verschillen in hart-en vaatziekten: Epidemiologie

- Verkeerde hormonen ?
  - Verkeerde oestrogenen ?
  - Verkeerde progestagenen ?
- Verkeerde vrouwen ?
  - Te oud?
  - Te lang in de menopauze
- Verkeerde onderzoeken?
  - Te vroeg gestopt?

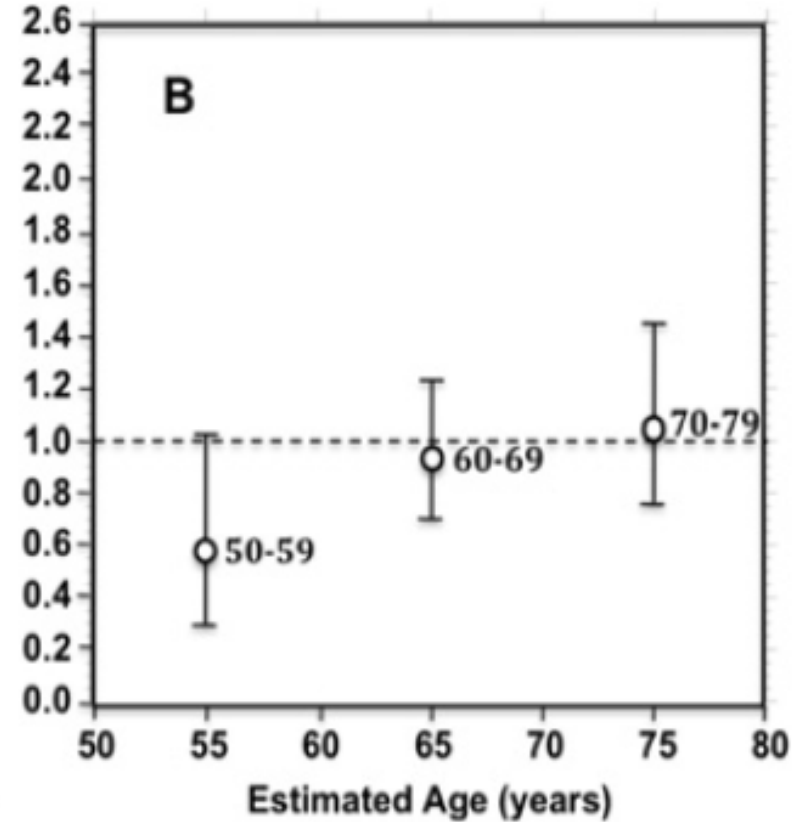
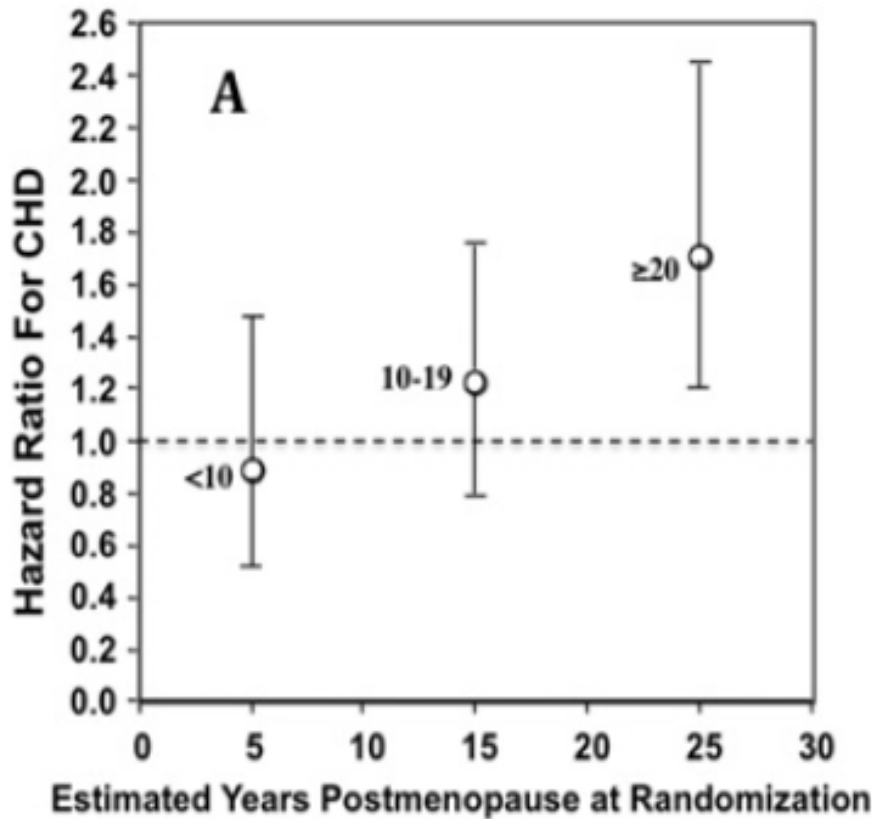
# Sekse/Gender verschillen in hart-en vaatziekten: Timing hypothesis



120 macacenen

1. Ovariectomie
2. 2 jr atherosclerotische dieet
3. Lip verlagend dieet + Randomisation E2/PLAC

## Sekse/Gender verschillen in hart-en vaatziekten: Timing hypothesis

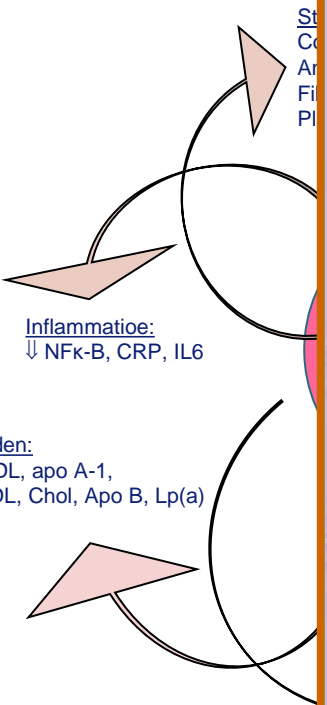
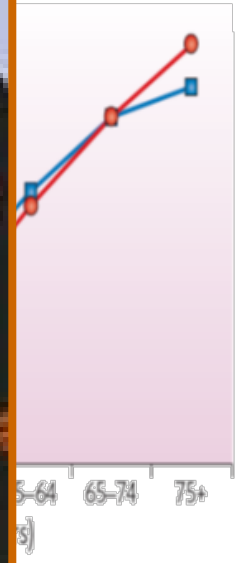


Anderson. JAMA 2004, Hsia Arch intern med 2006



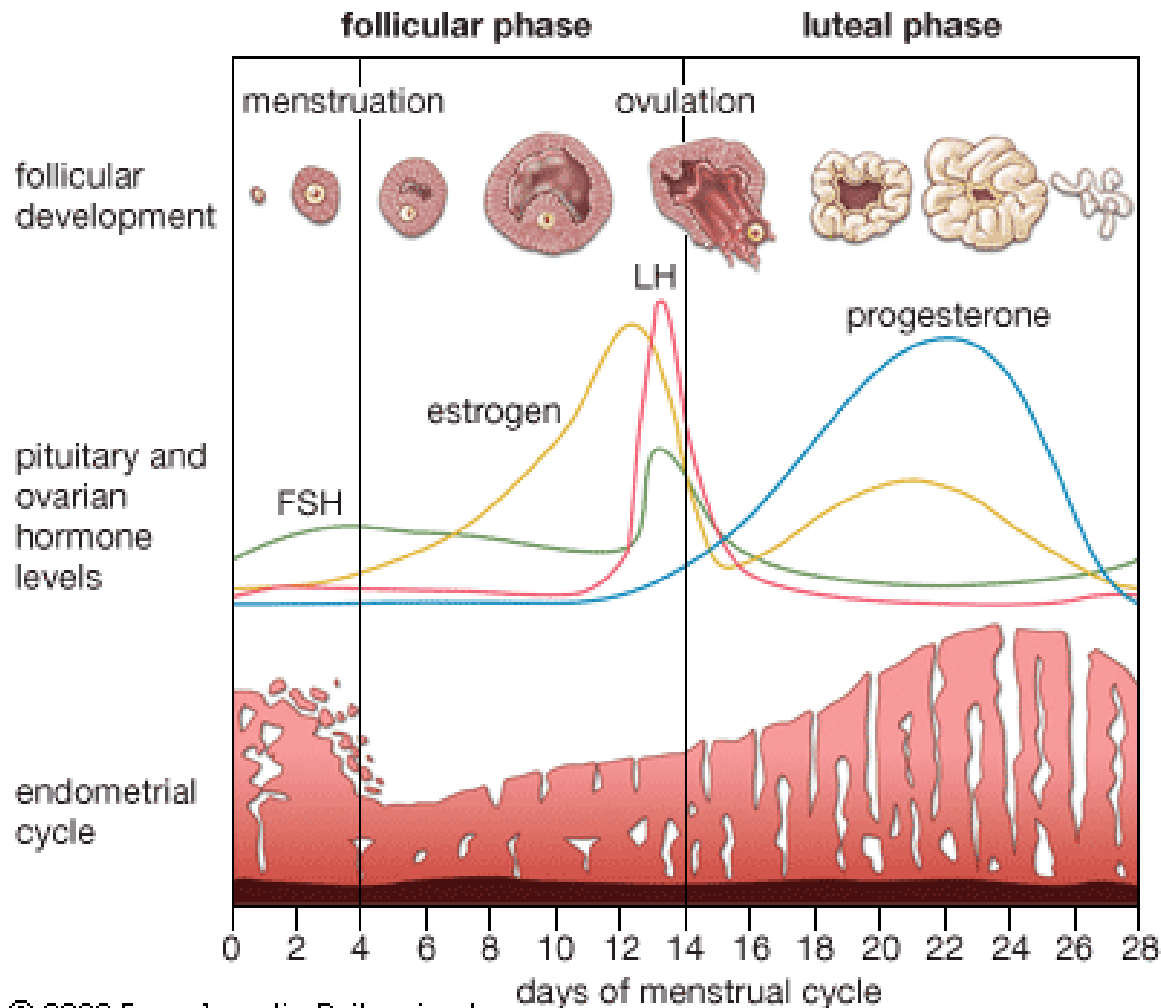
# Effecten oestrogenen op HVZ:

I don't think you understand how these hormones work... you're gonna make me do something that'll end up on the news.



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# Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus



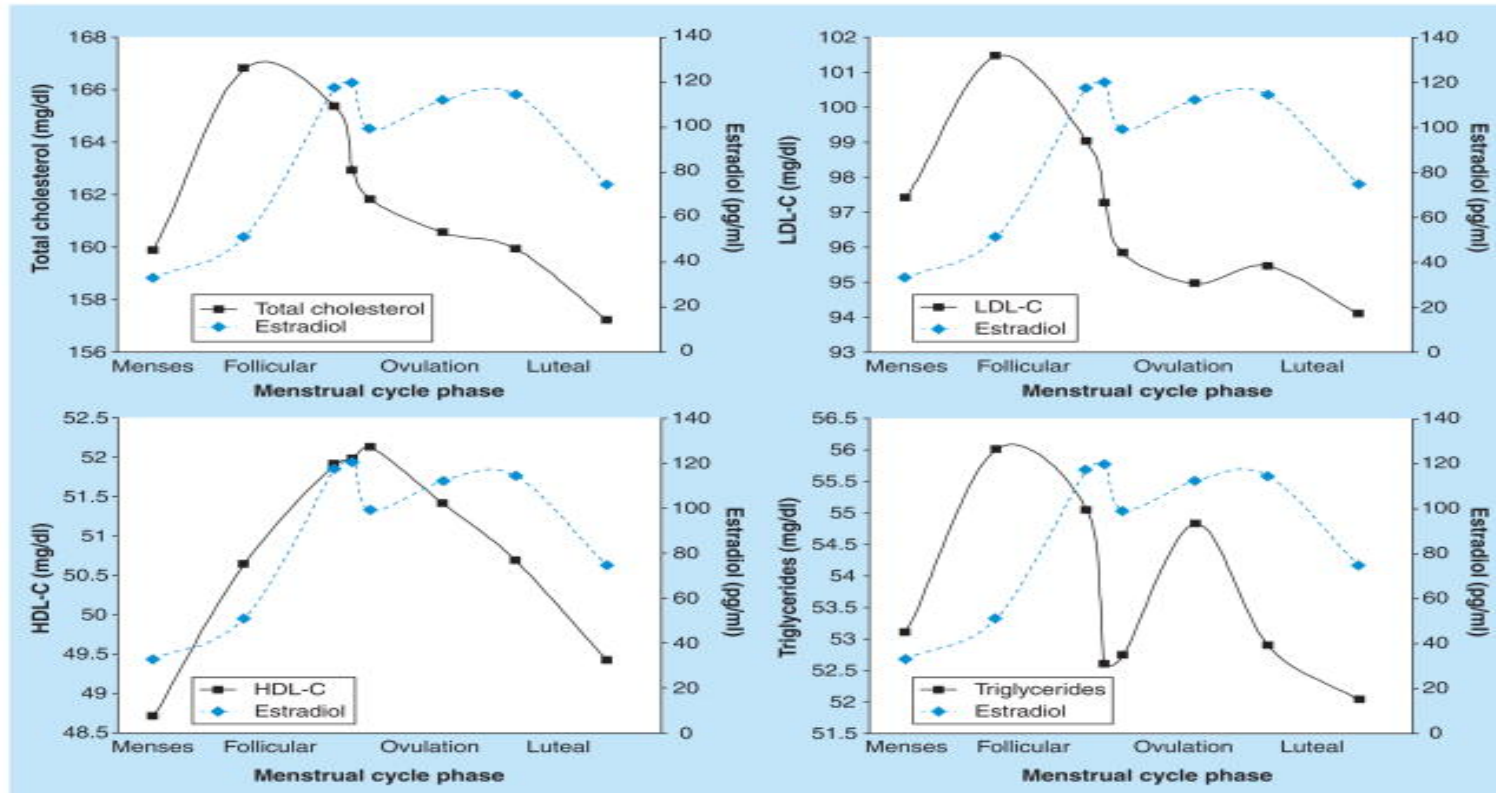
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## Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus

Eerder onderzoek naar invloed Menstruele cyclus:

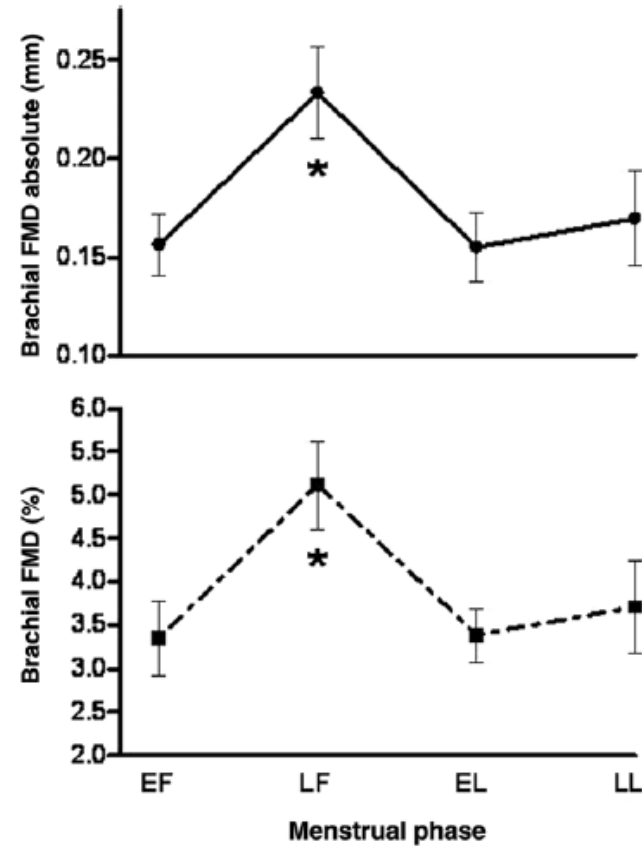
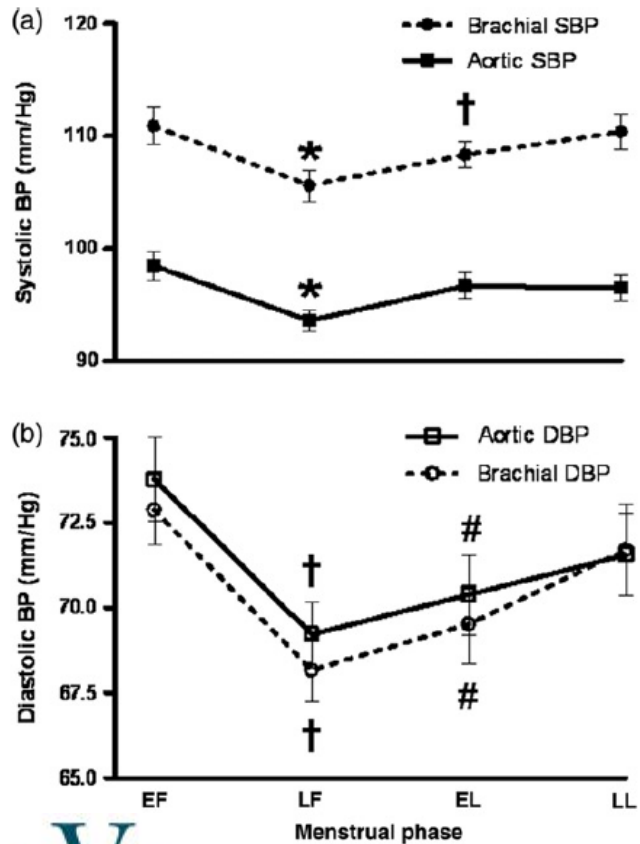
- Lipiden
- Endotheel functie/bloeddruk

## Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus- lipiden

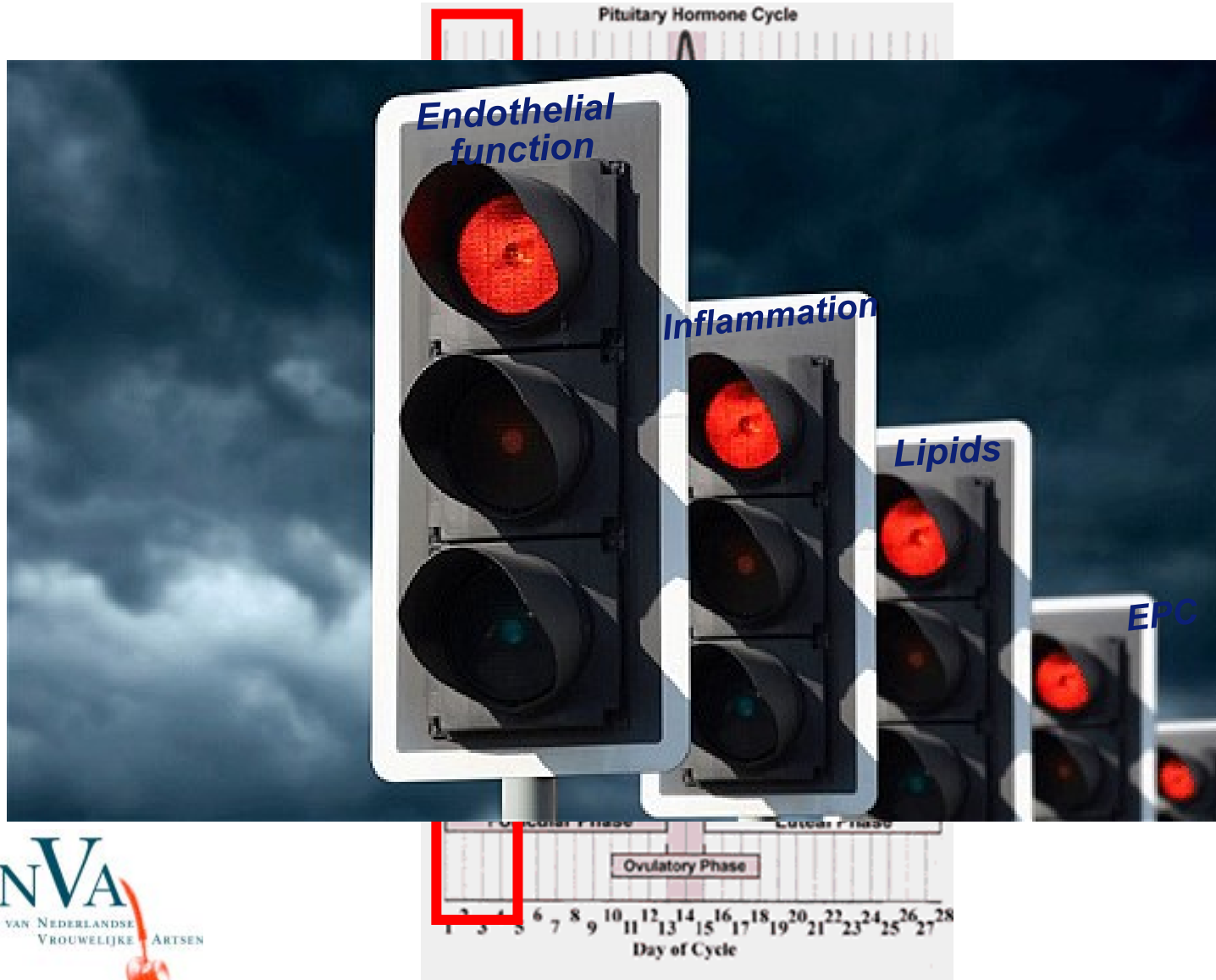


N= 256 gezonde vrouwen  
 2 keer cyclus- 8 metingen/cyclus

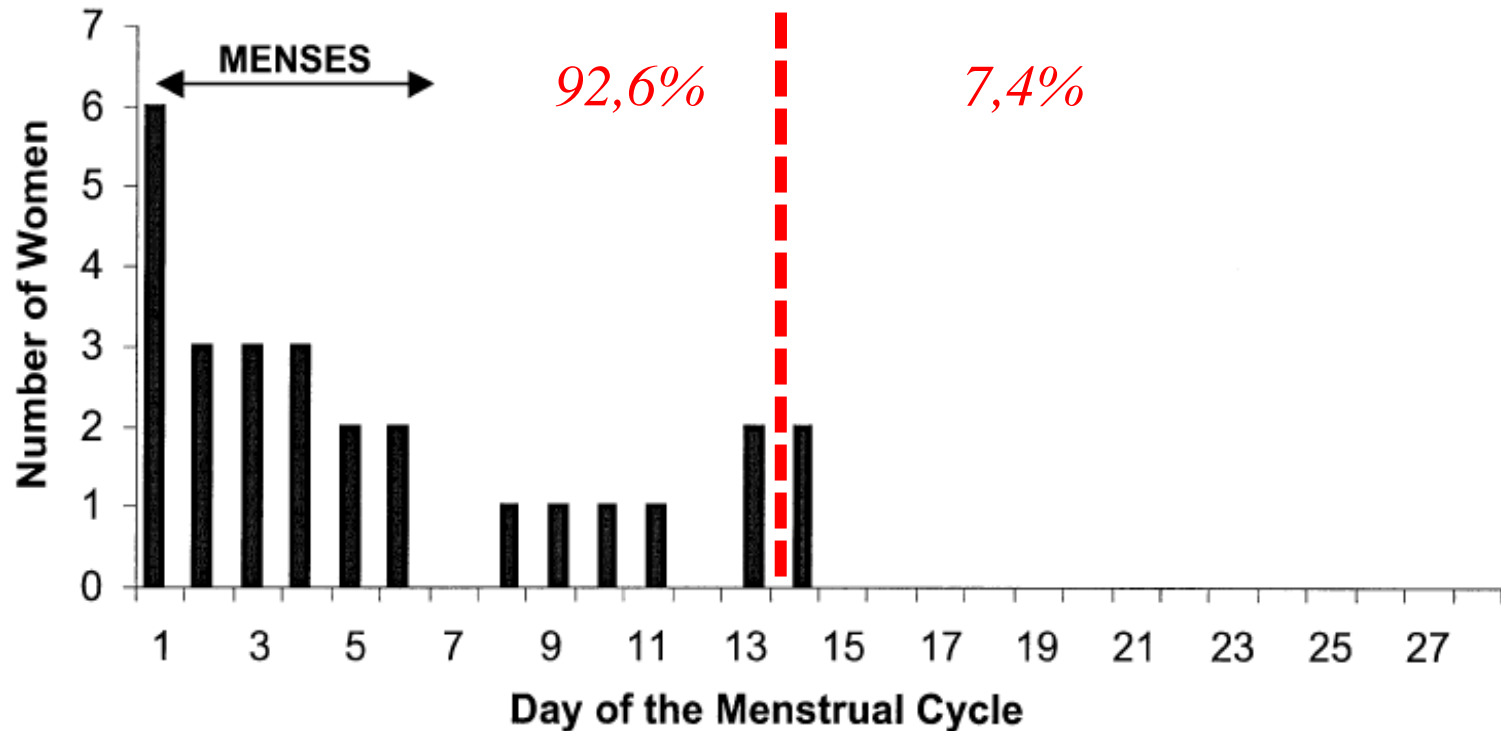
# Seks/Gender verschillen in hart-en vaatziekten: Menstruele cyclus- bloeddruk



# Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus & HVZ

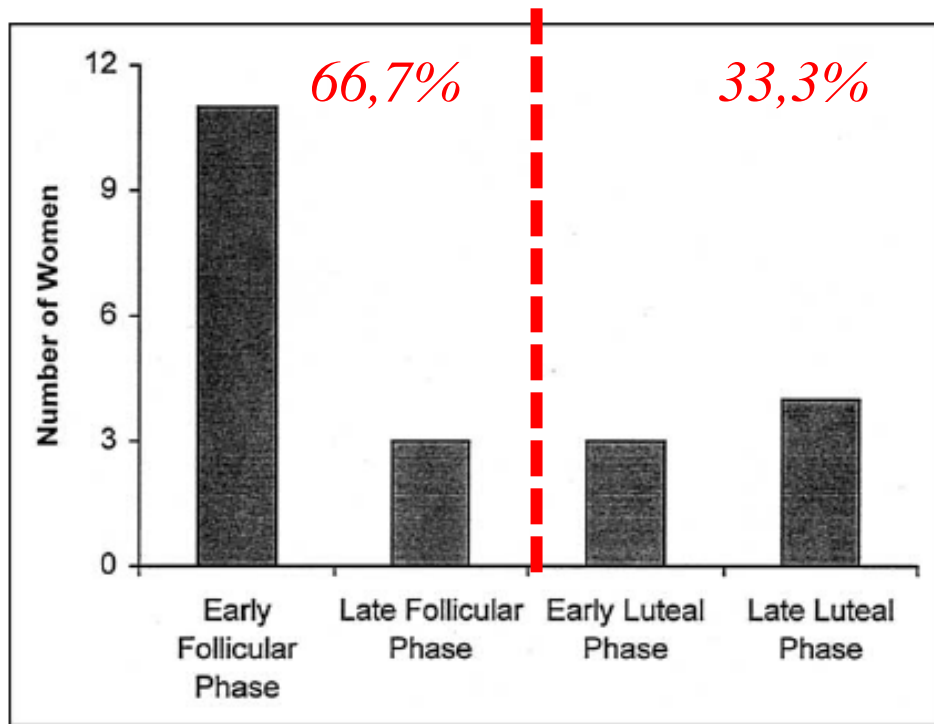


## Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus & HVZ



27 pre-menopauzale vrouwen met  
Myocardinfarct /instabiele angina pectoris

## Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus & HVZ



21 pre-menopauzale  
vrouwen met myocardinfarct

FIGURE 1. Distribution of onset of symptoms of acute myocardial infarction according to phase of the menstrual cycle. The number of women with ongoing menstrual cycles enrolled in the Onset Study whose symptoms began during each quarter of the menstrual cycle. The relative risk of onset during the early follicular % confidence interval, 1.4 to 7.7;  $p = 0.008$ ).



## Sekse/Gender verschillen in hart-en vaatziekten: Menstruele cyclus & HVZ

- Menstruele cyclus “model” voor bestuderen effect endogene vrouwelijke hormonen
- Treden acute HVZ (ook CVA/TIA's) vaker op in bepaalde fases cyclus?
- Worden testresultaten (fietsproeven/myocardscintigrafie) beïnvloed door fase cyclus?
- Verschilt invloed cyclus bij vrouwen met vs zonder HVZ

# CYCLE STUDY

# Take home messages



- Vrouwelijke geslachtshormonen lijken bescherming te bieden tegen HVZ
- Premature of chirurgische menopauze risicofactor voor HVZ
- HRT niet geadviseerd voor preventie HVZ bij postmenopauzale vrouwen
- Mogelijk invloed menstruele cyclus op HVZ
- Maar.. Raadsel vrouwelijke hormonen & HVZ nog niet opgelost

# Vragen?

WHY ARE THERE CELEBRITIES  
WHY DO SNAKES EXIST  
WHY DO OYSTERS HAVE PEARLS  
WHY ARE DUCKS CALLED DUCKS  
WHY DO THEY CALL IT THE CLAP  
WHY ARE KYLE AND CARTMAN FRIENDS  
WHY IS THERE AN ARROW ON PANG'S HEAD  
WHY ARE TEXT MESSAGES BLUE  
WHY ARE THERE MUSTACHES ON CLOTHES  
WHY ARE THERE MUSTACHES ON CARS  
WHY ARE THERE MUSTACHES ON  
WHY ARE THERE SO MANY  
WHY IS OHIO WEAT  
WHY ARE THE  
WHY ARE THERE  
WHY DO DYING PEOPLE REACH UP  
WHY AREN'T THERE VARIOUS  
WHY ARE OLD KINGDOMS DIFFERENT

WHY DO AMERICANS CALL IT SOCCER  
WHY ARE MY EARS RINGING  
WHY ARE THERE SO MANY AVENGERS  
WHY ARE THE AVENGERS FIGHTING THE X MEN  
WHY IS WOLVERINE NOT IN THE AVENGERS  
WHY ARE THERE ANTS IN MY LAPTOP  
WHY IS EARTH TILTED

WHY ARE THERE SO MANY CROWS IN ROCHESTER, MN  
WHY IS PSYCHIC WEAK TO BUG  
WHY DO CHILDREN GET CANCER  
WHY IS POSEIDON ANGRY WITH ODYSSEUS  
WHY IS THERE ICE IN SPACE  
WHY IS THERE AN OWL IN MY BACKYARD  
WHY ARE DOGS AFRAID OF FIREWORKS  
WHY IS THERE NO KING IN ENGLAND

*I don't know what the question is,  
but sex is always the answer*

*Woody Allen*



WHY DO KNEES CLICK  
WHY AREN'T THERE E GRADES  
WHY IS ISOLATION BAD  
WHY DO BOYS LIKE ME  
WHY DON'T BOYS LIKE ME  
WHY IS THERE ALWAYS A JAMA UPDATE  
WHY ARE THERE RED DOTS ON MY THIGHS  
WHY IS LYING GOOD



WHY ARE OCEANS BECOMING MORE ACIDIC  
WHY IS ARWEN DYING  
WHY AREN'T MY QUAIL LAYING EGGS  
WHY AREN'T MY QUAIL EGGS HATCHING  
WHY AREN'T THERE ANY FOREIGN MILITARY BASES IN AMERICA



WHY ARE ULTRASOUNDS IMPORTANT  
WHY ARE ULTRASOUND TYPHOIDS EXPENSIVE  
WHY IS STEALING WRONG