

Het belang van gezondheid in de menopauze

PROF. DR. H. DEPYPERE

Menopauze kliniek: Universitair Ziekenhuis, Gent.

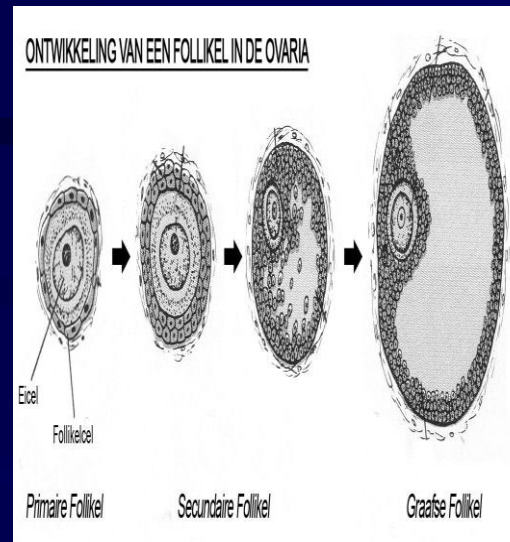
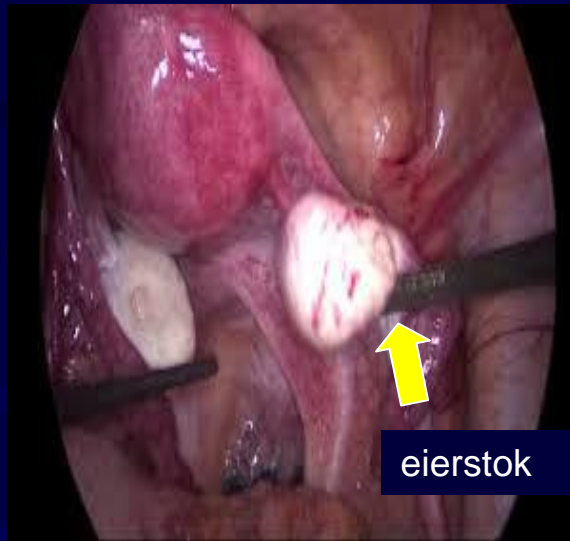
Privaat praktijk: Coupure rechts 4, Gent



Oestradiol/progesteron door de ovaria

Productie door follikel vanaf menarche tot menopauze \pm 51-52 jaar.

In België anno 1888: 46,6 jr; In Nigeria anno 2022: 54 jr. Bij de geboorte beide meisjes: 700 000 prim follikels.



Biologische discriminatie:

Man ~ testosteron

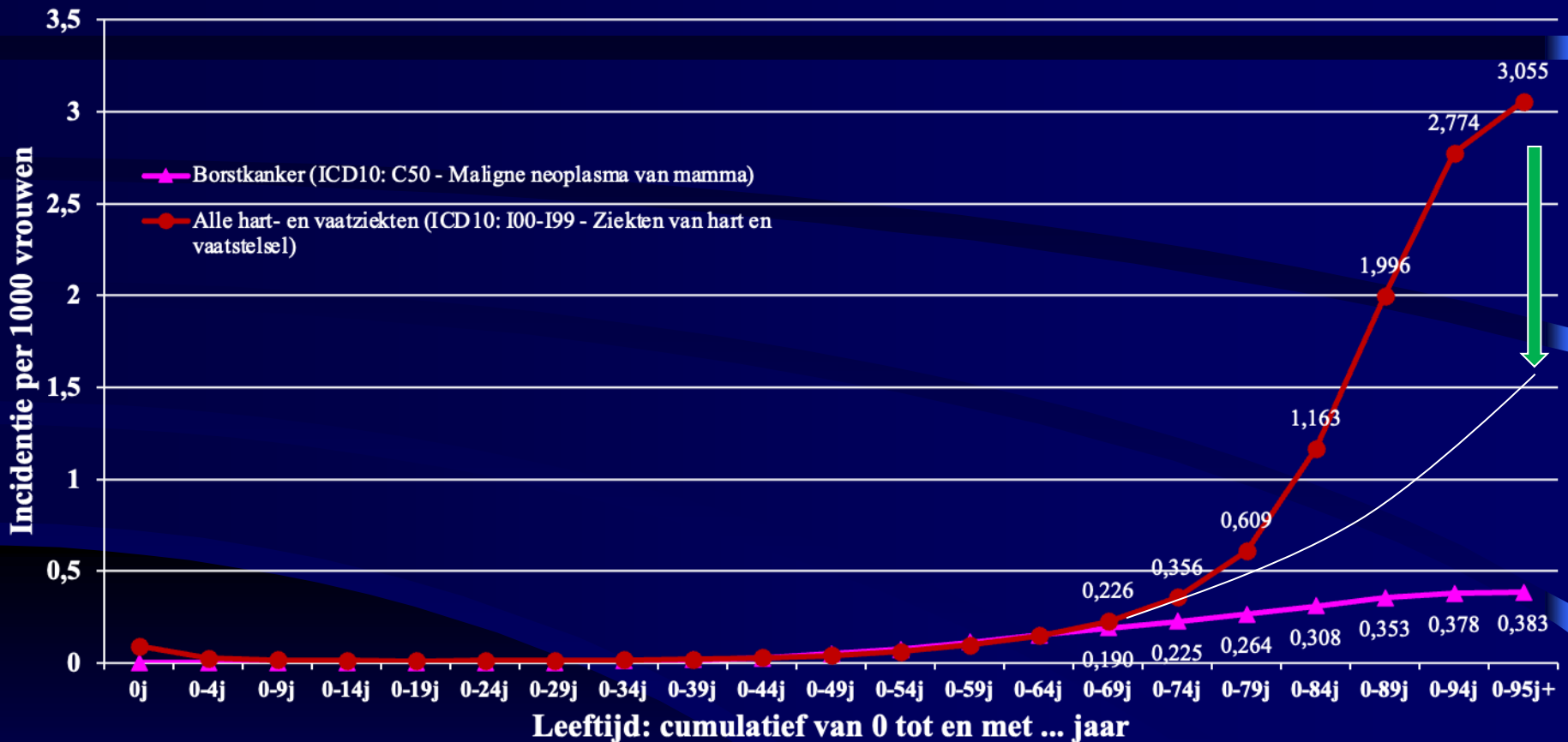
Vrouw oestrogeen $\downarrow\downarrow$

Hoog FSH en LH en laag oestradiol

Niet mogelijk onder de pil

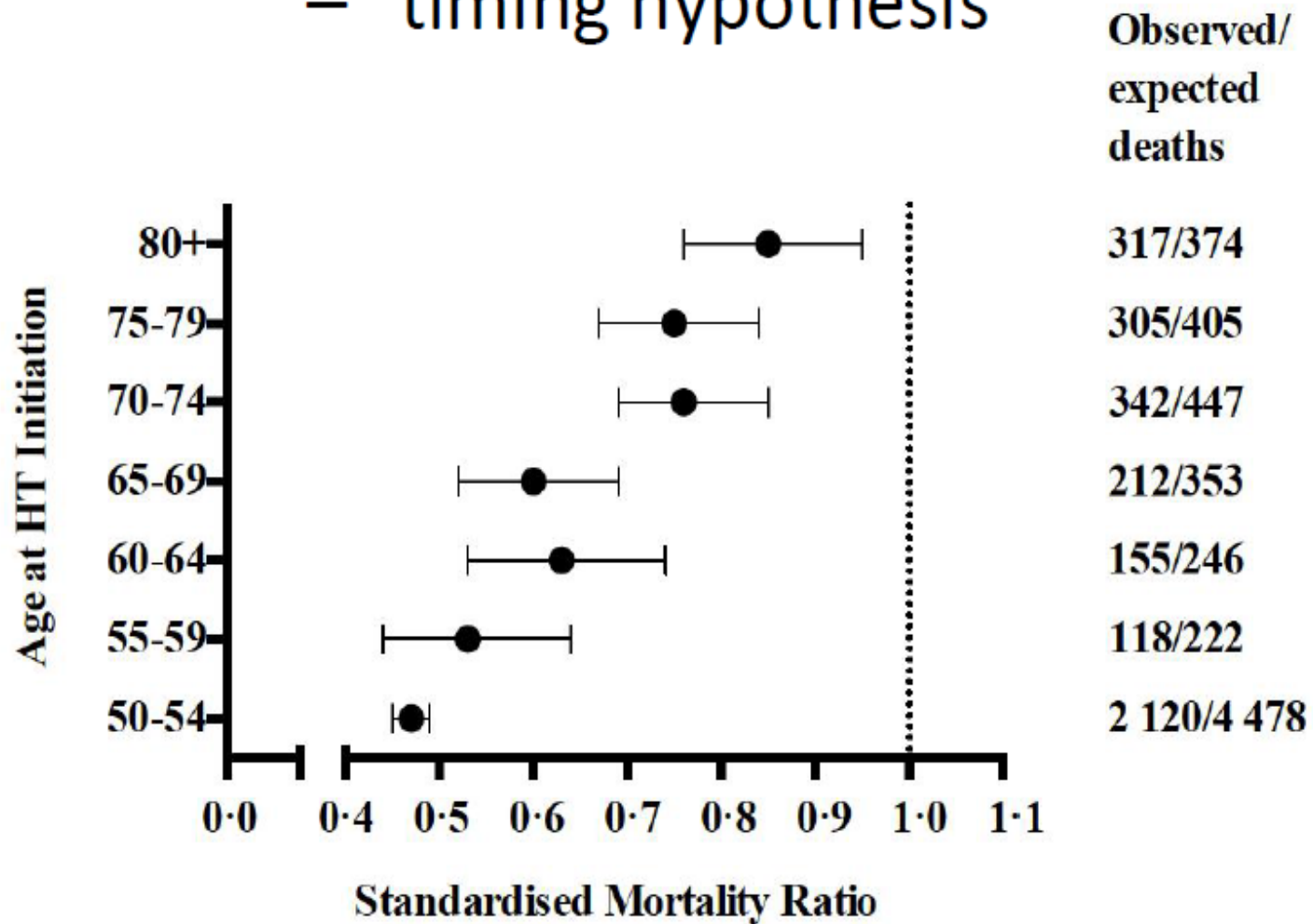
Wel mogelijk onder Mirena®, Kyleena®

Cumulatieve leeftijdsspecifieke incidentie van sterfte bij vrouwen voor enkele geselecteerde oorzaken, Vlaams Gewest, 2015



Bron: Agentschap Zorg en Gezondheid. *Cijfers over doodsoorzaken* [Online publicatie]. Brussel, [geraadpleegd op 16/01/2019].
 Beschikbaar op: <http://www.zorg-en-gezondheid.be/cijfers/> prof Koen Vanherck

Risk of cardiac death and the use of HT – “timing hypothesis”



Savolainen-Peltonen et al. JCEM 2016;101:2794-801

Be.stat.bel: women

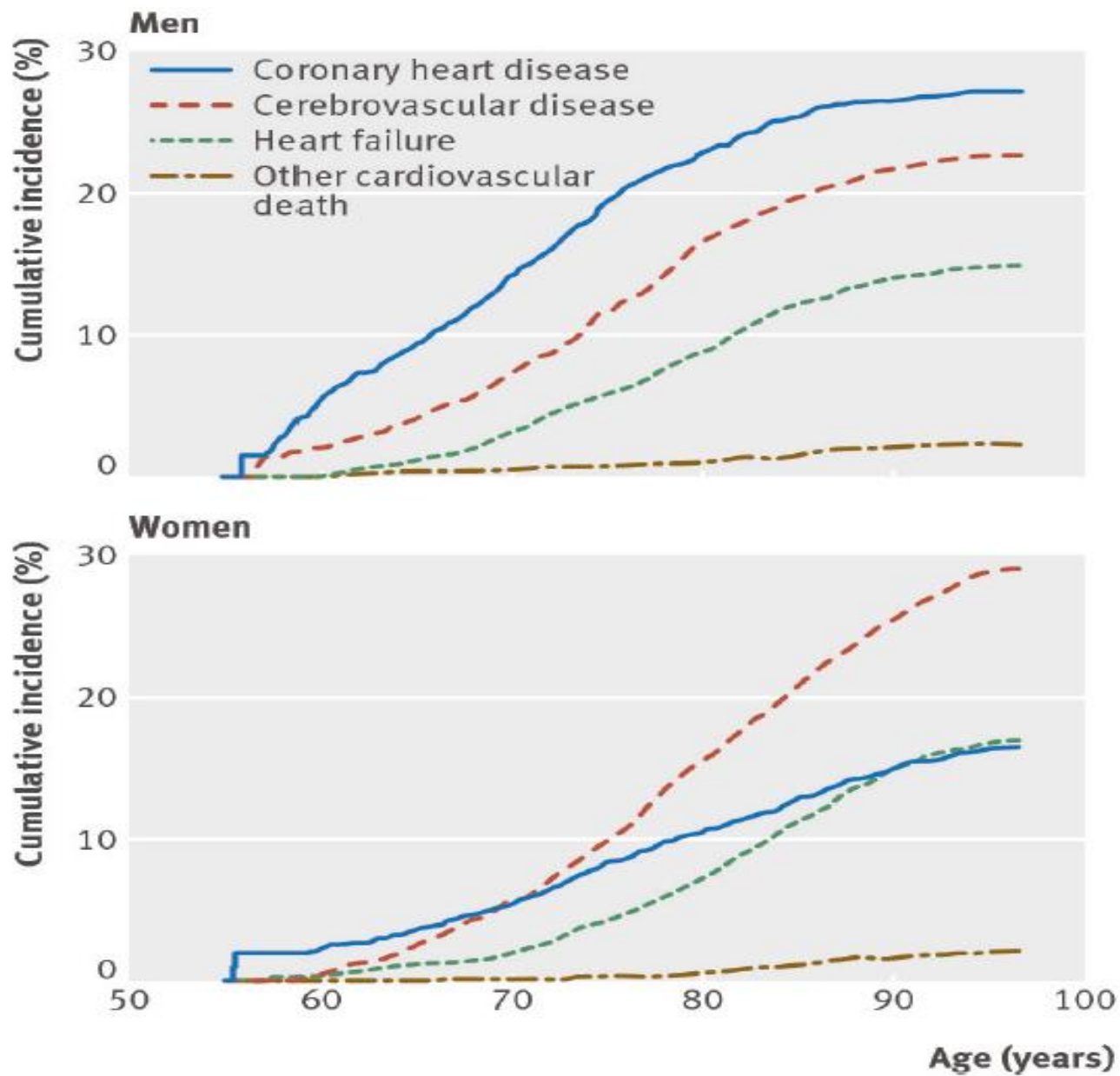
50-54 age: 390 376

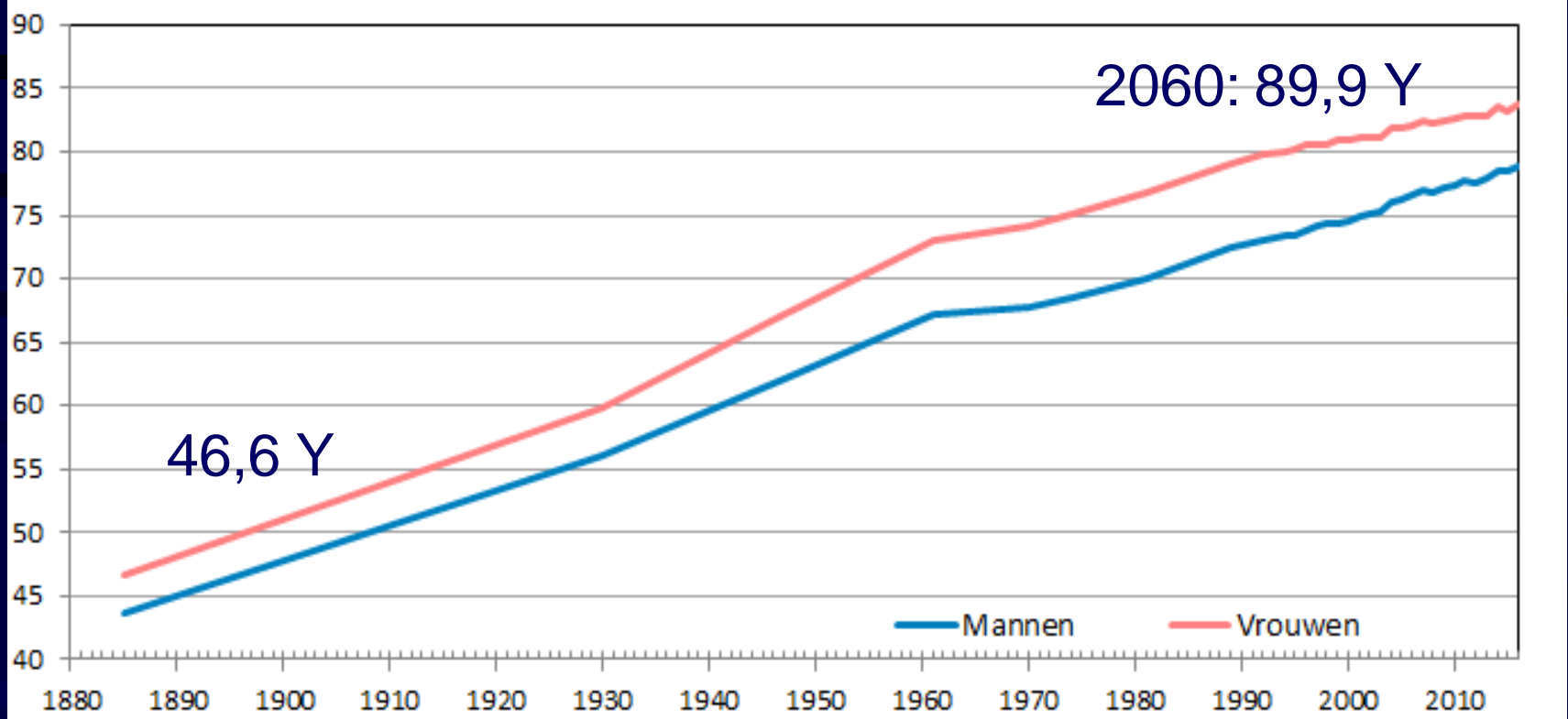
55-59 age: 398 908

789 284

2 op 100 vrouwen per 10 jaar opvolging zullen niet sterven door inname van hormonen.

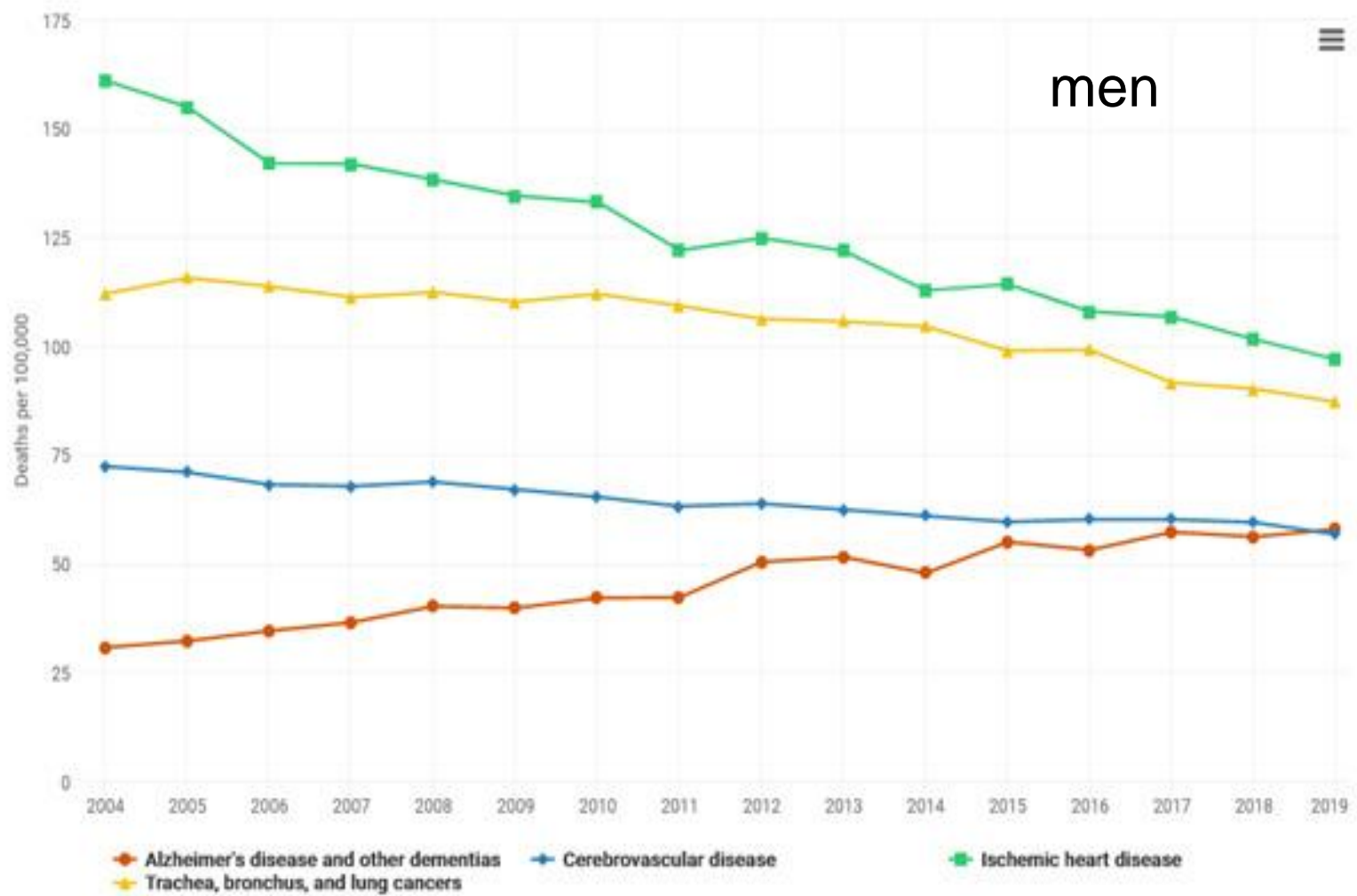
$789\ 284 / 100 \times 2 / 10 : 1579$ minder vrouwen die sterven per jaar. Dit gebaseerd op 19 gerandomiseerde studies.

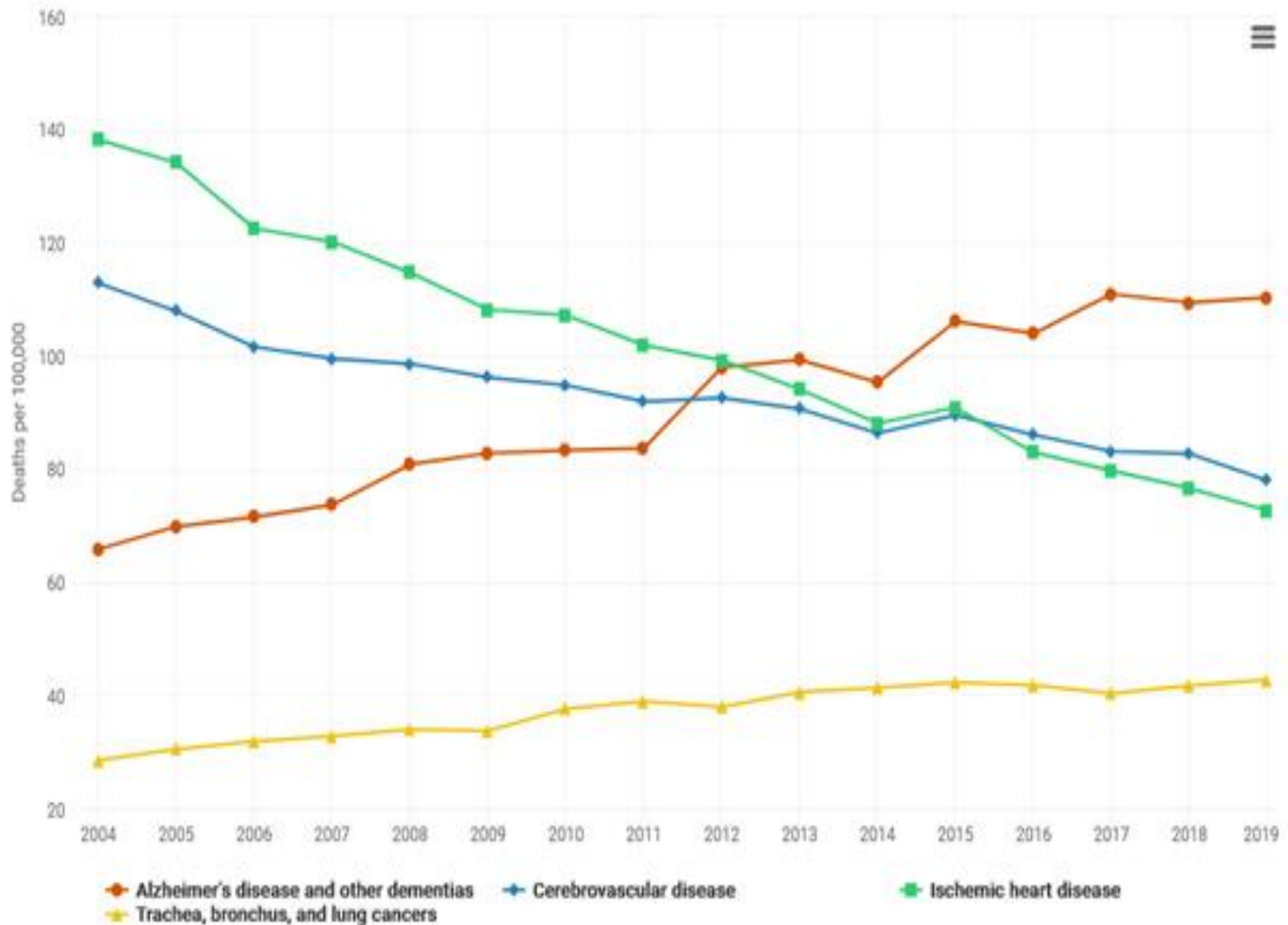




In 1956 werden gemiddeld 12 vrouwen op 1000 100 jaar.

Voor meisjes die 2016 werden geboren wordt verwacht dat 60 op 1000 100 jaar zullen worden (Statbel).






Only 6% of men die due to dementia. From 2013 dementia is the most important cause of death in women. In 2019 nearly 12 % of women died due to dementia.

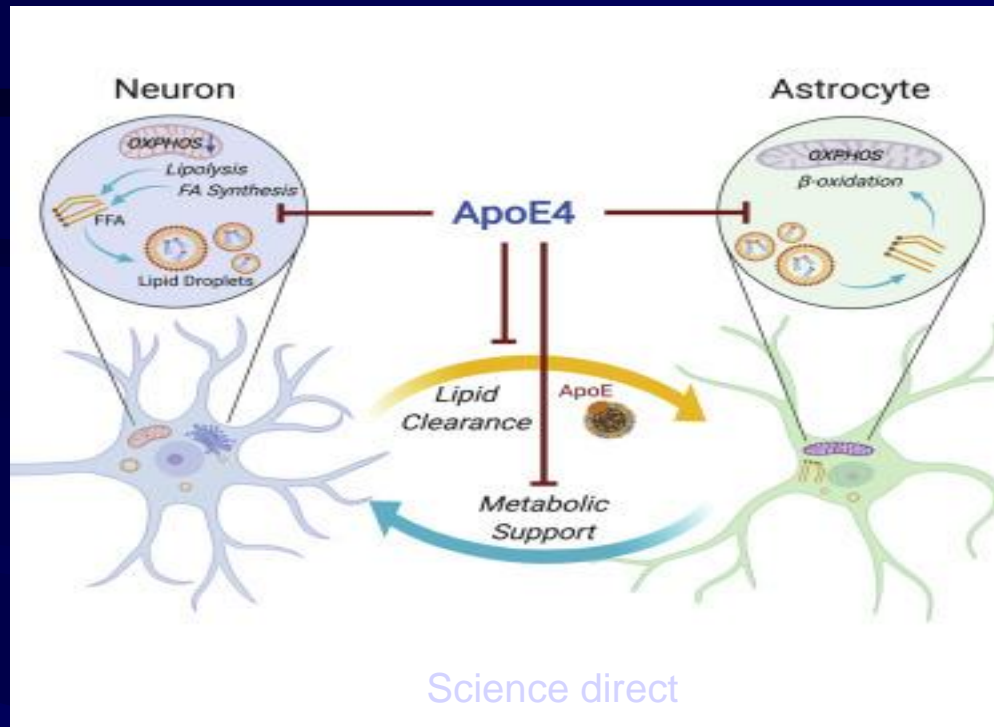


Review Article | Published: 09 July 2018

Sex differences in Alzheimer disease — the gateway to precision medicine

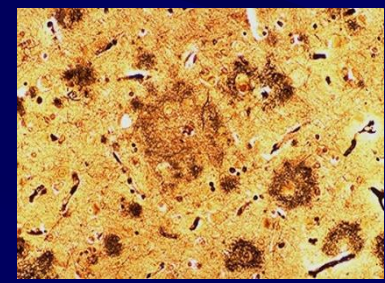
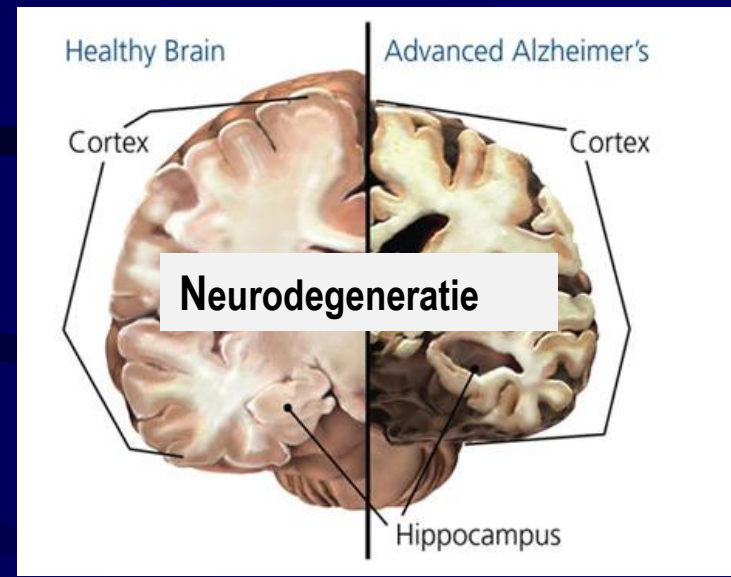
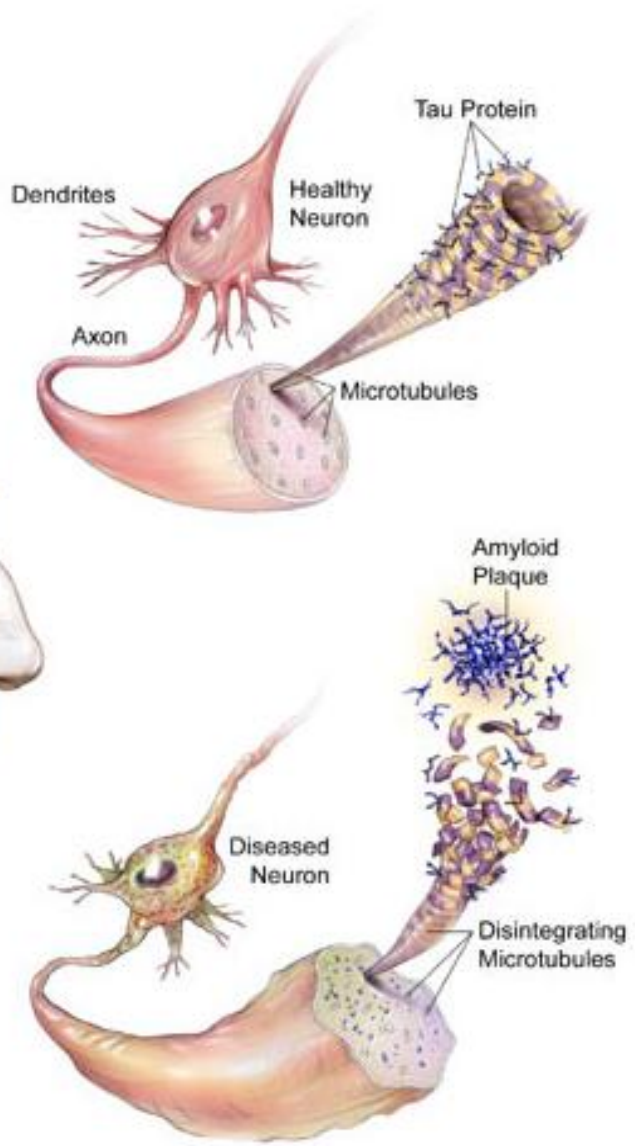
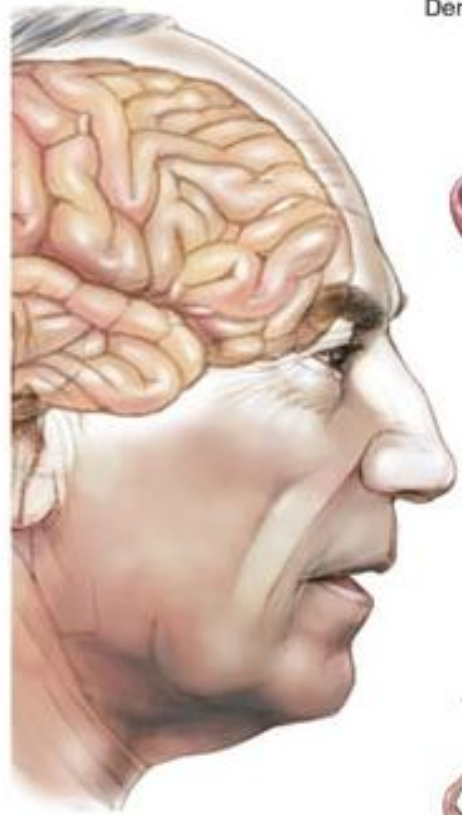
Maria Teresa Ferretti , Maria Florencia Iulita, Enrica Cavedo, Patrizia Andrea Chiesa, Annemarie Schumacher Dimech, Antonella Santuccione Chadha, Francesca Baracchi, Hélène Girouard, Sabina Misoch, Ezio Giacobini, Herman Depypere, Harald Hampel & for the Women's Brain Project and the Alzheimer Precision Medicine Initiative

Nature Reviews Neurology **14**, 457–469 (2018) | [Download Citation](#) ↓

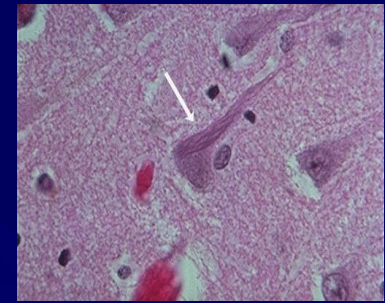


Possible isoforms of ApoE: E2E2, E2E3, E2E3, E2E4, E3E4, E4E4.

KENMERKEN VAN DE ZIEKTE VAN ALZHEIMER



Amyloid Plaques



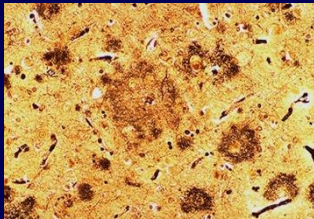
Neurofibrillaire kluwenvorming

ZIEKTE VAN ALZHEIMER

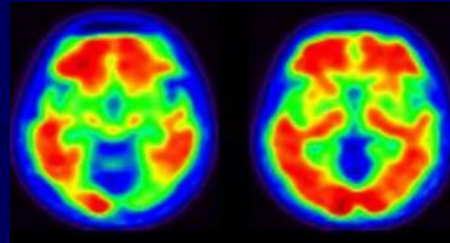
IN VIVO DETECTIE

SURROGAAT MERKERS

Amyloid Plaques



Amyloid PET



CSF/Plasma A β 1-42

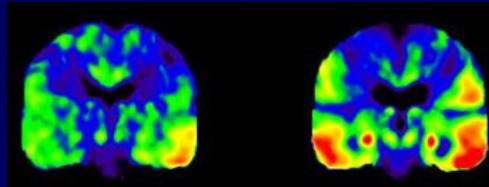
of



Neurofibrillaire kluwen



Tau PET

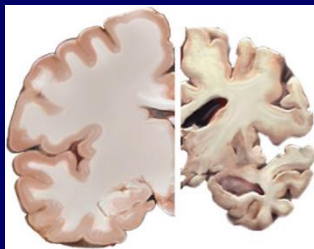


CSF/Plasma T-tau P-tau

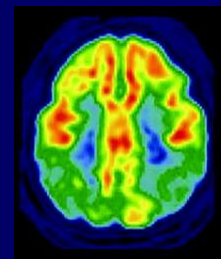
of



Neurodegeneratie

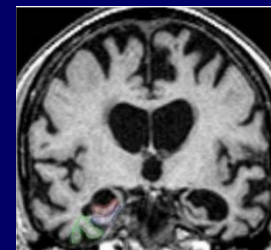


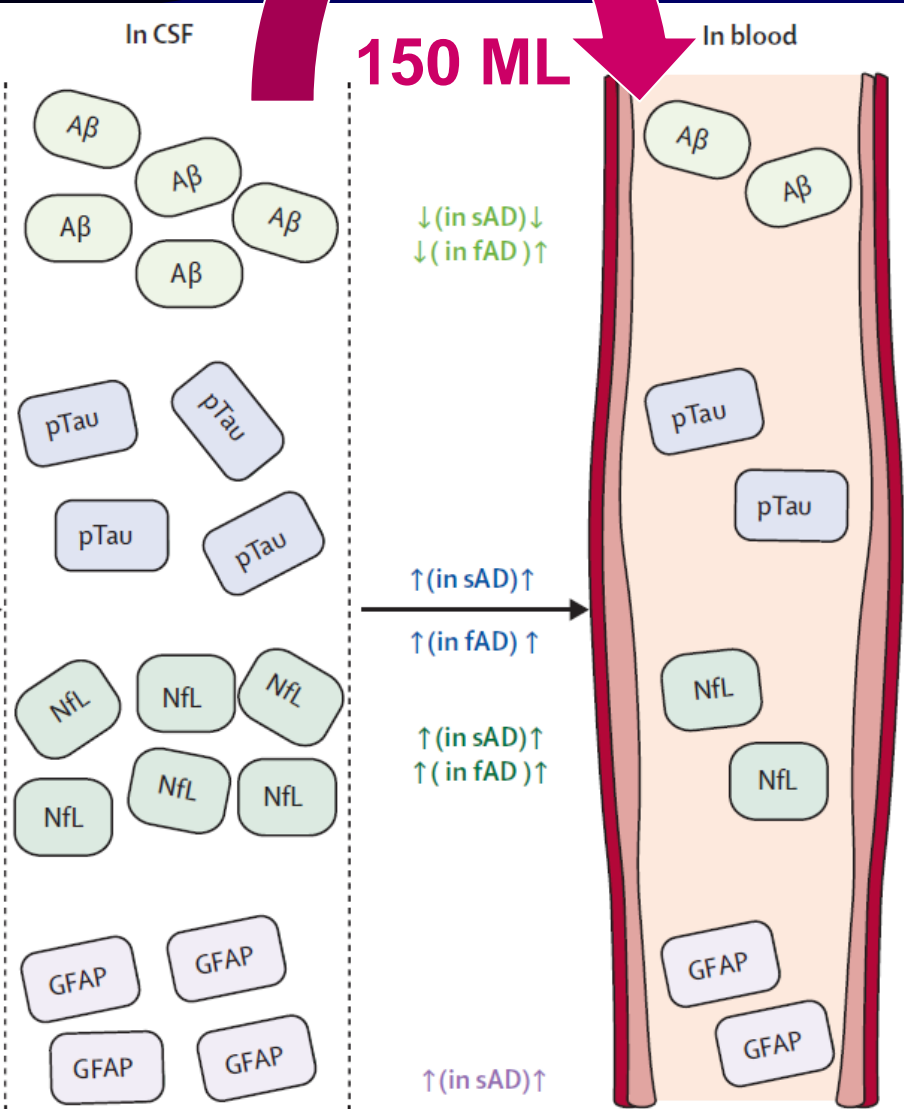
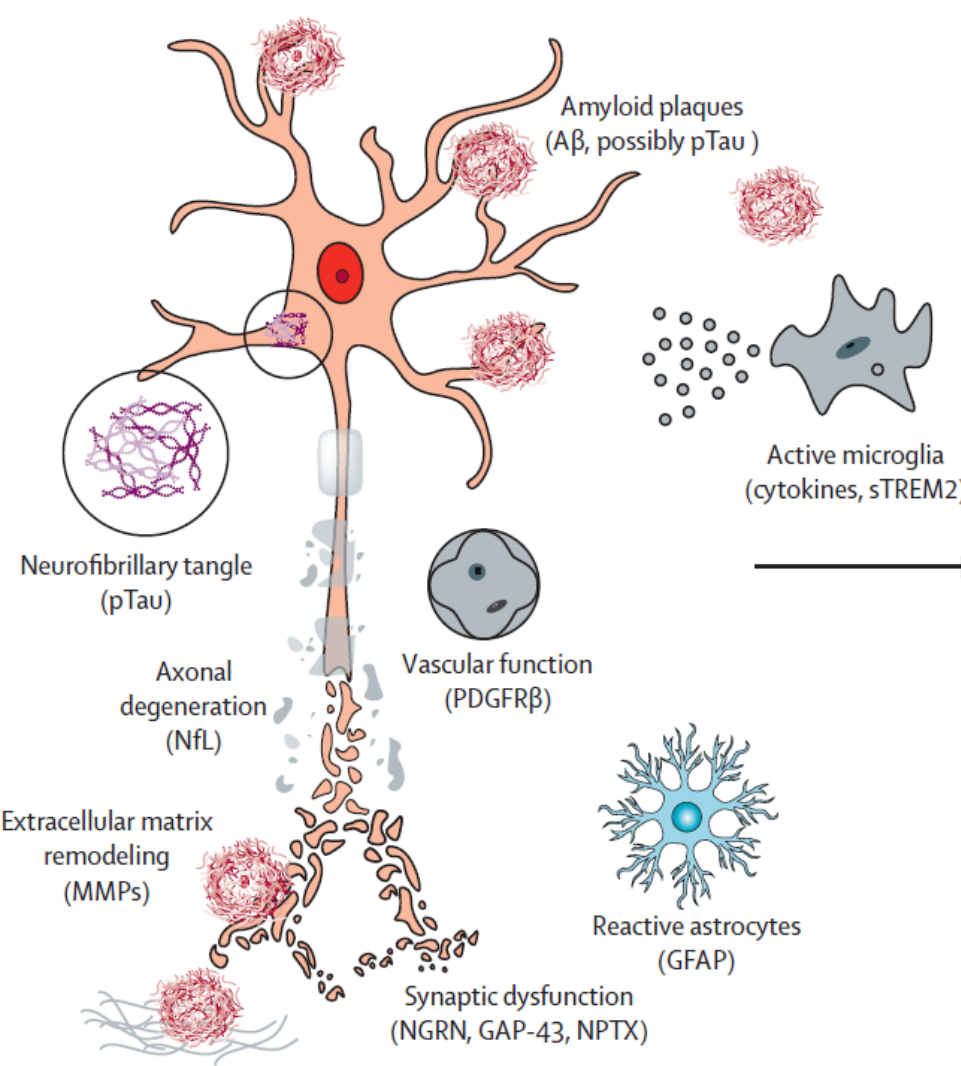
18-FDG PET



or

Brain Atrophy (MRI)





Depypere H¹, Vergallo A^{2*}, Lemercier P^{2*}, Lista S², Benedet AL³ Ashton NJ^{3,4,5,6}, Cavedo E, Zetterberg H^{3, 7, 8, 9, 10}, Blennow K^{3,7}, Vanmechelen E¹¹, Hampel H²; the Neurodegeneration Precision Medicine Initiative (NPMI).

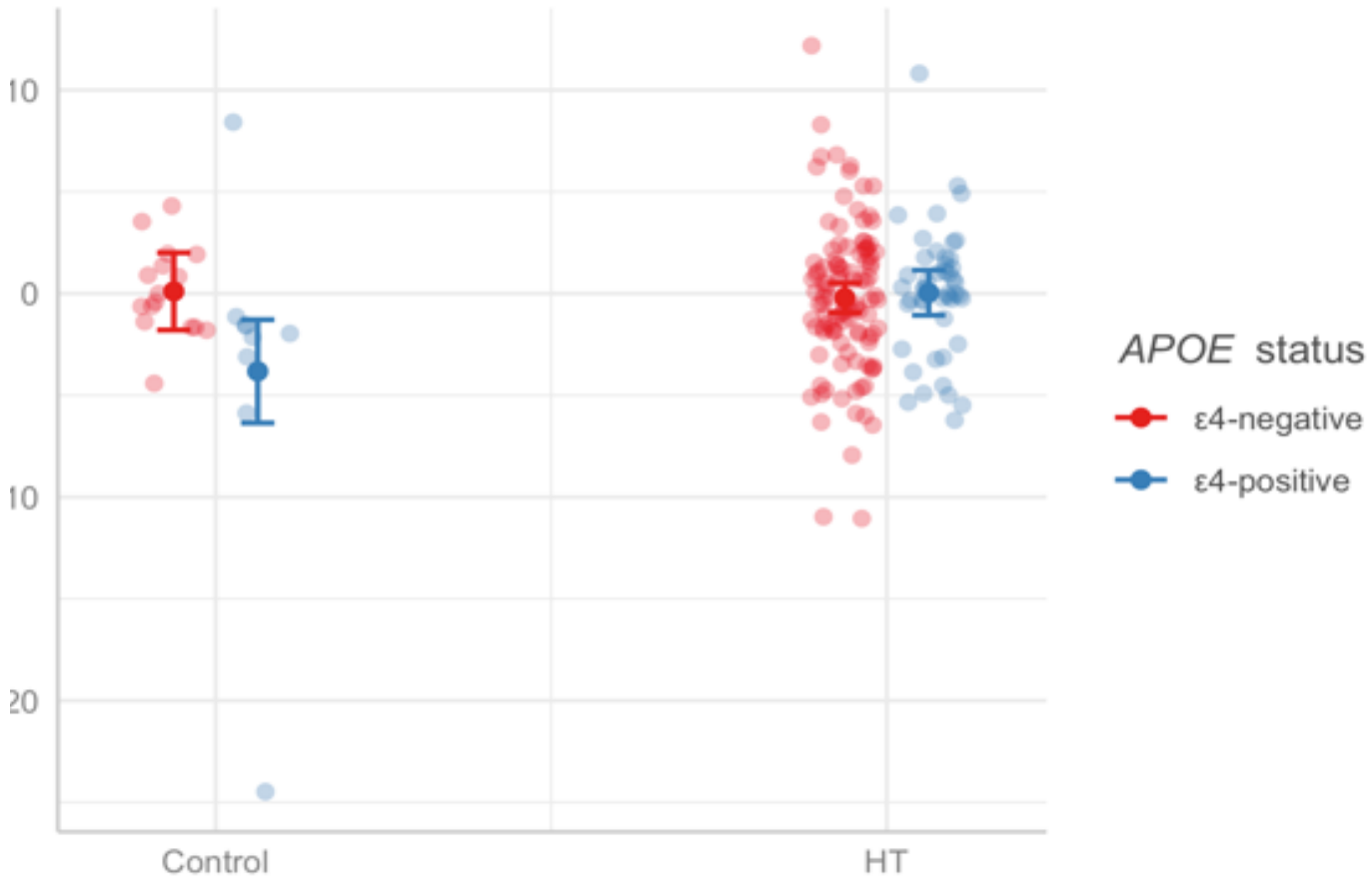
Menopause Hormone Therapy significantly alters Pathophysiological Biomarkers of Alzheimer's Disease

Alzheimer's and dementia: 2022 sept

alzheimer's 
association®

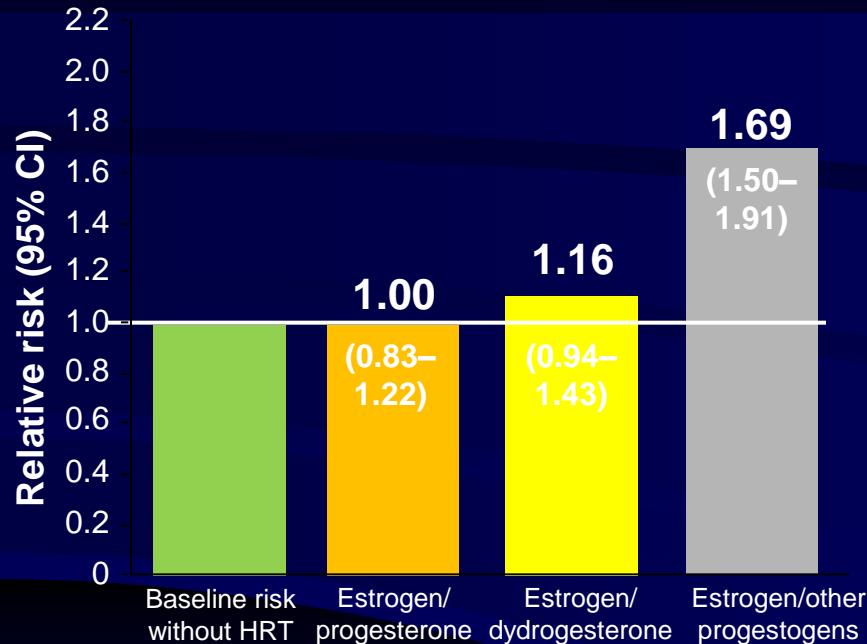
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Neurale serum parameters

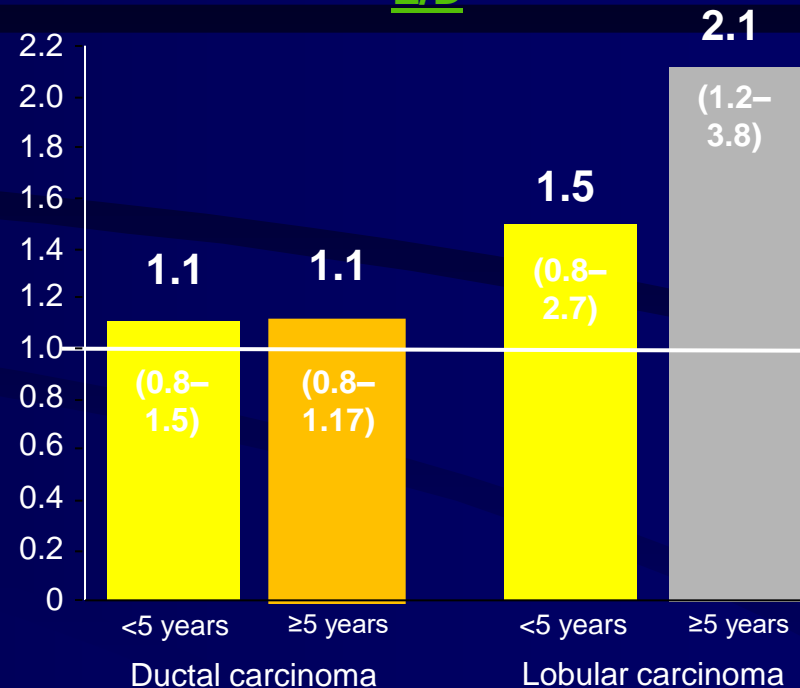


Choice of Progestogen and Breast Cancer Risk: E3N French Cohort Study

Risk of all breast cancer



Risk of breast cancer subtypes with E/D



■ Not statistically significantly different from risk without HRT
 ■ Significantly different from the risk without HRT

N = 80,377 women, for an average treatment duration of 8.1 years

Risk elevation may not be uniform for all progestogens

Outcome by Age 50-60 years of age at inclusion

	Hormone Therapy	Placebo	HR (95% CI)	P value
All-cause mortality				
Pooled trials	70 (0.23)	98 (0.34)	0.69 (0.51-0.94)	.01
CEE alone vs placebo	35 (0.28)	50 (0.39)	0.71 (0.46-1.09)	.04
CEE plus MPA vs placebo	35 (0.20)	48 (0.30)	0.67 (0.43-1.04)	.20
CVD mortality				
Pooled trials	18 (0.060)	22 (0.076)	0.79 (0.42-1.47)	.85
CEE alone vs placebo	8 (0.063)	10 (0.077)	0.81 (0.32-2.04)	.34
CEE plus MPA vs placebo	10 (0.058)	12 (0.075)	0.77 (0.33-1.79)	.47
Cancer mortality				
Pooled trials	37 (0.12)	48 (0.17)	0.74 (0.48-1.14)	.05
CEE alone vs placebo	20 (0.16)	26 (0.20)	0.78 (0.43-1.40)	.06
CEE plus MPA vs placebo	17 (0.099)	22 (0.14)	0.71 (0.38-1.33)	.37

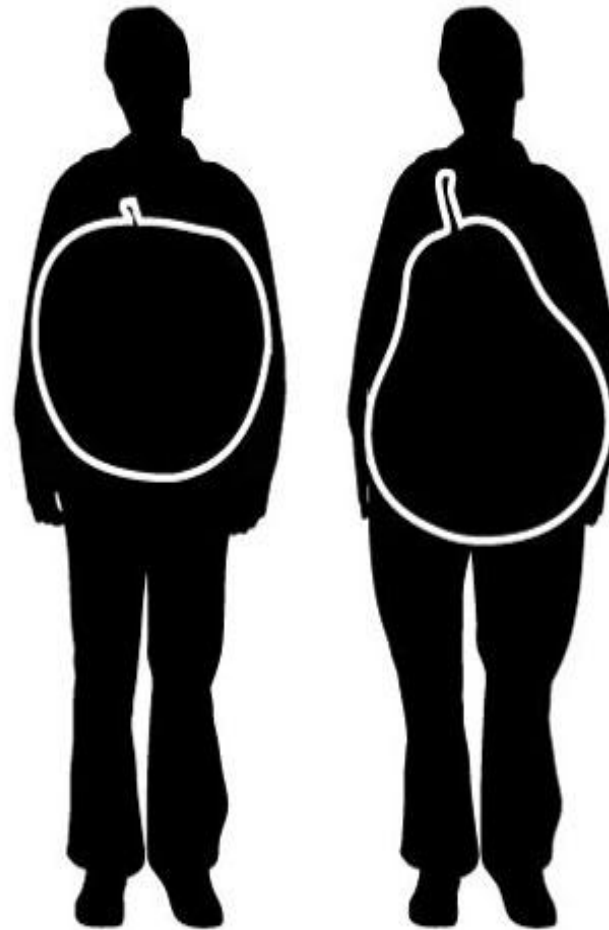
Menopausal Hormone Therapy and Long-term All-Cause and Cause-Specific Mortality: The Women's Health Initiative Randomized Trials
JoAnn E. Manson, MD, DrPH; Aaron K. Aragaki, MS; Jacques E. Rossouw, MD; Garnet L. Anderson, PhD; Ross L. Prentice, PhD; Andrea Z. LaCroix, PhD;
Rowan T. Chlebowski, MD, PhD; Barbara V. Howard, PhD; Cynthia A. Thomson, PhD; Karen L. Margolis, MD, MPH; Cora E. Lewis, MD, MSPH; JAMA 2017

But we aim to do better and decrease breast cancer
SERM- TSEC



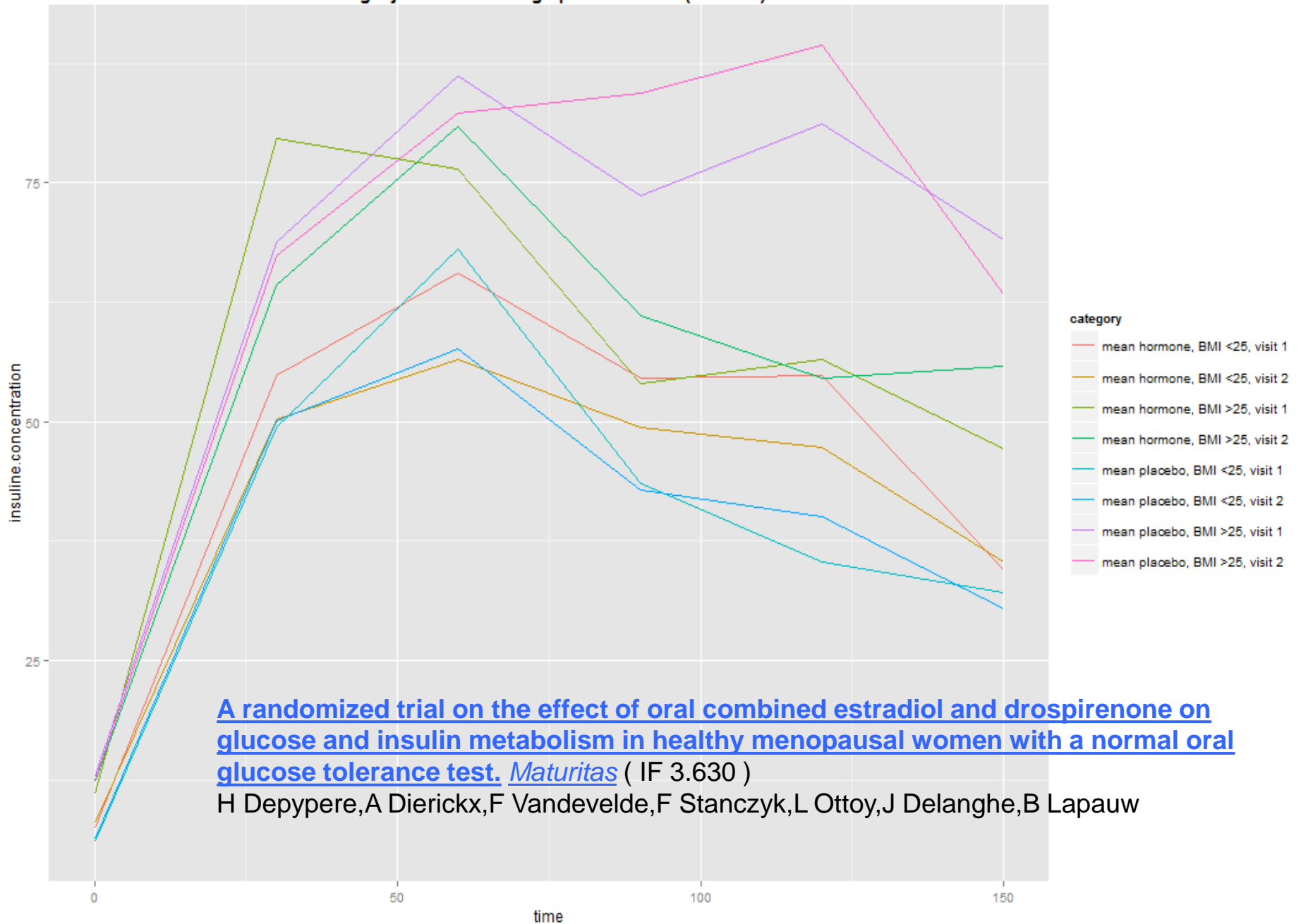
THE APPLE, by definition, is round. You have the body people want to cycle up to. But is it easy to dress? No, it's not. That's why you think it so much safer to cover yourself with yards of fabric, making absolutely sure not one centimeter of flesh can peep out.

Sometimes the thickened waist of the Apple maddens with the meromane. At the slender end of the scale is a little pugpy fit. Of all our shapes, the Apple tends to be the least confident. If, despite of your beautiful, soft, pillow-soft breasts and divinely sculpted ankles, you really don't like your body, but can't deprive others of a wonderful cleavage that can be enhanced with low tops and fitted jackets. Your body is easy to redefine with the right clothes.



Appelvorm – metabool syndroom

Vergelijken behandeling op visite 1 en 2 (insuline)



[A randomized trial on the effect of oral combined estradiol and drospirenone on glucose and insulin metabolism in healthy menopausal women with a normal oral glucose tolerance test. *Maturitas* \(IF 3.630 \)](#)

H Depypere, A Dierickx, F Vandeveldel, F Stanczyk, L Ottoy, J Delanghe, B Lapauw

Operate studie

Randomisatie:

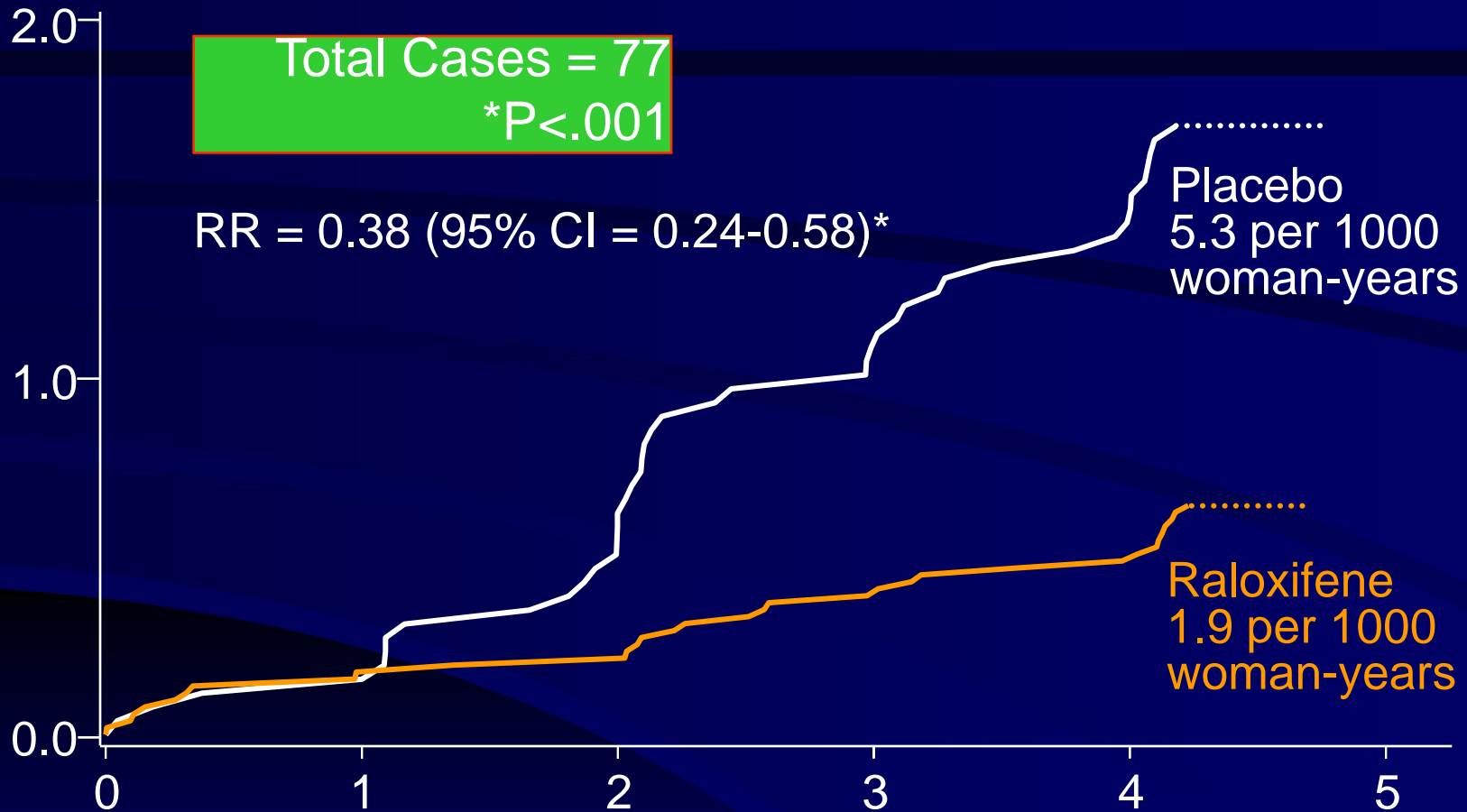
inspanning met lenzetto en progebel

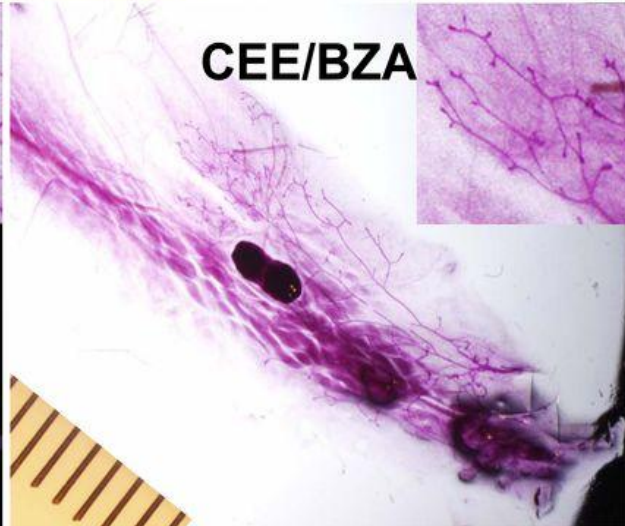
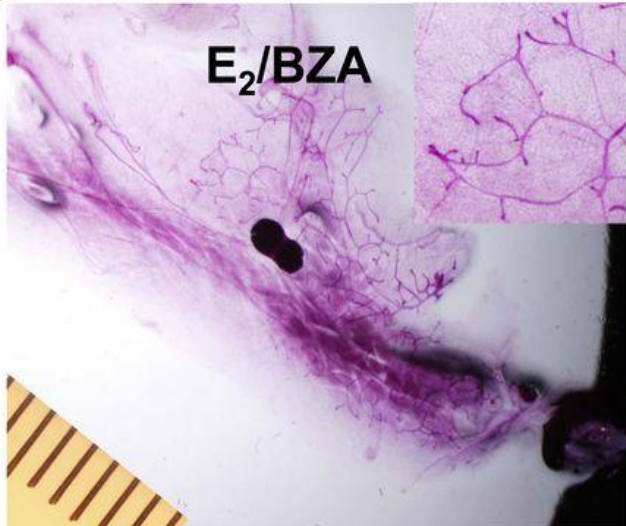
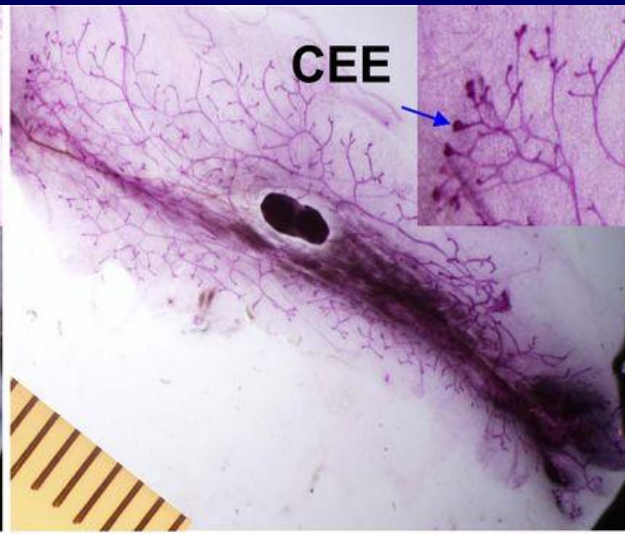
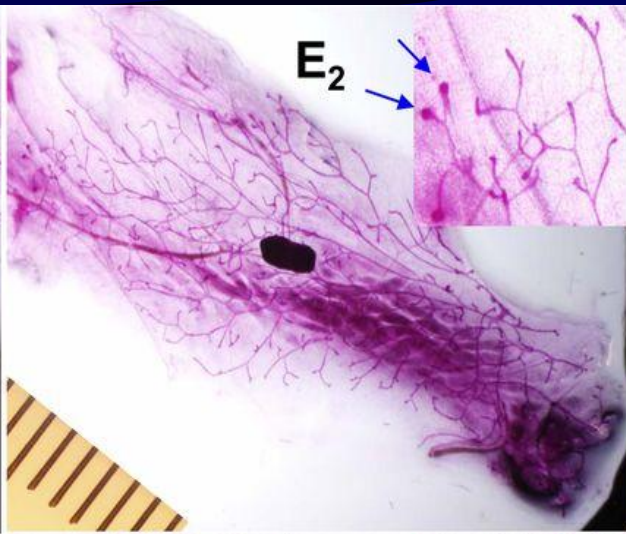
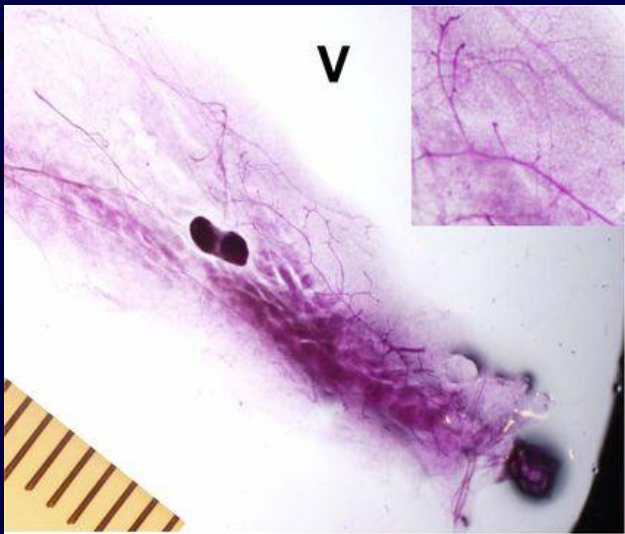
Lenzetto en progebel

Inspanning, uithouding, spierkracht, homa IR, ctx,
P1NP, DNA methylatie, amyloid, P tau, apo

Prof Calders, Prof Lapauw, Prof Kaufman, Prof
Depypere

More en core studie



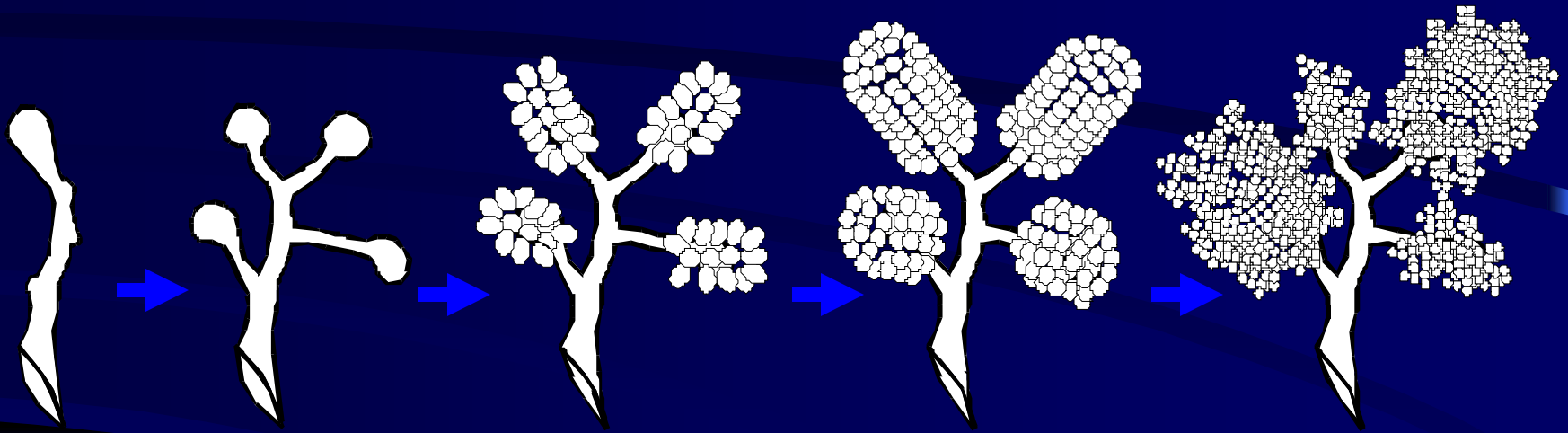


At birth

Development
of breast at
puberty

pregnancy

Lactation



*bud
formation*

*Lobule
Type 1*

*Lobule
Type 2*

*Lobule
Type 3*

*Lobule
Type 4*

Proliferation

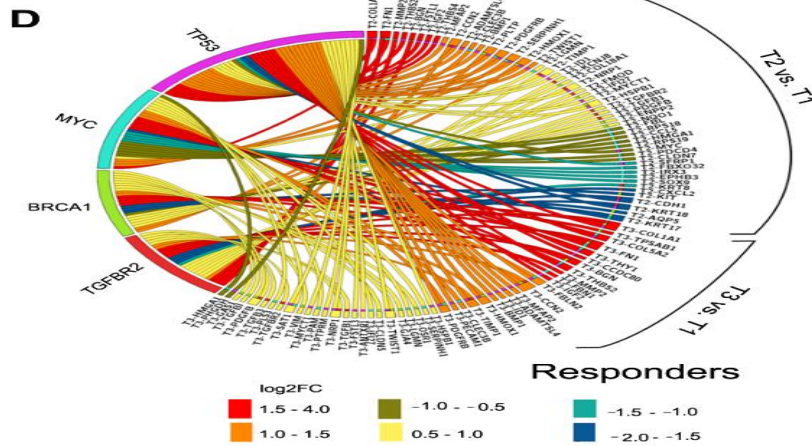
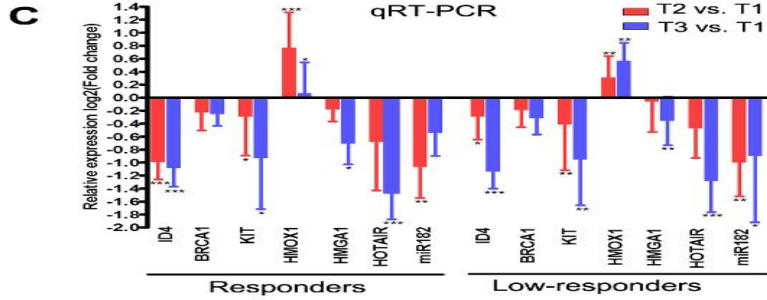
60

22

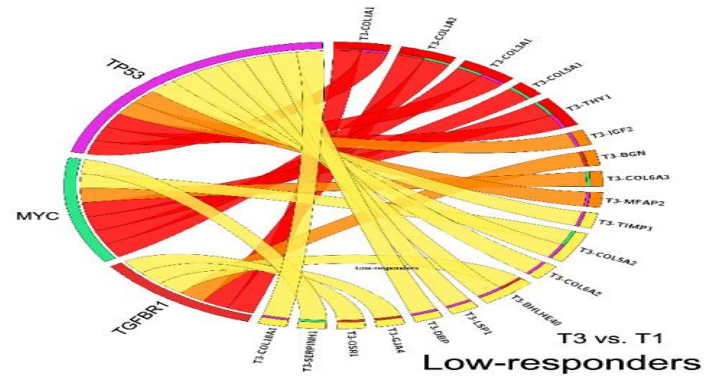
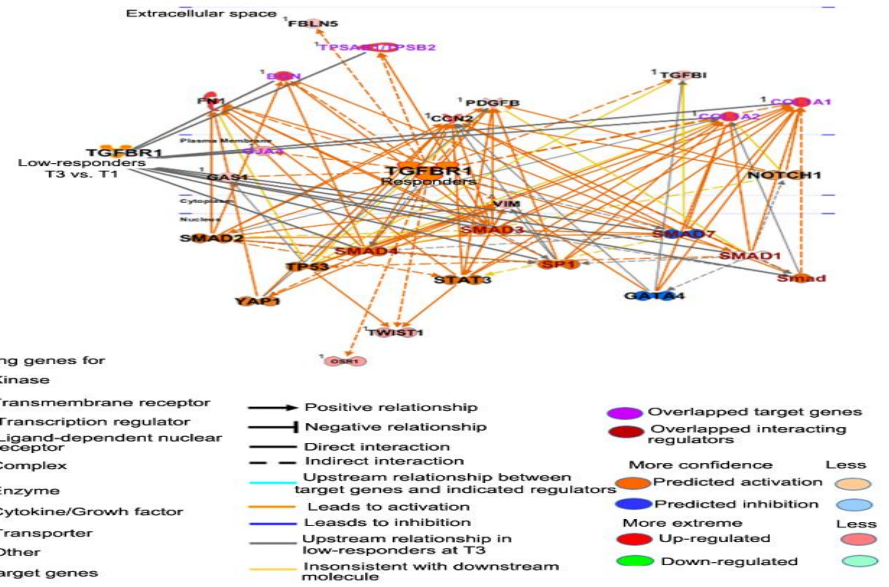
4

1

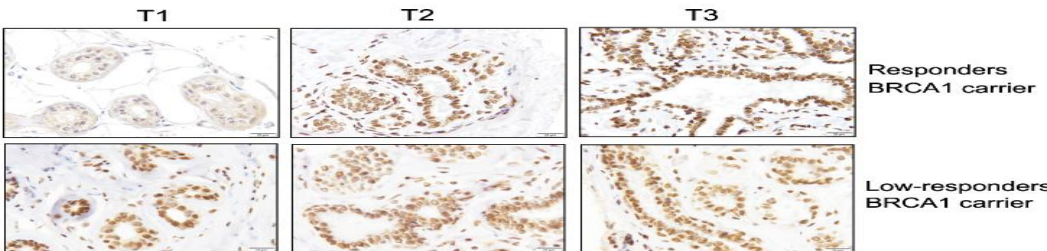
Responders (T2 vs. T1)			Responders (T3 vs. T1)			Low-responders (T3 vs. T1)		
Upstream regulators	Z-score	Prediction score	Upstream regulators	Z-score	Prediction score	Upstream regulators	Z-score	Prediction score
TGFBR2	Activated	2.4	TGFBR2	Increased activity	1.9	TGFBR2	Increased activity	1.7
TGFB1	Activated	5.6	TGFB1	Activated	6.31	TGFB1	Activated	4.2
TGFB1	Activated	3.1	TGFB1	Activated	3.1	TGFB1	Activated	2.2
TGFB2	Activated	2.3	TGFB2	Increased activity	1.9	TGFB2	Activated	2.7
BRCA1	Increased activity	1.0	BRCA1	Activated	2.1	TGFB3	Activated	2.9
TP53	Activated	2.0	TP53	Activated	2.7	TP53	Increased activity	1.8
MYC	Inhibited	-3.0	MYC	Inhibited	-2.6	MYC	Decreased activity	-0.8



B TGFBR1 is predicted activated at T2 and T3 in the responders, and at T3 in the low-responders



E BRCA1 expression in the breast of BRCA1/2 carriers

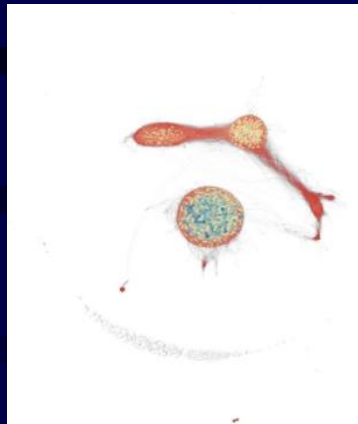
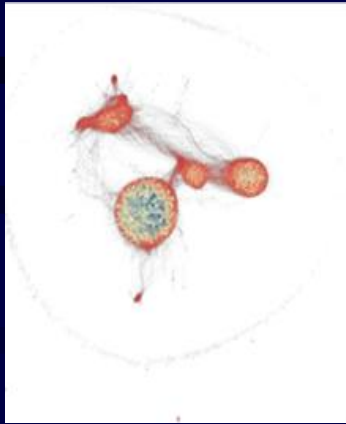


[Y Su, N Dang, H Depypere, et al. Recombinant Human chorionic gonadotropin induces signaling pathways towards cancer prevention in the breast of BRCA1/2 mutation carriers. Eur J Cancer Prev. 2023 Mar 1;32\(2\):126-138.](#)

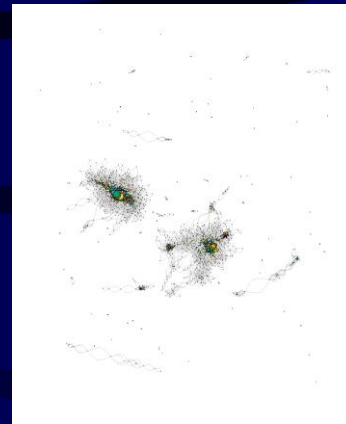
Nulliparous parous

T1

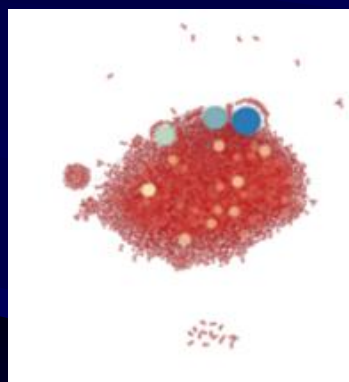
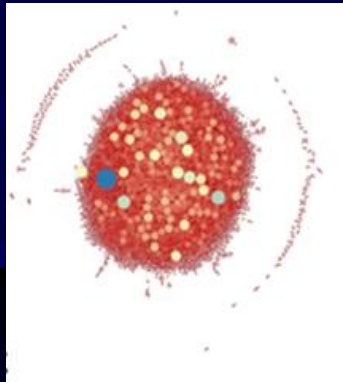
T3



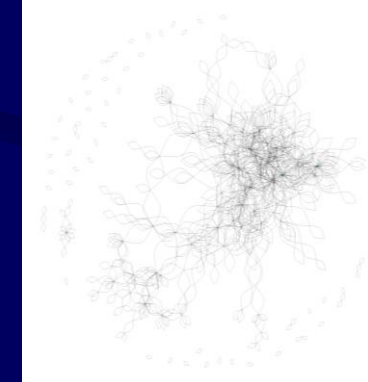
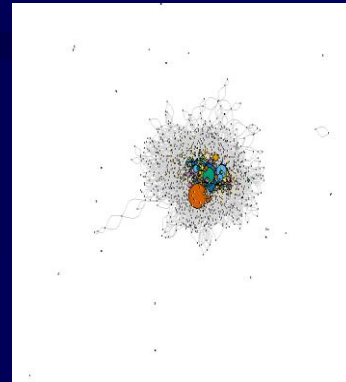
A



B



C



D

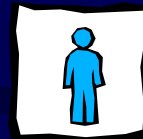
Fruchterman-Reingold figures, changes in high correlation networks after FFTP and r-hCG. A: Changes induced by FFTP in high positive correlation networks from nulliparous (NP) to parous (P). **B:** Changes induced by r-hCG in high positive correlation networks from T1 to T3. **C:** Changes induced by FFTP in high negative correlation networks from nulliparous (NP) to parous (P). **D:** Changes induced by r-hCG in high negative correlation networks from T1 to T3.

Menopauze en bot

Incidentie van osteoporose > 50 jaar :



1/3



1/8

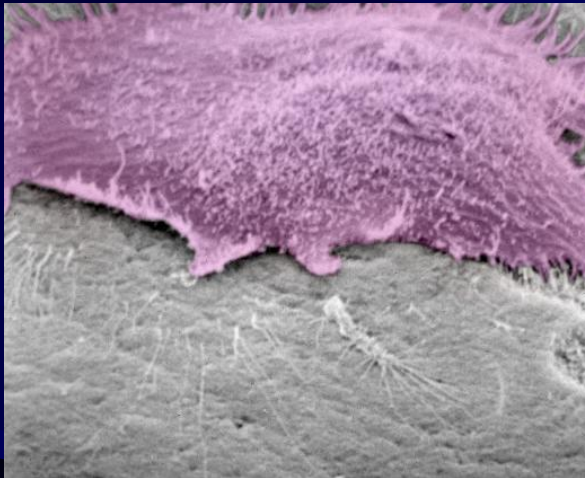
De incidentie zal de komende 50 jaar verdubbelen

2^{de} grootste gezondheidsprobleem na
cardiovasculaire ziekte



Osteoclasten en osteoblasten zijn essentieel voor de botombouw

Osteoclast



- De osteoclasten resorberen oud of beschadigd bot¹

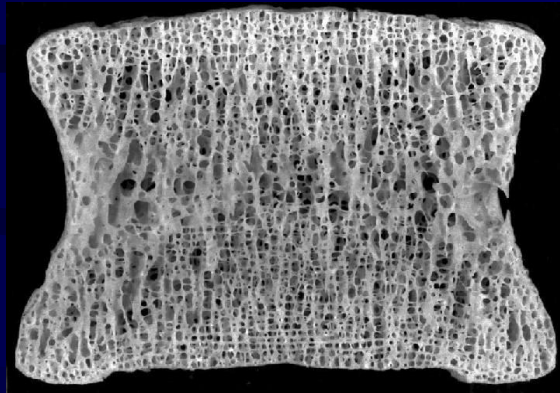
Osteoblast



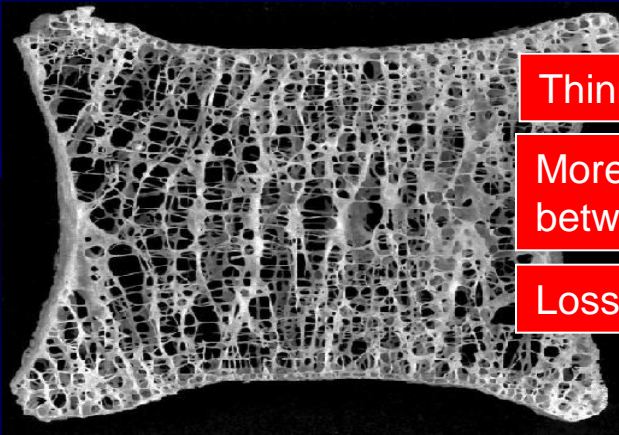
- De osteoblasten vormen nieuw bot nadat het geresorbeerd werd door de osteoclasten¹

1. Seeman E et al. *New Engl J Med* 2006;354:2250-2261.

Normal bone



Osteoporosis

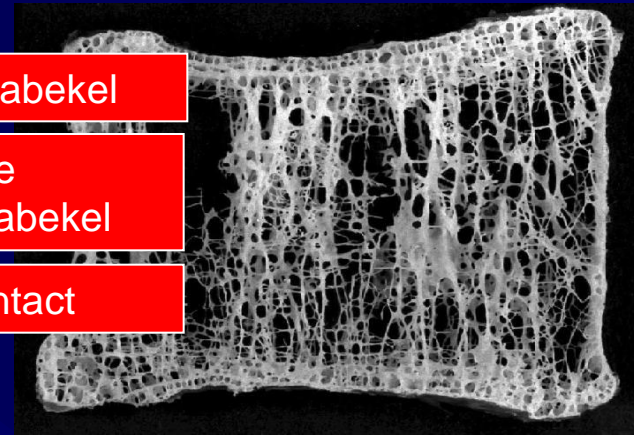


Thinning trabekel

More space
between trabekel

Loss of contact

Severe Osteoporosis



Vrouwen met klachten: IMS, EMAS, NAMS, BMS:
behandel met hormonen.

Wanneer starten?

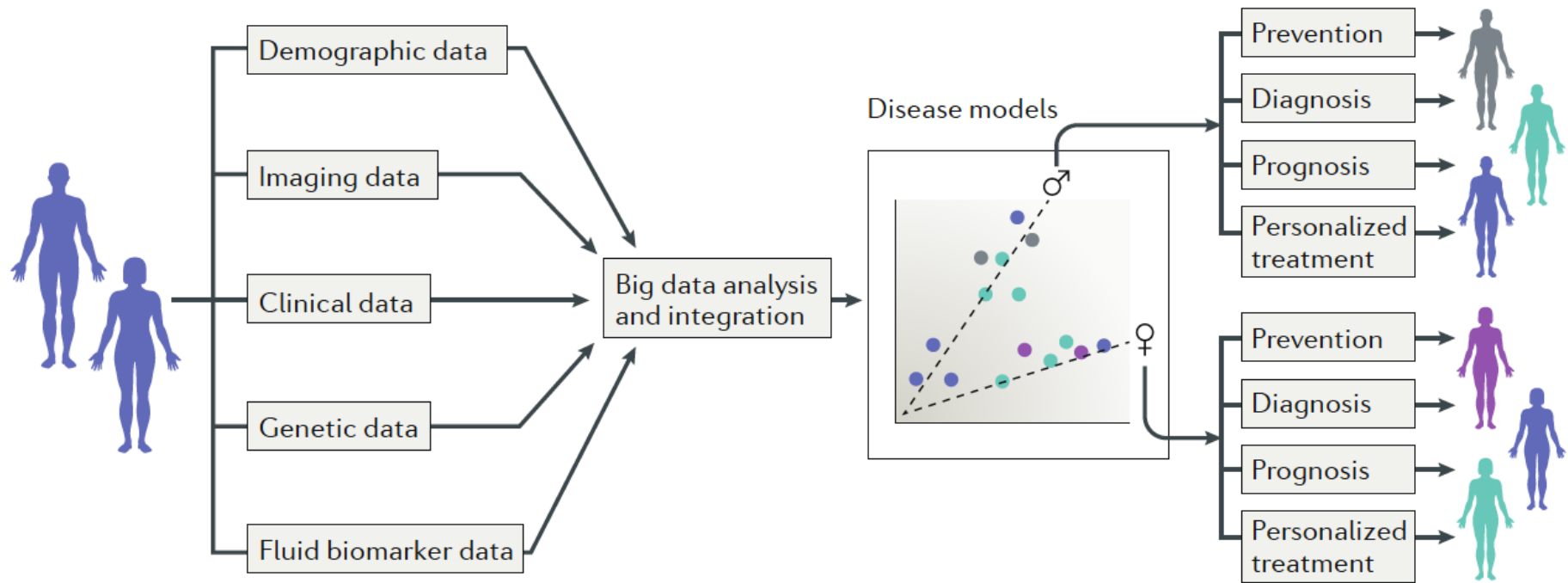
Hoe lang behandelen?

Welke producten? Indien baarmoeder nog aanwezig:


Oraal: Femoston® –conti of low-, Angeliq®, Activelle®,
Progynova® 1 mg en Utrogestan®, Progynova® met
Mirena® of Kyleena®, Bijuva®

Percutaan: Dermestril®, System®, Oestrogel®, Lenzetto®
met Utrogestan® of Mirena® of Duphaston® of
Kyleena®, feminova®

Indien geen baarmoeder dan enkel oestrogenen



Sex differences in Alzheimer disease — the gateway to precision medicine

Maria Teresa Ferretti , Maria Florencia Iulita, Enrica Cavedo, Patrizia Andrea Chiesa, Annemarie Schumacher Dimech, Antonella Santucci Chadha, Francesca Baracchi, H el ene Girouard, Sabina Misoch, Ezio Giacobini, Herman Depypere, Harald Hampel & for the Women's Brain Project and the Alzheimer Precision Medicine Initiative

Nature Reviews Neurology **14**, 457–469 (2018) | [Download Citation](#) 

Individuele aanpak voor: klachten en lange termijnsrisico's zoals, osteoporose, vaatlijden, dementie, borstkanker,...

Snel na de menopauze starten

Precutaan of lage dosis oraal

**Titreeren op de kliniek na controle afspraak kort na
initiatie van hormonen**

