



Cardiologie: Van Preventie tot herstel

Preventie meer dan ooit van belang!

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Voorzitter, Belgian Atherosclerosis Society / Belgian Lipid Club

Expert & Lid van het College, Hoge Gezondheidsraad (HGR-CSS)

Co-founder BELCHOL



ASKLEPIOS STUDY
Successful cardiovascular aging



Cardiologie: Van Preventie tot herstel

Preventie meer dan ooit van belang!

Belangenverklaring

1. Ik bezit geen aandelen van farmaceutische / medical device bedrijven
2. Grants/Research Support (unrestricted educational grants aan de Asklepios Studie) of Advisory Board Memberships, Consultancies of contracten als spreker: alle betalingen @ Universiteit Gent / UZ Gent; nooit persoonlijk.



ASKLEPIOS STUDY
Successful cardiovascular aging

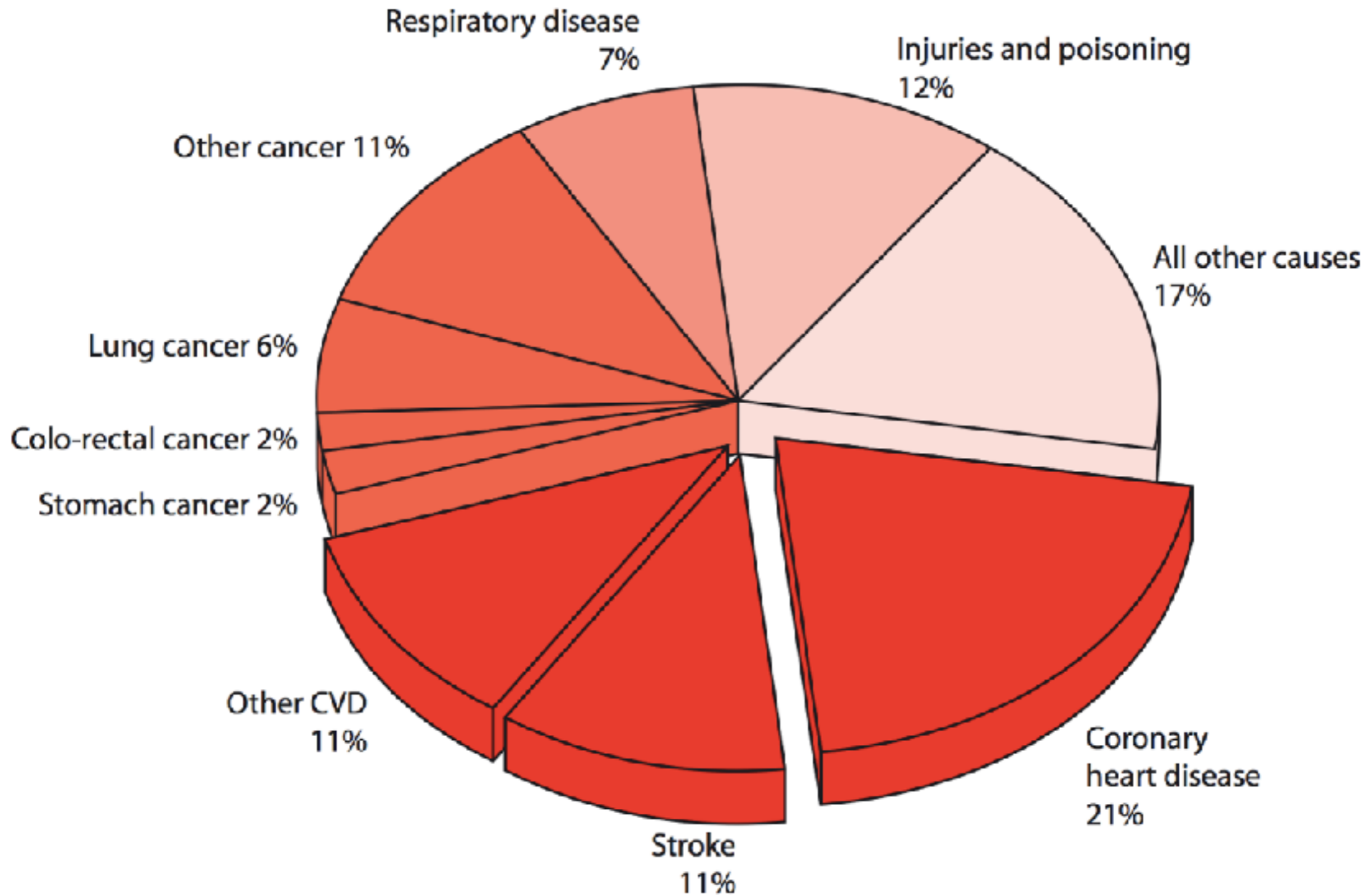


I) Epidemiologie



Overlijdensoorzaken

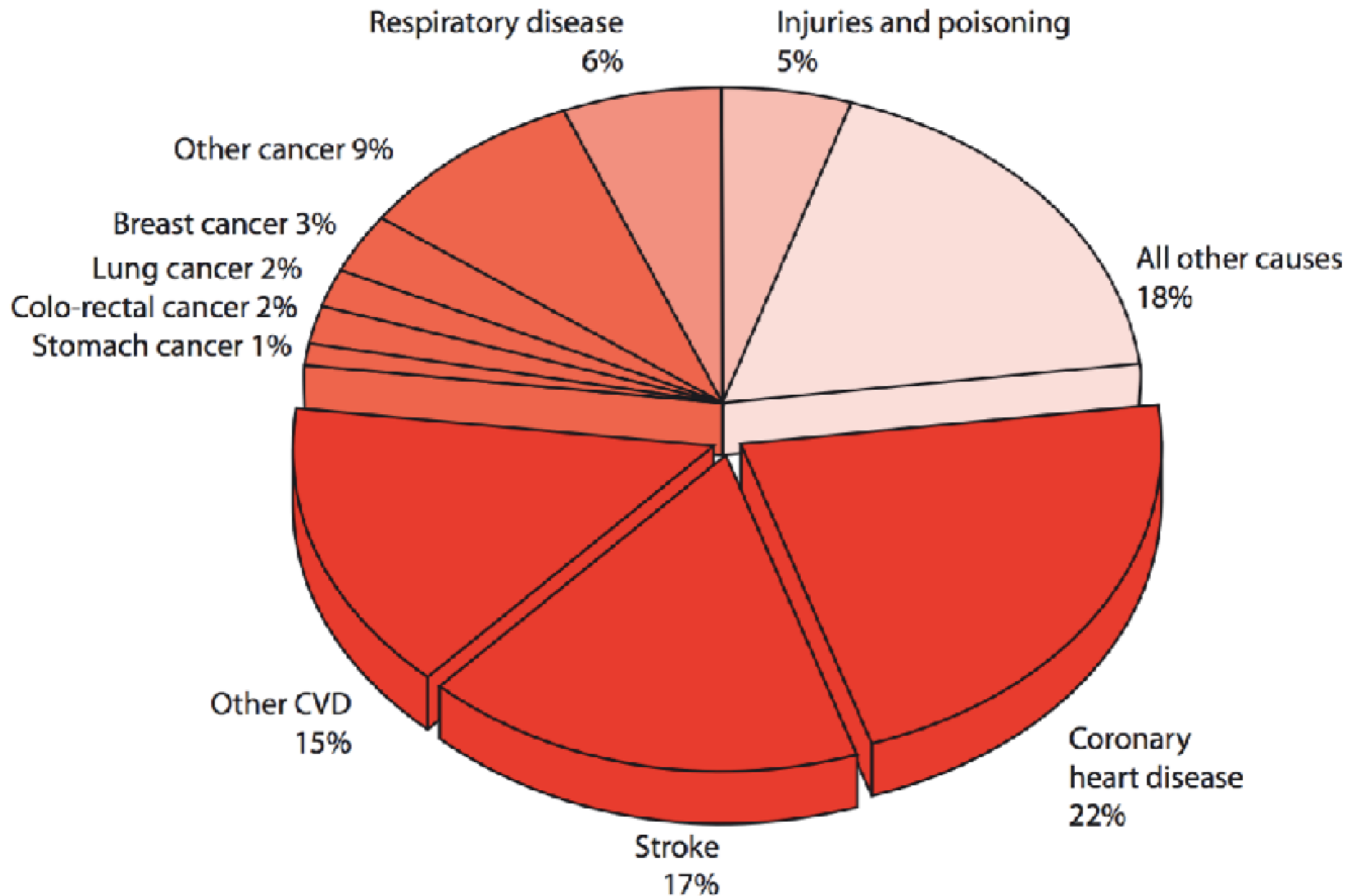
Overlijdens; Europese mannen





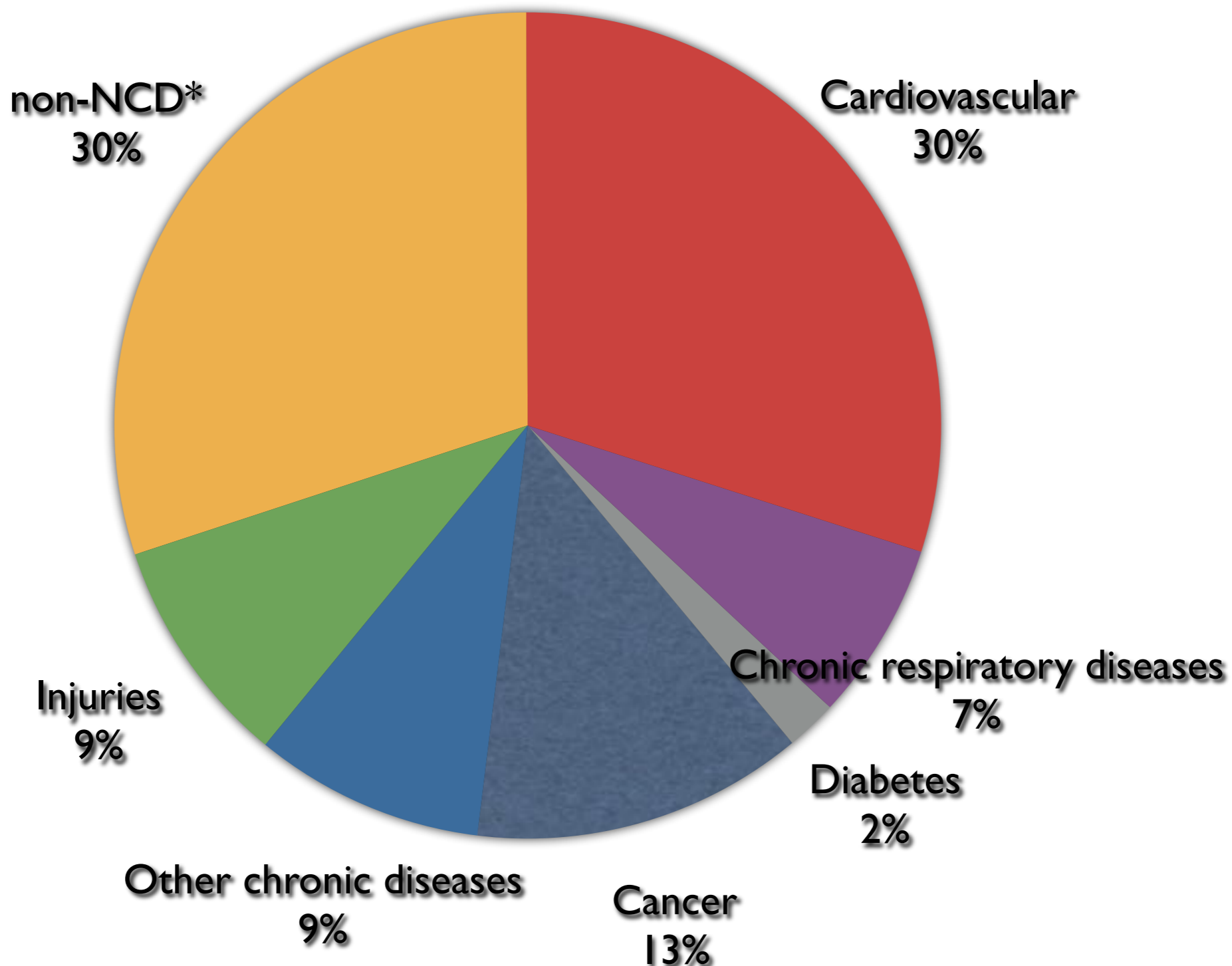
Overlijdensoorzaken

Overlijdens; Europese vrouwen





Overlijdensoorzaken wereldwijd



(*communicable diseases, maternal and perinatal conditions and nutritional deficiencies)



Global burden of diseases 1990-2015

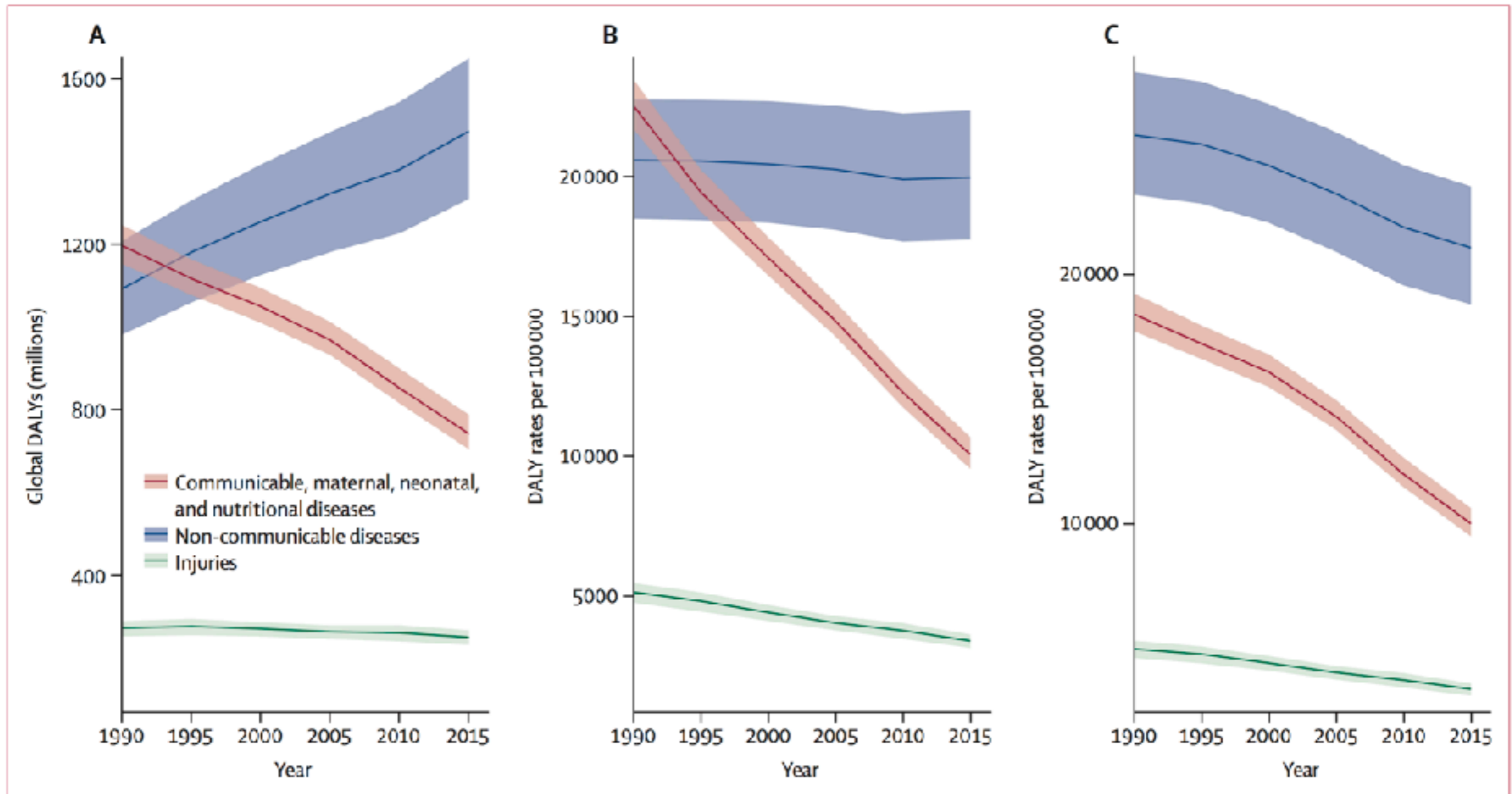


Figure 1: Trends from 1990 to 2015, by GBD Level 1 cause, in global DALYs (A), crude DALY rates (B), and age-standardised DALY rates (C)
The difference in trends between (A) and (B) is caused by population growth and the difference between (B) and (C) is caused by changes in the percentage distribution of the population by age. Shaded areas show 95% uncertainty intervals. DALYs=disability-adjusted life-years.

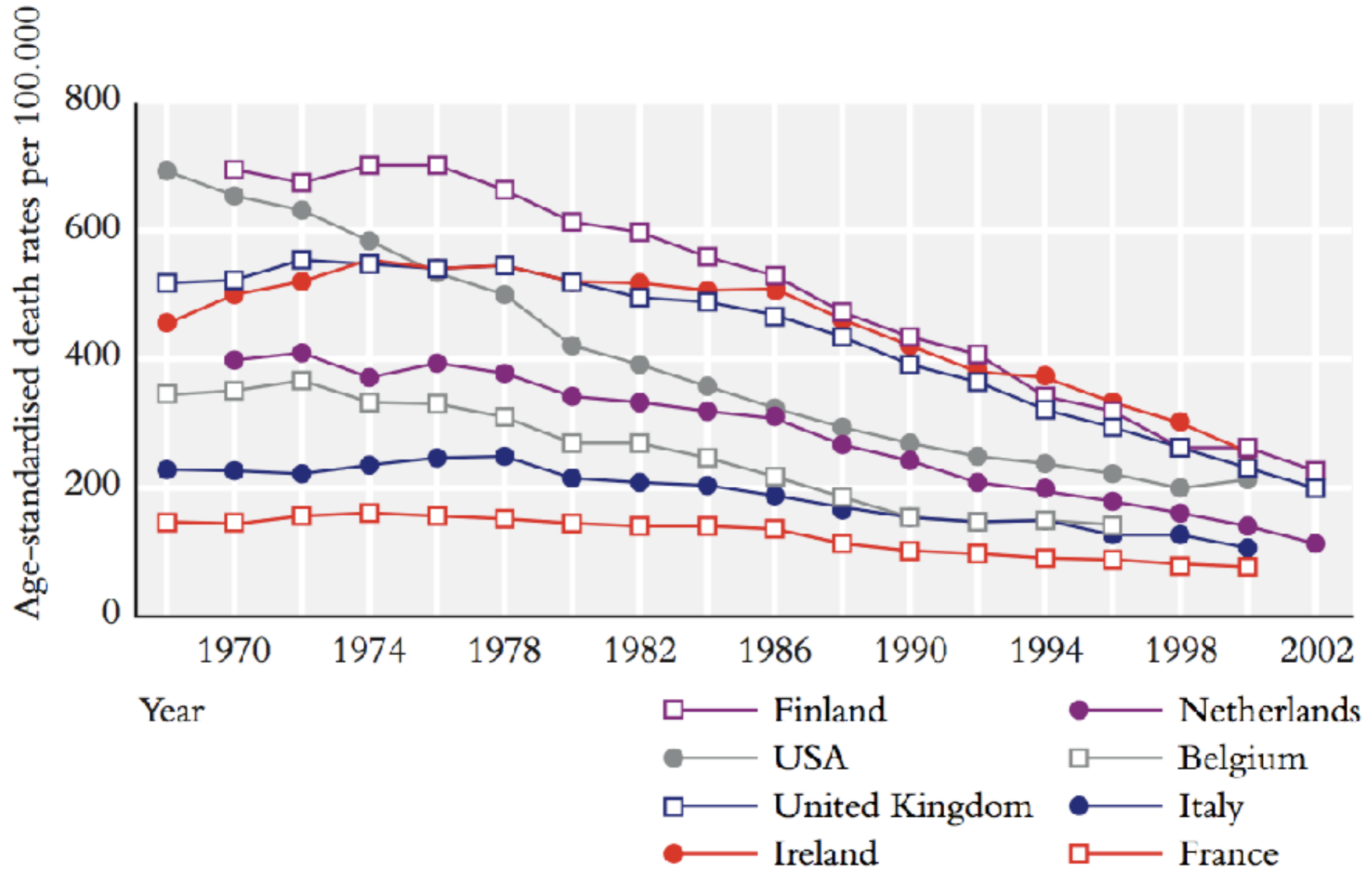


Humane & Economische Kost

- 30% van alle sterfte < 65 jaar.
- Voornaamste oorzaak van invaliditeit in de Westerse Wereld (>> CVA)
- *Kost (EU) : 192 € miljard/jaar (België, 2004: 3.5 miljard €)*
 - = 21.9 € miljoen/uur
 - = 6.100 € /seconde
- Humane kost (CVD, Europa) :
 - 4.3 miljoen overlijdens per jaar,
 - = 12.000 overlijdens per dag
 - = >8 overlijdens per minuut



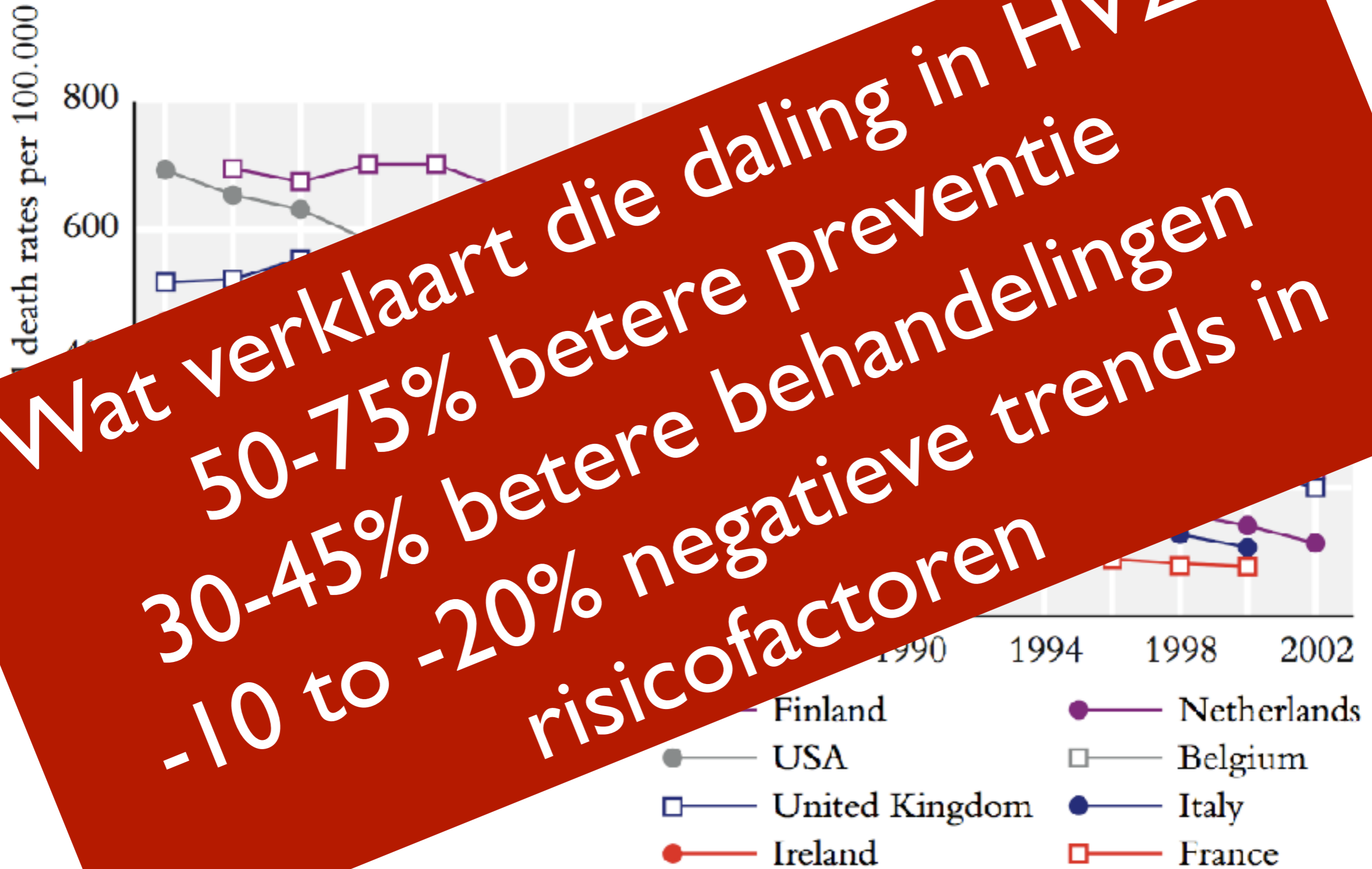
HVZ Evolutie 1965-2002



Age-standardized death rates per 100,000 population from CHD, men, 1968 to 2002, selected countries. Data from WHO Statistical Information System (WHOSIS) accessed at <http://www.who.int/whosis/en/> on March, 23rd, 2009 and from the British Heart Foundation Statistics Website (<http://www.heartstats.org/datapage.asp?id=744>). Notes: ICD codes 410-414 (8th and 9th Revision), I20-I25 (10th Revision). Age-standardized using the European Standard Population.



HVZ Evolutie 1965-2002



Wat verklaart die daling in HVZ?
 50-75% betere preventie
 30-45% betere behandelingen
 -10 to -20% negatieve trends in risicofactoren

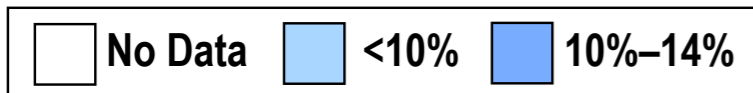
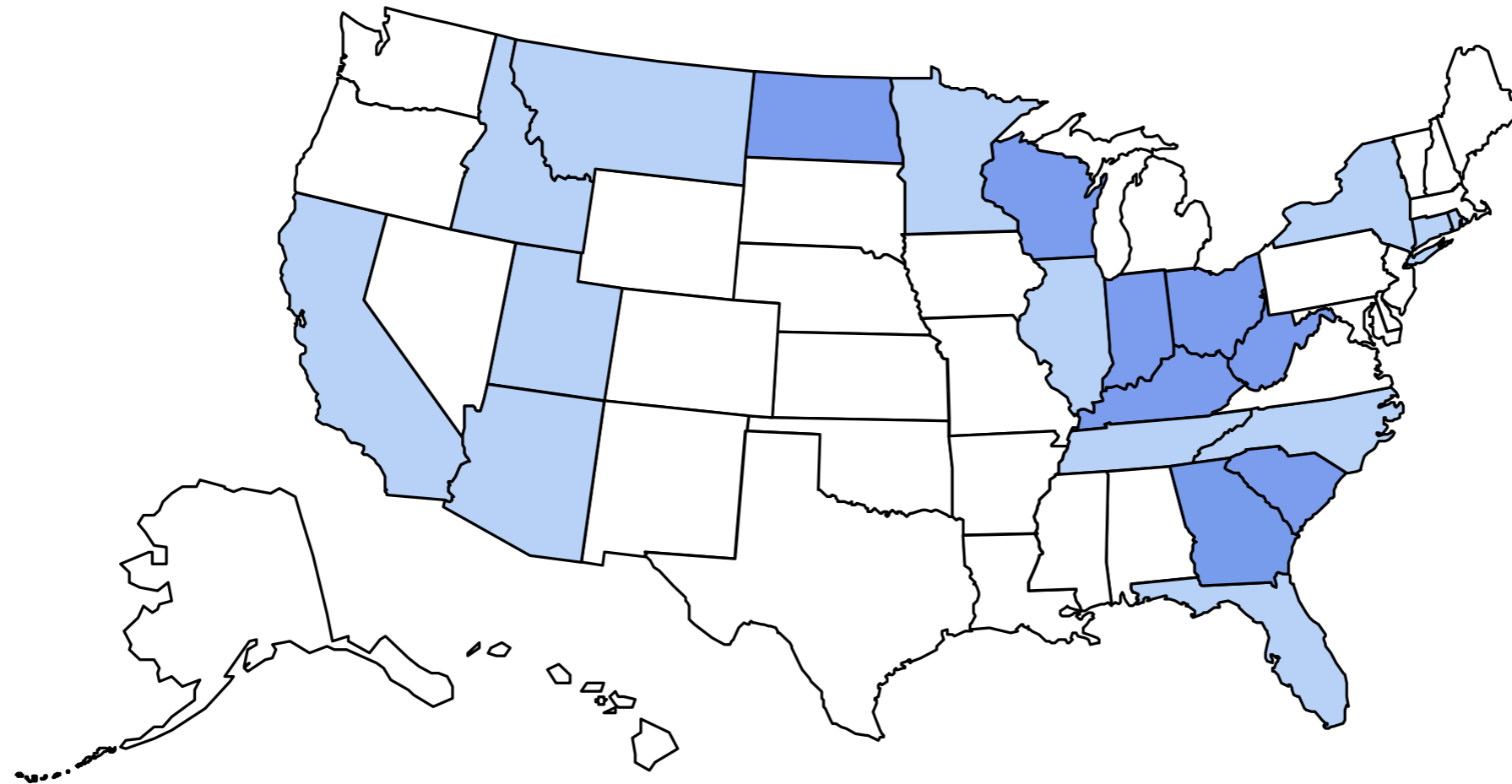
Age-standardized death rates per 100,000 population from CHD, men, 1968 to 2002, selected countries. Data from WHO Statistical Information System (WHOSIS) accessed at <http://www.who.int/whosis/en/> on March, 23rd, 2009 and from the British Heart Foundation Statistics Website (<http://www.heartstats.org/datapage.asp?id=744>). Notes: ICD codes 410-414 (8th and 9th Revision), I20-I25 (10th Revision). Age-standardized using the European Standard Population.



Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1985

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

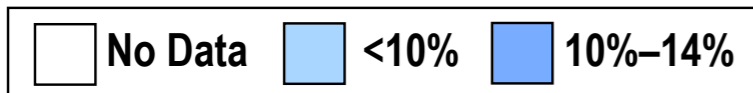
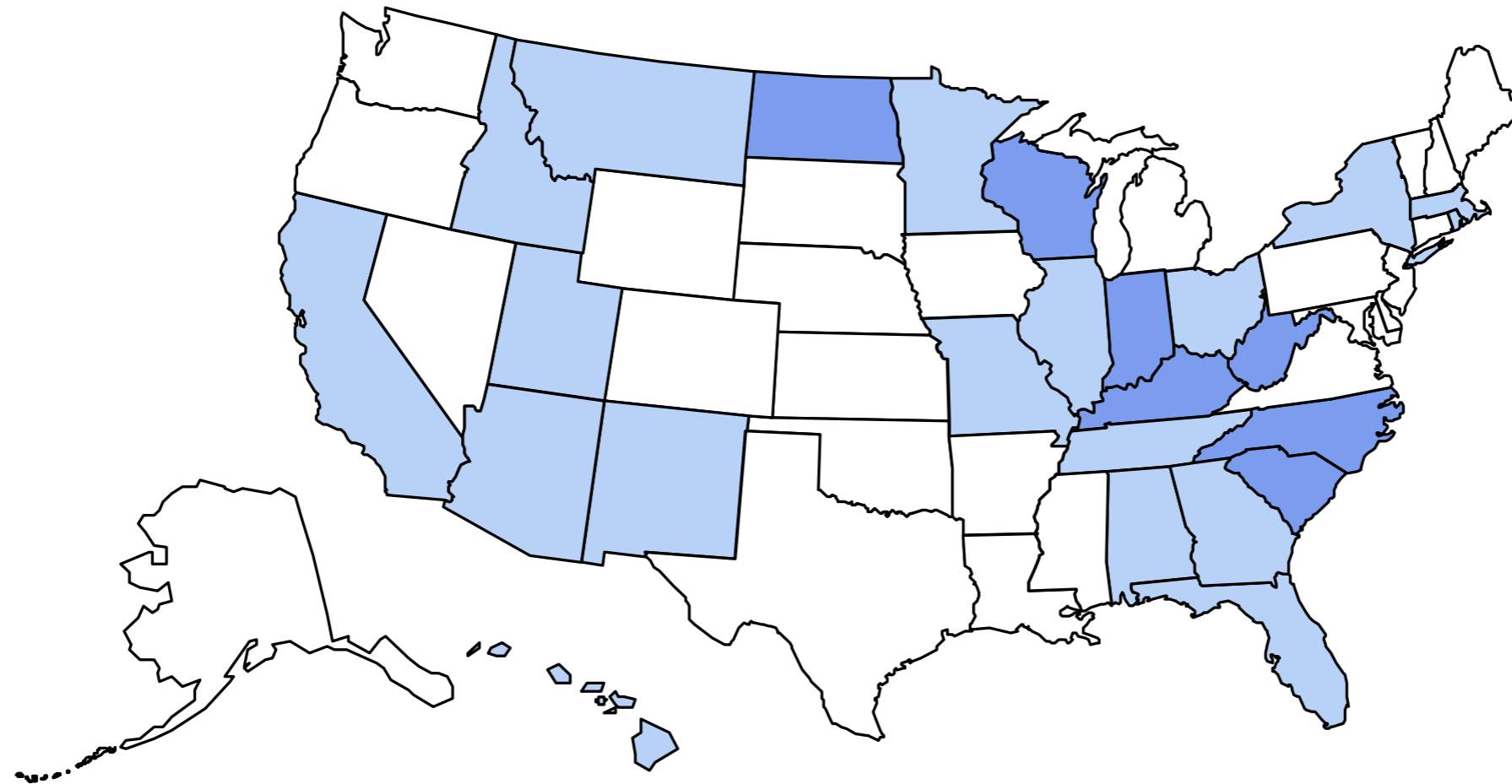




Obesitas evolutie

Obesity Trends* Among U.S. Adults **BRFSS, 1986**

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

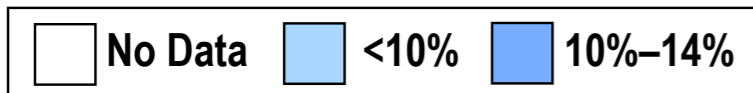
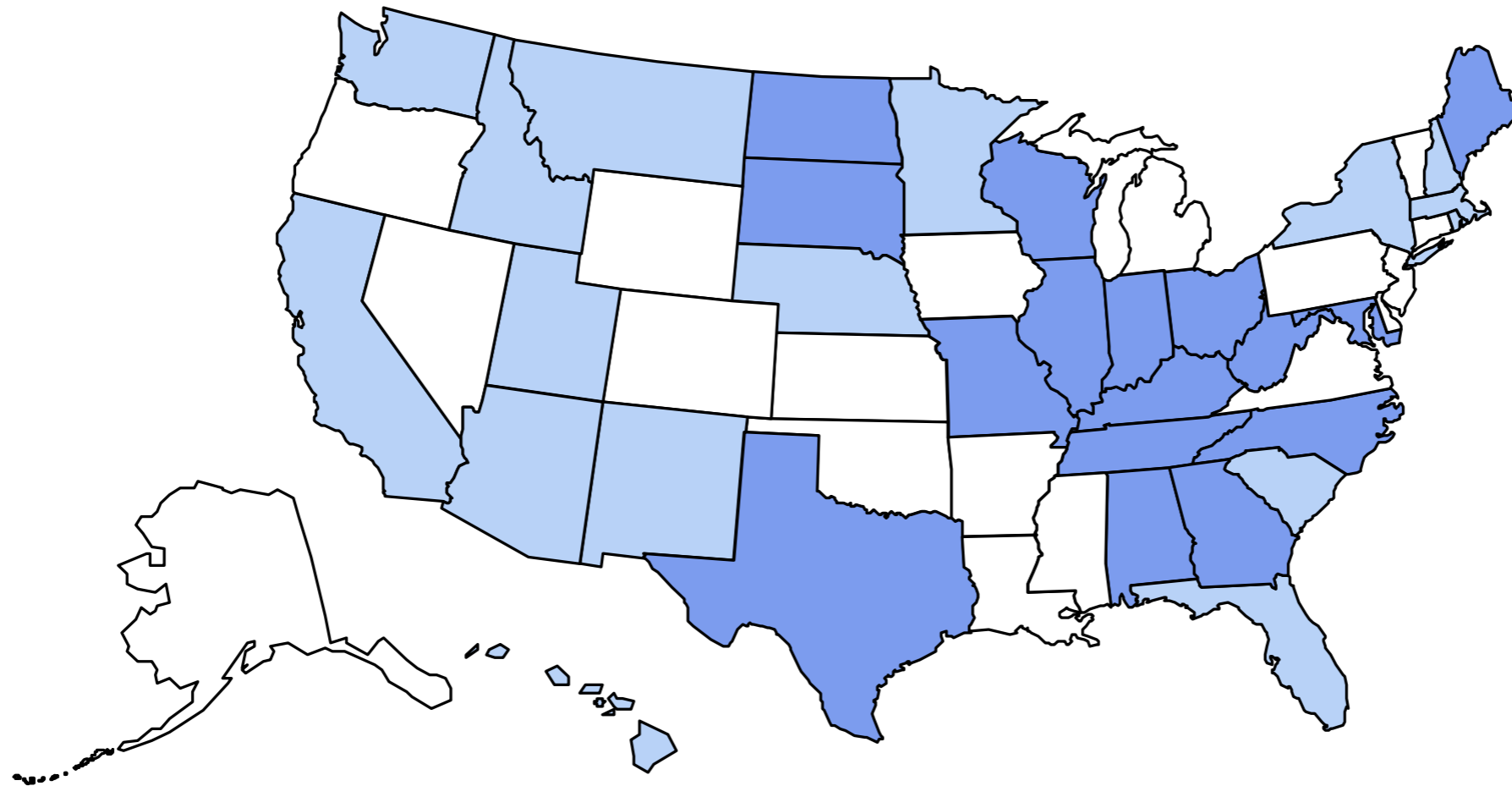




Obesitas evolutie

Obesity Trends* Among U.S. Adults **BRFSS, 1987**

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

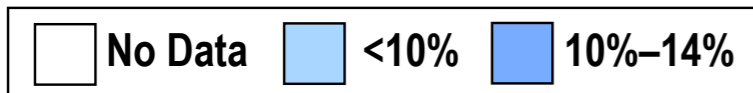
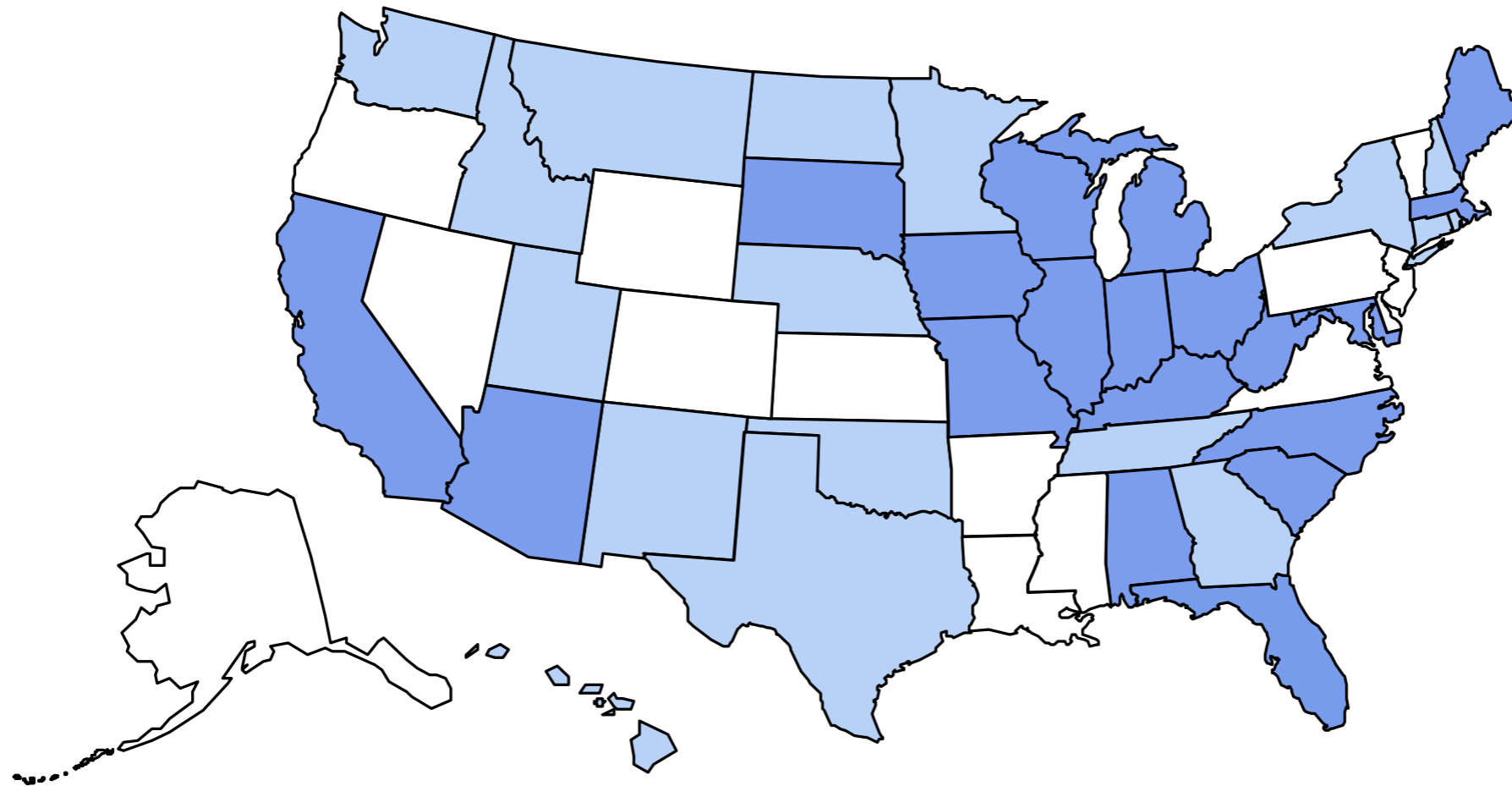




Obesitas evolutie

Obesity Trends* Among U.S. Adults **BRFSS, 1988**

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

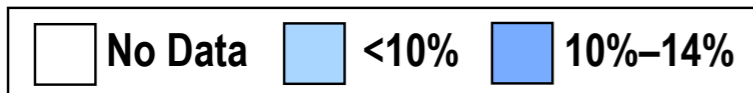
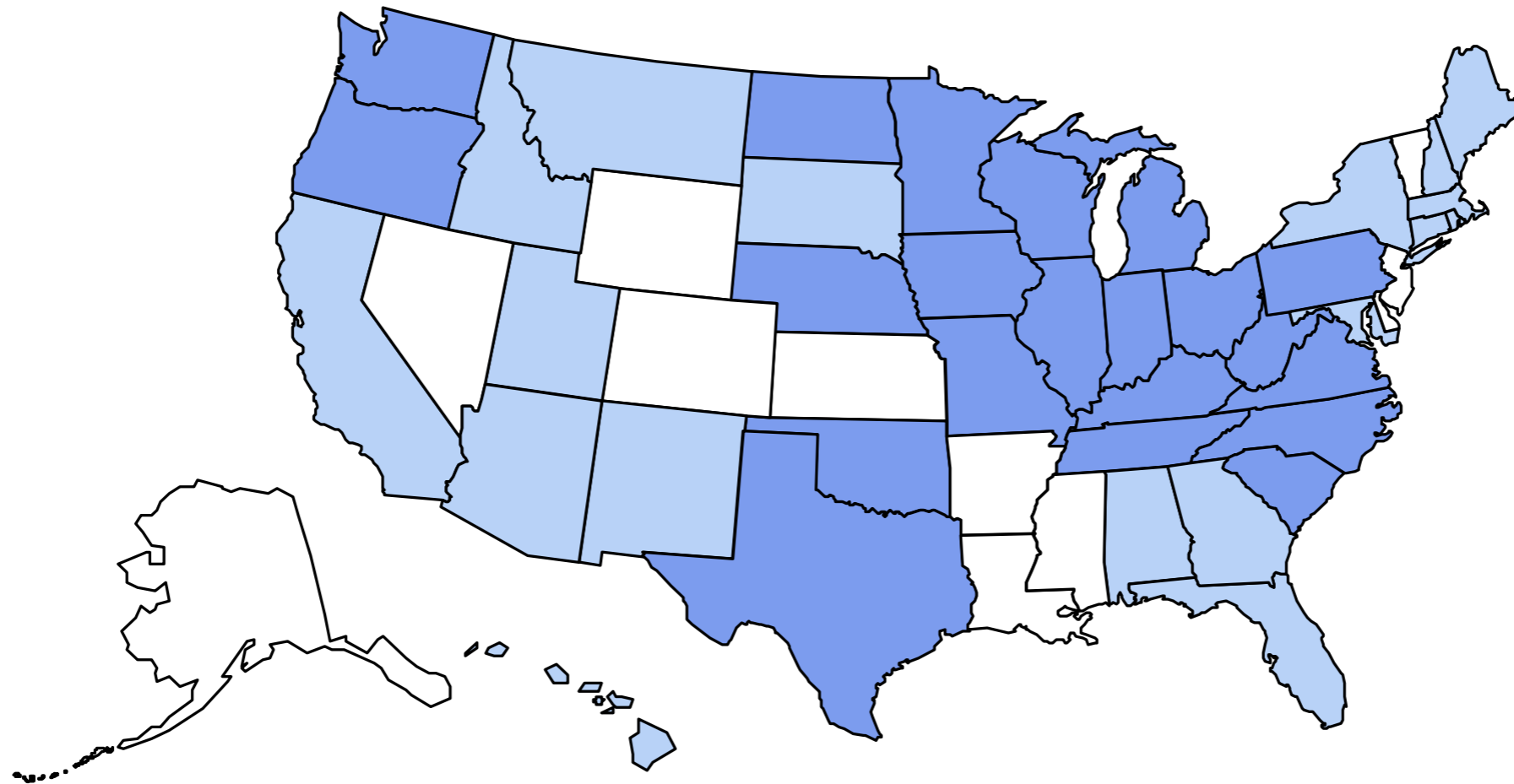




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1989

(*BMI ≥30, or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

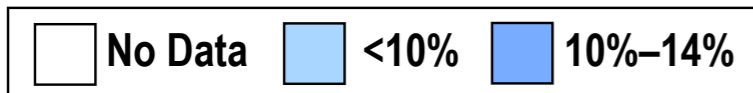
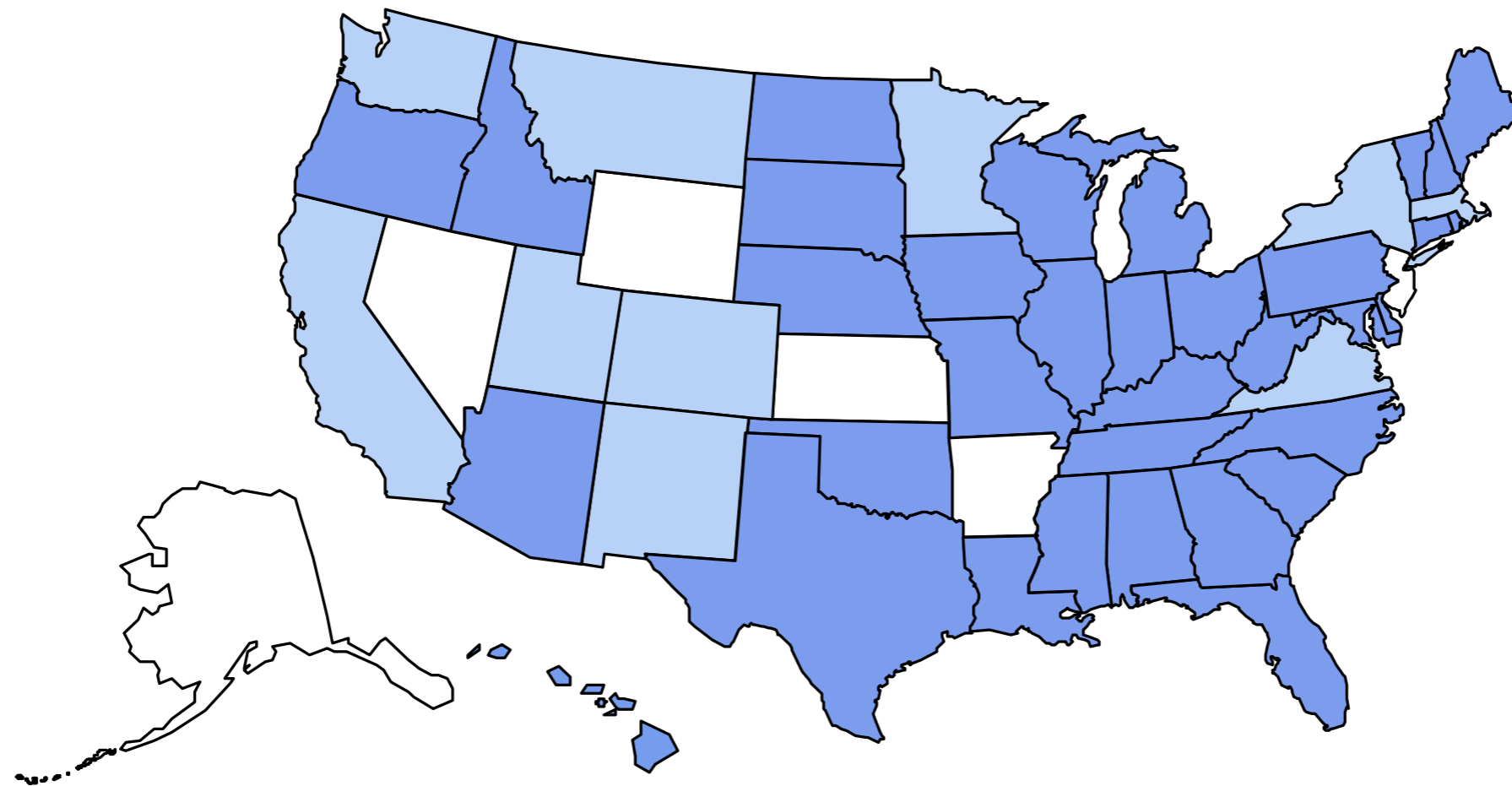




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1990

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

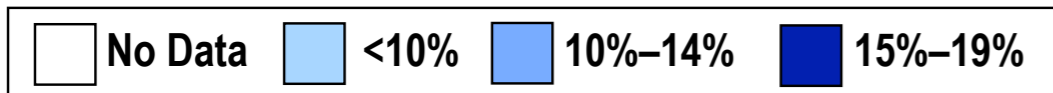
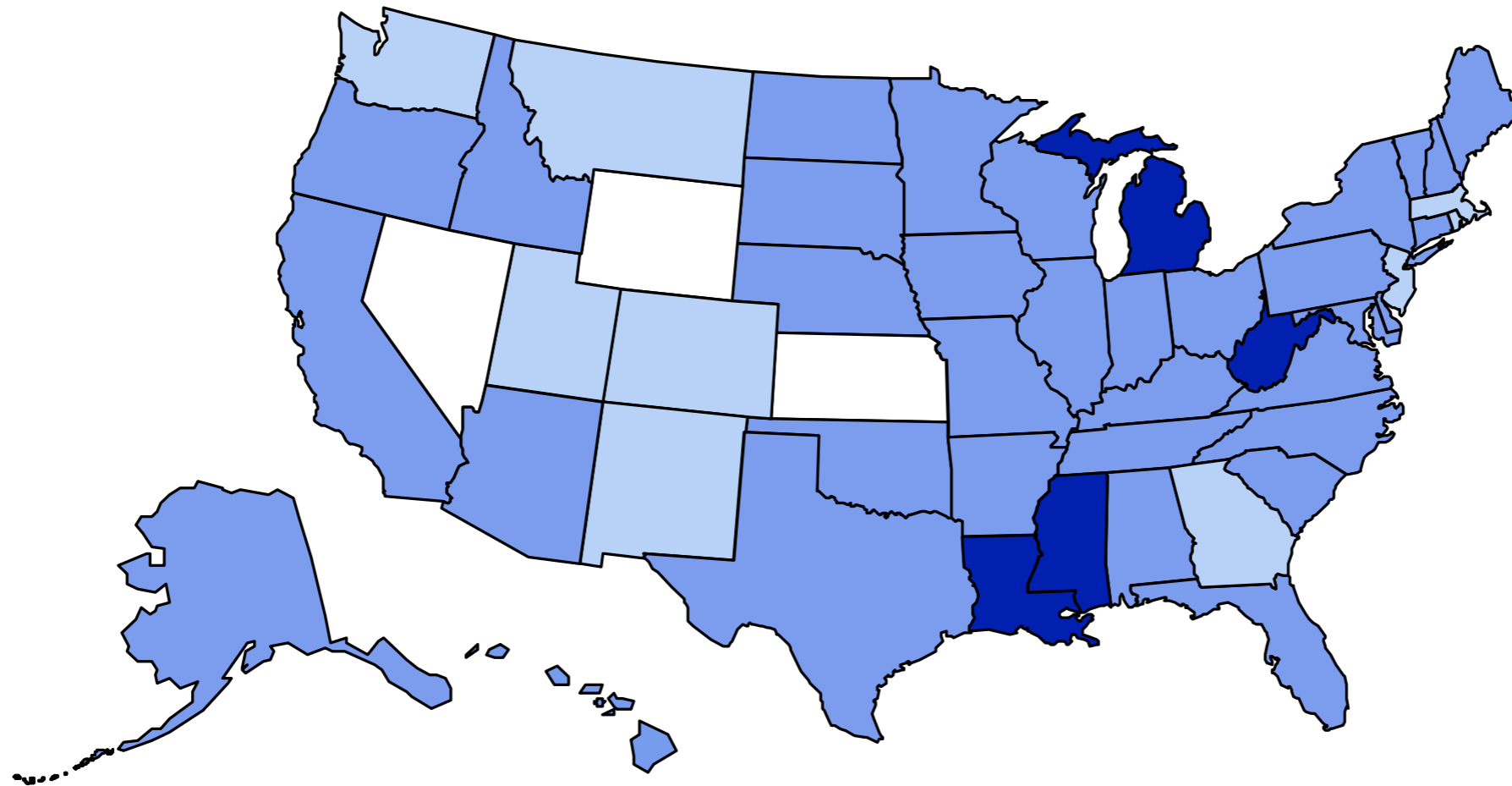




Obesitas evolutie

Obesity Trends* Among U.S. Adults **BRFSS, 1991**

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

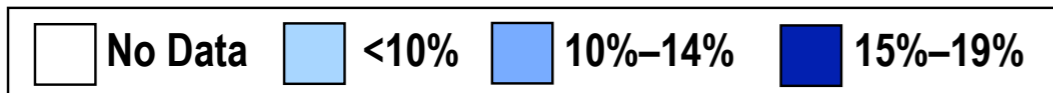
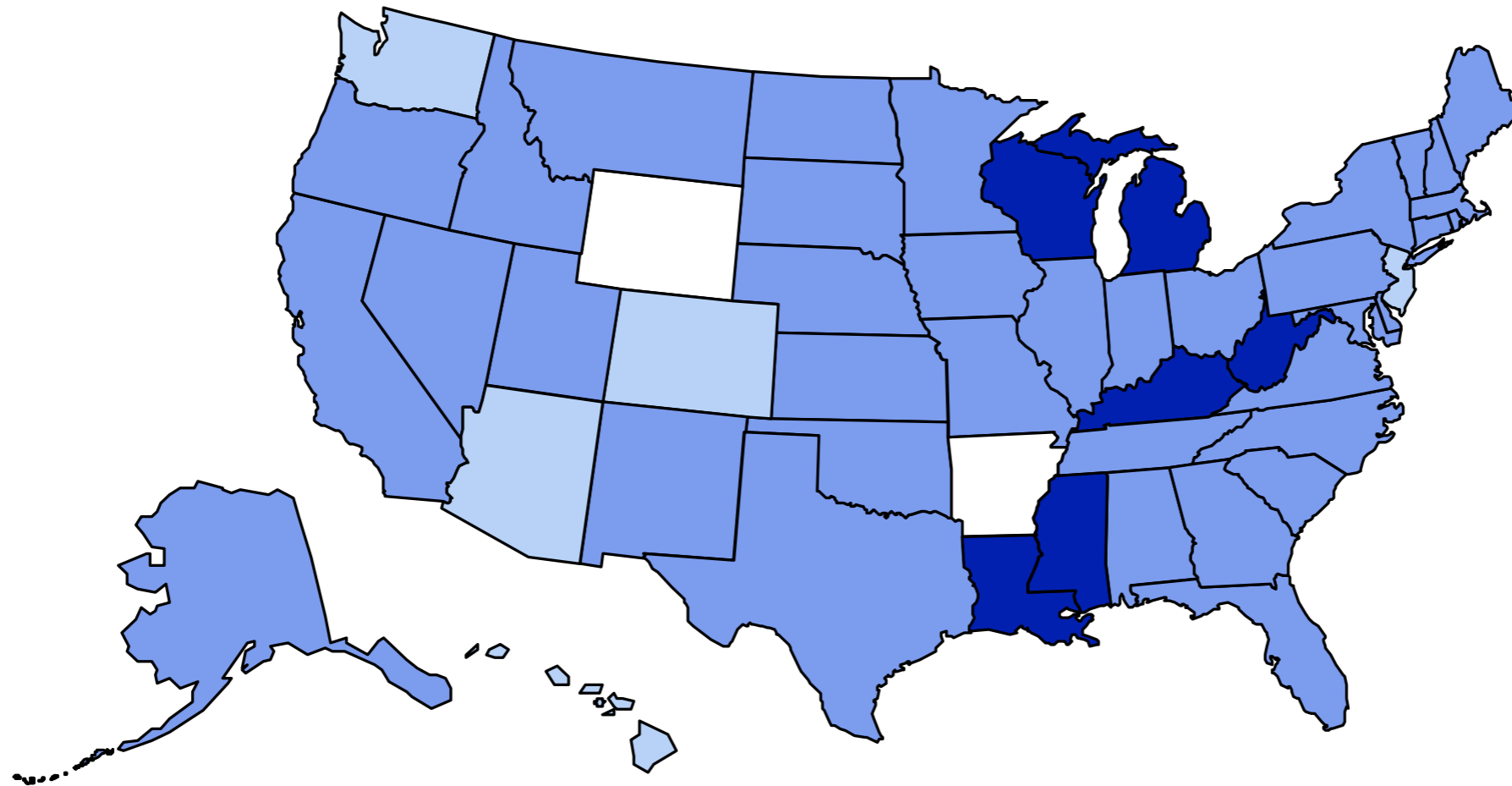




Obesitas evolutie

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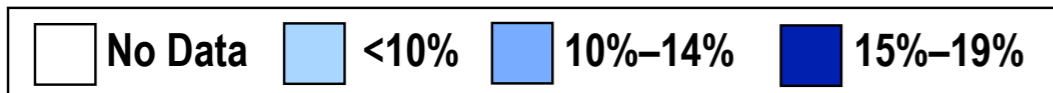
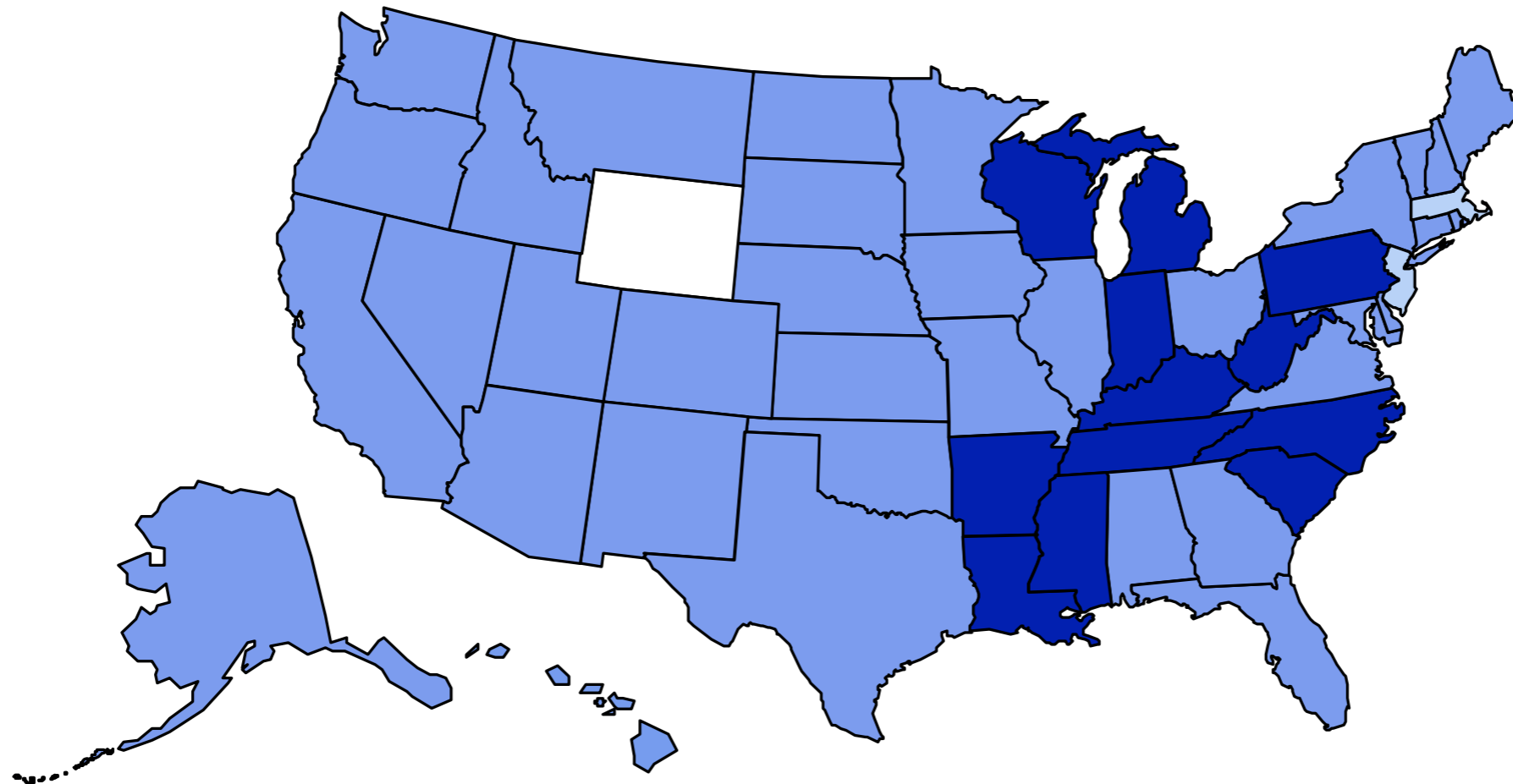




Obesitas evolutie

Obesity Trends* Among U.S. Adults **BRFSS, 1993**

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

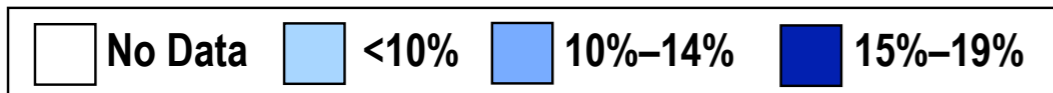
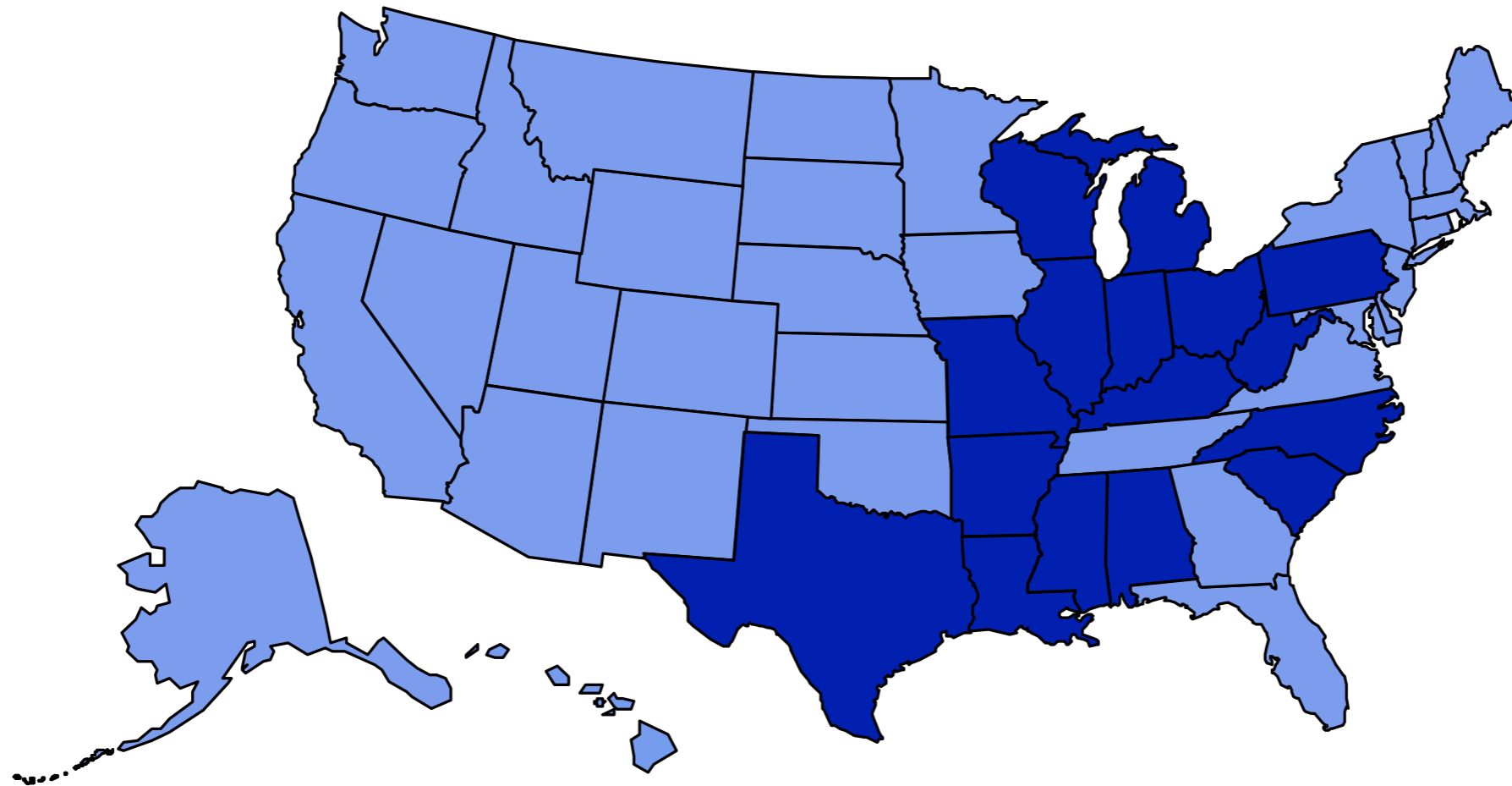




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1994

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

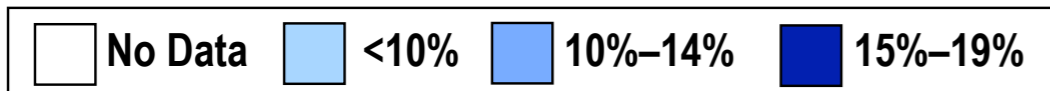
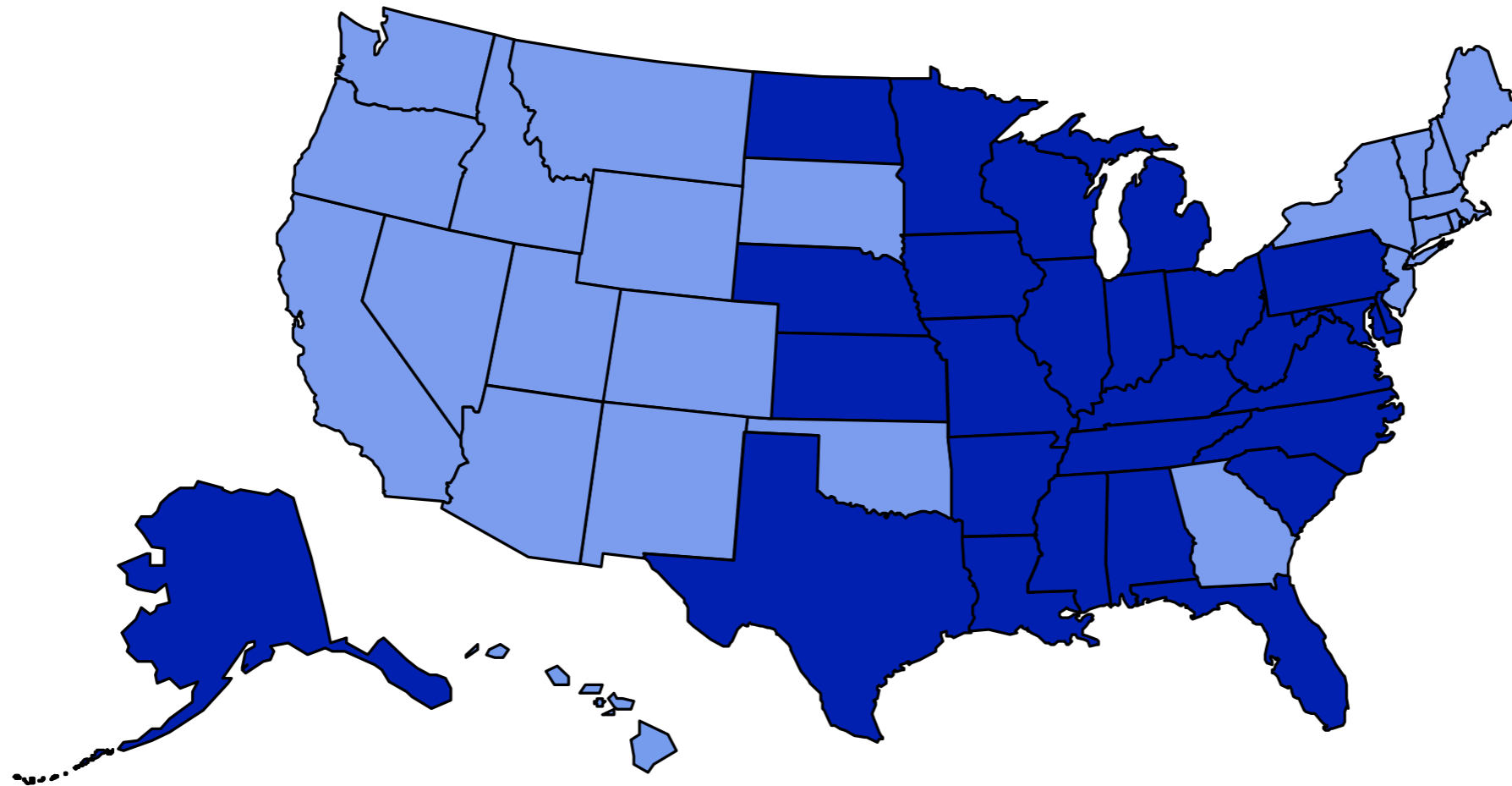




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1995

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

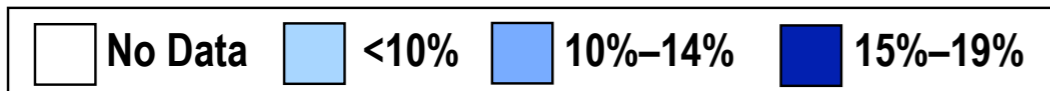
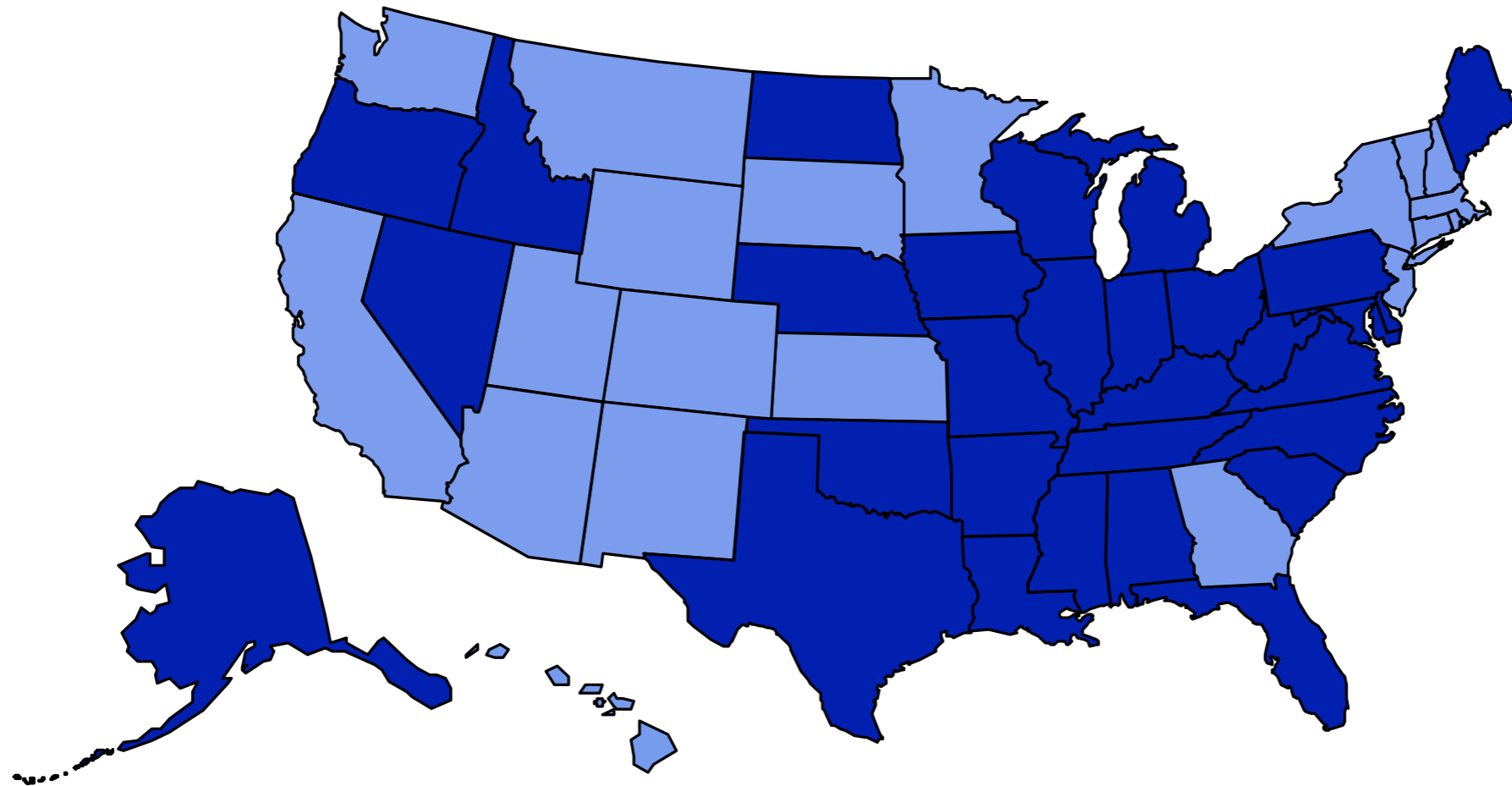




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1996

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

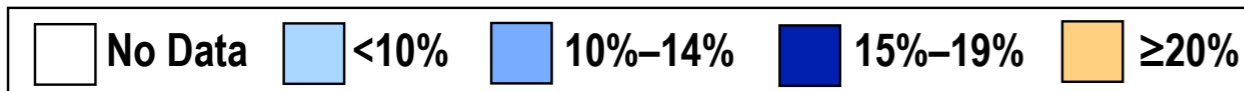
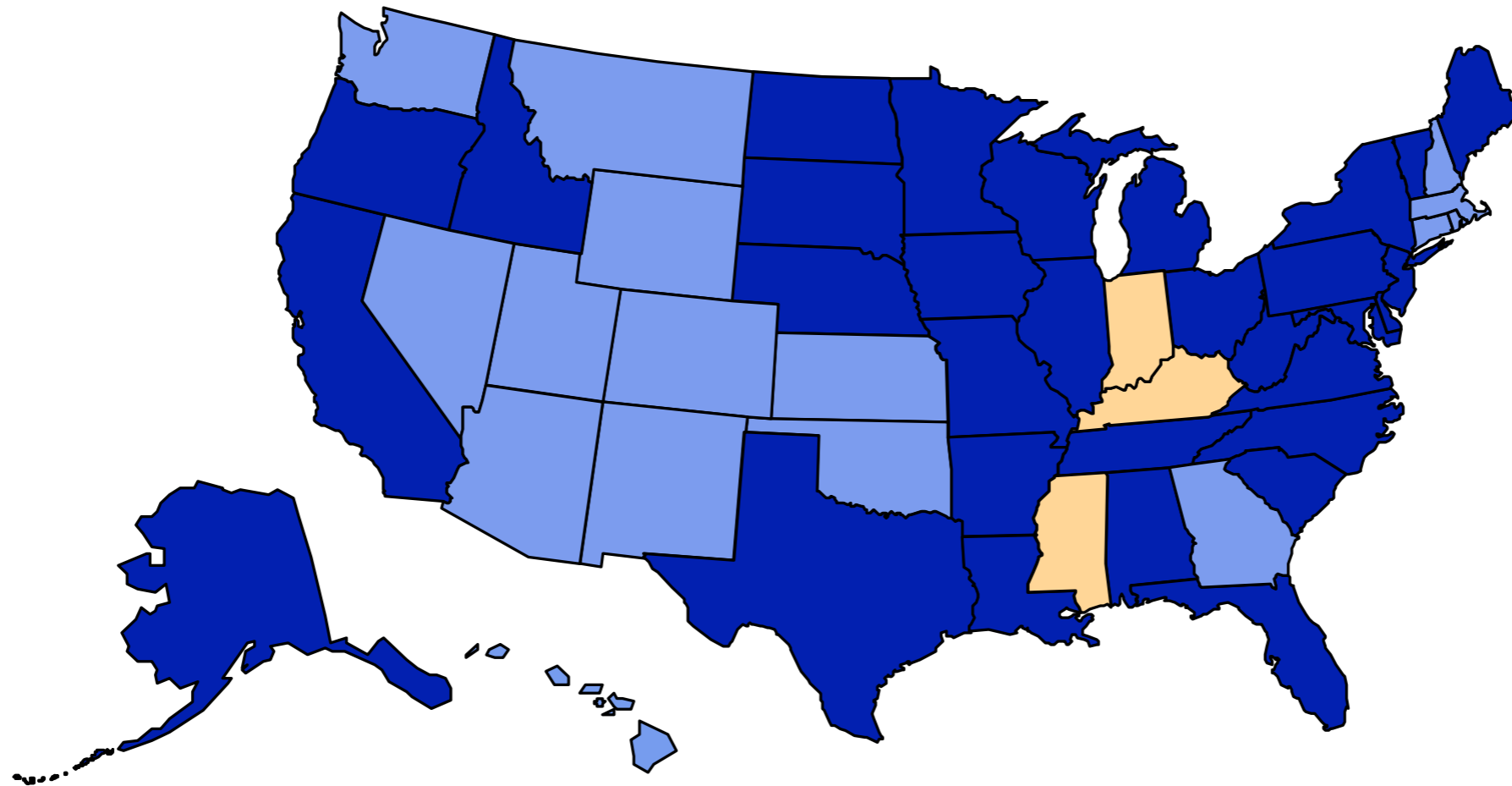




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1997

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

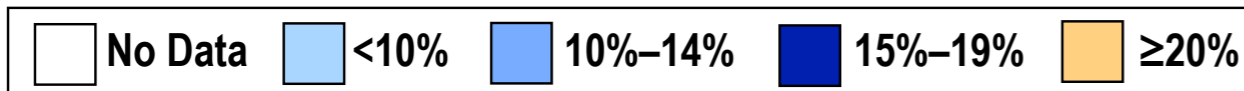
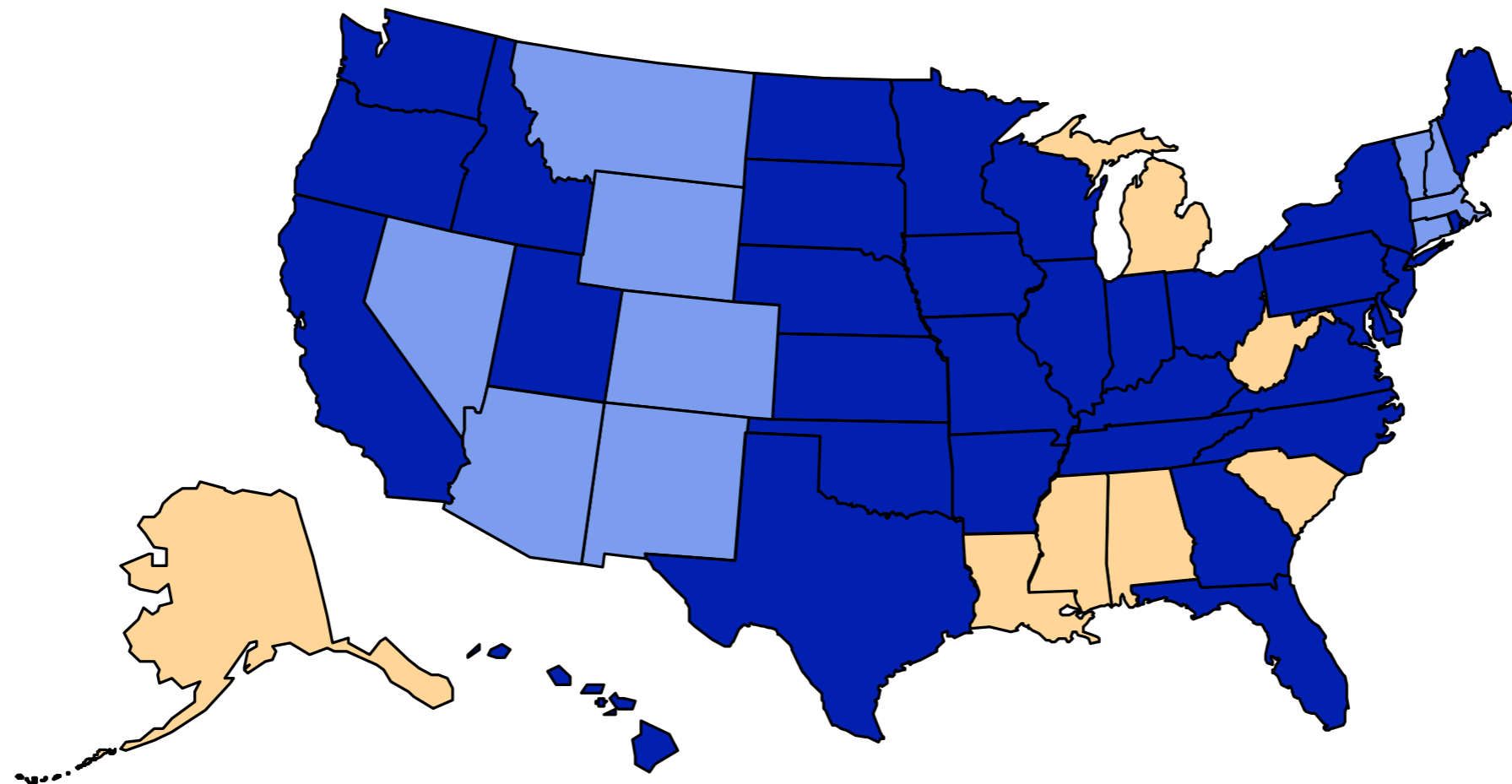




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1998

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

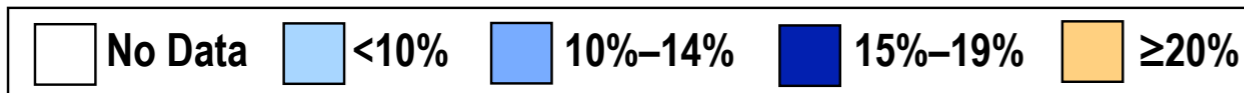
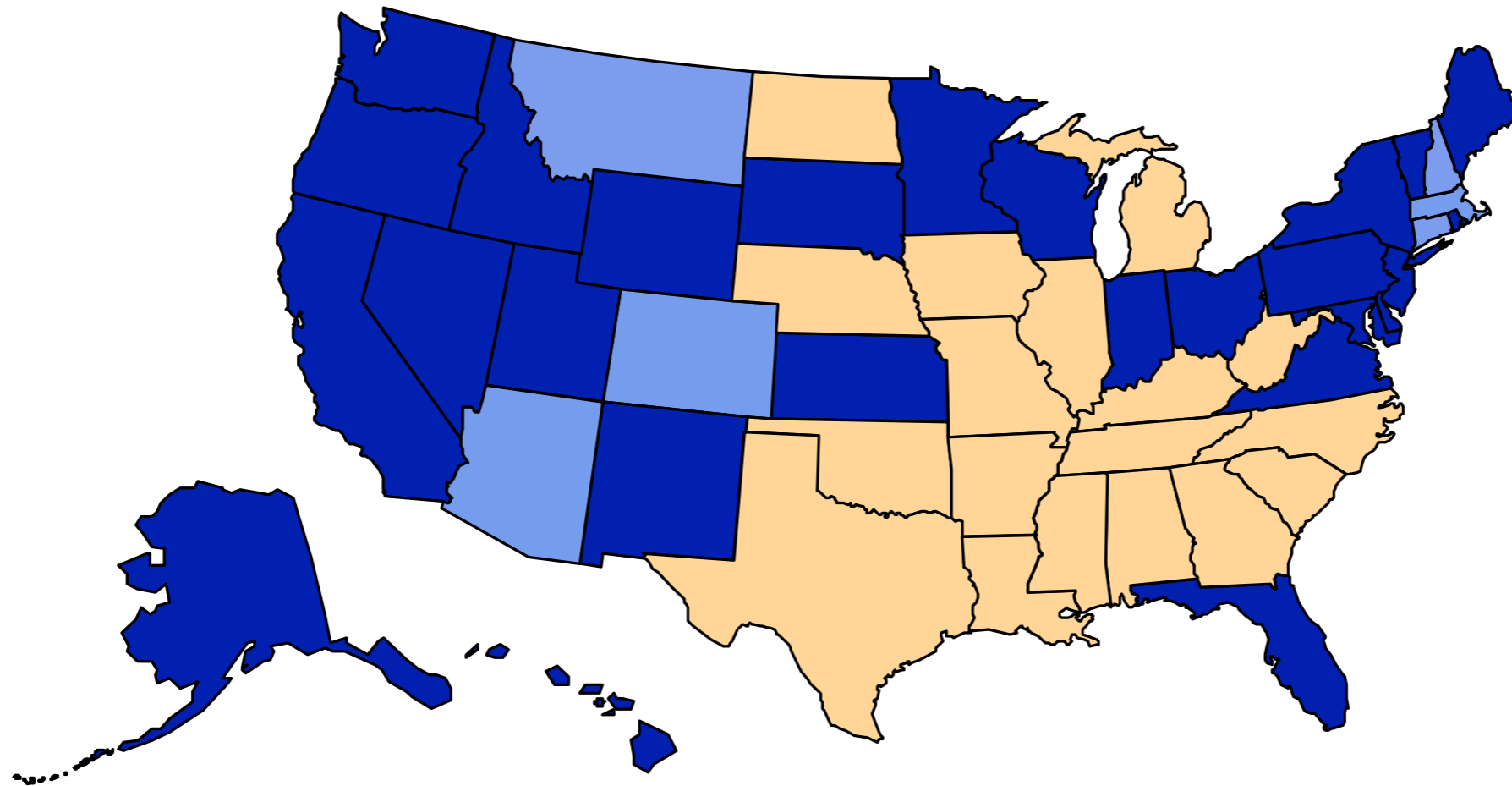




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 1999

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

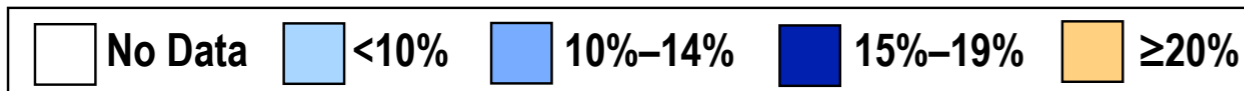
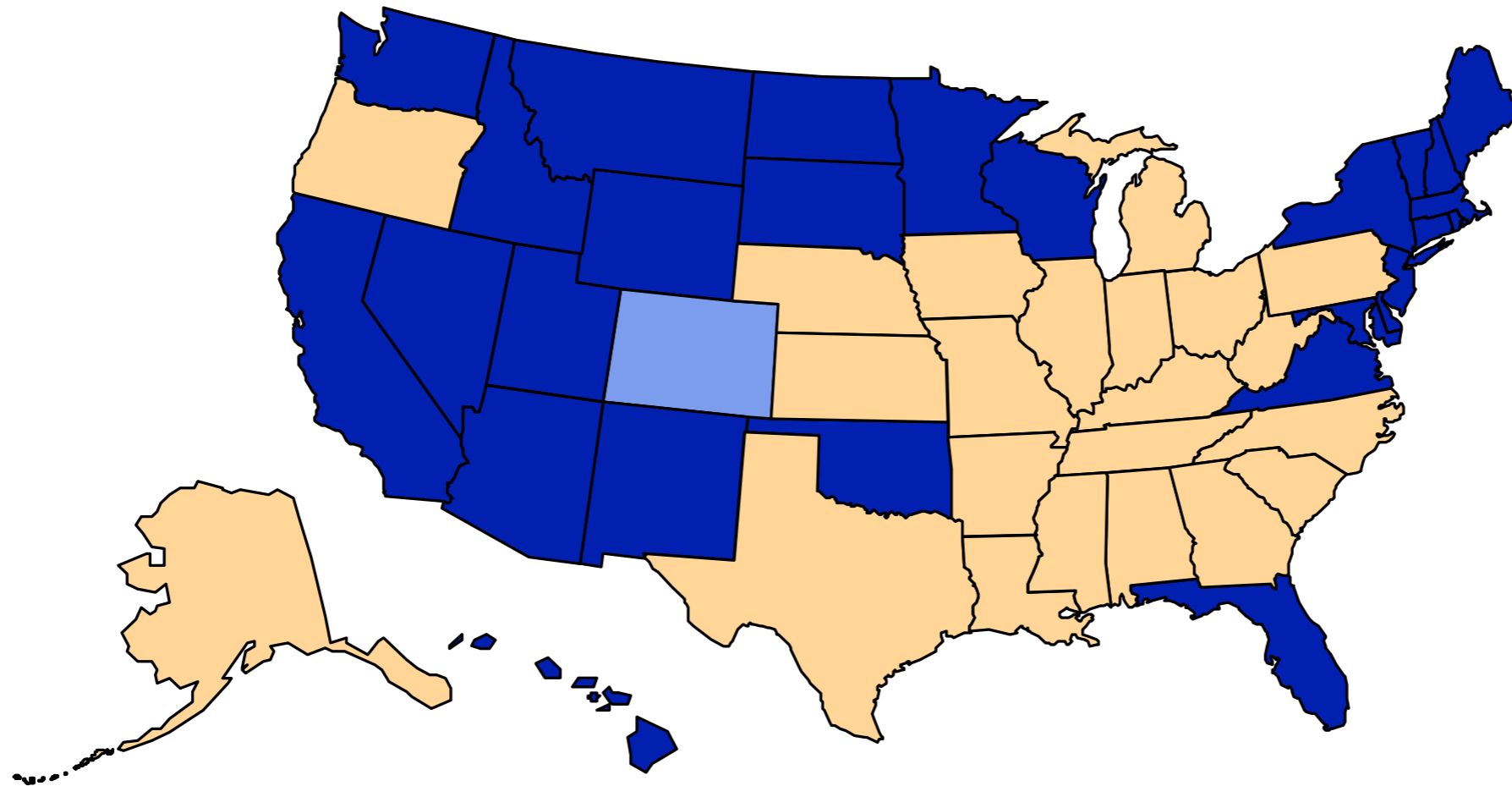




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2000

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

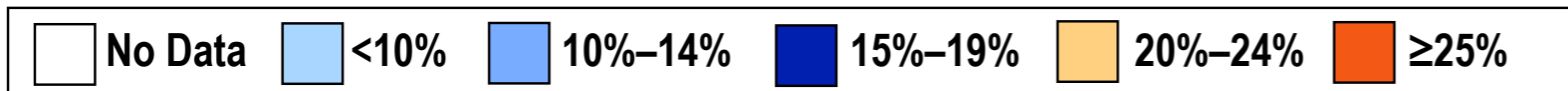
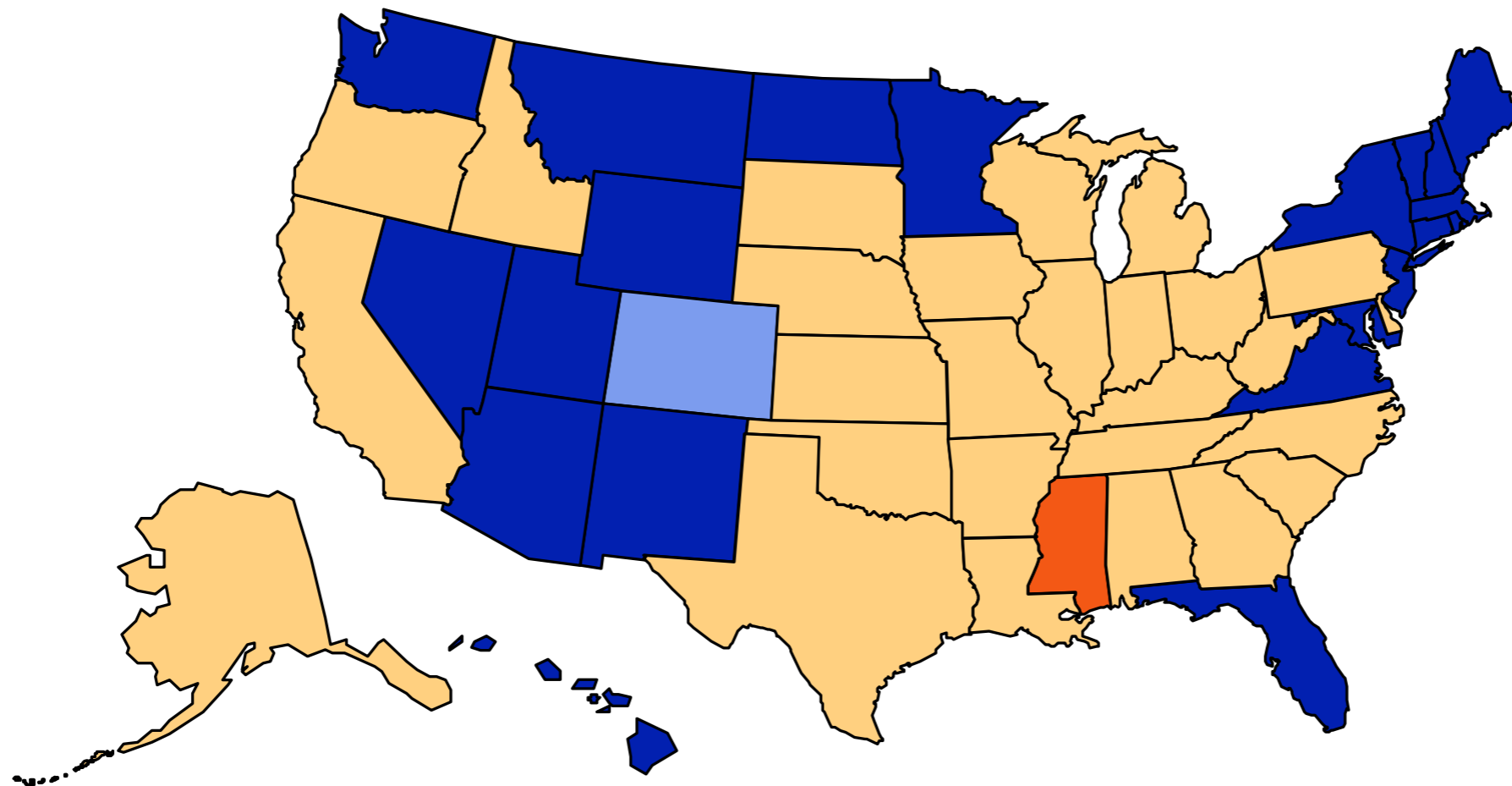




Obesitas evolutie

Obesity Trends* Among U.S. Adults **BRFSS, 2001**

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

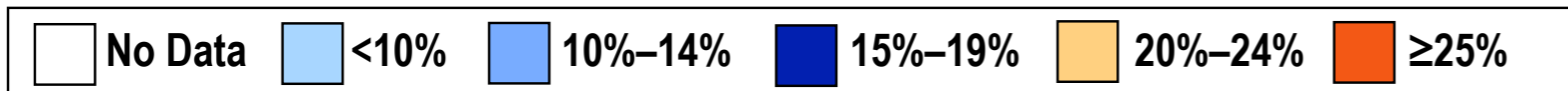
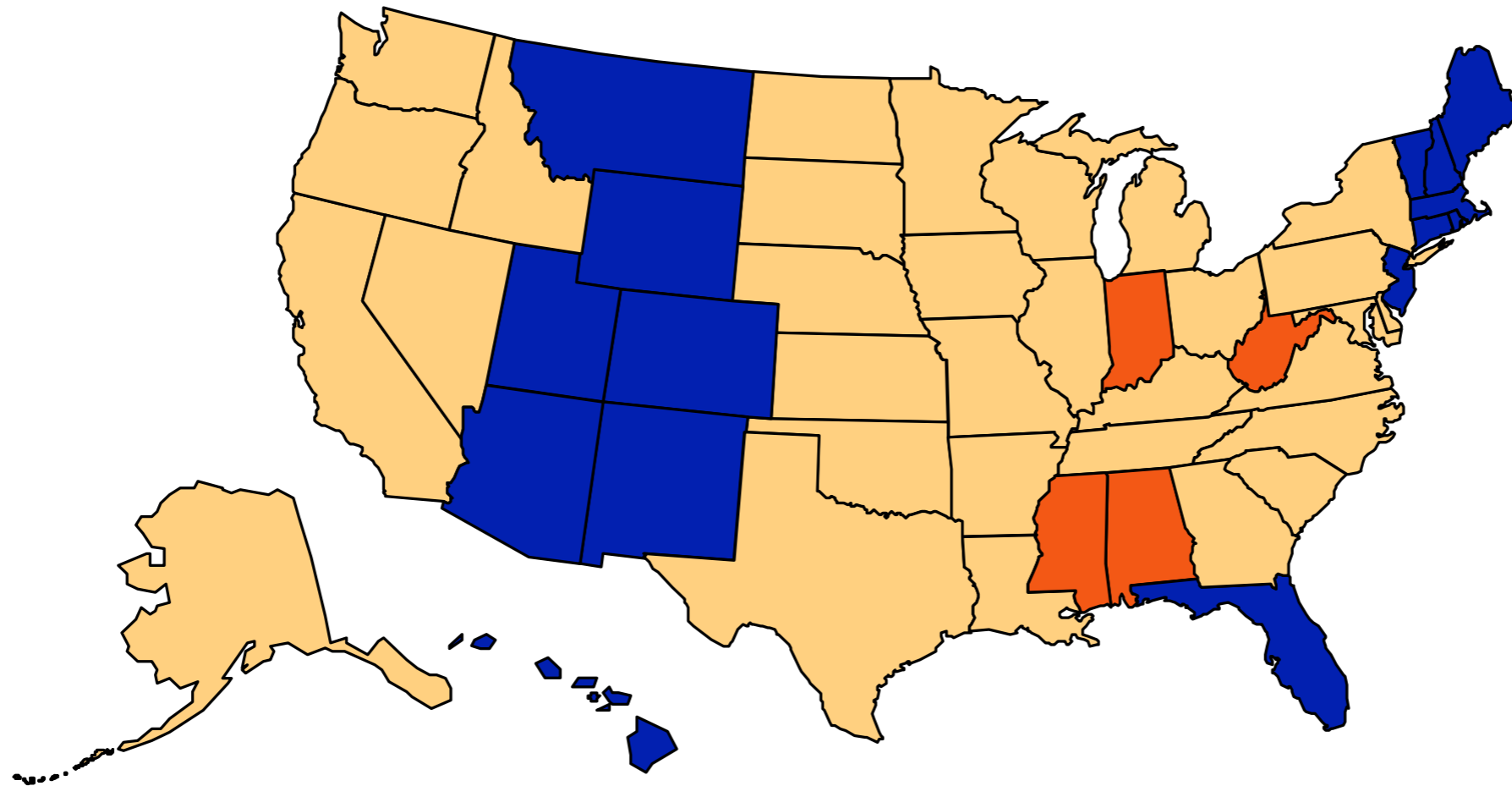




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2003

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

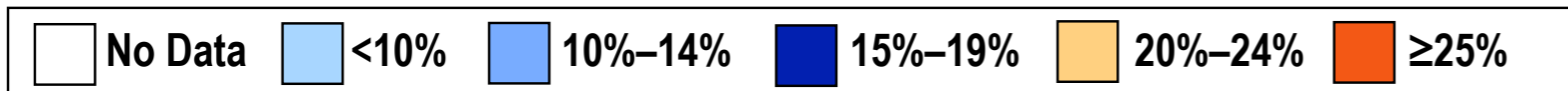
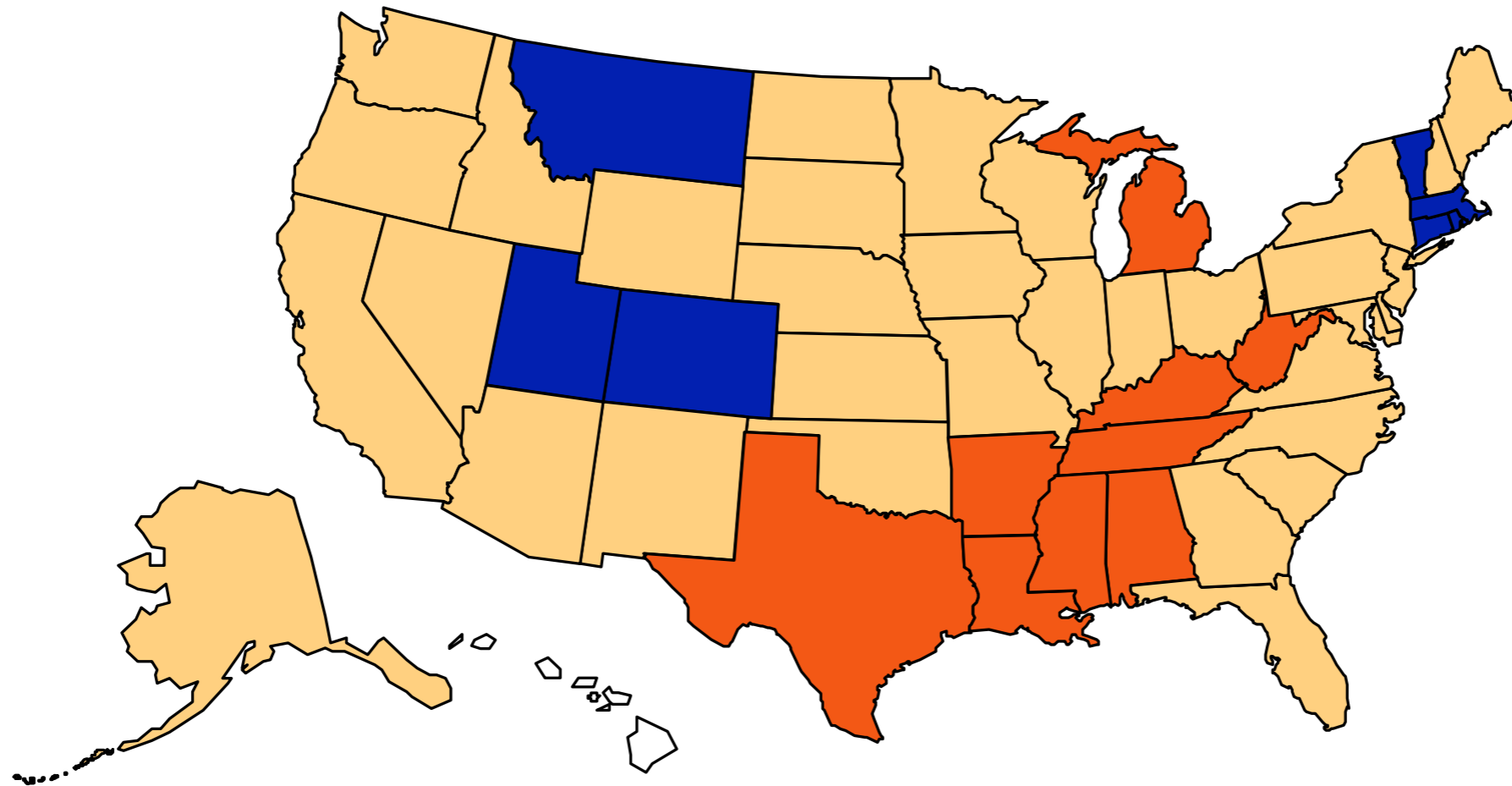




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2004

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

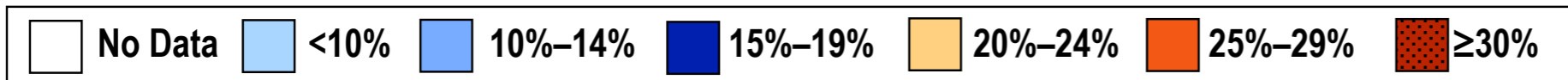
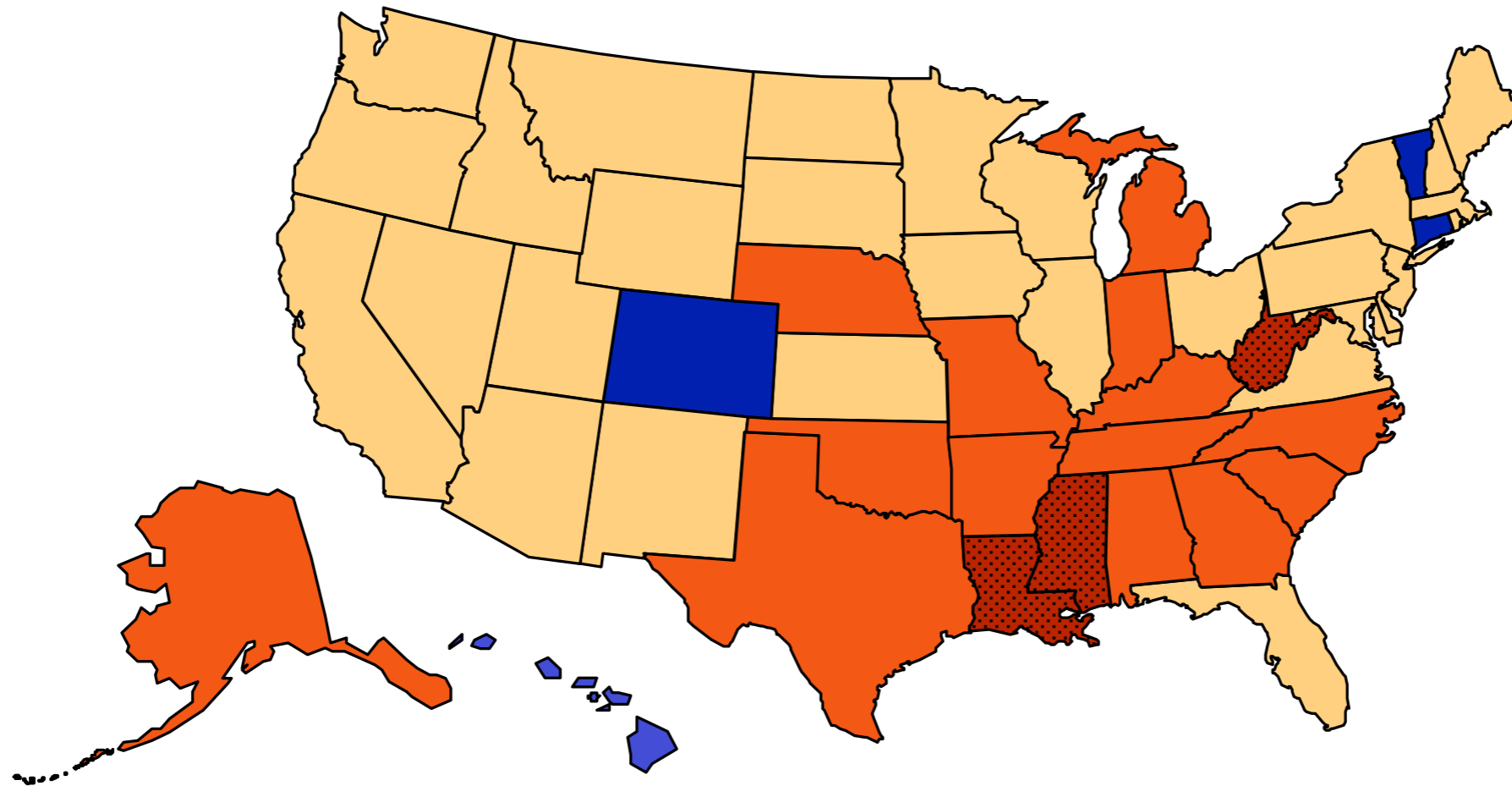




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2005

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

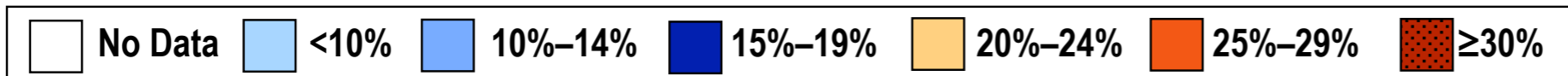
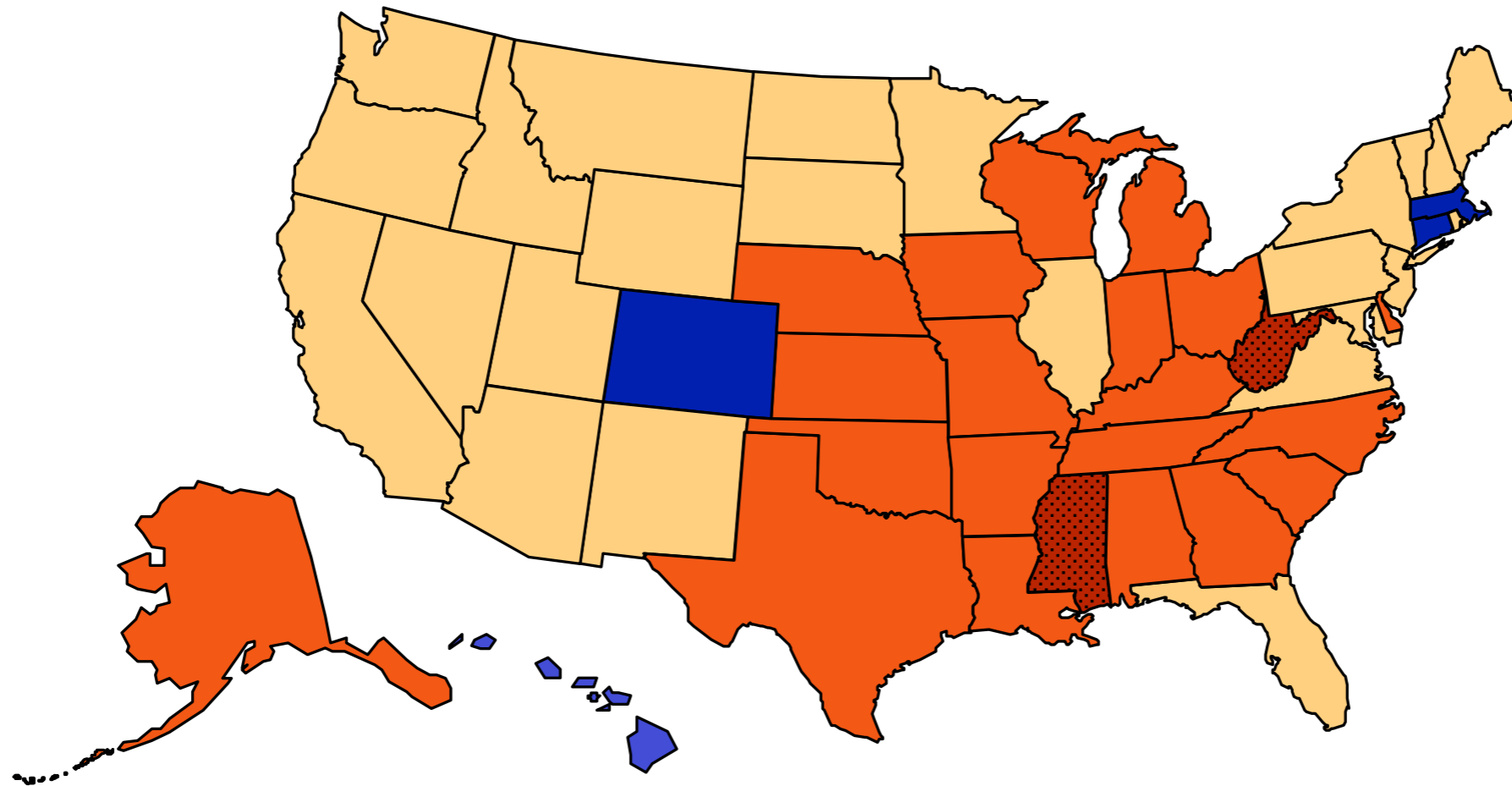




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2006

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

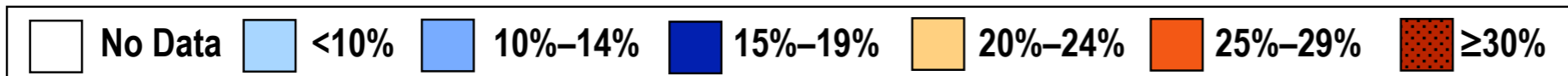
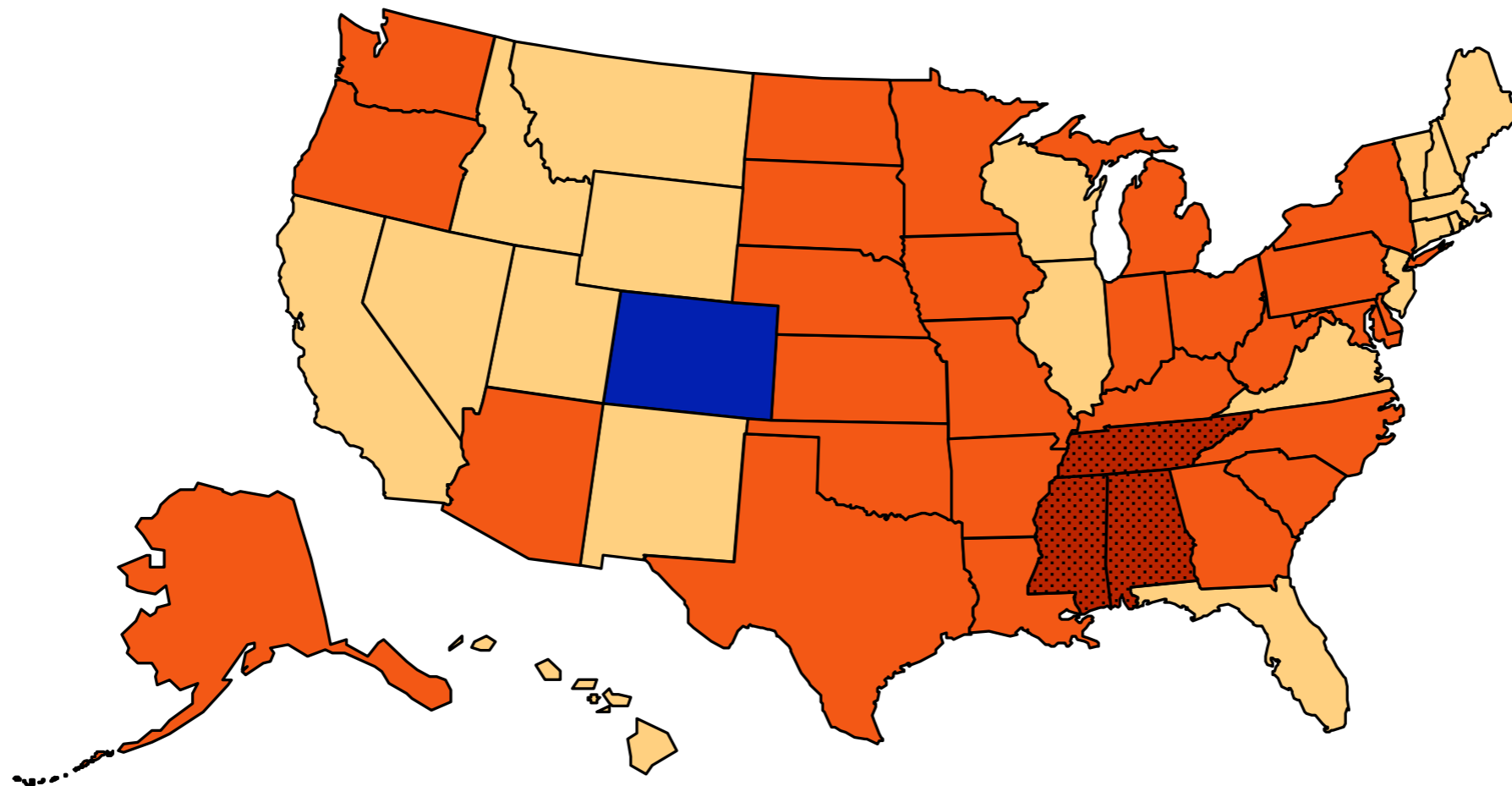




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2007

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

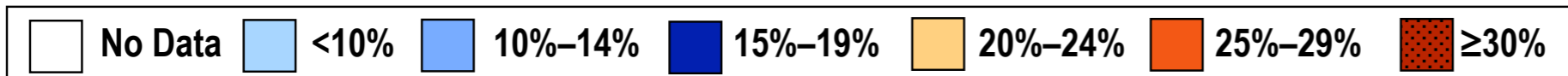
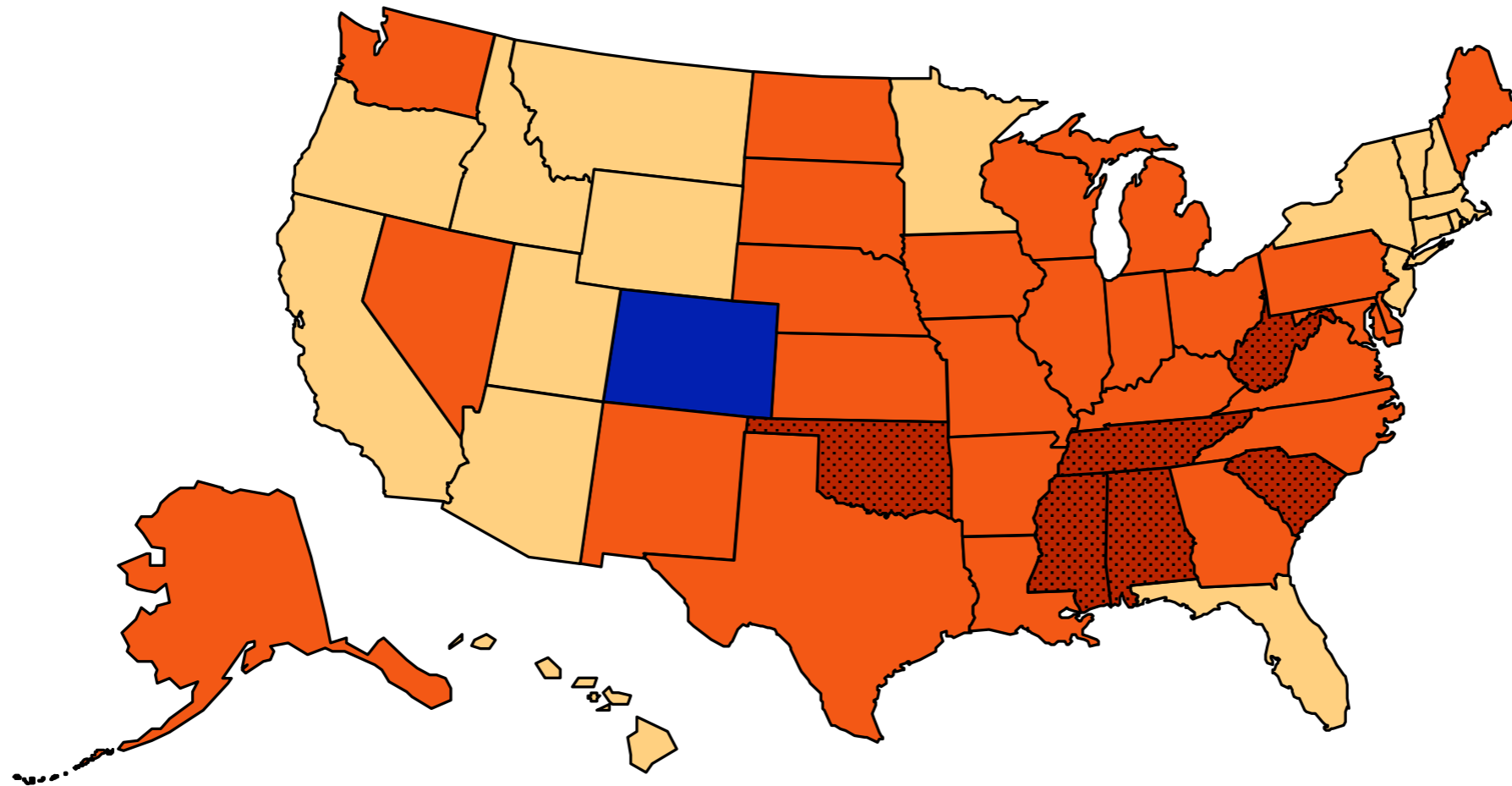




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2008

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.

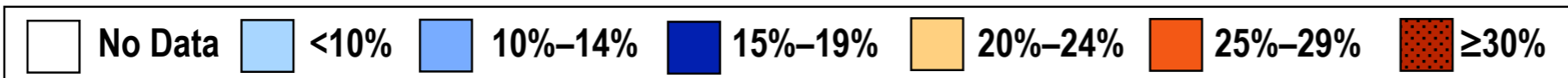
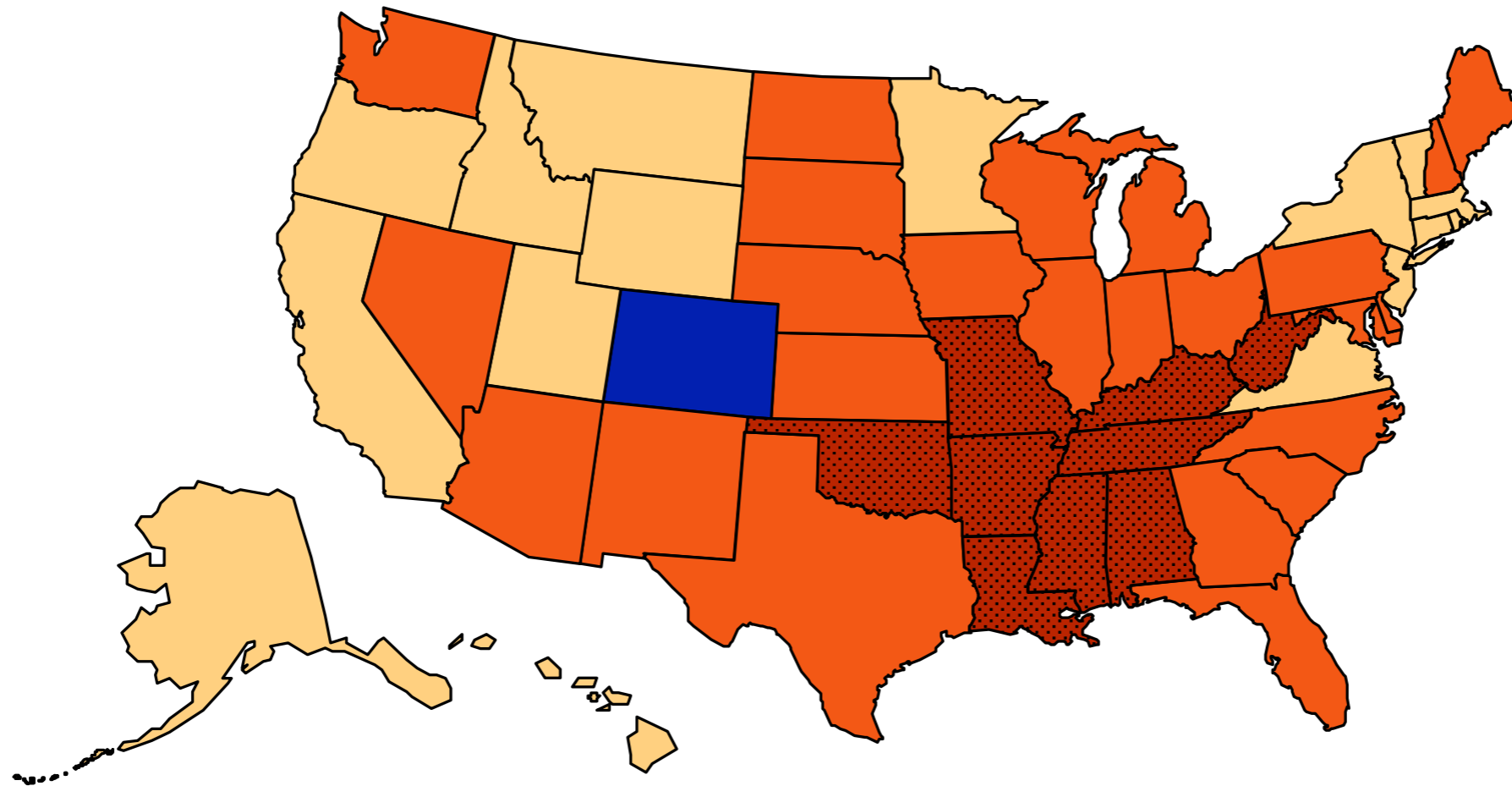




Obesitas evolutie

Obesity Trends* Among U.S. Adults BRFSS, 2009

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



Source: Behavioral Risk Factor Surveillance System, CDC.





Max, geboren september 2005

36





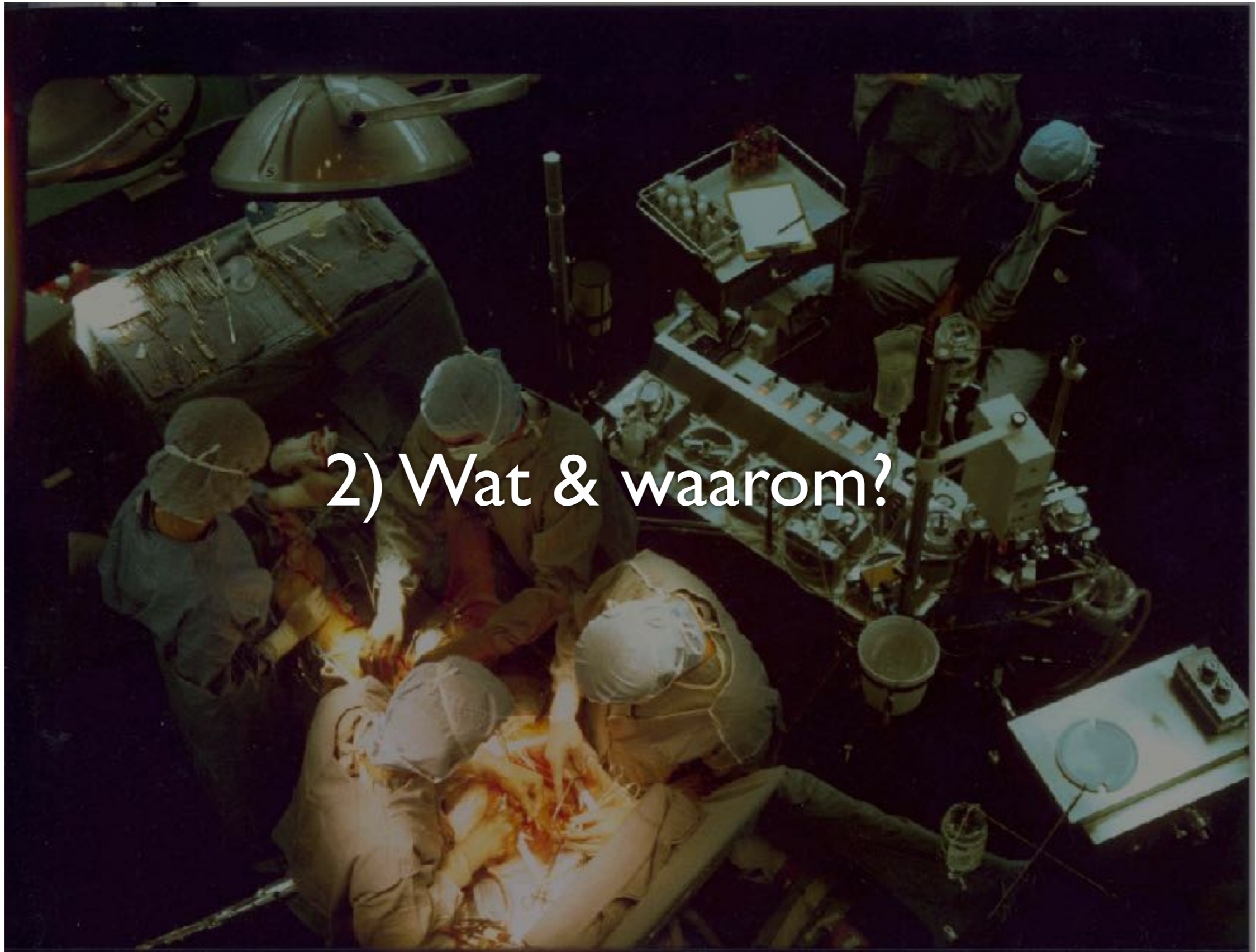
Max, geboren september 2005

37



Max, zoals elk kind geboren na 2000, heeft een “lifetime risk” voor ontwikkeling van diabetes van 33% (39% voor meisjes)

In zijn klasje van 24 kinderen, zullen er 9 suikerziekte krijgen.

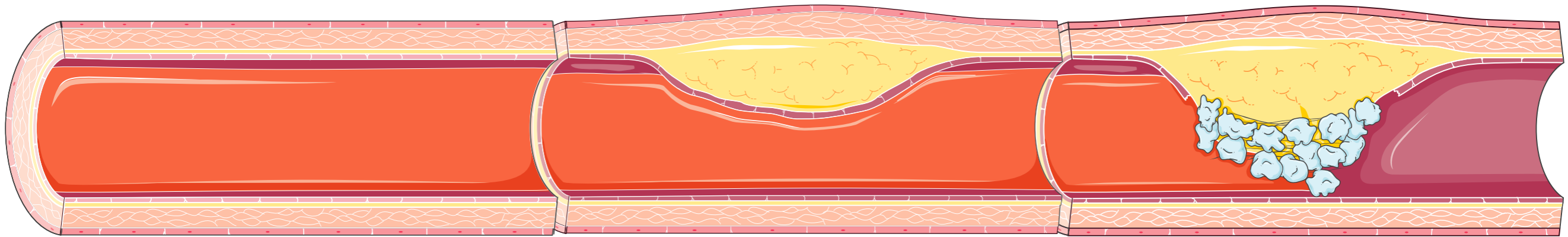


2) Wat & waarom?

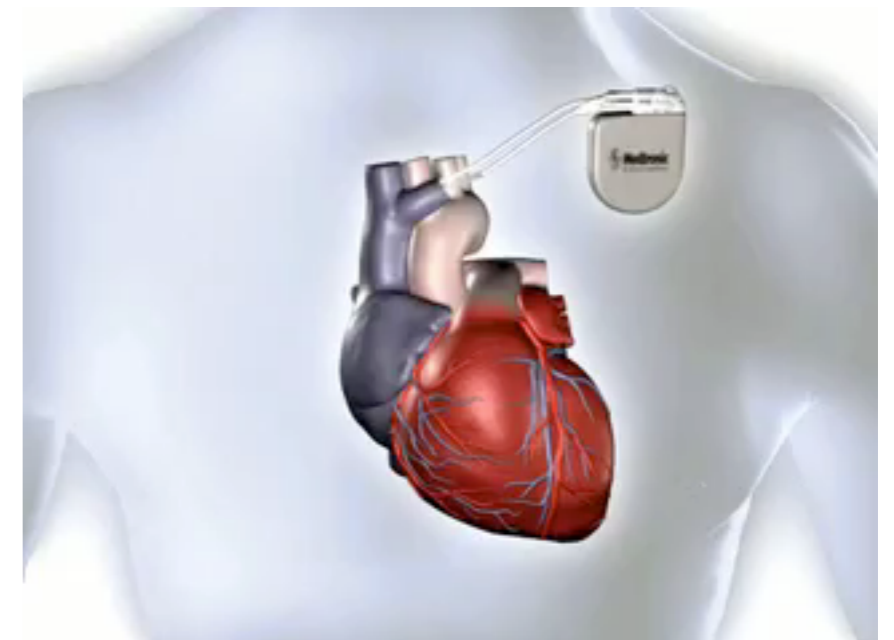


Wat zijn HVZ

1) slagaderverkalking



2) ritmestoornissen





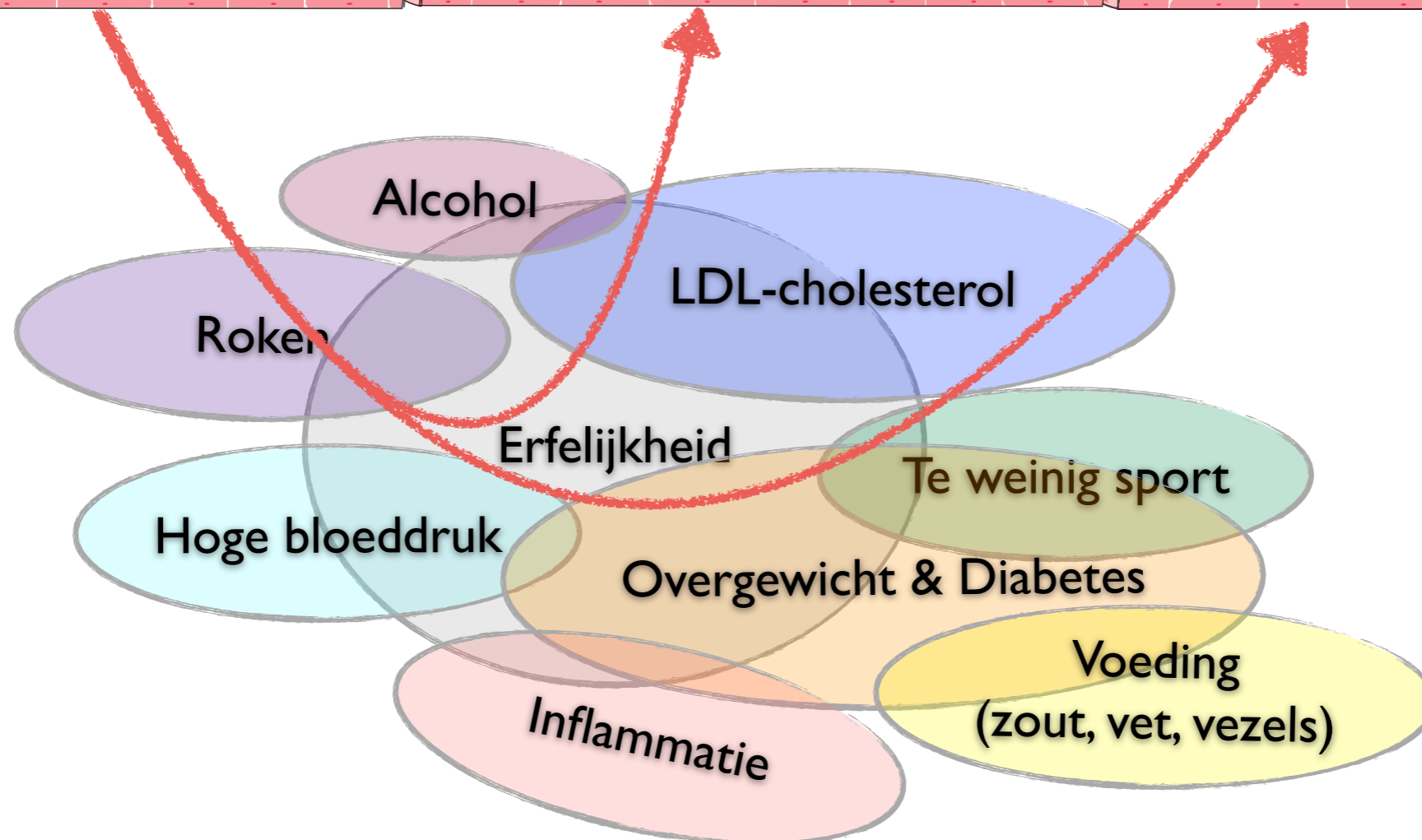
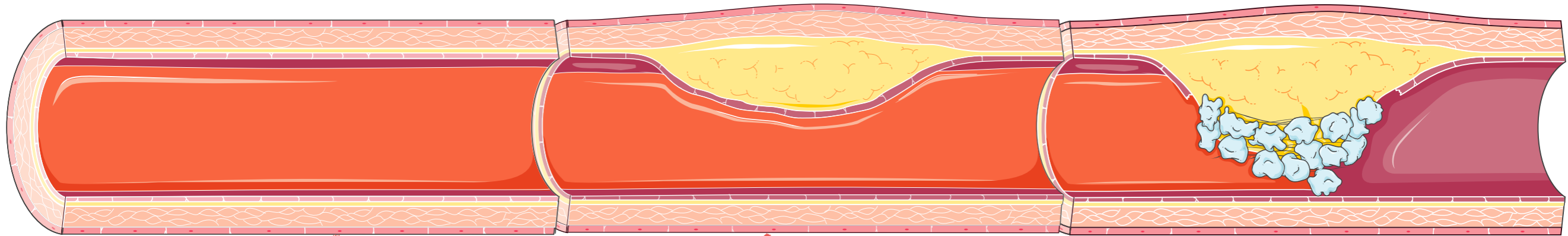
Normale slagader

“Plaque” / slagaderverkalking

De gecombineerde invloed van de risicofactoren leidt tot slagaderverkalking. Slagaderverkalking op zich geeft GEEN klachten!

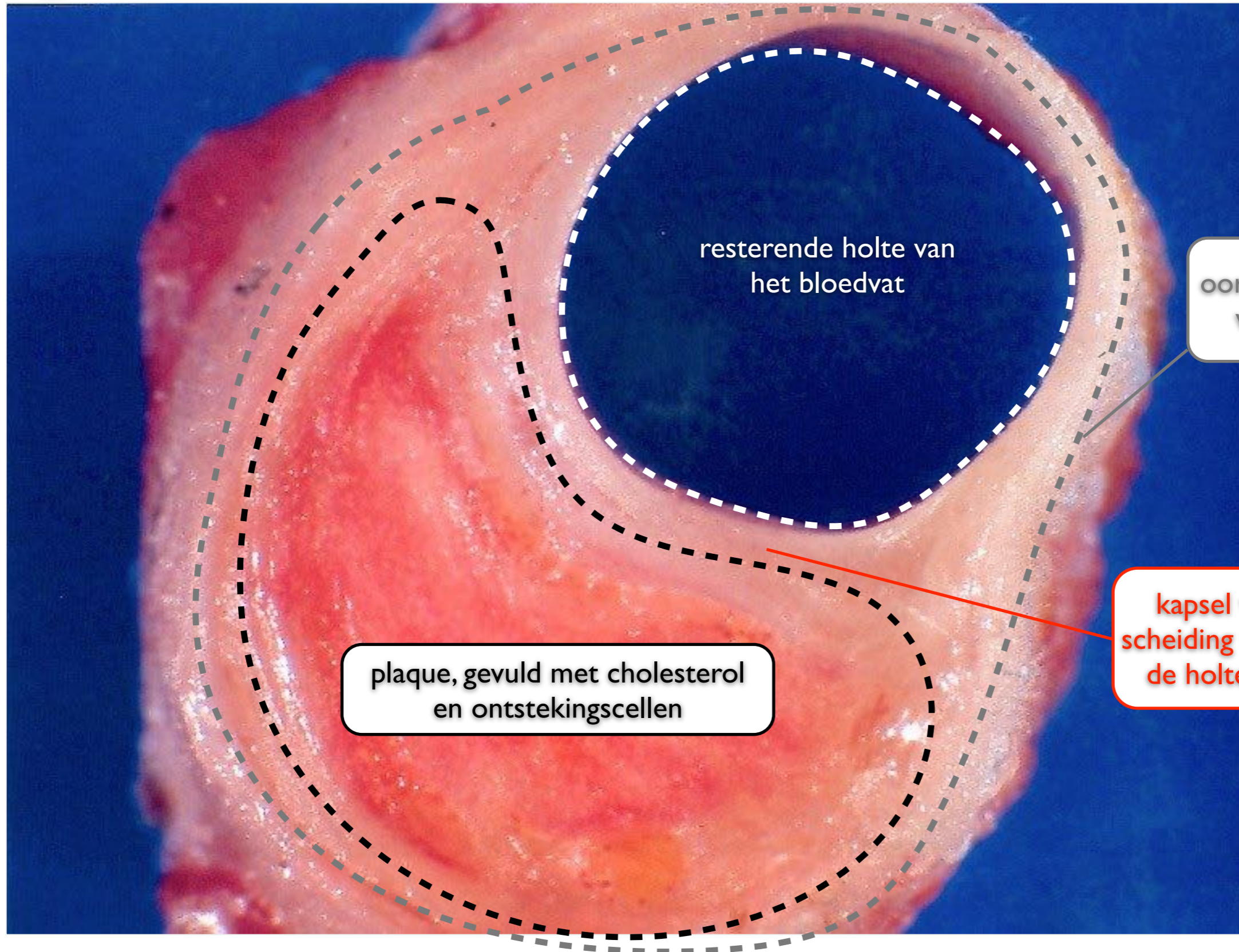
“Thrombus” / klonters

Op een plaque kan zich plots en onvoorspelbaar een klonters vormen die de slagader afsluit. Dit leidt dan tot een infarct, een plots overlijden of een beroerte (hersenen).





Slagaderverkalking



resterende holte van
het bloedvat

oorspronkelijke wand
van dit bloedvat

plaque, gevuld met cholesterol
en ontstekingscellen

kapsel van de plaque, de
scheiding tussen de plaque en
de holte van het bloedvat



De gevolgen van slagaderverkalking

Beroerte

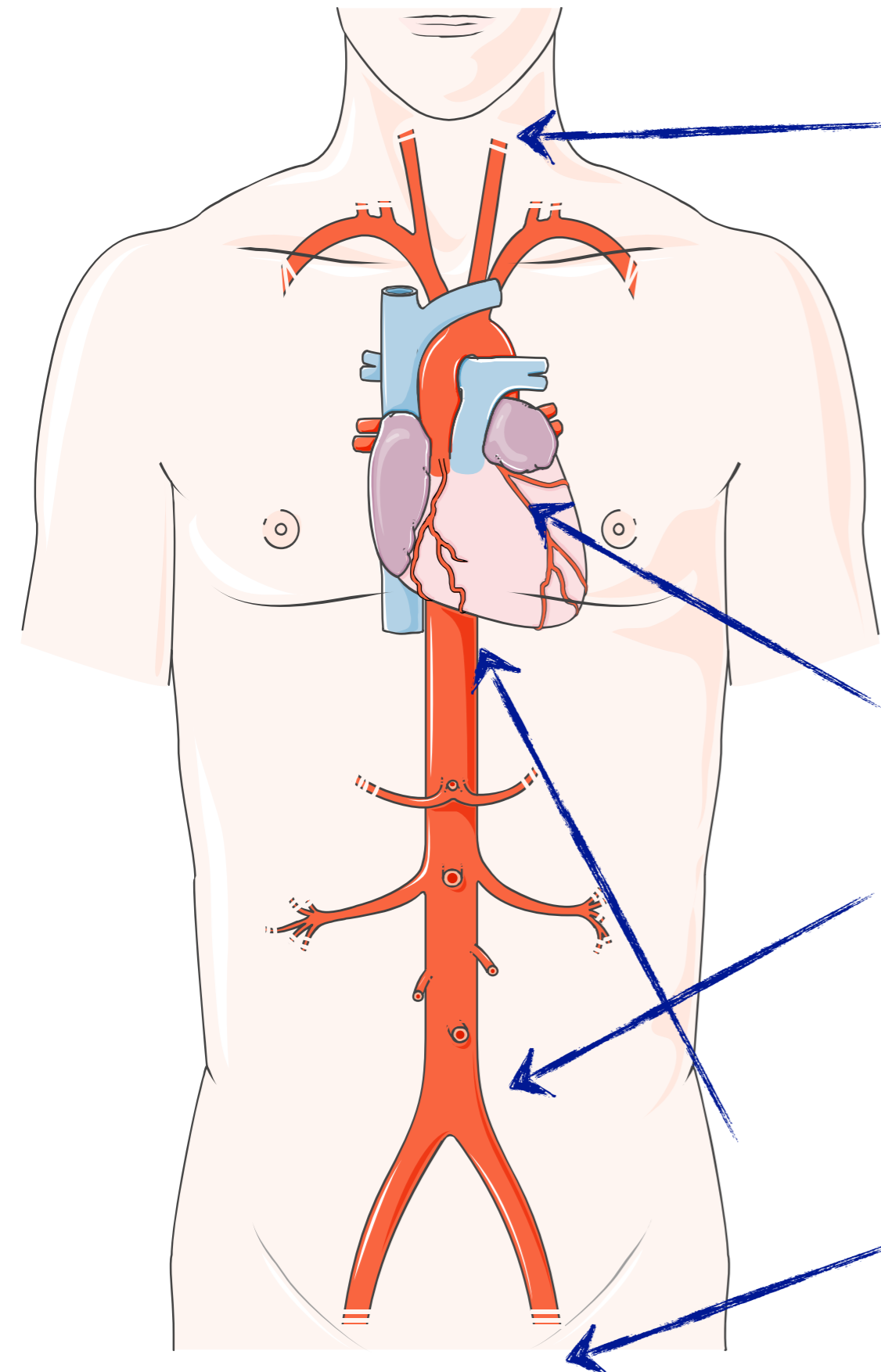
Hartinfarct

Aneurysma

Perifeer vaatlijden

Plotse dood

Hartfalen





Waarom krijgen we HVZ?

43

De natuur investeert niet in veroudering !





Waarom krijgen we HVZ?

44

(Over)gewicht is een voordeel op jonge leeftijd





Waarom krijgen we HVZ?

45

Hoge bloeddruk & agressieve bloedstolling idem





Waarom krijgen we HVZ?

46

De natuur investeert niet in veroudering van het individu enkel in de overleving van de soort!

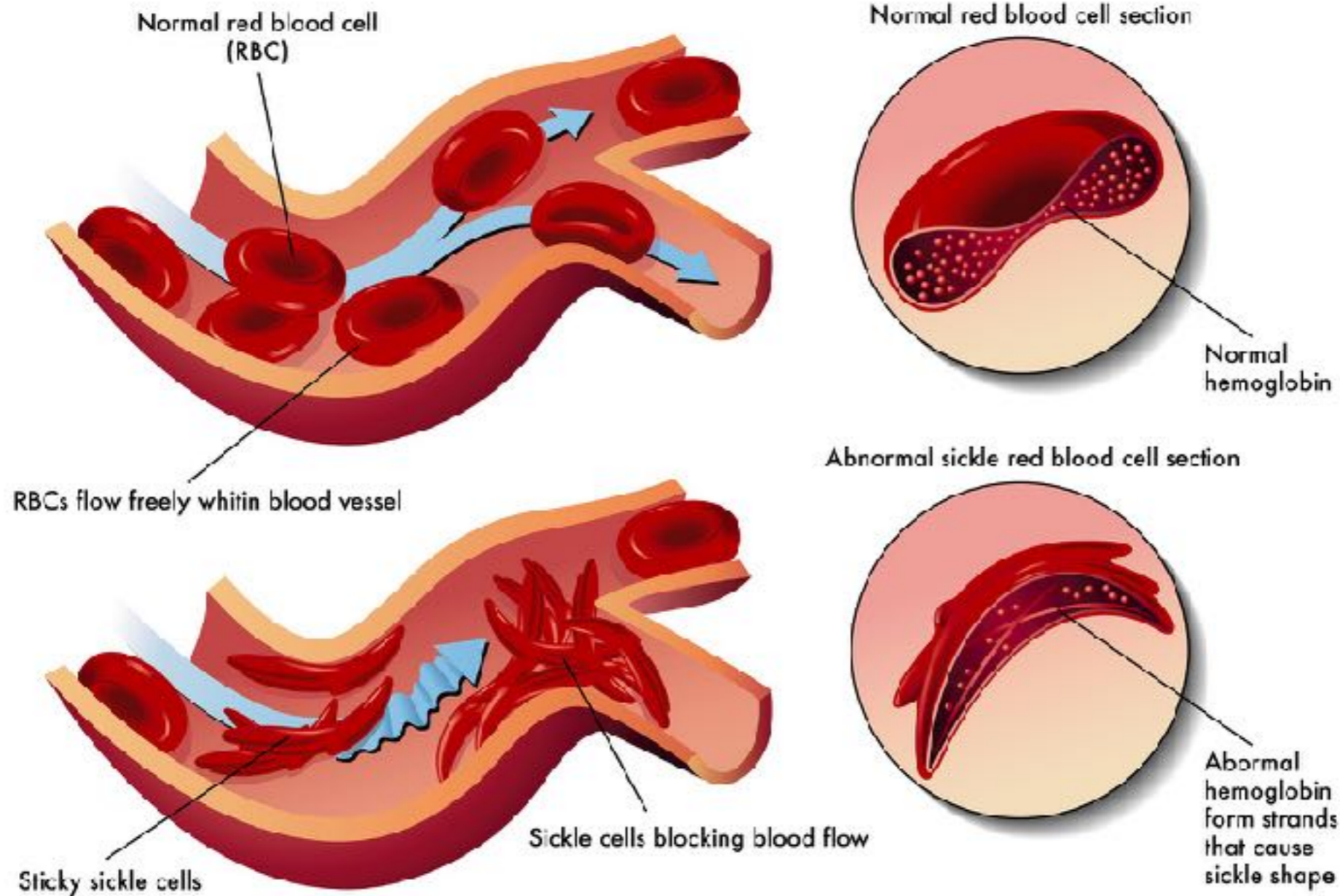
Sinds miljoenen jaren selectie van eigenschappen die de kans op het bereiken van de voortplantingsleeftijd verbeteren:

- *capaciteit om vet op te slaan en hongerperiodes te overleven*
- *een stevige bloedstolling om trauma's te overleven*
- *een vinnig reactief hart- en vaatstelsel*
- *cholesterol? (Sikkelcelanemie)*



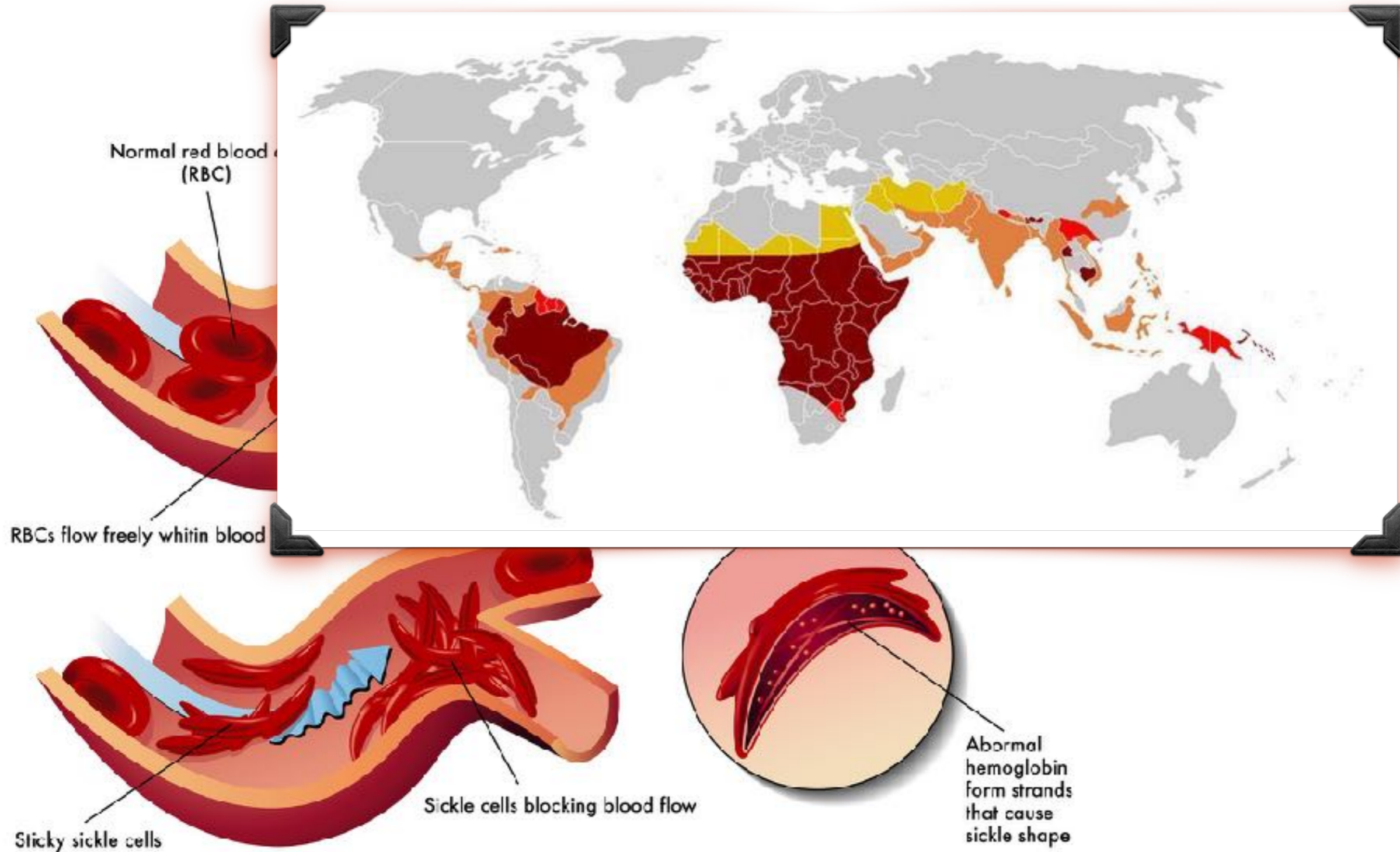
Waarom krijgen we HVZ?

Sickle-Cell Anemia



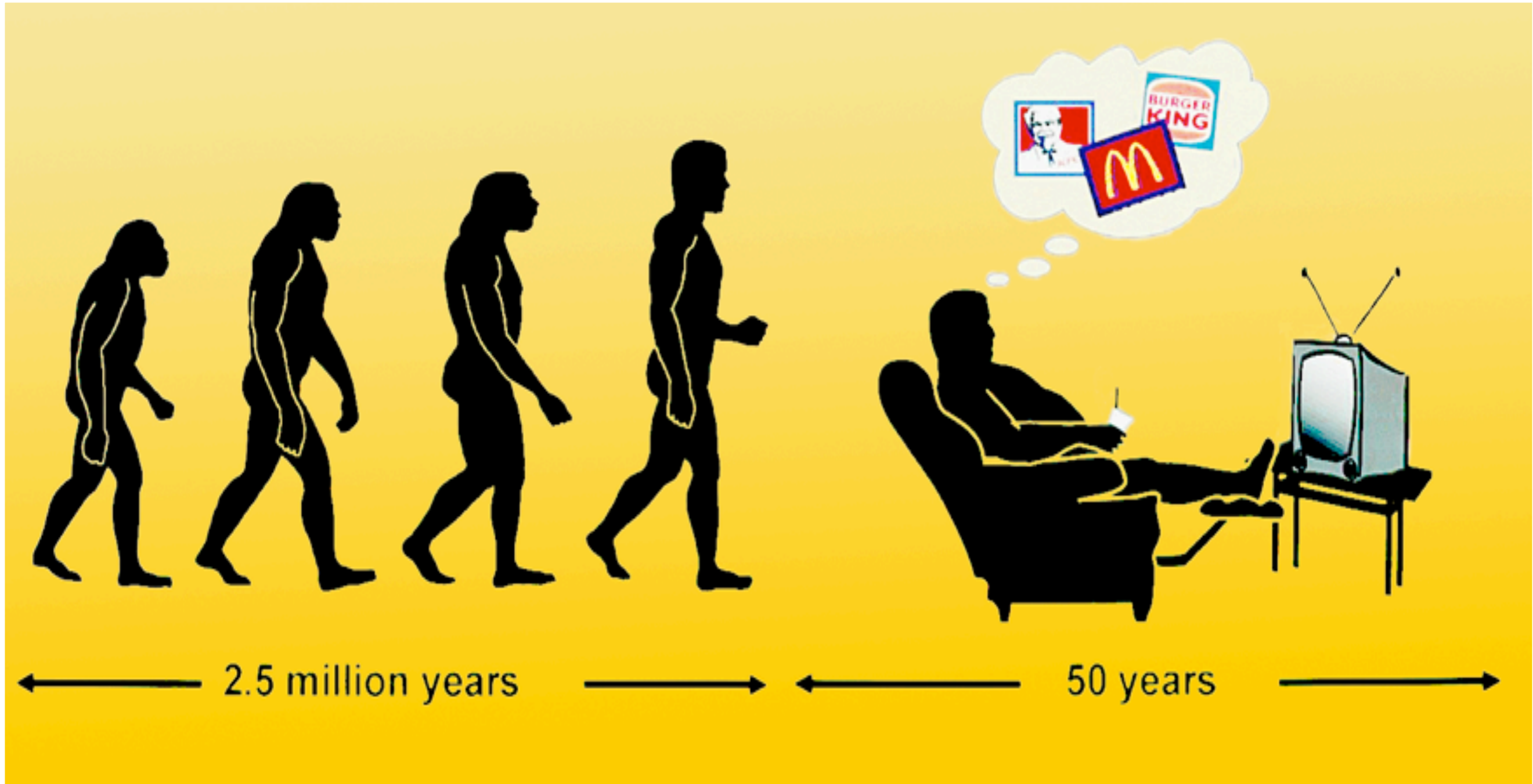


Waarom krijgen we HVZ?





Waarom krijgen we HVZ?

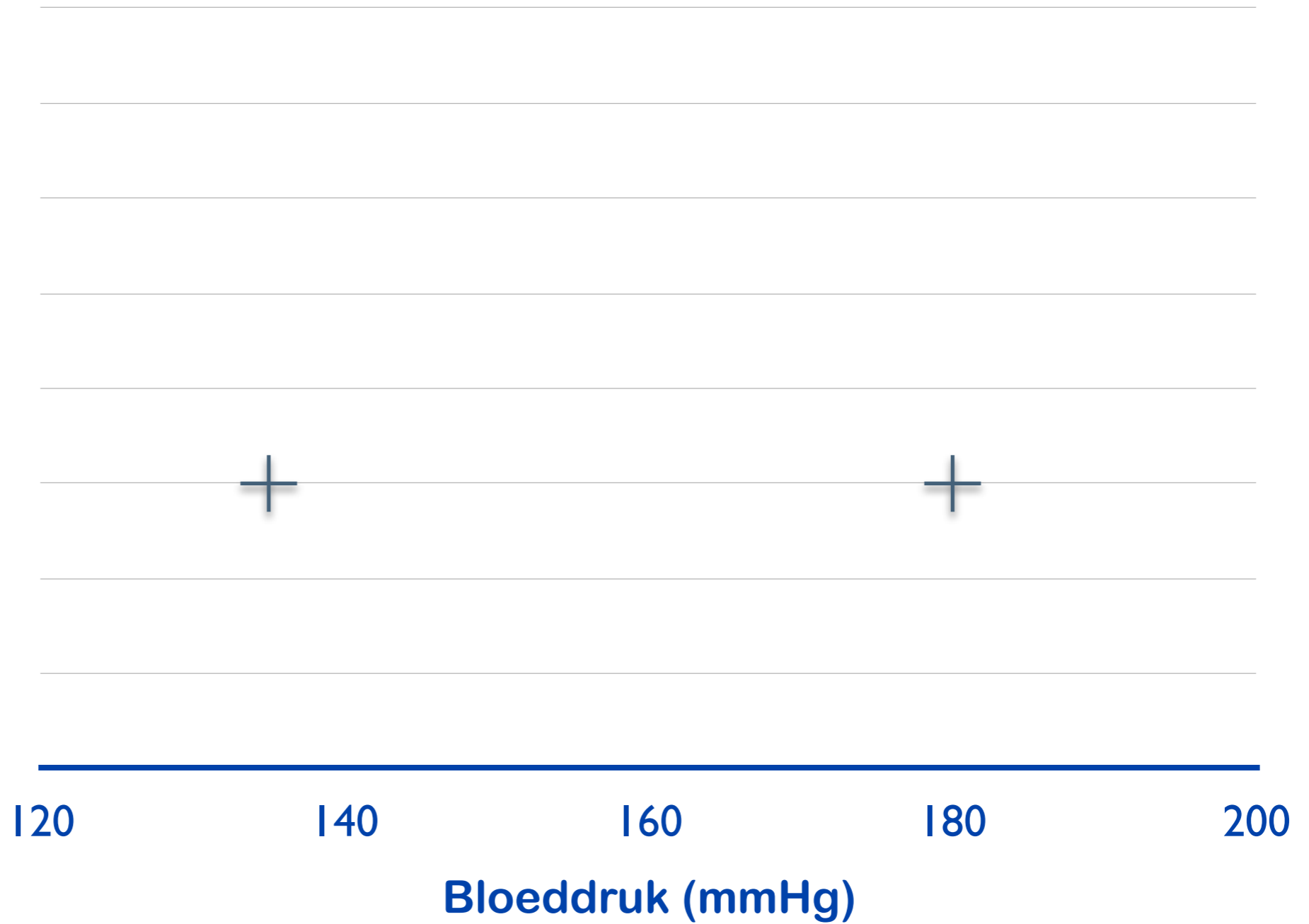




3) Strategieën?

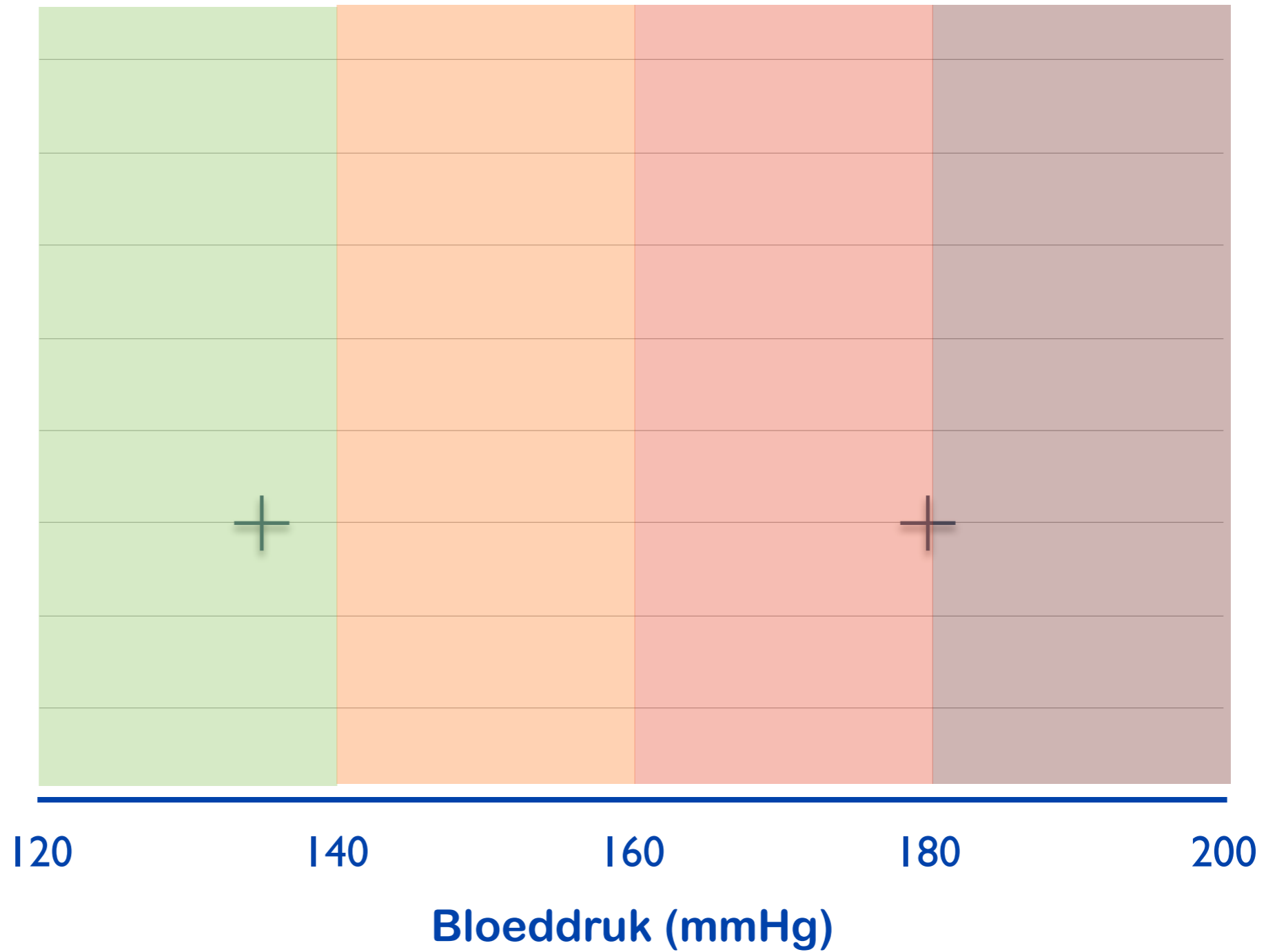


Wat is de grootste bedreiging?



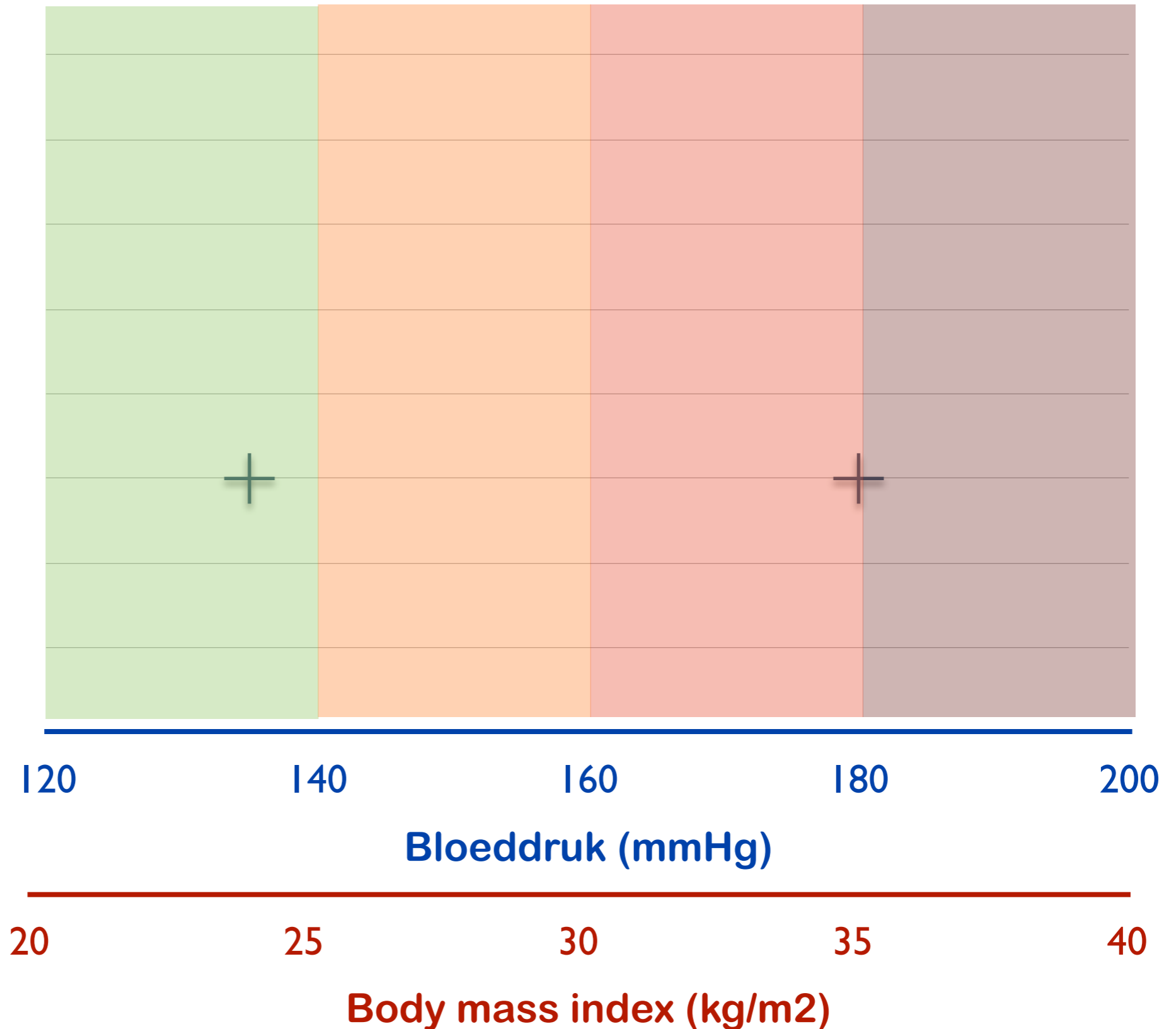


Wat is de grootste bedreiging?



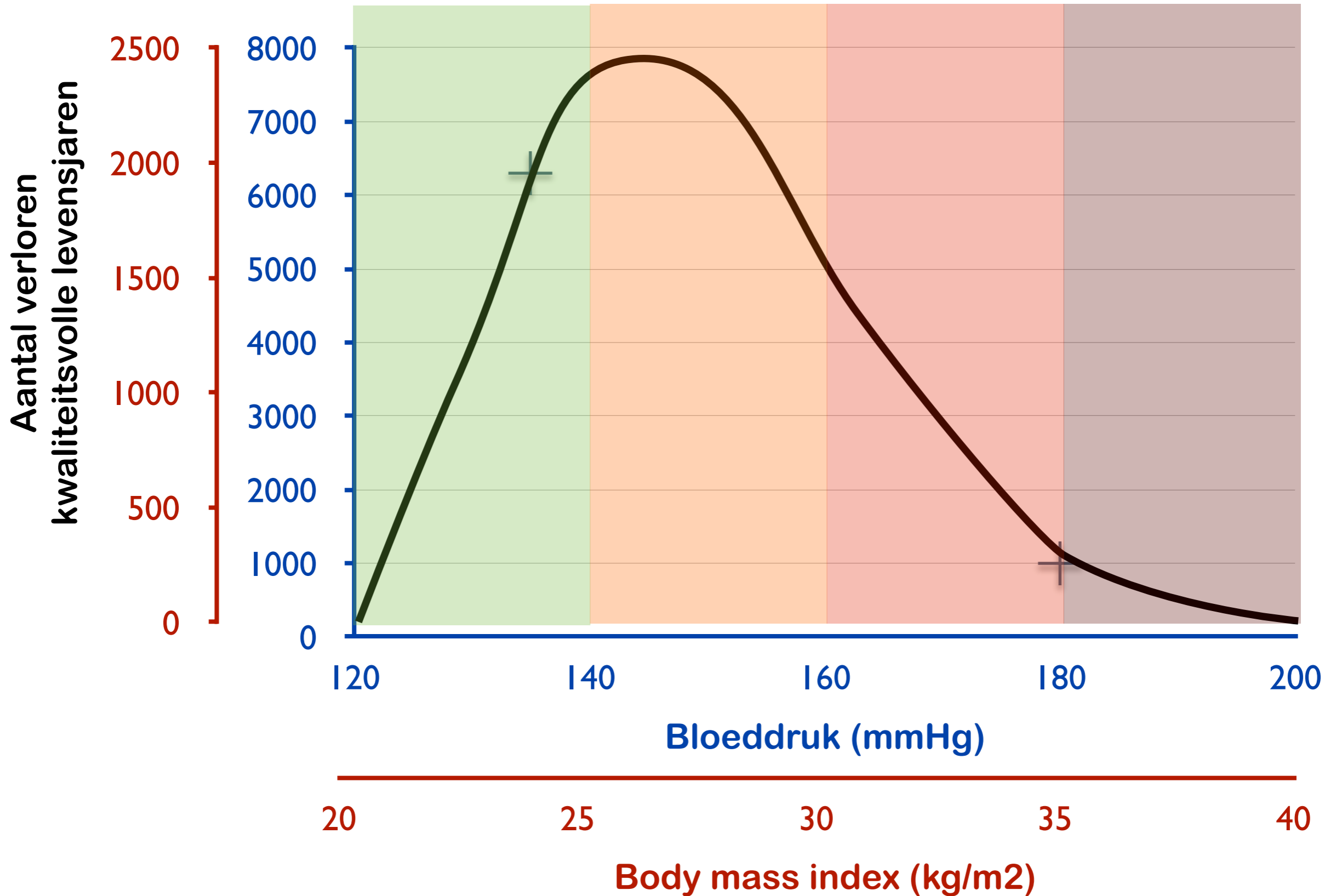


Wat is de grootste bedreiging?



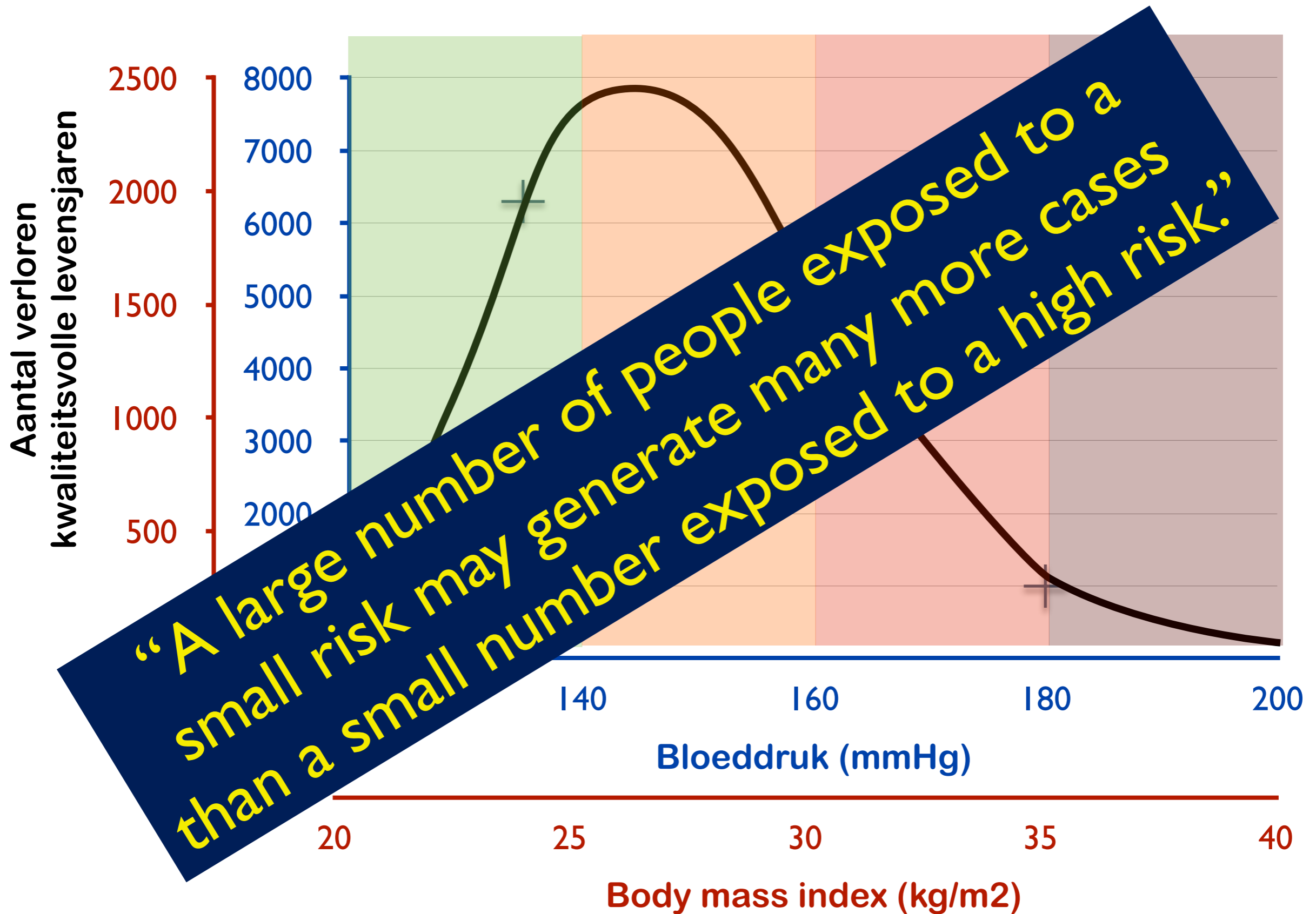


Wat is de grootste bedreiging?





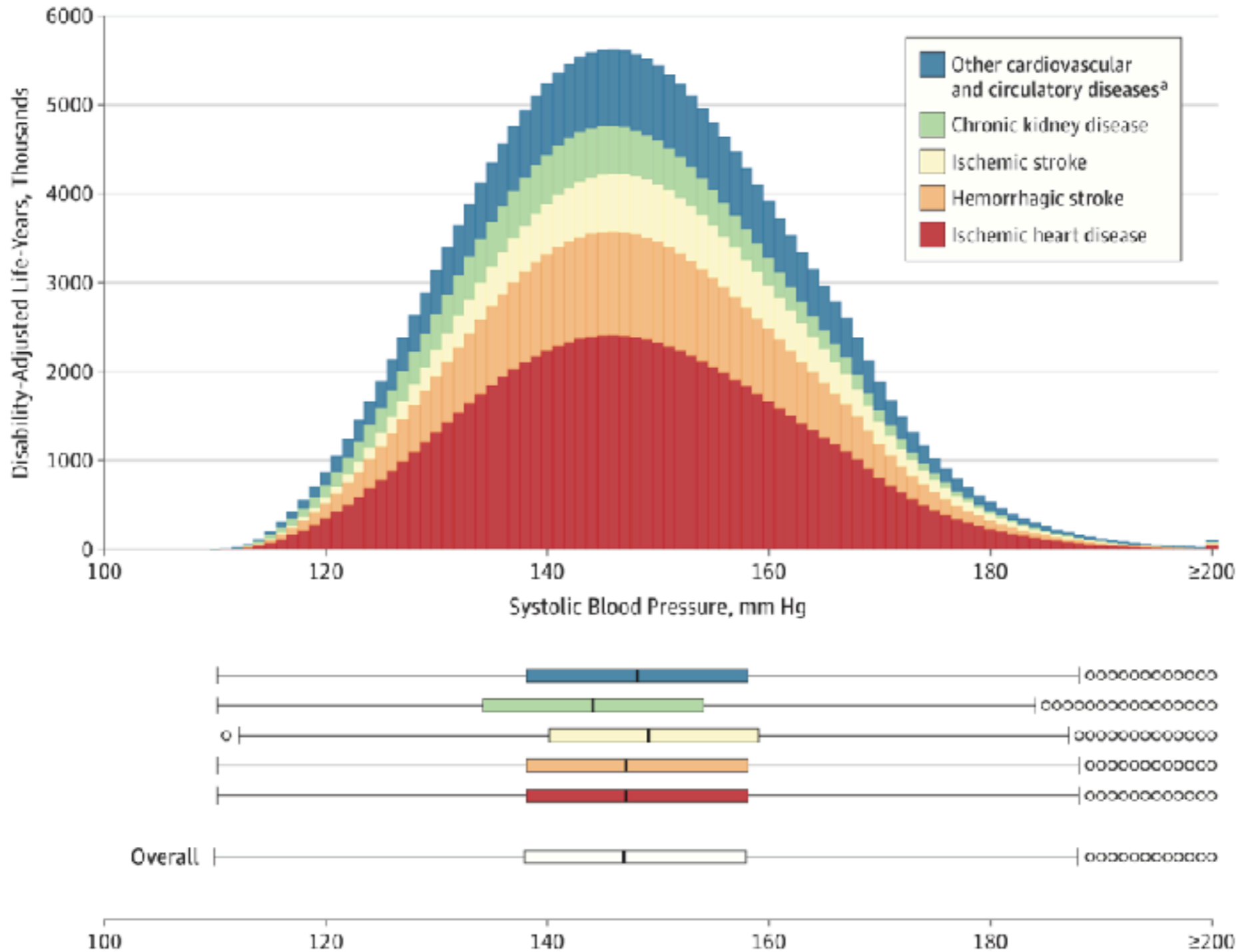
Wat is de grootste bedreiging?





Disability-Adjusted Life-Years by Systolic BP

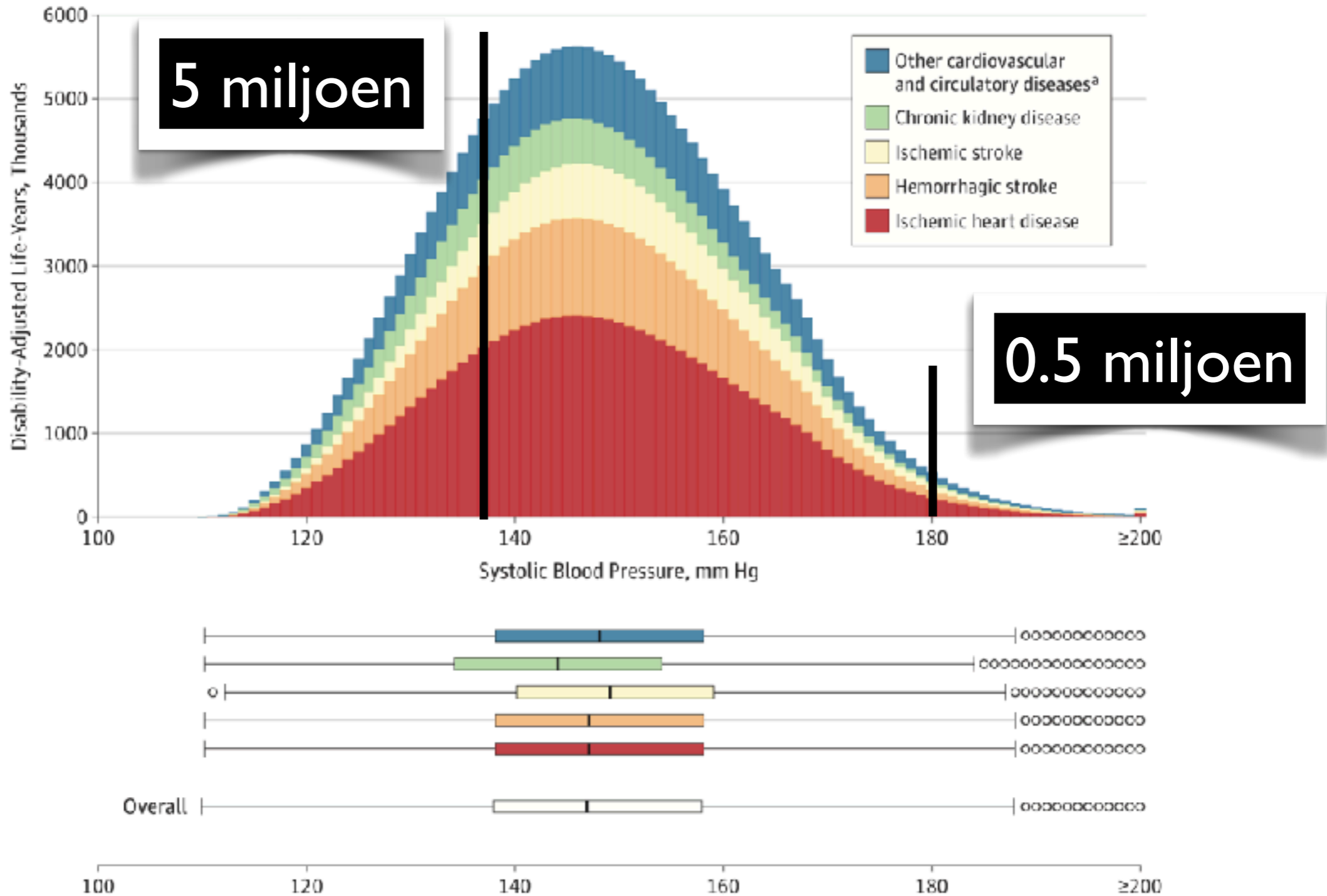
Figure 2. Projected Global Disability-Adjusted Life-Years by Systolic Blood Pressure Level and Cause, 2015





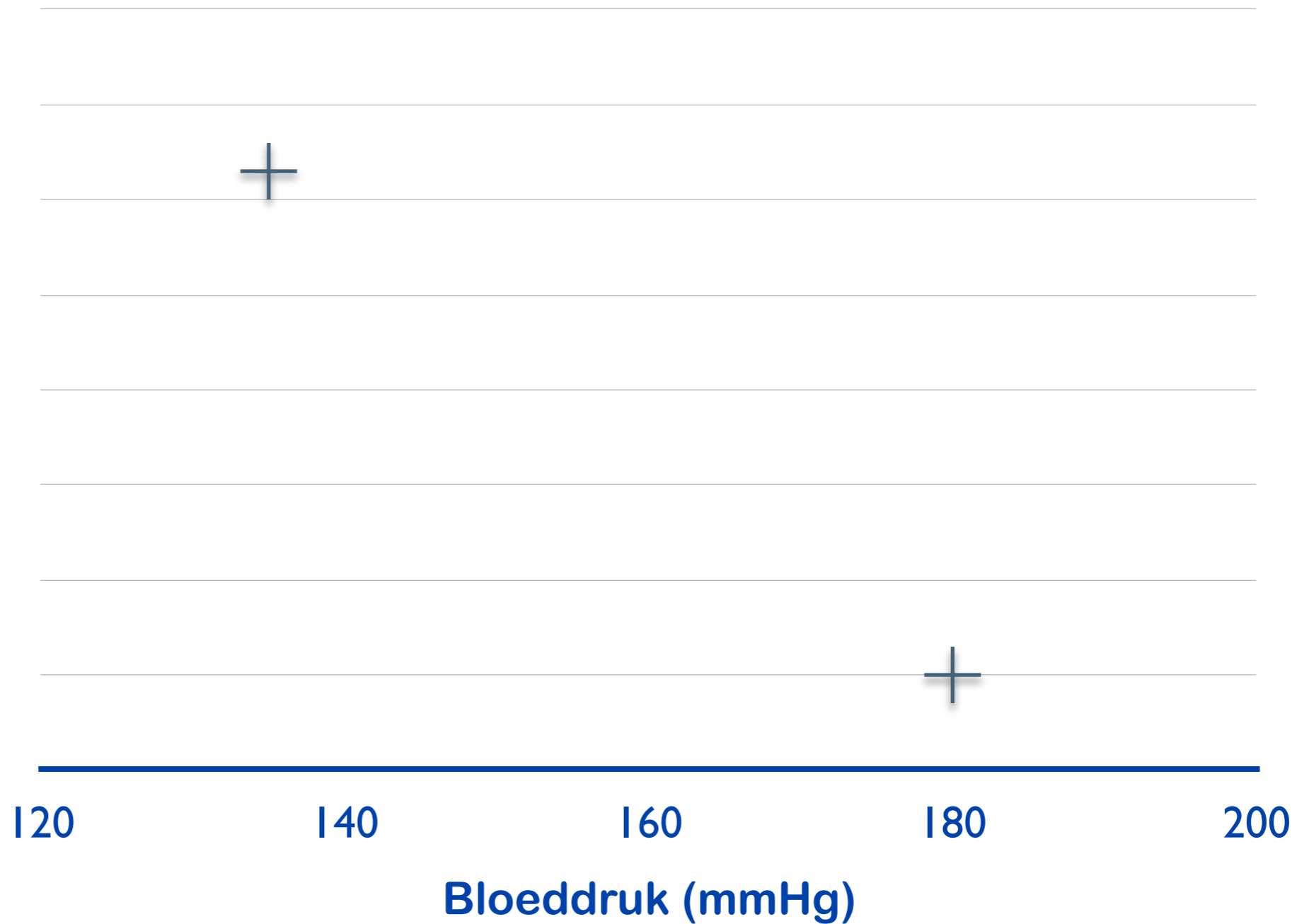
Disability-Adjusted Life-Years by Systolic BP

Figure 2. Projected Global Disability-Adjusted Life-Years by Systolic Blood Pressure Level and Cause, 2015



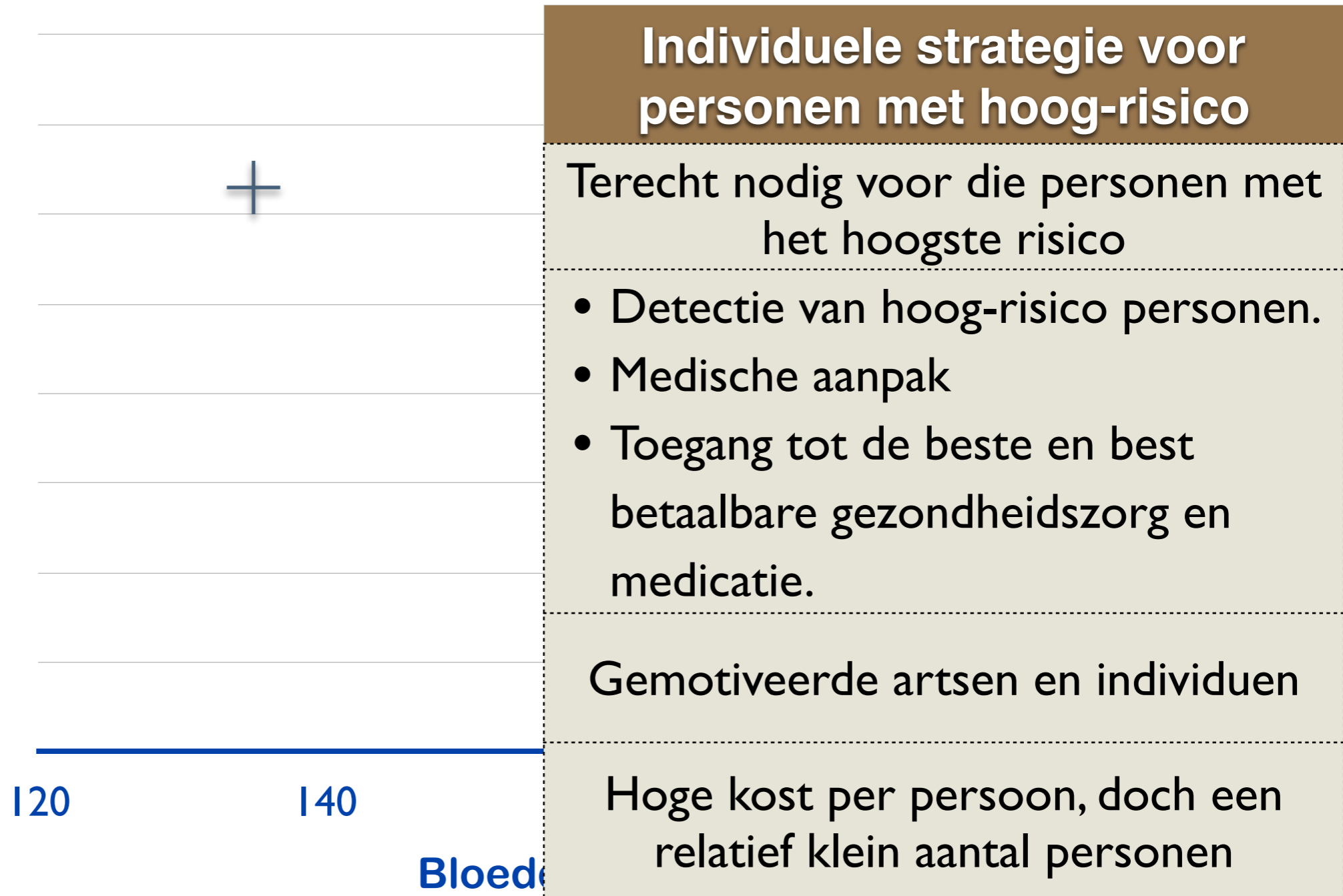


Wat is de grootste bedreiging?





Wat is de grootste bedreiging?





Wat is de grootste bedreiging?

Bevolkings-strategie

Terecht nodig voor die personen met het hoogste risico

- Streeft naar het verlagen -in beperkte mate- van het gewicht van de risicofactoren in de gehele bevolking.
- >> levensstijl aanpassingen & omgevingsveranderingen (wetten, stimulansen, opvoeding !!!)

Minder gemotiveerde artsen en individuen

Kleine cost per persoon, doch voor een hele bevolking

Individuele strategie voor personen met hoog-risico

Terecht nodig voor die personen met het hoogste risico

- Detectie van hoog-risico personen.
- Medische aanpak
- Toegang tot de beste en best betaalbare gezondheidszorg en medicatie.

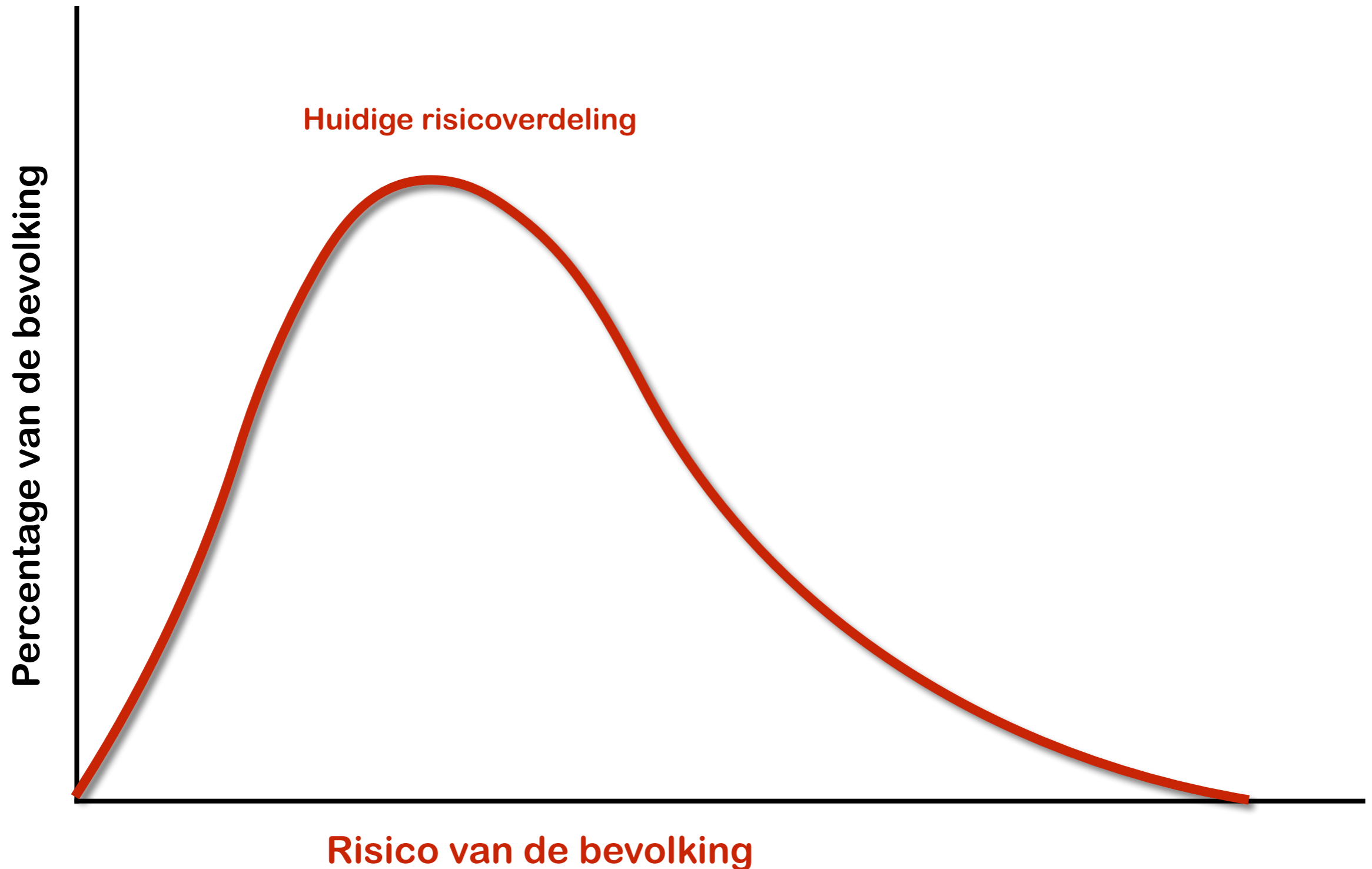
Gemotiveerde artsen en individuen

Hoge kost per persoon, doch een relatief klein aantal personen

oede



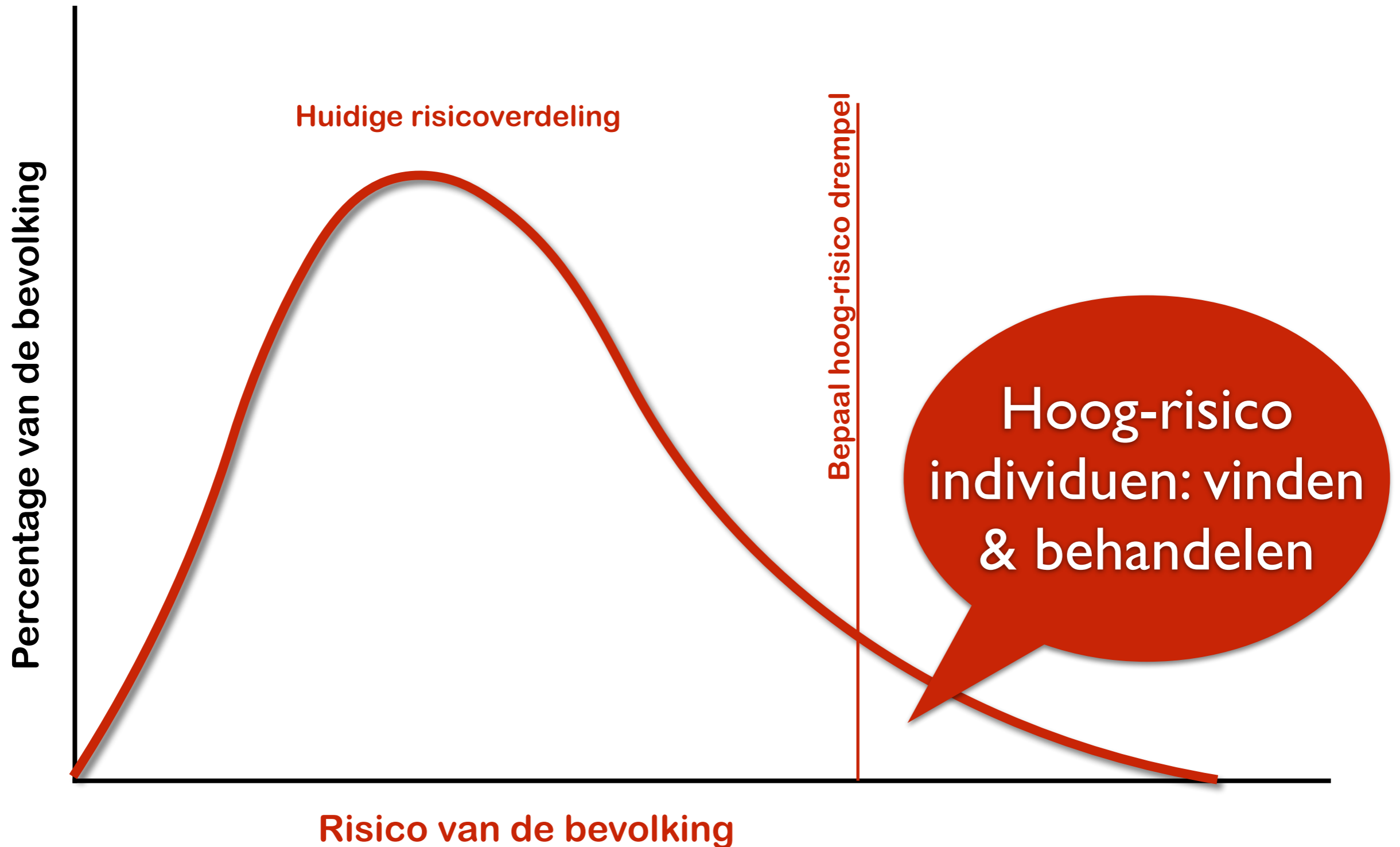
Een verhaal van 2 strategieën



Rose G. The strategy of preventive medicine. Oxford: Oxford University Press; 1992. Rose G. Sick individuals and sick populations. Int J Epidemiol 1985;14:32-8. Emberson et al. European Heart Journal 2004;25:484-491

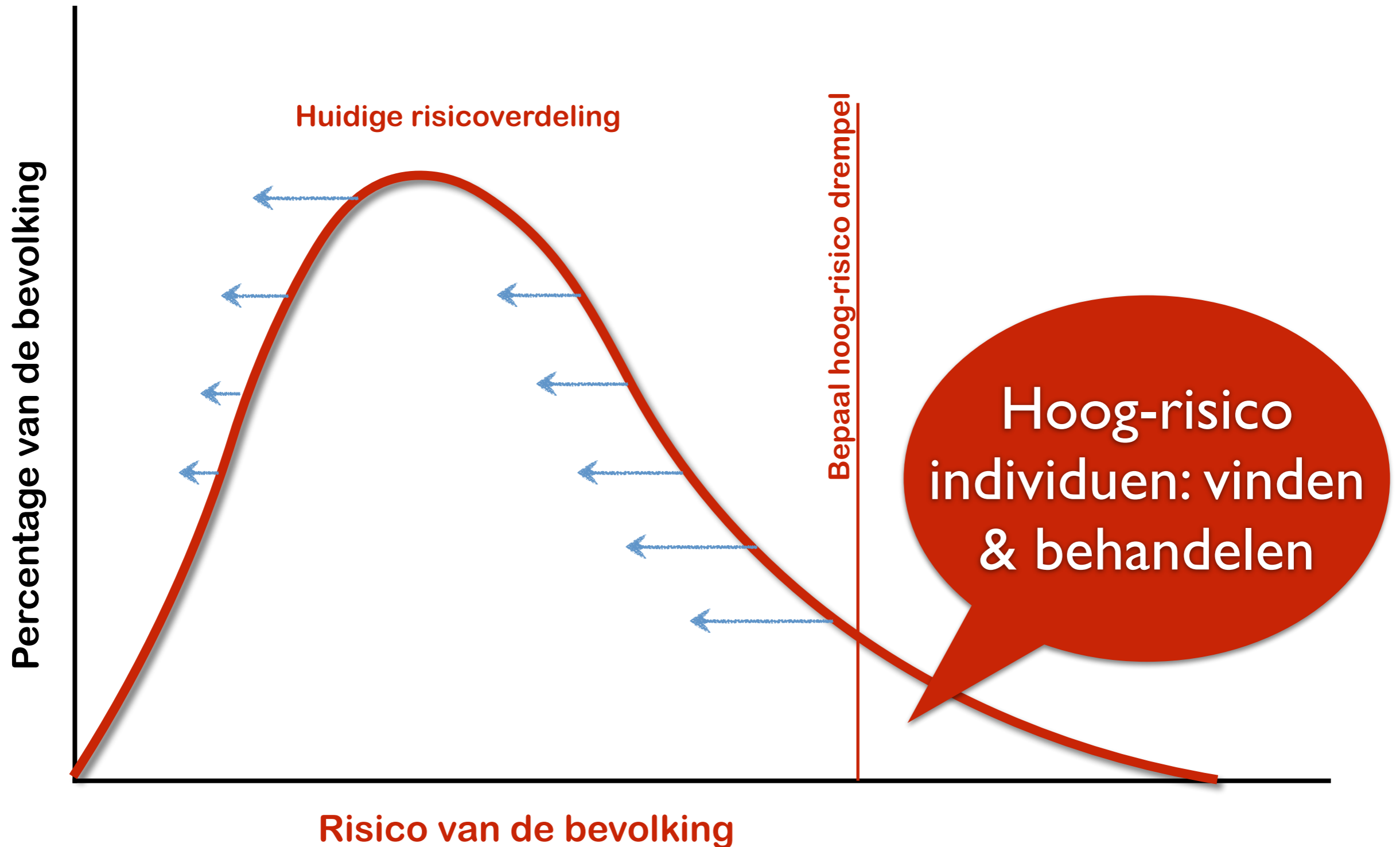


Een verhaal van 2 strategieën





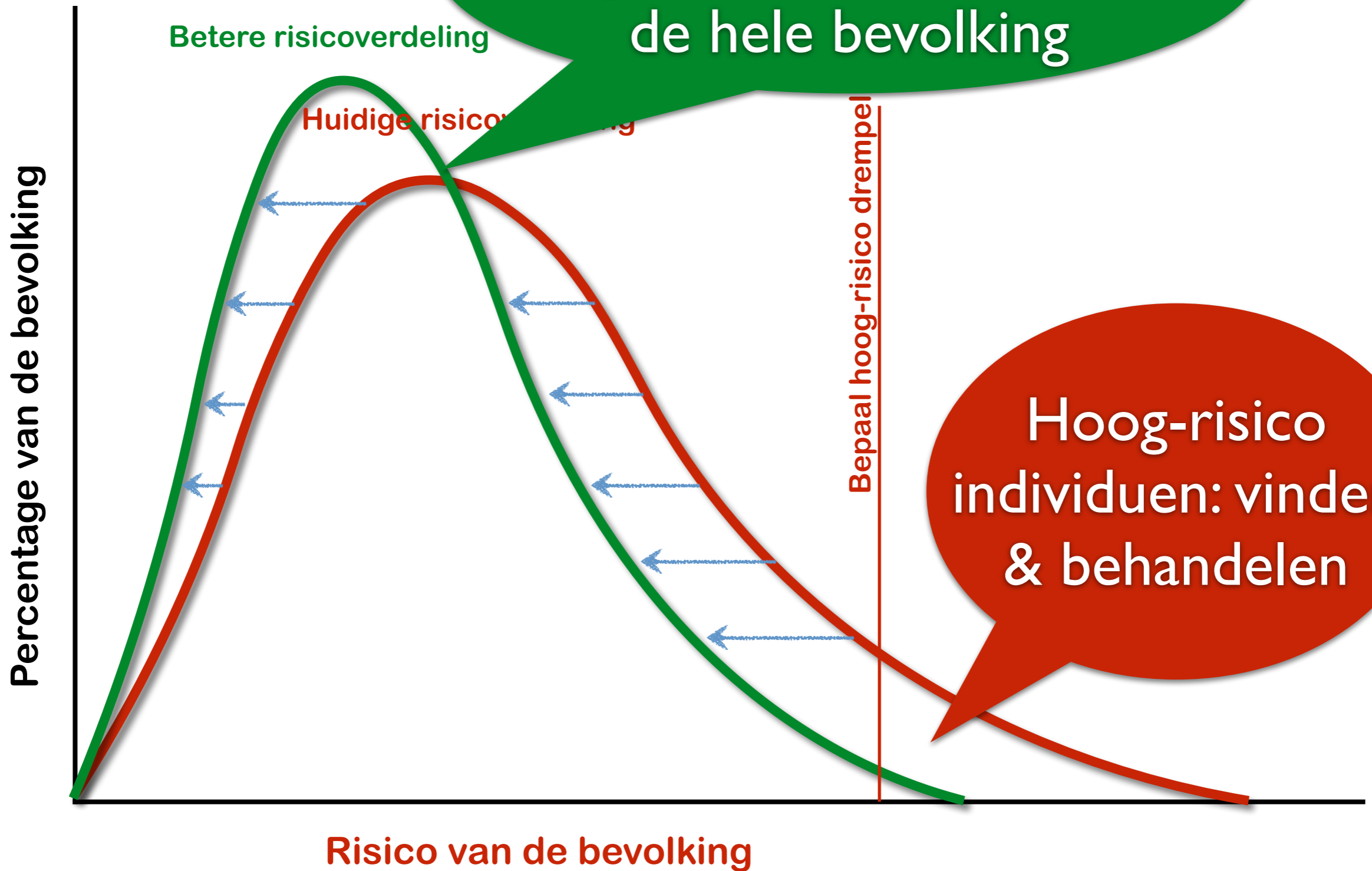
Een verhaal van 2 strategieën





Een verhaal van preventie strategieën

Kleine dalingen van risicofactoren in de hele bevolking





Wat is het doel van preventie?

65

Persoon X, overleden op 82 jaar aan hartfalen

Persoon Y, overleden op 78 jaar na een infarct



Wat is het doel van preventie?

66

Persoon X, overleden op 82 jaar aan hartfalen

- Beroerte op 54j met slechte recuperatie, waarna medisch pensioen (blijvend halfzijdig verlamd).

Persoon Y, overleden op 78 jaar na een infarct



Wat is het doel van preventie?

67

Persoon X, overleden op 82 jaar aan hartfalen

- Beroerte op 54j met slechte recuperatie, waarna medisch pensioen (blijvend halfzijdig verlamd).

Persoon Y, overleden op 78 jaar na een infarct



Wat is het doel van preventie?

Persoon X, overleden op 78 jaar

- Beroerte op 54j met hartinfarct
pensioen (blijft op pensioen)

Verlengen en verhogen van levenskwaliteit
De periode van ziekte tot een minimum beperken en zo ver mogelijk opschuiven naar hogere leeftijd.

Persoon Y, overleden op 78 jaar na een infarct



4) Levensstijl & risicofactoren



Primary prevention of CHD in Women through diet and lifestyle

- 84129 vrouwen (NHS)
- Gezonde levensstijl omschreven als: niet roken, BMI, sport > 30 min/d, matige alcohol intake, hartvriendelijke voeding.
- FU 14 years; 1128 hartinfarcten
- 83% minder infarcten in die 3% van de bevolking met de “beste” levensstijl.
- 82% van alle HVZ is vermijdbaar !



Levensstijl : een snapshot

71

2524 apparently healthy 35-55 year-old volunteers (median 45.9y; 48.5% male), free from overt cardiovascular disease.

- BMI >25 kg/m² : 53%
- BMI >30 kg/m² : 15%
- Teveel buikvet (abdominale obesitas) : 45%
- Ik rook nog steeds (1): 21%
- Ik eet te weinig groente en fruit (2): 63%
- Ik doe nooit aan sport (3): 65%
- Ik leef gezond (0/3): <4%
- Ik kom nooit uit de zetel en mijn enigste groenten zijn tabaksbladeren (3/3): 15%



Gemiddelde gewichtstoename in ASKLEPIOS

= + 5kg op 10 jaar

= + 9 kcal /d

= + 1/3 tot 1/2 suikerklontje



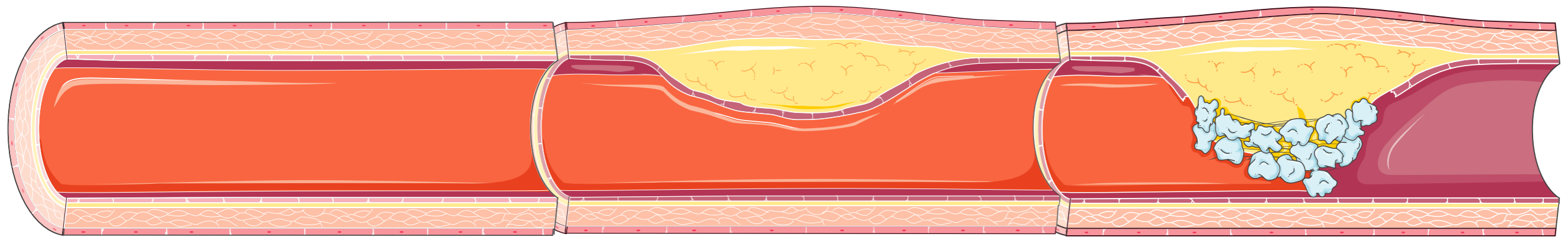
Table 1. Examples of Sedentary and Active Energy Expenditures for Common Activities*

Sedentary	kcal	Active	kcal
Using remote control device to change television channel	<1	Getting up and changing channel	3
Reclining for 30 min of phone calls	4	Standing for 3 10-min phone calls	20
Using garage door opener	<1	Raising garage door 2×/d	2-3
Hiring someone to clean and iron	0	Ironing and vacuuming each for 30 min	152
Waiting 30 min for pizza delivery	15	Cooking for 30 min	25
Buying presliced vegetables	0	Washing, slicing, chopping vegetables for 15 min	10-13
Using a leaf blower for 30 min	100	Raking leaves for 30 min	150
Using a lawn service	0	Gardening and mowing each for 30 min/wk	360
Using car wash 1×/mo	18	Washing and waxing car, 1 h/mo	300
Letting dog out the back door	2	Walking dog for 30 min	125
Driving 40 min, walking 5 min (parking)	22	Walking 15 min to bus stop 2×/d	60
Sending e-mail to colleague, 4 min	2-3	Walking 1 min, talking (standing) 3 min	6
Taking elevator up 3 flights	0.3	Walking up 3 flights	15
Parking as close as possible, 10-s walk	0.3	Parking in 1st spot, walking 2 min, 5×/wk	8
Letting cashier unload shopping cart	2	Unloading full shopping cart	6
Riding escalator 3×	2	Climbing 1 flight of stairs, 3×/wk in mall	15
Shopping online 1 h	30	Shopping at mall, walking 1 h	145-240
Sitting in car at drive-in window, 30 min	15	Parking and walking inside, 3×/wk, total of 30 min	70
Paying at the pump	0.6	Walking into station to pay, 1×/wk	5
Sitting and listening to lecture, 60 min	30	Giving lecture	70



Sporten is gezond?

sporten = trainen van herstelmechanismen

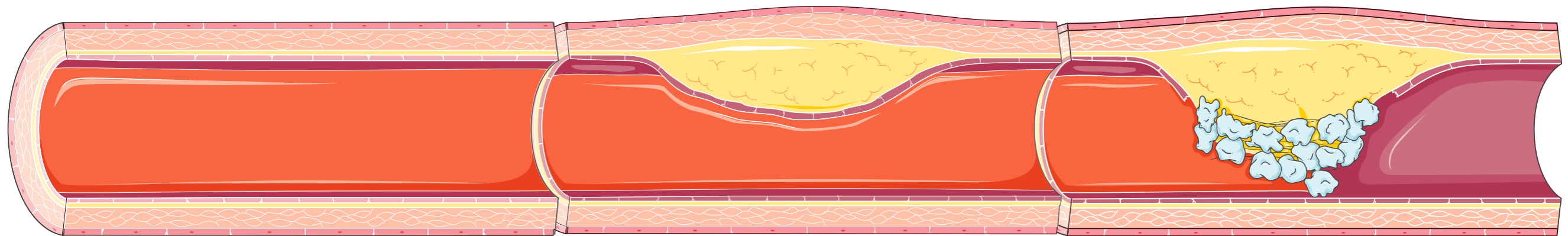




Sporten is gezond?

75

sporten = trainen van herstelmechanismen



3x/week 30 min inspanning waar je licht kortademig en zweterig van wordt.



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Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease

A Prospective Cohort Study

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Stephanie E. Chiuve, ScD,*‡ Laura Sampson, RD,* Kathryn M. Rexrode, MD, MPH,‡ Eric B. Rimm, ScD,*§||
Walter C. Willett, MD, DRPH,*§|| Frank B. Hu, MD, PhD*§||



CrossMark





- 84,628 women (Nurses' Health Study, 1980 to 2010) + 42,908 men (Health Professionals Follow-up Study, 1986 to 2010) free of diabetes, cardiovascular disease, and cancer at baseline.
- Diet was assessed by a semiquantitative food frequency questionnaire every 4 years.
- During 24 to 30 years of follow-up: 7,667 incident cases of CHD.



Healthy lifestyle & CVD

CENTRAL ILLUSTRATION Fat, Carbohydrates, and Heart Disease: Estimated Percentage of Changes in the Risk of Coronary Heart Disease Associated With Isocaloric Substitutions of 1 Dietary Component for Another

Isocaloric substitution of SFAs by equivalent energy from

Trans fat (2%)

MUFAs (5%)

PUFAs (5%)

Carbohydrates from refined starches/added sugars (5%)

Carbohydrates from whole grains (5%)

Isocaloric substitution of carbohydrates from refined starches/added sugars by equivalent energy from

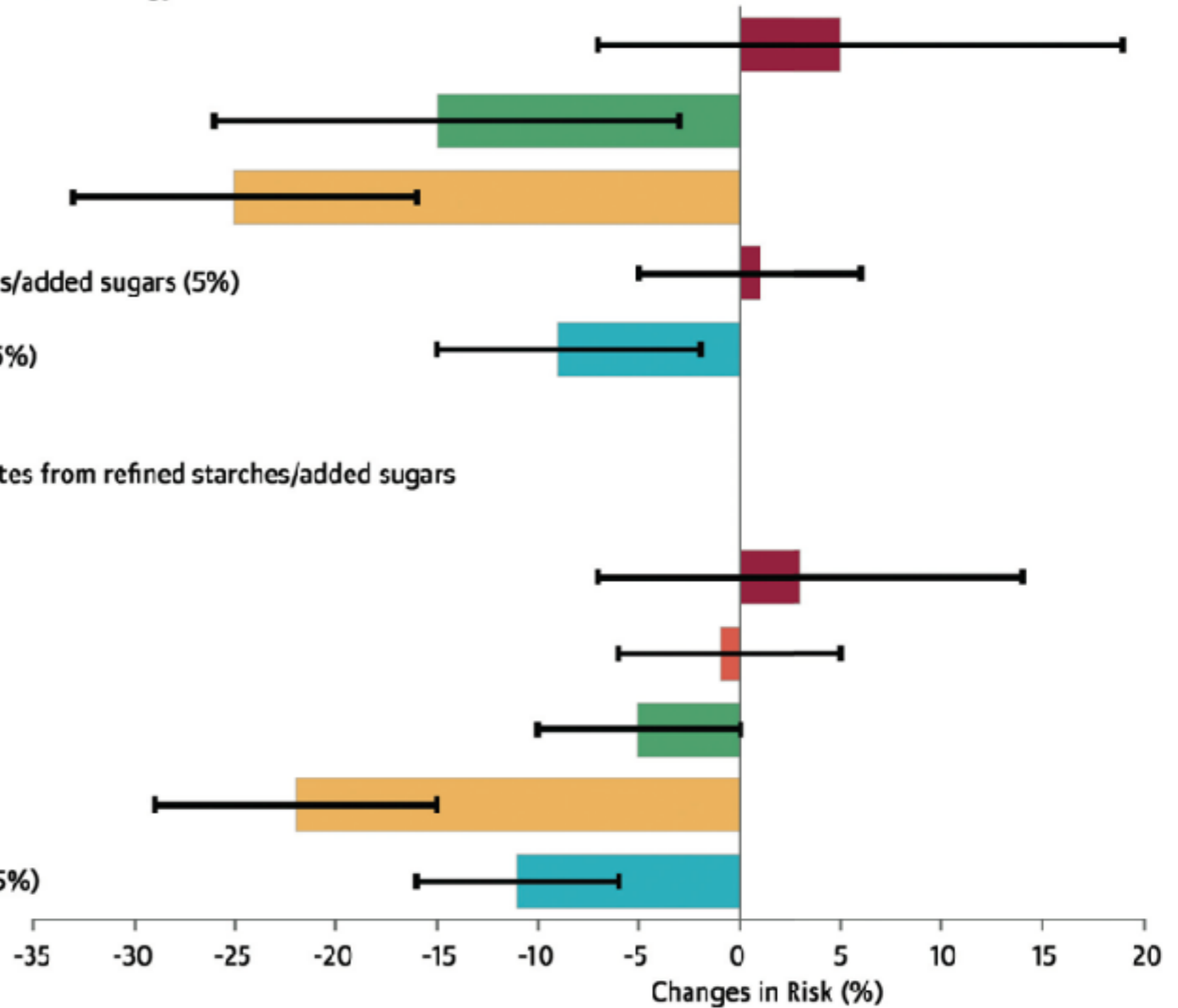
Trans fat (2%)

SFAs (5%)

MUFAs (5%)

PUFAs (5%)

Carbohydrates from whole grains (5%)





Look-AHEAD trial

- 5145 overweight or obese DM2
- Intensive lifestyle modification: the program included both group and individual counseling sessions, occurring weekly during the first 6 months, with decreasing frequency over the course of the trial.
- Primary outcome: death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina during a maximum follow-up of 13.5 years.
- Stopped after 9.6 years (futility).



Healthy lifestyle & CVD

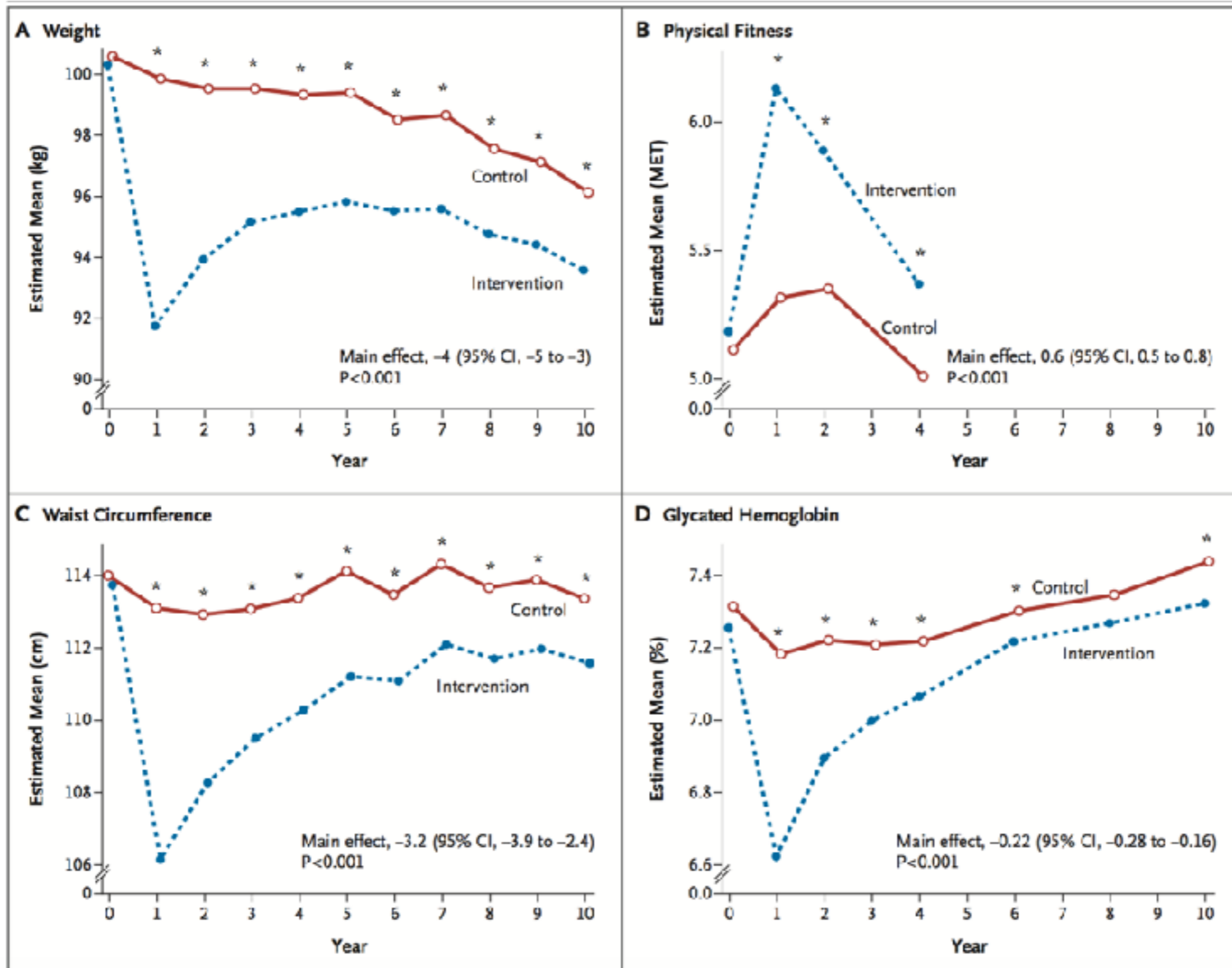
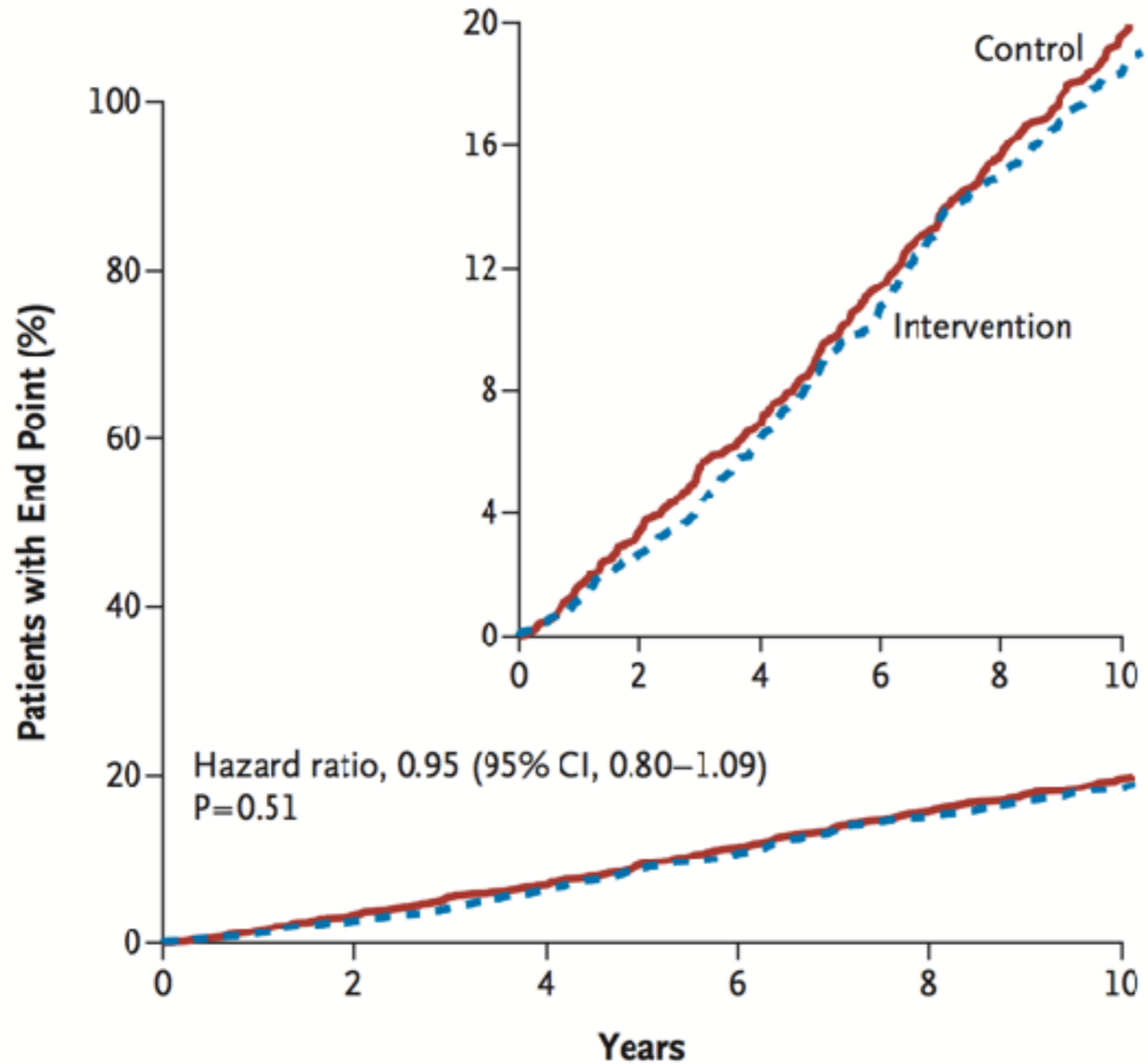


Figure 1. Changes in Weight, Physical Fitness, Waist Circumference, and Glycated Hemoglobin Levels during 10 Years of Follow-up.



Healthy lifestyle & CVD



No. at Risk

Control	2575	2425	2296	2156	2019	688
Intervention	2570	2447	2326	2192	2049	505

Figure 2. Cumulative Hazard Curves for the Primary Composite End Point.



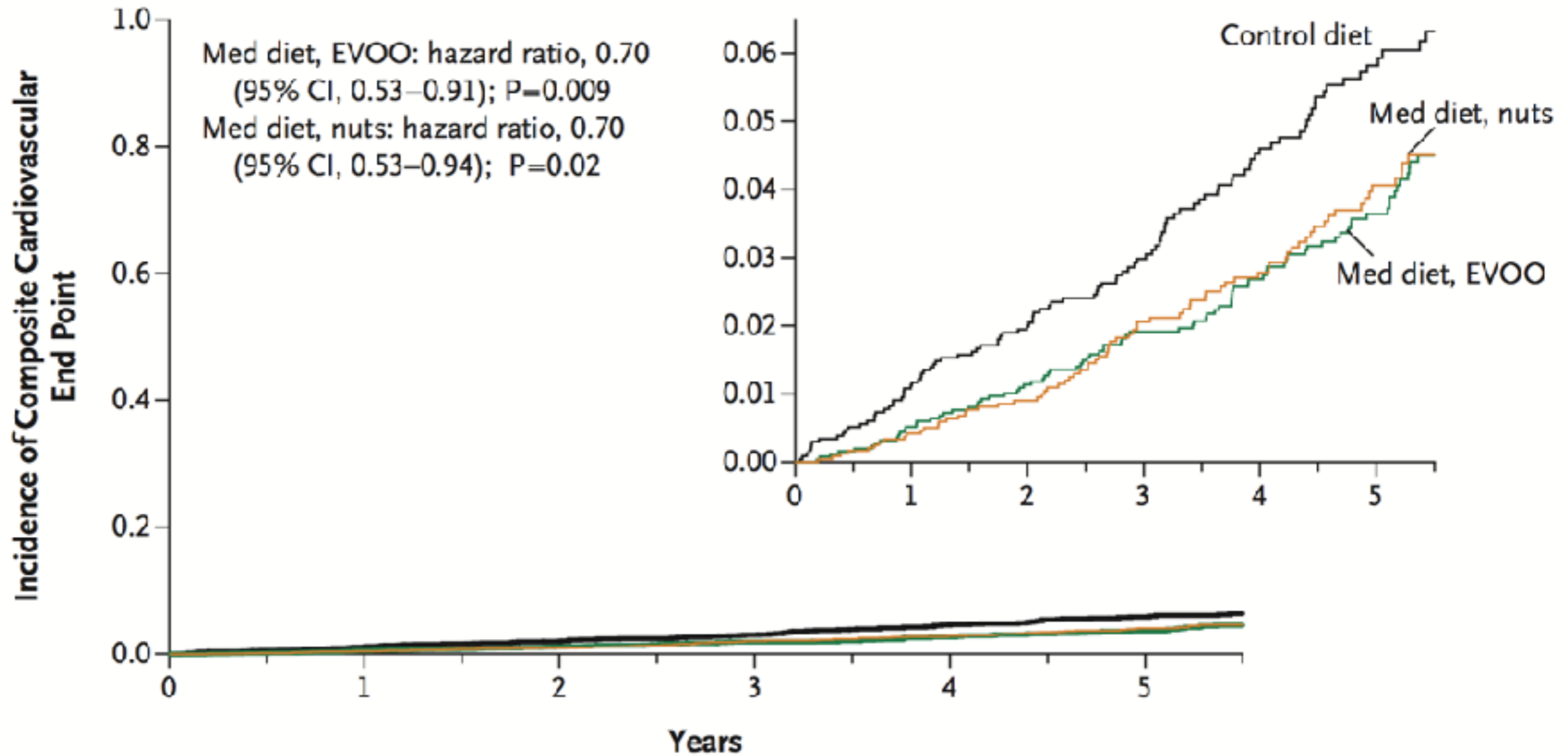
PREDIMED trial

- 7447 subjects at high cardiovascular risk (but no CVD); age range, 55 to 80 years; 57% women.
- Randomized to one of three diets: a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control diet (advice to reduce dietary fat).
- Primary end point: major cardiovascular events (myocardial infarction, stroke, or death from cardiovascular causes).
- Trial was stopped after a median follow-up of 4.8 years.



Healthy lifestyle & CVD

A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)



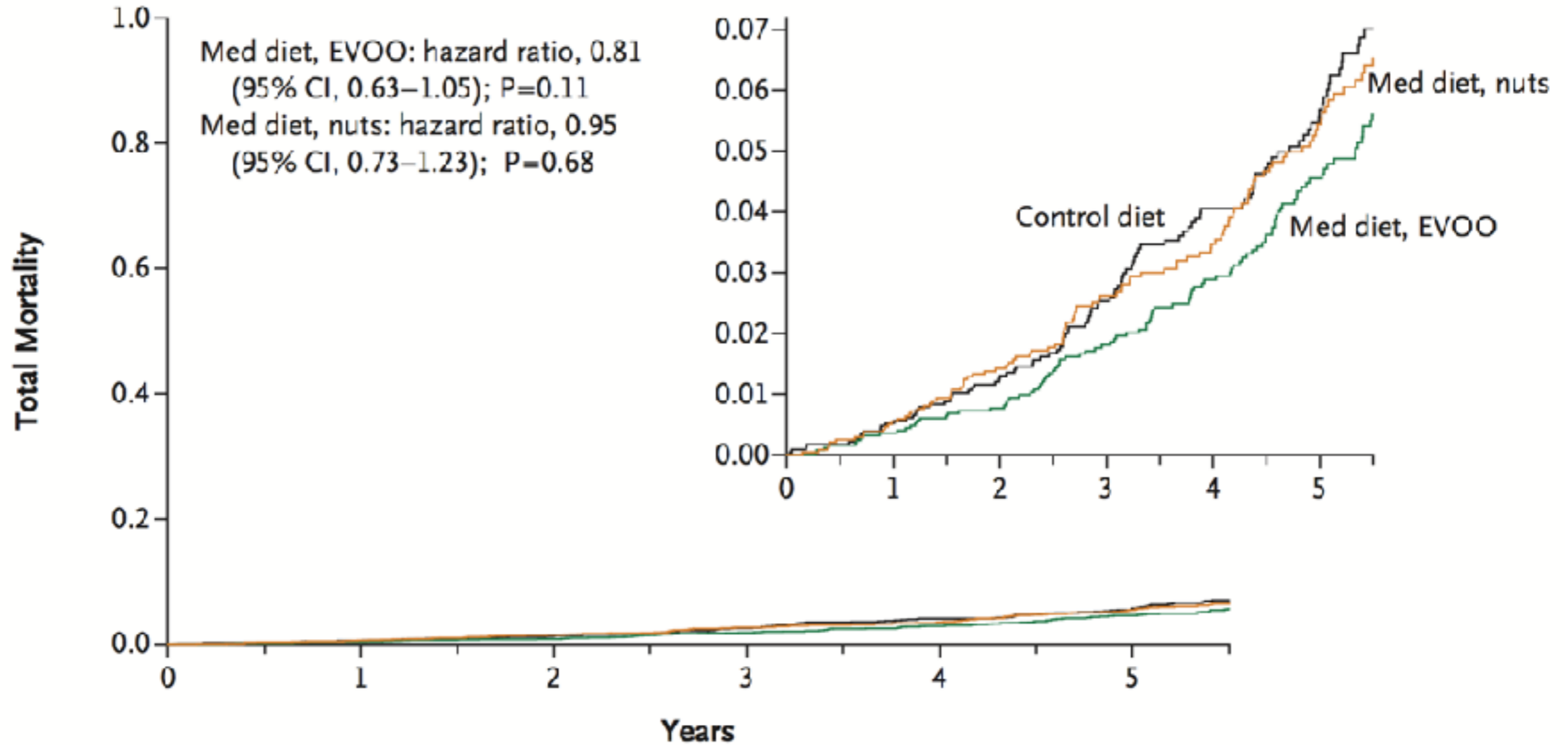
No. at Risk

	0	1	2	3	4	5
Control diet	2450	2268	2020	1583	1268	946
Med diet, EVOO	2543	2486	2320	1987	1687	1310
Med diet, nuts	2454	2343	2093	1657	1389	1031



Healthy lifestyle & CVD

B Total Mortality



No. at Risk

	0	1	2	3	4	5
Control diet	2450	2268	2026	1585	1272	948
Med diet, EVOO	2543	2485	2322	1988	1690	1308
Med diet, nuts	2454	2345	2097	1662	1395	1037



Predimed diet or running?

INTERVENTIONS AND MEASUREMENTS

The dietary intervention^{8,10-13} is detailed in the Supplementary Appendix. The specific recommended diets are summarized in Table 1. Participants in the two Mediterranean-diet groups received either extra-virgin olive oil (approximately 1 liter per week) or 30 g of mixed nuts per day (15 g of walnuts, 7.5 g of hazelnuts, and 7.5 g of almonds) at no cost, and those in the control group received small nonfood gifts. No total calorie restriction was advised, nor was physical activity promoted.



Wat mag ik wel / niet eten?

86





Wanneer is iets bewezen?

- Top evidentie:
 - *dubbelblinde (noch pt, noch onderzoeker weet wie wat neemt)*
 - *gerandomiseerde (lukraak toegewezen onderzoekersarm)*
 - *placebo-gecontroleerde studie*
 - *kostprijs, korte duur, werkt goed bij grote effecten, en als de onderzoeksgroep zeker is.*
- Epidemiologie: gegevens verzamelen over grote groepen mensen.
 - *Observationeel dus risico van “confounding”*



Wanneer is iets bewezen?

88

- Volvorijders krijgen minder kanker.
- Vegetariërs krijgen minder hart- en vaatziekten.
- In een steekproef mannen van 30 tot 70 jaar hadden die mannen met grijs haar meer HVZ —> kleurshampoo X zal hart- en vaatziekten verminderen.
- In het Middellandse zeegebied zijn er minder HVZ, ze gebruiken daar veel knoflook —> Lookpillen zullen HVZ verminderen



Compliance & prognosis

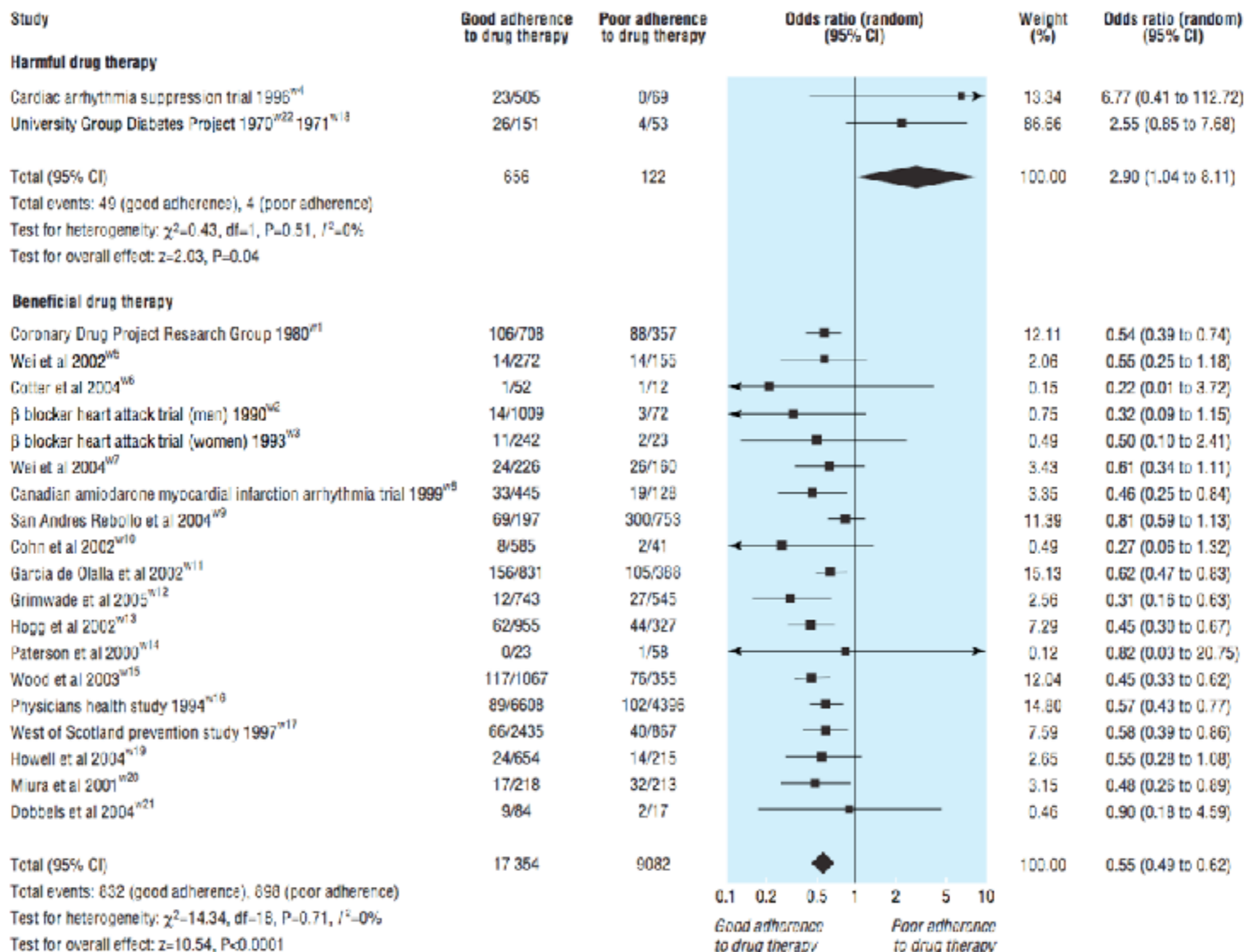


Fig 3 Association between adherence to harmful or beneficial drug therapy and mortality



Compliance & prognose

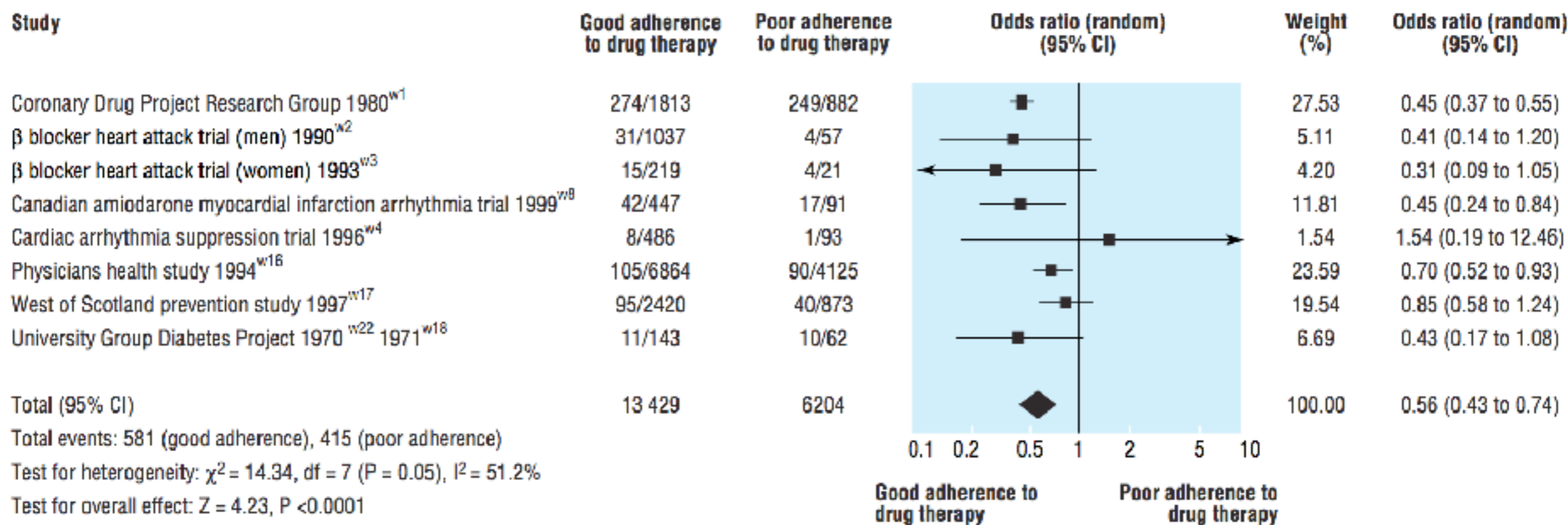


Fig 2 Association between adherence to placebo and mortality



Compliance & prognose

Elke dag stipt stijfsel innemen zorgt voor 44% daling in sterfte !!

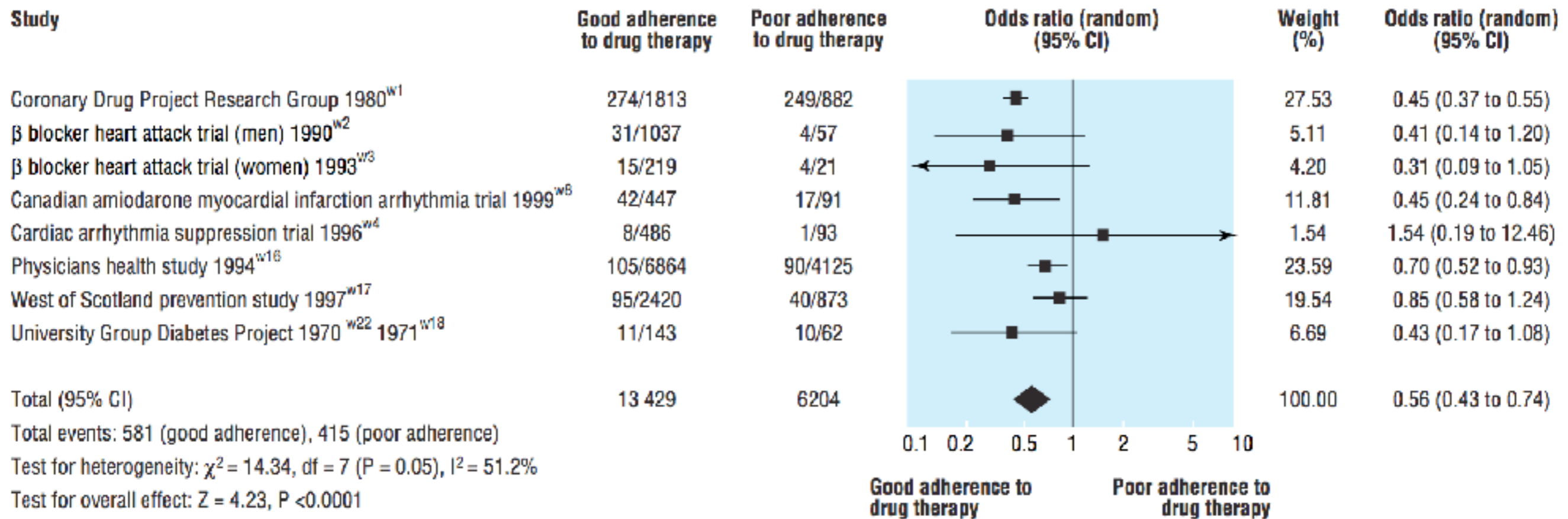


Fig 2 Association between adherence to placebo and mortality



Bridging the gap...

92

Levensstijl verandering
(interventie)

Levensstijl
(epidemiologie)

LDL -10 tot -20 mg/dl

HDL +10 mg/dl

Bloeddruk -5/-2.5 mmHg

Gewichtsverlies !

Rookstop

80% minder HVZ in
personen met de
gezondste levensstijl !



Efficacy and safety of more intensive lowering of LDL cholesterol. meta-analysis (n=170 000 indiv.; 26 RCT's)

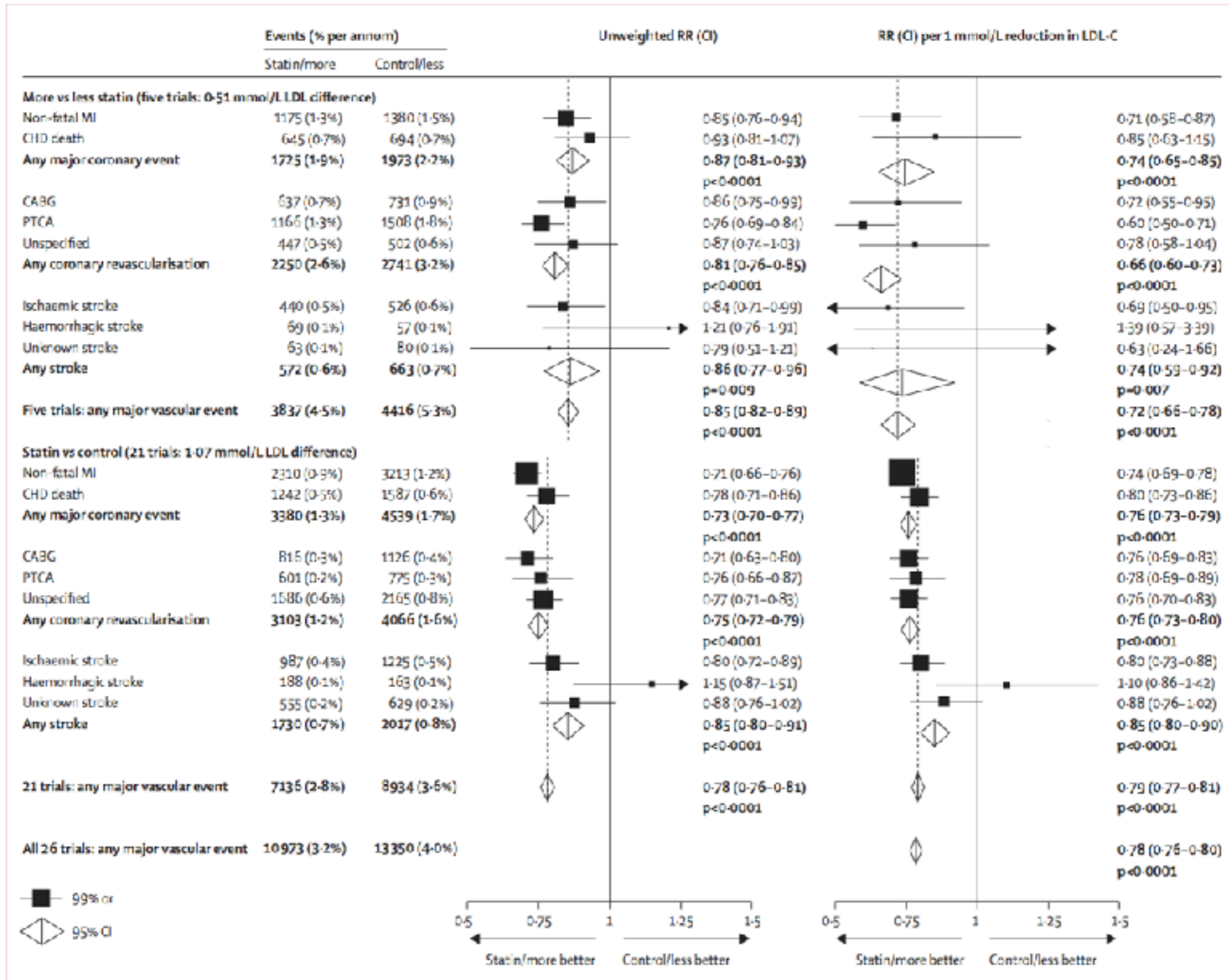


Figure 2: Effects on each type of major vascular event



Lipid lowering (CTT, n=170.000, 26 RCT)

94

Lowering LDL cholesterol by 1 mmol/l \equiv 39 mg/dl

-24% Revascularisation

-23% MI

-21% Vascular events

-19% Coronary deaths

-17% Stroke

-12% Overall mortality

These effects persist independent of:

- Primary or secondary prevention
- Age
- Hypertension
- Diabetes
- Baseline LDL cholesterol value



Efficacy and safety of more intensive lowering of LDL cholesterol. meta-analysis (n=170 000 indiv.; 26 RCT's)

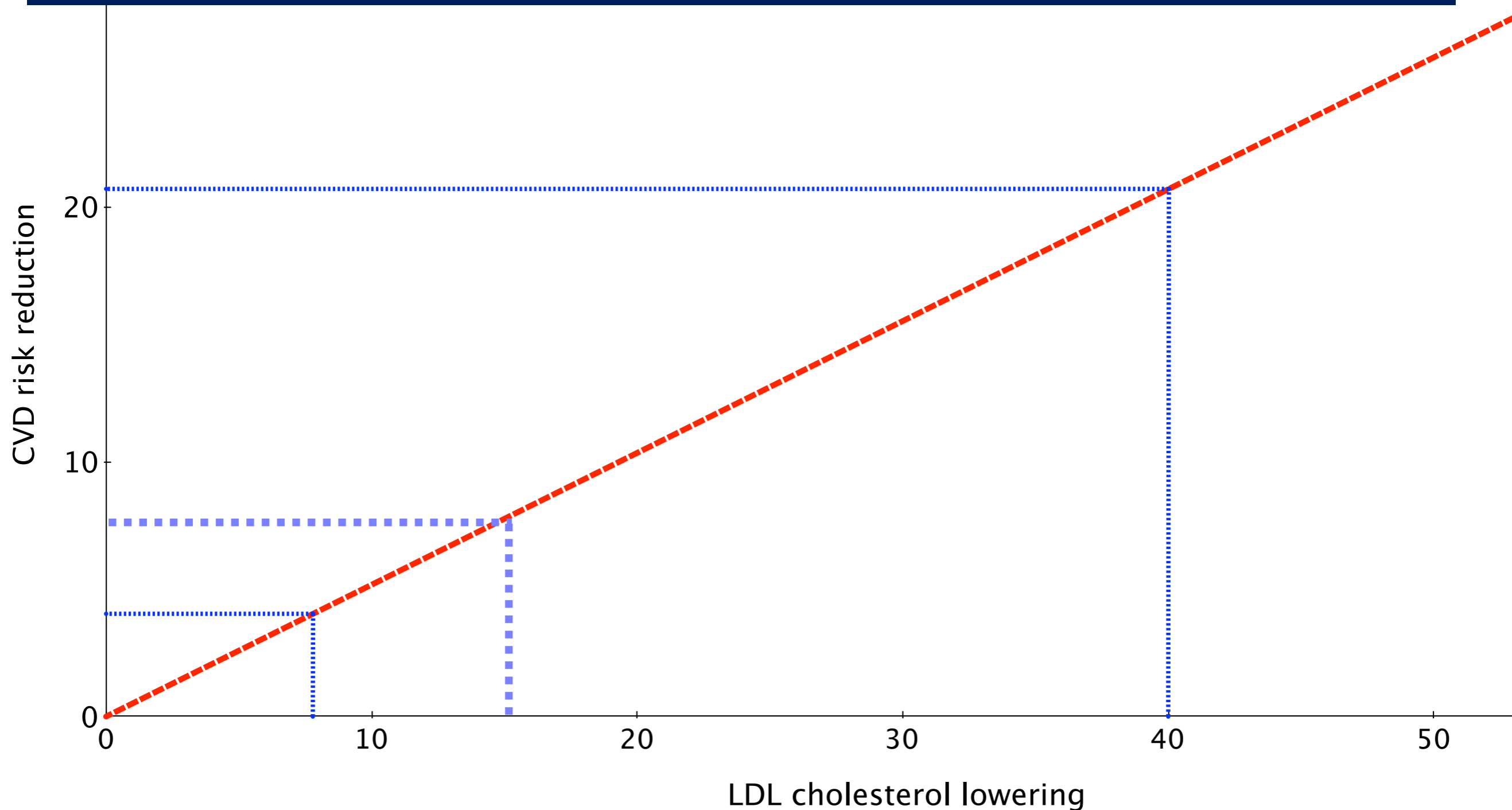
Statin vs Placebo: -21% CVD / 40mg/dl
More vs less statin: -15% CVD / 20 mg/dl

	Events (% per annum)		Unweighted
	Statin/more	Control/less	
More vs less statin (five trials: 0.51 mmol/L LDL difference)			
Non-fatal MI	1175 (1.3%)	1380 (1.5%)	0.86 (0.81-0.94)
CHD death	645 (0.7%)	694 (0.7%)	0.93 (0.81-1.07)
Any major coronary event	1725 (1.9%)	1875 (2.1%)	0.87 (0.81-0.93)
			p<0.0001
CABG	637 (0.7%)	637 (0.7%)	0.86 (0.75-0.99)
PTCA	637 (0.7%)	637 (0.7%)	0.76 (0.69-0.84)
Unspecified	637 (0.7%)	637 (0.7%)	0.87 (0.74-1.03)
Any coronary revascularisation	1911 (2.2%)	2011 (2.3%)	0.81 (0.76-0.85)
			p<0.0001
Ischaemic stroke	526 (0.6%)	526 (0.6%)	0.84 (0.71-0.99)
Haemorrhagic stroke	57 (0.1%)	57 (0.1%)	1.21 (0.76-1.91)
Stroke	583 (0.7%)	583 (0.7%)	0.79 (0.51-1.21)
Any vascular event	572 (0.6%)	663 (0.7%)	0.86 (0.77-0.96)
			p=0.009
Any vascular event	3837 (4.5%)	4416 (5.3%)	0.85 (0.82-0.89)
			p<0.0001



Lipid lowering CTT (n=170.000, 26 RCT)

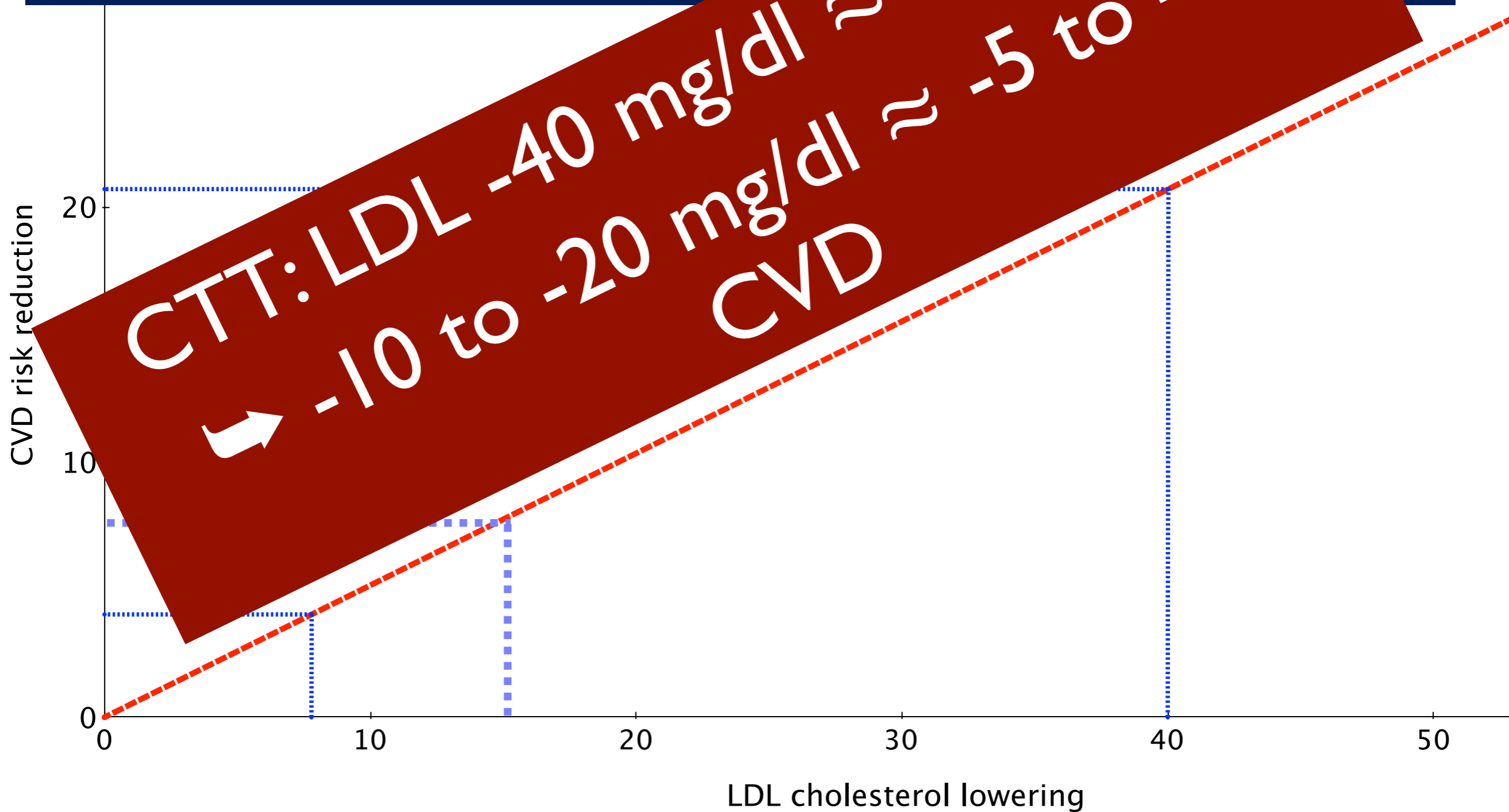
Lowering LDL-c by 40 mg/dl = -21% vascular events





Lipid lowering CTT (n=170,000)

Lowering LDL-c by 40 mg/dl





BP lowering (n = 464.000)

BMJ

RESEARCH

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

M R Law, professor of epidemiology | K Morris, professor of medical statistics | N J Wald, professor of environmental and preventive medicine

Coronary heart disease events

Strokes

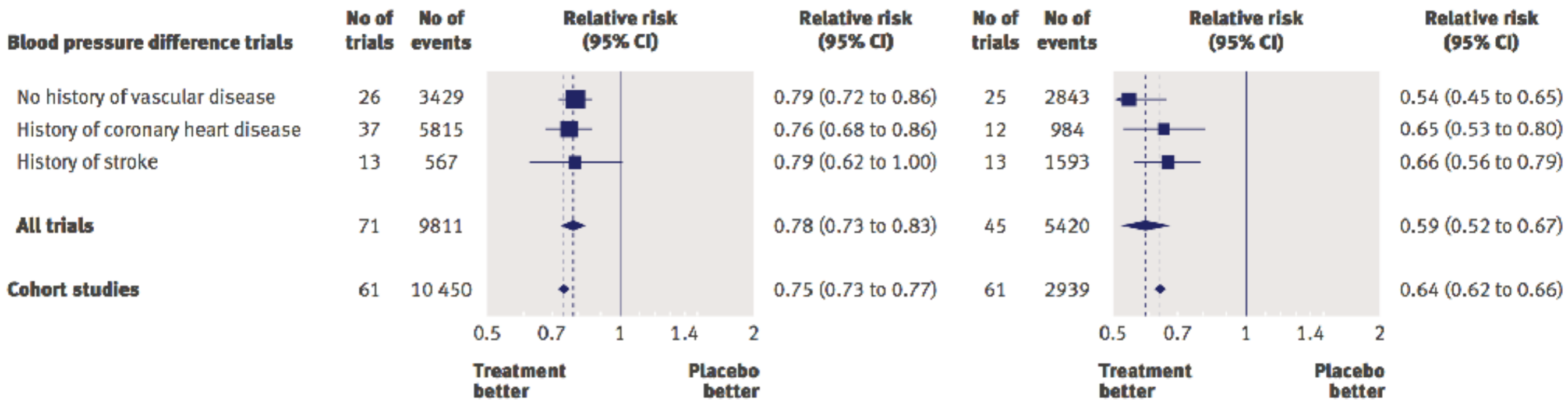


Fig 2 | Relative risk estimates of coronary heart disease events and stroke for a blood pressure reduction of 10 mm Hg systolic or 5 mm Hg diastolic in the blood pressure difference trials and in epidemiological cohort studies. (Total number of trials is fewer than the sum of the three categories as five included participants with and without vascular disease; see web extra figures 2a-f for individual trial results and summary estimates)



BP lowering (n = 464.000)

BMJ

RESEARCH

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

M P Law, professor of epidemiology, UK; M Morris, professor of medical statistics, NJ; W Wald, professor of

**-5/-2.5 mmHg
= -11% Coronair lijden
= -20% CVA**

Blood pressure difference trials

- No history of vascular disease
- History of coronary heart disease
- History of stroke

Relative risk (95% CI)

- 0.54 (0.45 to 0.65)
- 0.65 (0.53 to 0.80)
- 0.66 (0.56 to 0.79)

All trials

71 9811

0.78 (0.73 to 0.83)

45 5420

0.59 (0.52 to 0.67)

Cohort studies

61 10 450

0.75 (0.73 to 0.77)

61 2939

0.64 (0.62 to 0.66)



Fig 2 | Relative risk estimates of coronary heart disease events and stroke for a blood pressure reduction of 10 mm Hg systolic or 5 mm Hg diastolic in the blood pressure difference trials and in epidemiological cohort studies. (Total number of trials is fewer than the sum of the three categories as five included participants with and without vascular disease; see web extra figures 2a-f for individual trial results and summary estimates)



BP lowering (n = 464.000)

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-5/-2.5 mmHg
= -11% coronair lijden
= -20% CV

Relative risk (95% CI)

0.54 (0.45 to 0.65)

0.65 (0.53 to 0.80)

0.66 (0.56 to 0.79)

0.59 (0.52 to 0.67)

0.64 (0.62 to 0.66)

Blood pressure difference trials

No history of vascular disease

History of coronary heart disease

History of stroke

All trials

71 9811

0.78 (0.73 to 0.83)

45 5420

Cohort studies

61 10 450

0.75 (0.73 to 0.77)

61 2939

0.5 0.7 1 1.4 2

Treatment better

Placebo better

0.5 0.7 1 1.4 2

Treatment better

Placebo better

Fig 2 | Relative risk estimates of coronary heart disease events and stroke for a blood pressure reduction of 10 mm Hg systolic or 5 mm Hg diastolic in the blood pressure difference trials and in epidemiological cohort studies. (Total number of trials is fewer than the sum of the three categories as five included participants with and without vascular disease; see web extra figures 2a-f for individual trial results and summary estimates)



We hebben RCT data, dus...

We weten wat een grote LDL daling van 150 naar 75 mg/dl doet gedurende 5 jaar in een 60-jarige !

Maar weten wat een LDL daling van 122 naar 117 mg/dl in een 20 jarige doet als die LDL daling 25 jaar wordt volgehouden ?



How to test lifestyle ?

	Drugs	Lifestyle
Effect	large	small
Duration	short	long
Subjects	diseased	healthy
Follow up	excellent	drop-out !
Trial size	large	small
Blinded	yes	no



How to test lifestyle ?

	Drugs	Lifestyle
Effect	large	small
Duration	short	long
Subjects	diseased	healthy
Follow up	excellent	drop-out !
Trial size	large	small
Blinded	yes	no



How to test lifestyle ?

	Drugs	Genetics
Effect	large	small
Duration	short	long
Subjects	diseased	healthy
Follow up	excellent	perfect
Trial size	large	massive
Blinded	yes	yes



Effect of Long-Term Exposure to Lower Low-Density Lipoprotein Cholesterol Beginning Early in Life on the Risk of Coronary Heart Disease

A Mendelian Randomization Analysis

Brian A. Ference, MD, MPhil, MSc,*†‡ Wonsuk Yoo, PhD,§ Issa Alesh, MD,‡
Nitin Mahajan, MD, MPH,‡ Karolina K. Mirowska, MD,|| Abhishek Mewada, MD,|| Joel Kahn, MD,¶
Luis Afonso, MD,‡ Kim Allan Williams, SR, MD,‡ John M. Flack, MD, MPH*||

Detroit, Michigan; Oxford, United Kingdom; and Memphis, Tennessee

Data from 3 | 2.32 | non-overlapping participants!!



LDL SNP's & outcome

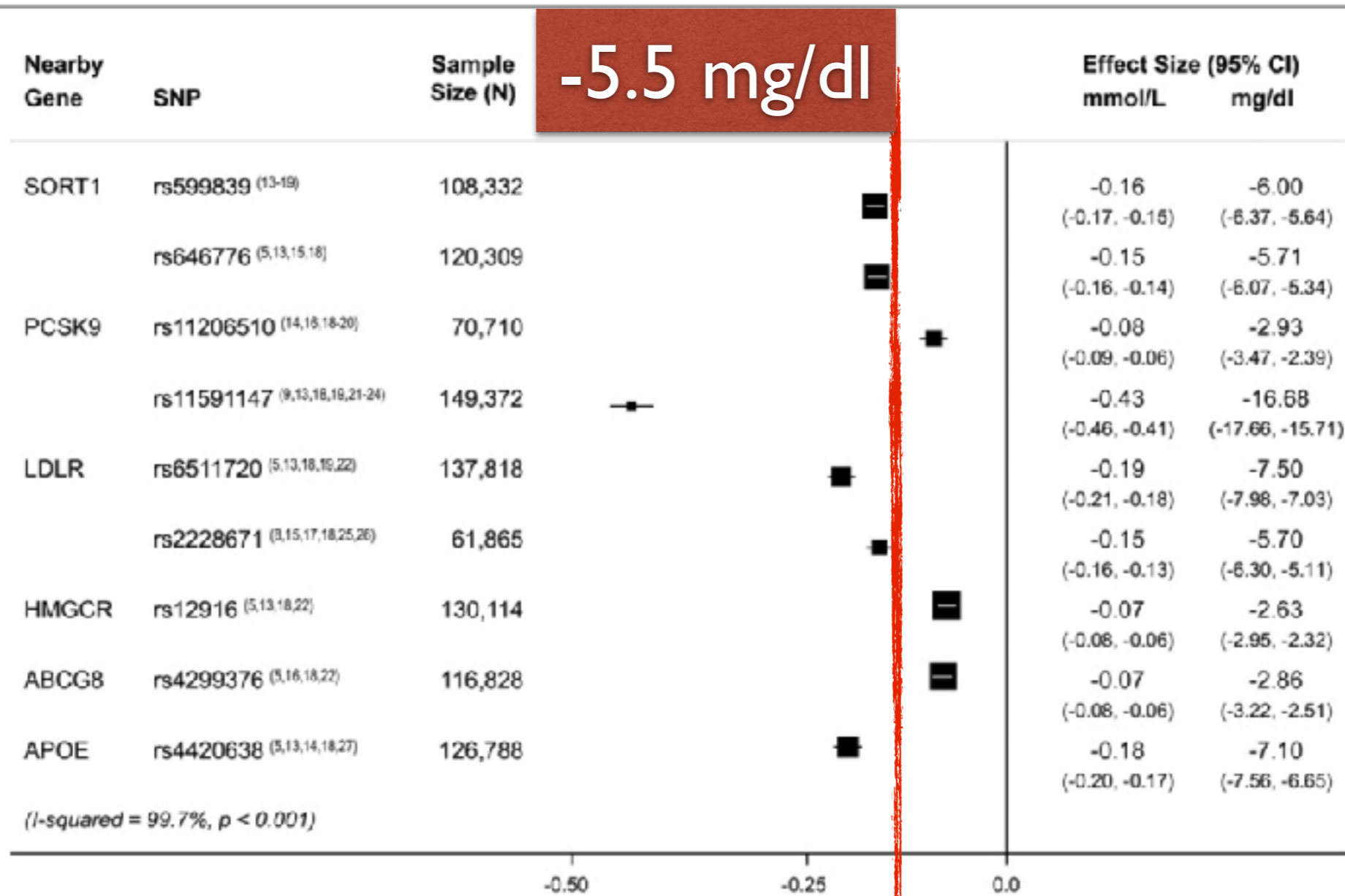


Figure 1 Association Between Exposure Alleles and LDL-C

Boxes represent the summary point estimate of effect for the association between each exposure allele and low-density lipoprotein cholesterol (LDL-C) measured in mmol/l. **Bars** represent 95% confidence interval (CI). SNP = single-nucleotide polymorphism.



LDL SNP's & outcome

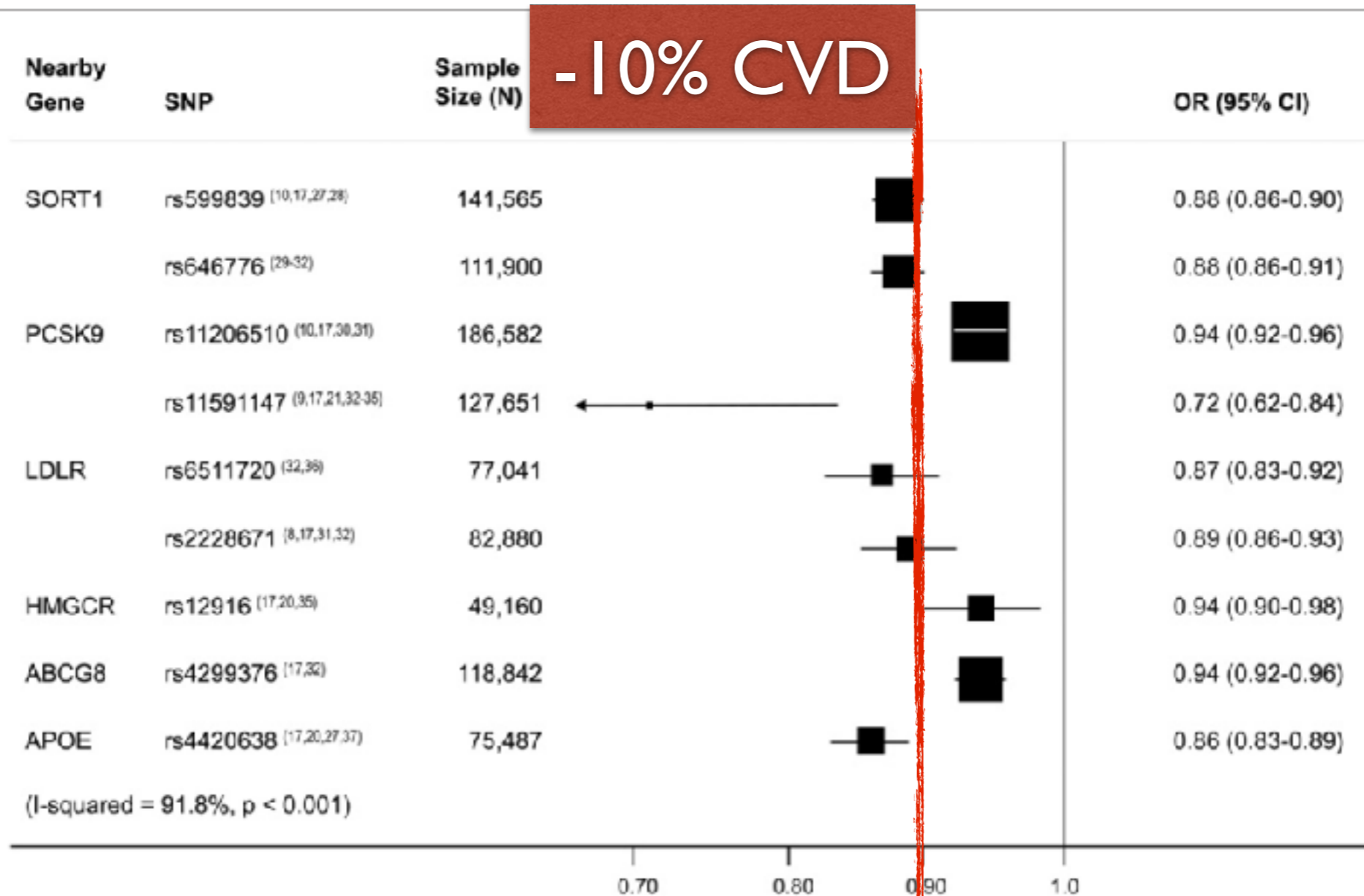
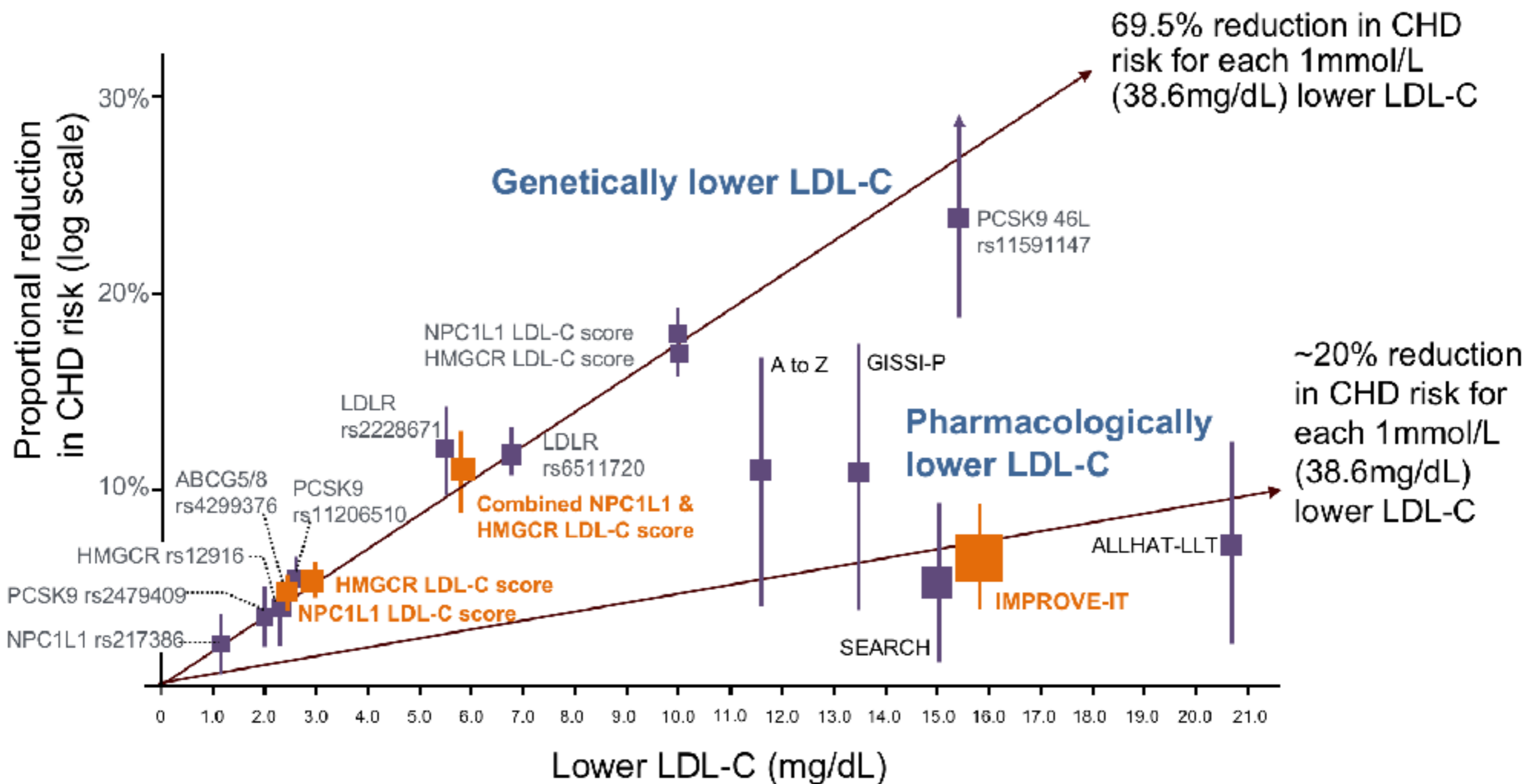


Figure 2 Association Between Exposure Alleles and Risk of CHD

Boxes represent the summary point estimate of odds ratio (OR) for the association between each exposure allele and risk of coronary heart disease (CHD). **Bars** represent 95% CI. (Unlike the other SNPs, the APOE C1-C2 SNP rs4420638 is associated with LDL-C, HDL-C, triglycerides, and C-reactive protein. We included this SNP specifically to assess for heterogeneity of effect on the risk of CHD.) Abbreviations as in Figure 1.



Clinical benefit of lower LDL is determined by duration & absolute exposure to lower LDL



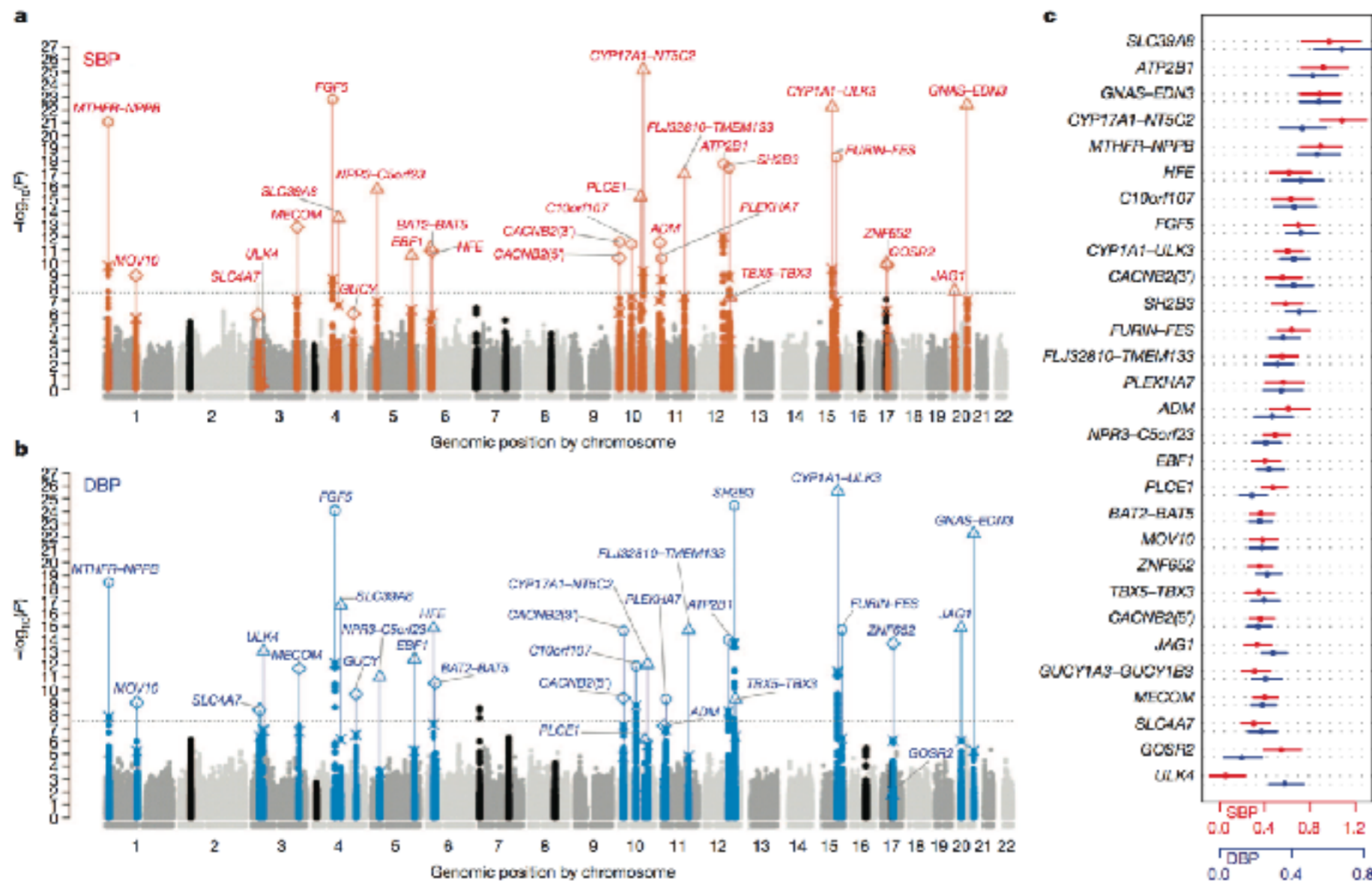


BP lowering (ICBP-GWAS)

doi:10.1038/nature10405

Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk

The International Consortium for Blood Pressure Genome-Wide Association Studies



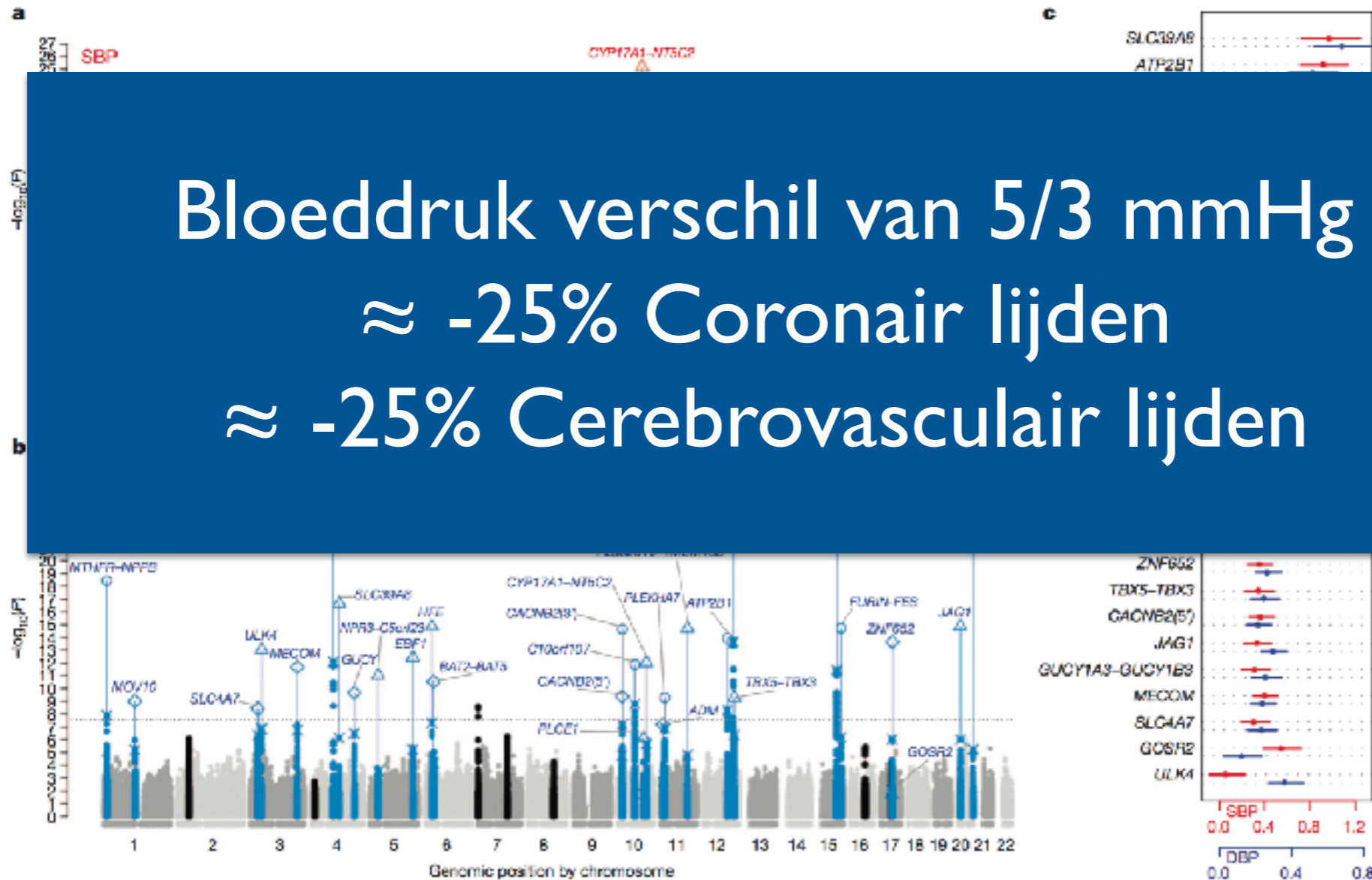


BP lowering (ICBP-GWAS)

doi:10.1038/nature10405

Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk

The International Consortium for Blood Pressure Genome-Wide Association Studies





Bridging the gap...



Levensstijl verandering
(interventie)

Levensstijl
(epidemiologie)

LDL -10 tot -20 mg/dl

HDL +10 mg/dl

Bloeddruk -5/-2.5 mmHg

Gewichtsverlies !

Rookstop

80% minder HVZ in
personen met de
gezondste levensstijl !

A Naturally Randomized Trial Comparing the Effect of Long-Term Exposure to Lower LDL-C, Lower SBP, or Both on the Risk of Cardiovascular Disease

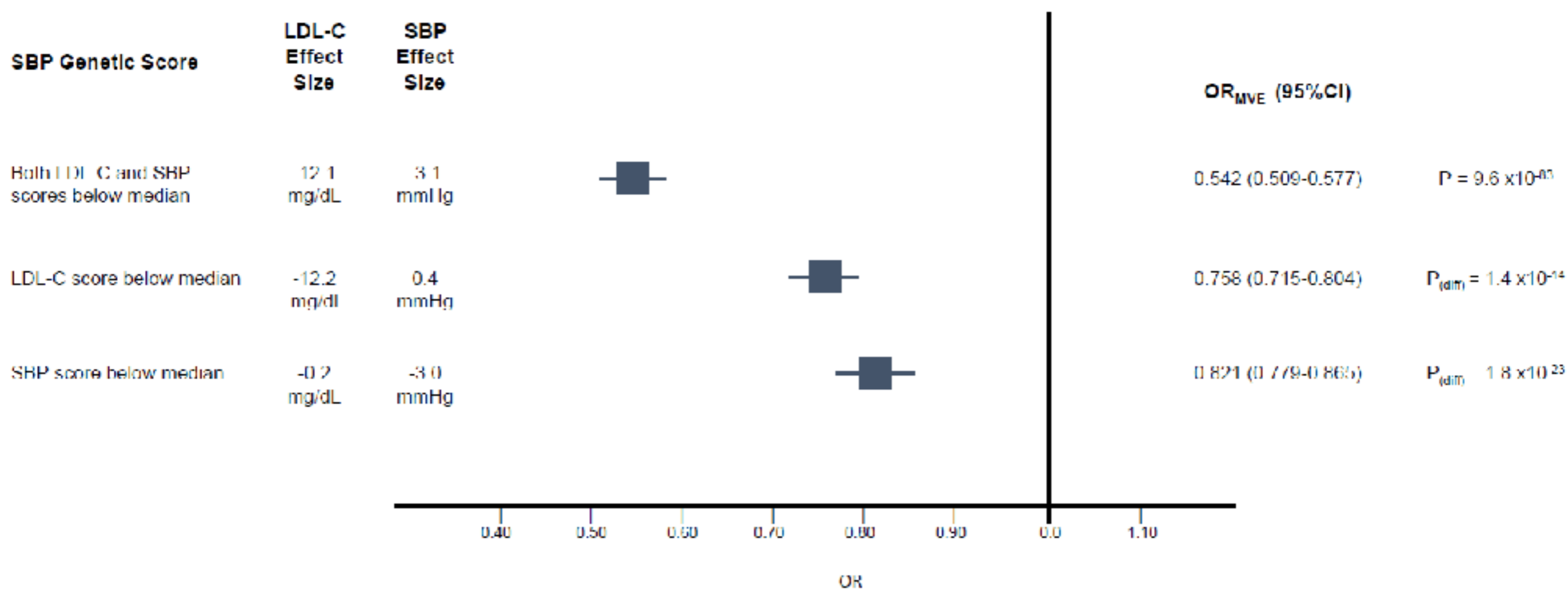
Brian A Ference MD, MPhil, MSc, Thatcher B Ference, Robert D Brook MD, Alberico L Catapano MSc, Christian T Ruff MD, MPH, David R Neff DO, George Davey Smith MD, DSc, Kausik K Ray MD, MPhil, Marc S Sabatine, MD, MPH



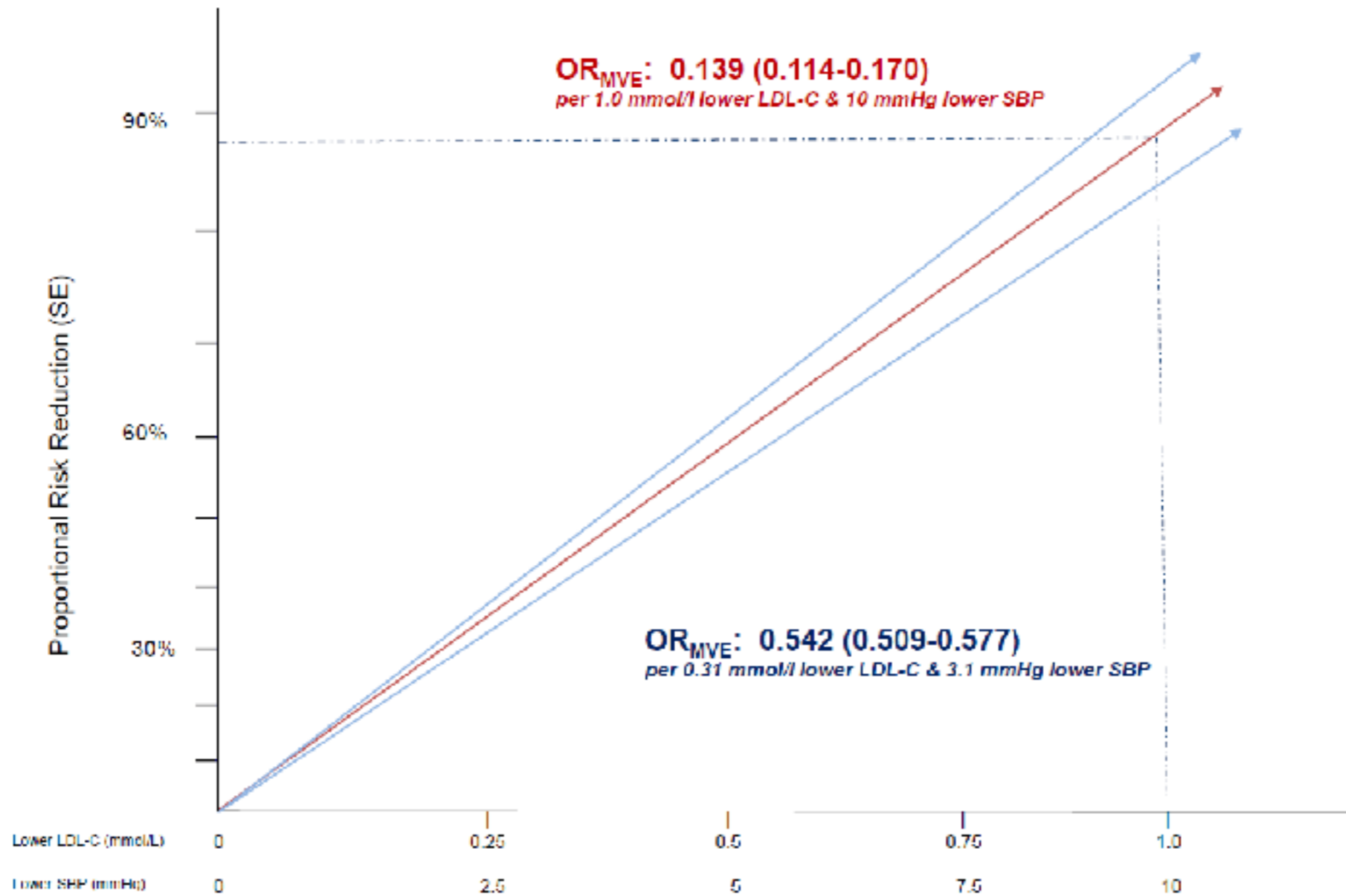
Division of Translational Research and Clinical Epidemiology (TRaCE)
Division of Cardiovascular Medicine
Wayne State University School of Medicine



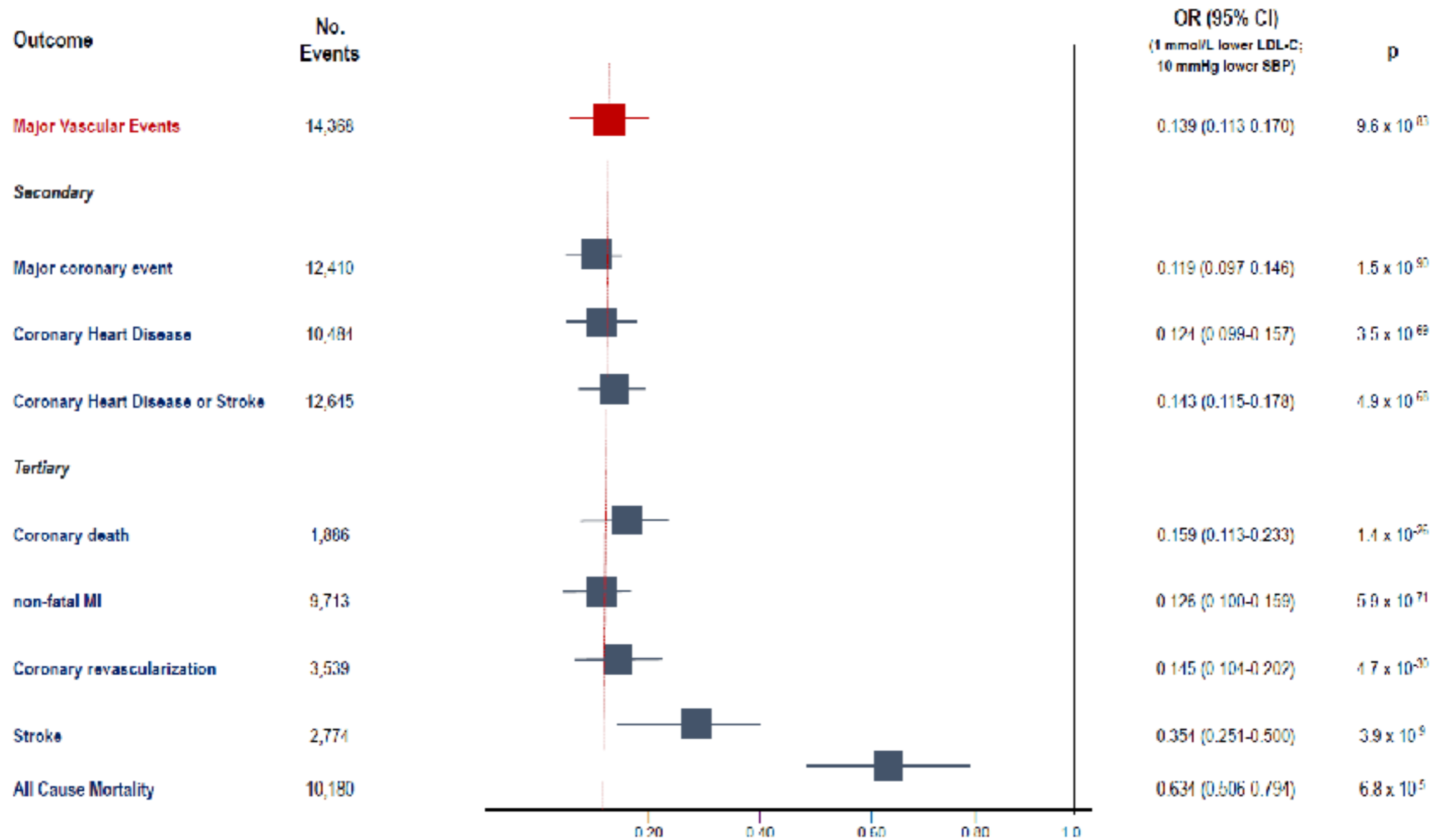
Combined effect of LDL-C & SBP on cardiovascular events



Effect of 1 mmol/L lower LDL-C & 10 mmHg lower SBP



Secondary and tertiary outcomes





Bridging the gap...

116

Interventional data

Epidemiological data

LDL -10 to -20 mg/dl
HDL +10 mg/dl
BP -5/-2.5 mmHg
Weight loss
Stop smoking

80% less CVD in
those with best
lifestyle !

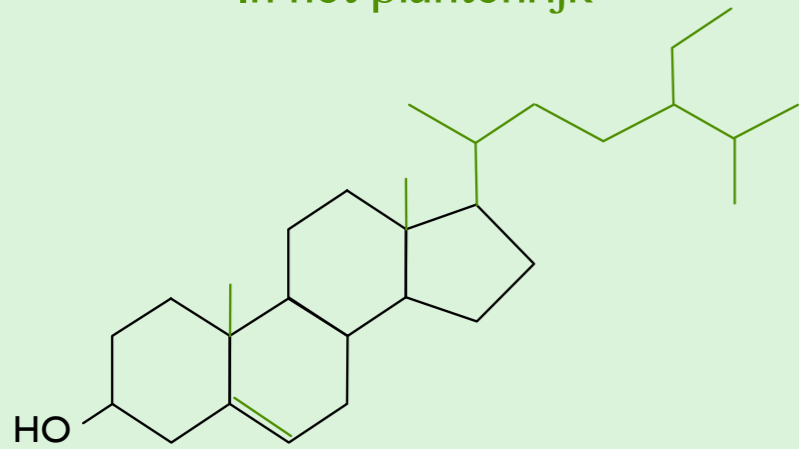


- Roken is en blijft een enorm doorwegende risicofactor op HVZ, longziekten & tumoren.
- Na rookstop:
 - *Na enkele weken rookstop daalt je risico op een infarct reeds.*
 - *Na 1 jaar rookstop is het extra risico op een hartziekte met ongeveer de helft gedaald.*
 - *Na 5 jaar is het risico op een beroerte hetzelfde als dat van een niet-roker*



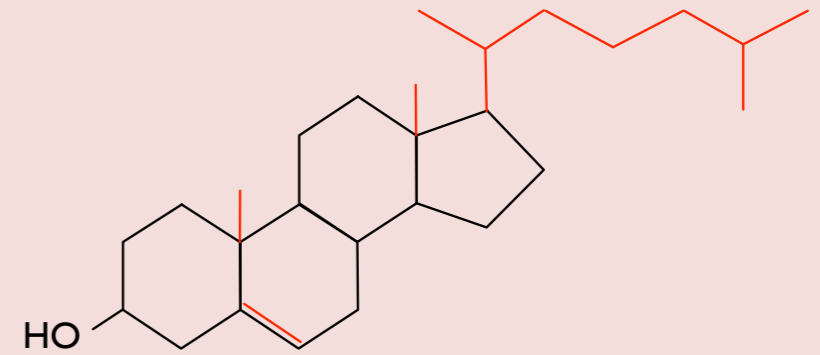
Cholesterol

In het plantenrijk

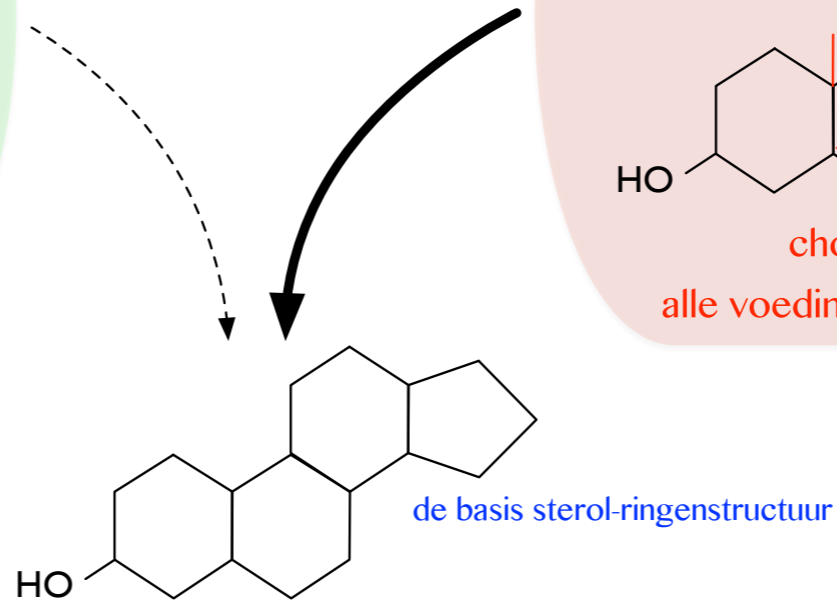


een plantensterol, ook wel phytosterol genoemd,
komt voor in noten, granen, fruit en groenten

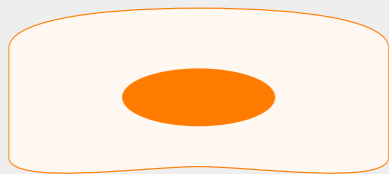
In het dierenrijk



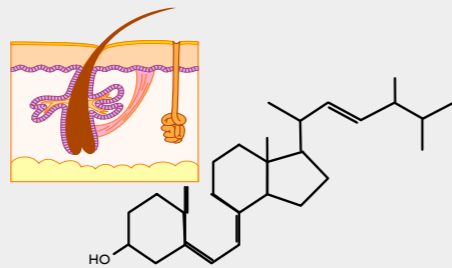
cholesterol, komt voor in
alle voeding die dierlijke vetten bevatten



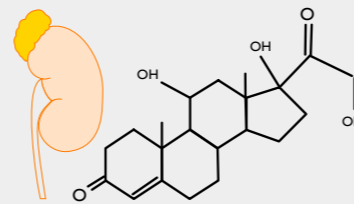
In ons lichaam wordt de sterol-ringenstructuur als bouwsteen gebruikt...



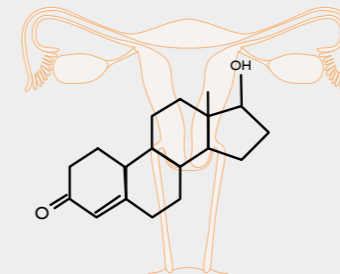
in elke cel voor de
opbouw van de
celwand



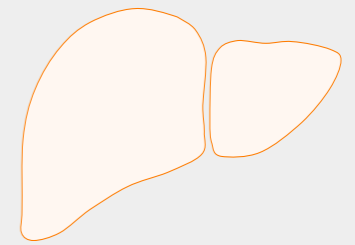
in de huid voor de
aanmaak van vitamine D



in de bijnier voor de
aanmaak van het hormonen
cortisol en aldosteron



voor de aanmaak van de
geslachtshormonen
testosteron, oestradiol en
progesterone



in de lever voor de
aanmaak van gal

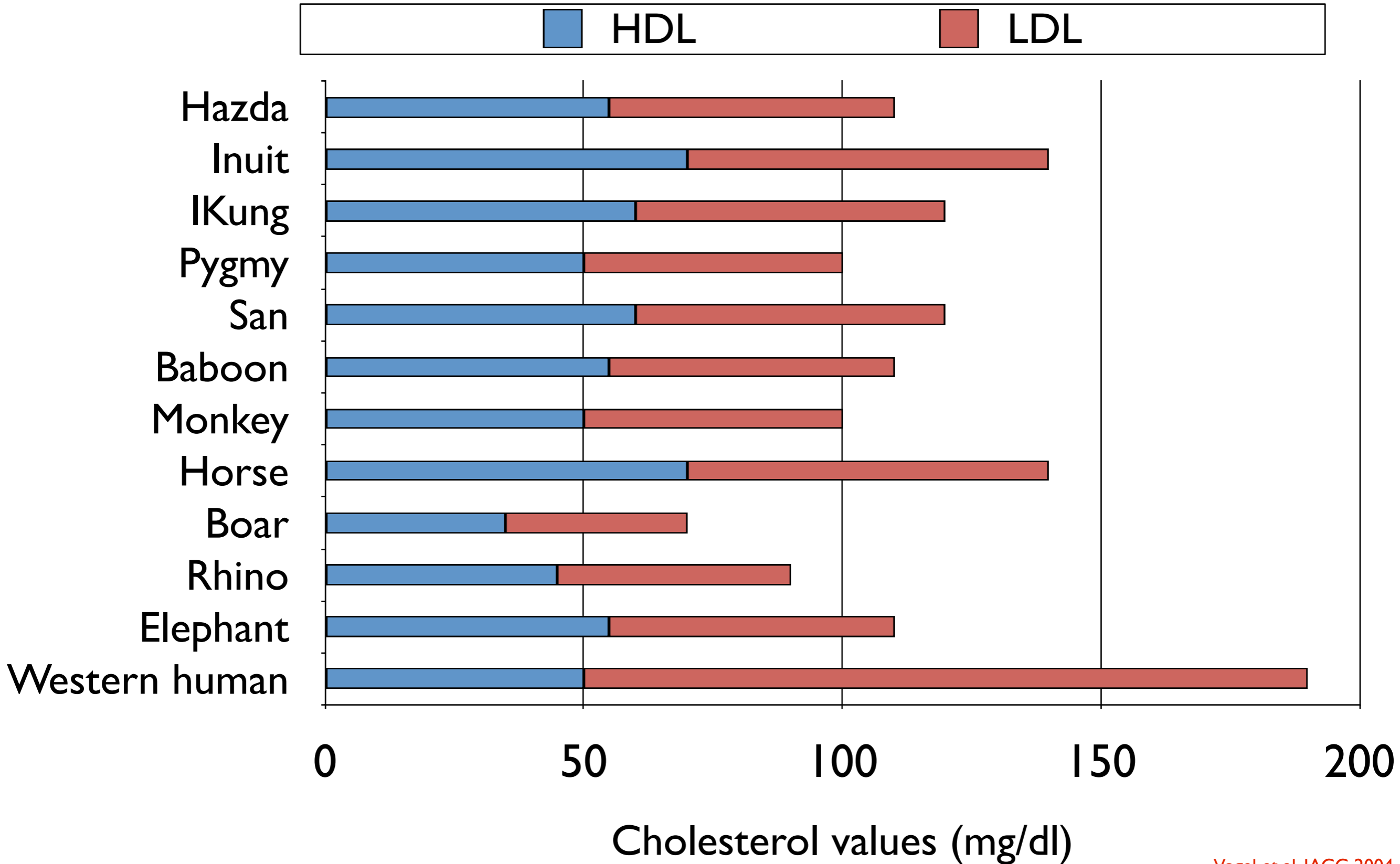


Cholesterol

1. LDL-cholesterol = “slechte cholesterol”
2. HDL-cholesterol = “goede cholesterol”
3. Ongeveer 80% van je cholesterolspiegel wordt door de lever aangemaakt; deze aanmaak is sterk erfelijk bepaald !
4. Voeding bepaalt (gemiddeld genomen) slechts 20% van onze cholesterolspiegel.
5. Het verband tussen hogere cholesterol en HVZ staat onomstotelijk vast !!!
6. 2/3 van onze bevolking heeft een te hoog LDL-chol.



Cholesterol levels in mammals





ESC

European Society
of Cardiology

European Heart Journal (2021) **42**, 3227–3337

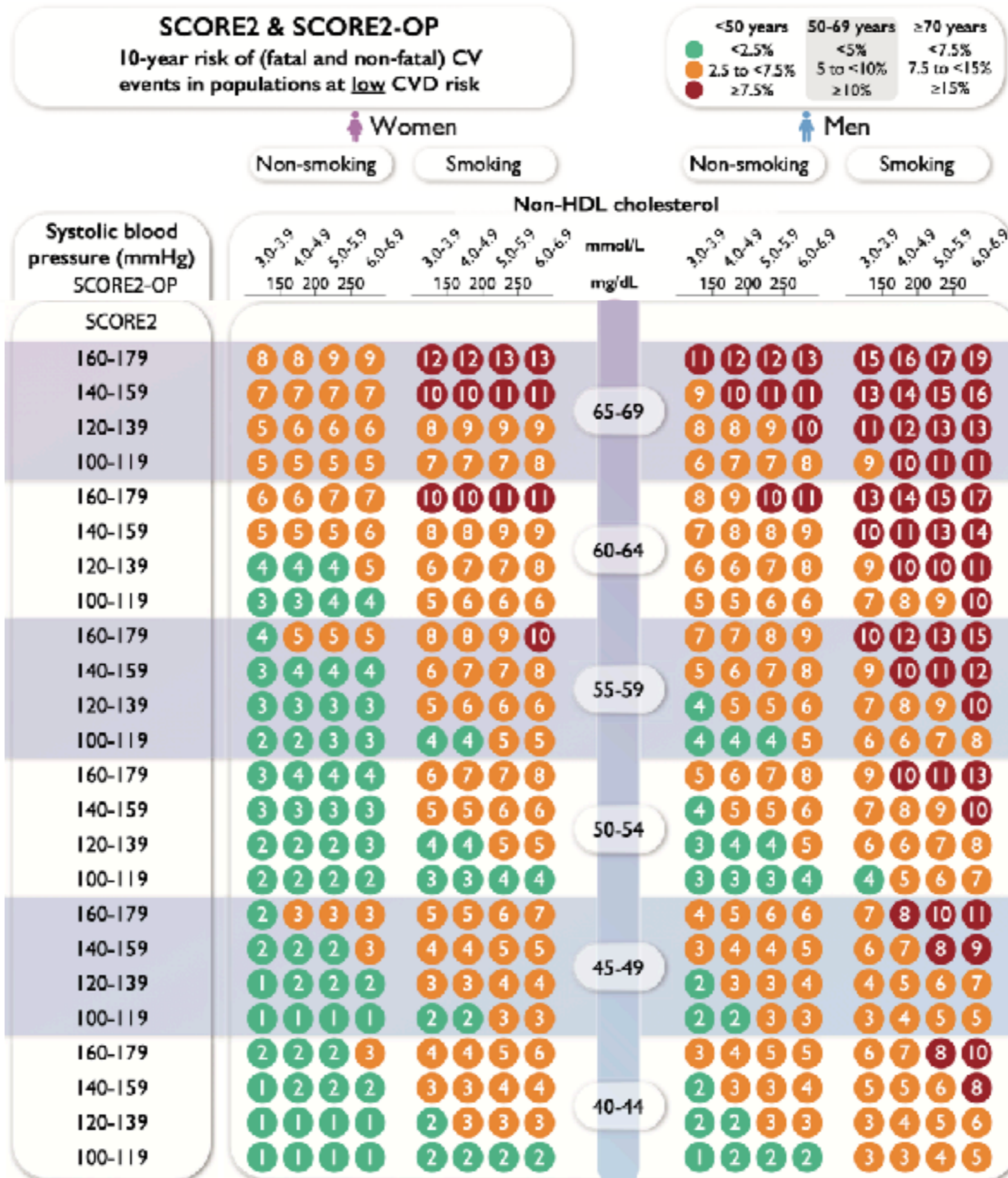
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)



SCORE2 & SCORE2-OP

10-year risk of (fatal and non-fatal) CV events in populations at **low** CVD risk

<50 years	50-69 years	≥70 years
● <2.5%	● <5%	● <7.5%
● 2.5 to <7.5%	● 5 to <10%	● 7.5 to <15%
● ≥7.5%	● ≥10%	● ≥15%

 **Women**

 **Men**

Non-smoking

Smoking

Non-smoking

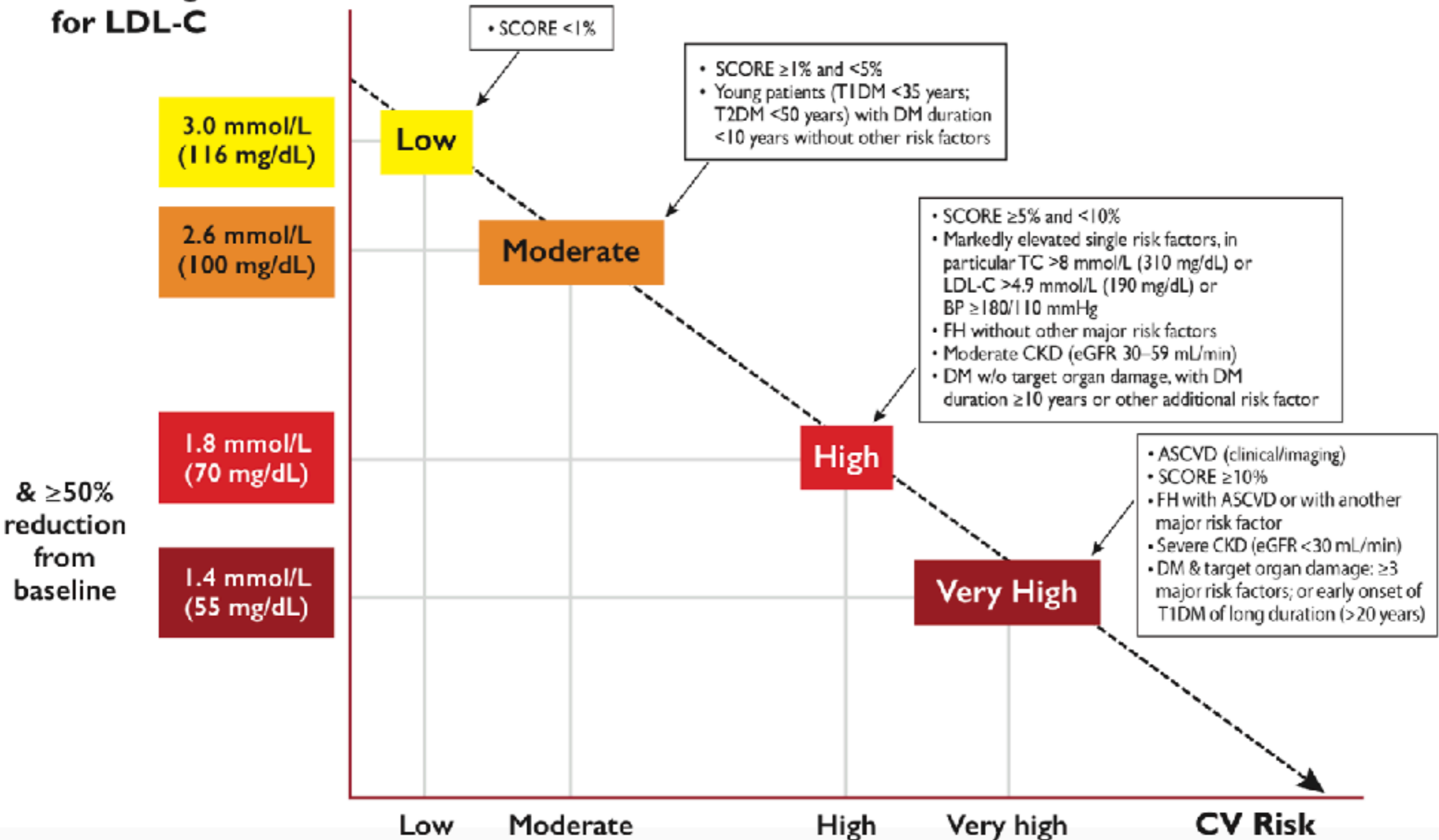
Smoking

Non-HDL cholesterol

Systolic blood pressure (mmHg) SCORE2-OP	3.0-3.9				4.0-4.9				5.0-5.9				6.0-6.9				mmol/L mg/dL	Age (y)	3.0-3.9				4.0-4.9				5.0-5.9				6.0-6.9										
	150	200	250		150	200	250		150	200	250		150	200	250				150	200	250		150	200	250		150	200	250												
160-179	28	29	30	31	31	32	33	34	29	35	42	49	29	35	42	49	85-89	29	35	42	49	28	33	40	47	27	33	40	47	26	32	38	45	26	32	38	45				
140-159	26	27	28	29	29	30	31	32	23	27	32	37	21	25	29	34	80-84	21	25	29	34	19	22	26	31	22	25	30	34	17	20	24	28	19	23	27	31				
120-139	24	25	26	27	27	28	29	30	16	17	18	19	16	18	21	23	75-79	16	18	21	23	14	15	18	20	18	20	23	26	12	13	15	17	15	17	19	22				
100-119	23	24	25	26	25	26	27	28	15	15	16	17	11	11	12	13	70-74	11	11	12	13	9	10	10	11	13	14	15	15	10	11	12	13	15	16	18	19	12	13	14	16
160-179	20	21	22	23	25	26	28	29	10	11	12	12	10	11	12	12		10	11	12	13	15	16	18	19	22	24	26	28	15	16	18	19	22	24	26	28				
140-159	18	19	20	21	23	24	25	26	9	9	10	10	9	9	10	10		9	9	10	10	12	13	14	16	18	19	21	23	12	13	14	16	18	19	21	23				
120-139	16	17	18	19	20	21	22	23	7	7	8	8	7	7	8	8		7	7	8	8	10	11	12	13	14	16	17	19	10	11	12	13	14	16	17	19				
100-119	15	15	16	17	18	19	20	21	6	6	6	7	6	6	6	7		6	6	6	7	8	8	9	10	12	13	14	15	8	8	9	10	12	13	14	15				

Risico-inschatting & doelen

Treatment goal
for LDL-C





Wie behandelen?

125

Jef, 50 jaar

- LDL-cholesterol 160 mg/dl
- Bloeddruk 120/80 mmHg, niet-roker, actief, geen HVZ in familie
- 3% kans op HVZ de komende 10 jaar
- Effect van statine (30% daling risico)=1%
- 100 mensen 10 jaar behandelen om 1 event te voorkomen

Zulma, 50 jaar

- LDL-cholesterol 110 mg/dl
- Bloeddruk 160/90 mmHg, rookster, DM, HVZ in familie
- 45% kans op HVZ de komende 10 jaar
- Effect van statine (30% daling risico)=15%
- 7 mensen 10 jaar behandelen om 1 event te voorkomen



Lipid lowering (CTT, n=170.000, 26 RCT)

126

Lowering LDL cholesterol by 1 mmol/l \equiv 39 mg/dl

-24% Revascularisation

-23% MI

-21% Vascular events

-19% Coronary deaths

-17% Stroke

-12% Overall mortality

These effects persist independent of:

- Primary or secondary prevention
- Age
- Hypertension
- Diabetes
- Baseline LDL cholesterol value



Veiligheid van statines?

OPEN ACCESS Freely available online



Lack of Effect of Lowering LDL Cholesterol on Cancer: Meta-Analysis of Individual Data from 175,000 People in 27 Randomised Trials of Statin Therapy

Cholesterol Treatment Trialists' (CTT) Collaboration¹

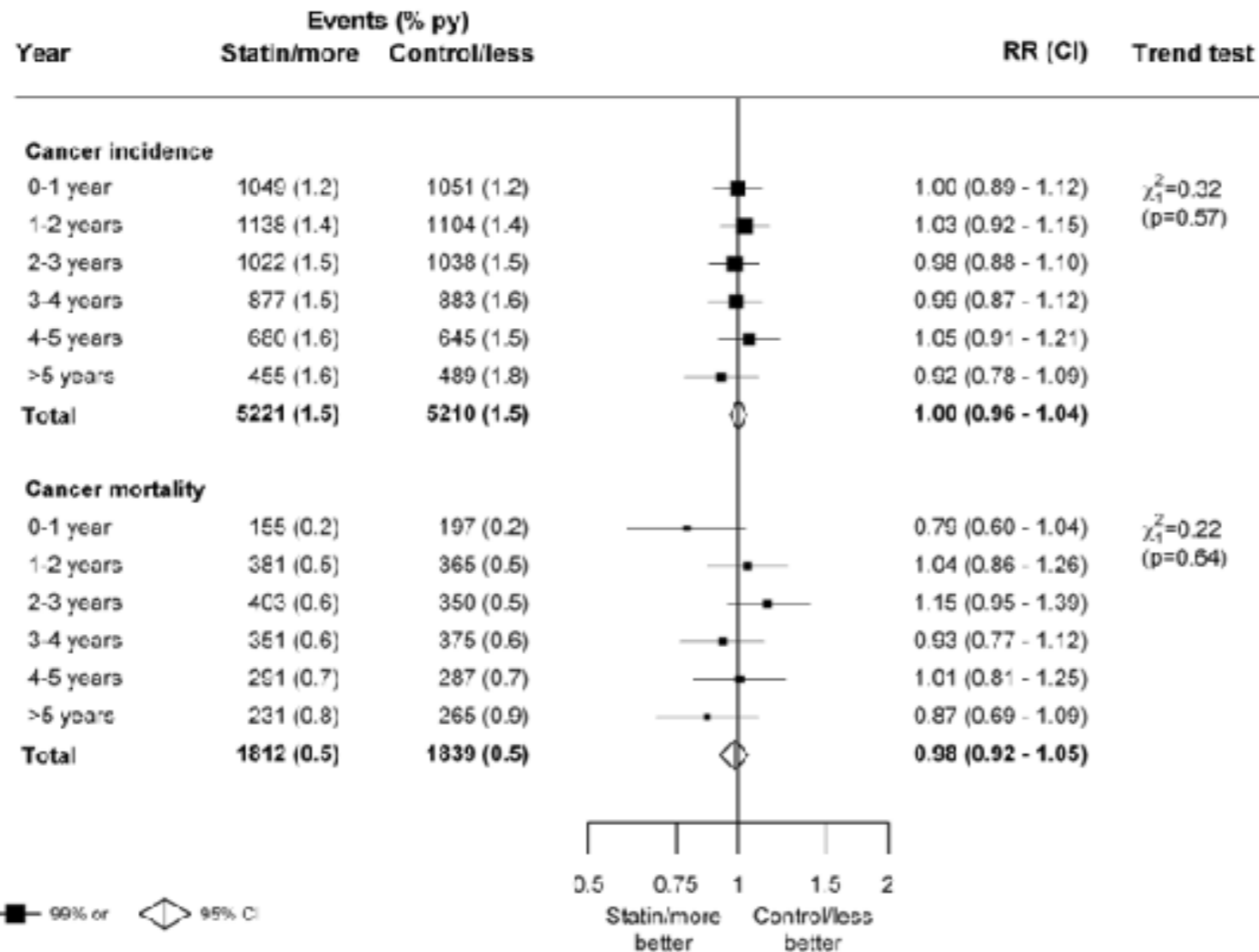


Figure 3. Effects of statin therapy on cancer incidence and mortality, by duration of treatment. Symbols and conventions as in Figure 1. doi:10.1371/journal.pone.0029849.g003



Statin associated muscle symptoms

- In observational/unblinded data up to 20% report statin associated muscle symptoms (SAMS).
- In unblinded / RCT data only 1-5% ! report statin associated muscle symptoms (SAMS). E.g. in HOPE-3: 5% muscle pain in the placebo group versus 6% in the statin group.
- Currently no biomarker to show/exclude that someone has SAMS.



ASCOT-LLA open label results

Adverse events associated with unblinded, but not with blinded, statin therapy in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid-Lowering Arm (ASCOT-LLA): a randomised double-blind placebo-controlled trial and its non-randomised non-blind extension phase

Ajay Gupta, David Thompson, Andrew Whitehouse, Tim Collier, Bjorn Dahlof, Neil Poulter, Rory Collins, Peter Sever, on behalf of the ASCOT Investigators

- Lipid-Lowering Arm of the Anglo-Scandinavian Cardiac Outcomes Trial.
- Patients aged 40–79 years with hypertension, at least three other cardiovascular risk factors, and fasting total cholesterol concentrations of 6.5 mmol/L or lower, and who were not taking a statin or fibrate, had no history of myocardial infarction, and were not being treated for angina.
- Atorvastatin 10 mg daily or matching placebo in a randomised double-blind placebo-controlled study.



ASCOT-LLA open label results

Randomised phase

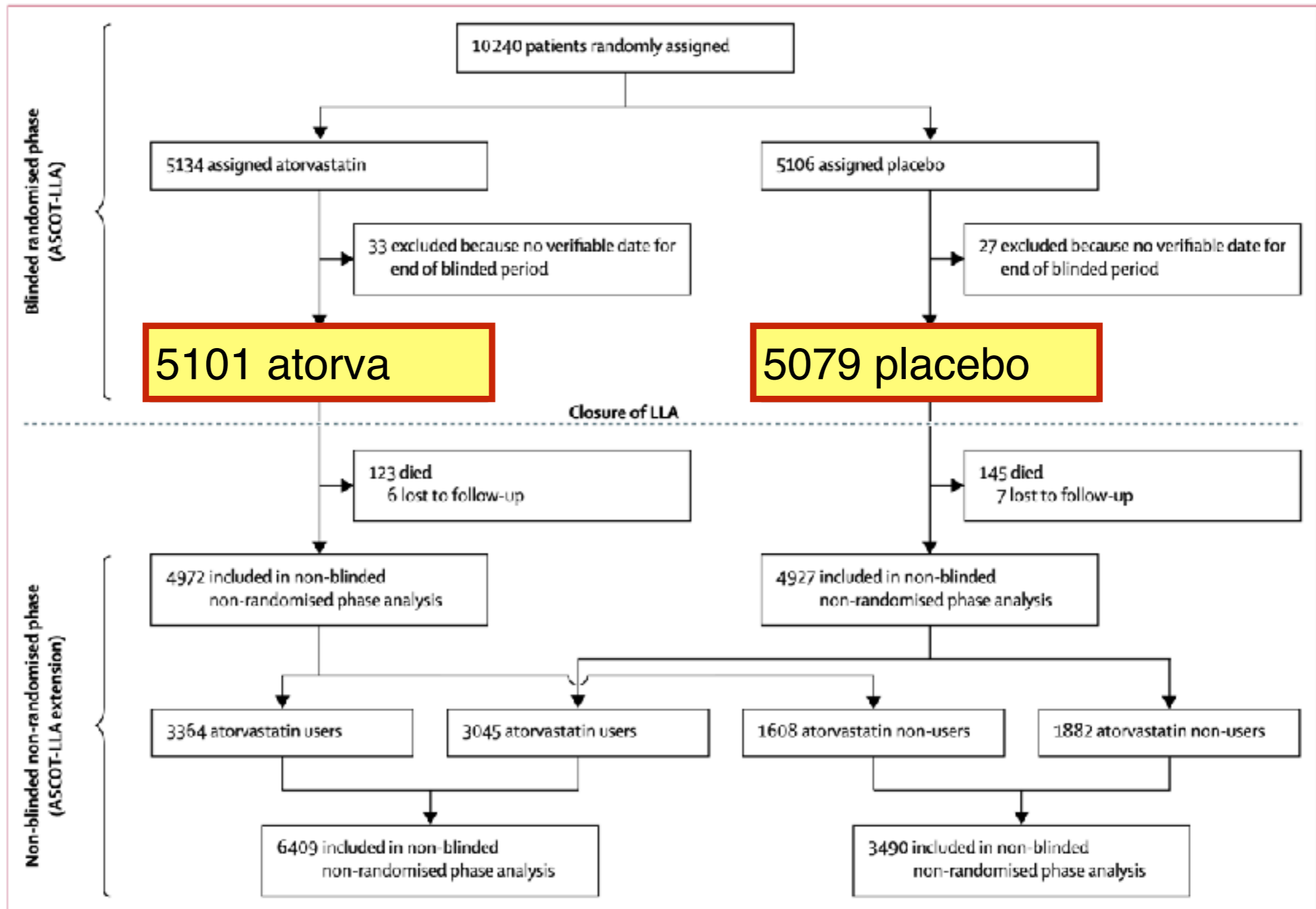


Figure 1: Trial profile

ASCOT=Anglo-Scandinavian Cardiac Outcomes Trial. LLA=Lipid-Lowering Arm.



ASCOT-LLA open label results

Randomised phase

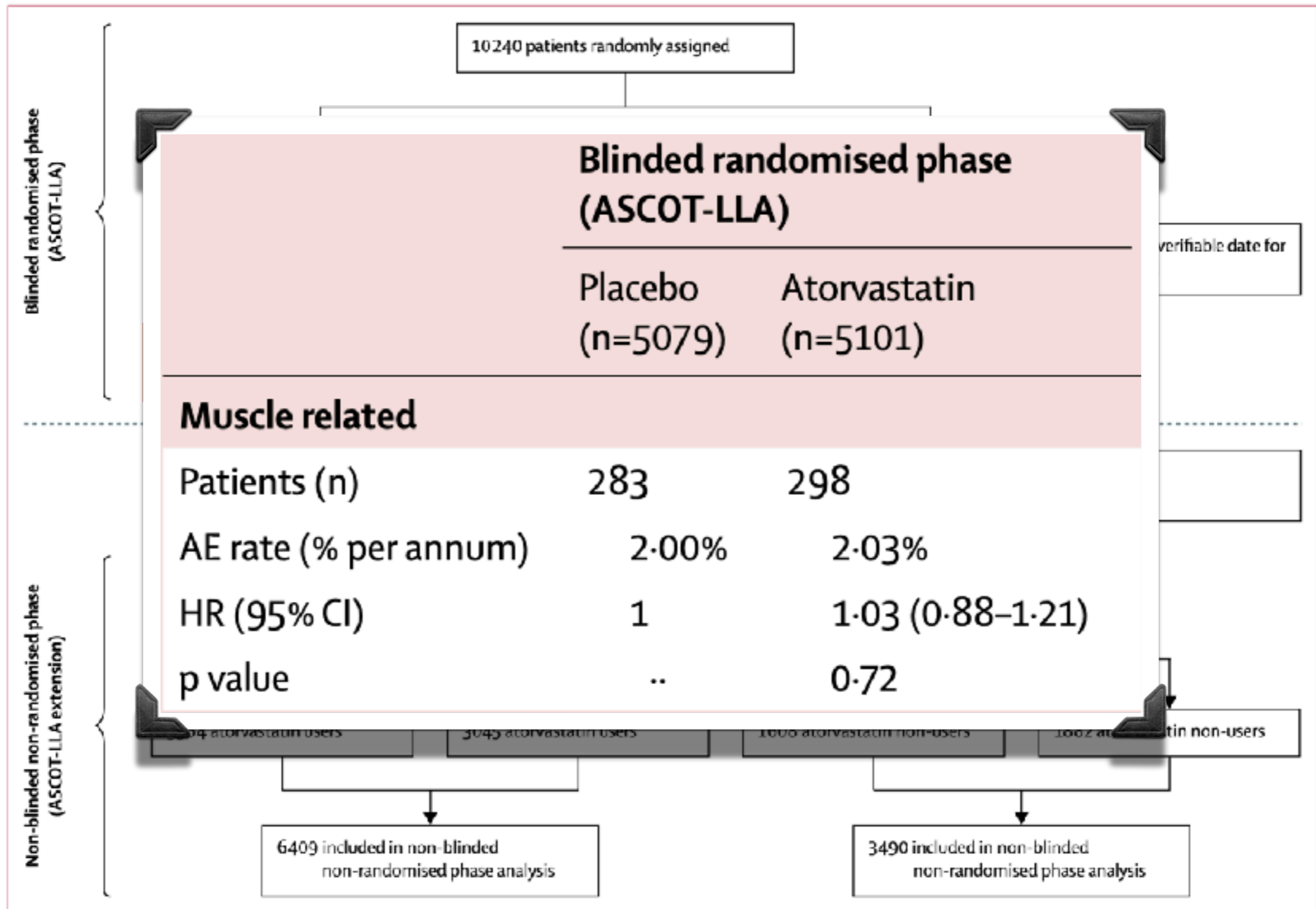


Figure 1: Trial profile

ASCOT=Anglo-Scandinavian Cardiac Outcomes Trial. LLA=Lipid-Lowering Arm.



ASCOT-LLA open label results

Randomised phase

Non-randomised
OLE

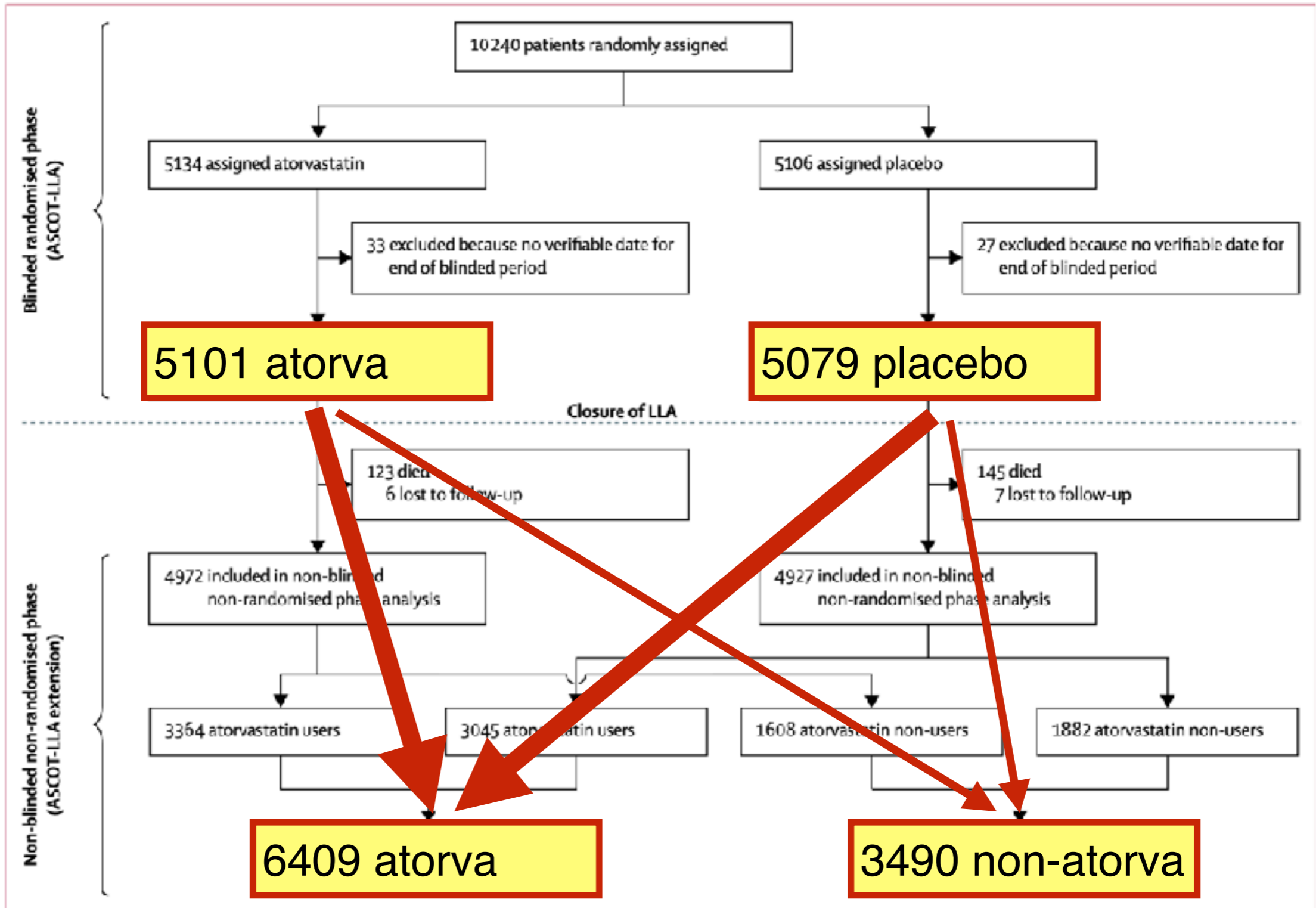


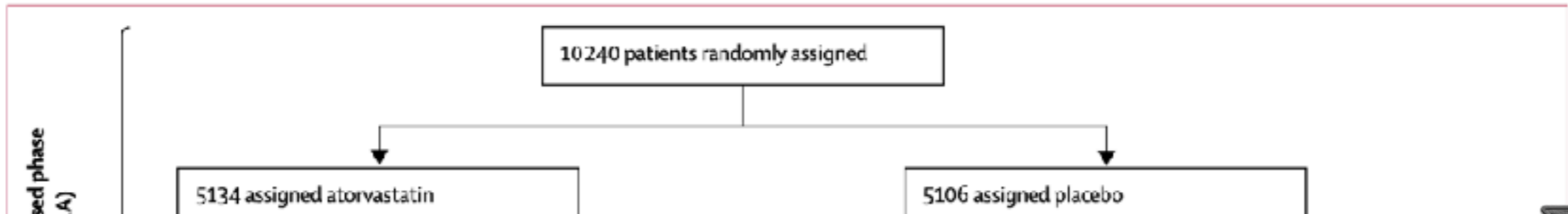
Figure 1: Trial profile

ASCOT=Anglo-Scandinavian Cardiac Outcomes Trial. LLA=Lipid-Lowering Arm.



ASCOT-LLA open label results

Blinded phase



Blinded randomised phase (ASCOT-LLA)

Non-blinded non-randomised phase

	Placebo (n=5079)	Atorvastatin (n=5101)	Atorvastatin non-user (n=3490)	Atorvastatin user (n=6409)
--	---------------------	--------------------------	-----------------------------------	-------------------------------

Muscle related

Patients (n)	283	298	124	161
AE rate (% per annum)	2.00%	2.03%	1.00%	1.26%
HR (95% CI)	1	1.03 (0.88-1.21)	1	1.41 (1.10-1.79)
p value	..	0.72	..	0.006

Non-blinded phase

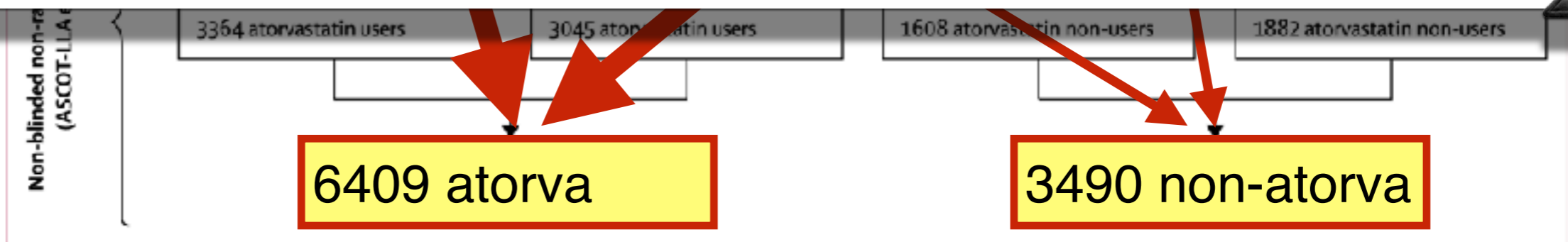


Figure 1: Trial profile

ASCOT=Anglo-Scandinavian Cardiac Outcomes Trial. LLA=Lipid-Lowering Arm.



ASCOT-LLA open label results

	Blinded randomised phase (ASCOT-LLA)		Non-blinded non-randomised phase	
	Placebo (n=5079)	Atorvastatin (n=5101)	Atorvastatin non-user (n=3490)	Atorvastatin user (n=3490)
Muscle related				
Patients (n)	283	298		
AE rate (% per annum)	2.00%	2.03%		
HR (95% CI)	1	1		
p value				
Erectile dysfunction				
Patients (n)				
AE rate (% per annum)			0.66%	0.56%
HR (95% CI)		0.59 (0.56-0.85)	1	0.87 (0.63-1.20)
p value		0.0005	..	0.40
Patients (n)	32	31	36	22
AE rate (% per annum)	0.22%	0.20%	0.29%	0.17%
HR (95% CI)	1	0.94 (0.57-1.54)	1	0.59 (0.34-1.02)
p value	..	0.81	..	0.06

Evidence for a clear NOCEBO-effect!
 ...these analyses could well underestimate the magnitude of the nocebo effect because the ASCOT-LLA was done during 1998–2005, before claims that statin therapy causes high rates of side-effects had become as common as they are now.



SAMS-CI score

Klinische symptomen (nieuwe of onverklaarde spierklachten)	
Regionaal patroon (selecteer hoogste toepasbare puntenaantal)	
Symmetrisch heupflexoren / dijbeen	3
Symmetrische kuitspierpijn	2
Symmetrische pijn proximaal bovenste ledematen	2
Aspecifieke, assymetrische of intermitterende pijn	1
Tijdspatroon	
Klachten starten binnen de 4 weken na start statine	3
Klachten starten tussen 4-12 weken na start statine	2
Klachten starten >12 weken na start statine	1
De-challenge (evolutie na stoppen statine)	
Beterschap na stoppen <2 weken	2
Beterschap na stoppen pas binnen 2-4 weken	1
Geen beterschap na stoppen binnen de 4 weken	0
Re-challenge (evolutie na herstarten statine)	
Zelfde klachten treden terug op binnen de 4 weken	3
Zelfde klachten treden terug op pas na 4-12 weken	1
Statin Myalgia Clinical Index Score	
<i>Pijn waarschijnlijk statine gerelateerd</i>	<i>9-11 punten</i>
<i>Pijn mogelijks statine gerelateerd</i>	<i>7-8 punten</i>
<i>Pijn waarschijnlijk NIET statine gerelateerd</i>	<i><7 punten</i>



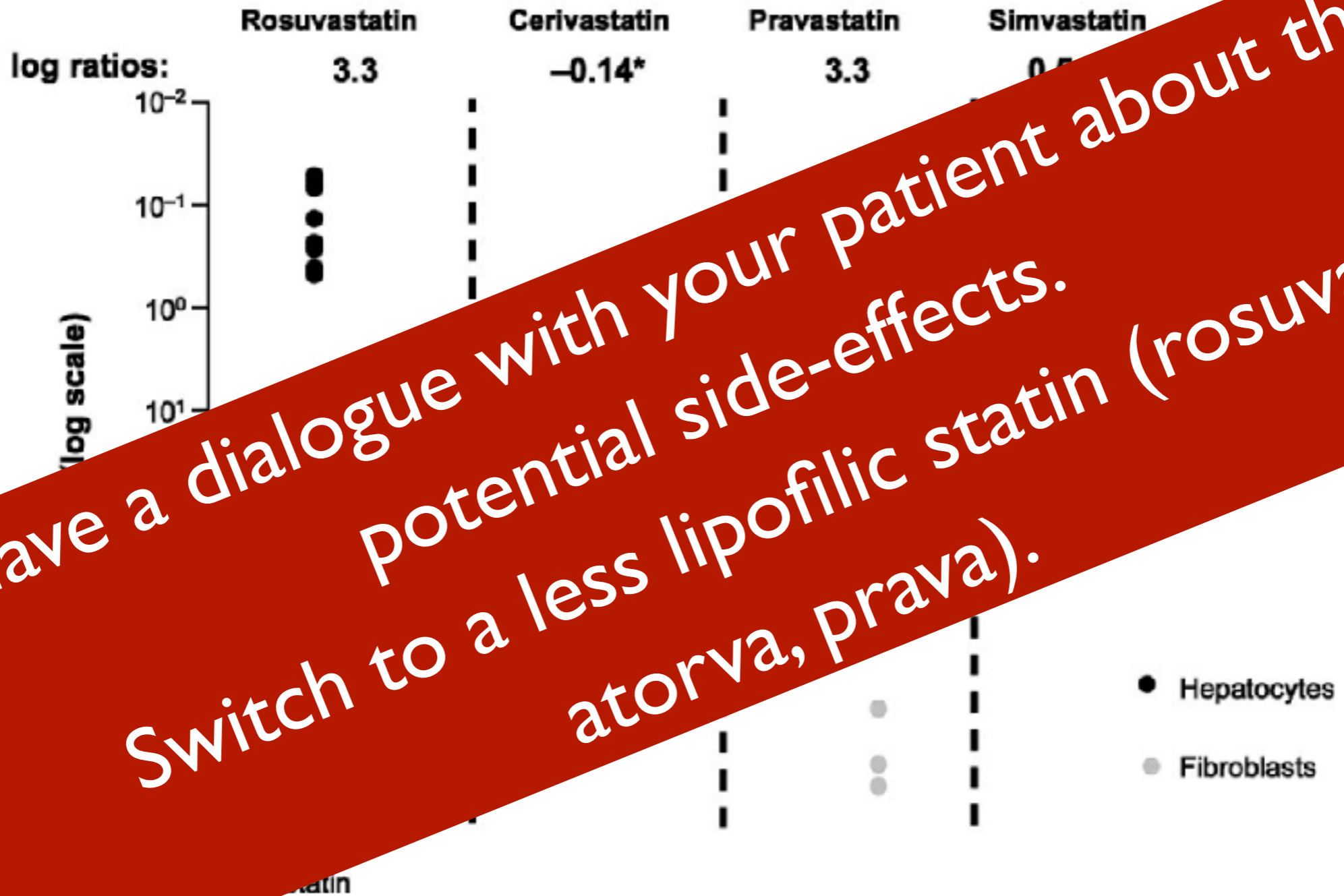
SAMS-CI score

Klinische symptomen (nieuwe of onverklaarde spierklachten)	
Regionaal patroon (selecteer hoogste toepasbare puntenaantal)	
Symmetrisch heupflexoren / dijbeen	
Symmetrische kuitspierpijn	
Symmetrische pijn proximaal bovenste ledematen	
Aspecifieke, assymetrische of intermitterende pijn	
Tijdspatroon	
Klachten starten binnen de 4 weken na start statine	3
Klachten starten tussen 4-12 weken na start	2
Klachten starten >12 weken na start	1
De-escalatie (evolutie na herstarten statine)	
Beterschap na stopzetting statine	2
Beterschap na herstarten statine	1
Geen beterschap na 4 weken	0
Statine Myalgia Clinical Index Score	
Pijn waarschijnlijk statine gerelateerd	9-11 punten
Pijn mogelijks statine gerelateerd	7-8 punten
Pijn waarschijnlijk NIET statine gerelateerd	<7 punten

1. Have a dialogue with your patient about the potential side-effects.



Comparative pharmacology of statins



1. Have a dialogue with your patient about the potential side-effects.

2. Switch to a less lipophilic statin (rosuva, atorva, prava).

Fig. 2. The 50% inhibitory concentration (IC₅₀) values for inhibition of cholesterol synthesis in primary rat hepatocytes and cultured fibroblasts by rosuvastatin and other statins, and log ratios of the IC₅₀ values. From McTaggart et al. [10].



Comparative pharmacology of statins



1. Have a dialogue with your patient about the potential side-effects

2. Switch to a less lipophilic statin (rosuva, atorva, prava)

3. Alternate day dosing !!

Fig. 2. The 50% inhibitory (IC₅₀) values for inhibition of cholesterol synthesis in primary rat hepatocytes and cultured fibroblasts by rosuvastatin and cerivastatin. The log ratios of the IC₅₀ values. From McTaggart et al. [10].



StatinWISE & SAMSON

Statin treatment and muscle symptoms: series of randomised, placebo controlled n-of-1 trials

Emily Herrett,¹ Elizabeth Williamson,² Kieran Brack,³ Danielle Beaumont,³ Alexander Perkins,² Andrew Thayne,³ Haleema Shakur-Still,³ Ian Roberts,³ Danielle Prowse,³ Ben Goldacre,⁴ Tjeerd van Staa,⁵ Thomas M MacDonald,⁶ Jane Armitage,⁷ Jon Wimborne,⁸ Paula Melrose,⁸ Jayshreen Singh,⁹ Lucy Brooks,¹⁰ Michael Moore,¹¹ Maurice Hoffman,¹² Liam Smeeth,¹ on behalf of the StatinWISE Trial Group

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

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Side Effect Patterns in a Crossover Trial of Statin, Placebo, and No Treatment

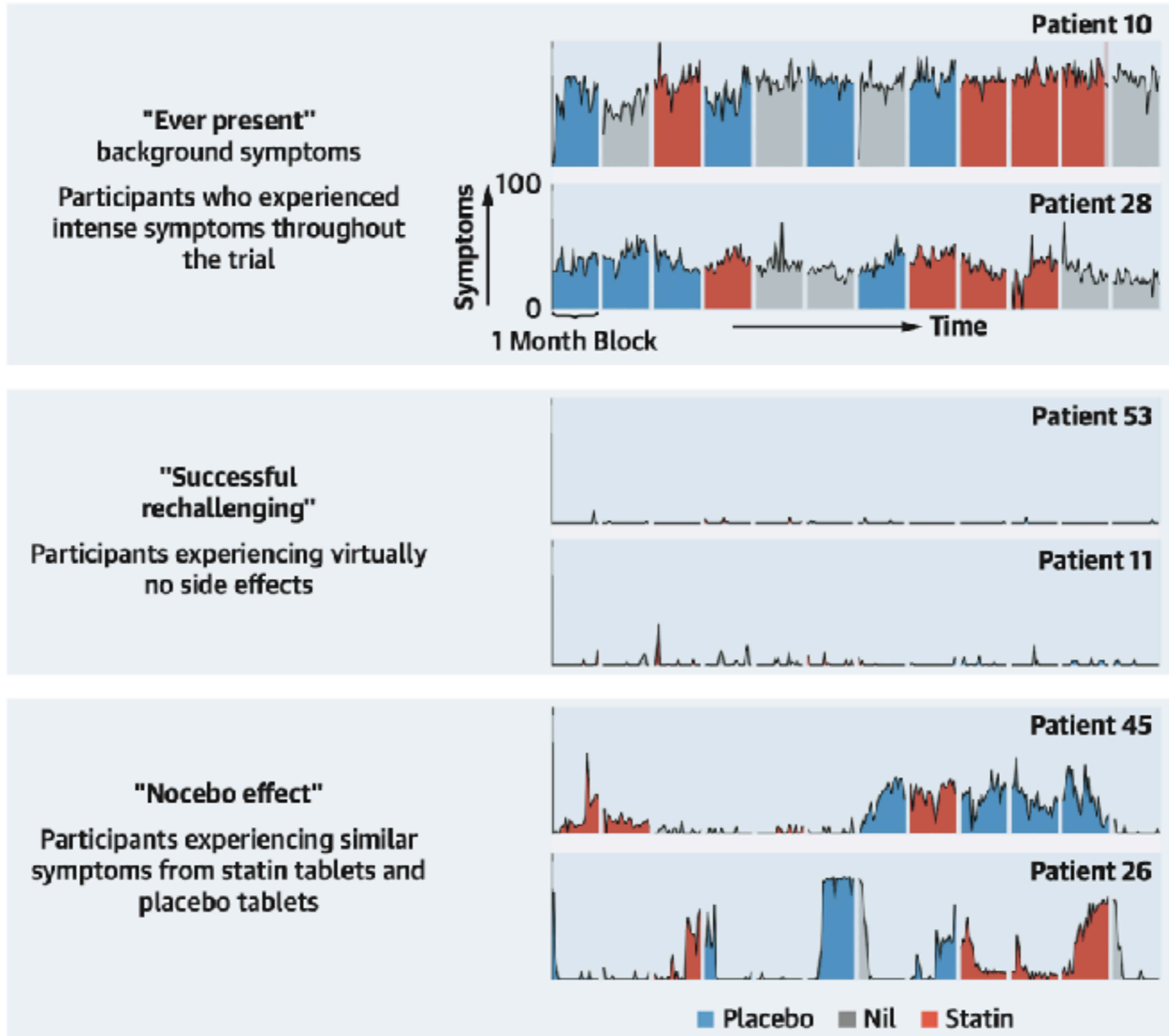


James P. Howard, PhD,^{a,*} Frances A. Wood, MPhil,^{a,*} Judith A. Finegold, PhD,^a Alexandra N. Nowbar, MBBS,^a David M. Thompson, PhD,^a Ahran D. Arnold, MBBS,^a Christopher A. Rajkumar, MBBS,^a Susan Connolly, PhD,^a Jaimini Cegla, PhD,^b Chris Stride, PhD,^c Peter Sever, PhD,^a Christine Norton, PhD,^d Simon A.M. Thom, MD,^a Matthew J. Shun-Shin, PhD,^a Darrel P. Francis, MA^a



StatinWISE & SAMSON

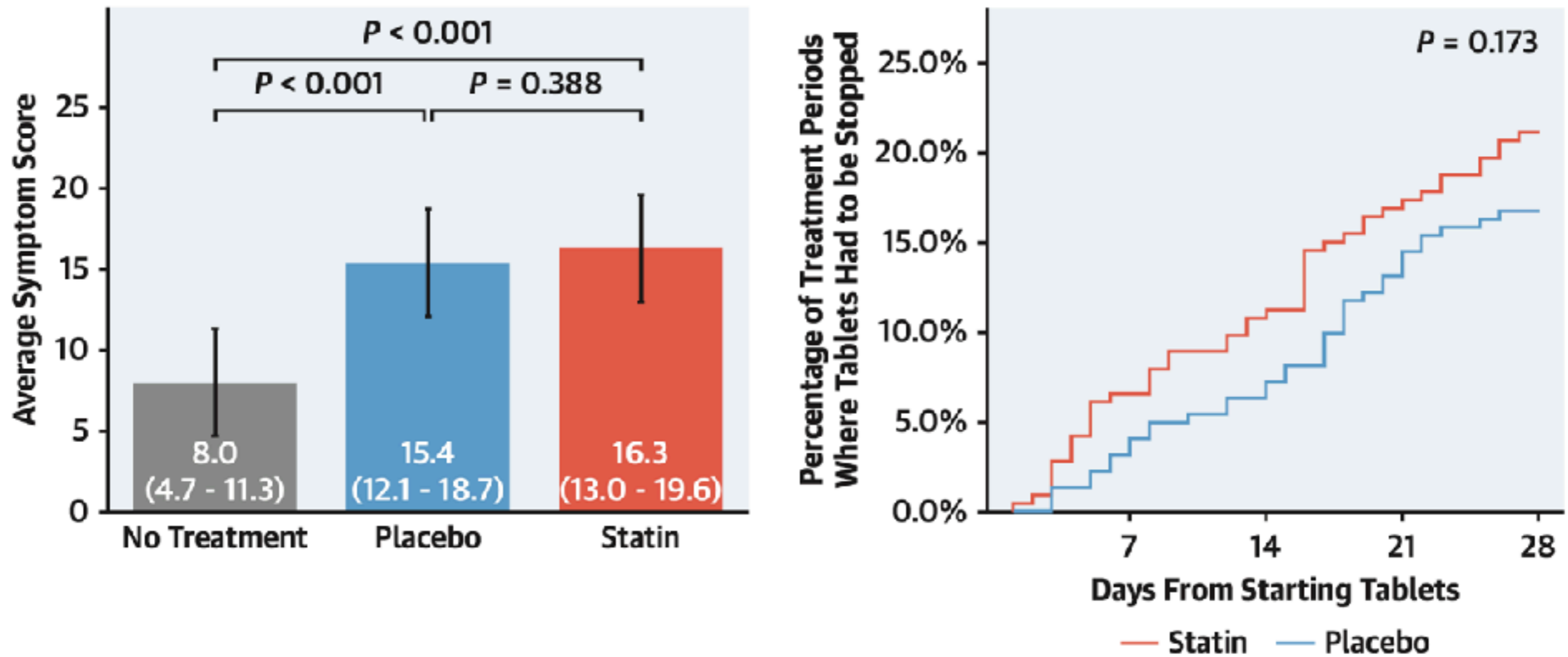
Some Symptomatic Patterns Seen During SAMSON





StatinWISE & SAMSON

CENTRAL ILLUSTRATION Symptom Scores and Cumulative Early Tablet Stopping Rates by Treatment



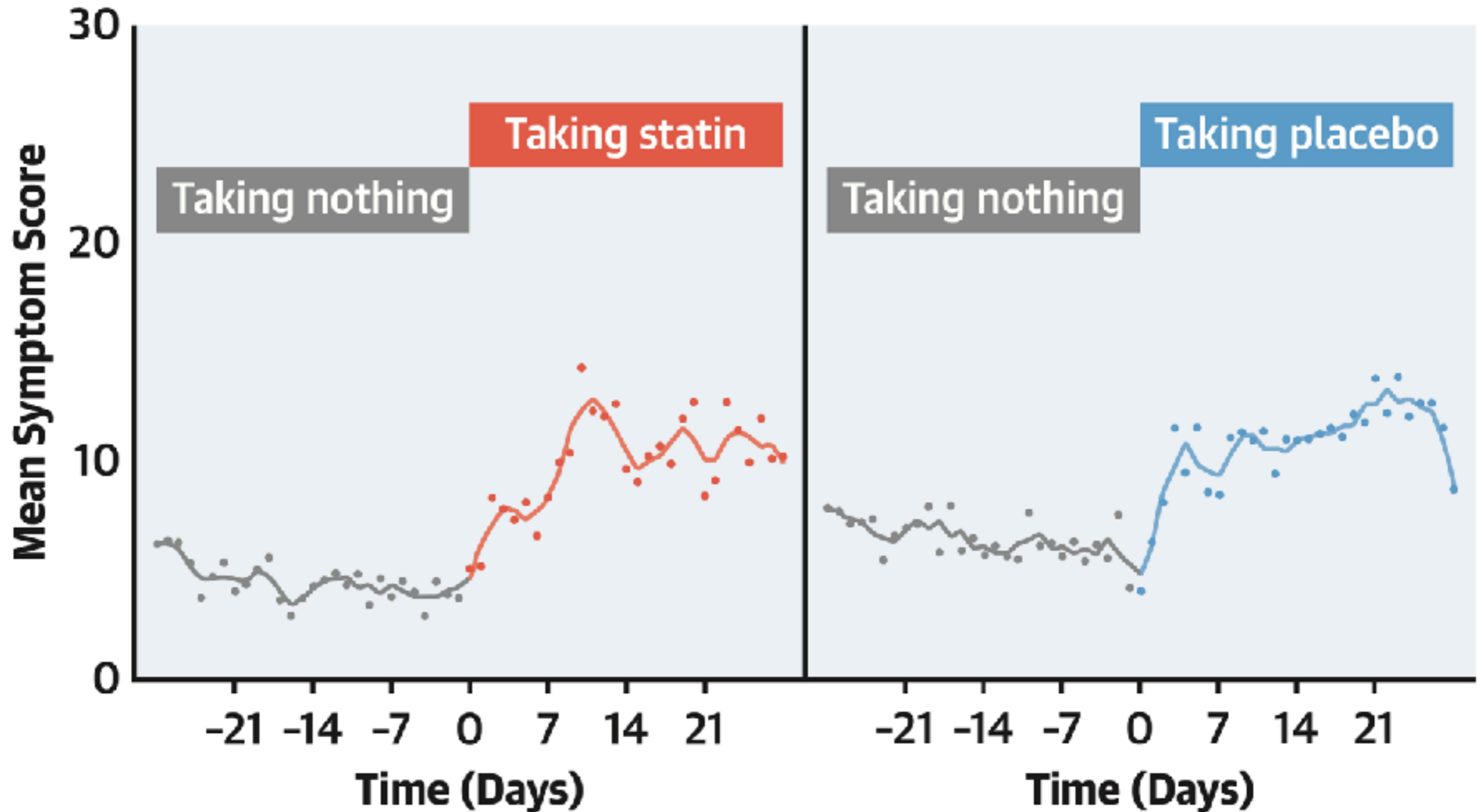
Howard, J.P. et al. J Am Coll Cardiol. 2021;78(12):1210-1222.

(Left) The mean symptom scores across the 3 treatment types (statin, placebo, and no treatment). **Whiskers** indicate the associated 95% CIs. **(Right)** The cumulative rate of stopping tablets for patients starting a statin (**red**) or placebo (**blue**) after a no-tablet month. *P* value derived from a mixed-effects logistic regression model.



StatinWISE & SAMSON

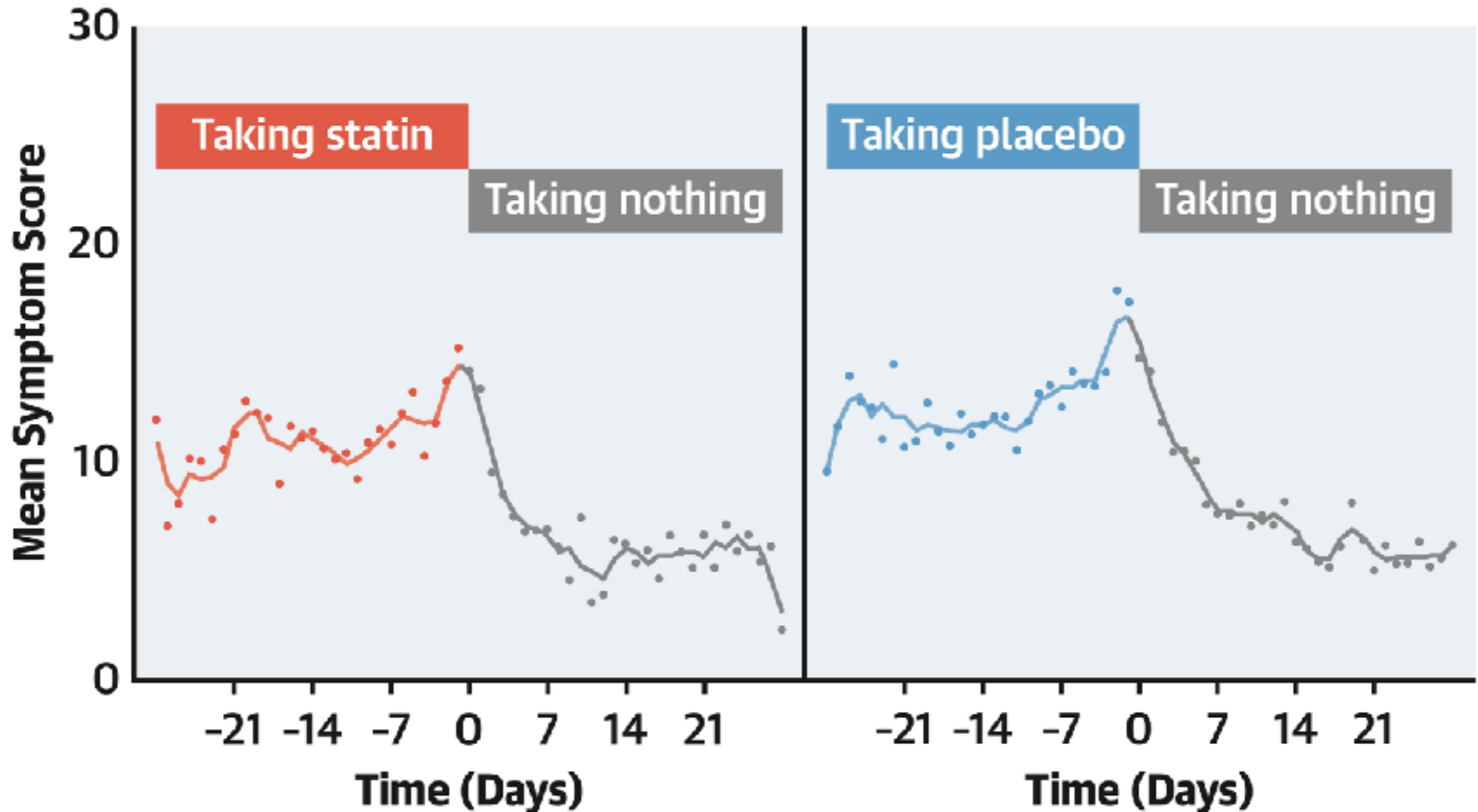
Symptom Time Course in Days Before and After Starting Tablets





StatinWISE & SAMSON

Symptom Time Course in Days Before and After Stopping Tablets





SAMSON

- Majority of symptoms caused by statin tablets are verifiable but are driven by the act of taking tablets rather than whether the tablets contain a statin (nocebo).
- Clinicians should not interpret symptom intensity or timing of symptom onset or offset as indicating pharmacological causation, because the pattern is identical for placebo.
- The cues and informal experiments patients and clinicians use to test causation can ***paradoxically*** confirm a nonexistent association.
- This error is prevented by a scheduled, 3-armed, crossover trial containing no-tablet periods. Participating in such a protocol allows one-half of patients with reported side effects to successfully restart statins



StatinWISE & SAMSON

Global Spotlights

Nocebo/drucebo effect in statin-intolerant patients: an attempt at recommendations

Peter E. Penson ^{1,2*} and Maciej Banach ^{3,4}

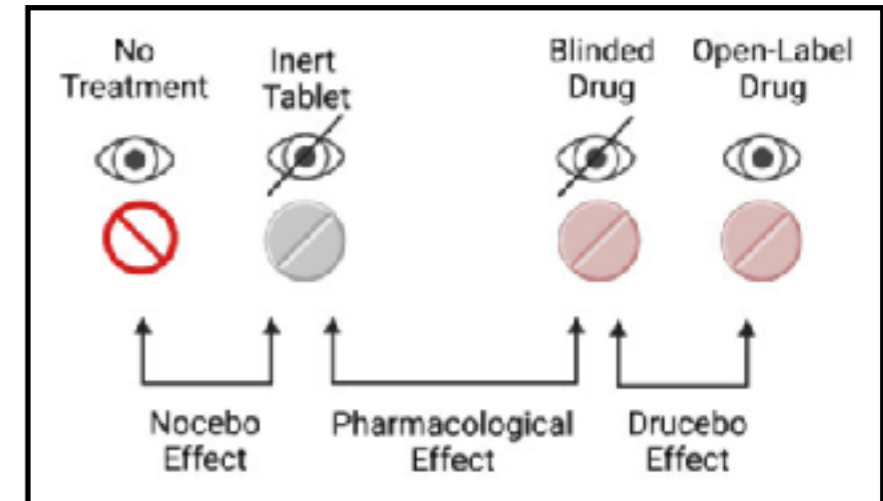


Table 1 A summary of major studies investigating the nocebo/drucebo effect with statin therapy

	Design	Participants	Intervention	Comparator	Nocebo/drucebo contribution to SAMS	Resumption of therapy
IILEP and LBPMCG	Meta-analysis	11 180	Open-label statin (various)	Blinded statin (various)	Drucebo contributed to between 38% and 78% of muscle pain.	NR
SAMSON	Series of n-of-1 RCTs	60 patients reporting statin side-effects	Atorvastatin 20 mg/day	Placebo and no treatment	No difference in symptom intensity between statin and placebo.	57% had, or intended to restart statin 6 months after trial
StatinWISE	Series of n-of-1 RCTs	200 with SAMS	Atorvastatin 20 mg/day	Placebo	No difference in symptom intensity between statin and placebo.	66% had or intended to restart statin at trial end.

IILEP, International Lipid Expert Panel; LBPMCG, Lipid and Blood Pressure Meta-analysis Collaboration Group; NR, not reported; RCT, randomized controlled trial; SAMS, statin-associated muscle symptoms; SAMSON, Statin Side-effects Or Nocebo Trial.



Empowerment

Uiteindelijk is een individu is verantwoordelijk voor zijn gezonde levensstijl



Empowerment

Uiteindelijk is een individu is verantwoordelijk voor zijn gezonde levensstijl, op voorwaarde dat dat individu begrijpt wat een gezonde levensstijl is, de middelen heeft en de omgeving het toelaat om gezond te leven.



Empowerment

Uiteindelijk is een individu is verantwoordelijk voor zijn gezonde levensstijl, op voorwaarde dat dat individu “empowered” is!



Empowerment

EMPOWERMENT :

“...the process of shifting a patient’s mentality from a passive recipient of health care towards an active role where they understand their condition, their role in the health care process, and take self-initiated actions to benefit their health...”



1. Je hebt hoge bloeddruk als je bloeddruk gemiddeld
 - meer is dan 140 mmHg bovendruk en/of
 - meer dan 90 mmHg onderdruk (bij suikerziekte > 85 mmHg)
2. Bij twijfel: laat je bloeddruk regelmatig controleren. Een bloeddruk schommelt, dit is normaal.
3. Als je zelf meet: op vaste tijdstippen
4. Meestal is er niet echt een oorzaak van hoge bloeddruk behalve de veroudering (verstijving) van je slagaders. Zoeken naar een oorzaak (via specialist) is meestal niet nuttig.



1. Wat kun je zelf doen?

- Vermageren: 10% vermagering kan gemakkelijk de bloeddruk 10-20 mmHg doen zakken
- Sporten
- Zoutbeperking (alles met mate)

2. Wat zal je huisarts (of specialist) doen?

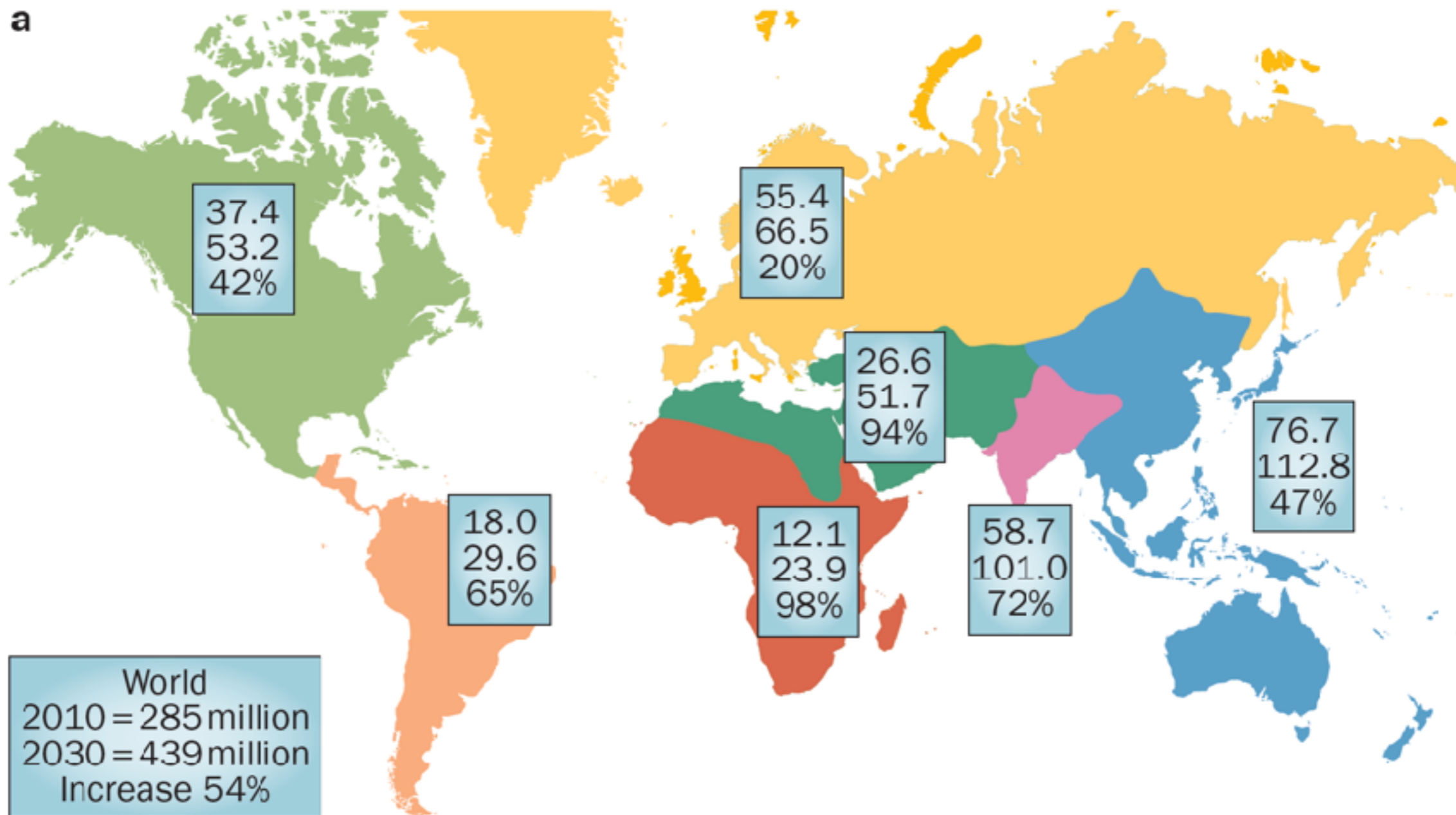
- Vaak hebben we meerdere producten in combinatie nodig hebben om de bloeddruk onder controle te krijgen.

Stockbeheer en diabetes





Diabetes wereldwijd 2010-2030





ApneaLink AL-plus

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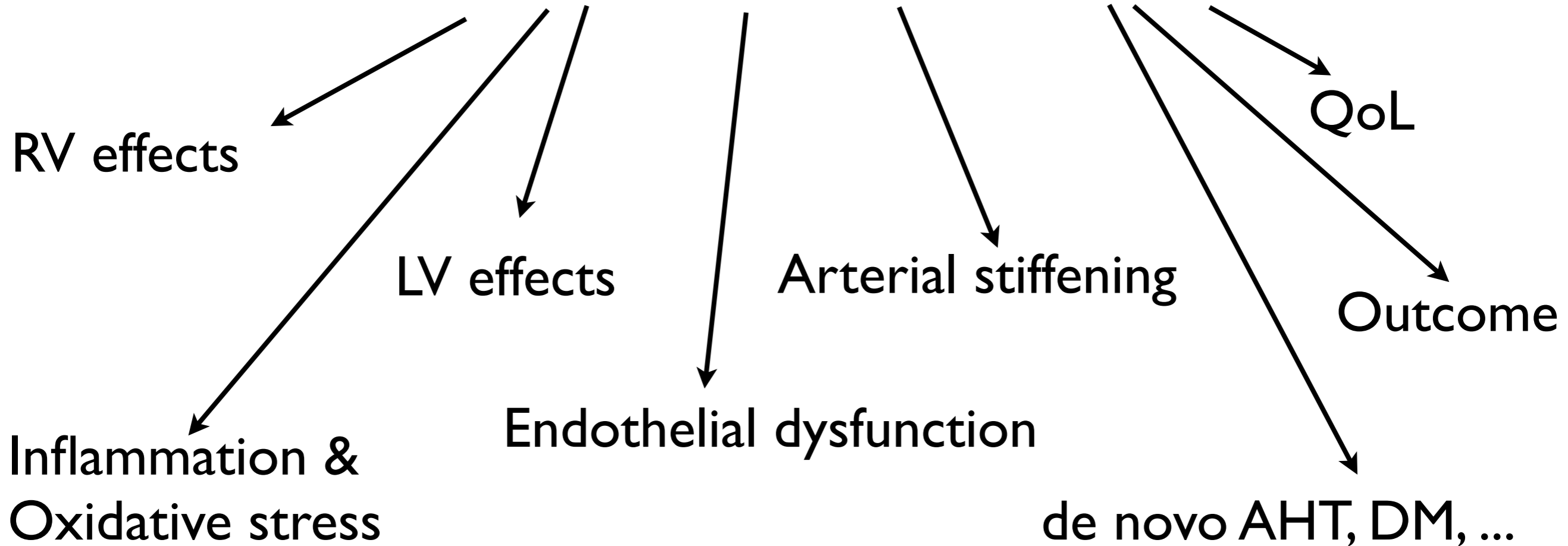
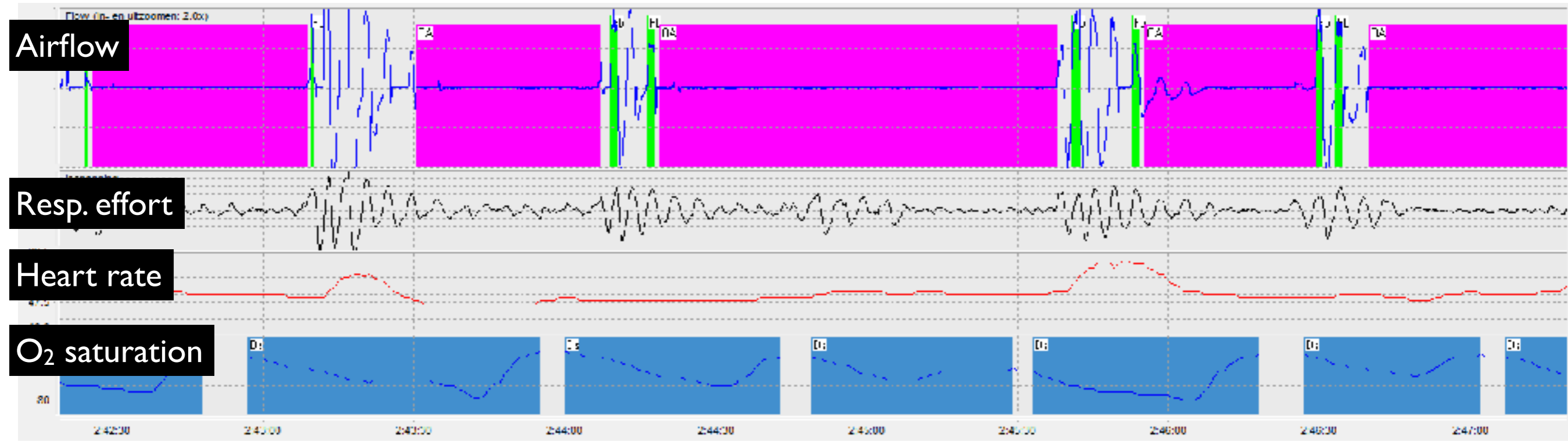


ApneaLink is a simple, cost-effective sleep-screening tool that objectively identifies patients at risk for obstructive sleep apnea (OSA).



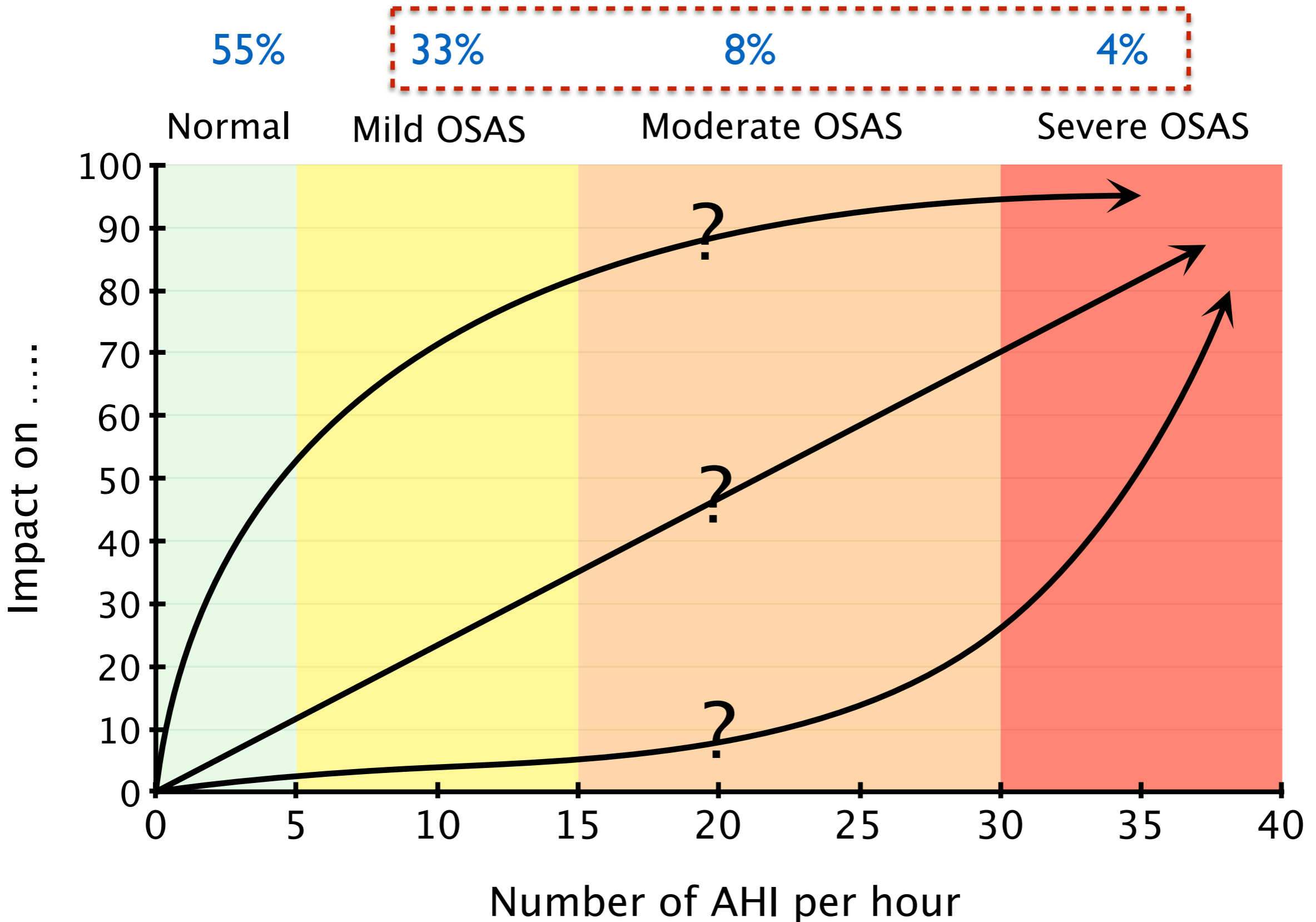


ASKLEPIOS sleep disordered breathing



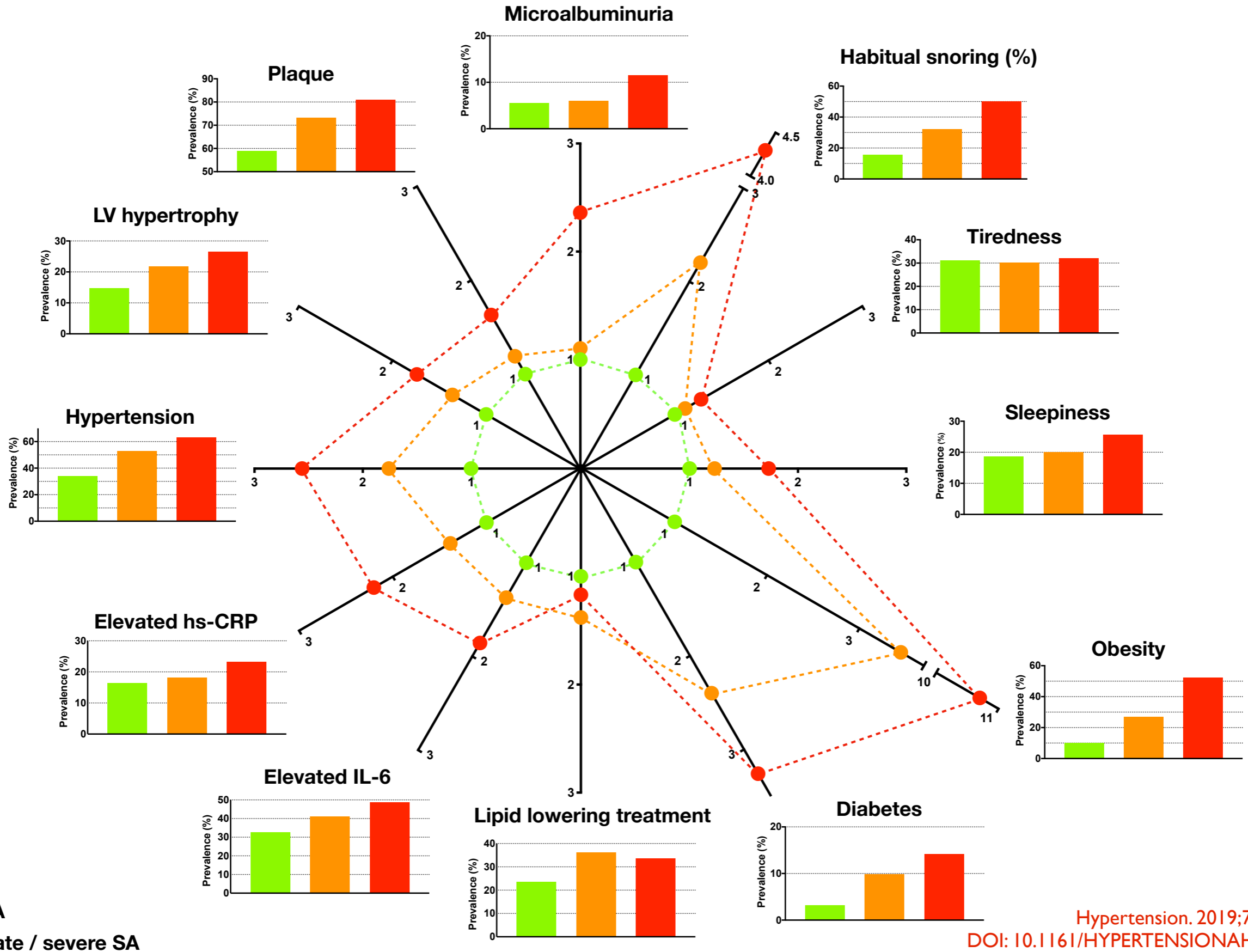


ASKLEPIOS sleep disordered breathing





ASKLEPIOS sleep disordered breathing





5) "Lifecourse" prevention



THE LANCET



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A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the *Lancet* Commission on hypertension

Michael H Olsen, Sonia Y Angell, Samira Asma, Pierre Boutouyrie, Dylan Burger, Julio A Chirinos, Albertino Damasceno, Christian Delles, Anne-Paule Gimenez-Roqueplo, Dagmara Hering, Patricio López-Jaramillo, Fernando Martinez, Vlado Perkovic, Ernst R Rietzschel, Giuseppe Schillaci, Aletta E Schutte, Angelo Scuteri, James E Sharman, Kristian Wachtell, Ji Guang Wang*



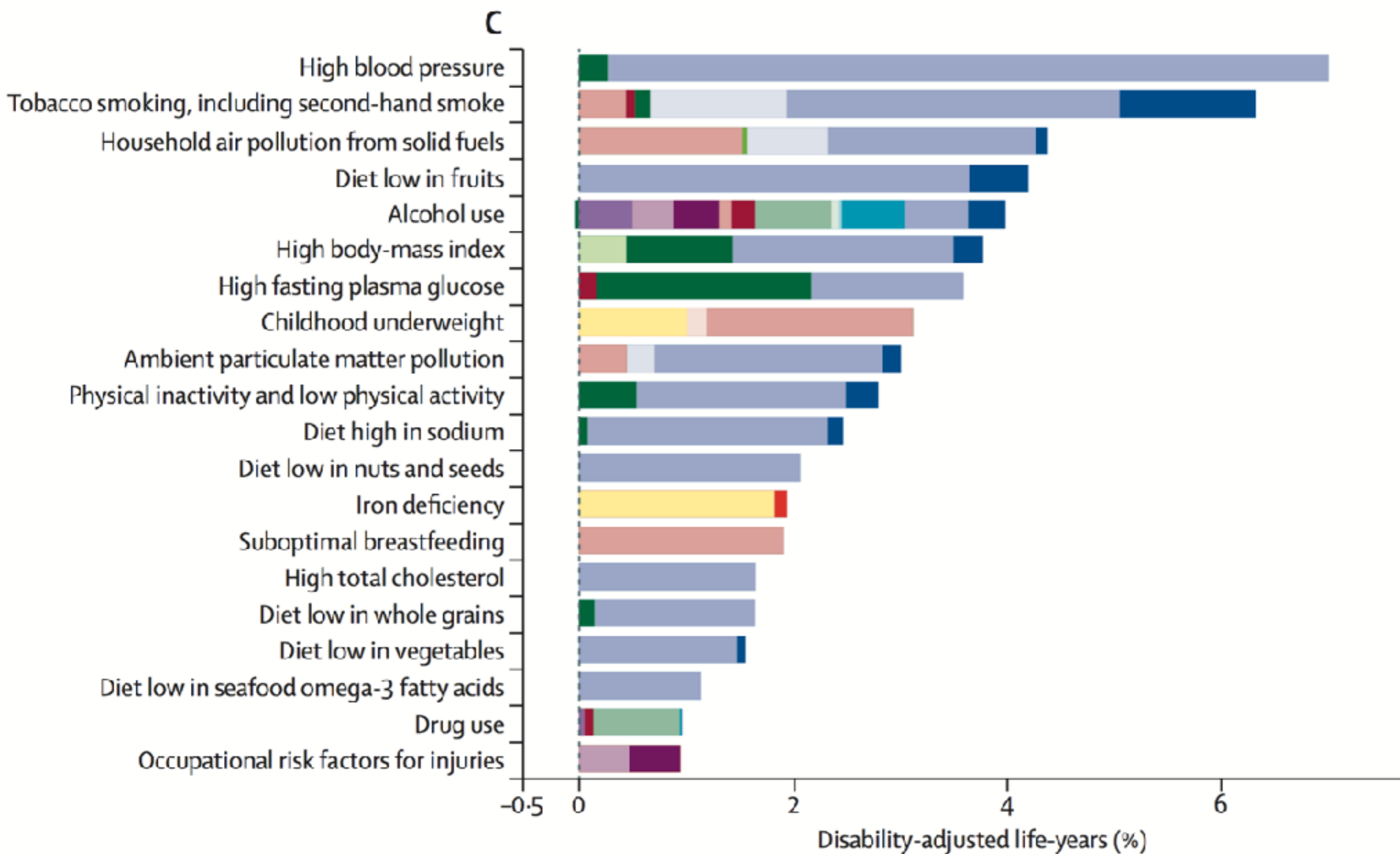
A global view....

- (i) Roken is vooral een prioriteit in?
- (ii) Welke technologie deed de laatste 25 jaar de bloeddruk van een heel continent dalen?
- (iii) Wat is in Mozambique de medicamenteuze top-prioriteit voor de aanpak van hypertensie?
- (iv) Web-connected mobiele ECG's gaan een grote impact hebben op infarctoverleving in Latur, Maharashtra, India?



Global burden of diseases

161





A global view....

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Public health-a-lease

163

- Decoupling of seasonal fresh fruit and vegetable intake



- Decoupling of seasonal fresh fruit and vegetable intake





A global view....

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GLOBAL STATUS REPORT on noncommunicable diseases 2014

"Attaining the nine global noncommunicable diseases targets: a shared responsibility"



People | 2.15 World Development Indicators: Health systems

	Health expenditure				per capita	Health workers		Hospital beds per 1,000 people 2007-12	Completeness of birth registration 2008-14 %	Completeness of death registration 2007-13 %	
	Total	Public	Out of pocket	External resources		Physicians /1 000 people	Nurses /1 000 people				
	% of GDP	% of total	% of total	% of total							\$
2013	2013	2013	2013	2013			2007-12	2008-14	2007-13		
Belgium	11.2	75.8	19.9	..	5,093	4,526	4.9	16.8	6.5	100.0	100.0
Mozambique	46.4	6.4	48.4	40	71	0.0	0.4	0.7	47.9	..	

Belgium

Mozambique

Physicians
/1 000 people

4.9

0.0

... in low-income countries there is only 0.1 physician and 0.5 nurse for every 1 000 people, and even in high-income countries, figures of 3.1 physicians and 8.6 nurses per 1 000 are insufficient to carry out this important task effectively...



Mozambique gets 64 new doctors

6:44 CAT | 20 Dec 2018

0 Comments  Print  Share



in file CoM

Mozambique has added 64 new doctors specialised in several areas to its national total of 694.



Hypertension Detection in Barbershops

Barbershops as Hypertension Detection, Referral, and Follow-Up Centers for Black Men

Paul L. Hess, Jason S. Reingold, Jennifer Jones, Melissa A. Fellman, Premere Knowles, Joseph E. Ravenell, Stacey Kim, Jamie Raju, Erica Ruger, Sharonda Clark, Chibuike Okoro, Ore Ogunji, Patricia Knowles, David Leonard, Ruth P. Wilson, Robert W. Haley, Keith C. Ferdinand, Anne Freeman, Ronald G. Victor

1. BP fell by 16.3/9.2 mmHg in the enhanced intervention group but was unchanged in the comparison group ($p=0.0001$, adjusted for age and BMI).
2. HTN treatment increased from 47% to 92% ($p=0.001$)
3. HTN control increased from 19% to 58% ($p=0.001$)



Lancet Commission on Hypertension

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A global view....

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Latur, India





Lancet Commission in Latur, India





Lancet Commission in Latur, India





Lancet Commission in Latur, India





Lancet Commission in Latur, India

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Lancet Commission in Latur, India





Lancet Commission in Latur, India





Lancet Commission in Latur, India





Lancet Commission in Latur, India

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Lancet Commission in Latur, India

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THE LANCET

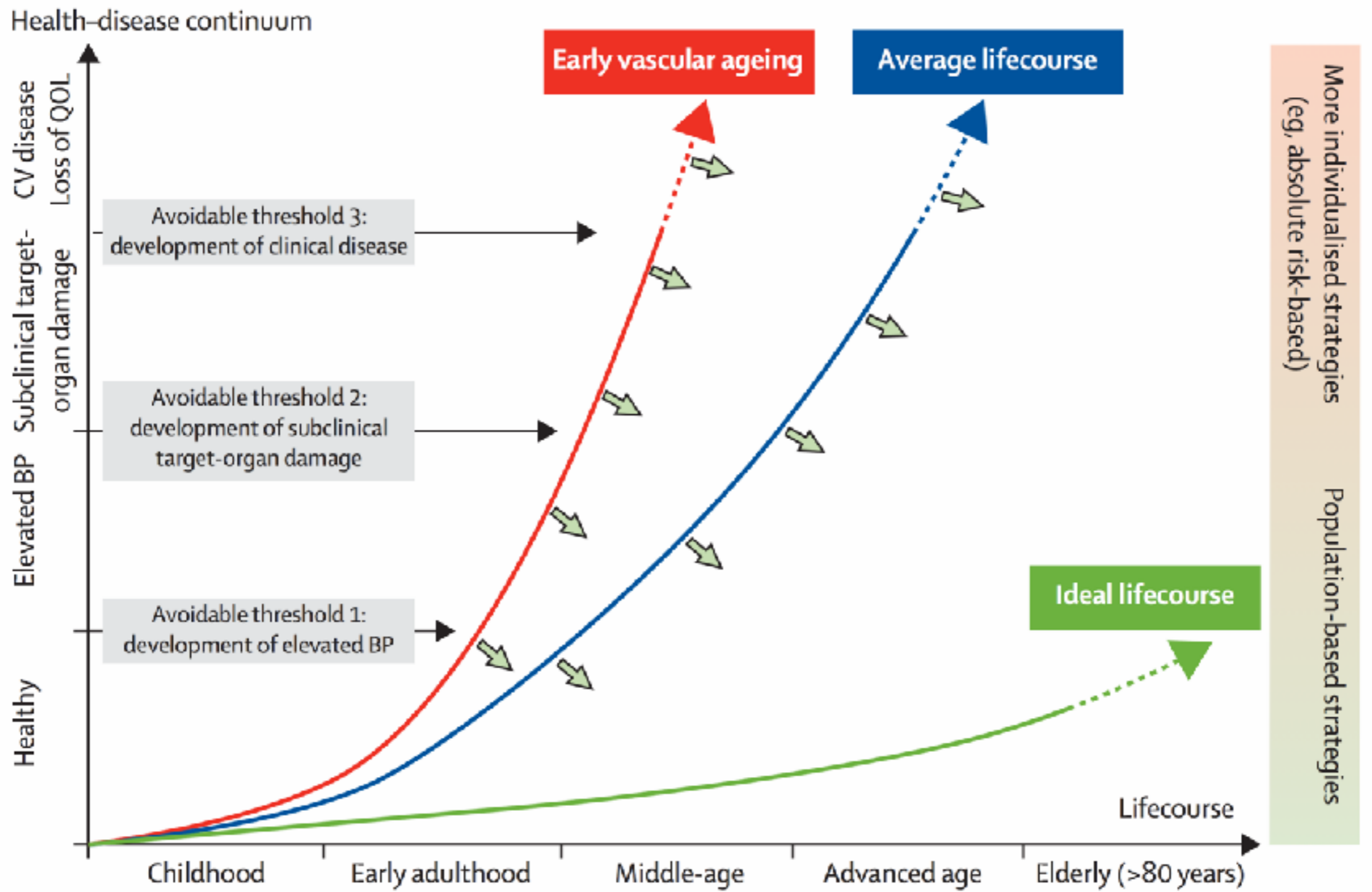


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A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the *Lancet* Commission on hypertension

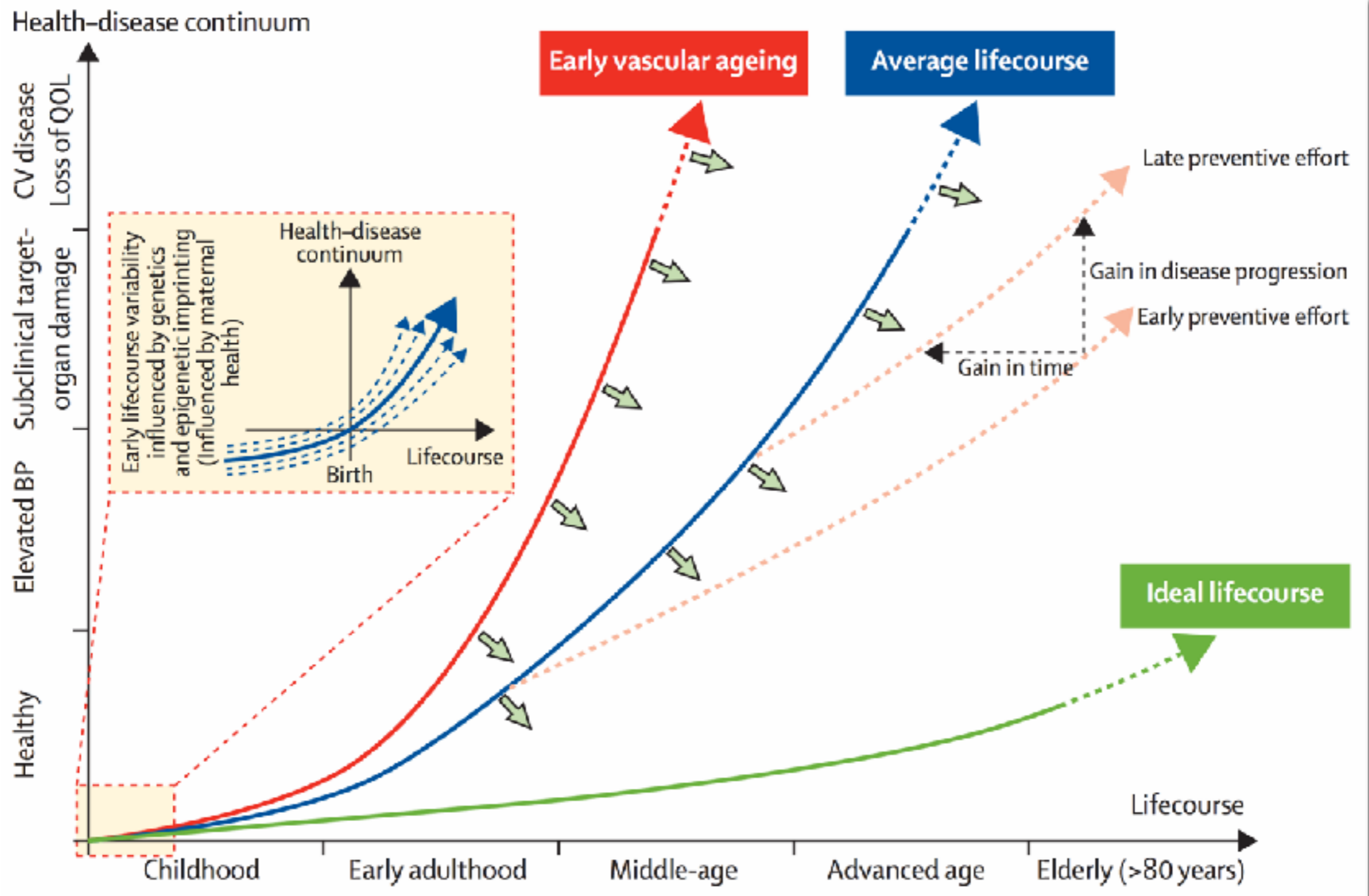
Michael H Olsen, Sonia Y Angell, Samira Asma, Pierre Boutouyrie, Dylan Burger, Julio A Chirinos, Albertino Damasceno, Christian Delles, Anne-Paule Gimenez-Roqueplo, Dagmara Hering, Patricio López-Jaramillo, Fernando Martinez, Vlado Perkovic, Ernst R Rietzschel, Giuseppe Schillaci, Aletta E Schutte, Angelo Scuteri, James E Sharman, Kristian Wachtell, Ji Guang Wang*

The lifecourse approach ⁽¹⁾

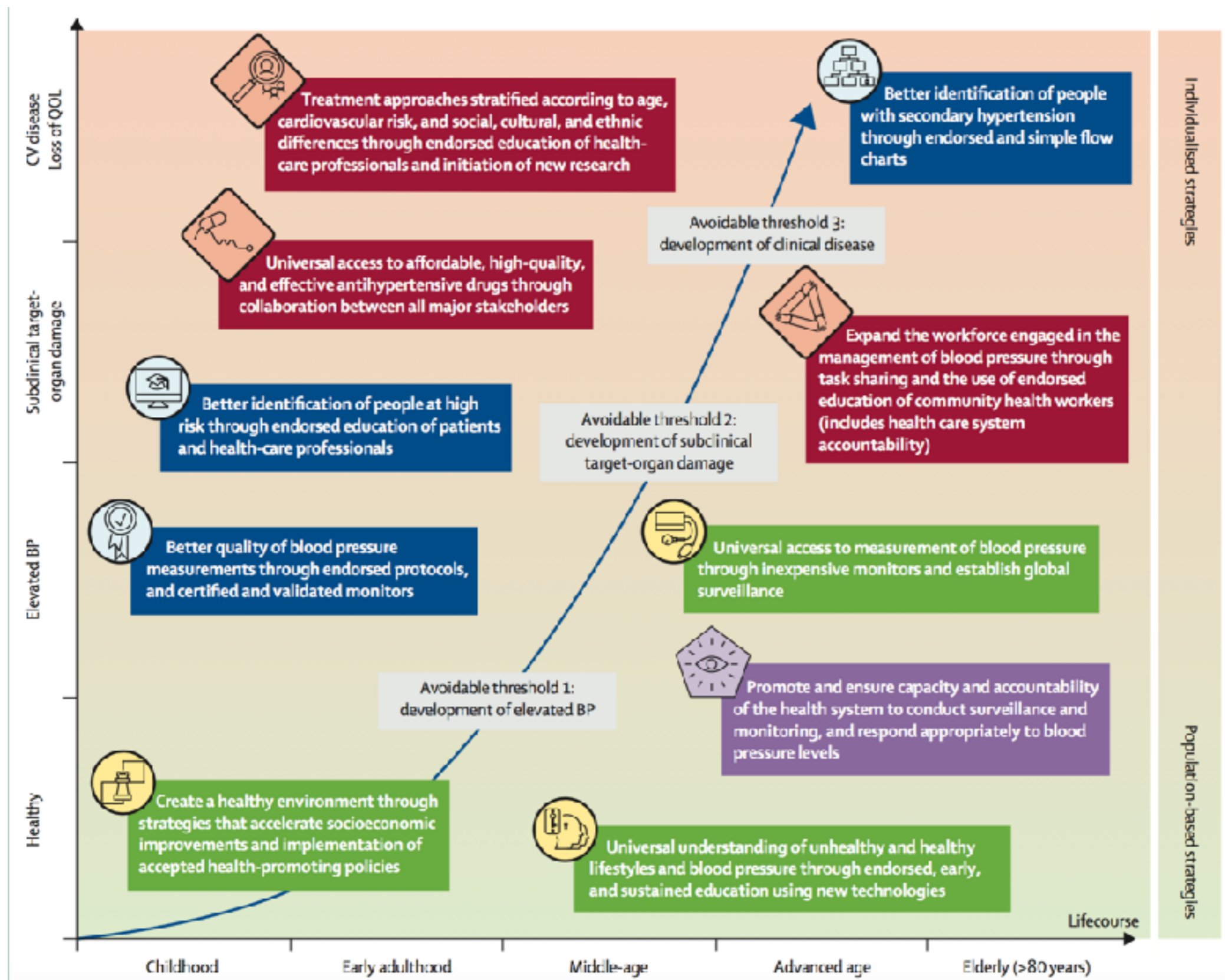


CV=cardiovascular. QOL=quality of life. BP=blood pressure.

The lifecourse approach ⁽¹⁾

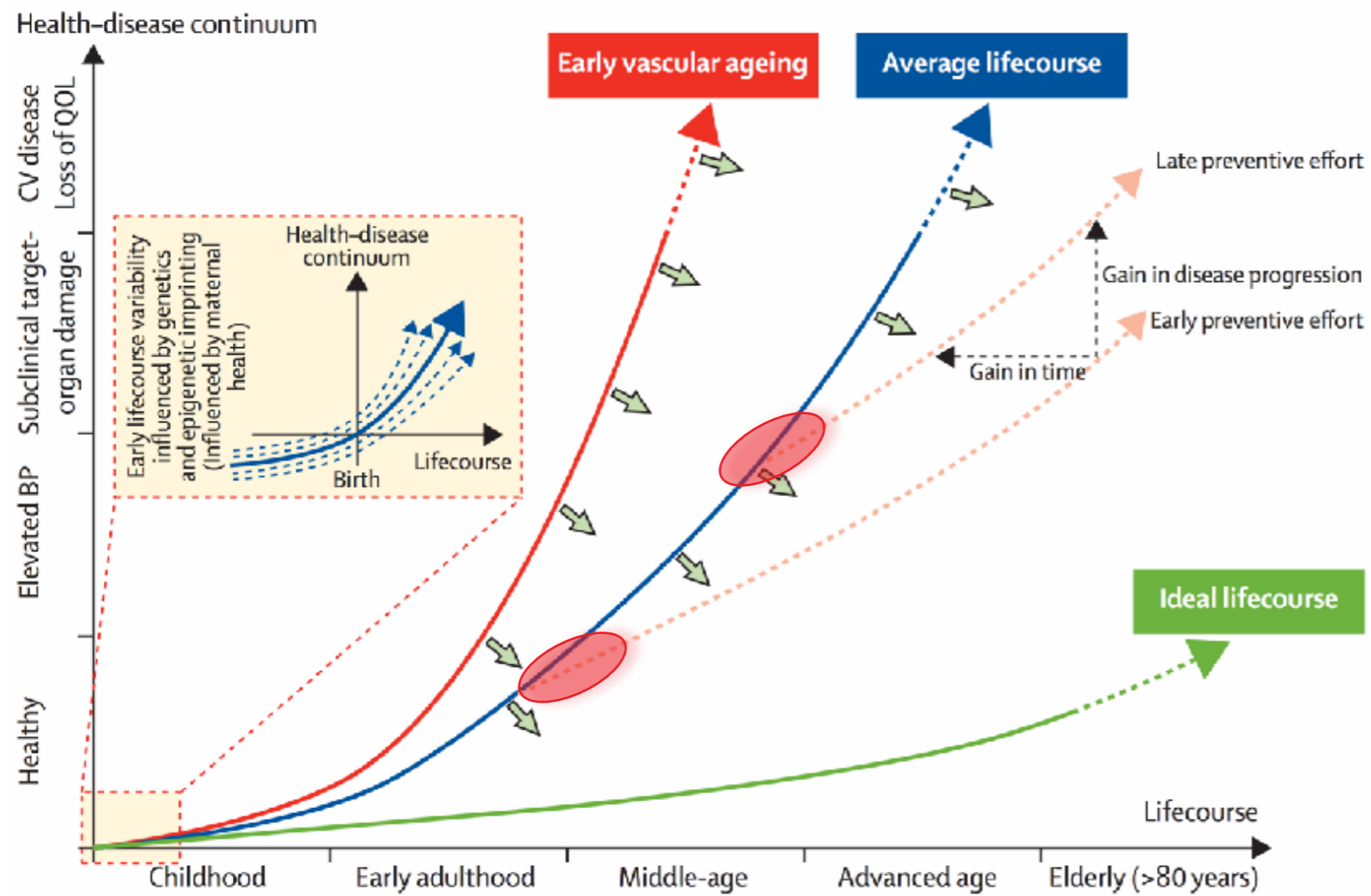


CV=cardiovascular. QOL=quality of life. BP=blood pressure.



Lifecourse net clinical benefit of a treatment

Timeframe for which benefits/risks of a treatment are known



- Data about the benefit / harms of antihypertensive treatment derive from short-term RCT's (FU typically 5 years).
- In most individuals, treatment duration by far exceeds the event horizon provided by most clinical trials.
- Information about the accrual of benefits and potential harms over the lifecourse of



The lifecourse approach

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The Commission strongly suggests that decisions about treatment should be made with the lifecourse framework in mind, whereby not only immediate cardiovascular benefits but also long-term remote target-organ or metabolic harms are taken into account in a unifying concept of “lifecourse net clinical benefit”.

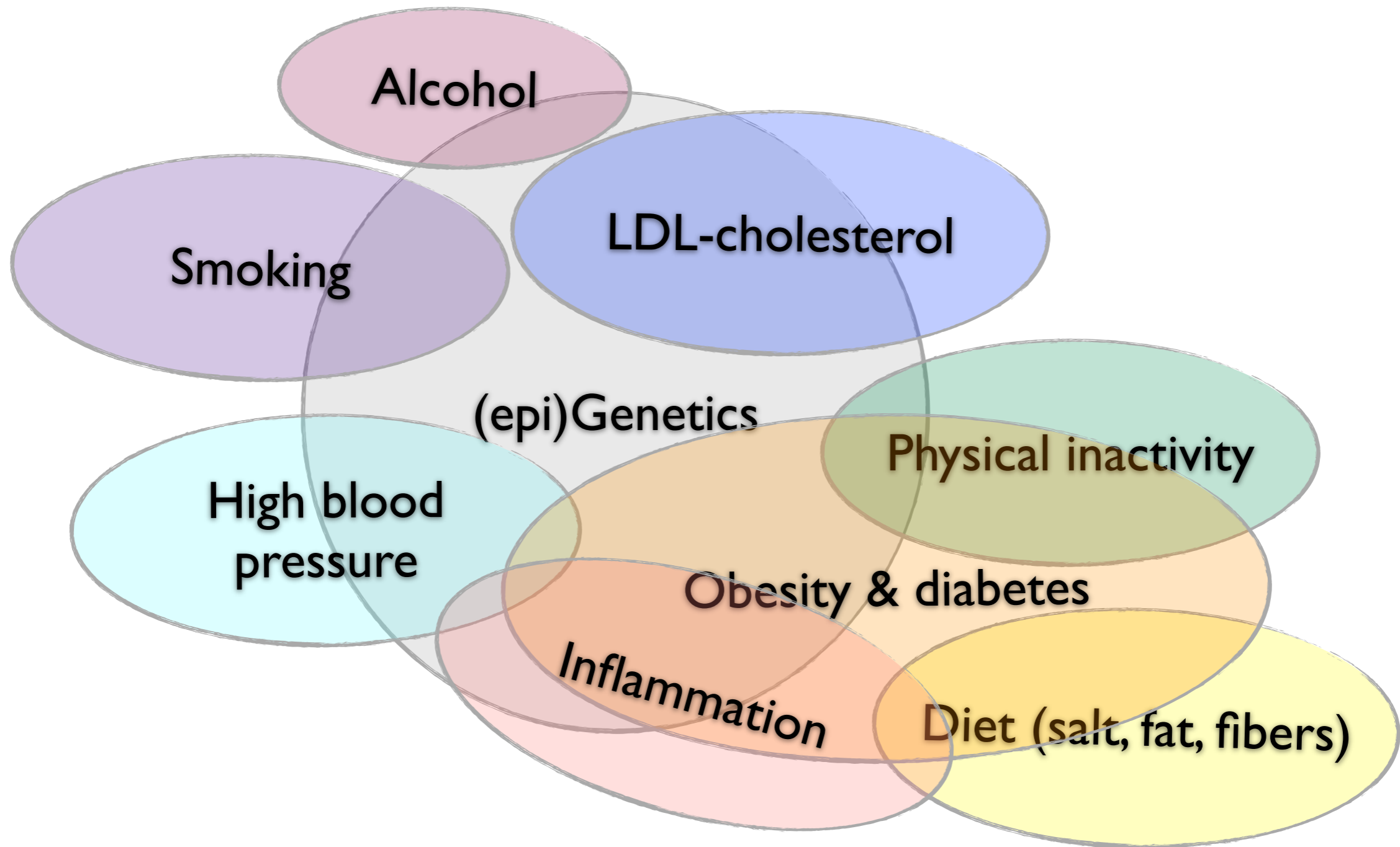
- The potential of big data to fill in this important knowledge gap cannot be overstated.
- The Commission strongly recommends research into the lifecourse net clinical balance between benefits and harms of different antihypertensive drugs and of different blood pressure targets.

A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the Lancet Commission on hypertension. *Lancet* 2016; 388: 2665–712

Olsen MH, Angell SY, Asma S, Boutouyrie P, Burger B, Chirinos JA, Damasceno A, Delles C, Gimenez-Roqueplo AP, Hering D, López-Jaramillo P, Martinez F, Perkovic V, Rietzschel ER, Schillaci G, Schutte AE, Scuteri A, Sharman JE, Wachtell K, Wang JG

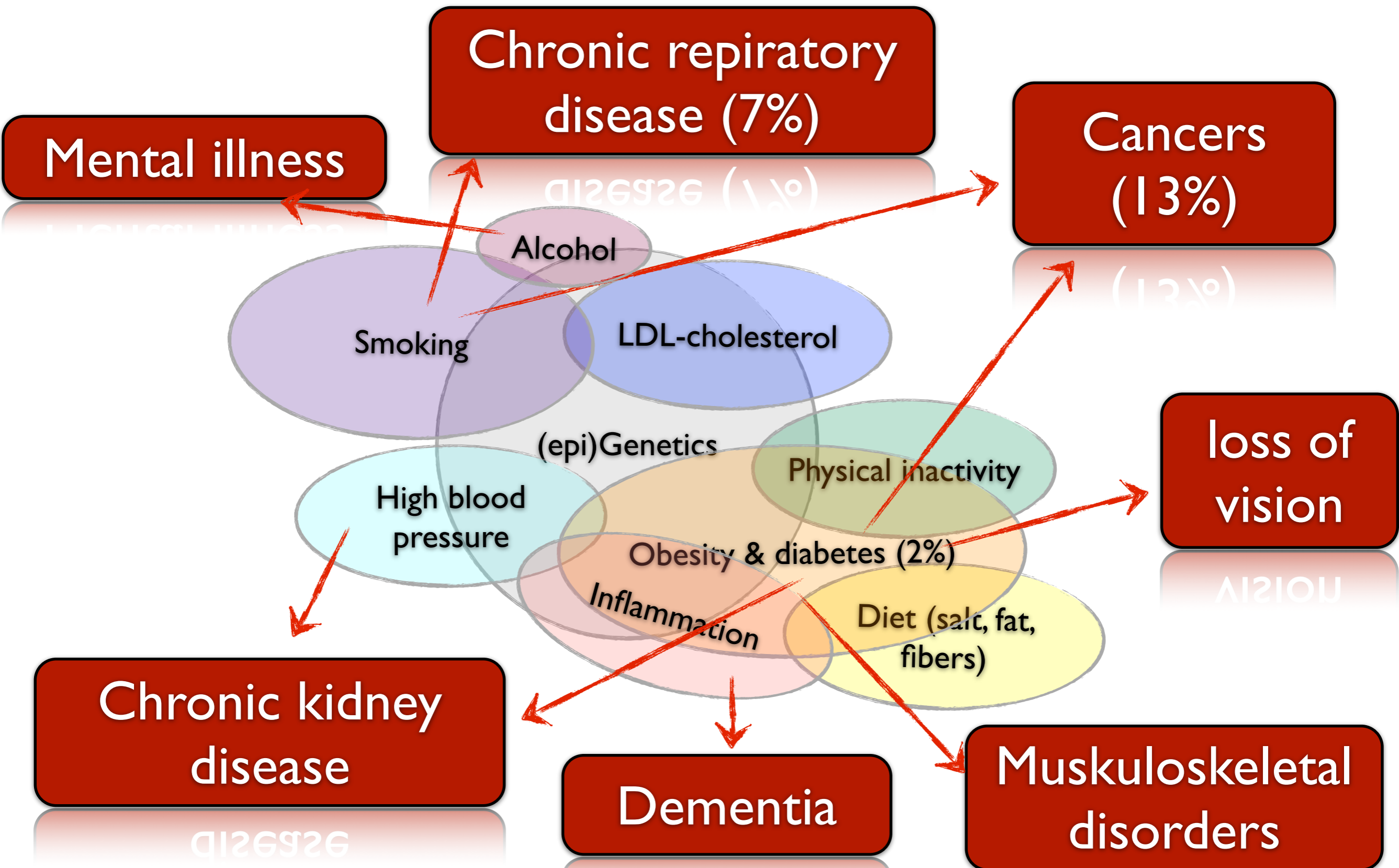


Oorzaken van HVZ





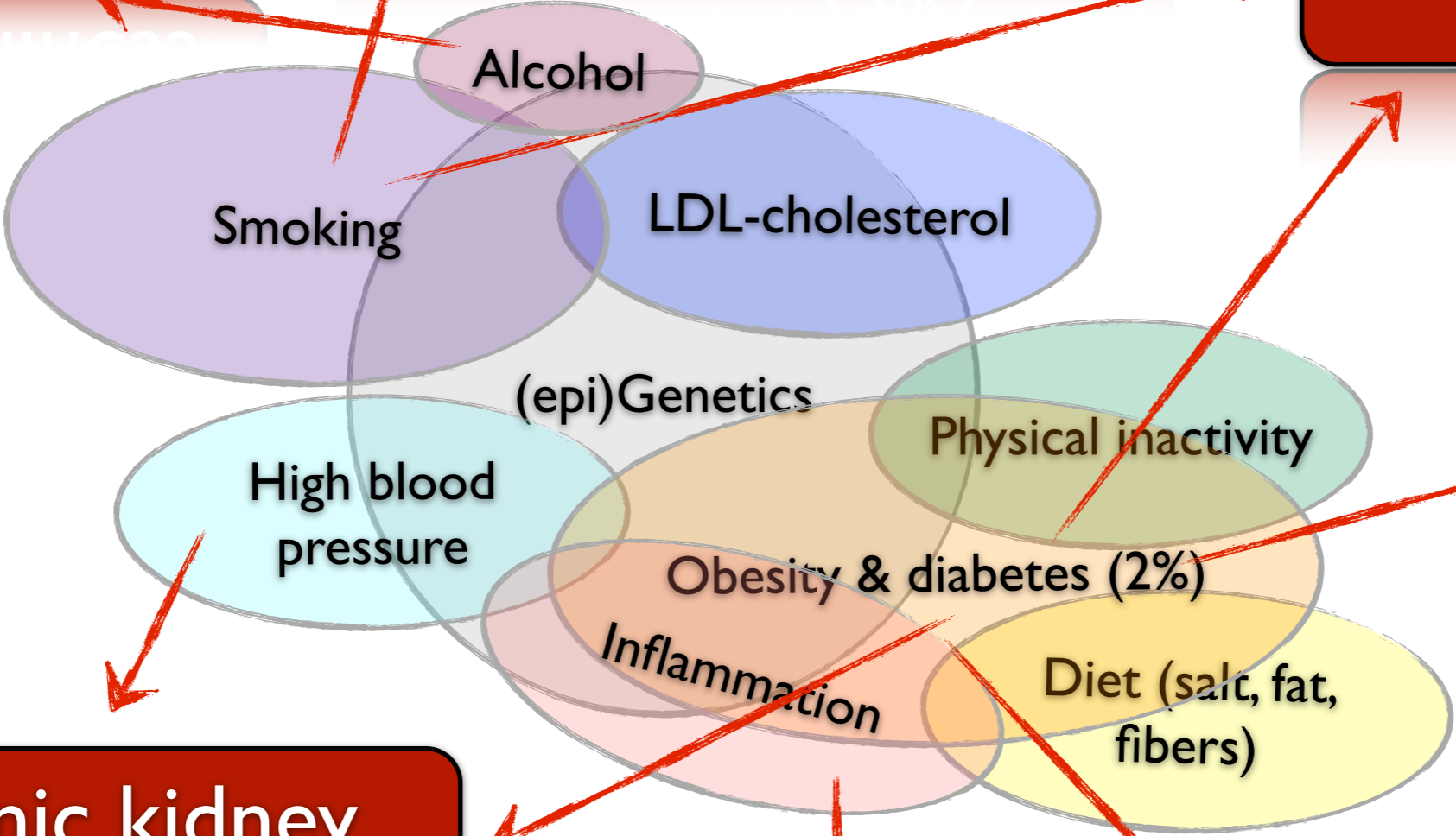
Oorzaken van HVZ (30% of globale sterfte)



Chronic respiratory disease (7%)

Mental illness

Cancers (13%)



loss of vision

Chronic kidney disease

Dementia

Musculoskeletal disorders



Vragen ?