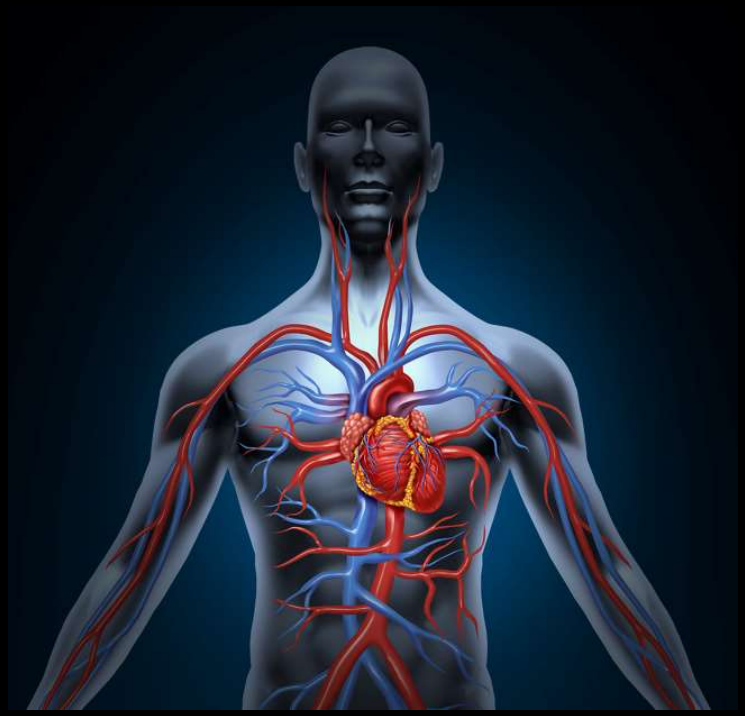
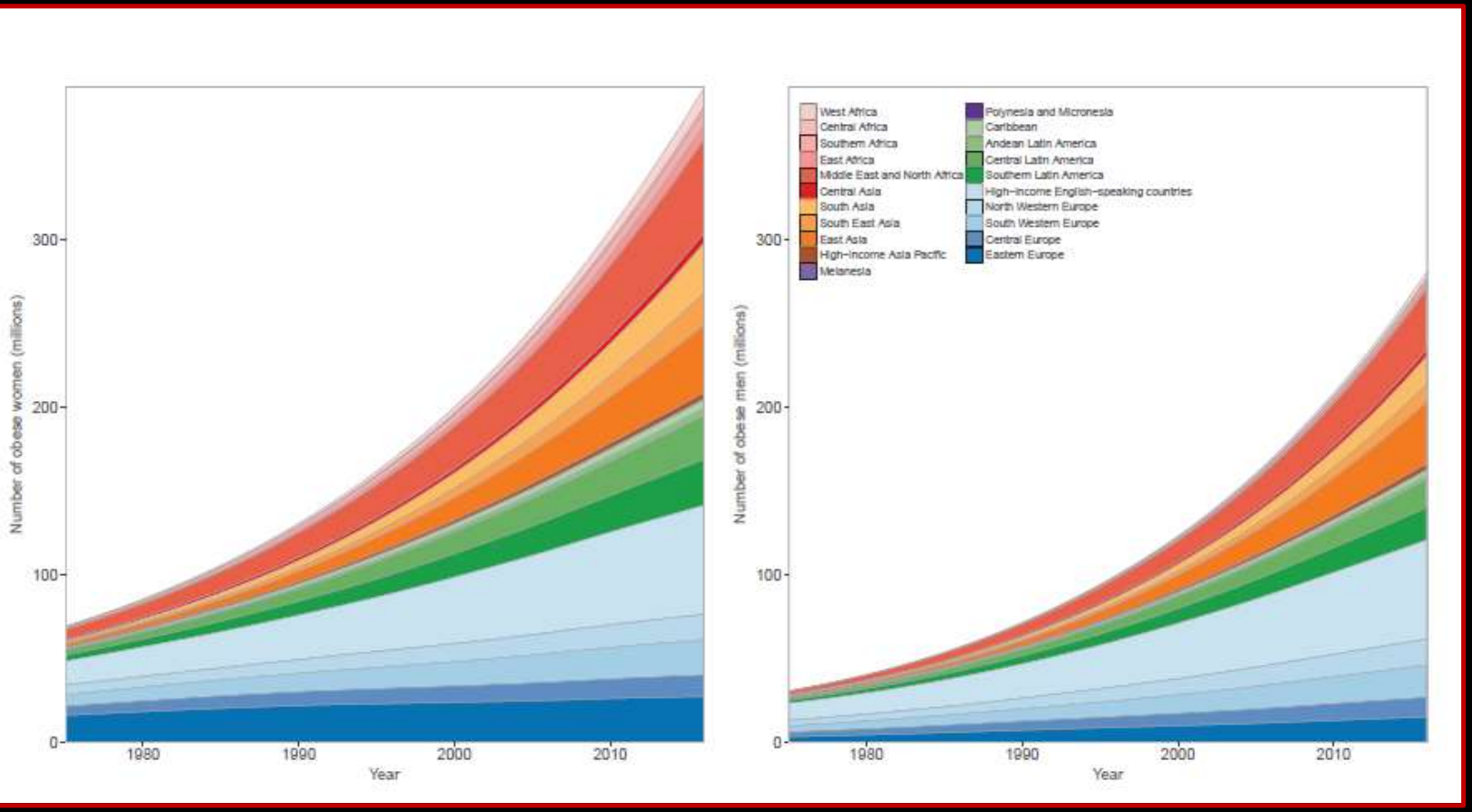
Fetma – läkemedelsbehandling och risk för stroke.



Annika Rosengren, MD, professor

Sahlgrenska Academy and Sahlgrenska University Hospital/Östra

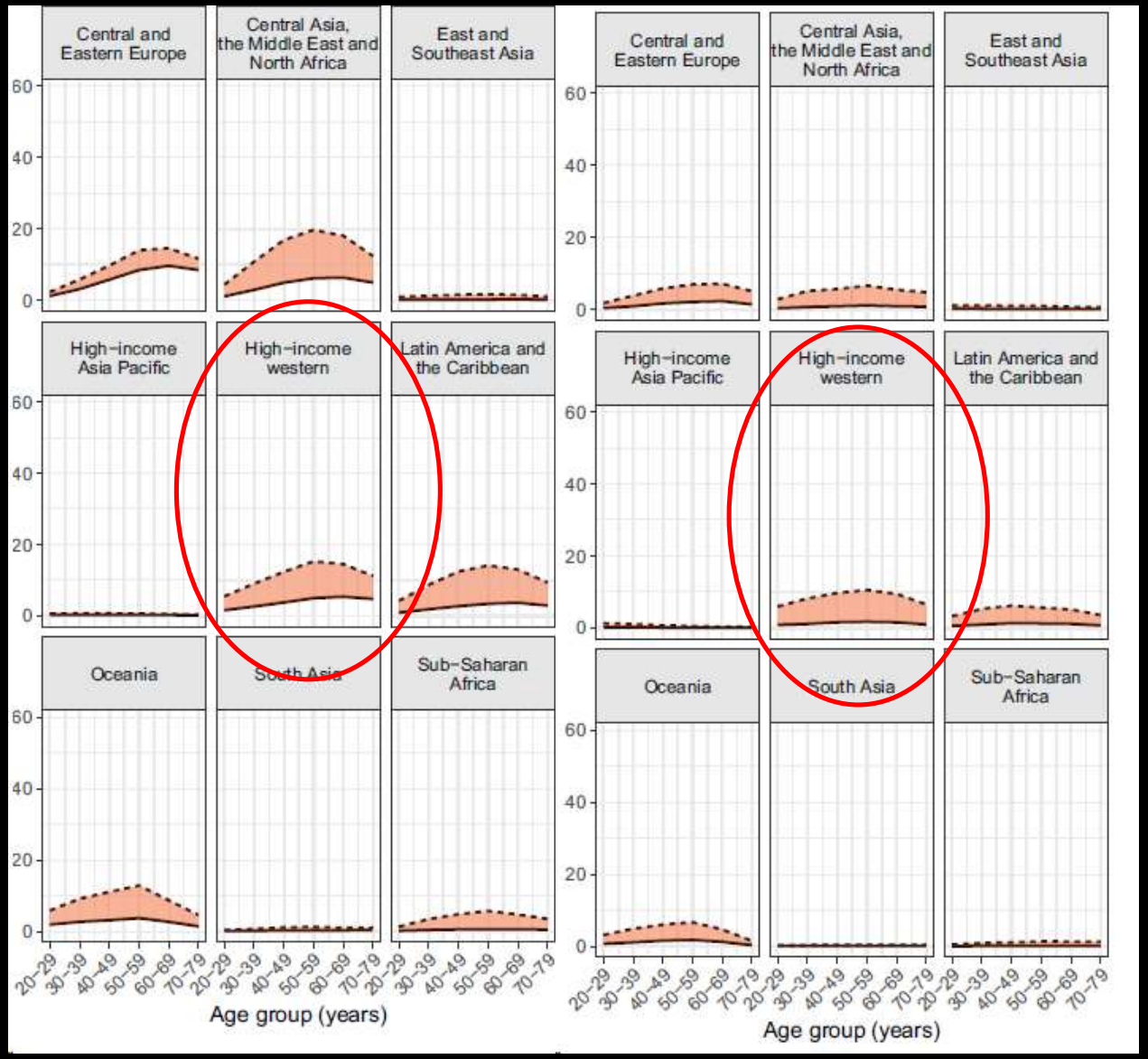
Worldwide trends in obesity in women and men 1975-2016



The number of adult women with obesity increased from 69 million in 1975 to 390 million in 2016; the number of men with obesity increased from 31 million in 1975 to 281 million

Latest WHO estimate: 890 million adults living with obesity, and 160 million children and adolescents, bringing the total up to over 1 billion altogether.

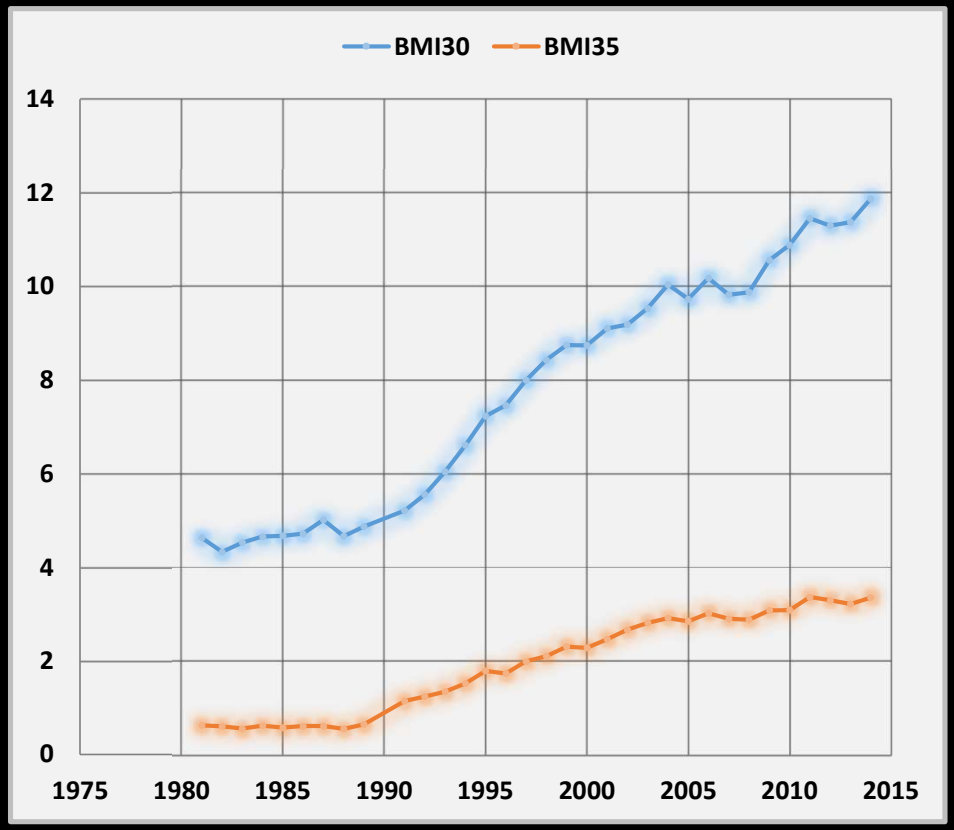
NCD Risk Factor Collaboration (NCD-RisC). Lancet. 2017;390:2627-2642 (appendix).



Global förändring 1985-2016 i förekomst av svår fetma(BMI ≥35) bland män (t v) och kvinnor (t h) i relation till ålder

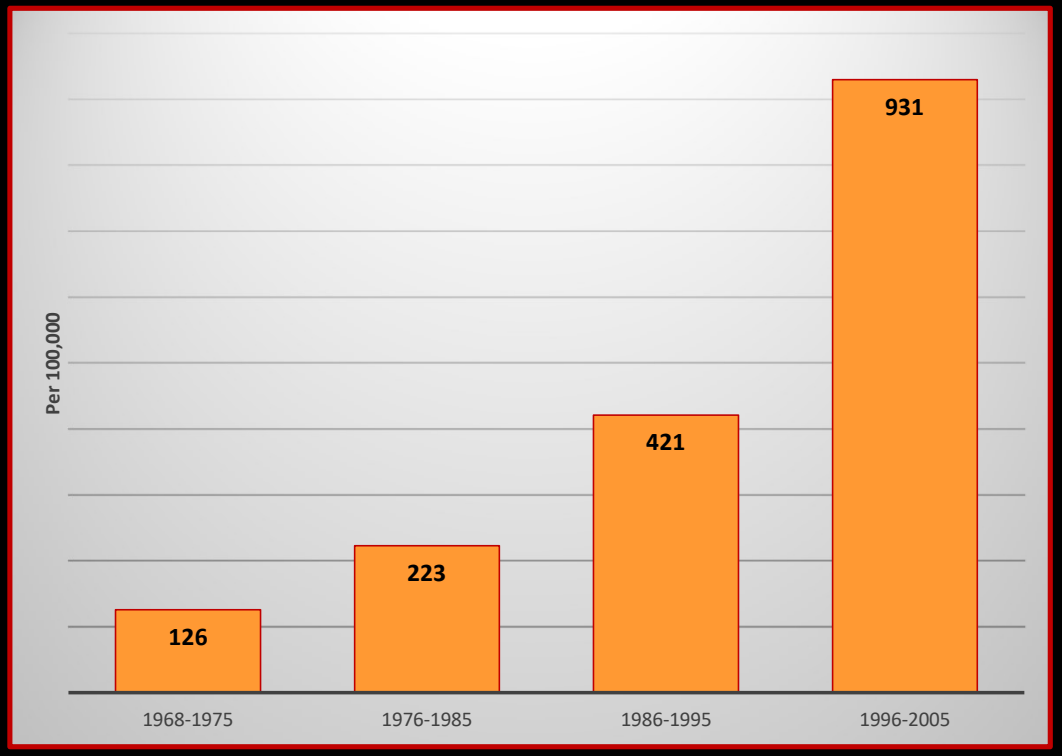
NCD Risk Factor Collaboration (NCD-RisC) eLife 2021;10:e60060

Andel (%) unga kvinnor i Sverige med BMI ≥30 och BMI ≥35, 1981-2015. Snittålder 29 år.



Lundberg CE, et al. Sci Rep 2021;11:12056

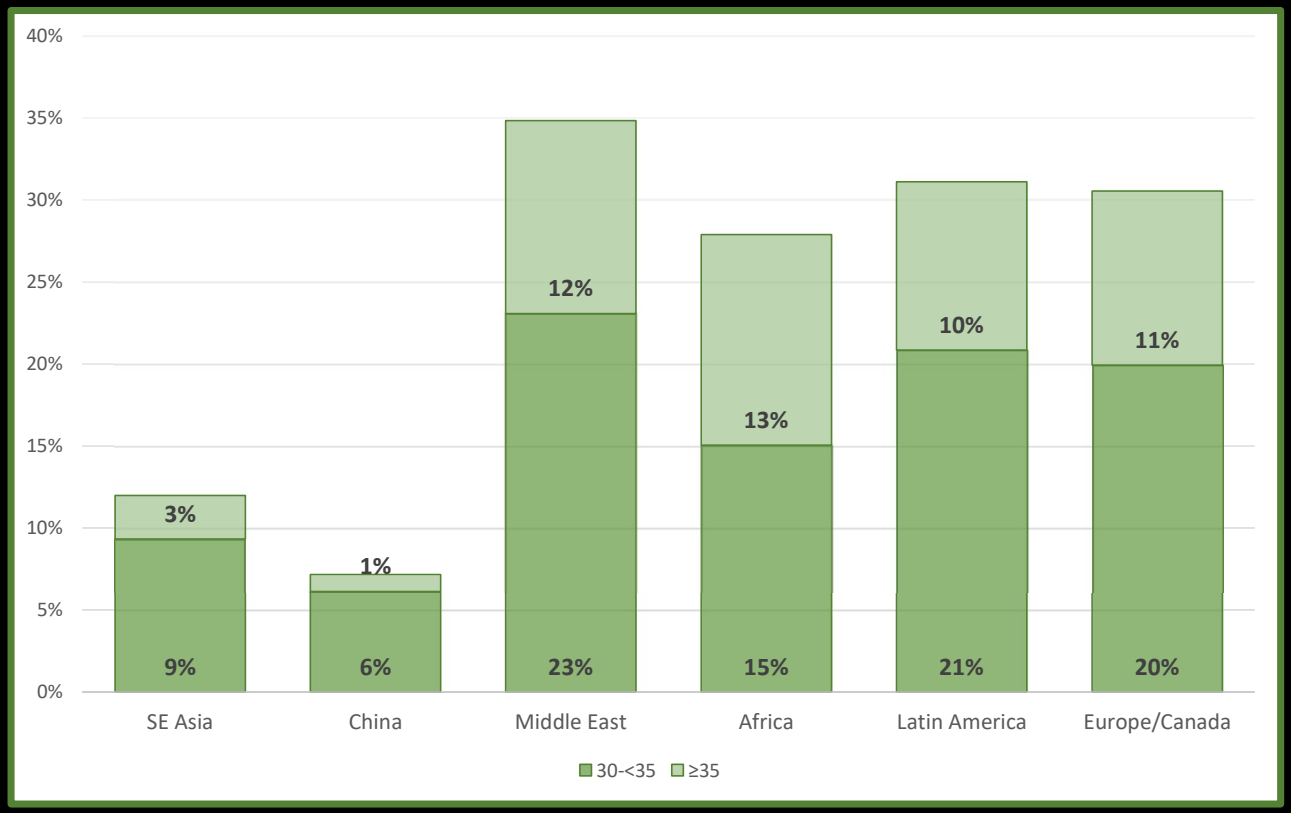
Andel 18-åriga män per 100,000 med ”severe obesity” (BMI ≥35) 1968-2005



Män födda 1949-1987

Lissner L, et al. J Adolesc Health 2019;65:232-238.

Fetma klass 1 (BMI 30-<35) och klass 2-3 (BMI≥ 35) (%) bland vuxna 35-70 år i olika regioner i PURE



PURE = Prospective Urban Rural Epidemiologic study

EE = energy expenditure
EI = energy intake

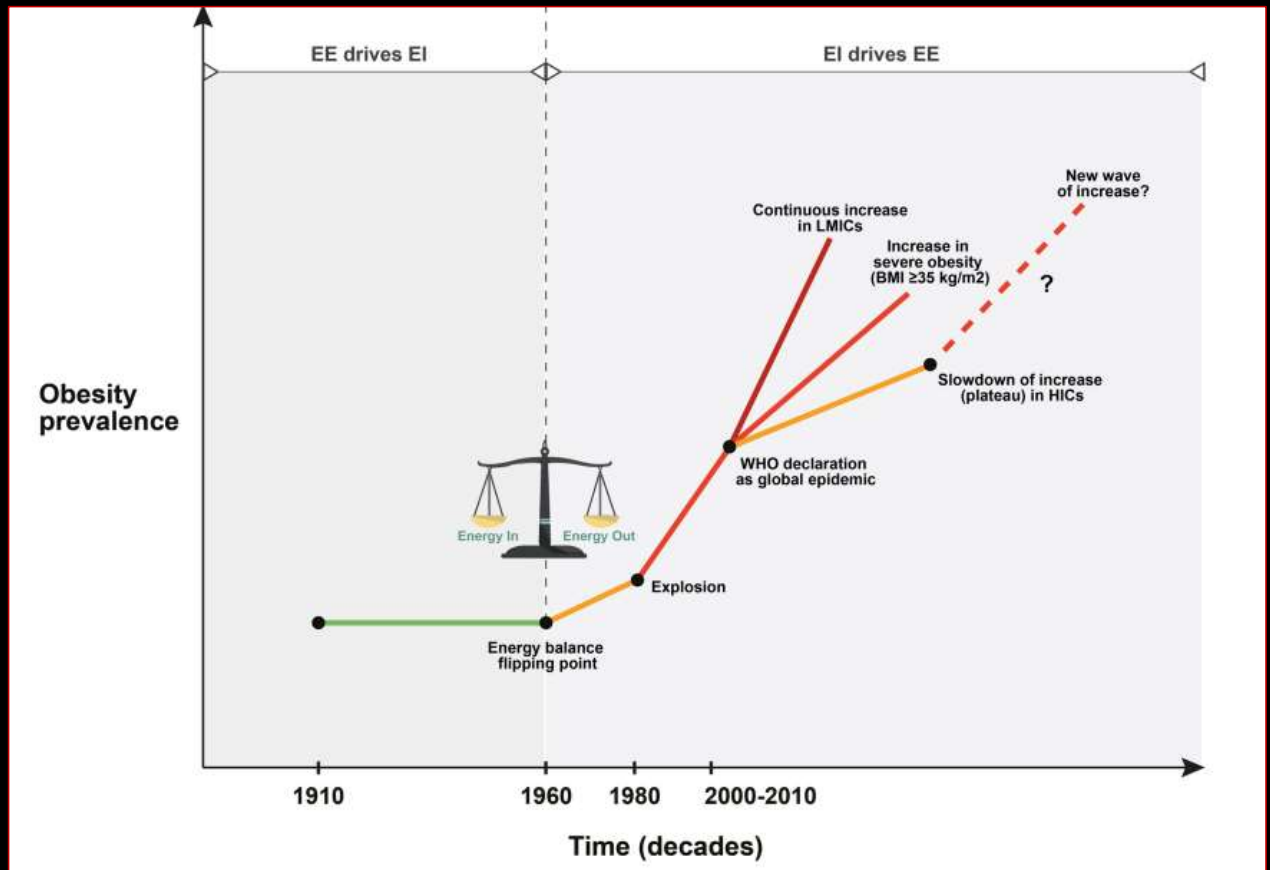


Fig. 2 A graphical summary of global obesity prevalence trends over decades of the twentieth and twenty-first century

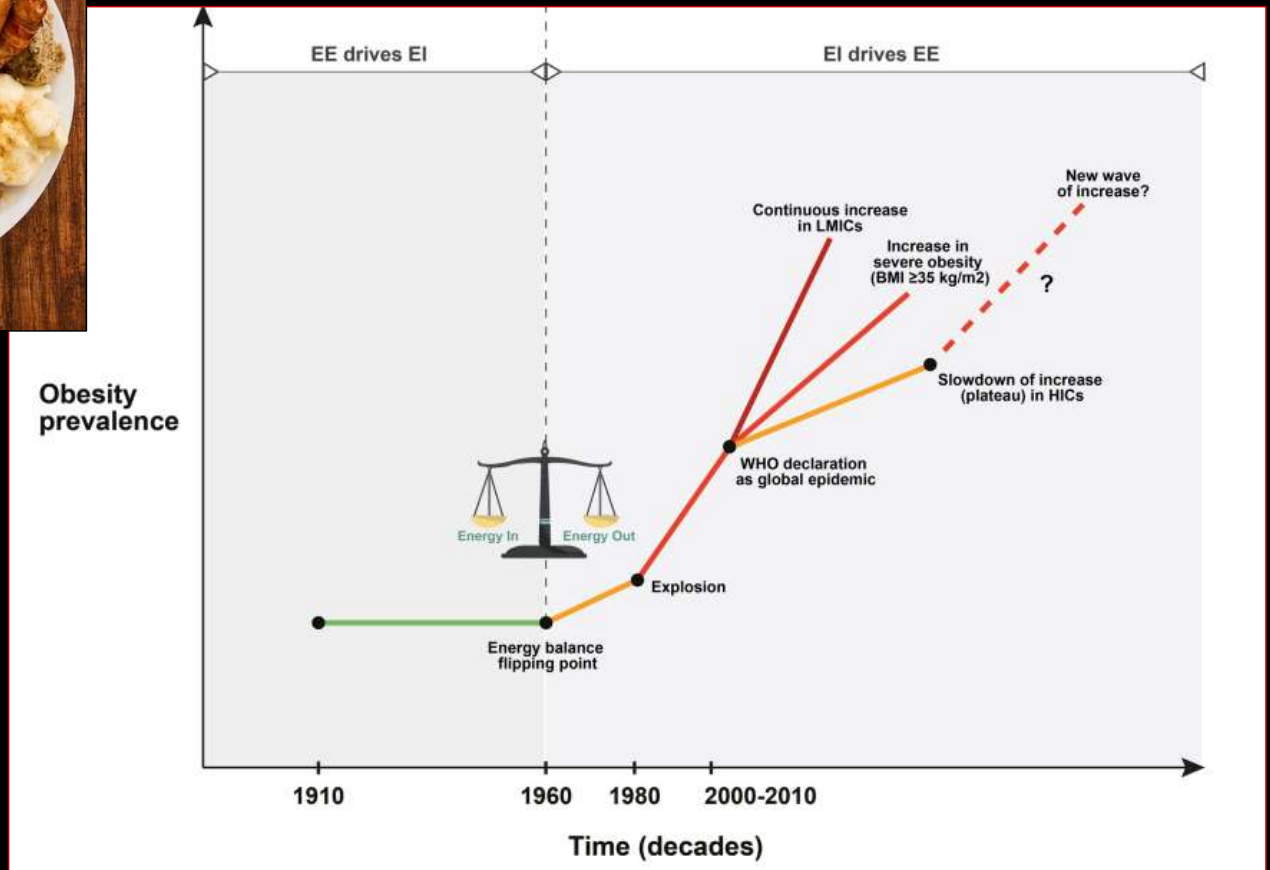
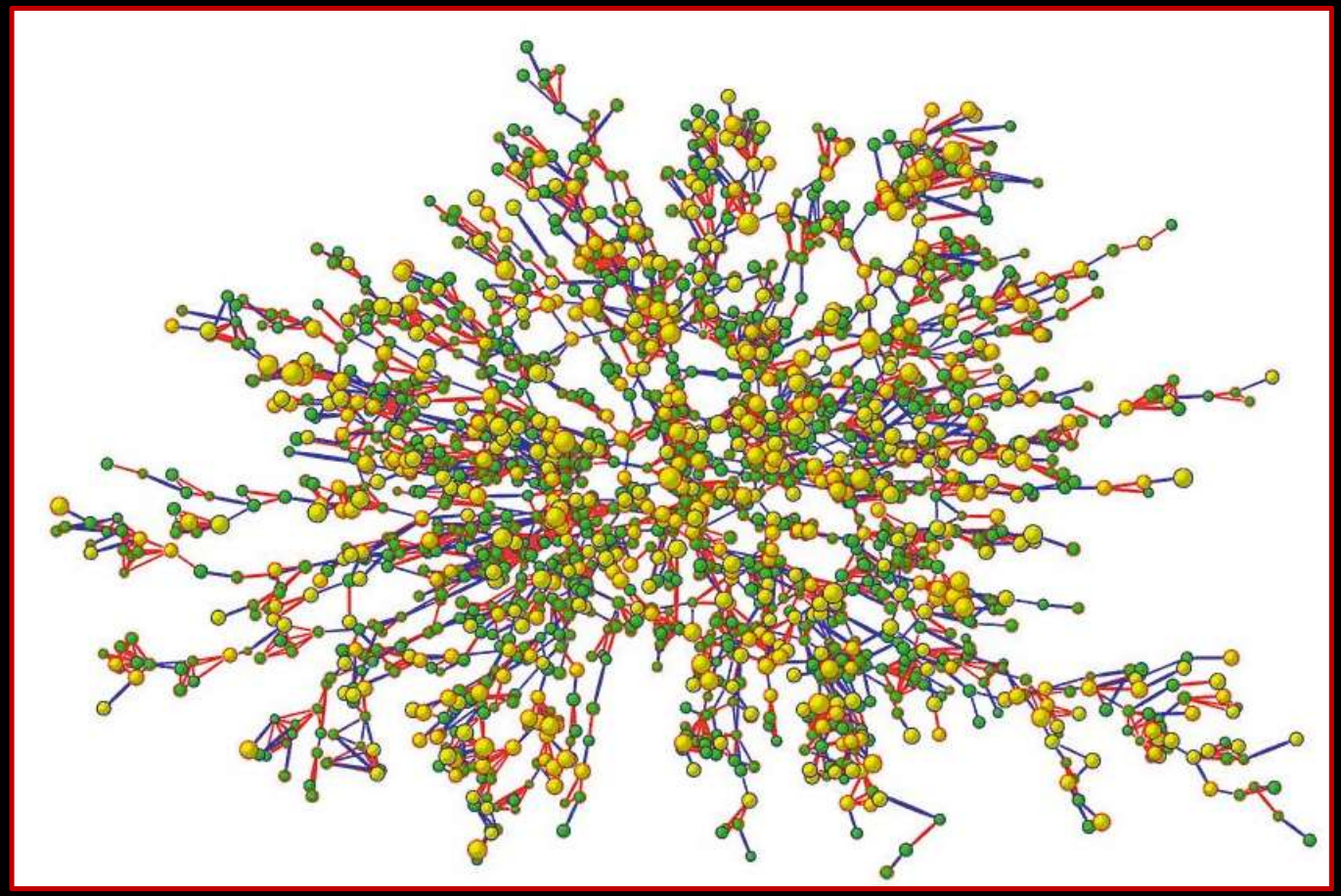


Fig. 2 A graphical summary of global obesity prevalence trends over decades of the twentieth and twenty-first century

Clustering of obesity in a social network of 2200 people in the Framingham Heart Study in the year 2000.

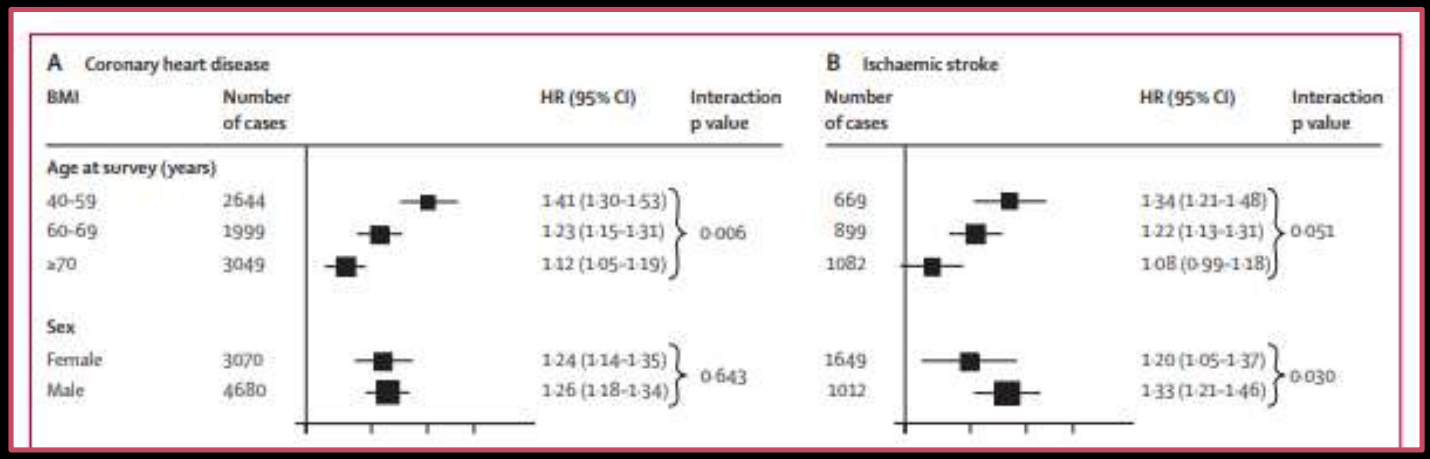


Each circle represents one person. Red borders=women, blue borders=men. The size of each circle is proportional to the person's BMI. Yellow circles denote a person with BMI ≥30 and green denotes BMI<30.

Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. N Engl J Med. 2007;357:370-9.

Högt BMI som riskfaktor för CHD och stroke i olika åldrar

Hazard ratios HRs coronary heart disease (A) and ischaemic stroke (B) per 1 SD higher baseline values of BMI according to age, sex, and BMI at baseline

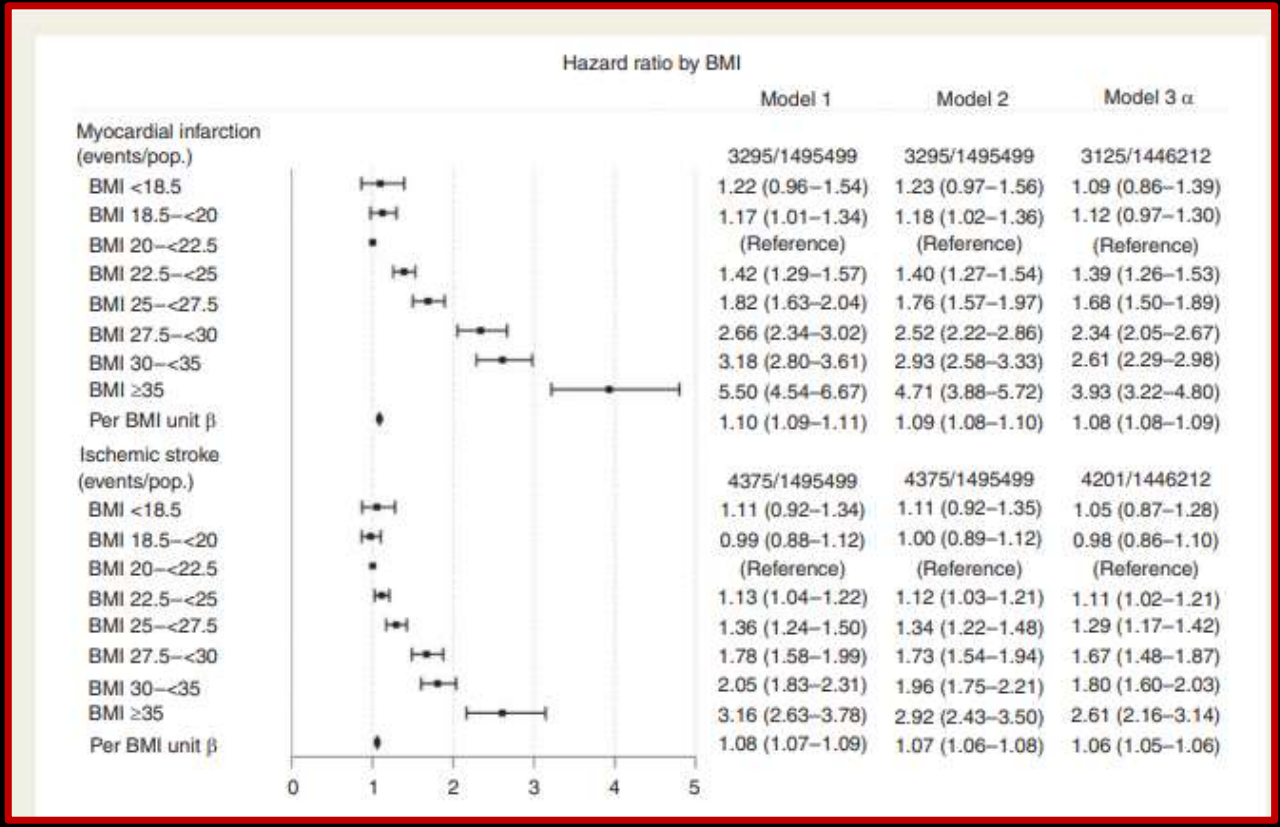


Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents

oa The Global BMI Mortality Collaboration*

Global BMI Mortality Collaboration, Di Angelantonio E, et al. Lancet. 2016;388:776-86.

Hazard ratios for early AMI and ischemic stroke according to prepregnancy body mass index (BMI) groups (reference: BMI 20– < 22.5). Medical Birth Registry 1982-2014, 1,5 million women.



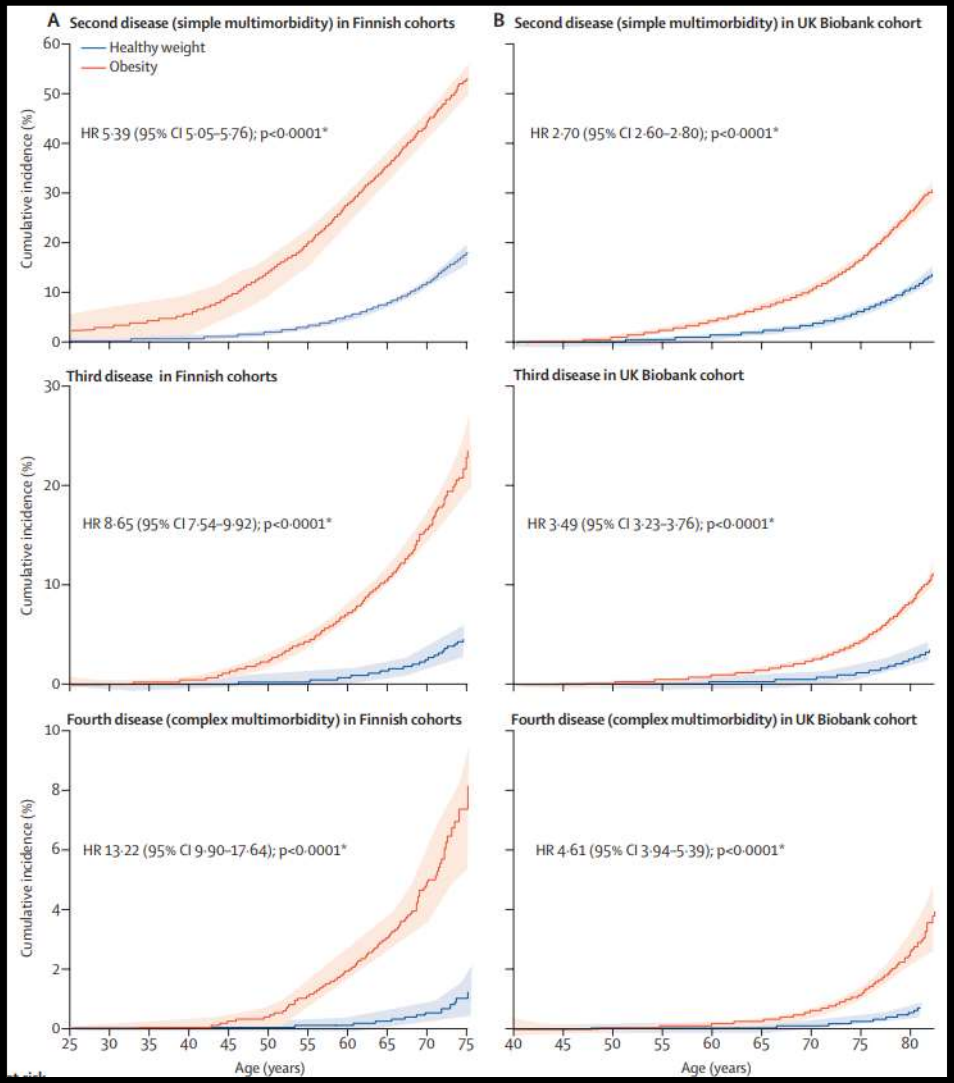
	Model 1	Model 2	Model 3 α
Myocardial infarction (events/pop.)	3295/1495499	3295/1495499	3125/1446212
BMI <18.5	1.22 (0.96–1.54)	1.23 (0.97–1.56)	1.09 (0.86–1.39)
BMI 18.5–<20	1.17 (1.01–1.34)	1.18 (1.02–1.36)	1.12 (0.97–1.30)
BMI 20–<22.5	(Reference)	(Reference)	(Reference)
BMI 22.5–<25	1.42 (1.29–1.57)	1.40 (1.27–1.54)	1.39 (1.26–1.53)
BMI 25–<27.5	1.82 (1.63–2.04)	1.76 (1.57–1.97)	1.68 (1.50–1.89)
BMI 27.5–<30	2.66 (2.34–3.02)	2.52 (2.22–2.86)	2.34 (2.05–2.67)
BMI 30–<35	3.18 (2.80–3.61)	2.93 (2.58–3.33)	2.61 (2.29–2.98)
BMI ≥35	5.50 (4.54–6.67)	4.71 (3.88–5.72)	3.93 (3.22–4.80)
Per BMI unit β	1.10 (1.09–1.11)	1.09 (1.08–1.10)	1.08 (1.08–1.09)
Ischemic stroke (events/pop.)	4375/1495499	4375/1495499	4201/1446212
BMI <18.5	1.11 (0.92–1.34)	1.11 (0.92–1.35)	1.05 (0.87–1.28)
BMI 18.5–<20	0.99 (0.88–1.12)	1.00 (0.89–1.12)	0.98 (0.86–1.10)
BMI 20–<22.5	(Reference)	(Reference)	(Reference)
BMI 22.5–<25	1.13 (1.04–1.22)	1.12 (1.03–1.21)	1.11 (1.02–1.21)
BMI 25–<27.5	1.36 (1.24–1.50)	1.34 (1.22–1.48)	1.29 (1.17–1.42)
BMI 27.5–<30	1.78 (1.58–1.99)	1.73 (1.54–1.94)	1.67 (1.48–1.87)
BMI 30–<35	2.05 (1.83–2.31)	1.96 (1.75–2.21)	1.80 (1.60–2.03)
BMI ≥35	3.16 (2.63–3.78)	2.92 (2.43–3.50)	2.61 (2.16–3.14)
Per BMI unit β	1.08 (1.07–1.09)	1.07 (1.06–1.08)	1.06 (1.05–1.06)

Dikaiou P, et al. Obesity, overweight and risk for cardiovascular disease and mortality in young women. Eur J Prev Cardiol. 2021;28:1351-1359.

Tidig stroke i relation till BMI i värnpliktsregistret

	Hazard ratio (95% CI) p-value		
	Model 1	**Model 2**	**Model 3**
Hospitalization for stroke	8539 / 1610352	7582 / 1454228	6241 / 1116880
<18.5	1.01 (0.93-1.09)	0.98 (0.90-1.08)	0.90 (0.81-0.99)
18.5 to <20.0 (reference)			
20.0 to <22.5	0.99 (0.93-1.05)	0.98 (0.92-1.04)	1.07 (1.00-1.15)
22.5 to <25.0	1.13 (1.05-1.21)	1.09 (1.01-1.17)	1.21 (1.11-1.32)
25.0 to <27.5	1.49 (1.36-1.63)	1.41 (1.28-1.55)	1.54 (1.38-1.72)
27.5 to <30.0	1.86 (1.64-2.12)	1.77 (1.55-2.03)	1.99 (1.71-2.33)
30.0 to <35.0	2.55 (2.21-2.93)	2.30 (1.98-2.68)	2.49 (2.08-2.98)
≥35.0	3.82 (2.94-4.95)	3.31 (2.49-4.40)	3.60 (2.52-5.14)

Rosengren A, et al. Eur Heart J. 2017 21;38:1926-33.



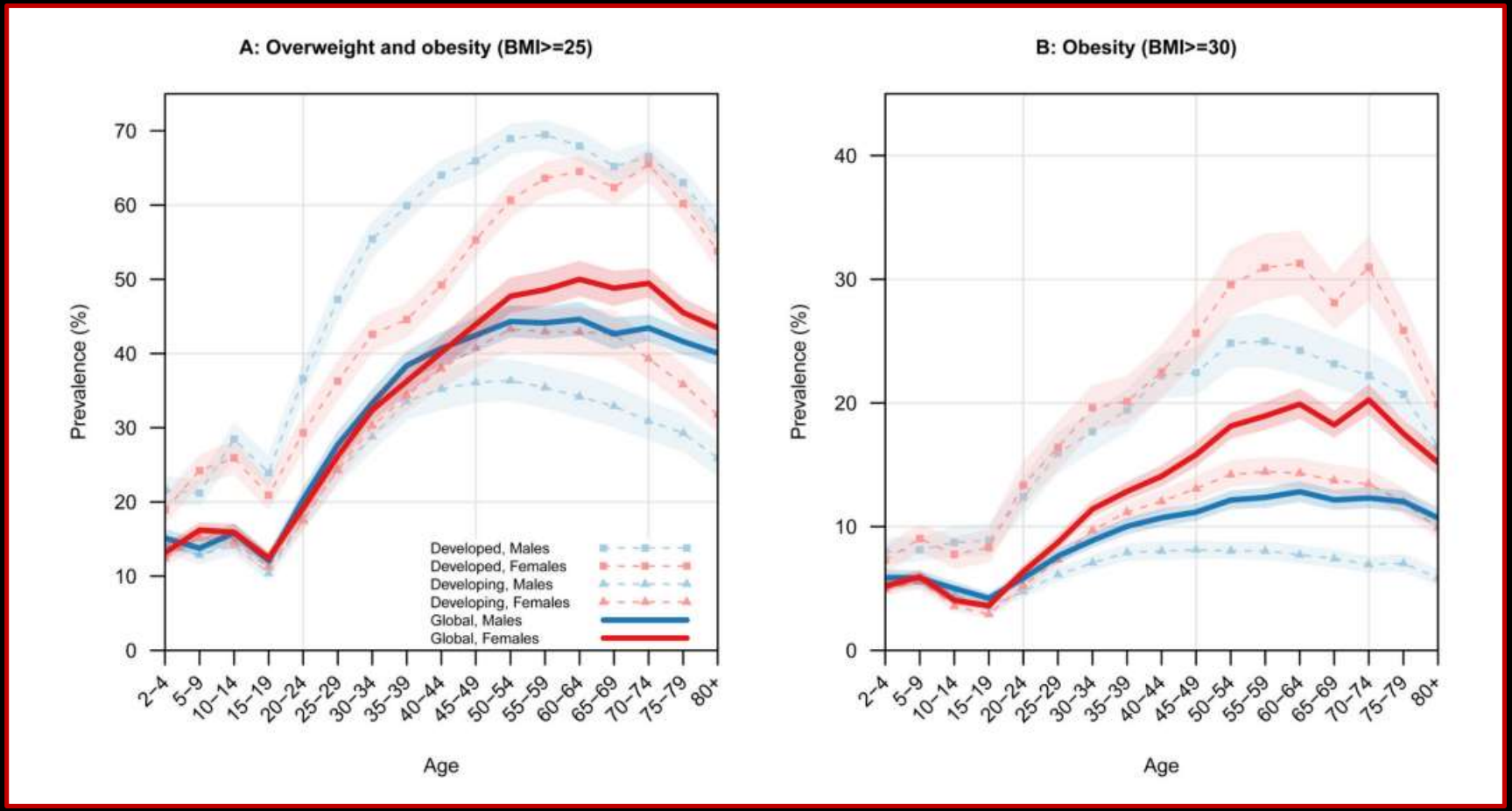
Obesitas och risk för multisjuklighet I två finska populationer (t v) och en från UK biobank (t h)

Body-mass index and risk of obesity-related complex multimorbidity: an observational multicohort study

Mika Kivimäki, Timo Strandberg, Jaana Pentti, Solja T Nyberg, Philipp Frank, Markus Jokela, Jenni Ervasti, Sakari B Suominen, Jussi Vahtera, Pyry N Sipilä, Joni V Lindbohm, Jane E Ferrie

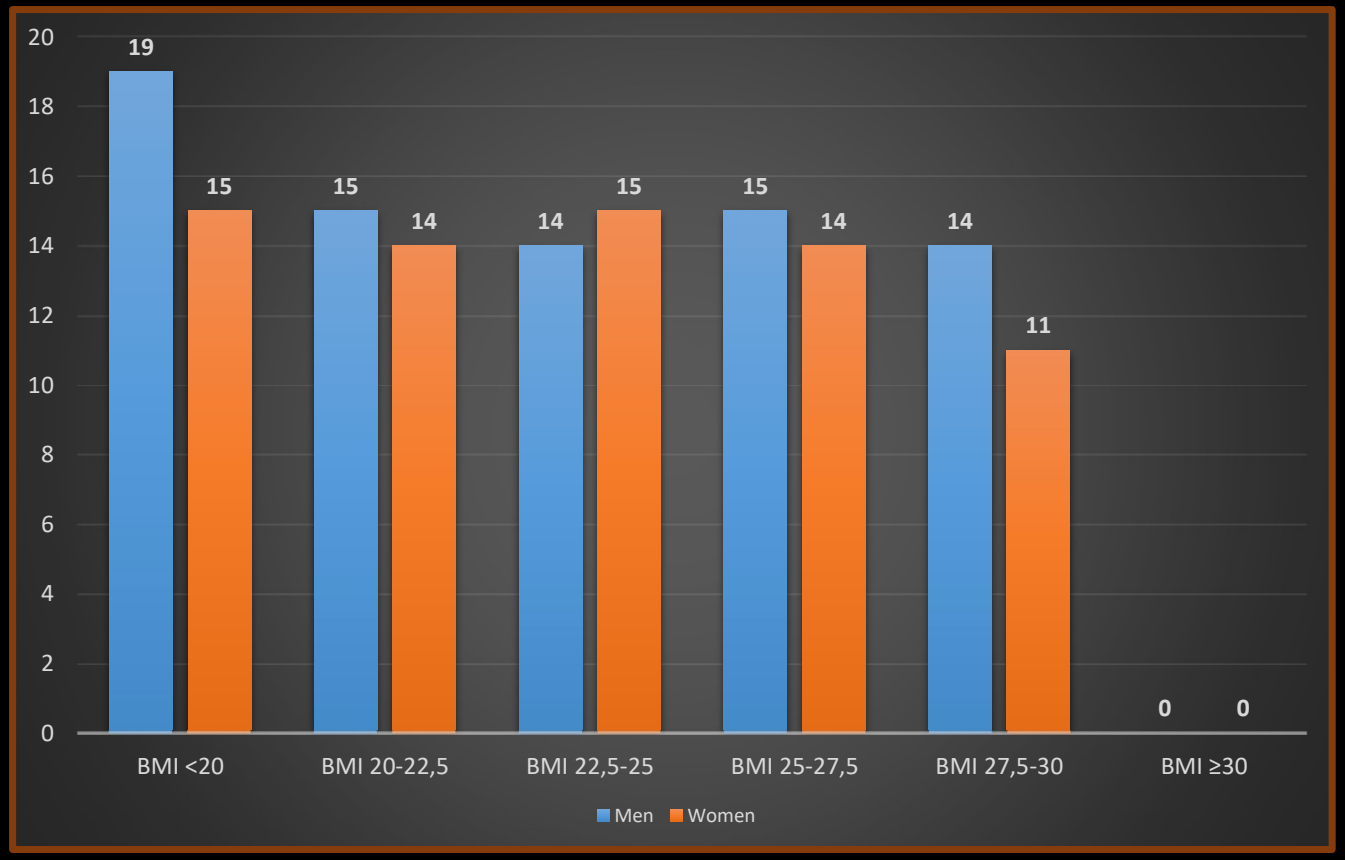
Lancet. 2022;10:253-63.

Övervikt (BMI≥25) och fetma (BMI≥30) bland män och kvinnor i olika åldrar i världen 2013



Ng M, et al. Lancet 2014

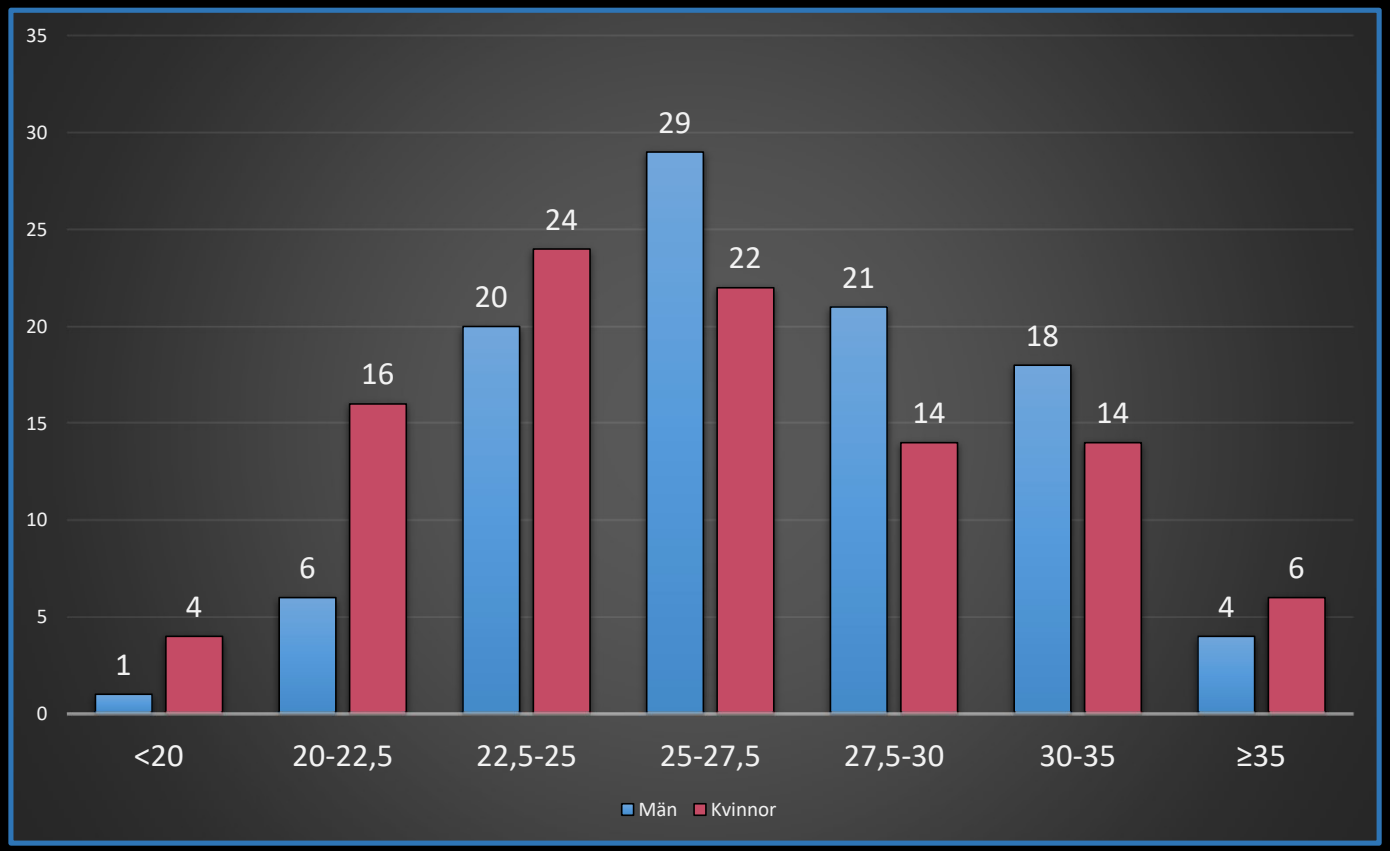
Viktökning från 20 års ålder till 50-64 år (kg) i relation till vikt vid 20 (självuppgiven vikt)



<u>Genomsnittlig viktökning</u>
Män: 14.8 kg (20.7%)
Kvinnor: 14.5 kg (25.8%)

Manuskript

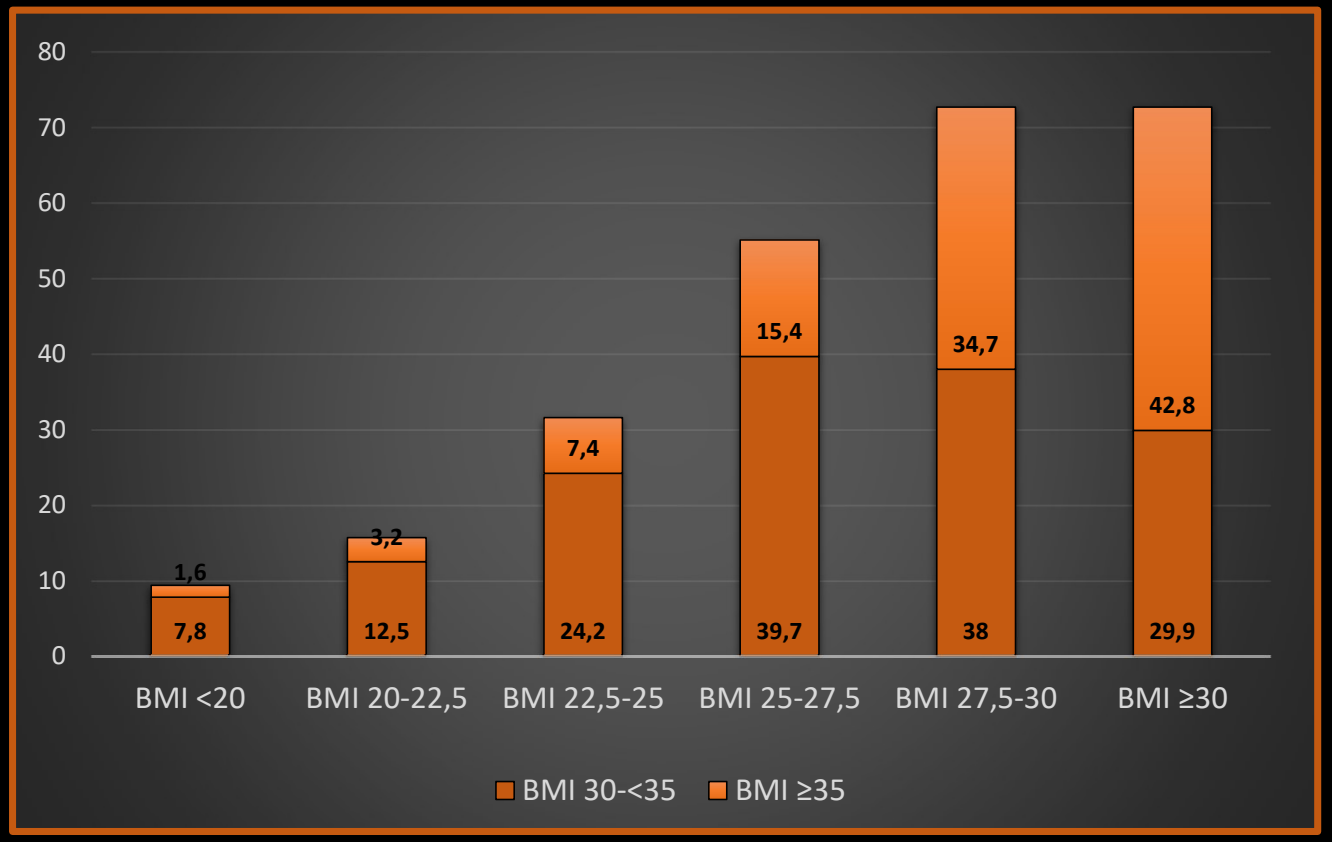
Fördelning av BMI (%) bland vuxna män och kvinnor 50-64 år i SCAPIS 2014-2018



<u>Normalviktiga (BMI<25)</u>:

- Män: 27%
- Kvinnor: 44%

BMI 30-<35 och ≥35 i SCAPIS (%) i relation till vikt vid 20 års ålder



Manuscript

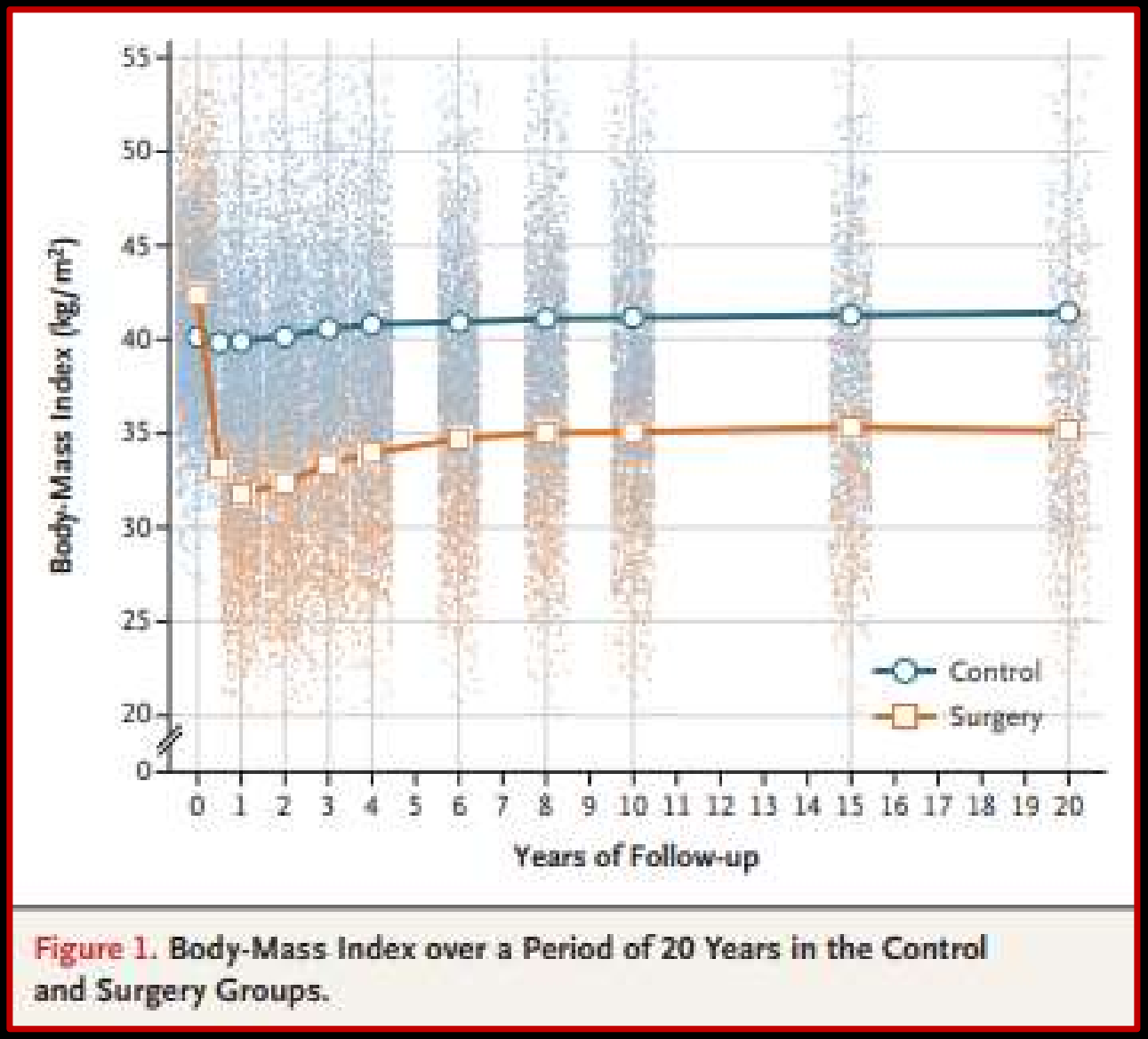
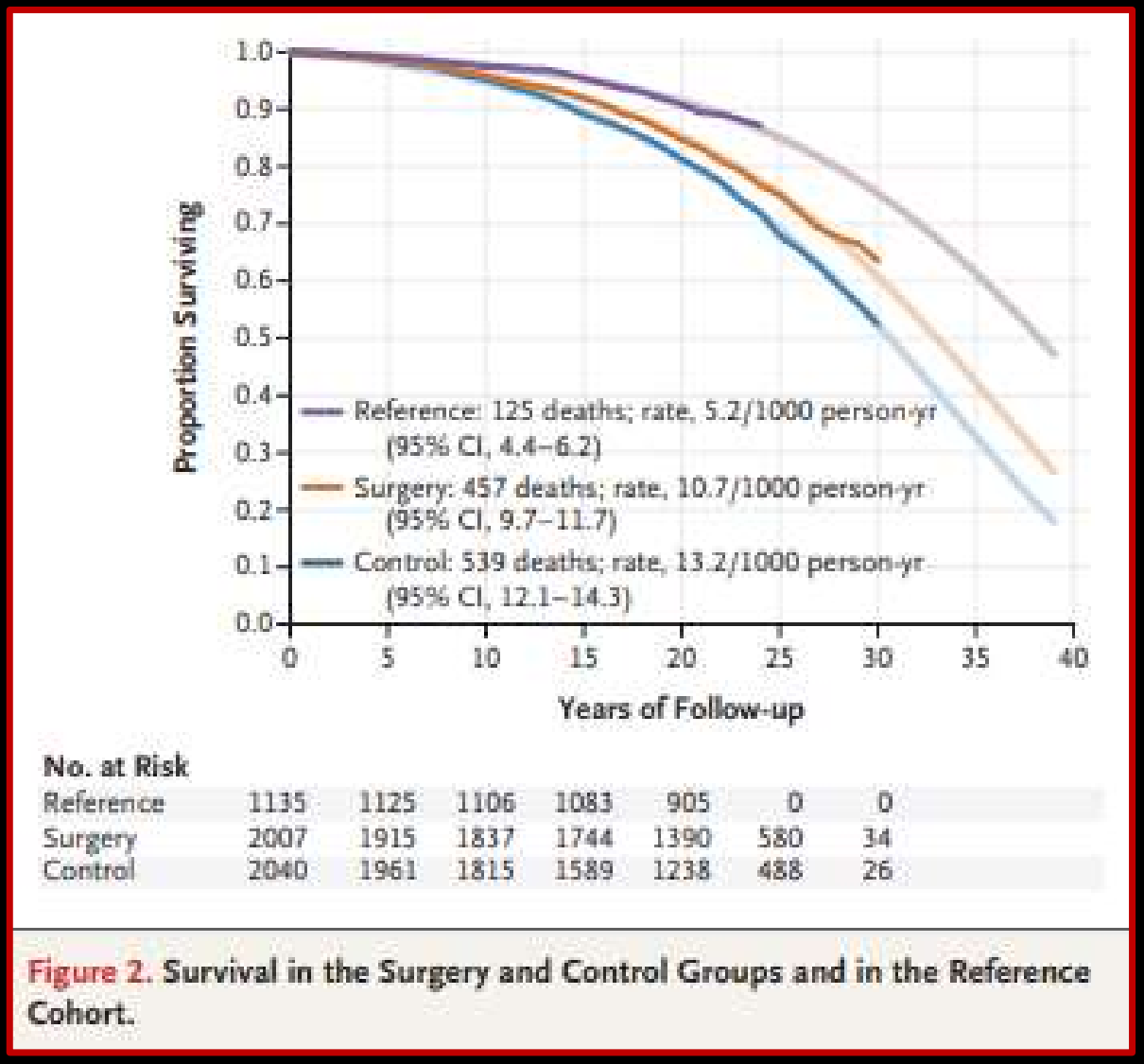


Figure 1. Body-Mass Index over a Period of 20 Years in the Control and Surgery Groups.

Viktminskning efter viktreducerande krirurgiska ingrepp i SOS-studien

Carlsson LMS, et al. N Engl J Med. 2020;383:1535-1543.



No. at Risk							
Reference	1135	1125	1106	1083	905	0	0
Surgery	2007	1915	1837	1744	1390	580	34
Control	2040	1961	1815	1589	1238	488	26

Figure 2. Survival in the Surgery and Control Groups and in the Reference Cohort.

Överlevnad efter viktreducerande kirurgiska ingrepp i SOS-studien

Carlsson LMS, et al. N Engl J Med. 2020;383:1535-1543.

ORIGINAL ARTICLE

OPEN

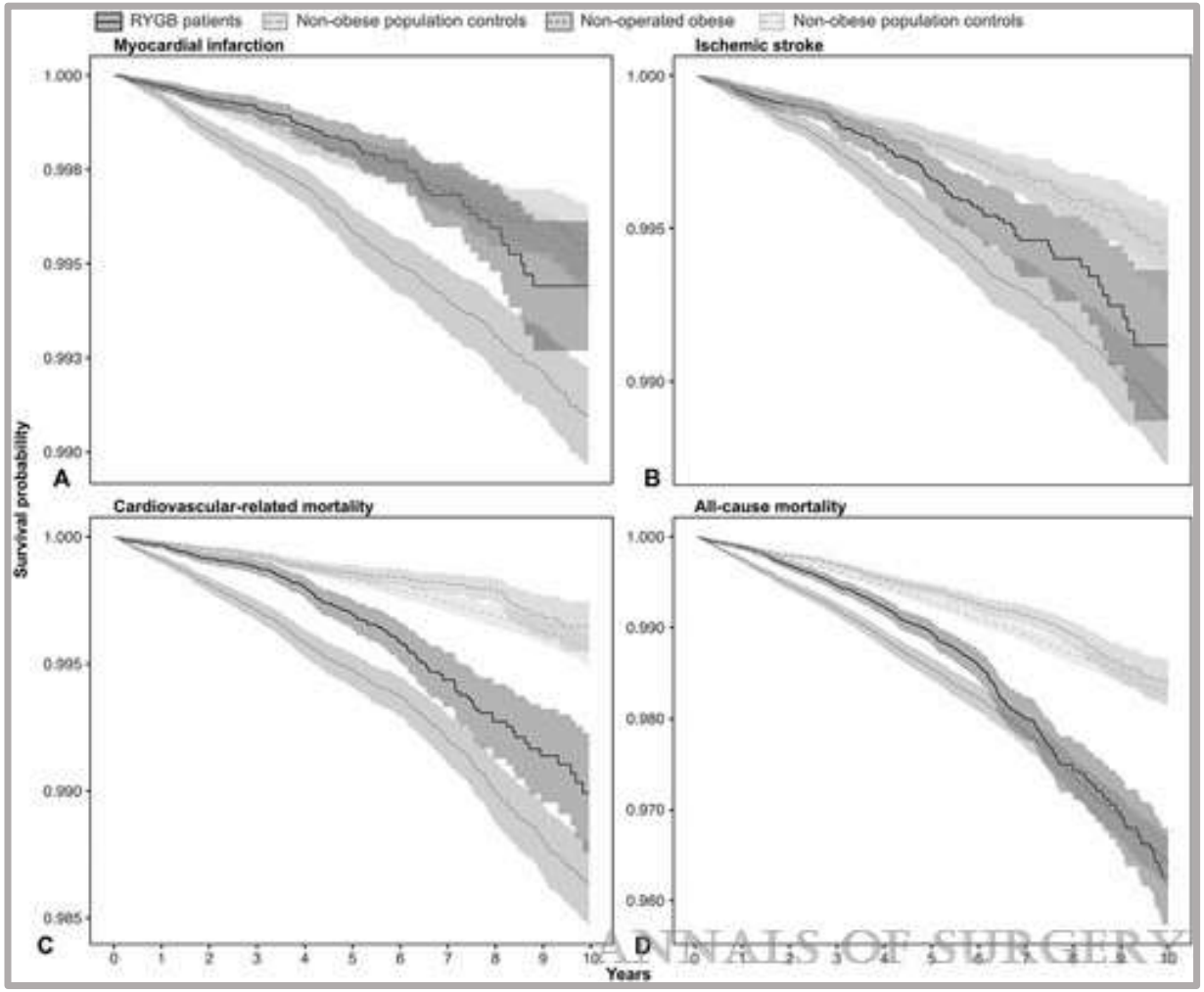
Risk of Myocardial Infarction, Ischemic Stroke, and Mortality in Patients Who Undergo Gastric Bypass for Obesity Compared With Nonoperated Obese Patients and Population Controls

Christina E. Lundberg, PhD, MPH,✉ Lena Björck, PhD,*† Martin Adiels, PhD,*‡ Jesper Lagergren, MD, PhD,§‖ and Annika Rosengren, MD, PhD*†*

"Compared with nonoperated patients with obesity, RYGB patients had a reduced risk of myocardial infarction [HR = 0.44 (95% CI 0.28-0.63)], similar risk of ischemic stroke [HR = 0.79 (95% CI 0.54– 1.14)], and decreased risks of cardiovascular-related [HR = 0.47 (95% CI 0.35–0.65)] and all-cause mortality [HR = 0.66 (95% CI 0.54–0.81)] within the first 3 years of follow-up, but not later"

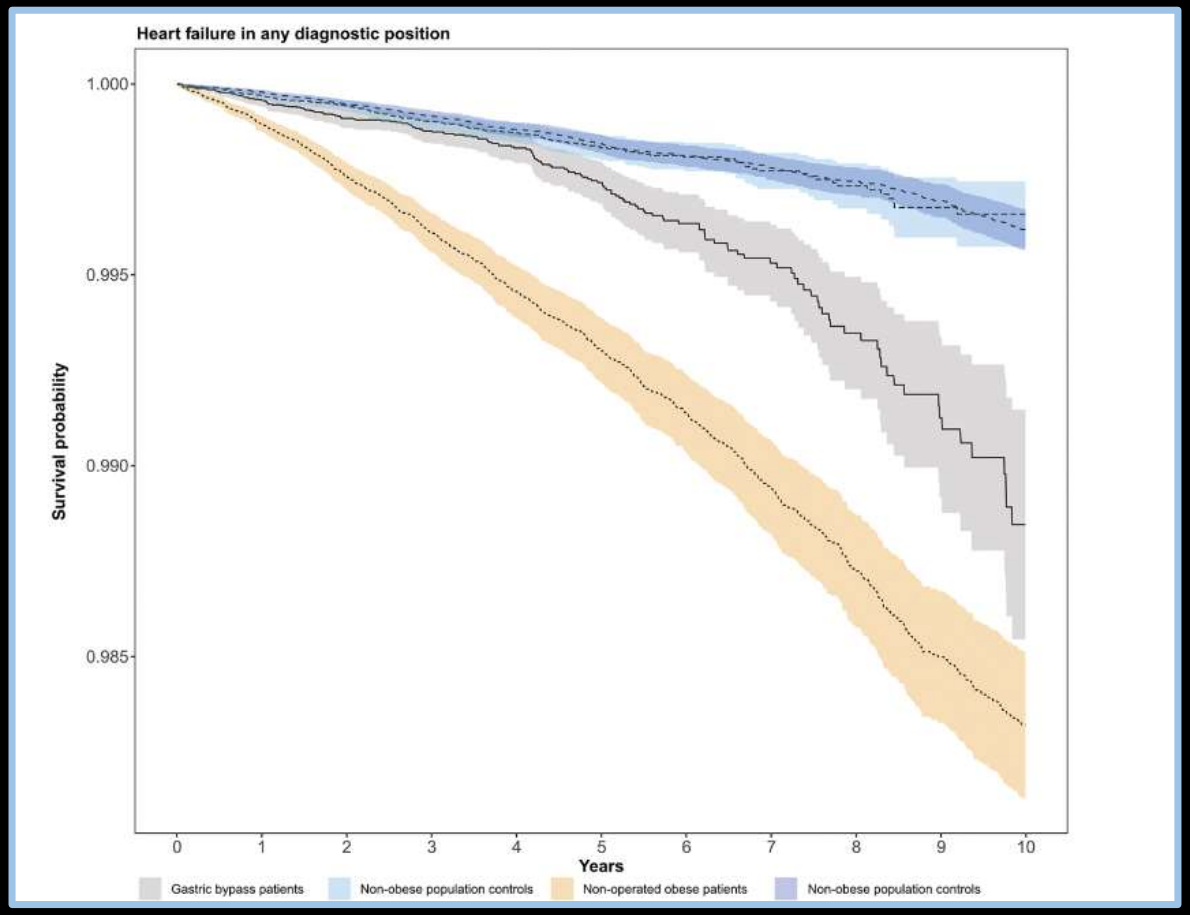
Lundberg CE, et al. Ann Surg. 2023 Feb 1;277(2):275-283.

AMI, ischemisk stroke, CVD-död, död: viktreducerande ingrepp, ej opererade individer med obesitas, och befolkningskontroller



Lundberg CE, et al. Ann Surg 2023; 277:275-283.

Hjärtsvikt: viktreducerande ingrepp (n=27,882) och ej opererade individer med obesitas (n=39,564), och befolkningskontroller (n=55,149+78,004)



Lundberg CE, et al. ESC Heart Failure. 2022;9:1844-1852.

https://investor.lilly.com/news-releases/news-release-details/tirzepatide-demonstrated-significant-and-superior-weight-loss

GLP-1 agonists

Glucagon-like peptide-1 (GLP-1) receptor agonists, also known as GLP-1 analogs:

- a class of drugs that reduce blood sugar and energy intake by activating the GLP-1 receptor in the gut
- mimic the actions of the endogenous incretin hormone GLP-1 that is released by the gut after eating.

RESEARCH SUMMARY

Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

Kosiborod MN et al. DOI: 10.1056/NEJMoa2306963

CLINICAL PROBLEM

Patients with heart failure with preserved ejection fraction often have obesity, a condition that is associated with a greater burden of heart failure–related symptoms, worse functional capacity, and more impaired quality of life. Whether therapies that target obesity in such patients can alleviate symptoms and physical limitations is unknown.

CLINICAL TRIAL

Design: A multinational, double-blind, randomized, placebo-controlled trial evaluated whether treatment with semaglutide — a glucagon-like peptide 1 receptor agonist approved for long-term weight management — would reduce heart failure–related symptoms and improve physical function, in addition to inducing weight loss, in adults with heart failure with preserved ejection fraction and obesity.

Intervention: 529 patients with a body-mass index of ≥30 were assigned to receive subcutaneous semaglutide (2.4 mg) or placebo once weekly for 52 weeks. The dual primary end points were the change in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS), which quantifies heart failure–related symptoms and physical function, and the change in body weight from baseline to week 52.

RESULTS

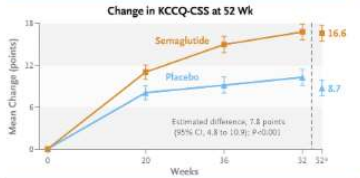
Efficacy: The mean change in KCCQ-CSS and the mean percentage change in body weight were significantly greater with semaglutide than with placebo.

Safety: Serious adverse events occurred less often with semaglutide than with placebo, primarily because fewer cardiac disorders occurred in the semaglutide group. Adverse events leading to treatment discontinuation were more common with semaglutide.

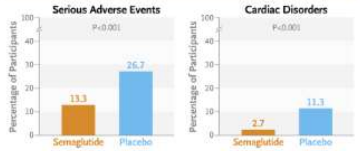
LIMITATIONS AND REMAINING QUESTIONS

- The number of non-White trial participants was low.
- The trial was not sufficiently powered to evaluate the effects of semaglutide on clinical events, such as hospitalization for heart failure.
- Whether the observed effects of semaglutide would last beyond 1 year is unknown.

Links: Full Article | NEJM Quick Take | Editorial



Week 52 data are based on ANCOVA and imputation of missing data.



CONCLUSIONS

In adults with heart failure with preserved ejection fraction and obesity, once-weekly treatment with semaglutide was associated with greater reductions in heart failure–related symptoms and physical limitations and greater weight loss than placebo over 52 weeks.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 21, 2023 VOL. 389 NO. 12

Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C Petrie, for the STEP-HFpEF Trial Committees and Investigators*

Table 1. Baseline Demographic and Clinical Characteristics of the Participants.*

Characteristic	Semaglutide (N=263)	Placebo (N=266)	Total (N=529)
Female sex — no. (%)	149 (56.7)	148 (55.6)	297 (56.1)
Median age (IQR) — yr	70 (62–75)	69 (62–75)	69 (62–75)
Ethnic group — no. (%)†			
Hispanic or Latino	15 (5.7)	21 (7.9)	36 (6.8)
Not Hispanic or Latino	248 (94.3)	245 (92.1)	493 (93.2)
Race — no. (%)†			
Black	8 (3.0)	13 (4.9)	21 (4.0)
White	255 (97.0)	252 (94.7)	507 (95.8)
Other	0	1 (0.4)	1 (0.2)
Median body weight (IQR) — kg	104.7 (92.4–120.1)	105.3 (92.4–122.0)	105.1 (92.4–120.8)
Median BMI (IQR)	37.2 (33.9–41.1)	36.9 (33.3–41.6)	37.0 (33.7–41.4)
BMI stratum — no. (%)			
30 to <35	89 (33.8)	91 (34.2)	180 (34.0)
≥35	174 (66.2)	175 (65.8)	349 (66.0)

The NEW ENGLAND JOURNAL of MEDICINE

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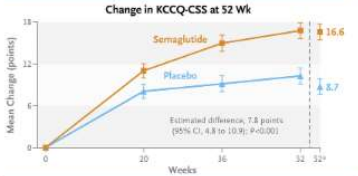
Links: Full Article | NEJM Quick Take | Editorial



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In adults with heart failure with preserved ejection fraction and obesity, once-weekly treatment with semaglutide was associated with greater reductions in heart failure–related symptoms and physical limitations and greater weight loss than placebo over 52 weeks.

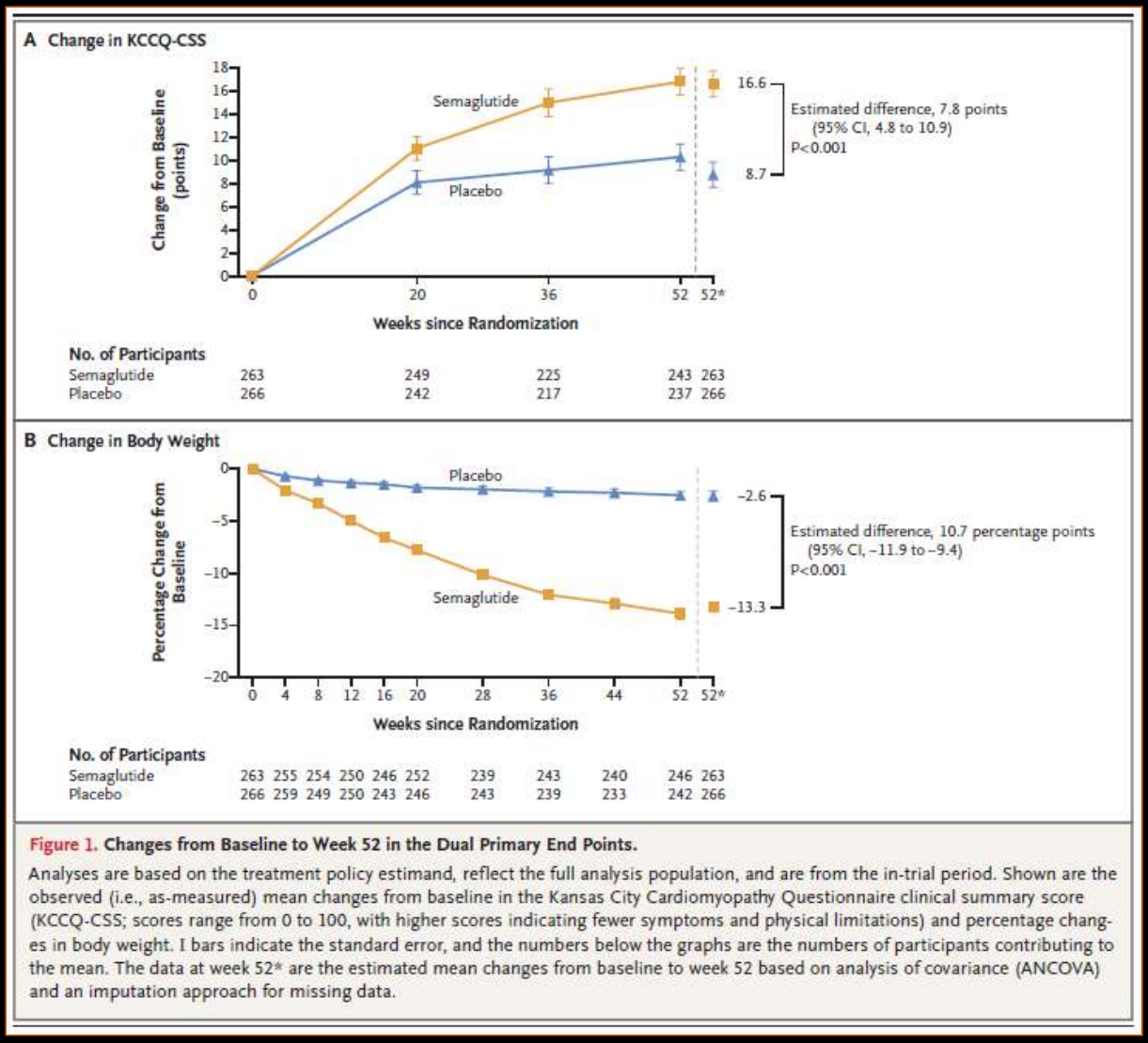


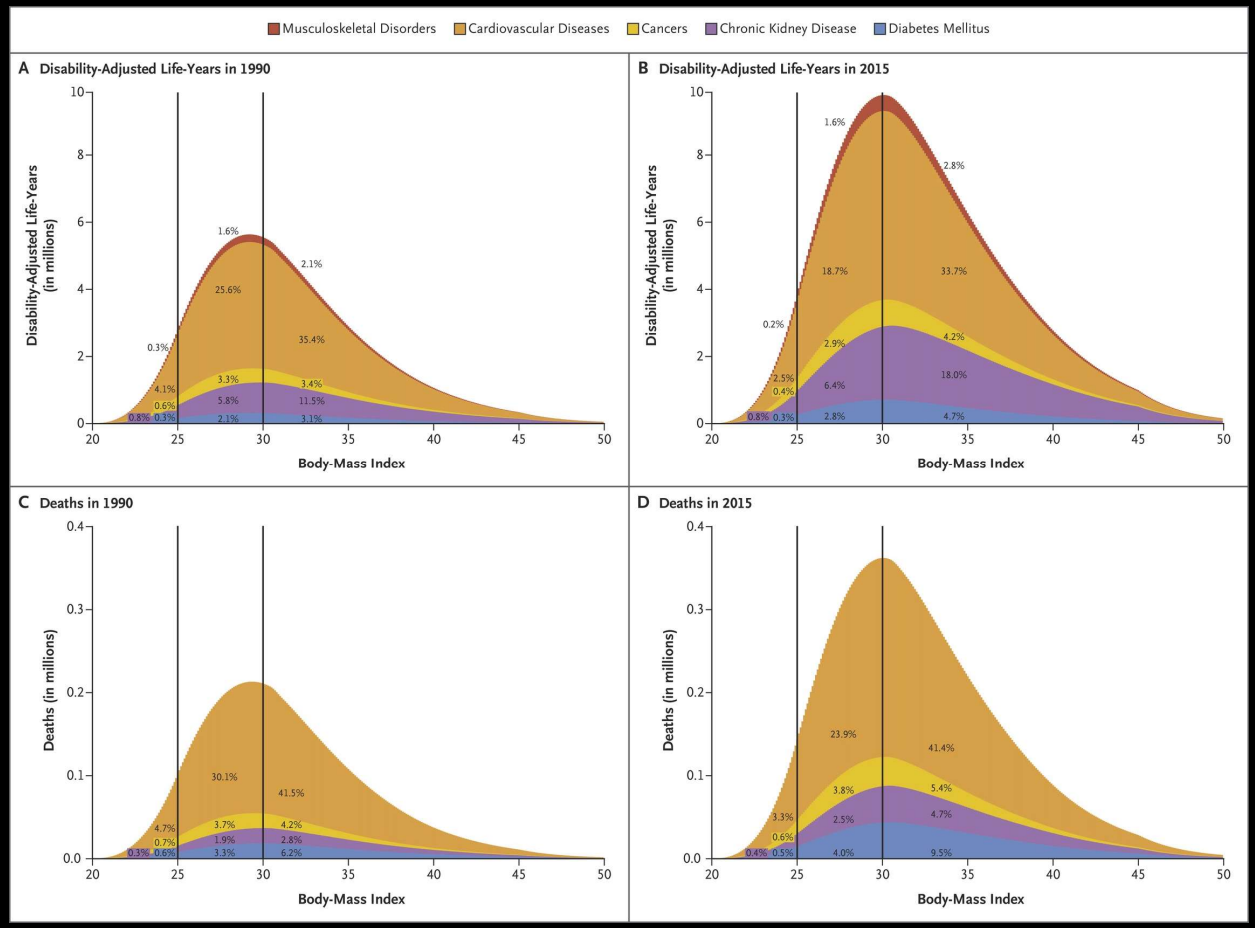
Figure 1. Changes from Baseline to Week 52 in the Dual Primary End Points.

Analyses are based on the treatment policy estimand, reflect the full analysis population, and are from the in-trial period. Shown are the observed (i.e., as-measured) mean changes from baseline in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating fewer symptoms and physical limitations) and percentage changes in body weight. I bars indicate the standard error, and the numbers below the graphs are the numbers of participants contributing to the mean. The data at week 52* are the estimated mean changes from baseline to week 52 based on analysis of covariance (ANCOVA) and an imputation approach for missing data.

Löser GLP1-agonister det globala fetmaproblemet..?

- Varje år går tusentals unga människor enbart i Sverige in i vuxenlivet med fetma, och många med svår fetma – kanske 5-10,000, respektive 2-3000 per årskull.
- Drygt 1 miljard människor har en ohälsosam övervikt
- Risken för tidig hjärtinfarkt, hjärtinfarkt, stroke, och förtidig död ökar från låga BMI-nivåer - en hälsosam vikt vid 18-20 år ligger runt BMI 20-22
- De flesta fall av såväl CVD som övrig sjuklighet inträffar bland den stora gruppen med måttlig övervikt
- Bariatrisk kirurgi: effektivt men stort ingrepp och övergående effekt
- GLP1-agonister: viktigt vid etablerad fetma och samsjuklighet men sannolikt rätt liten inverkan på CVD i stort – vikten reduceras men normaliseras inte
- Dyrt: ett års behandling med Wegovy = 57 300 kr (källa: Dagens Medicin)
- ***Fortsatt väsentligt att förebygga övervikt/fetma hos unga och viktuppgång från ungdom till medelålder***

Global Disability-Adjusted Life-Years and Deaths Associated with a High Body-Mass Index (1990–2015).



The GBD 2015 Obesity Collaborators. N Engl J Med ;377:13-27

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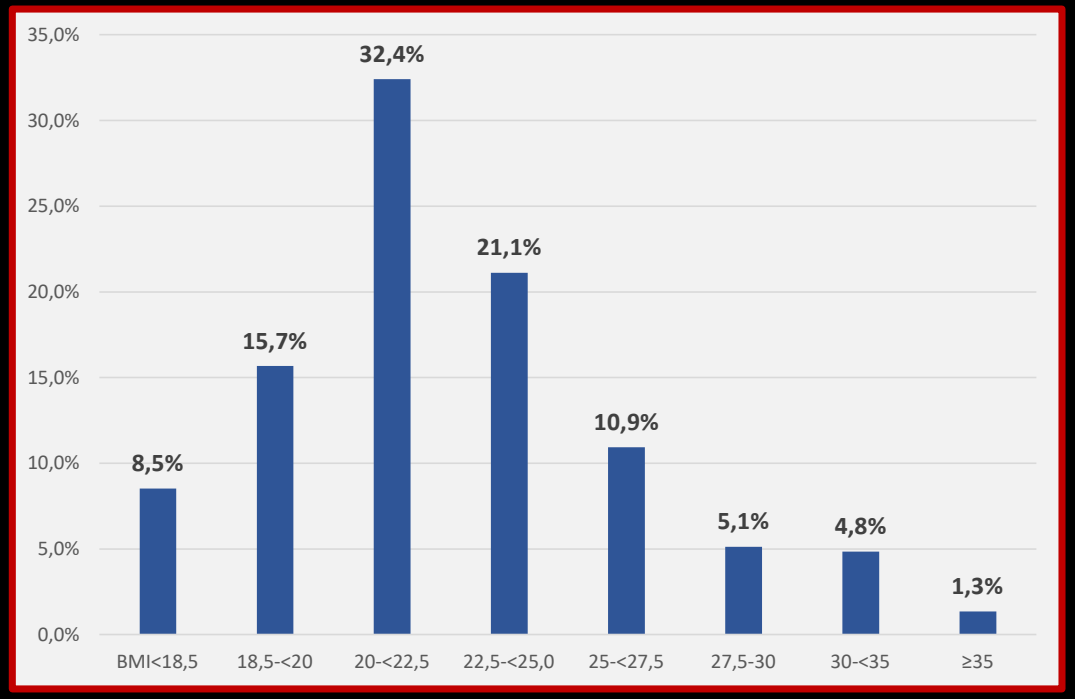
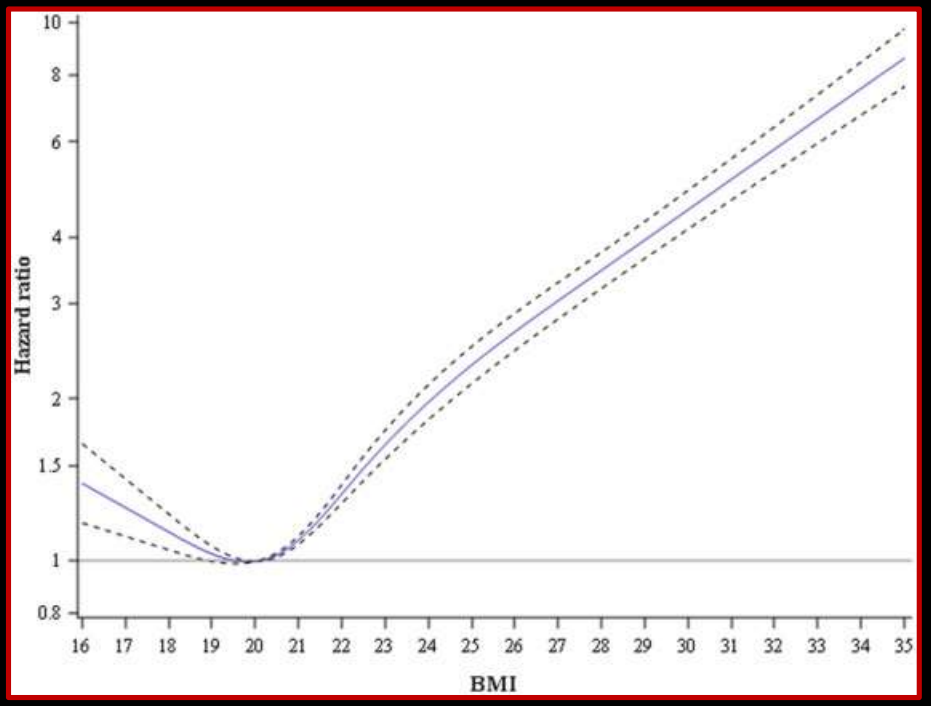
Fördelning av fall (%) av tidig hjärtsvikt och risk efter BMI vid 18 års ålder. Värnpliktsregistret.





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