Professor John Dixon

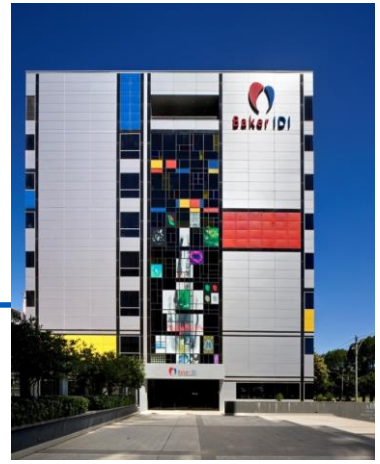
Head of Clinical Obesity Research
Baker IDI Heart and Diabetes Institute
Melbourne

Friday, August 09, 2019

(Plenary)

9:10 - 9:30 BMI is a Great Metric, But Do We Understand It?

BMI is a great metric? - But do we understand it?



Professor John B Dixon, MBBS PhD

Professorial Research Fellow
Head, Clinical Obesity Research
Baker IDI Heart & Diabetes Institute
Melbourne, Australia

South GP CME South Meeting
08 Aug 2019 - 11 Aug 2019

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Disclosures: Professor John B Dixon

Bariatric Advantage	Consultant
BUPA	Research Support
I-Nova	Consultant
Nestle Health Science	Consultant
NACOS	Chair accreditation
NHMRC	Research Support
Nova Nordisk	Advisory board and speaker fees
MISS	Co-director US surgical conference
Obesity Australia	
RACGP	Research Support

Everything You Know About Obesity Is Wrong

For decades, the medical community has ignored mountains of evidence to wage a cruel and futile war on fat people, poisoning public perception and ruining millions of lives.

HUFFINGTON POST
SEPTEMBER 19, 2018

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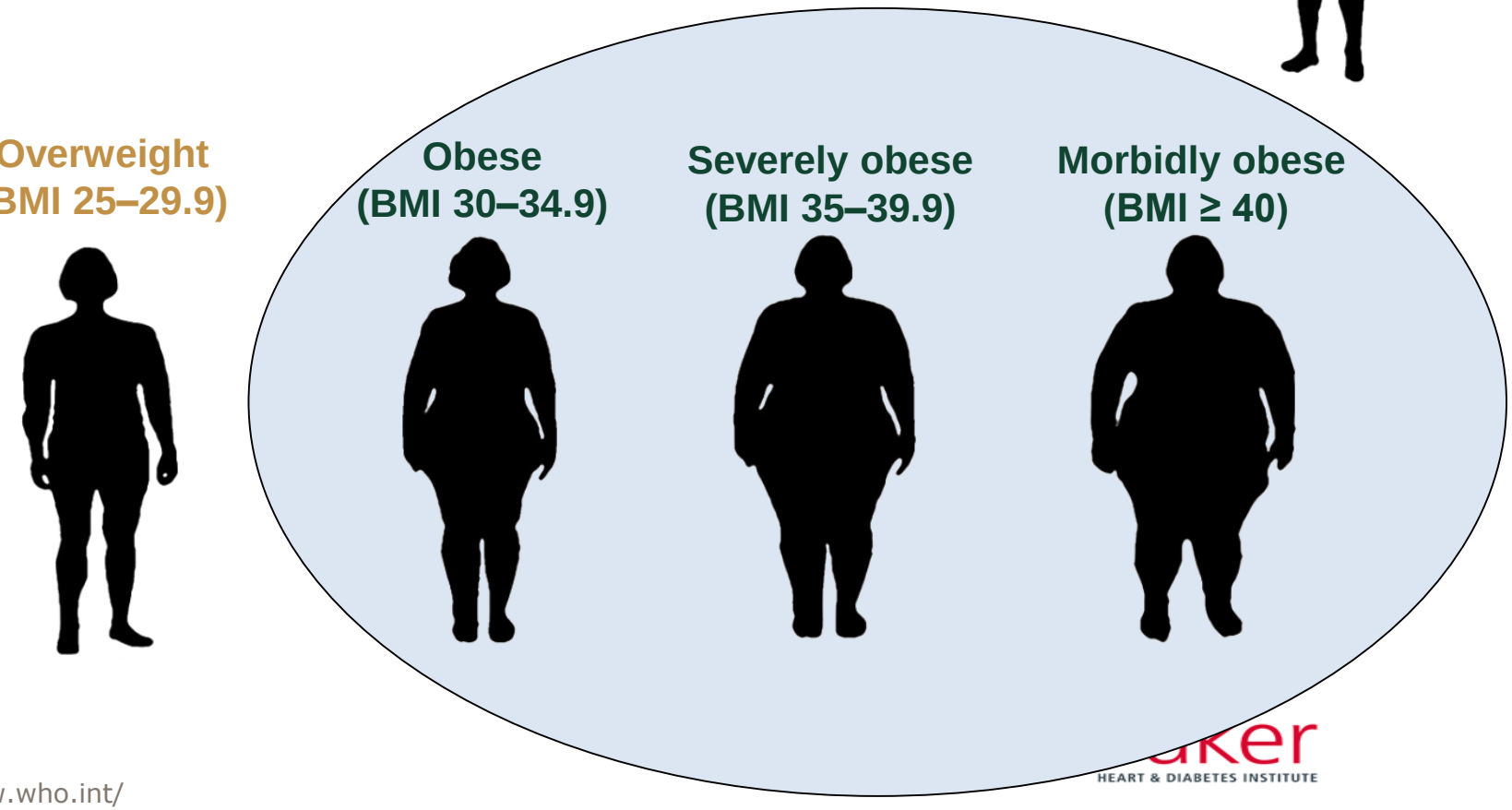
What is Obesity?

Excessive accumulation of fat that may impair health

Latin: *obesus*: from *ob-* (intensive) + *edere* (to eat)

$$BMI = \frac{weight\ (kg)}{height\ (m)^2}$$

WHO BMI cutoffs (kg/m²)²		
White European	Overweight	≥25
	Obese	≥30
Asian	Overweight	**>23**
	Obese	**>27.5**



BMI, body mass index

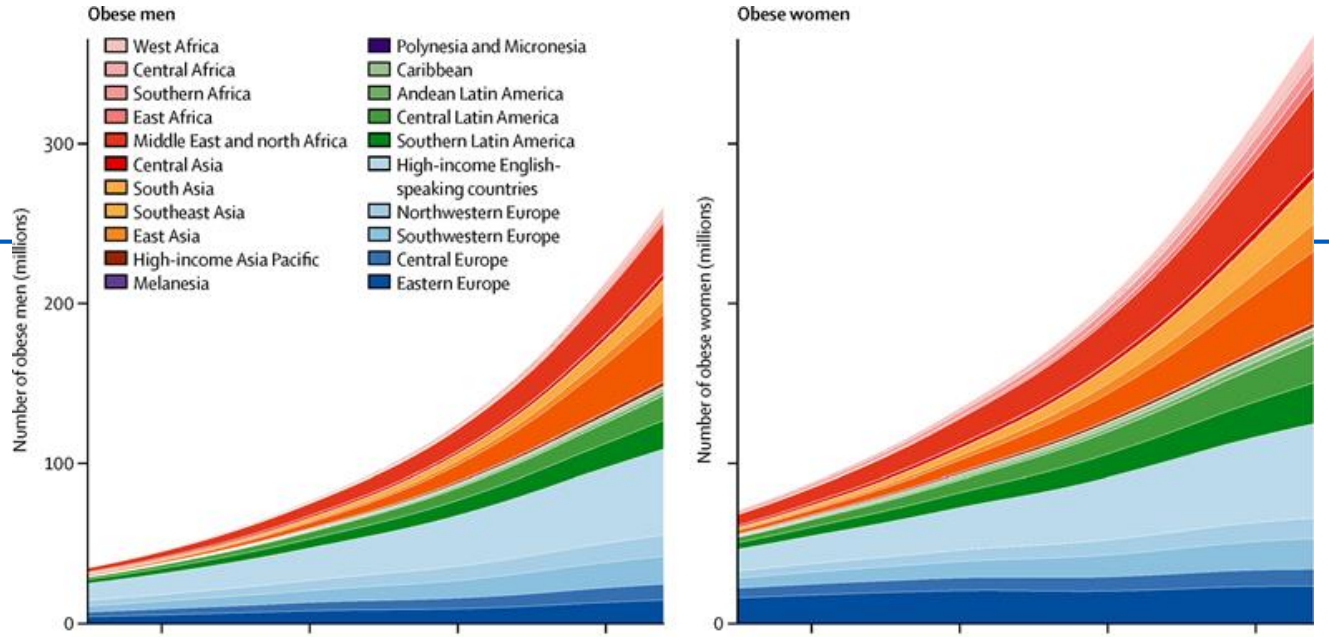
WHO. Factsheet 311. 2014. http://www.who.int/

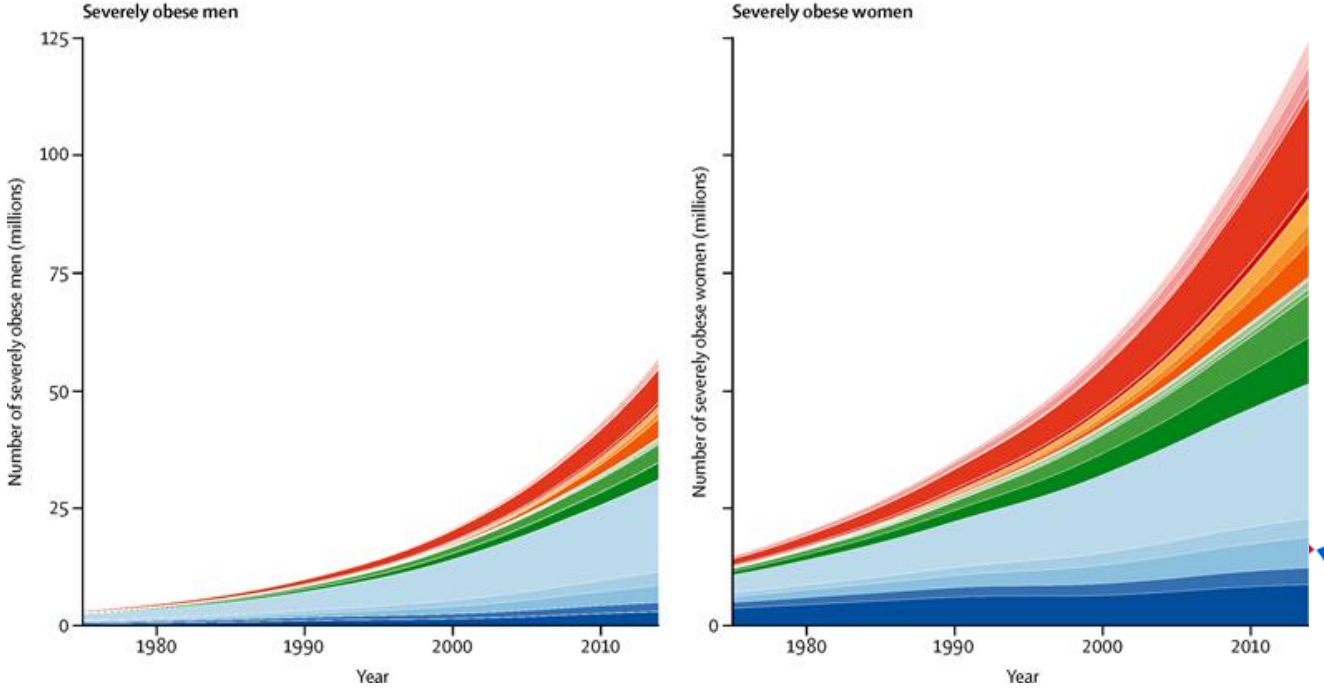
Global & Regional Obesity

High income English speaking countries

BLUE

Global & Regional Severe obesity





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Is BMI a good measure of body composition?

- Percentage fat mass or fat free mass

BMI and its relationship with mortality?

- Age
- Risk of disease
- Living with disease

What are the implications for weight management?

- Indications based on BMI
- Targets for weight loss

BMI has major limitations as it does not measure body fat? Surely we can find a better metric?

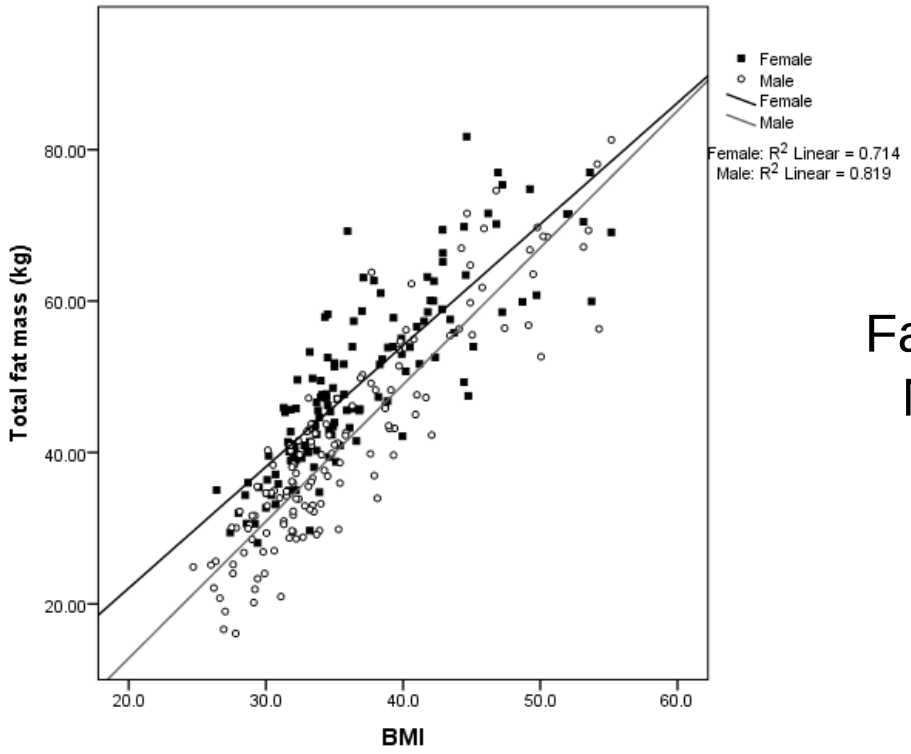
Is BMI a good measure of body composition?

- Percentage fat mass or fat free mass

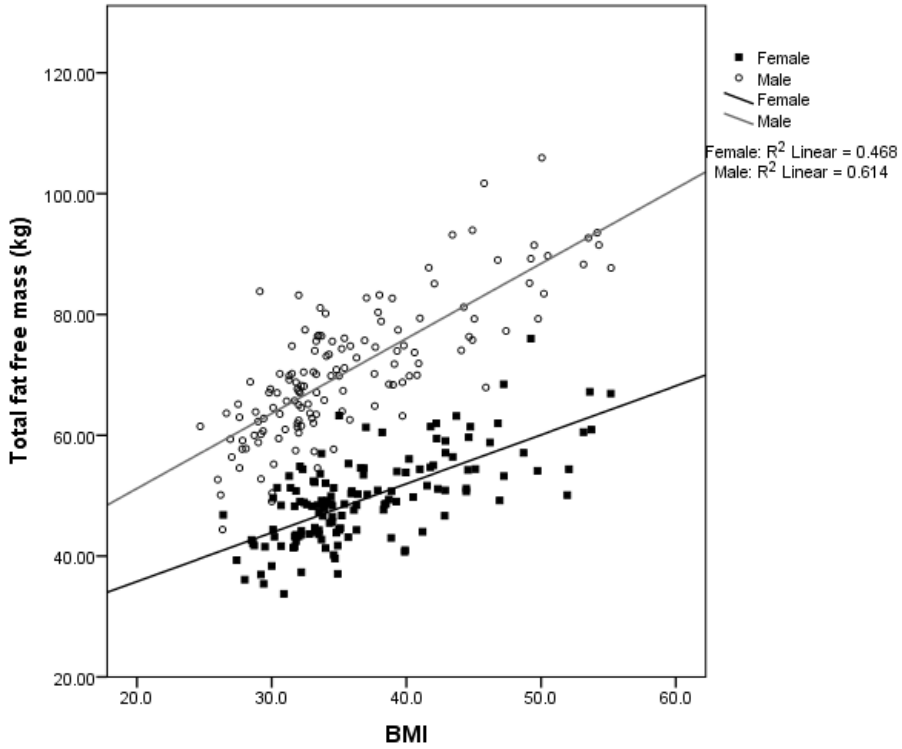
Body composition and body mass index

275 weight stable obese white adults 50% M&F

Fat Mass



Fat Free Mass



DEXA body composition

Females ■

Males ○

Diabetes, obesity & metabolism. Jan 2015;17(1):91-93.

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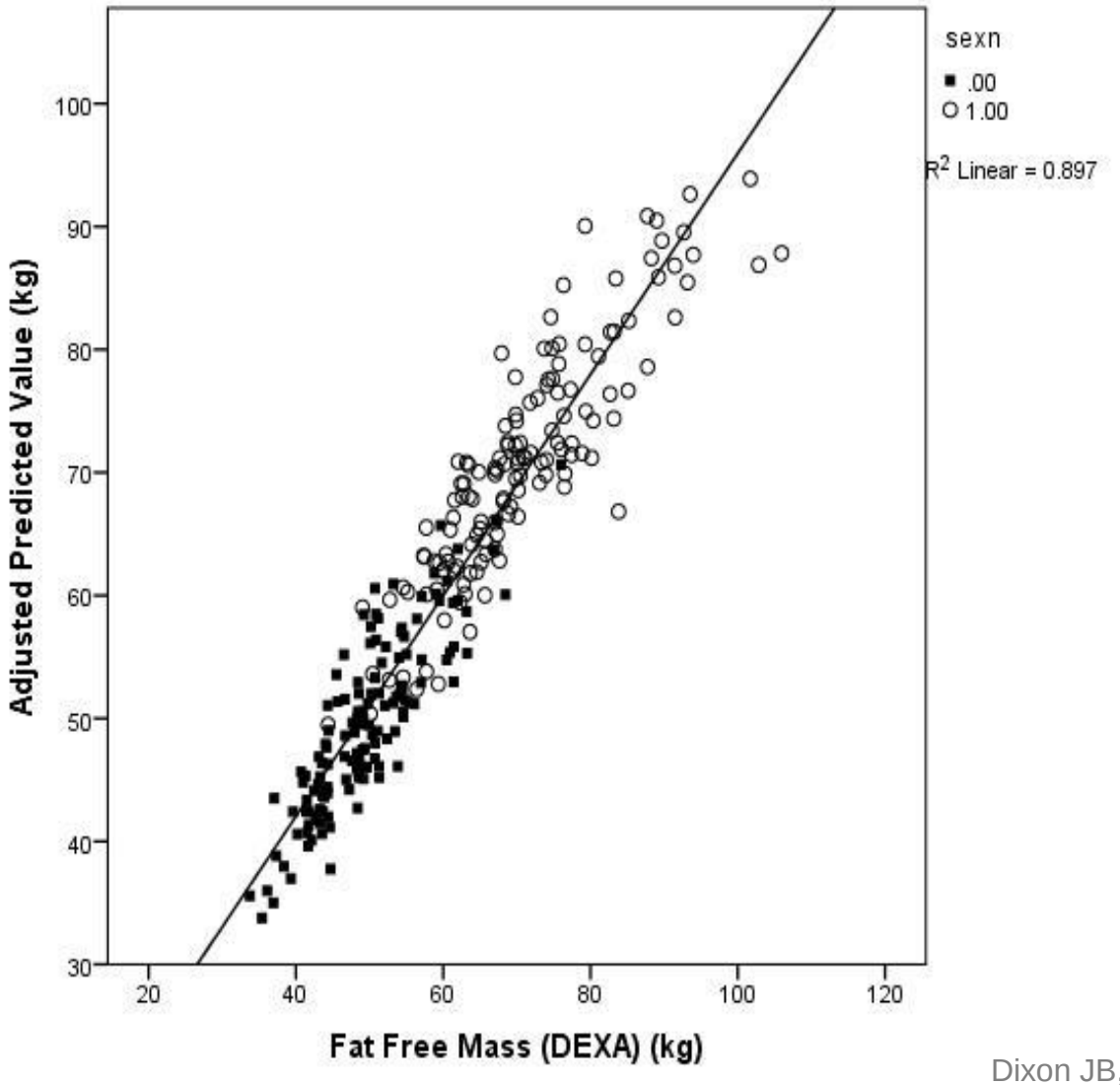
DEXA measures FFM and FM without any additional inputs. How well are the DEXA results explained by what we know?



90% of variance explained by height, weight, sex and age

Height, weight, sex, and age (European population) provide the most remarkable biologically explanation of body composition in these overweight and obese adults

If we replace the height and weight with BMI the explanation of variance drops to 89%

Dixon JB, et al *Diabetes, obesity & metabolism.* 2014.

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BMI is an excellent measure of body composition -

- With sex, age, weight, height, and ethnicity we have an excellent measure of Fat Mass and Fat Free Mass
- It is NOT a measure of fat distribution
- It is NOT a measure of risk
- We do NOT design our useful metrics around extreme outliers

- **What is Obesity?**
  Excessive accumulation of fat that may impair health

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BMI and its relationship with mortality?

- Age
- Risk of disease
- Living with disease

BMI – Quetelet's Index -

Body mass index (BMI), more properly Quetelet's index, was developed by Lambert Adolphe Jacques Quetelet (1796–1874).

Quetelet, a Belgian mathematician, made contributions to astronomy, mathematics, sociology, anthropometry, and statistics

BMI was little used until the late 1970's

- October 1980 - Reuben Andres, Clinical Director of the US National Institute on Aging, was asked to talk to Association of Life Insurance Medical Directors Annual Meeting
- Studies looked at heights and weights of over 4 million people (time of buying a policy) and 106,000 deaths
- Five conclusions

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Mortality data presented to life insurance companies in 1980

BMI and mortality is U- or J-shaped

BMI associated with minimal (NADIR) mortality increases with age

Accounting for smoking, pre-existing disease, or early mortality had little effect on BMI of minimal mortality

The best BMI for a given age is the same in men and women

Frame size was not a useful metric

Conclusion: BMI should be used

The first 2 of these conclusions
proved controversial because they questioned the “beautiful hypotheses”

Andres R. The obesity-mortality association: where is the nadir of the U-shaped curve? Trans Assoc Life Insur Med Dir Am 1980;64: 185–97.

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Conclusion: BMI should be used

Is BMI a good metric for estimating body *"Fatness"* ?

Classification	BMI(kg/m^2)
	Principal cut-off points
Normal range	**18.5 - 24.9**
Pre-obese	**25.0 - 29.9**
Obese class I	**30.0 - 34.9**
Obese class II	**35.0 - 39.9**
Obese class III	**≥40.0**

Ruben Andres. The obesity-mortality association: where is the nadir of the U-shaped curve? Trans Assoc Life Insur Med Dir Am 1980;64: 185–97. Ruben
Review and commentary:Am J Clin Nutr 2014;99:759–60.

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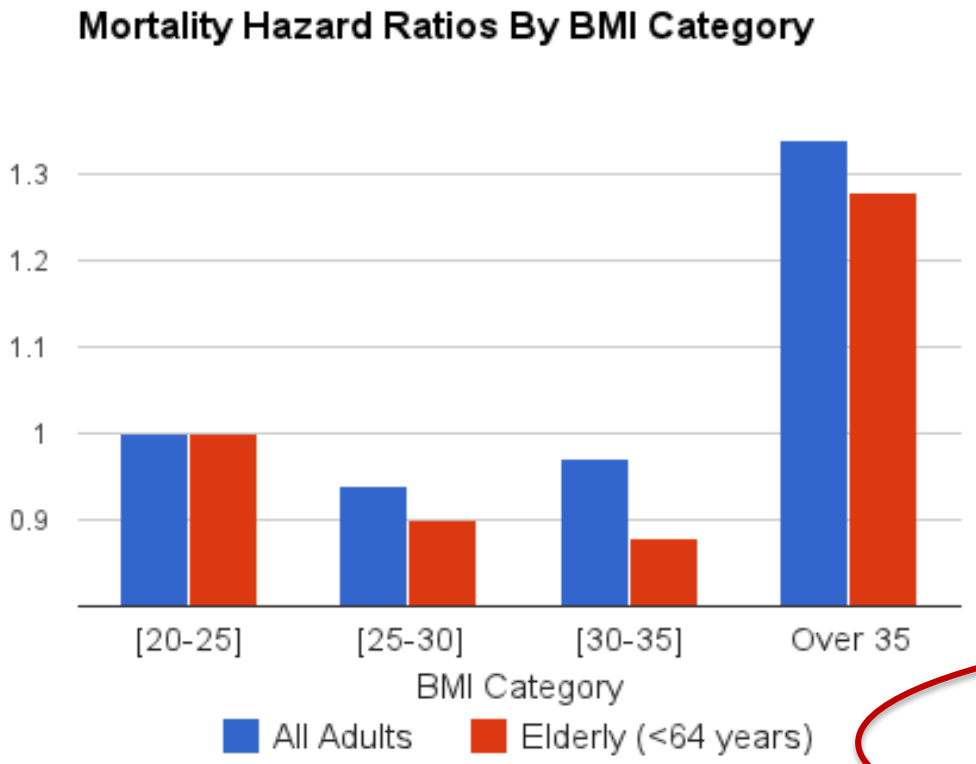
Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis

2.88 million with 270,000 deaths



	Self-reported or Measured Height and Weight		
	No. of HRs	Summary HR (95% CI)	I^2, %
BMI of 25-<30			
All ages	86	0.94 (0.90-0.97)[a]	87.6
Mixed ages	68	0.95 (0.91-0.99)[a]	89.3
Age ≥65 y only	18	0.90 (0.86-0.95)	27.9
BMI of ≥30			
All ages	42	1.21 (1.12-1.31)[a]	89.3
Mixed ages	33	1.26 (1.16-1.37)[a]	89.7
Age ≥65 y only	9	1.05 (0.92-1.21)[a]	63.9
BMI of 30-<35			
All ages	42	0.97 (0.90-1.04)[a]	83.8
Mixed ages	33	0.98 (0.91-1.06)[a]	84.8
Age ≥65 y only	9	0.88 (0.69-1.12)[a]	78.0
BMI of ≥35			
All ages	42	1.34 (1.21-1.47)[a]	81.2
Mixed ages	33	1.35 (1.22-1.50)[a]	82.2
Age ≥65 y only	9	1.28 (0.93-1.76)[a]	75.2

Flegal, K. M., B. K. Kit, et al. (2013). JAMA **309(1): 71-82.**

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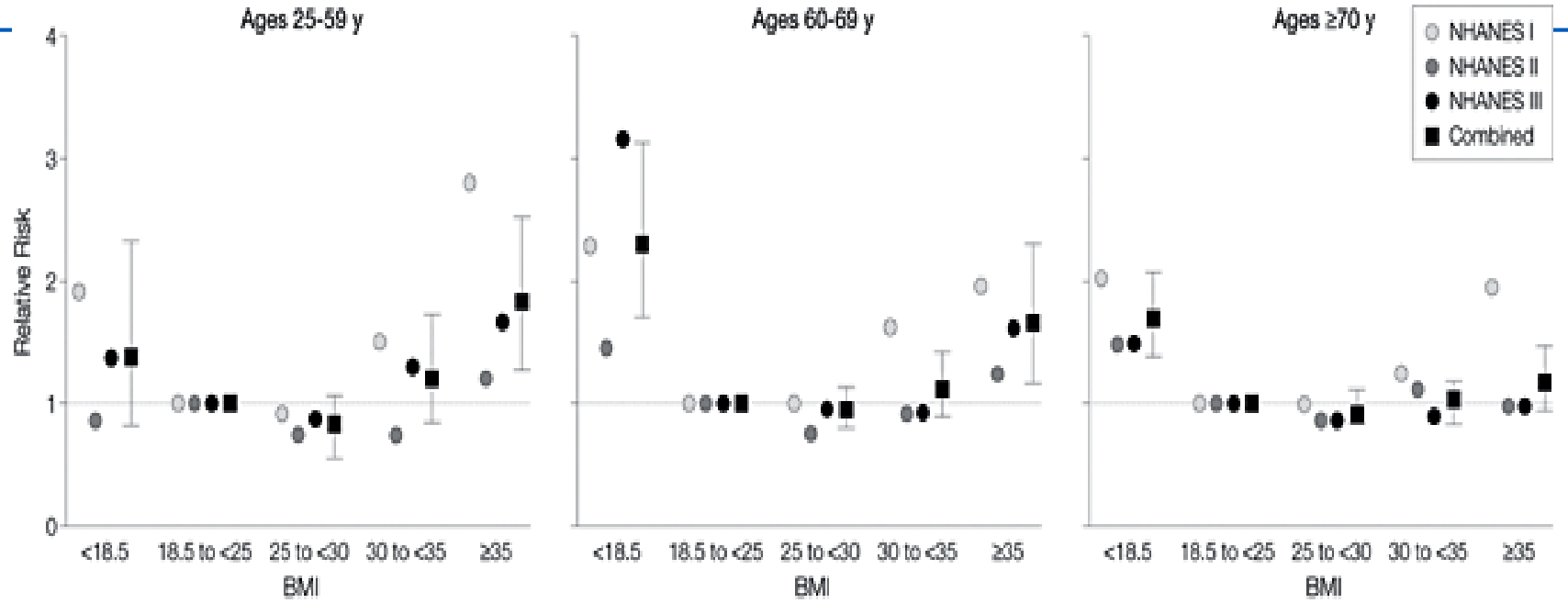
Relative Risks of Mortality by BMI Category, Survey, and Age



Varying follow-up periods of NHANES I-III

Flegal, K. M. et al. JAMA 2005;293:1861-1867

For a review including many countries

Oreopoulos, A., K. Kalantar-Zadeh, A. M. Sharma and G. C. Fonarow (2009). "The obesity paradox in the elderly: potential mechanisms and clinical implications." Clin Geriatr Med **25(4): 643-659, viii.**

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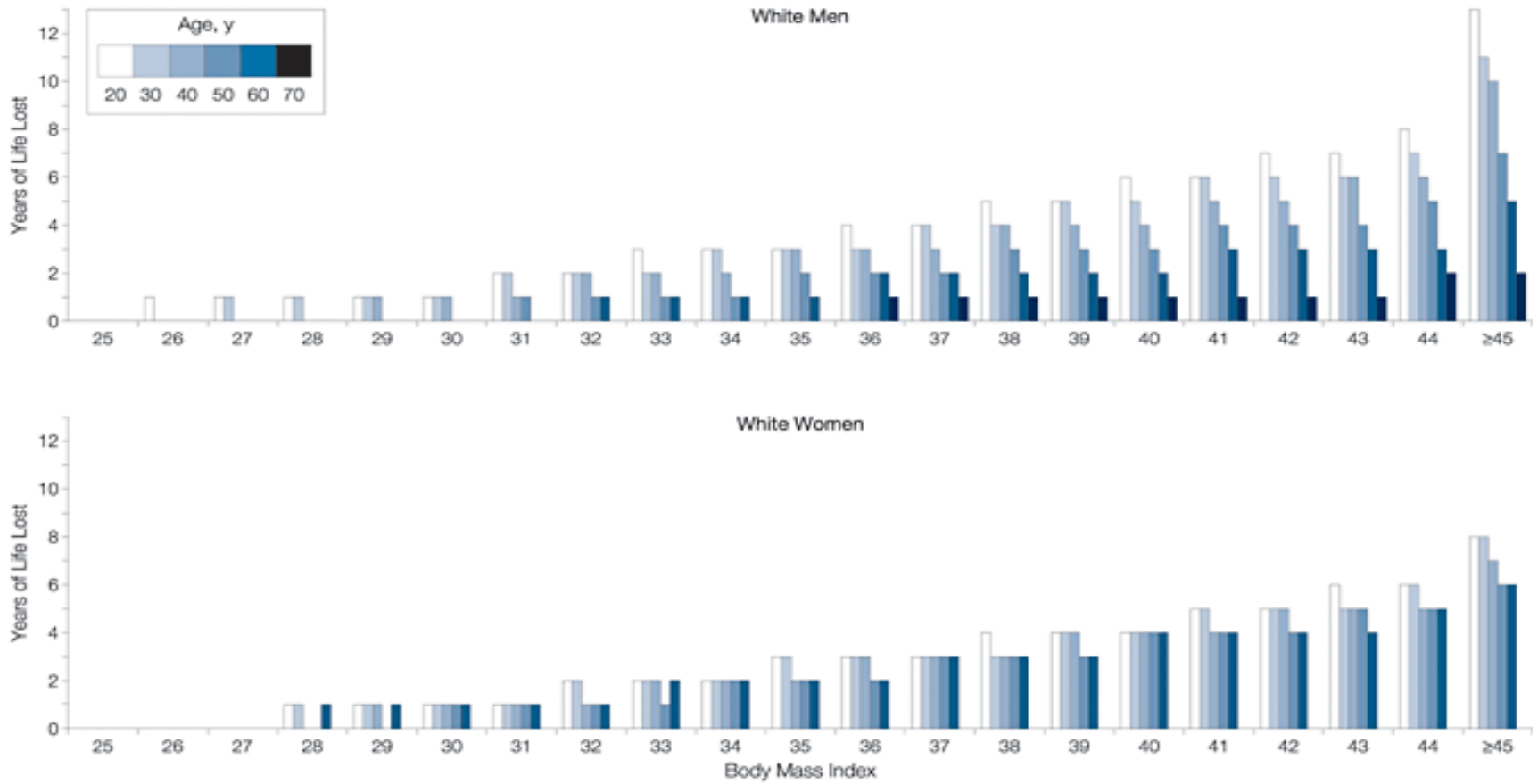
Years of life lost associated with BMI



Fontaine, KR et.al. JAMA 289:187, January 8, 2003

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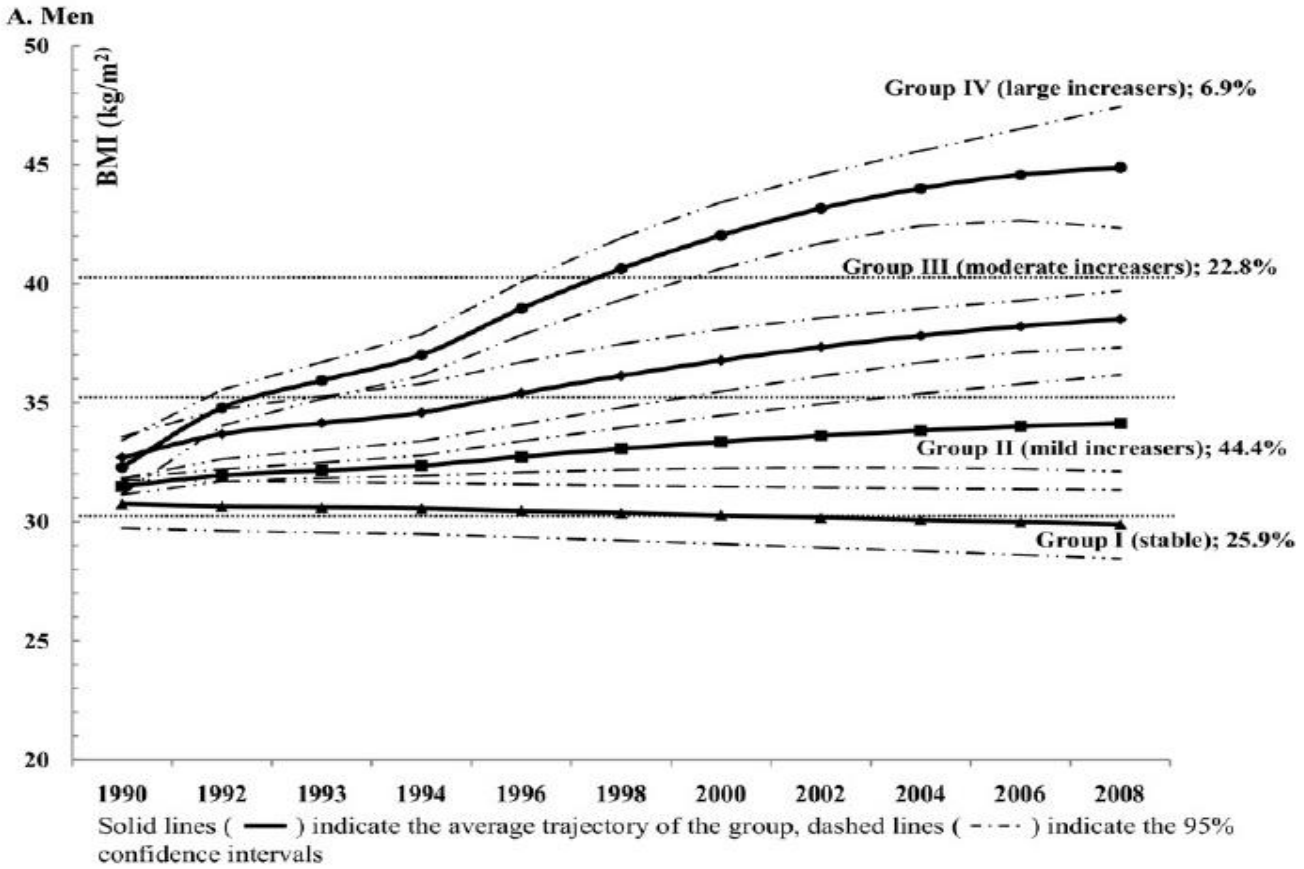
Body mass trajectories through midlife among adults with class I obesity

National longitudinal study of youth 1979

Age 25 -33 Class 1 obesity 1990 – followed to 2008

Men



Solid lines (——) indicate the average trajectory of the group, dashed lines (- - - -) indicate the 95% confidence intervals

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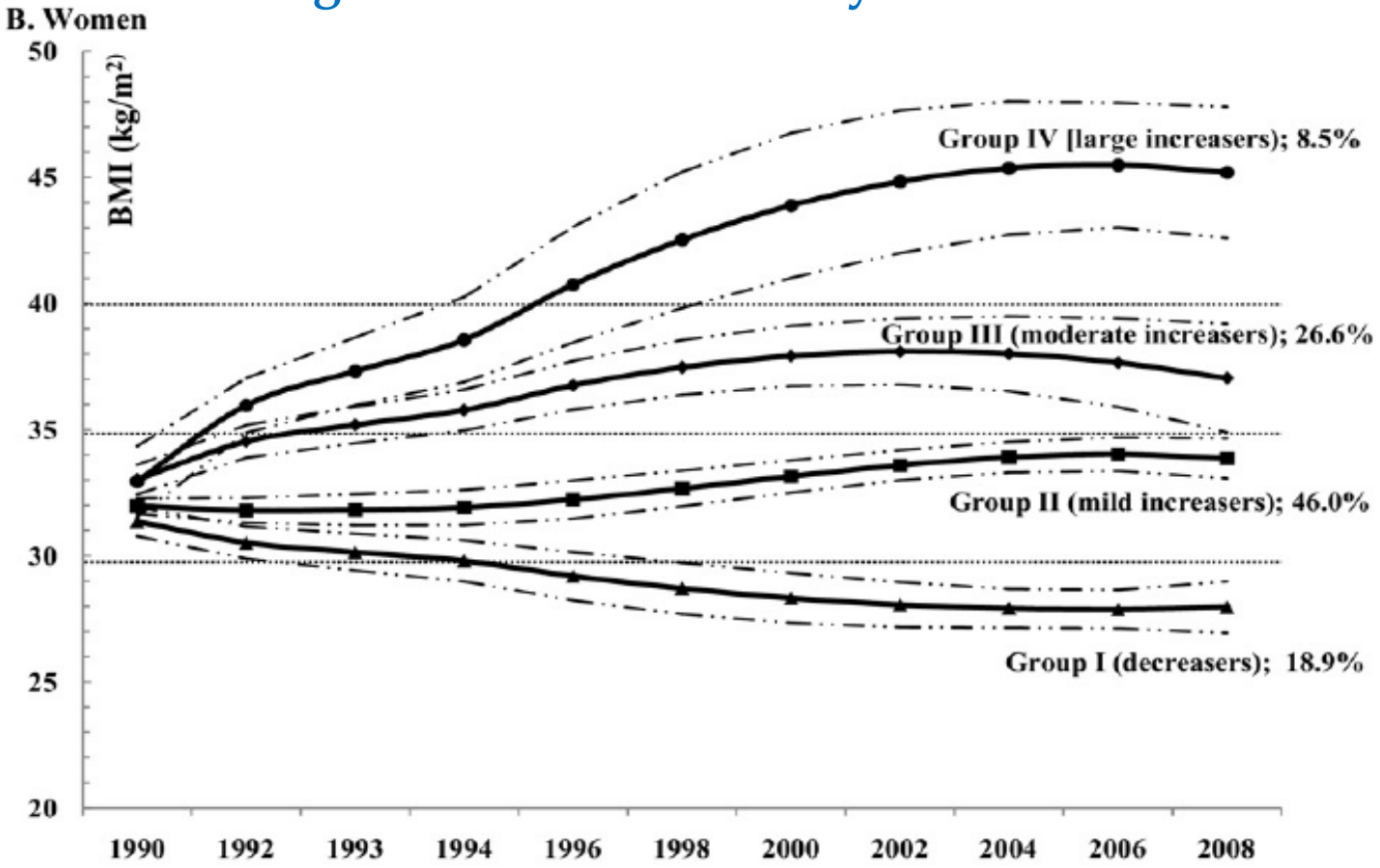
Body mass trajectories through midlife among adults with class I obesity

National longitudinal study of youth 1979
Age 25 -33 Class 1 obesity 1990 – followed to 2008

Women



Solid lines (——) indicate the average trajectory of the group, dashed lines (- - -) indicate the 95% confidence intervals

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BMI and risk of mortality – Cause of death

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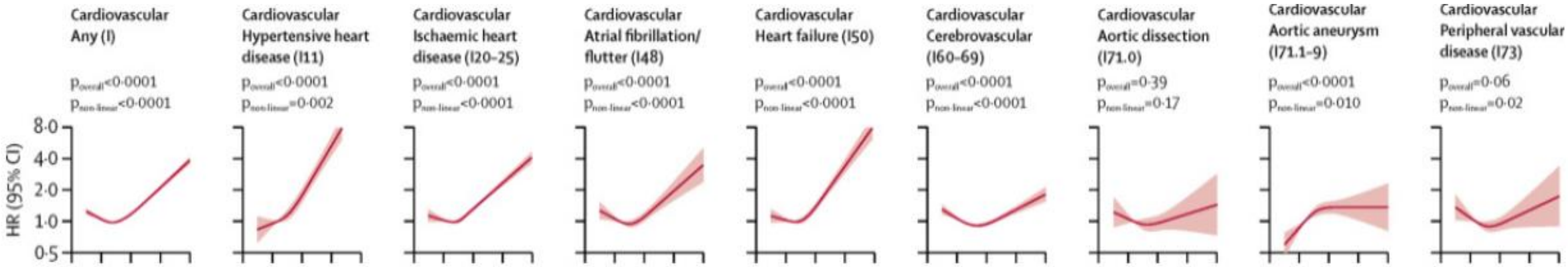
Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3.6 million adults in the UK

Cardiovascular Deaths

Clinical Practice Research Datalink (CPRD) linked to national mortality registration data BMI and all-cause mortality, and between BMI and a comprehensive range of cause-specific mortality. Based on ICD 10 classification.

BMI data collected at age 16 years and older and with subsequent follow-up time available from the 5-year anniversary of the first BMI record, or on Jan 1, 1998 follow-up ended at death or on March 8, 2016.

Fully adjusted models were stratified by sex and adjusted for baseline age, smoking, alcohol use, diabetes, index of multiple deprivation, and calendar period.



BMI scale 10-20-30-40-50

Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. *The lancet Diabetes & endocrinology.* 2018;6(12):944-953.

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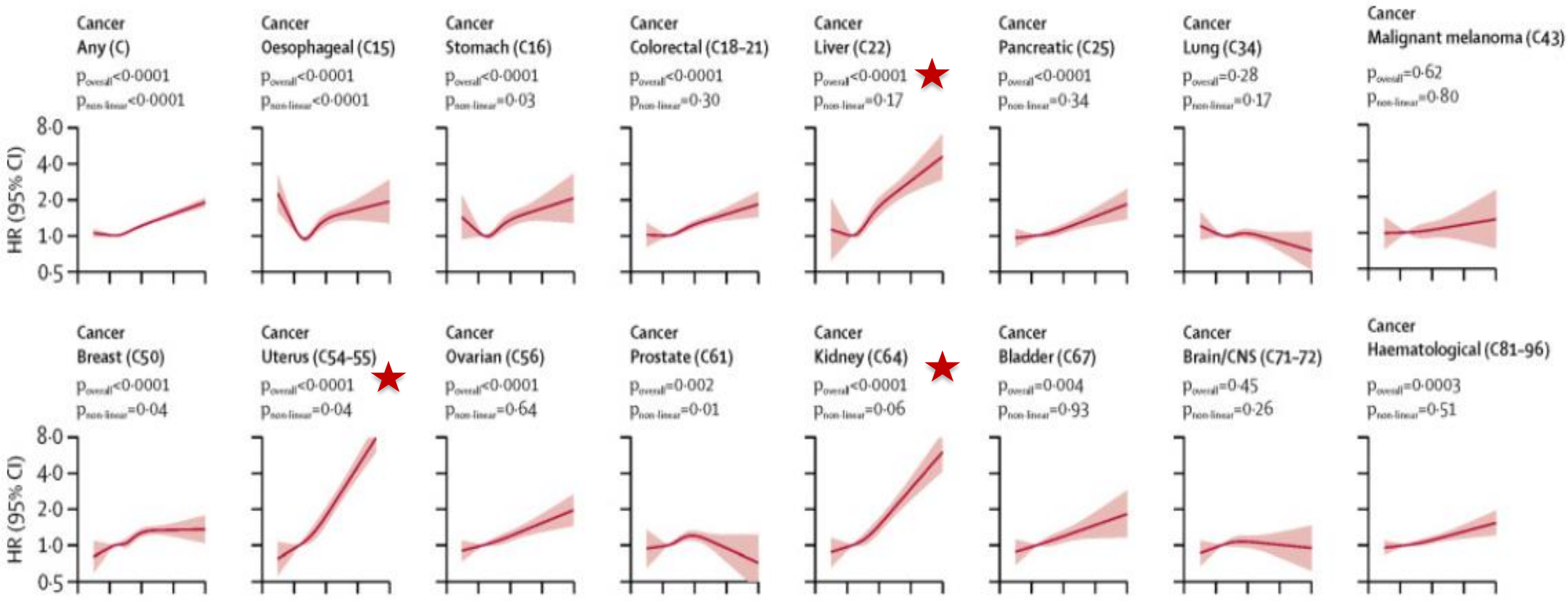
Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3 · 6 million adults in the UK

Cancer Deaths



BMI scale 10-20-30-40-50

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BMI and mortality in those with established disease

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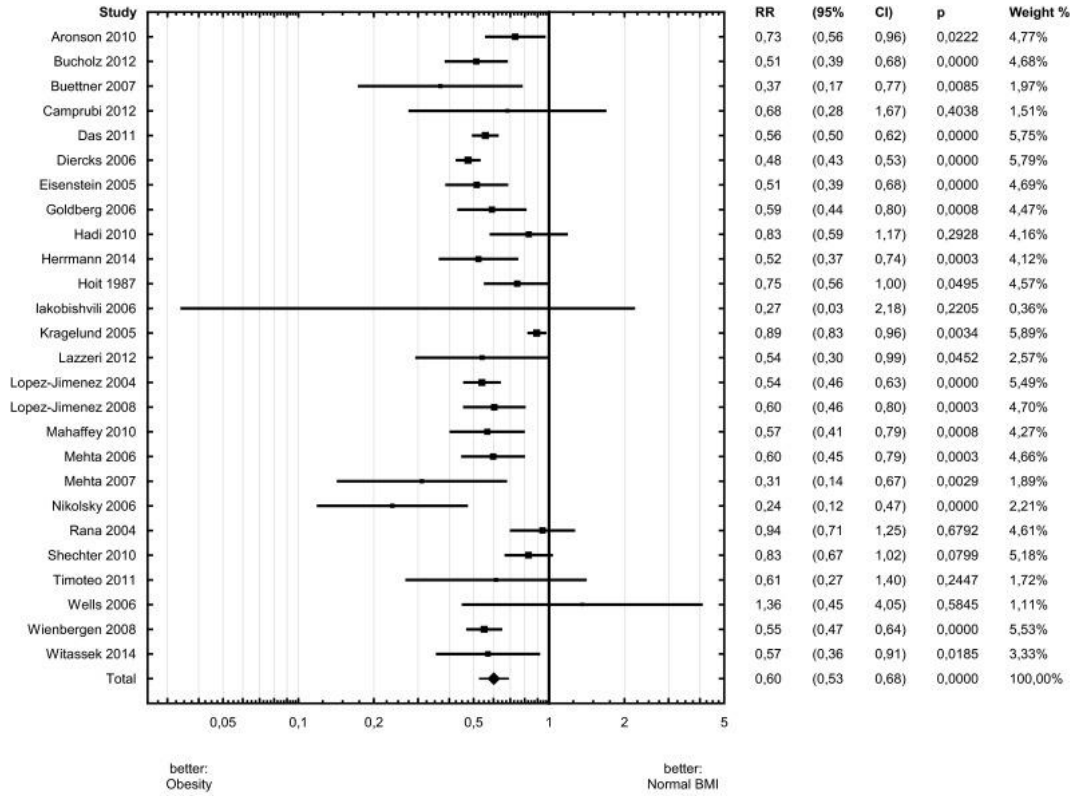
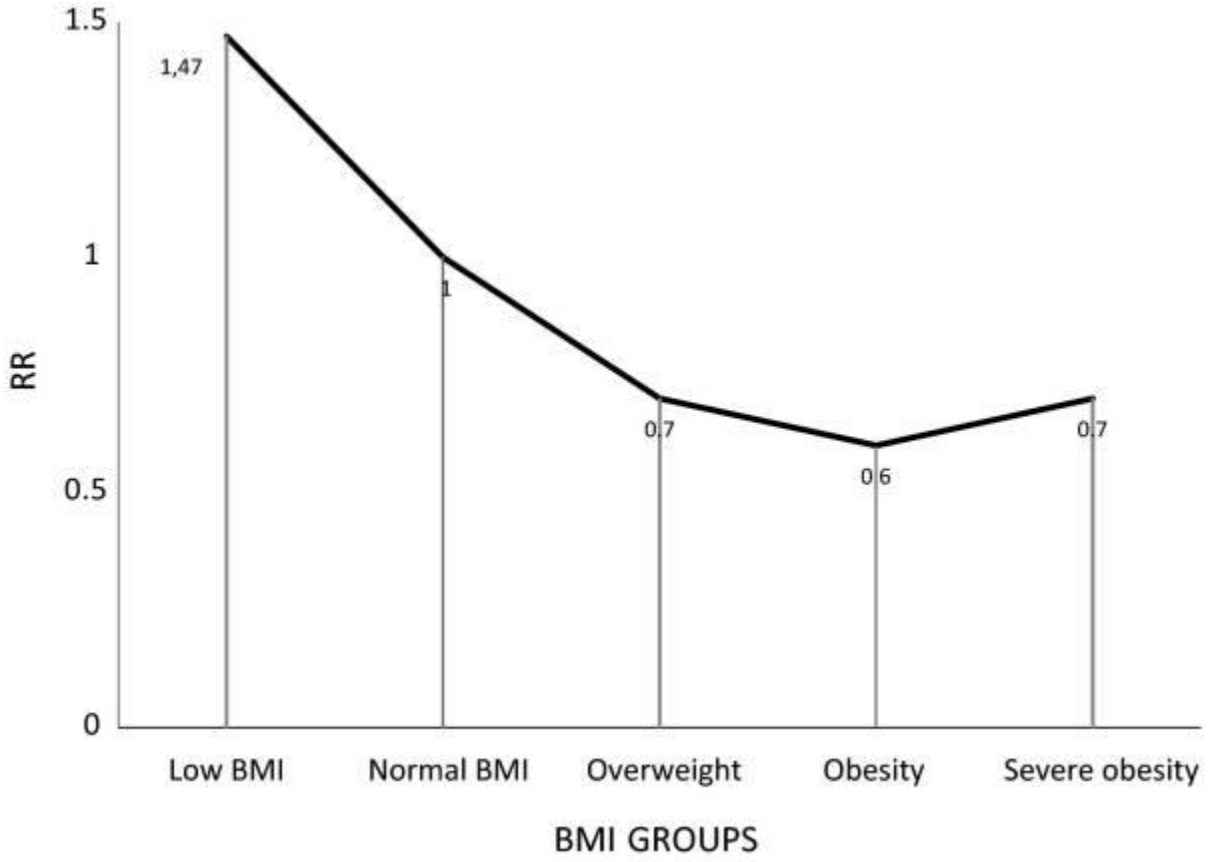
Meta-analysis: total mortality risk for Obesity versus Normal BMI in patients with acute coronary syndrome





RR 0.60 (0.53 – 0.68) for Obese vs Normal weight

Niedziela J, Hudzik B, Niedziela N, et al. *Eur J Epidemiol.* 2014;29(11):801-812.

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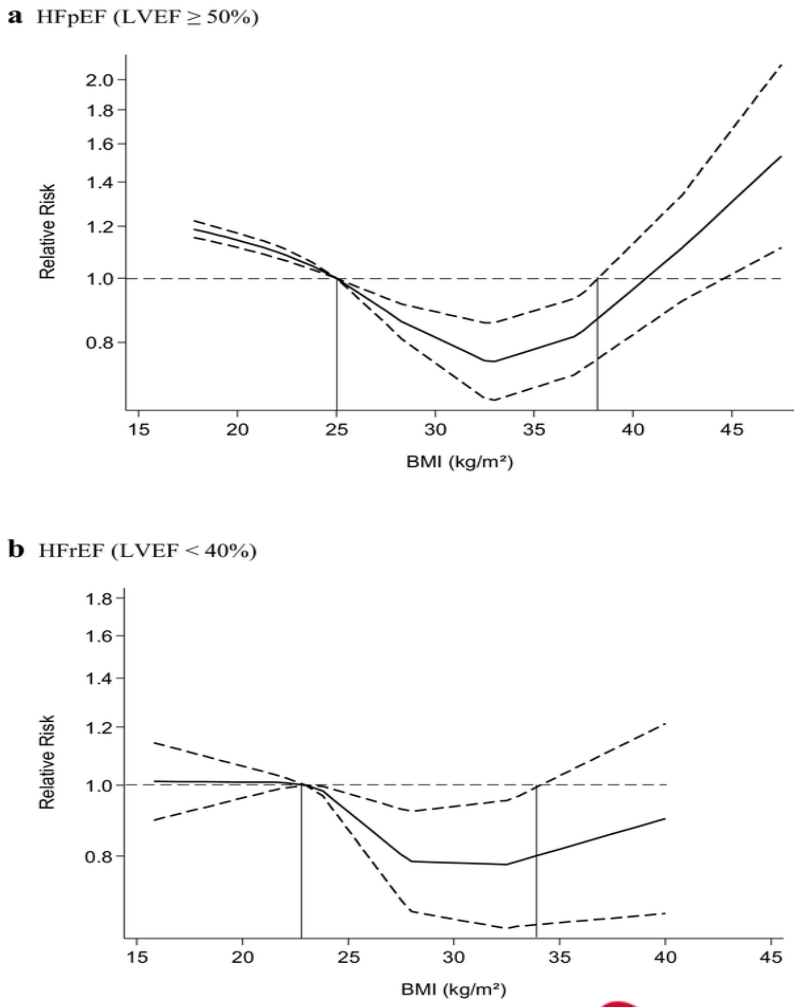
Body mass index and all-cause mortality in heart failure patients with normal and reduced ventricular ejection fraction: a dose–response meta-analysis

Study	Pub year	Number of patients	Source	Follow-up (years)	HF phenotype	Age (years) mean (SD)	Women (%)	NYHA class (%)
Haass	2011	4109	USA	4.1	HFpEF	72	60.4	II/III/IV 3/9/0
DeShutter	2014	47,866	USA	3.1	HFpEF	61.6 (15.4)	55	–
Kapoor	2010	1236	USA	1.0	HFpEF	71 (12)	4	–
Padwal	2014[#]	22,009	MAGGIC	3.0	HFrEF:15,956 patients HFpEF: 6053 patients	66.8	32	II/III: 46/50
Vest	2015	3811	USA	6.0	HFrEF	54.1 (11.6)	100	I/II/III/IV 8/31/59/2
Curtis	2005	7767	USA and Canada	3.1	HFrEF	64 (11)	24.6	I/II/(III or IV) 14.3/54.5/31.3
Zafrir	2015	630	Israel	3.3	HFrEF	65 (13)	20	III or IV: 53
Clark	2015	1675	USA	2.0	HFrEF	52.2 (11.6)	22.6	III or V: 79.1
Wu	2009	446	USA	0.8	HFrEF	62.2	27.6	–
McAuley	2007	6876	USA	7.5	HFrEF	58 (11)	10	–

NYHA class New York Heart Association functional classification, *HFpEF* heart failure with preserved ejection fraction, *HFrEF* heart failure with reduced ejection fraction

[#]The MAGGIC meta-analysis was based on studies originally reported between 1992 and 2006; data collection will have occurred several years earlier [9]



Zhang J, Begley A, Jackson R, et al. Body mass index and all-cause mortality in heart failure patients with normal and reduced ventricular ejection fraction: a dose-response meta-analysis. *Clin Res Cardiol.* 2019;108(2):119-132.

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OW & Obese patients diagnosed with type 2 diabetes lower mortality

5 longitudinal cohort studies:

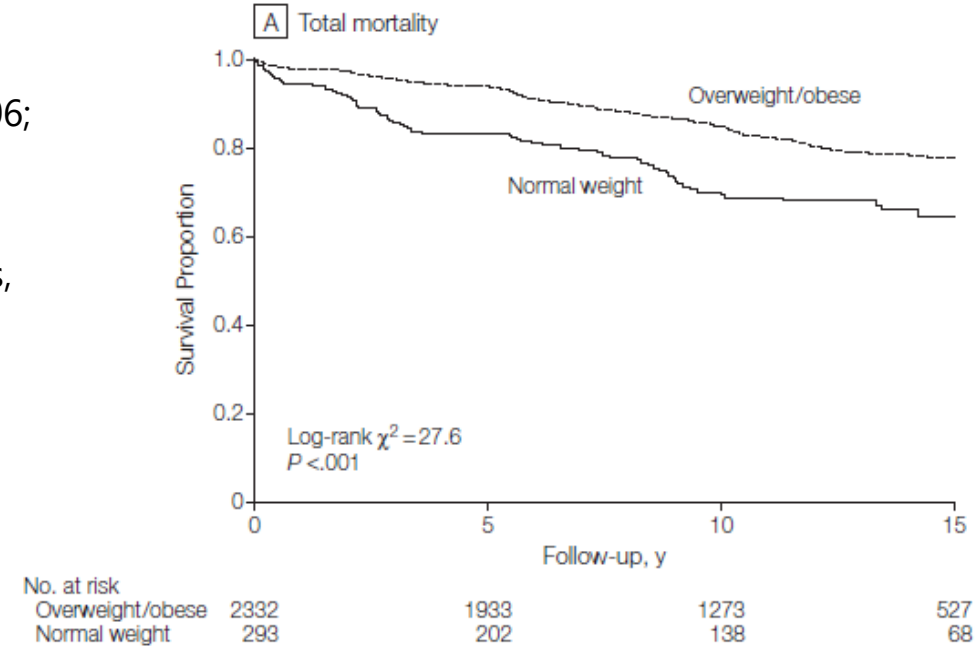
Atherosclerosis Risk in Communities study, 1990-2006;

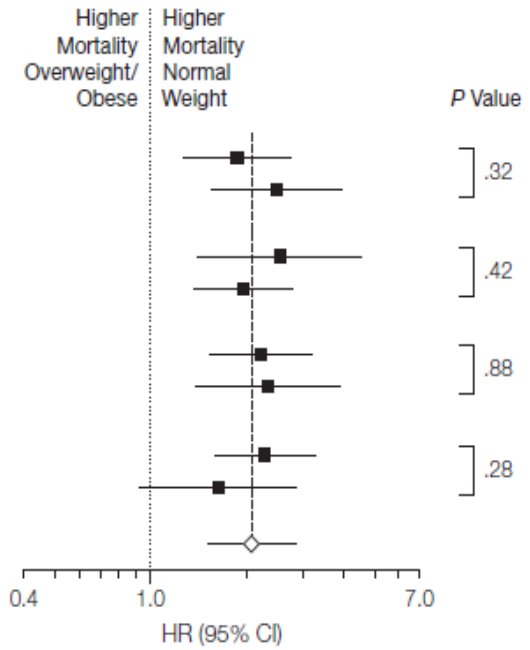
Cardiovascular Health Study, 1992-2008;

Coronary Artery Risk Development in Young Adults, 1987-2011;

Framingham Offspring Study, 1979-2007; and

Multi-Ethnic Study of Atherosclerosis, 2002-2011.





A total of 2625 participants with incident diabetes contributed 27,125 person-years of follow-up. Included were men and women (age >40 years)

Carnethon, M. R., P. J. De Chavez, et al. (2012). "Association of weight status with mortality in adults with incident diabetes." JAMA **308(6): 581-590.**

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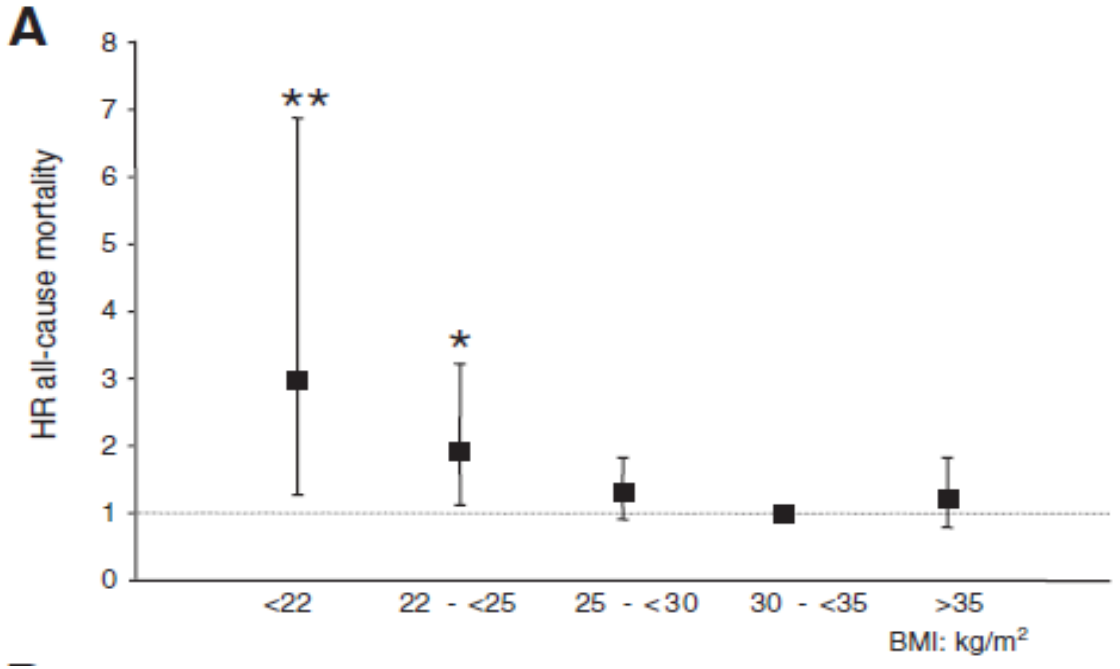
Inverse relation of body weight and weight change with mortality and morbidity in patients with type 2 diabetes and cardiovascular co-morbidity: An analysis of the PROactive study population

Wolfram Doehner [a,b,*], Erland Erdmann [c], Richard Cairns [d], Andrew L. Clark [e], John A. Dormandy [f], Ele Ferrannini [g], Stefan D. Anker [b,h]

5202 patients with type 2 diabetes and established cardiovascular disease

Randomized to pioglitazone or placebo



Weight loss during the study increased mortality

Weight gain did not

Doehner, W., E. Erdmann, R. Cairns, A.L. Clark, J.A. Dormandy, E. Ferrannini, et al., *J Cardiol, (2011).*

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Lowest mortality higher than the “normal” range

Chronic disease

Cardiac failure, type 2 diabetes, chronic renal disease, acute coronary syndrome, hypertension with established coronary artery disease, chronic pulmonary disease, and following CABGs, dementia in the elderly, valve surgery and general surgery.

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Can intentional weight loss save lives?

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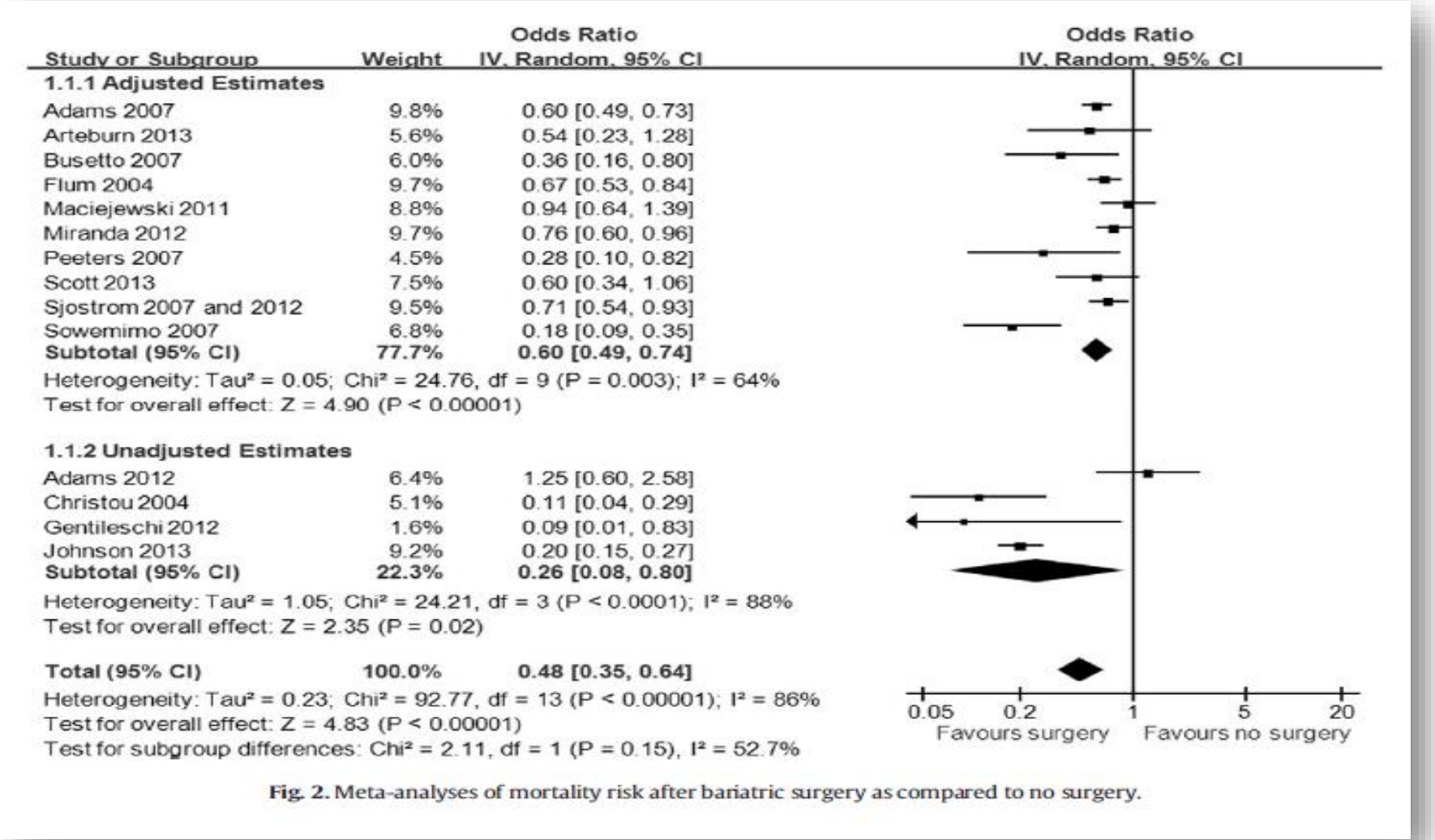
Bariatric-Metabolic Surgery saves lives

14 studies; 29,208 underwent bariatric surgery and 166,200 nonsurgical controls



Study or Subgroup	Weight	Odds Ratio IV, Random, 95% CI
1.1.1 Adjusted Estimates		
Adams 2007	9.8%	0.60 [0.49, 0.73]
Arteburn 2013	5.6%	0.54 [0.23, 1.28]
Busetto 2007	6.0%	0.36 [0.16, 0.80]
Flum 2004	9.7%	0.67 [0.53, 0.84]
Maciejewski 2011	8.8%	0.94 [0.64, 1.39]
Miranda 2012	9.7%	0.76 [0.60, 0.96]
Peeters 2007	4.5%	0.28 [0.10, 0.82]
Scott 2013	7.5%	0.60 [0.34, 1.06]
Sjostrom 2007 and 2012	9.5%	0.71 [0.54, 0.93]
Sowemimo 2007	6.8%	0.18 [0.09, 0.35]
Subtotal (95% CI)	**77.7%**	**0.60 [0.49, 0.74]**
Heterogeneity: Tau² = 0.05; Chi² = 24.76, df = 9 (P = 0.003); I² = 64%		
Test for overall effect: Z = 4.90 (P < 0.00001)		
1.1.2 Unadjusted Estimates		
Adams 2012	6.4%	1.25 [0.60, 2.58]
Christou 2004	5.1%	0.11 [0.04, 0.29]
Gentileschi 2012	1.6%	0.09 [0.01, 0.83]
Johnson 2013	9.2%	0.20 [0.15, 0.27]
Subtotal (95% CI)	**22.3%**	**0.26 [0.08, 0.80]**
Heterogeneity: Tau² = 1.05; Chi² = 24.21, df = 3 (P < 0.0001); I² = 88%		
Test for overall effect: Z = 2.35 (P = 0.02)		
Total (95% CI)	**100.0%**	**0.48 [0.35, 0.64]**
Heterogeneity: Tau² = 0.23; Chi² = 92.77, df = 13 (P < 0.00001); I² = 86%		
Test for overall effect: Z = 4.83 (P < 0.00001)		
Test for subgroup differences: Chi² = 2.11, df = 1 (P = 0.15), I² = 52.7%		

Fig. 2. Meta-analyses of mortality risk after bariatric surgery as compared to no surgery.

Hazard Ratio

0.6 (0.49 to 0.74)

50% reduction in CV deaths

50% reduction in cancer deaths

All studies to date have been in class II and III obesity

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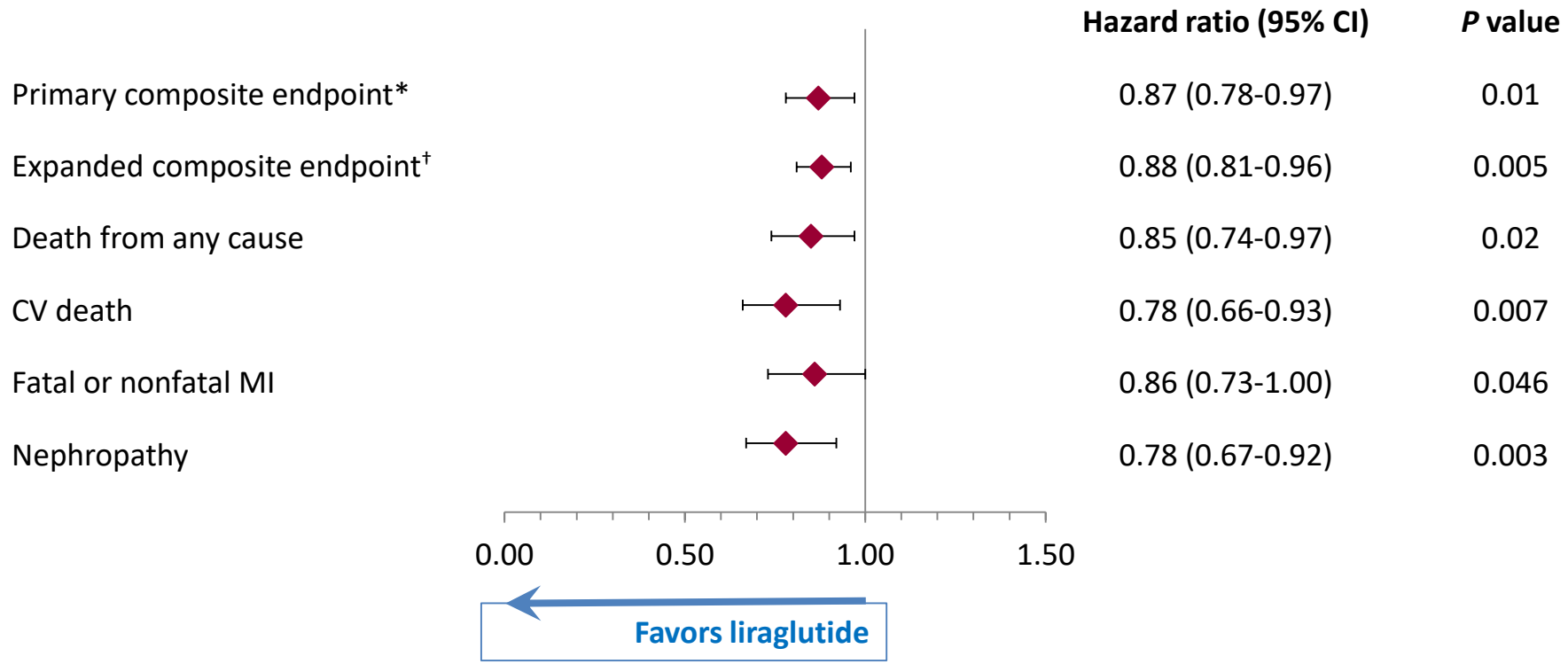
Kwok CS et al. Int J Cardiol 2016

Clinical Outcomes with Liraglutide

LEADER (N=9340)



*CV death, nonfatal MI (including silent MI), or nonfatal stroke; †CV death, nonfatal MI (including silent MI), nonfatal stroke, coronary revascularization, and hospitalization for unstable angina or HF.

CI, confidence interval; CV, cardiovascular; MI, myocardial infarction.

Marso SP, et al. *N Engl J Med*. 2016 Jun 13. [Epub ahead of print]

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We need to take a more critical look at intentional weight loss!

Should it surprise that increased fatness (to a point) may have benefits?

Elderly
Chronic Disease
Organ Failure
Injury

Greater reserve of fat mass and fat free mass

The young and the fit are in a better competitive position to obtain food during tough times

A persons age and state of health influences the relationship between BMI and mortality

Intentional weight loss has great benefit on mortality when the risk of mortality in individuals with clinically severe obesity is higher than population age, sex, and disease status matched controls

(The extensive Bariatric Surgery data)

We cannot assume similar benefit when an individuals weight is not associated with higher mortality than population age, sex and disease status matched controls

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There is more to living than dying!

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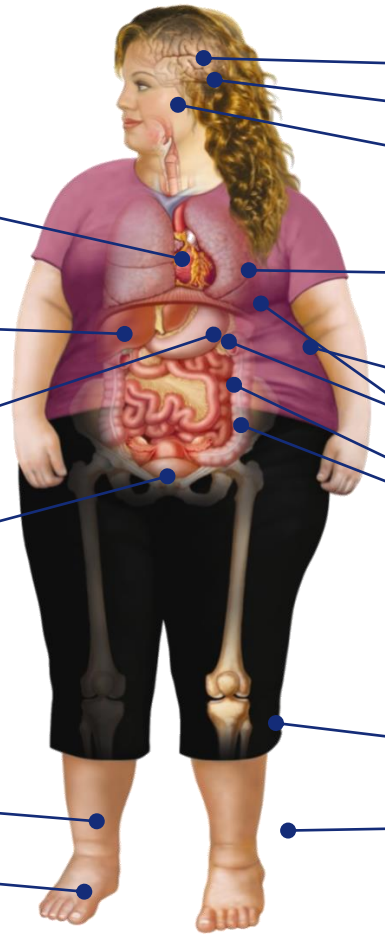
Obesity the canary in the mineshaft for obesity related complications



Pulmonary Disease
- Abnormal Function
- Obstructive Sleep Apnea
- Hypoventilation Syndrome
- Asthma

Nonalcoholic Fatty Liver Disease
- Steatosis
- Steatohepatitis
- Cirrhosis

Gall Bladder Disease

Gynecologic Abnormalities
- Abnormal Menses
- Infertility
- Polycystic Ovarian Syndrome

Skin Problems

Gout

Idiopathic Intracranial Hypertension

Stroke

Cataracts

Coronary Heart Disease
- Dyslipidemia
- Hypertension

Diabetes

Severe Pancreatitis

Cancer
- Breast, Uterus, Cervix,
- Colon, Esophagus, Pancreas, Kidney, Prostate

Osteoarthritis

Phlebitis
- Venous Stasis

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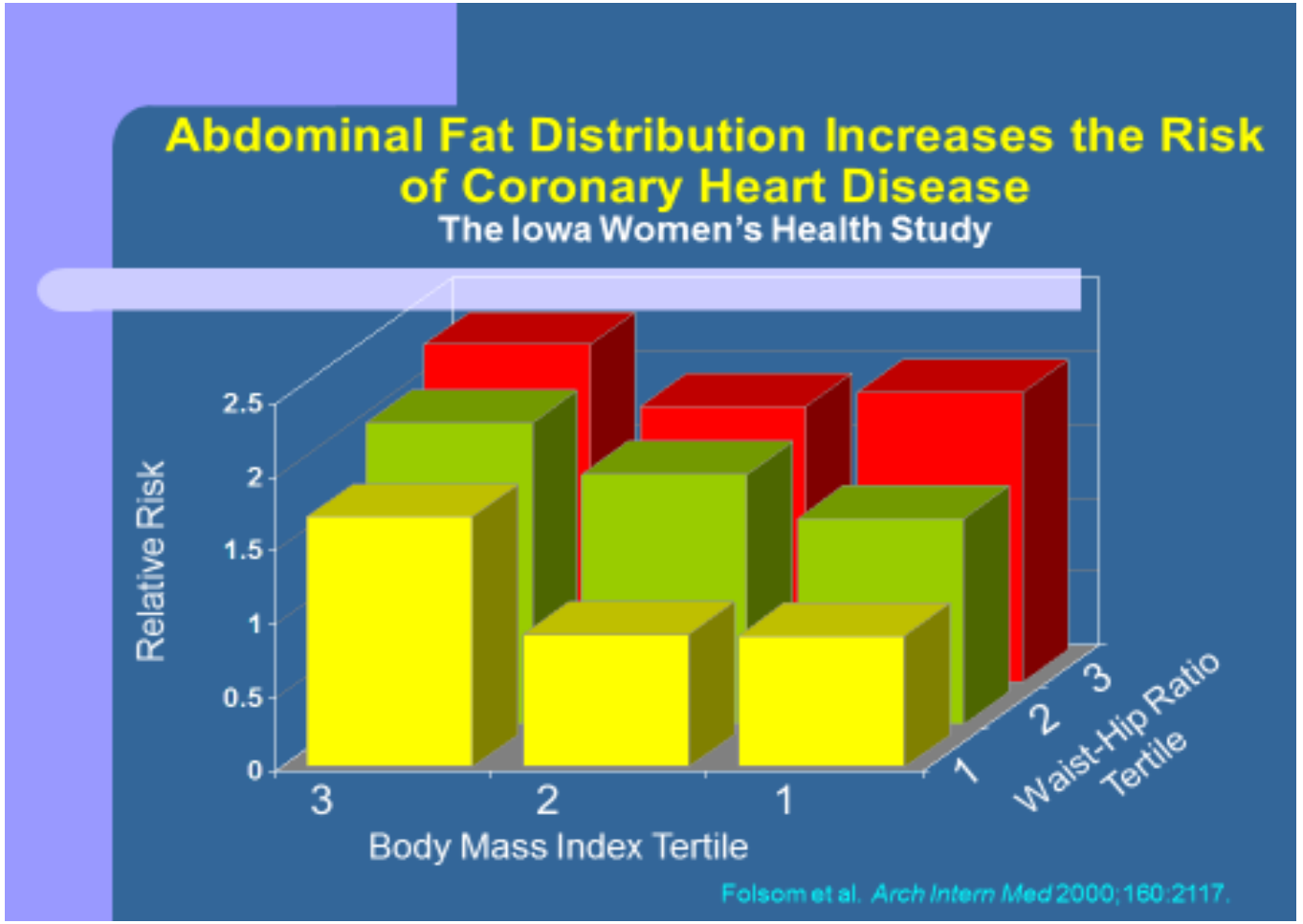
What are the implications for weight management?

- Indications based on BMI
- Targets for weight loss

Anthropometric measures add colour to BMI



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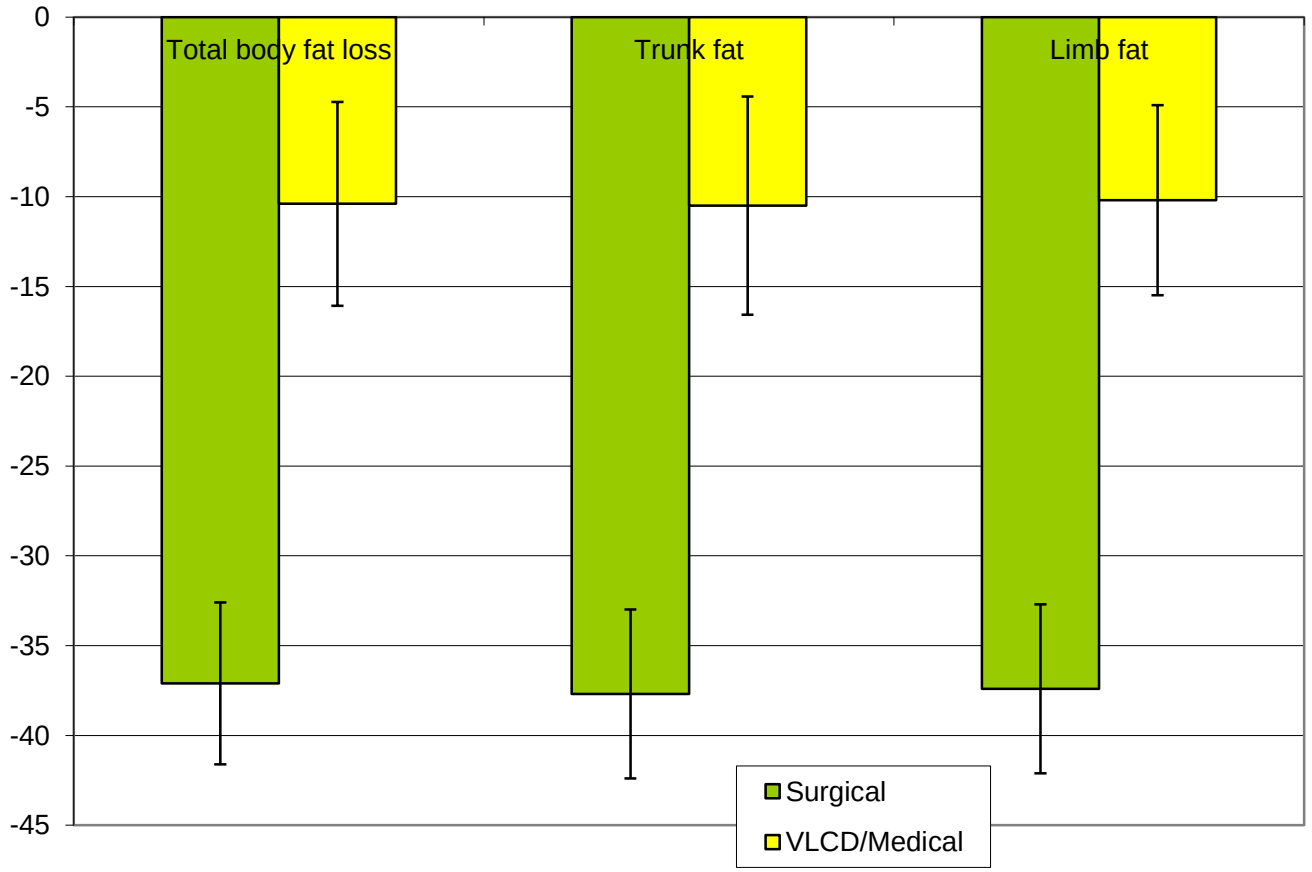
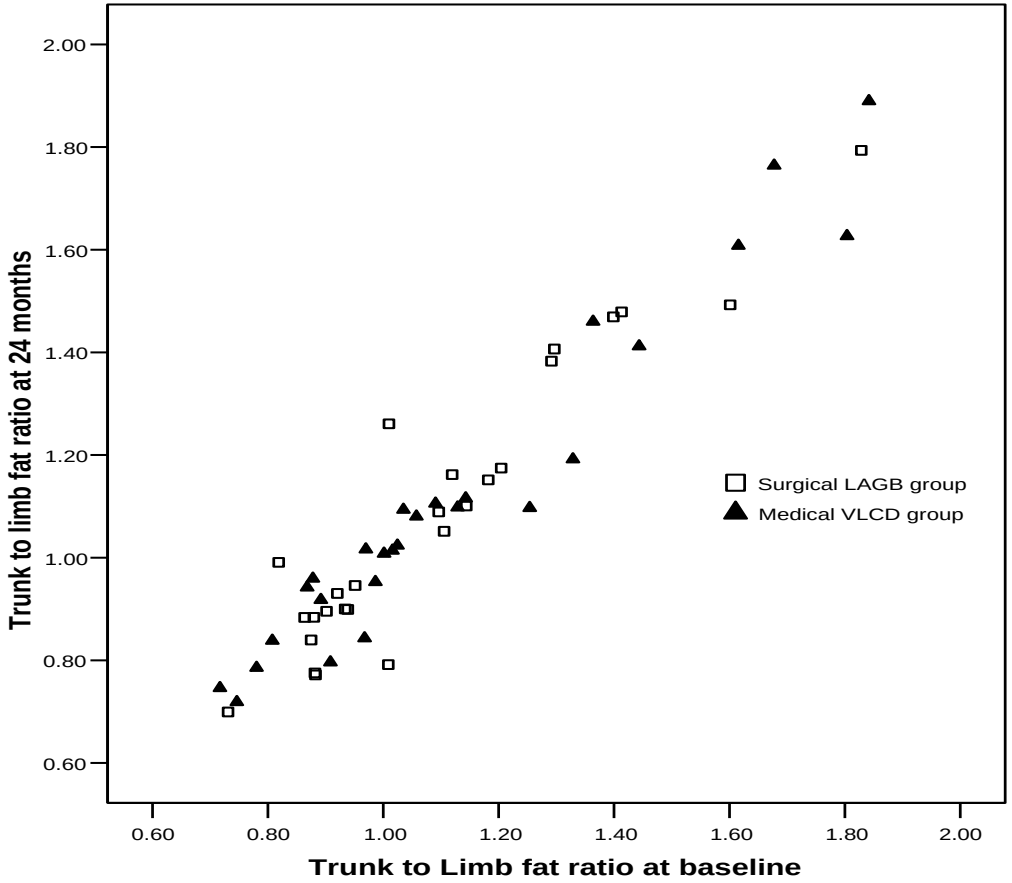
What happens to fat distribution with weight loss?





Dixon JB, Strauss BJ, Laurie C, et al. *Obesity (Silver Spring).* 2007;15:1187-98.

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'Obesity paradox' misunderstands the biology of optimal weight throughout the life cycle.

There is no ‘obesity paradox’ to explain, if we accept the premise that varying ideal weight ranges apply to individuals over different stages of the life span, accordingly allowing us to abandon the rigid biologically implausible concept of a single‘ideal weight’ (for height) or weight range.

Perhaps lifestyle advice should focus less on biologically difficult to achieve intentional weight loss for those in the overweight and class I obese range, and instead focus more on quality nutrition, physical activity, fitness and maintaining function in chronic disease states and with aging.

Dixon JB, Egger GJ, Finkelstein EA, Kral JG, Lambert GW. *International journal of obesity.* 2015;39(1):82-84.

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Using BMI Intelligently

- BMI is a good measure of body fatness: Weight, Height, Sex, Age, & Ethnicity
- Age modifies risk associated with BMI: Focus on the young and track trajectory
- Understand when overweight is a risk
- Established health issues modify the risk of a higher BMI
- In older patients assess if intentional weight loss will be of benefit. A healthy diet and age appropriate physical activity may be the pathway to improved quality of live and health while forgetting about the scales
- When people have chronic disease think about when intentional weight loss may be of benefit? Is there benefit? What are the risks?
- Provide advice regarding intentional weight loss to those who need it. This will focus resources on where they are really needed

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Conclusions and key messages

Obesity is a killer disease: Especially for those with a BMI >35 almost all causes of death are increased. The NADIR BMI for mortality varies throughout the lifecycle and on individual health.

Obesity, like CVD, Type 2 Diabetes and Cancer, is not a lifestyle choice

Challenge our hard-wired thinking about BMI

- BMI is a very good indicator of body compositions if age, sex and ethnicity are known. Don't dismiss it because outliers can occur
- Healthy weight vs unhealthy weight
- What is a healthy weight for my patient now?
  - Age, disease, weight trajectory, weight journey, cardio-metabolic risk, quality of life, psychological wellbeing

When is intentional weight loss recommended? (When is it not recommended?)

- Most of our current hard outcome mortality and CV event data comes from case-control studies in patients with a BMI >35 having surgical interventions – those clearly at high risk
- We need specific quality data regarding those with established health conditions
- MACE, Quality of Life, Body composition, Activities of daily living
- *"There is more to living than dying"*

Obesity is very poorly understood: Unfortunately we will not advance prevention and management unless we stop the shaming and blaming

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