Lifestyle Interventions First, Foremost, Forever

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Micronutrient deficiencies in people living with obesity

- Energy dense, micronutrient poor diets
- Obesity related metabolic changes, inflammation and gut flora affect micronutrient absorption and metabolism
- Calorie restriction without optimising dietary micronutrient content exacerbates pre-existing deficiencies.
- One third of older people with obesity have poor overall nutritional status - decreased functional capacity, impairment in balance and gait, falls, and depressed mood.

Soysal P et al. Aging Clin Exp Res. 202

Pellegrini M, et al. J Endocrinol Invest. 2021

McKay J et al BMC Nutr. 2020

Jalali M et al. Biomed Res Int. 2022

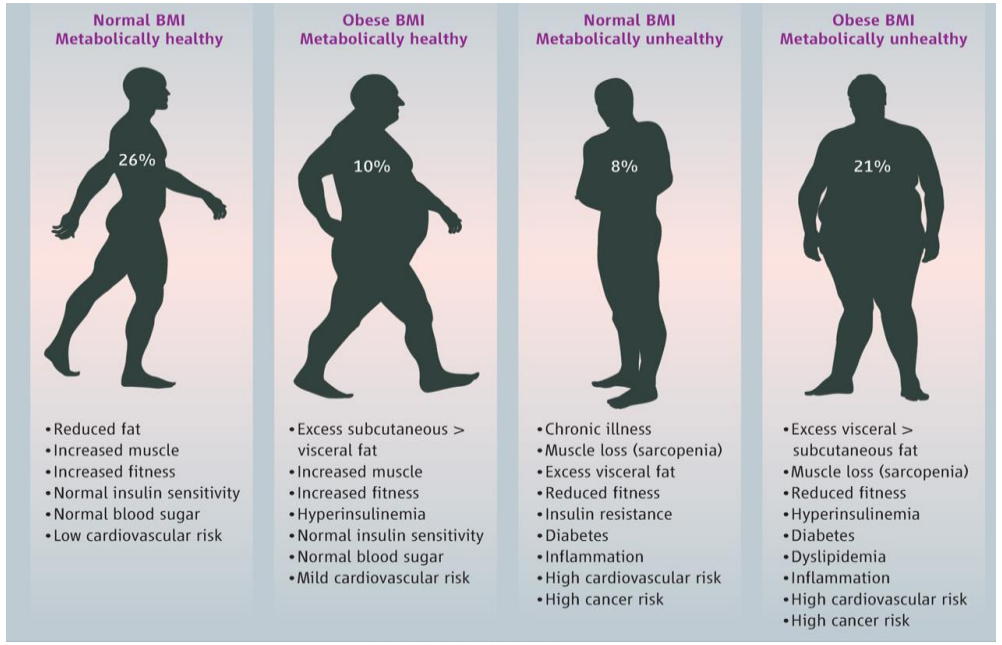
Kobylińska M et al. Obes Facts. 2022

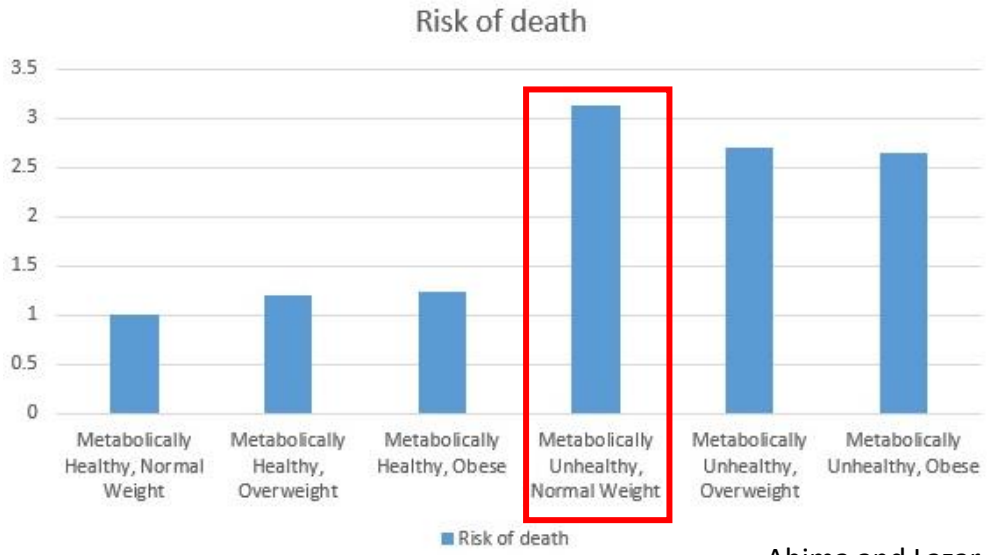
Prevalence of micronutrient deficiency

Micronutrient	Obesity	Diabetes
Thiamine B1	15–29%	17–79%[a]
Pyridoxine B6	0–11%	—
Cobalamin B12	3–8%	22%
Folic Acid	3-4%	—
Ascorbic acid	35–45%	—[b]
Vitamin A	17%	—
Vitamin D	80–90%[c]	85–90%[c]
Vitamin E	0%	0%
Zinc	14–30%	—
Chromium	—	20–40%
Selenium	58%	—

Via M. Endocrinol. 2012

Risk of premature mortality is not only about obesity

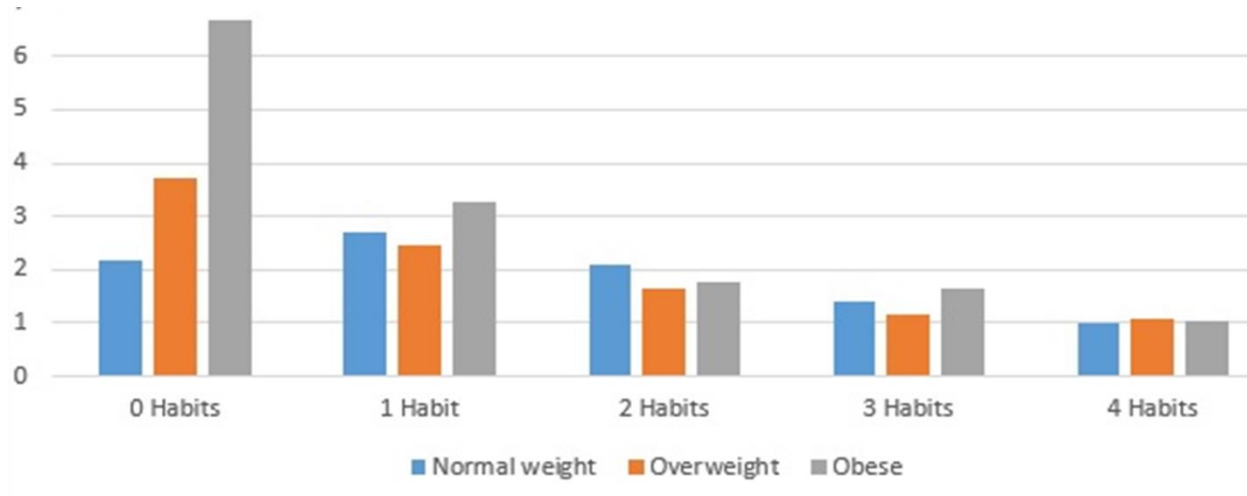




Ahima and Lazar, Science, 2013

Even less so if measured by BMI

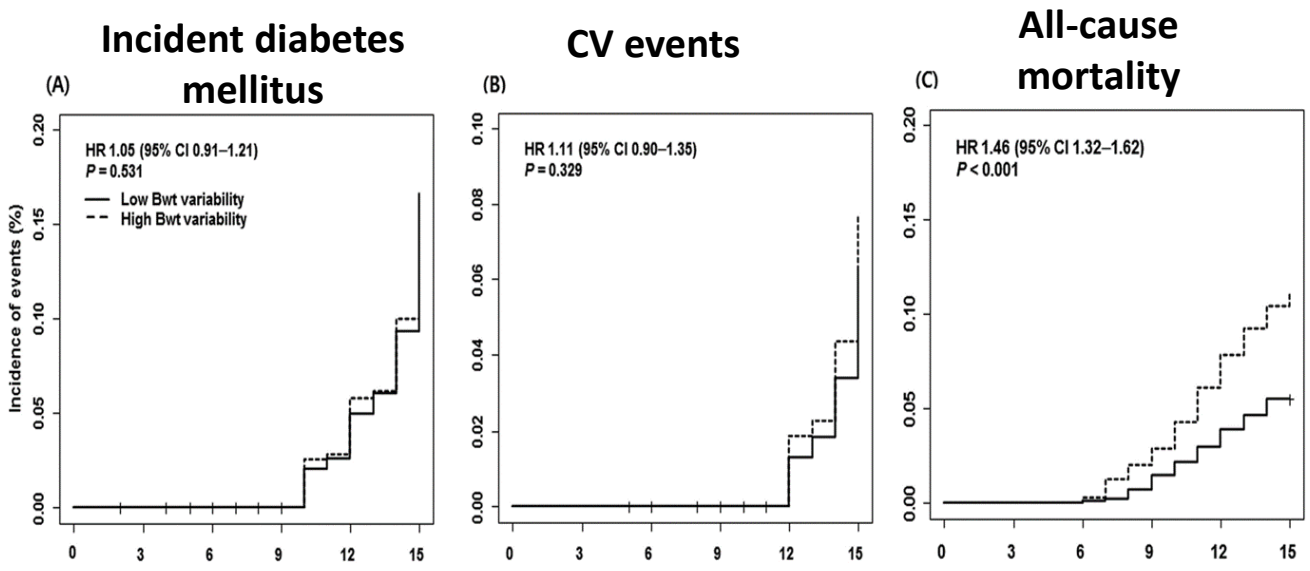
Adoption of healthy lifestyle without weight loss reduces risk from unfavourable to favourable across all weight categories



Matheson EM et al J Am Board Fam Med 2012

High body weight variability increases mortality

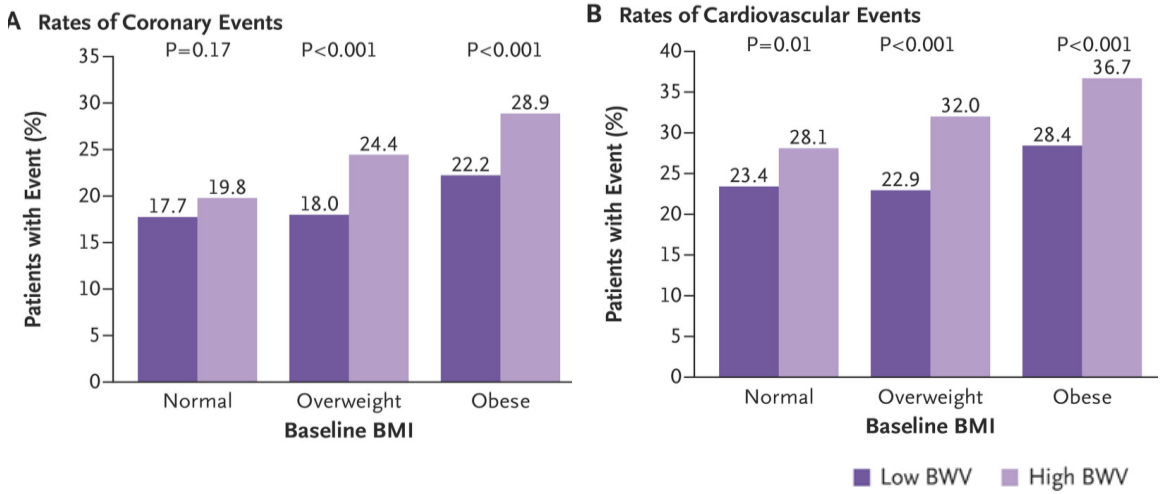
Korean Genome and Epidemiology Study:16-year prospective cohort study, N=3608 participants



Tae Jung Oh et al J Clin Endocrinol Metab, 2019

Cologne J. et al JAMA Netw Open. 2019
Choi D et al Sci Rep. 2019

Body-Weight Variability and Rates of Coronary and Cardiovascular Events as a Function of Baseline Body-Mass Index. (N = 9509)



Adjusted models, quintile with highest variation compared to lowest variation in body weight. **Risk of events:**

Coronary 64% higher,

CV 85% higher,

Death 124% higher.

Bangalore, S et al N Engl J Med 2017

Adverse Health Effects of Ultra Processed Foods

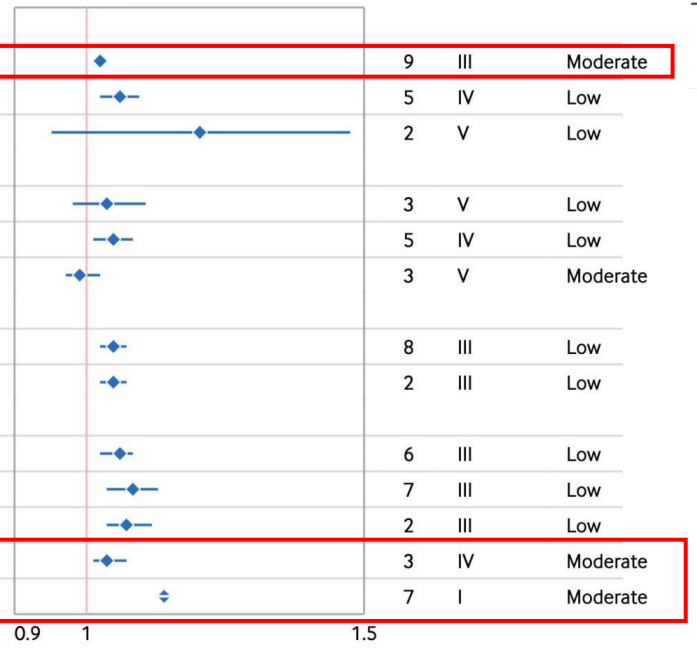
Summary — Higher dietary exposure to ultra-processed foods was associated with a higher risk of adverse health outcomes in 32 out of 45 pooled analyses (71%)

Study design — Umbrella review | 14 meta-analysis studies; 45 pooled analyses; Ultra-processed foods; defined by the Nova classification

Population — 9 888 373 participants included; irrespective of health status and age

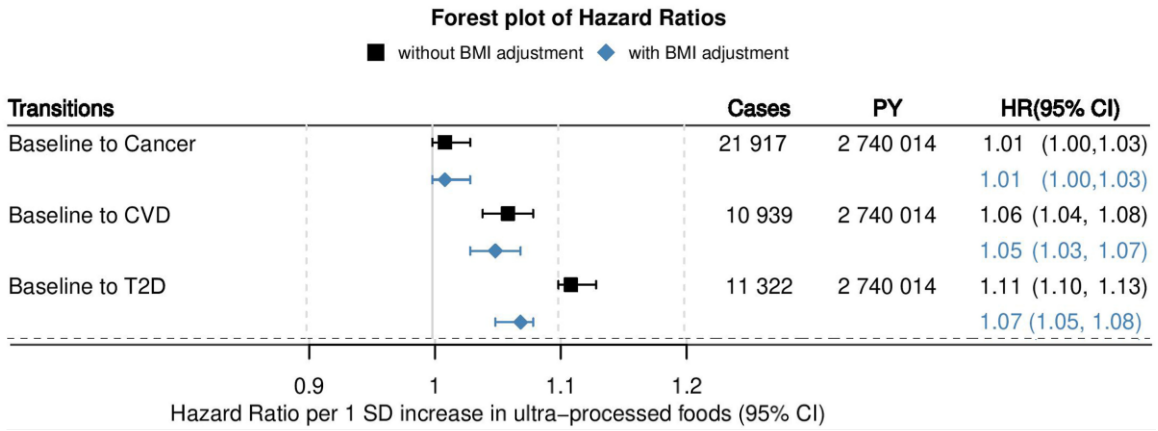
Dose response relationships between greater exposure to ultra-processed food and adverse health outcomes

Outcome	Equivalent odds ratio (95% CI)	k	Credibility	GRADE
Mortality				
All cause mortality (dose)	1.02 (1.01 to 1.03)	9	III	Moderate
Cardiovascular disease related mortality (dose)	1.05 (1.02 to 1.08)	5	IV	Low
Heart disease related mortality (dose)	1.18 (0.95 to 1.47)	2	V	Low
Cancer				
Breast cancer (dose)	1.03 (0.98 to 1.09)	3	V	Low
Colorectal cancer (dose)	1.04 (1.01 to 1.07)	5	IV	Low
Prostate cancer (dose)	0.99 (0.97 to 1.02)	3	V	Moderate
Cardiovascular Health				
Cardiovascular disease events combined (dose)	1.04 (1.02 to 1.06)	8	III	Low
Cardiovascular disease morbidity (dose)	1.04 (1.02 to 1.06)	2	III	Low
Metabolic Health				
Abdominal obesity (dose)	1.05 (1.02 to 1.07)	6	III	Low
Obesity (dose)	1.07 (1.03 to 1.11)	7	III	Low
Overweight (dose)	1.06 (1.03 to 1.10)	2	III	Low
Overweight + obesity (dose)	1.03 (1.01 to 1.06)	3	IV	Moderate
Type 2 diabetes (dose)	1.12 (1.11 to 1.13)	7	I	Moderate



Lane M, et al BMJ 2024

Ultra-processed food consumption and risk of cancer, CVD, T2D, and cancer



Cordova, R et al , The Lancet 2023

Overall diet quality has a stronger influence on long-term health than ultra-processed food consumption.

Fang, Z et al BMJ 2024

The Importance of Dietary Quality in weight loss interventions

Less of a nutritionally insufficient diet is not necessarily of benefit even if weight is lost

	LCD (n=19) 8 weeks	CSIRO(n=12) 8 weeks	LCD# (n=9) 52 weeks	CSIRO (n=7) 52 weeks
Weight (kg)	- 9.5 ± 4.8**	- 4.8 ± 2.7**	-12.9 ± 3.8**	-8.1 ± 6.3**
Waist circumference (cm)	- 12.1 ± 4.8**	- 5.4 ± 4.1**	-15.2 ± 6.1**	-7.7 ± 5.4**
Plasma hsCRP (mg/L)	1.2 ± 4.4	- 4.1 ± 5.8*	0.49 ± 1.87	-4.4 ± 3.7*
Plasma IL-6 (pg/ml)	0.6 ± 1.7	- 1.4 ± 1.8*	0.04 ± 0.60	-1.10 ± 0.86*
Plasma sE-selectin (ng/dl)	- 11.8 ± 11.5*	- 19.0 ± 16.9*	-12.0 ± 11.4*	-30.4 ± 13.7**

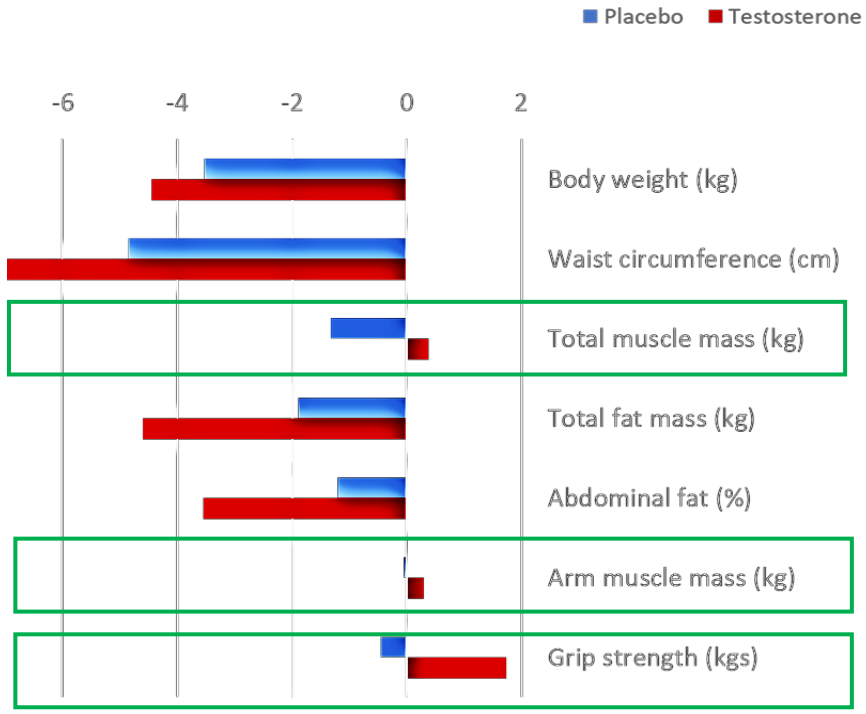
Khoo J Wittert G et l, et al J Sex Med. 2011 Oct;8(10):2868-75

Weight Loss and Lean Body Mass

- Weight loss by diet, pharmacotherapy or surgery causes loss of muscle and bone
- Substantially mitigated by resistance exercise
- Accelerated by increased lean mass loss

Study	Blundell et al., 2017		McCrimmonn et al., 2020		Wilding et al., 2021	
Dose	Once weekly, 1mg		Once weekly, 1mg		Once weekly, 1mg	
Duration	12 weeks		52 weeks		68 weeks	
Funder	Novo Nordisk		Novo Nordisk		Novo Nordisk	
Change in Body Composition	Fat Mass	Lean Mass	Fat Mass	Lean Mass	Fat Mass	Lean Mass
	-3.5kg	-1.1kg	- 3.4kg	-2.3kg	-8.36kg	-5.36kg

Anthropometric effects of a 2-year WW program on middle aged and older men with and without testosterone treatment



Wittert G, et al, Lancet Diabetes and Endocrinology, 2021

Is there a dietary pattern for optimal health?

	Low-carbohydrate	Low-fat/ vegetarian/vegan	Low-glycemic	Mediterranean	Mixed/balanced	Paleolithic
Health benefits relate to:	Emphasis on restriction of refined starches and added sugars in particular.	Emphasis on plant foods direct from nature; avoidance of harmful fats.	Restriction of starches, added sugars; high fiber intake.	Foods direct from nature; mostly plants; emphasis on healthful oils, notably monounsaturates.	Minimization of highly processed, energy-dense foods; emphasis on wholesome foods in moderate quantities.	Minimization of processed foods. Emphasis on natural plant foods and lean meats.
Compatible elements:	Limited refined starches, added sugars, processed foods; limited intake of certain fats; emphasis on whole plant foods, with or without lean meats, fish, poultry, seafood.					
And all potentially consistent with:	**Food, not too much, mostly plants[a,b,c].**					

Mixed or Balanced Diets

Figured prominently in the intervention trials of the National Institutes of Health (NIH). The Dietary Approaches to Stop Hypertension (DASH) diet and the dietary pattern used in the Diabetes Prevention Program (DPP)

A diet of minimally processed foods close to nature, predominantly plants, is decisively associated with health promotion and disease prevention and is consistent with the salient components of seemingly distinct dietary approaches

D.L. Katz and S. Meller. Annual Review of Public Health. 2014

Lyon (Mediterranean) Diet

Very low - refined carbohydrate and processed foods
Low - saturated fat
High - monounsaturated fat, antioxidants, potassium, fiber
Adequate - protein

- LDL cholesterol reduction
- Elevates HDL
- Triglyceride reduction
- Anti-inflammatory
- Anti-hypertensive

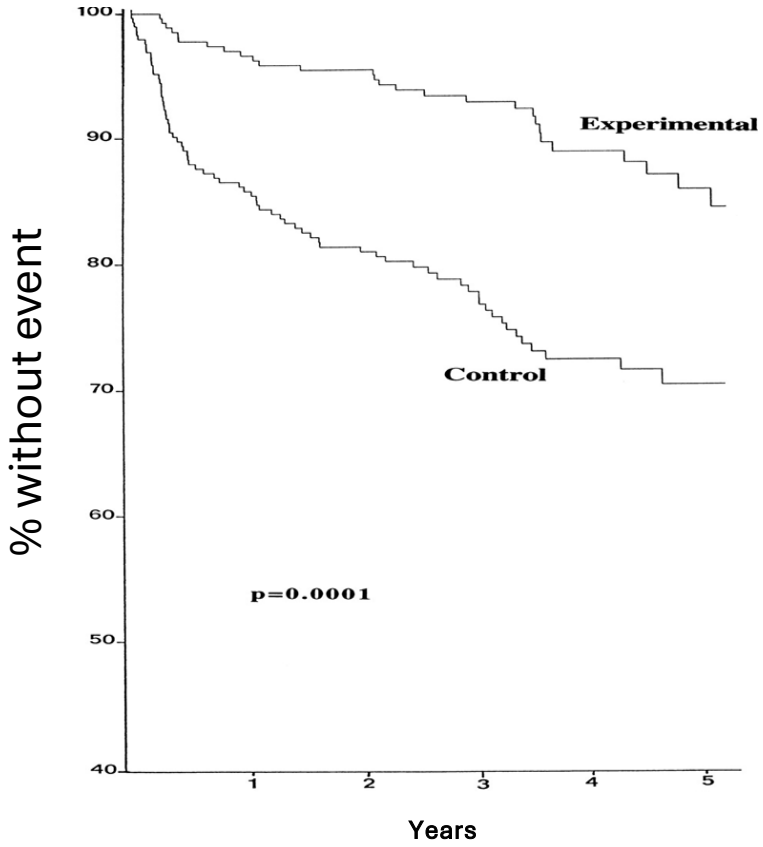
All cause mortality reduced by 70%
Ethics committee stopped study prematurely to make results available to the public immediately

Strict adherence to a Mediterranean diet reduced

- Risk of dying from cancer – 9%
- Risk of dying from CV disease – 6%
- Risk of developing Parkinson's and Alzheimer's – 13 %

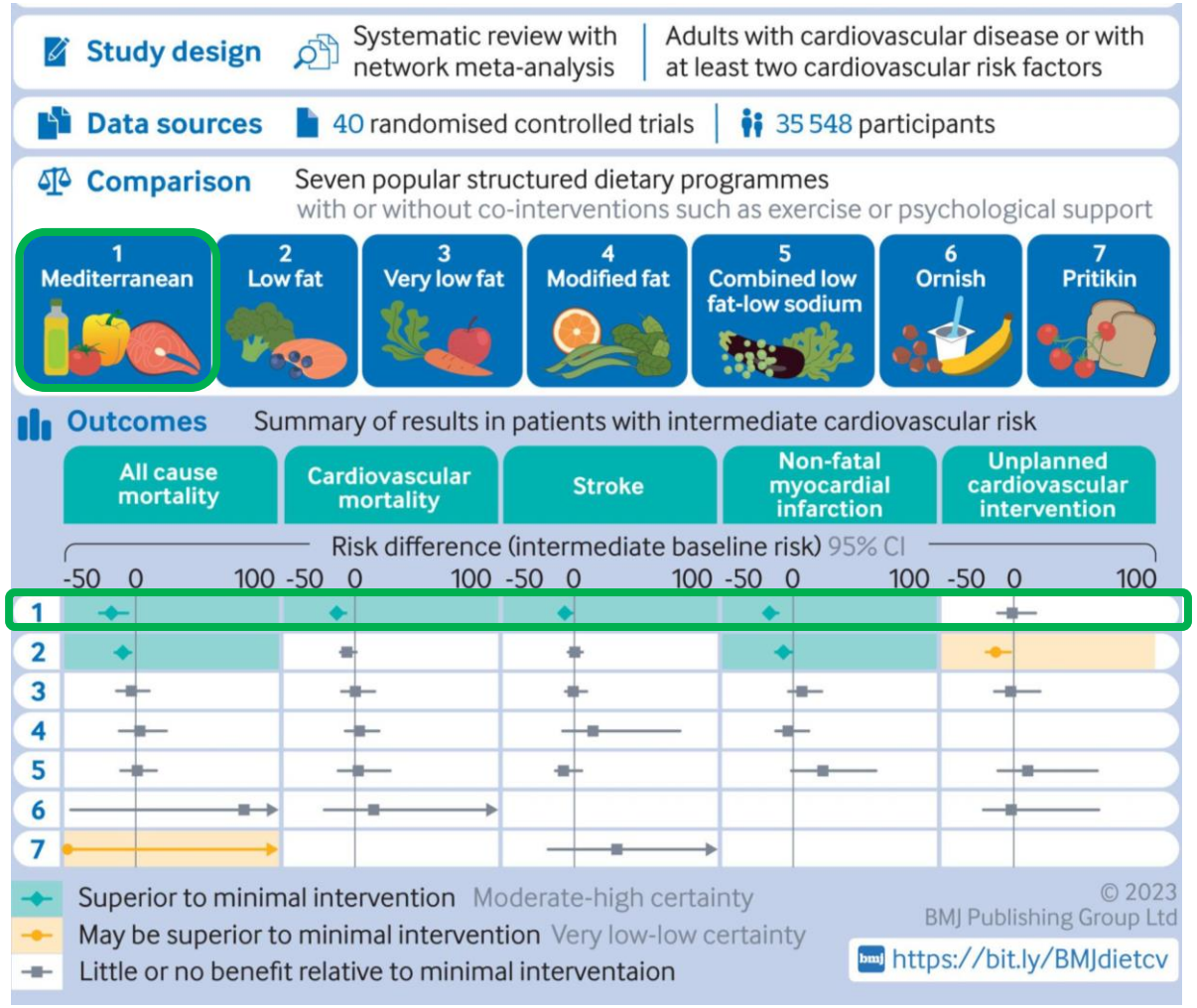
Sofi F, et al. BMJ 2008
Papdaki, A. et al Nutrients, 2020

Cumulative survival without non-fatal MI or major secondary end points



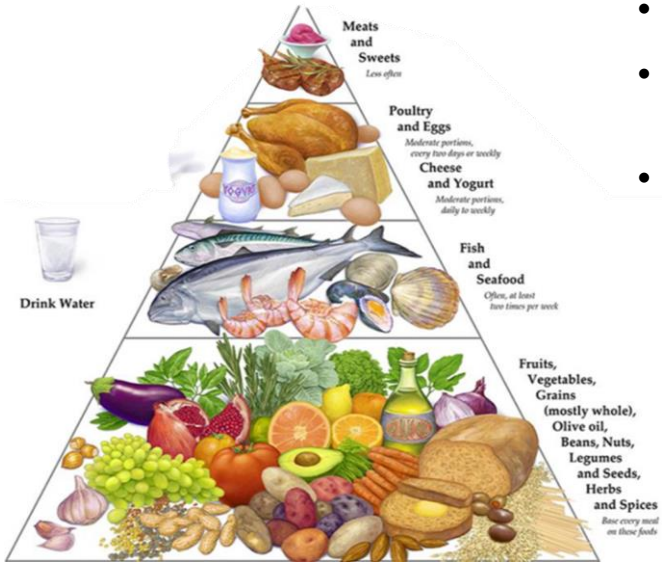
De Lorgeril et al. Lancet 1994, Circulation 1999

7 popular diets & CV events in at risk patients
Systematic review & network meta-analysis



Karam, G et al BMJ 2023

Dietary Best Bets



- Avoid processed foods
- Eat more plant-based foods than animal foods
- choose wholegrains and legumes over refined grains.

  Eat fish and chicken, eggs and dairy

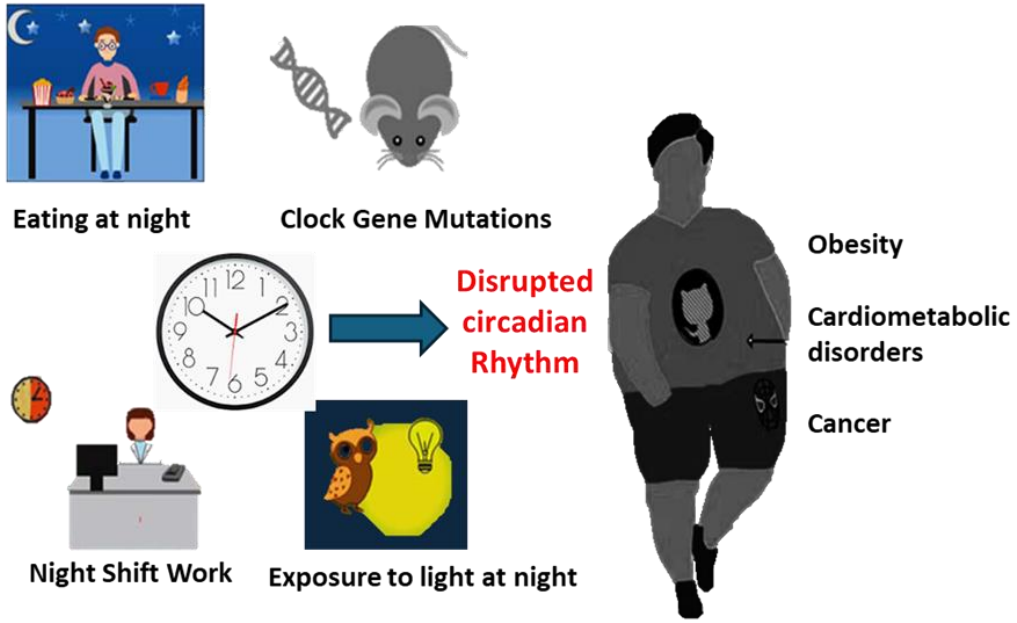
  Some red meat

  Avoid processed meat.

  Drink water
- Eat in phase with the normal circadian rhythm
- Go without eating for 8-12 hours a day i.e. overnight.

Alcohol - major contributor to weight gain, impedes weight loss, disrupts sleep, increases cancer and T2D risk and does not have a CVD (or any other benefit)

Chrononutrition and Intermittent Fasting

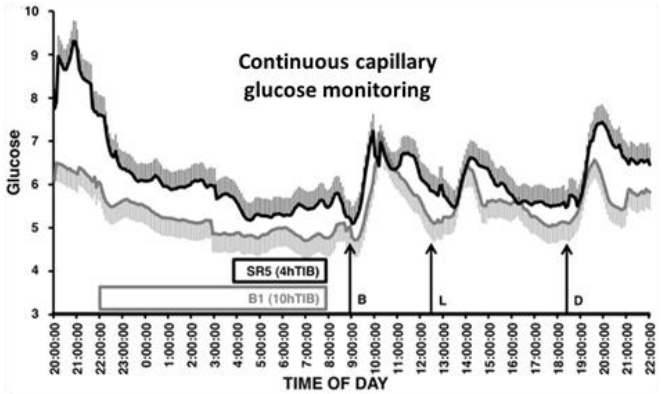


Sleep Restriction

N = 14 healthy men
Age 27.4 ± 3.8
BMI 23.5 ± 2.9

Slept 22 00 – 08 00
Slept 04 00 – 08 00

Measurements
baseline
day 5



Reynolds AC, et al. PLoS ONE 2012

Intermittent early time-restricted eating versus calorie restriction and standard care in adults at risk of T2D

AUS-D risk score ≥12, age, 35–75 years
N = 209, 58 ± 10 years, 34.8 ± 4.7 kg m
3 groups (1:2:2) – 6-month intervention and 12 months follow-up

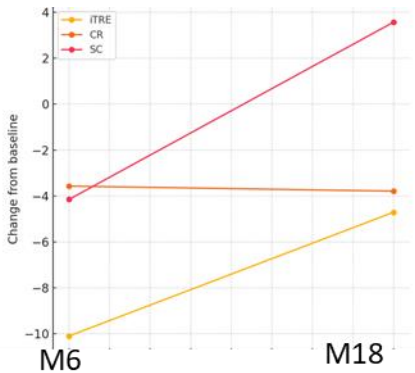
- Control (SC);
- Caloric restriction (CR) – 70% of daily energy requirement
- Intermittent Time Restricted Intake (iTRE) 30% energy requirement 8am-12pm 3 non-consecutive days. Ad lib eating on other days.

No difference in weight, fat mass or fat free mass, WC -5.10 vs -1.66

Change from Baseline to month 6 and 18

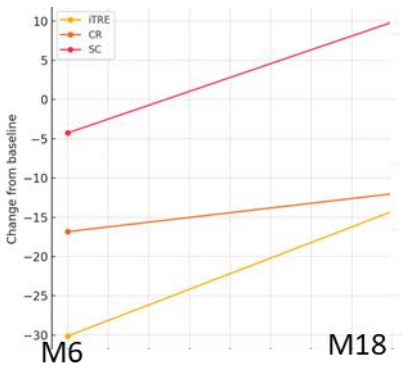
P Values iTRE vs CR

Glucose AUC



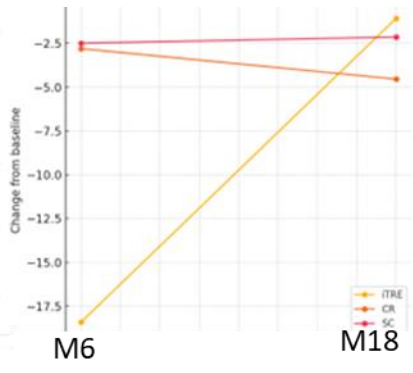
P=0.03 P=NS

Insulin AUC



P=0.04 P=NS

Fasting Triglycerides



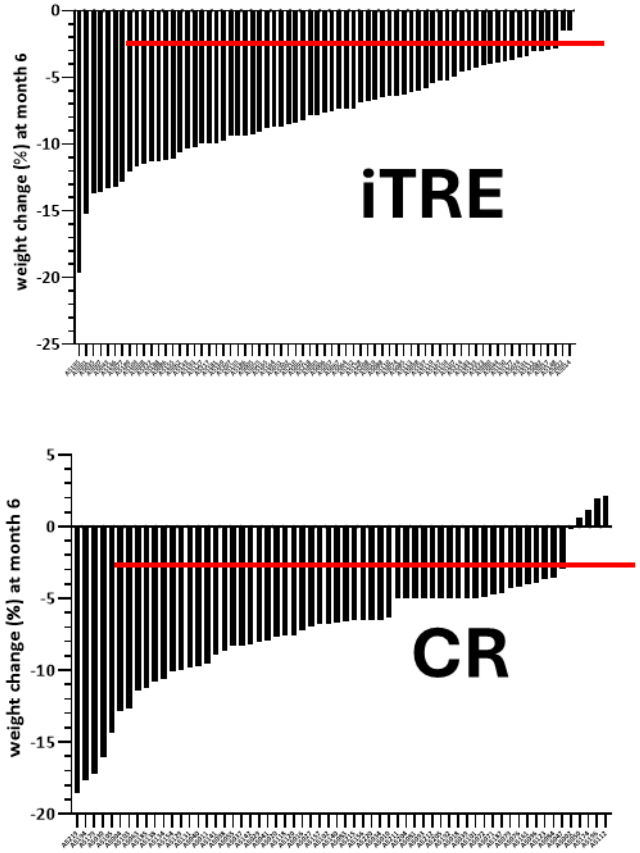
P=0.04 P=NS

Helbronn, Wittert et al. Nature Med, 2023

Obesity is a highly heterogenous condition

- Age of onset
- Associated abnormalities and presumptive cause
- Dependence on how you define and measure the excess adipose tissue, age, sex and various the risk modifiers
  - Amount & distribution of fat
  - Muscle mass and function
  - Level of physical activity
  - Nutritional sufficiency
  - Sleep
  - Stress
  - Other health behaviours & exposures (smoking, alcohol consumption, environmental toxins)
- The effects on physical and psychological function
- Psychosocial and environmental factors
- Response to treatment

Metabolic heterogeneity in weight loss in response to intervention



Helbronn, Wittert et al. Nature Med, 2023

Skeletal Muscle Mass and Physical Activity

- People with obesity have more muscle mass but poorer muscle quality
- Weight loss by decreasing energy intake (incl pharmacotherapy and surgery) reduces muscle mass.
- Weight loss improves global physical function.
- Adequate intake of high-quality protein reduces the loss of muscle mass.
- Both endurance- and resistance exercise help preserve muscle mass during weight loss. Resistance has the greater effect. Both have metabolic benefits independent of weight loss.
- Resistance-type exercise improves muscle strength and lower HbA1c independent of fat mass

Jansson AK, BMJ Open 2022
Cava, E et al Advances in Nutrition 2017

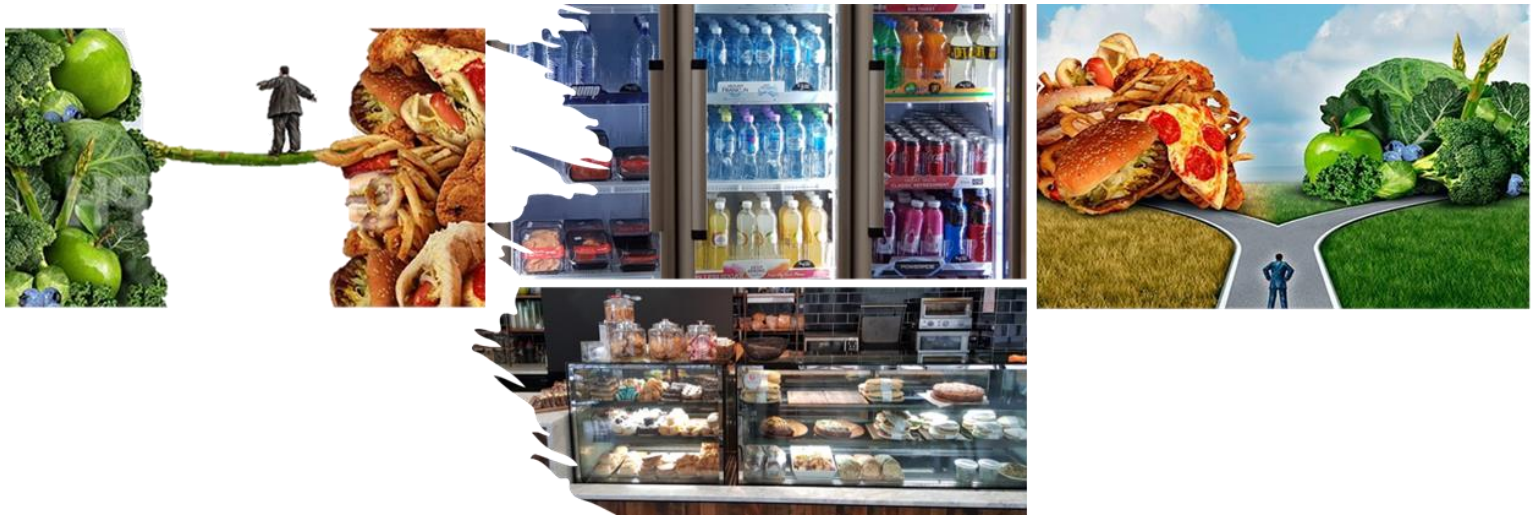
A recent systematic review and network meta-analysis:

The most effective strategy for nearly all body composition outcomes during energy restrictionj was combining energy restriction with resistance training or mixed exercise and high (adequate) protein.

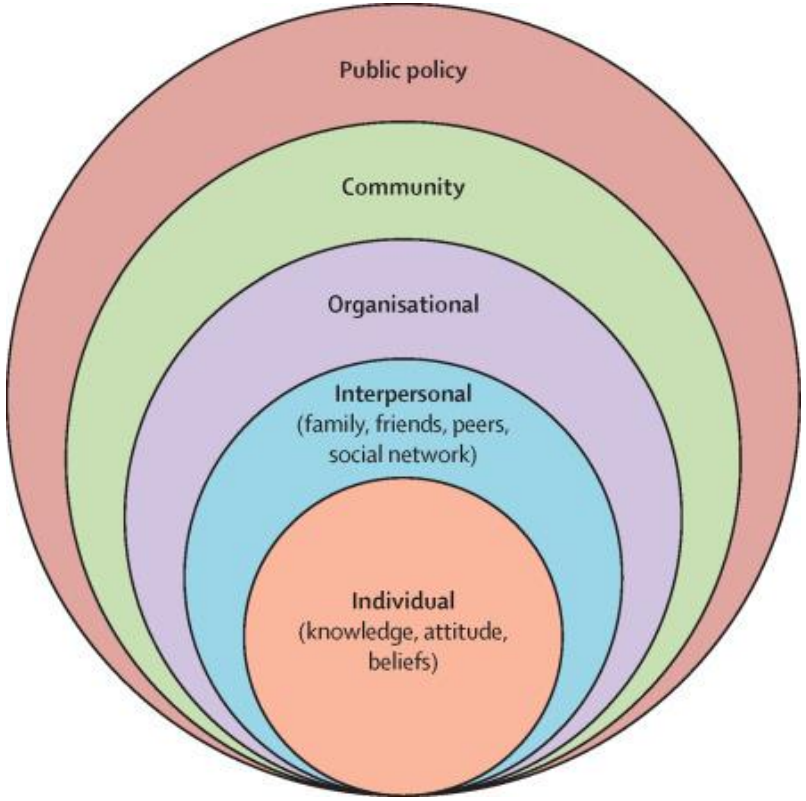
Eglseer, D et al. Advances in Nutrition, 2023

Role Modelling Healthy Behaviours an Promoting Healthy and Supportive Environments

- The food environment impacts human health
- Ready availability of highly hedonic, energy dense, nutrient limited foods impairs health
- Healthy choice should be the only choice
- This approach is environmentally sustainable

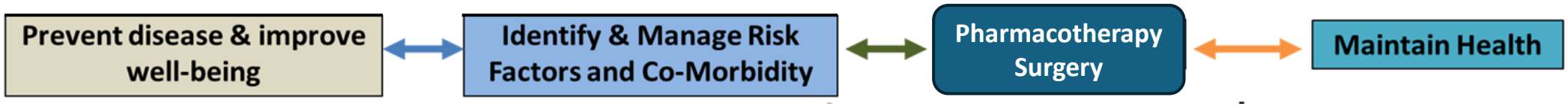


Creating and supporting a healthy food environment



Liu B et al The Lancet Planetary Health, 2 (10):e423-e424 (2018)

Obesity is a chronic lifelong condition. Whether ameliorated by pharmacotherapy or surgery – lifestyle measures and attention to psychosocial function are pivotal



- Personalised management requires integration of nutrition and physical activity with pharmacotherapy, metabolic surgery, behavioural and psychosocial approaches.
- Hypocaloric, nutrient dense diet, adequate protein, appropriately timed with avoidance of snacking and resistance as well as aerobic activity
- Advocacy for a supportive environment and avoidance of stigma are essential elements for successful long-term outcomes
- Good health rather than weight loss should be the goal

Thank You