The Cardiometabolic Consequences of Obesity and Nutritional Strategies for Prevention

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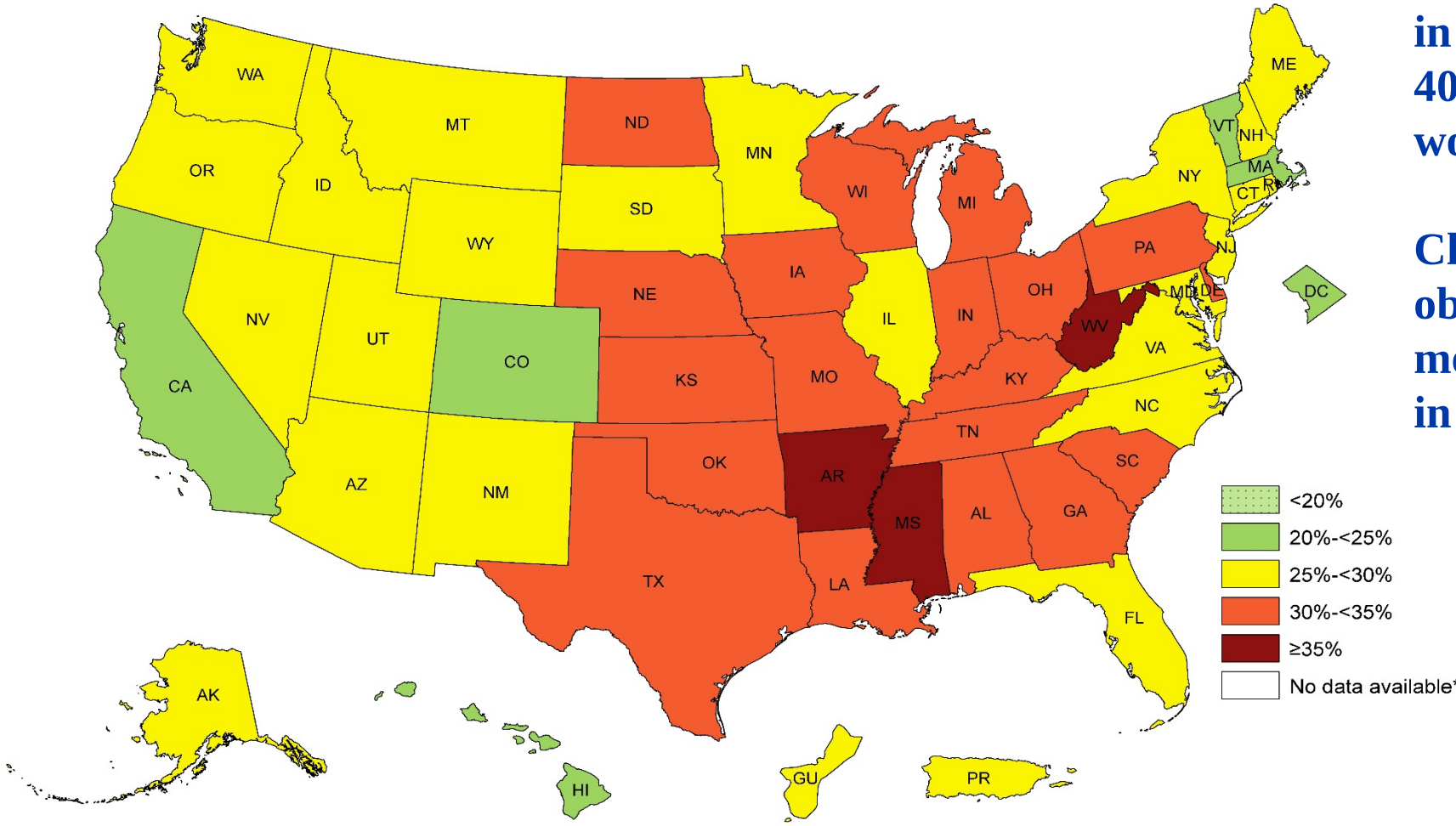
Prevalence of Self-Reported Obesity Among U.S. Adults 2014

¶ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



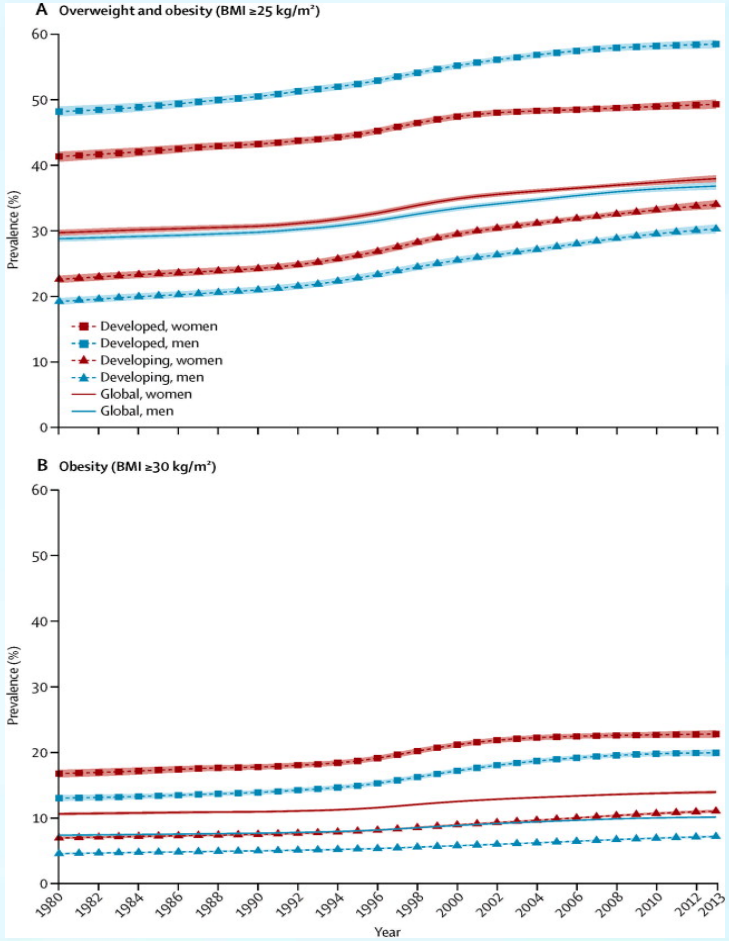
Prevalence of obesity: 35% in men and 40% in women

Class 3 obesity: 6% in men and 10% in women

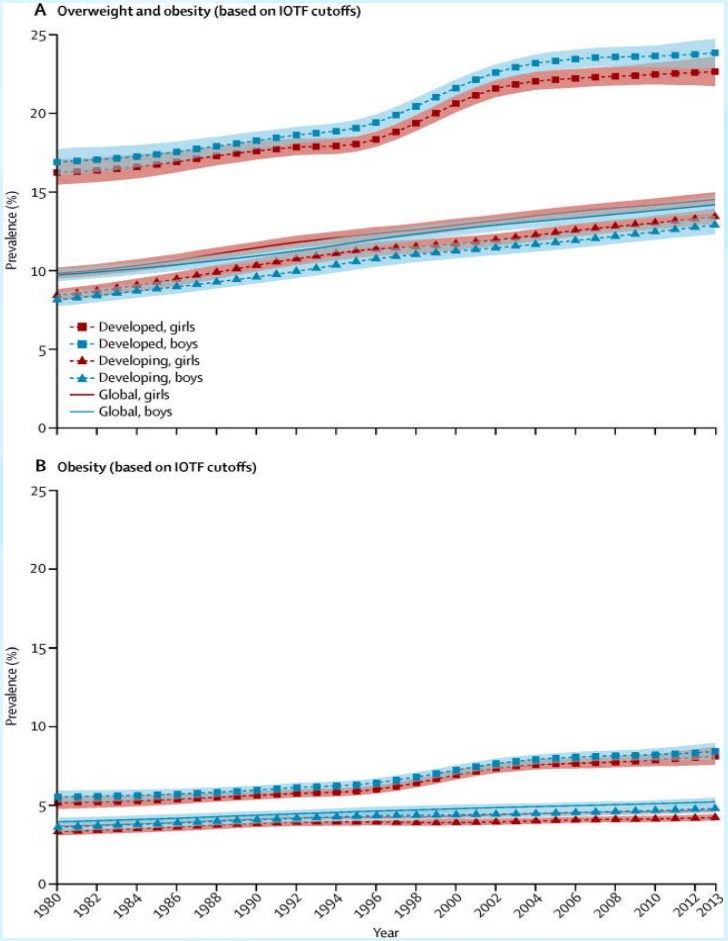
*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.

Global trends in obesity: 1980-2013

Adults



Children



Ng et al. Lancet 2014; 384: 766-81

After ‘The Biggest Loser,’ Their Bodies Fought to Regain Weight

Contestants lost hundreds of pounds during Season 8, but gained them back. A study of their struggles helps explain why so many people fail to keep off the weight they lose.

GINA KOLATA

MAY 2, 2016

- Decreased leptin (satiety hormone)
- Increased ghrelin (hunger hormone)
- Decreased metabolism
- Genetic predisposition

http://www.nytimes.com/2016/05/02/h
loser-weight-loss.html

Atherogenic factors in metabolic syndrome

Insulin resistance

Glucotoxicity

Lipotoxicity

↓ Adiponectin

Type 2 diabetes and glycemic disorders

Dyslipidemia
- Low HDL
- Small, dense LDL
- Hypertriglyceridemia

Hypertension

Endothelial dysfunction/ inflammation (hsCRP)

Impaired thrombolysis
↑ PAI-1

Atherosclerosis

Courtesy of Selwyn AP, Weissman PN.

Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories

A Systematic Review and Meta-analysis

Katherine M. Flegal, PhD
Brian K. Kit, MD
Heather Orpana, PhD
Barry I. Graubard, PhD

Importance Estimates of the relative mortality risks associated with normal weight, overweight, and obesity may help to inform decision making in the clinical setting.

Objective To perform a systematic review of reported hazard ratios (HRs) of all-cause mortality for overweight and obesity relative to normal weight in the general population

97 studies were included in the analysis (2.88 million individuals and 270,000 deaths).

Normal weight (18.5-<25): reference group
Overweight (25-<30): 0.94 (95% CI, 0.91-0.96)
Class 1 obesity (30-<35): 0.95 (95% CI, 0.88-1.01)
Class 2 & 3 obesity (≥35): 1.29 (95% CI, 1.18-1.41)

Methodological Issues in BMI-mortality Studies

- **Reverse causation (weight loss due to preexisting diseases)**
- **Residual confounding by cigarette smoking (Smokers tend to be leaner but have higher mortality rates)**
- **Over-adjustment for intermediates (e.g., blood pressure, lipids, glucose)**

Elderly populations

- **High prevalence of comorbid conditions & illness-weight loss**
- **Body mass index (BMI) less reliable measurement of adiposity**
- **Depletion of susceptibles**
- **High baseline mortality risk dilutes individual risk factors**

Manson JE, et al JWH. 2007; 16: 168-176

Obesity researchers must distinguish between two issues

- Role of excess body fat (high BMI) in causing illness and premature death.
  (Here BMI is a cause of disease)

- Role of chronic illness in causing involuntary weight loss (low BMI).

(Here low BMI is a consequence of disease)

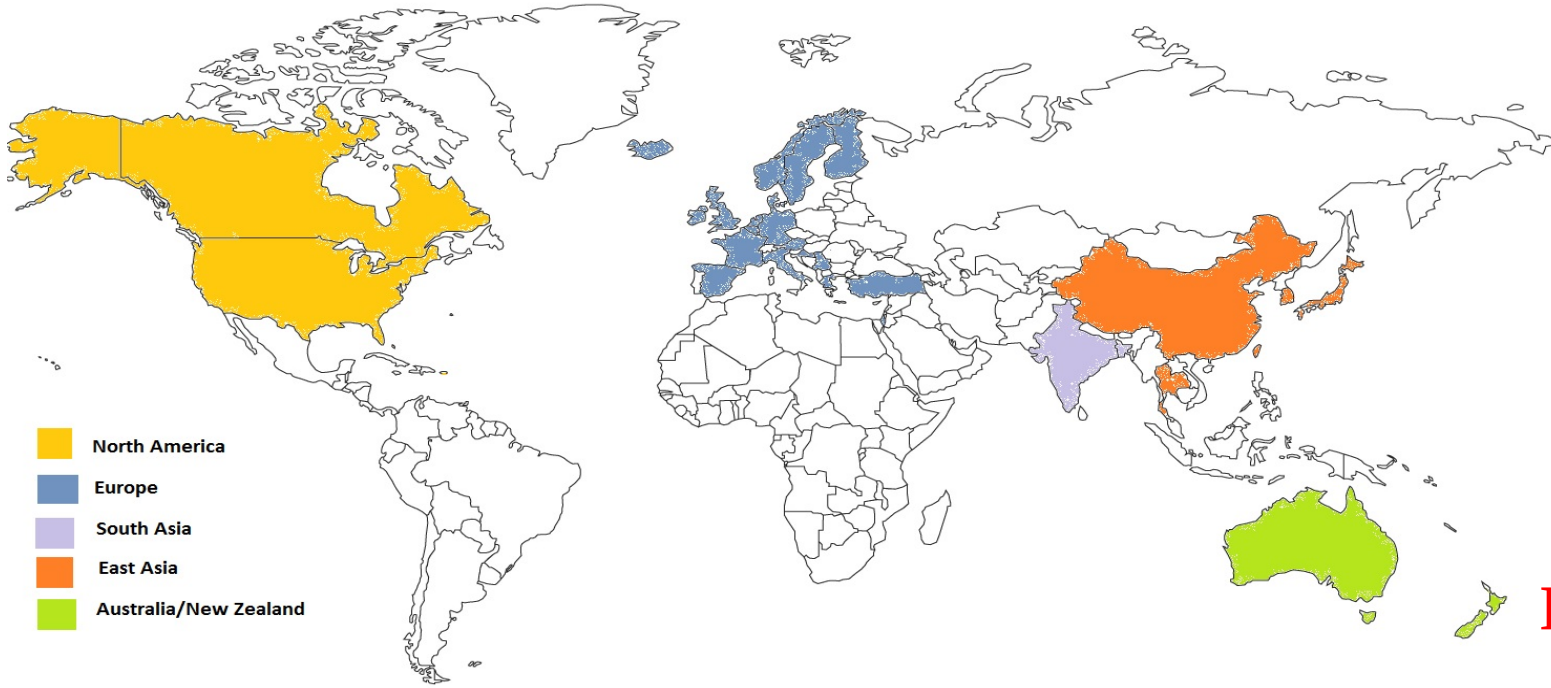
Michael Thun

Three Approaches to Minimize Bias In This Situation

- Restrict analyses to healthy never-smokers
- Exclude initial years of follow-up
- Consider disease incidence & risk factors as well as mortality

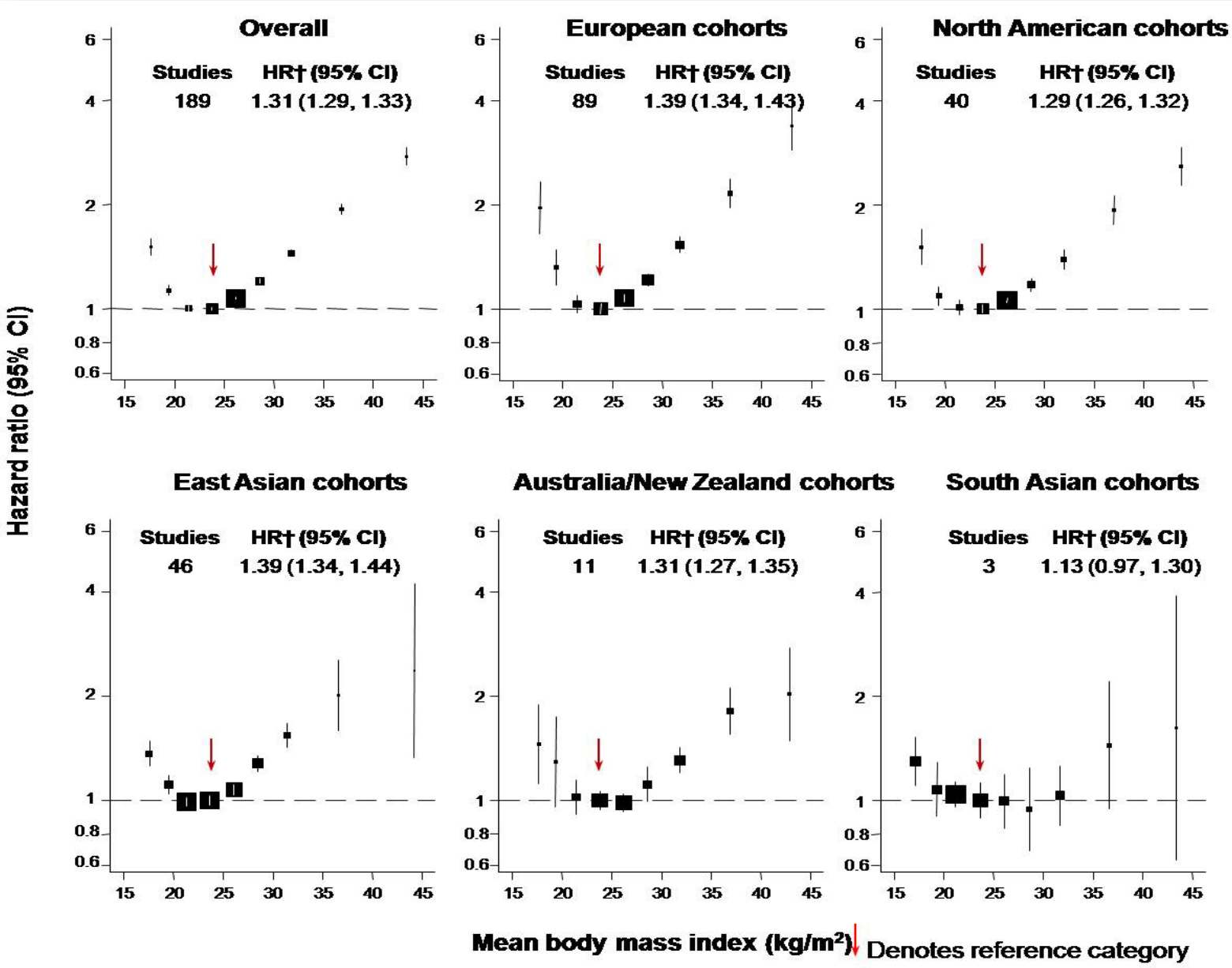
The Global BMI Mortality Collaboration

- Goal
  - Provide valid estimates of the associations of overweight and obesity with all-cause mortality across populations in major global regions
  - Conduct individual-level meta-analysis using the same protocol for data analysis
- Who we are
  - 500 investigators, 300 institutions, 32 countries, 4 continents
  - 239 prospective studies, 10.6 million participants



Lancet 2016

HRs for all-cause mortality by pre-defined categories of BMI



Summary and Conclusions

1. After accounting for residual confounding by smoking and reverse causation as well as possible, the lowest mortality is at BMI less than 25 in the general population.
2. One likely explanation for the “obesity paradox” is that chronically ill patients who lose weight and become frail are the ones who tend to die early.
3. Associations were substantially higher at younger than at older ages of baseline assessment
   - Policies to curb obesity to start early in life
4. Associations were higher in males than females
   - Greater insulin resistance, ectopic (e.g., liver) fat levels and type 2 diabetes prevalence at equivalent BMI levels

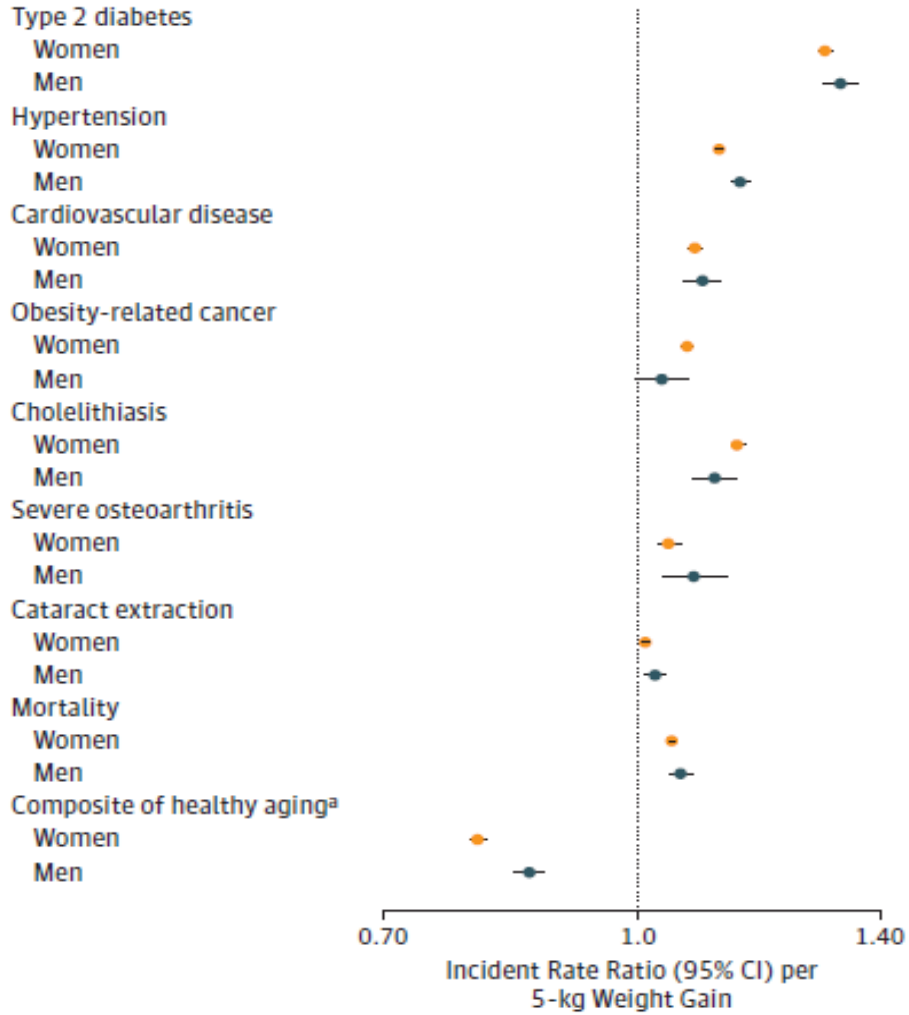
JAMA | Original Investigation

Associations of Weight Gain From Early to Middle Adulthood With Major Health Outcomes Later in Life

Yan Zheng, MD, PhD; JoAnn E. Manson, MD, DrPH; Changzheng Yuan, MD, ScD; Matthew H. Liang, MD, MPH; Francine Grodstein, ScD; Meir J. Stampfer, MD, DrPH; Walter C. Willett, MD, DrPH; Frank B. Hu, MD, PhD

Associations of weight change (per 5 kg) with

Figure 2. Associations of Weight Gain From Early to Middle Adulthood With Risk of Individual Health Outcomes



In the meta-analysis of data from women and men, per 5 kg weight gain was associated with

30% higher risk of type 2 diabetes,

14% higher risk of hypertension,

8% higher risk of cardiovascular disease,

6% higher risk of obesity-related cancer,

5% higher risk of deaths in never-smokers,

17% lower likelihood of achieving healthy aging in later life.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men

Dariush Mozaffarian, M.D., Dr.P.H., Tao Hao, M.P.H., Eric B. Rimm, Sc.D., Walter C. Willett, M.D., Dr.P.H., and Frank B. Hu, M.D., Ph.D.

Mozaffarian et al. NEJM 2012

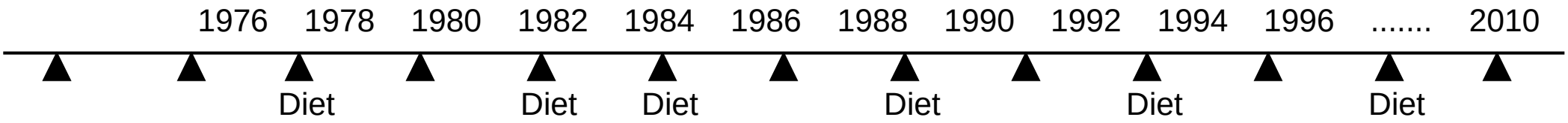
Determinants of Long-Term Weight Gain

- The average adult gains about 1 lb (0.45 kg) per year.
- Subtle, but adds up: 20 lbs over 20 years !
- This gradual pace makes it very difficult for individuals to perceive specific causes or remedies.
- Many RCTs have tested short-term weight loss strategies in obese/overweight persons. Such findings may have little relevance to determinants of long-term, gradual weight gain in non-obese populations.

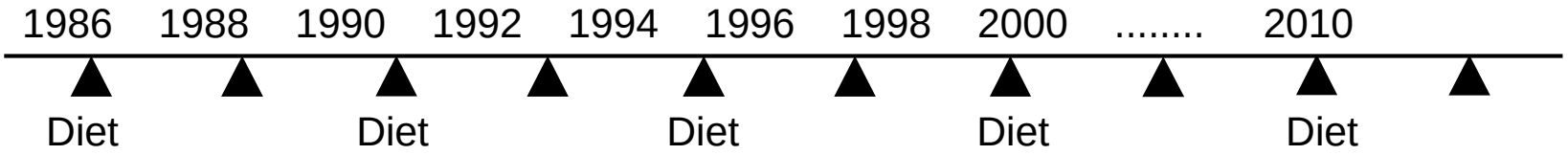
Courtesy of Mozaffarian

Lifestyle Changes and Long-Term Weight Gain

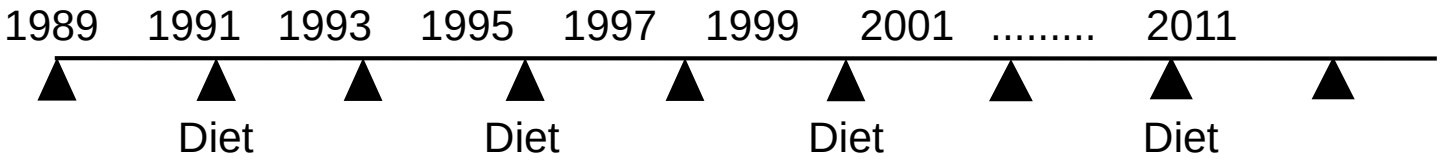
Nurses' Health Study (121,701 women)



Health Professionals Follow-up Study (51,529 men)

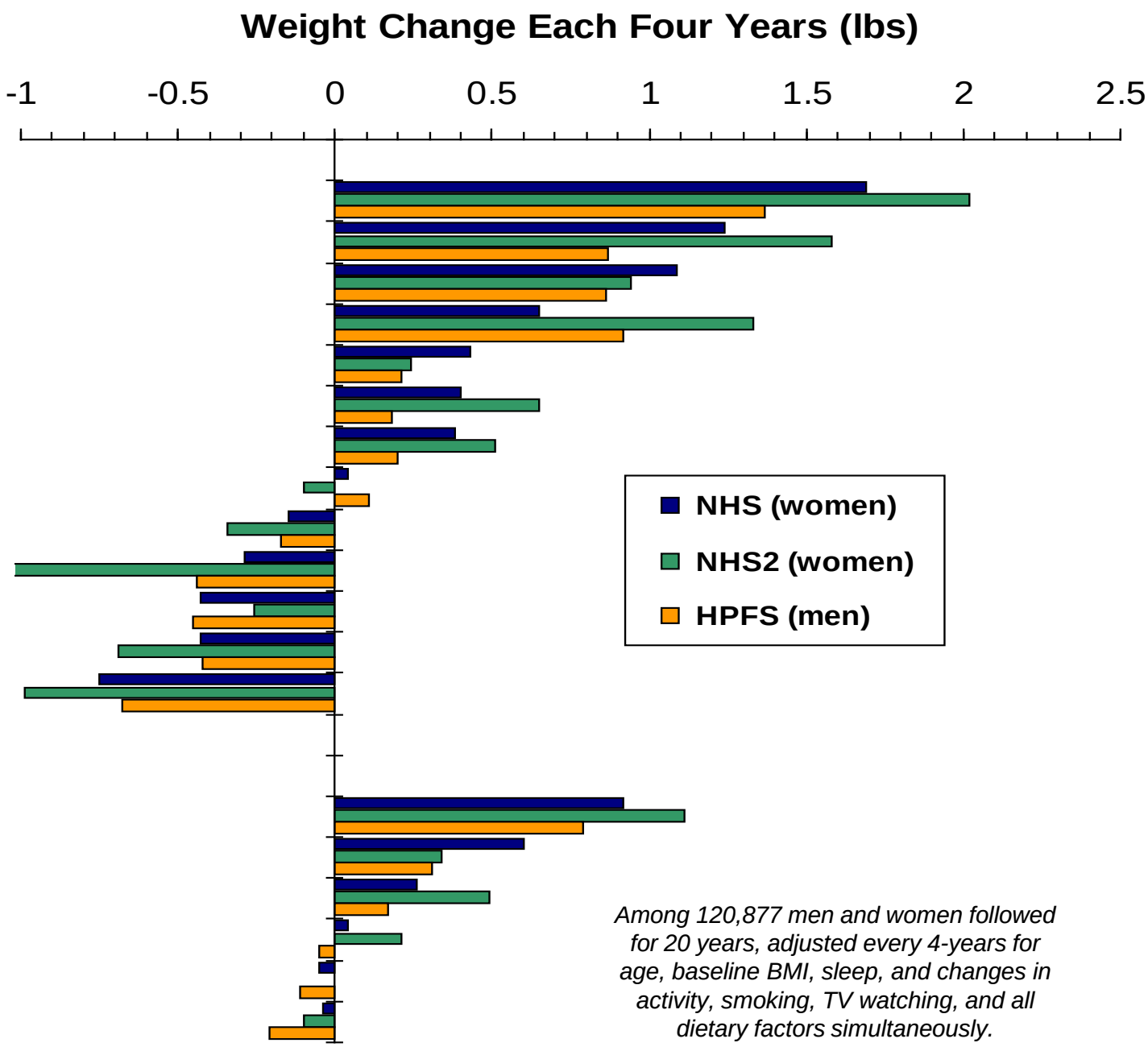


Nurses' Health Study II (116,686 young women)



Every Two Years: Weight, smoking, physical activity, CVD risk factors, diseases.

Every Four Years: Detailed dietary habits.



Among 120,877 men and women followed for 20 years, adjusted every 4-years for age, baseline BMI, sleep, and changes in activity, smoking, TV watching, and all dietary factors simultaneously.

Weight Change Associated with Each Increased Daily Serving of:

Foods

Potato chips

Potatoes/fries

Processed meats

Unprocessed red meats

Butter

Sweets and desserts

Refined grains

Cheese

Vegetables

Nuts

Whole grains

Fruits

Yogurt

Beverages

Sugar-sweetened beverages

Alcohol

100% fruit juice

Low fat or skim milk

Whole fat milk

Diet (zero calorie) soda

Take Home Messages

- **Diet quality is likely to influence diet quantity.**
  → not simply "eat less", but also "eat better."
- **Current emphasized metrics based on total amounts of fat or carbohydrates may not be very helpful.**
- **Carbohydrate quality and extent of food processing appear to be potentially key metrics.**
- **Weight gain is very gradual → Difficult to detect/combat.**
- **Small diet and lifestyle changes can make big difference**
  → Tremendous opportunity for prevention!

Courtesy of Mozaffarian

Prospective Urban Rural Epidemiology (PURE) Study

- 135,000 participants, 18 countries
- 7 years of follow up
- Findings
  - Highest fat intake (35% daily calories) 23% lower mortality risk than lowest intake (10% daily calories)
  - Highest carbohydrate intake (77% daily calories) 28% higher mortality risk than lowest intake (46% daily calories)

Dehghan et al. Lancet 2017

STAT News

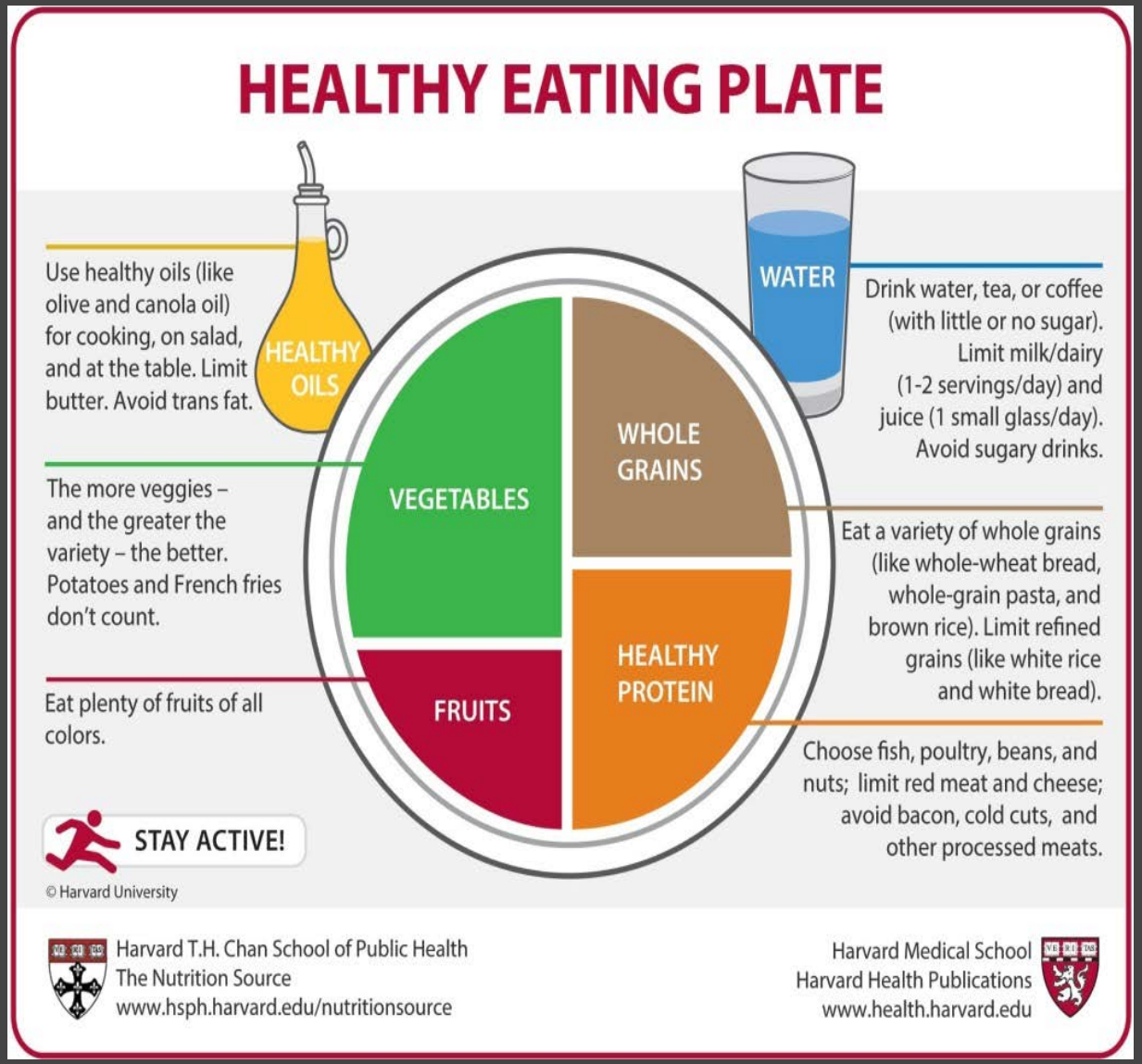
Conclusions: Carbs are bad and fats are good.

Methodological Problems

- "Total carbohydrates" is over-simplified
  - High quality vs. low quality carbs
- Very high carbohydrate intake may indicate poverty diet
  - Confounding from poverty and undernutrition
- Assessment and analysis of types of fat
  - No trans fat data
  - Did not examine replacing saturated fat with polyunsaturated fat
- Reliability of data
  - Fat intake in Chinese cohort 17.7% vs. 30% in other surveys

Beyond the Headlines and Abstract

- Large studies assessing diet in developing countries are needed
- Interpret findings with caution
- Dietary guidance:
  - Enjoy whole grains and unsaturated fat
  - Limit saturated fat and refined grains/added sugars



JAMA Internal Medicine
Formerly *Archives of Internal Medicine*

Research

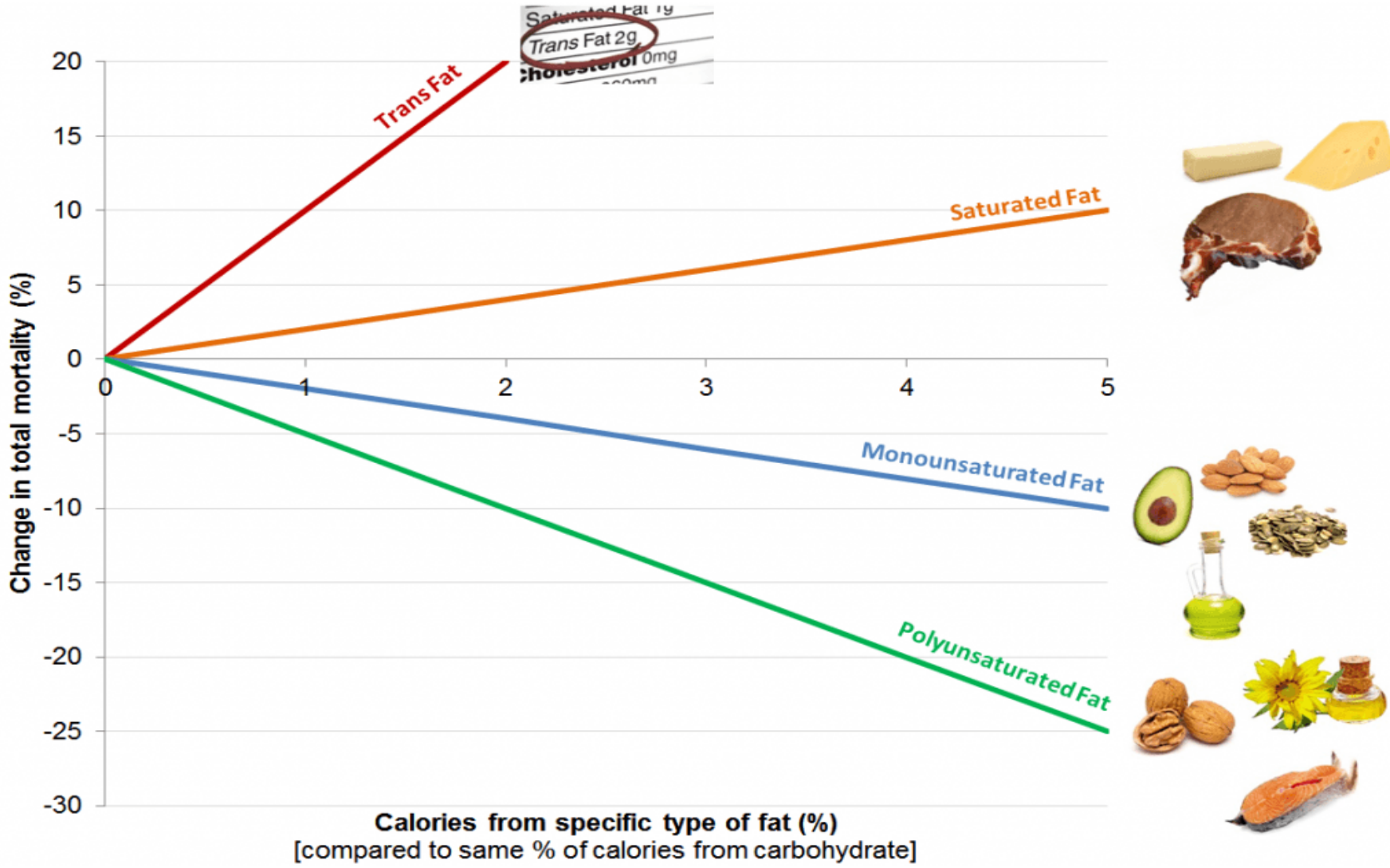
Original Investigation

Association of Specific Dietary Fats With Total and Cause-Specific Mortality

Dong D. Wang, MD, MSc; Yanping Li, PhD; Stephanie E. Chiuve, ScD; Meir J. Stampfer, MD, DrPH; JoAnn E. Manson, MD, DrPH; Eric B. Rimm, ScD; Walter C. Willett, MD, DrPH; Frank B. Hu, MD, PhD

Wang et al. *JAMA Intern Med*. July 2016

Types of Fats and Mortality



Dietary Pattern Analysis: A New Direction in Nutritional Epidemiology

Frank B. Hu

Current Opinion in Lipidology 2002; 13:3-9

Conceptually, dietary patterns represent a broader picture of food and nutrient consumption, and may thus be more predictive of disease risk than individual foods or nutrients.

Dietary patterns: from nutritional epidemiologic analysis to national guidelines

Elizabeth M Cespedes and Frank B Hu

Am J Clin Nutr 2015;101:899–900.

The American Journal of Clinical Nutrition

Establishing a robust evidence base for the dietary patterns described by national guidelines is essential to test the public health relevance of these guidelines.

Scientific Report of the 2015 Dietary Guidelines Advisory Committee

Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture

The DGAC recommends 3 healthy dietary patterns

- Healthy U.S.- style Pattern
- Healthy Mediterranean-style Pattern
- Healthy Vegetarian Pattern

Common components of healthy dietary patterns:

- Rich in vegetables, fruit, whole grains, seafood, legumes, and nuts
- Moderate in low-/non-fat dairy products and alcohol
- Lower in red/processed meat
- Low in sugar sweetened foods/beverages and refined grains
- Low in saturated fat, added sugars, and sodium

HARVARD T.H. CHAN | SCHOOL OF PUBLIC HEALTH

Changes in Diet Quality and Total and Cause-Specific Mortality

Sotos-Prieto M, Bhupathiraju SN, Mattei J, Fung TT, Li Y, Pan A, Willett WC, Rimm EB, Hu FB.

New England Journal of Medicine (July 2017)

Overall dietary quality

The Alternate Healthy Eating Index-2010 (AHEI) score

- Based on recommendations for food and nutrient consumption with
- Current scientific evidence of beneficial health effects

The Alternate Mediterranean diet (AMED) score

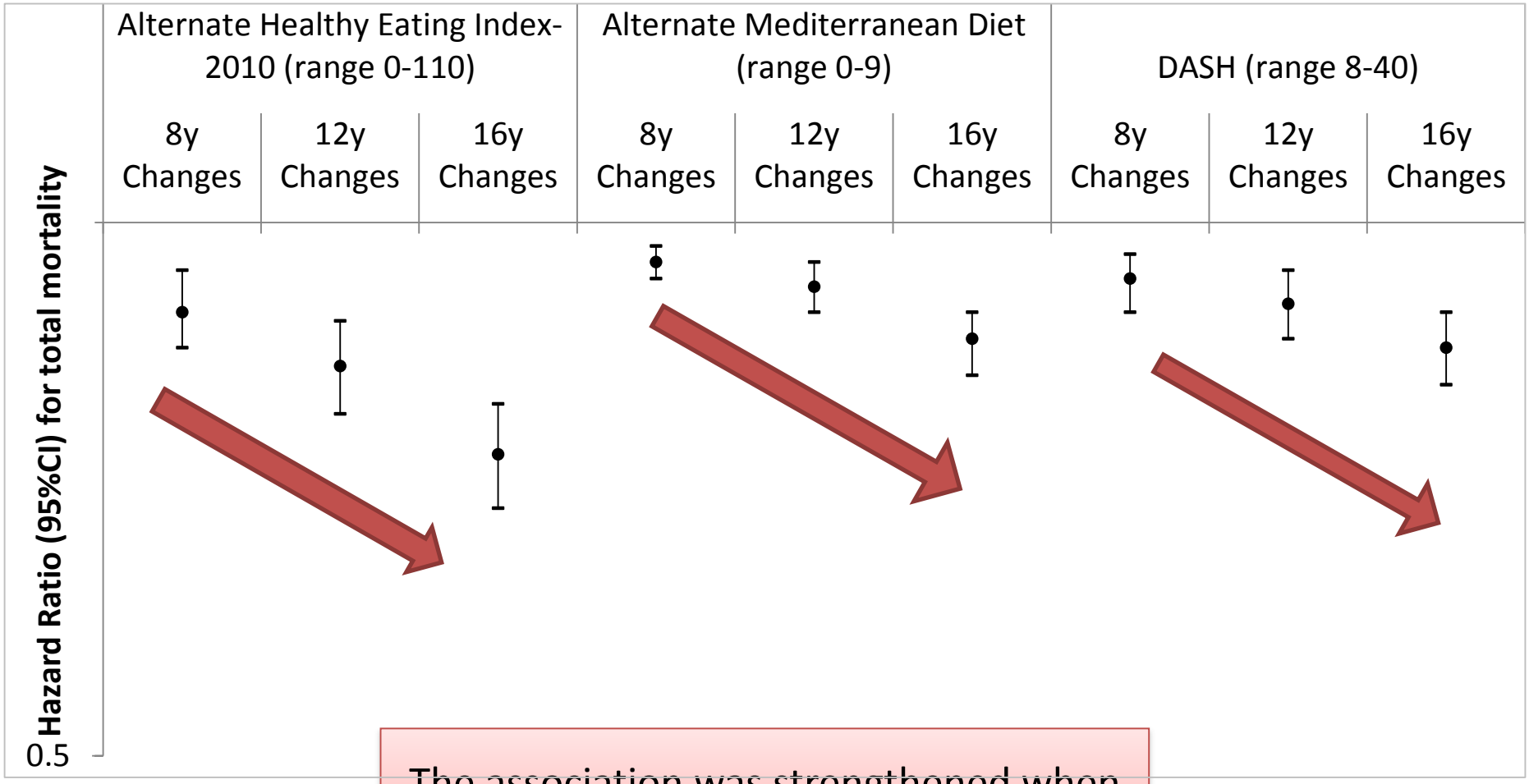
- Comprised of foods and nutrients characteristic of the Mediterranean Pattern

The Dietary Approach to Stop Hypertension (DASH) score

- Developed from the DASH dietary recommendations aiming to reduce blood pressure

AHEI: Chiuve et al., 2012. J Nutr. **AMED** Fung TT et al., 2009. Circulation. **DASH:** Fung TT et al., 2008 Arch Intern Med.

Shorter- and longer-term changes in diet quality



The association was strengthened when longer changes were evaluated

Translating the Public Health Message

- Even a modest improvement in diet quality (i.e. ~22 points or 20%) out of 110 for the AHEI score over a 12-year lower the risk of total mortality by 17%

- This change can be achieved by swapping out just one serving of red or processed meat for one daily serving of nuts or legumes

- Underscore the importance of promoting dietary changes as part of nutrition and public health policies.

Plant-based diets and risk of type 2 diabetes and coronary heart disease

Satija et al. PloS Medicine 2016

Satija et al. J Am College of Cardiology 2017

Plant-based diets are not equivalent to “vegetarian” diets

Foods excluded in different types of dietary patterns

	RED MEAT & POULTRY	FISH & SEAFOOD	EGGS	DAIRY
NON-VEGETARIAN				
PESCO-VEGETARIAN				
LACTO-OVO-VEGETARIAN				
LACTO-VEGETARIAN				
VEGAN				

The three plant-based diet indices

Overall Plant-based Diet Index (PDI)

High animal, low plant food intake

High plant, low animal food intake

Healthful Plant-based Diet Index (hPDI)

High animal, high unhealthy plant, and low healthy plant food intake

High healthy plant, low unhealthy plant, and low animal food intake

Unhealthful Plant-based Diet Index (uPDI)

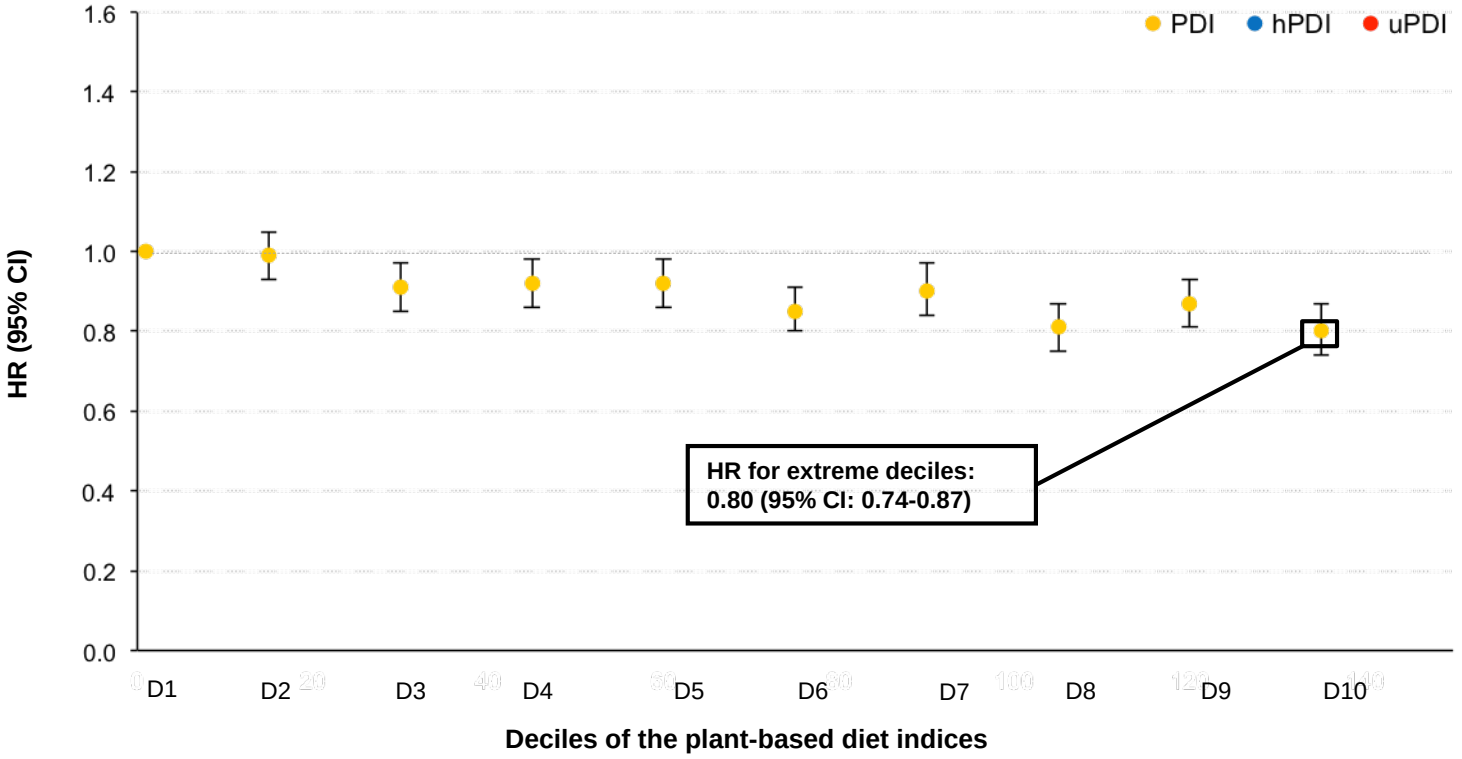
High animal, high healthy plant, and low unhealthy plant food intake

High unhealthy plant, low healthy plant, and low animal food intake

Results

Associations with T2D

Pooled HRs (95% CI) for T2D according to deciles of the plant-based diet indices



Multivariable model. P trend<0.001 for all analyses

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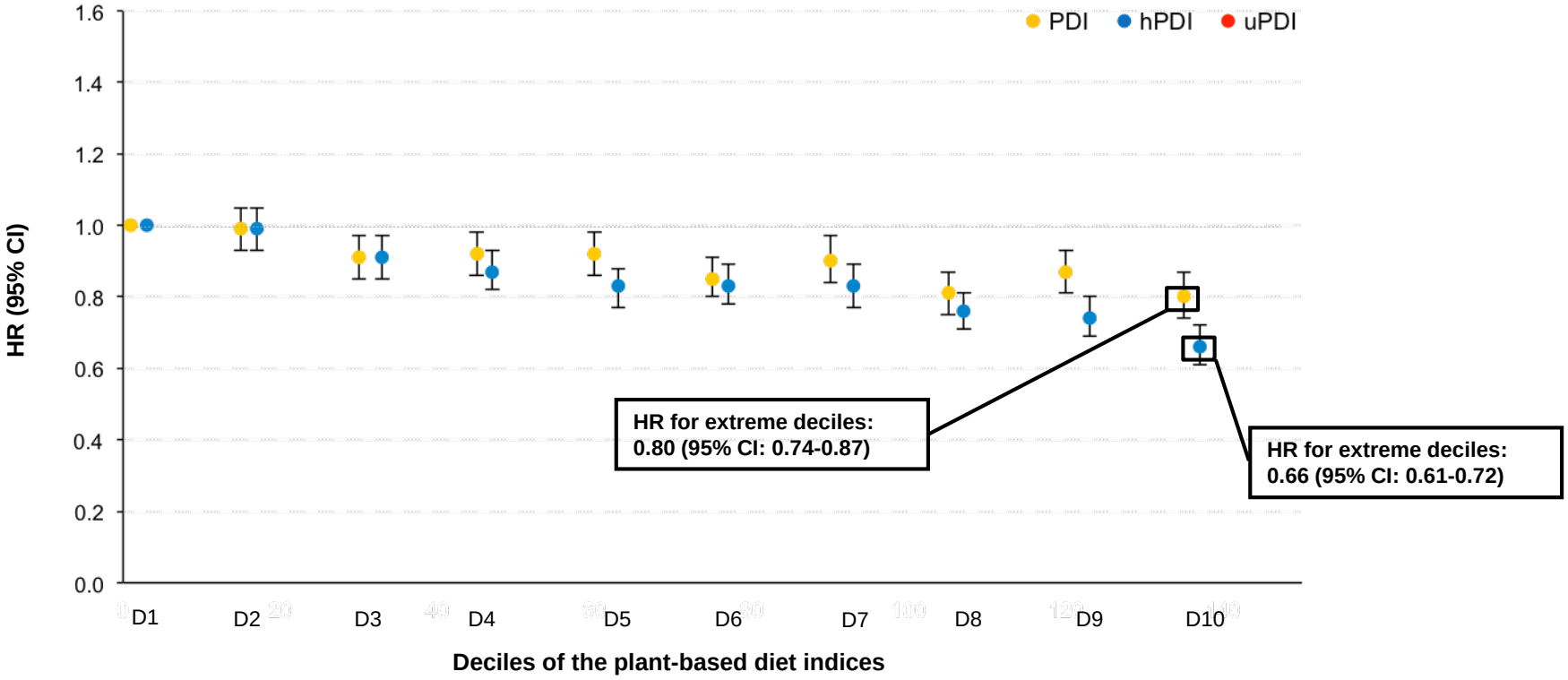

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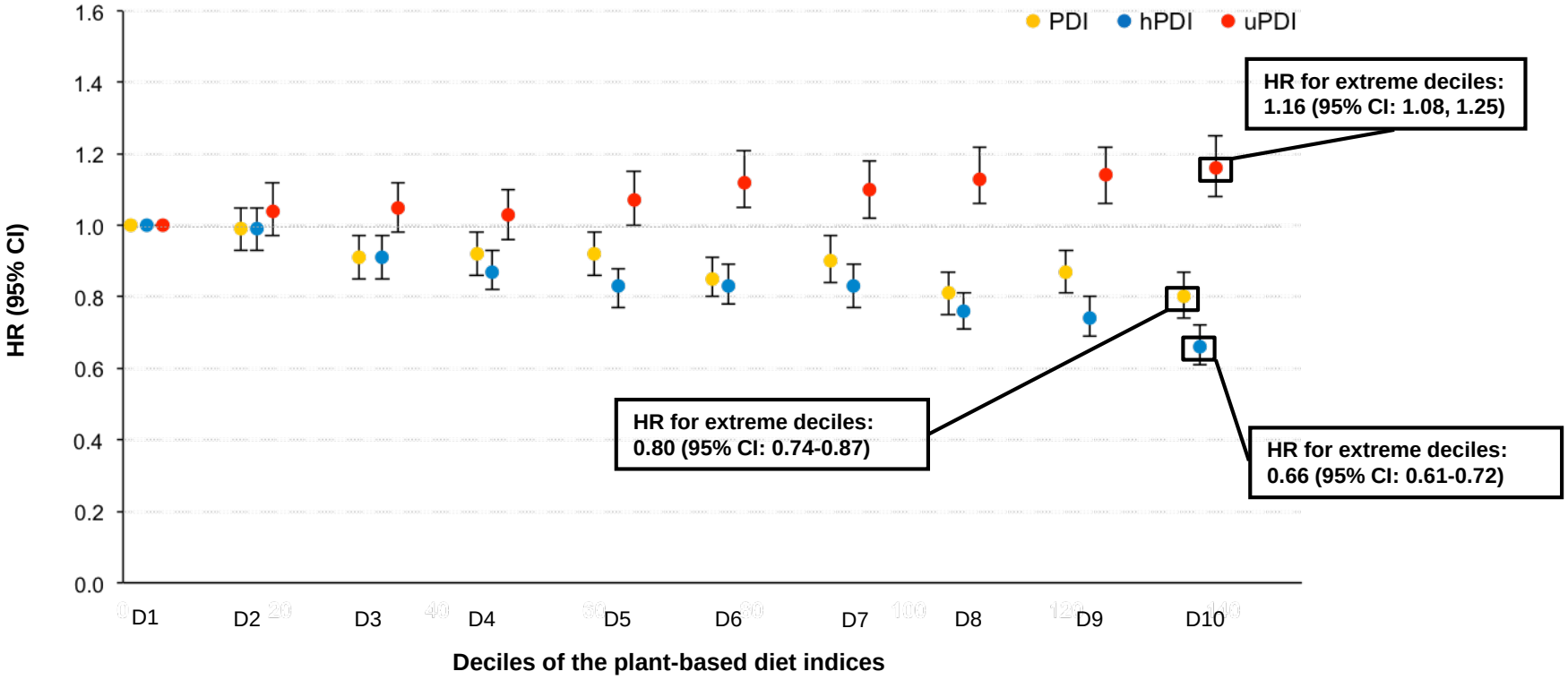
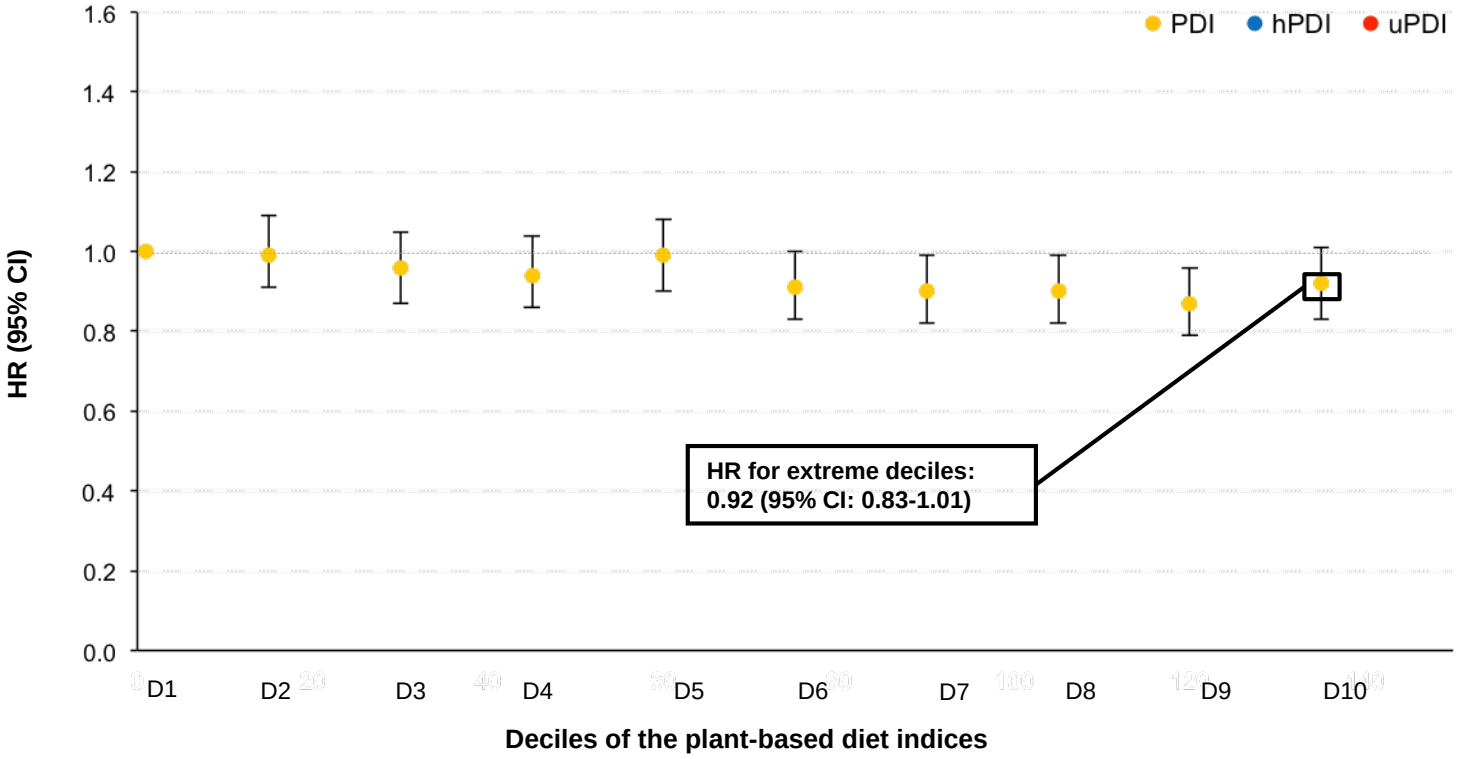


Multivariable model. P trend<0.001 for all analyses

Results

Associations with CHD

Pooled HRs (95% CI) for CHD according to deciles of the plant-based diet indices

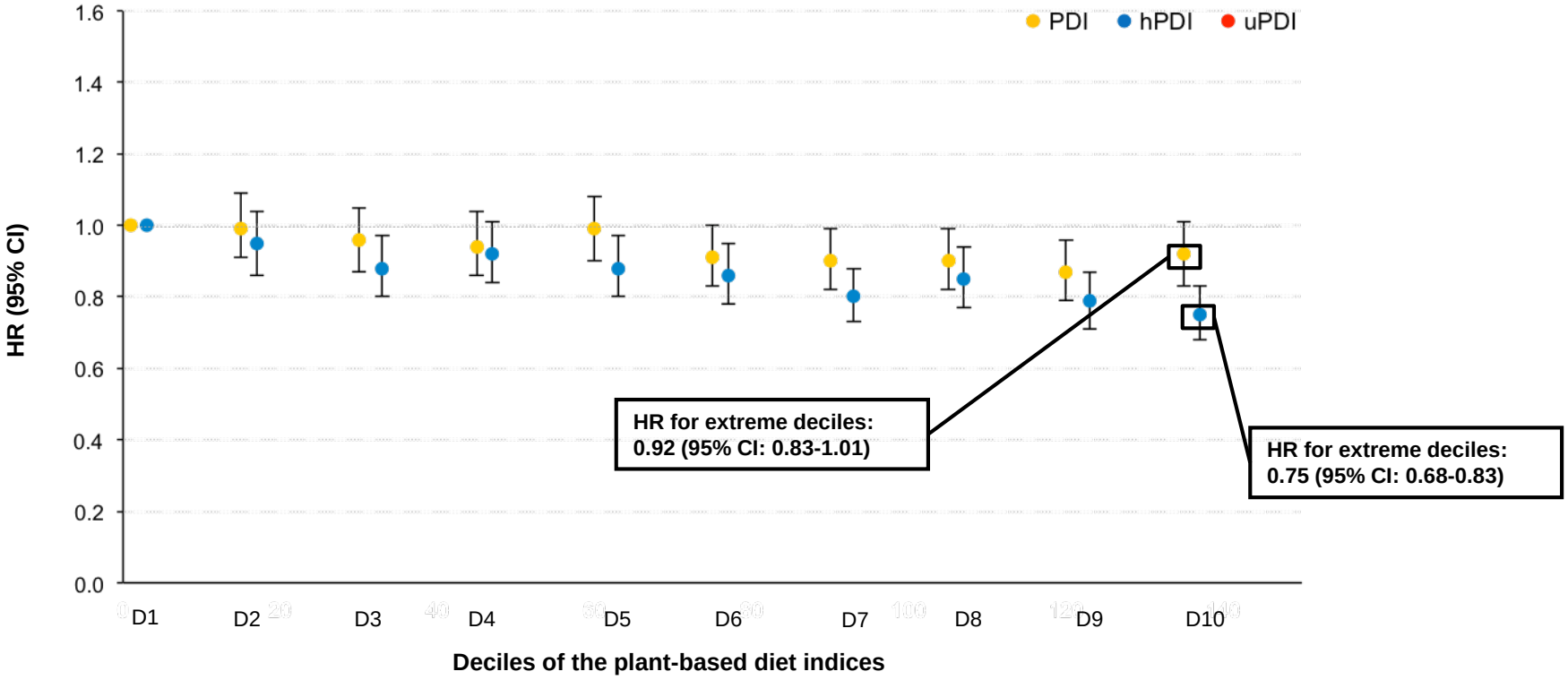


Multivariable model. P trend=0.003 for PDI, and <0.001 for hPDI and uPDI

Results

Associations with CHD

Pooled HRs (95% CI) for CHD according to deciles of the plant-based diet indices



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Results

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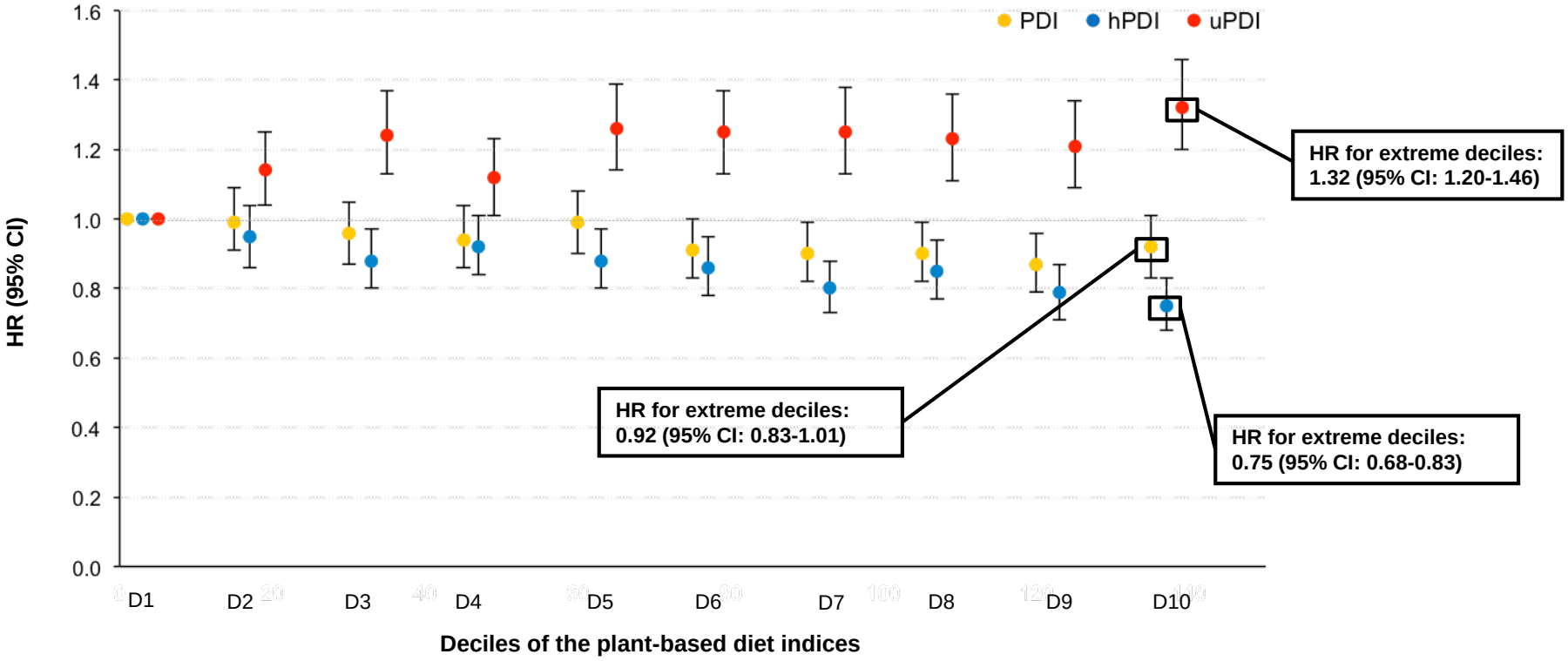

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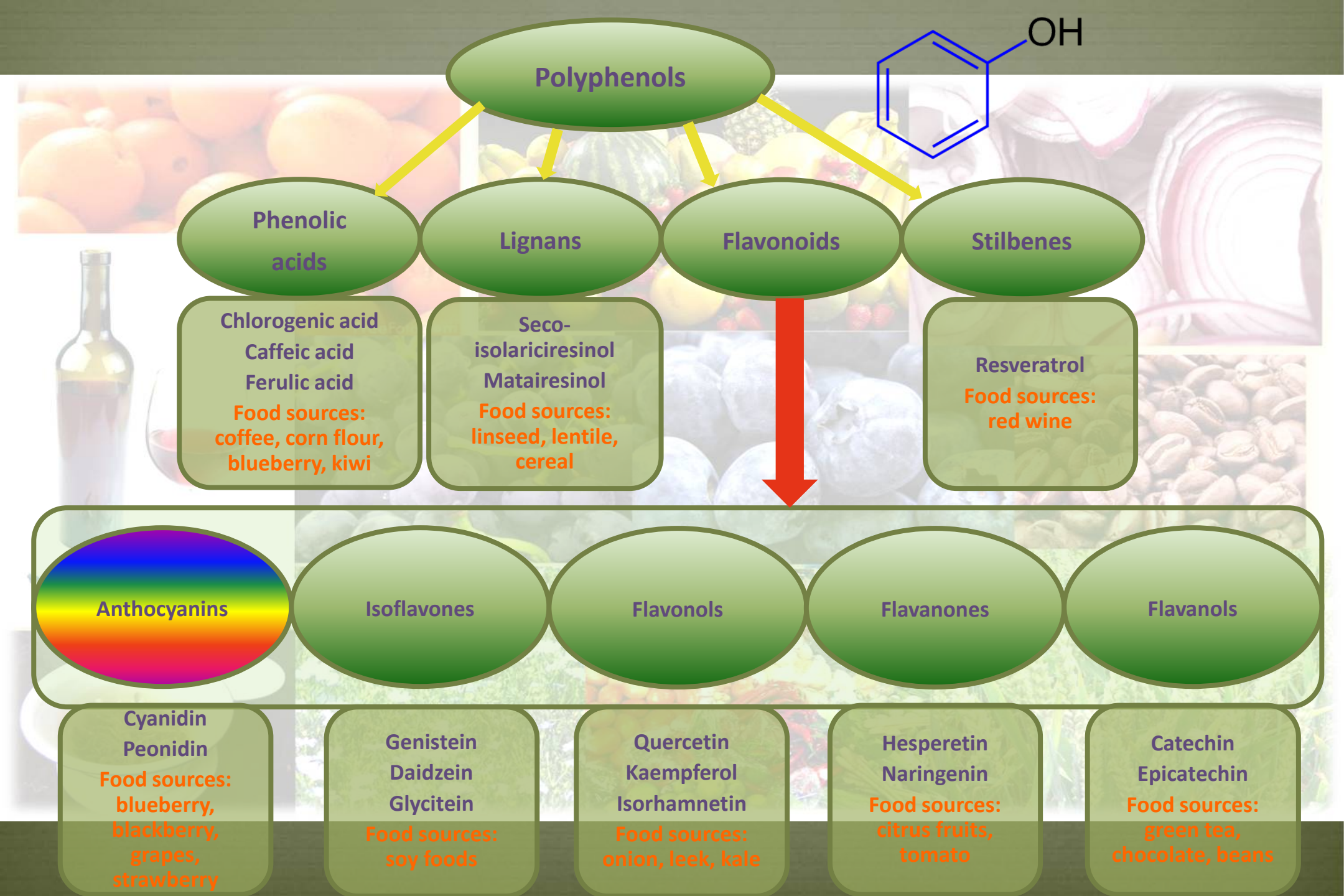
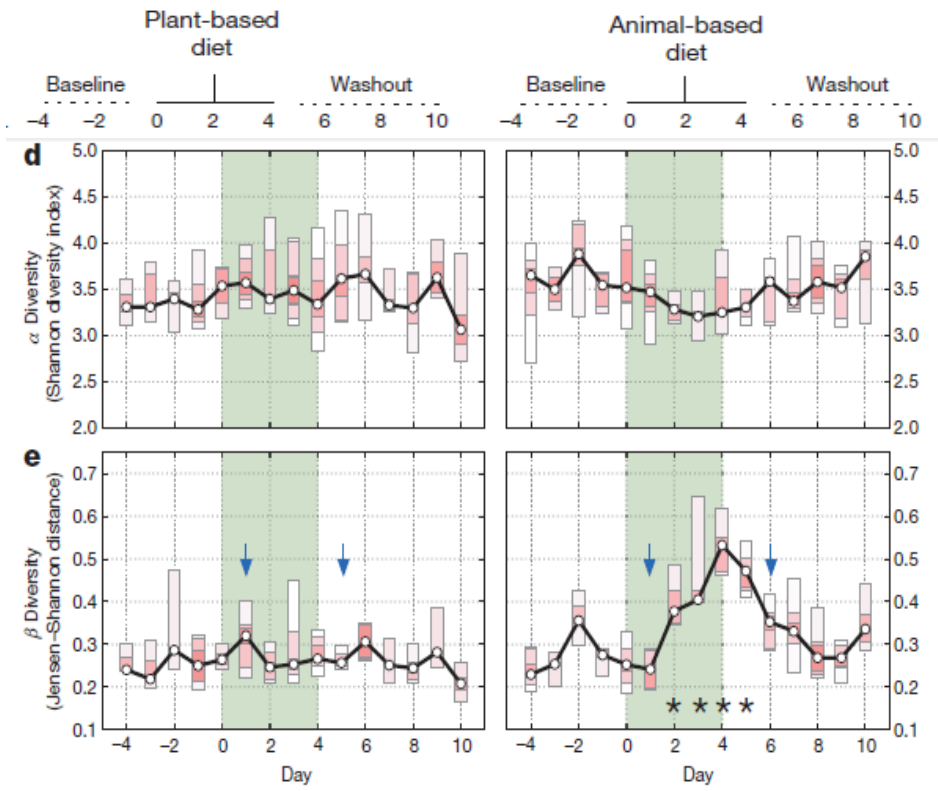
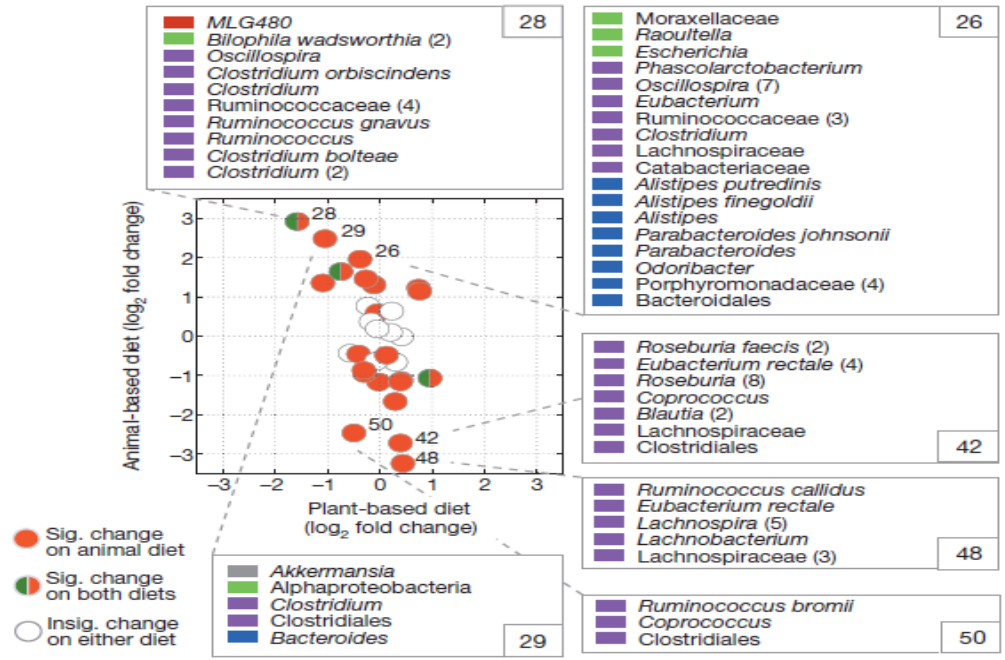

Polyphenols
OH
Phenolic acids
Lignans
Flavonoids
Stilbenes
Chlorogenic acid
Caffeic acid
Ferulic acid
Food sources: coffee, corn flour, blueberry, kiwi
Seco-isolariciresinol
Matairesinol
Food sources: linseed, lentile, cereal
Resveratrol
Food sources: red wine
Anthocyanins
Isoflavones
Flavonols
Flavanones
Flavanols
Cyanidin
Peonidin
Food sources: blueberry, blackberry, grapes, strawberry
Genistein
Daidzein
Glycitein
Food sources: soy foods
Quercetin
Kaempferol
Isorhamnetin
Food sources: onion, leek, kale
Hesperetin
Naringenin
Food sources: citrus fruits, tomato
Catechin
Epicatechin
Food sources: green tea, chocolate, beans

Diet alters human gut microbiome



Ab libitum 'plant-based diet' and 'animal-based diet' for five consecutive days by six male and four female.



Bacterial cluster response to dietary arm

The similarity of each individual's gut microbiota to their baseline communities (B diversity) decreased on the animal-based diet (dates with q,0.05 identified with asterisks; Bonferroni-corrected, two-sided Mann–Whitney U test).

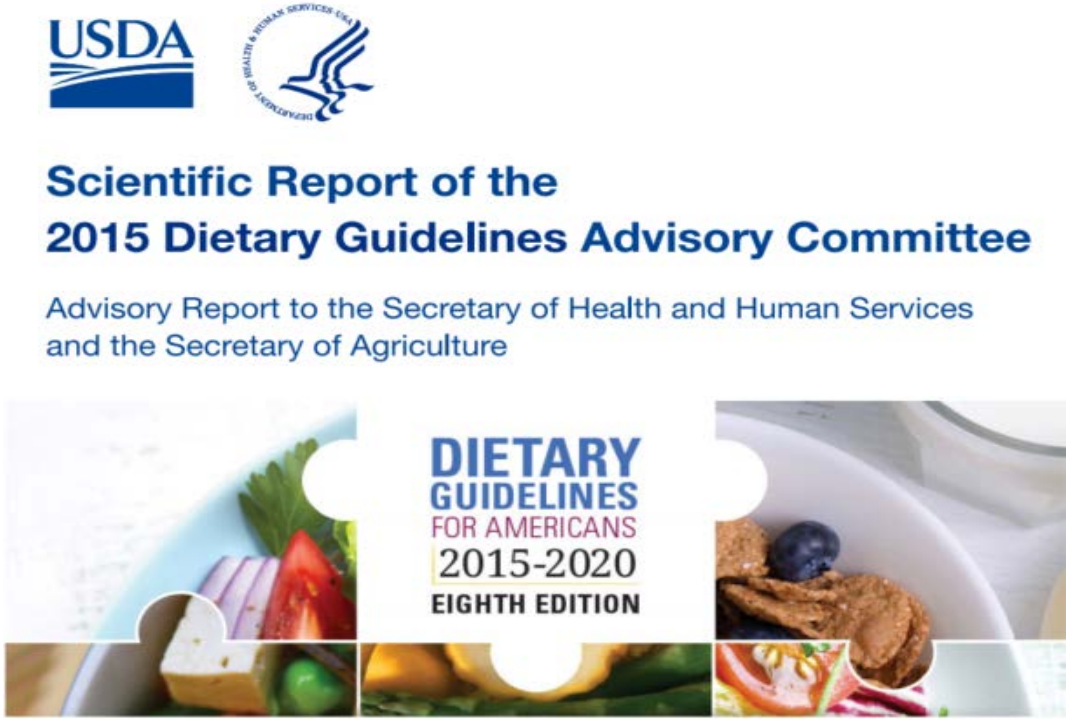
David LA et al. Nature 2013; 500(7464): 585-8

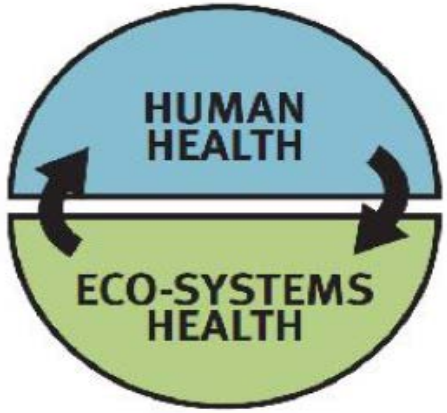
Conclusions & Implications

- An overall plant-based diet score was associated with lower risk of T2D & CHD.
- This inverse association became substantially stronger for a healthier version of the diet, but was positive for an unhealthful version
- Not all plant-based diets are created equal.

Increasing intake of healthy plant-foods, while reducing intake of less healthy plant foods and certain animal foods, may be beneficial for T2D and CHD prevention

Conclusions & Implications





Increasing intake of healthy plant-foods, while reducing intake of less healthy plant foods and certain animal foods (e.g. red and processed meats), is also beneficial for the health of the planet.

Acknowledgements

- *Shilpa N Bhupathiraju*
- *Lea Borgi*
- *Stephanie E Chiuve*
- *JoAnn E Manson*
- *Kathryn M Rexrode*
- *Eric B Rimm*
- *Donna Spiegelman*
- *Qi Sun*
- *Walter C Willett*