Trends and development in the assessment of nutritional health benefits of consumption of foods

Walter C. Willett, MD, DrPH

Department of Nutrition

Harvard T. H. Chan School of Public Health

February 15, 2022

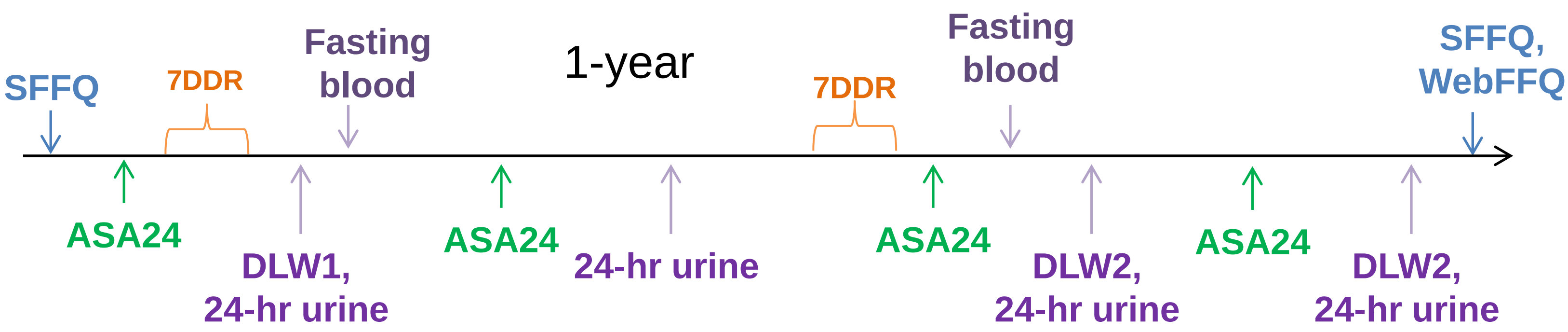
Challenges in Studies of Specific Foods and Health

- Lags between intake and disease can be decades
- Range of intake may be limited
- Effects of single foods are likely to be small
- Intakes may be correlated with other foods
- Confounding by non-dietary factors
- Long-term randomized trials usually not feasible

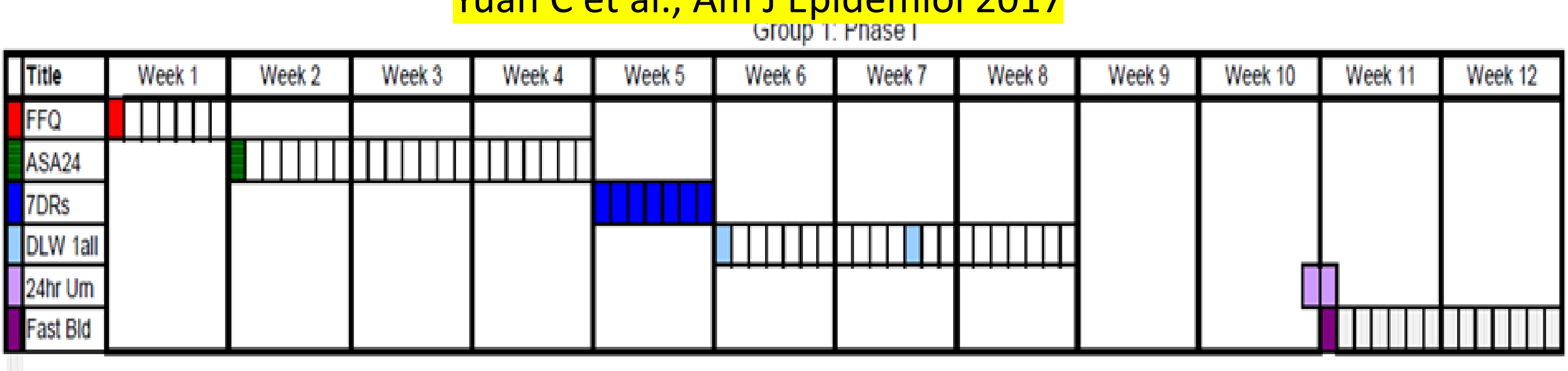
Approaches to study of specific foods and health outcomes

- Long-term prospective cohort studies (? Dietary assessment method)
- Use of biomarkers as outcomes
- Surrogate outcomes, e.g., blood pressure, blood lipids
- Animal studies
- Nutrient profiling
- Combinations of the above

Women's Lifestyle Validation Study (WLVS)
-Study timeline

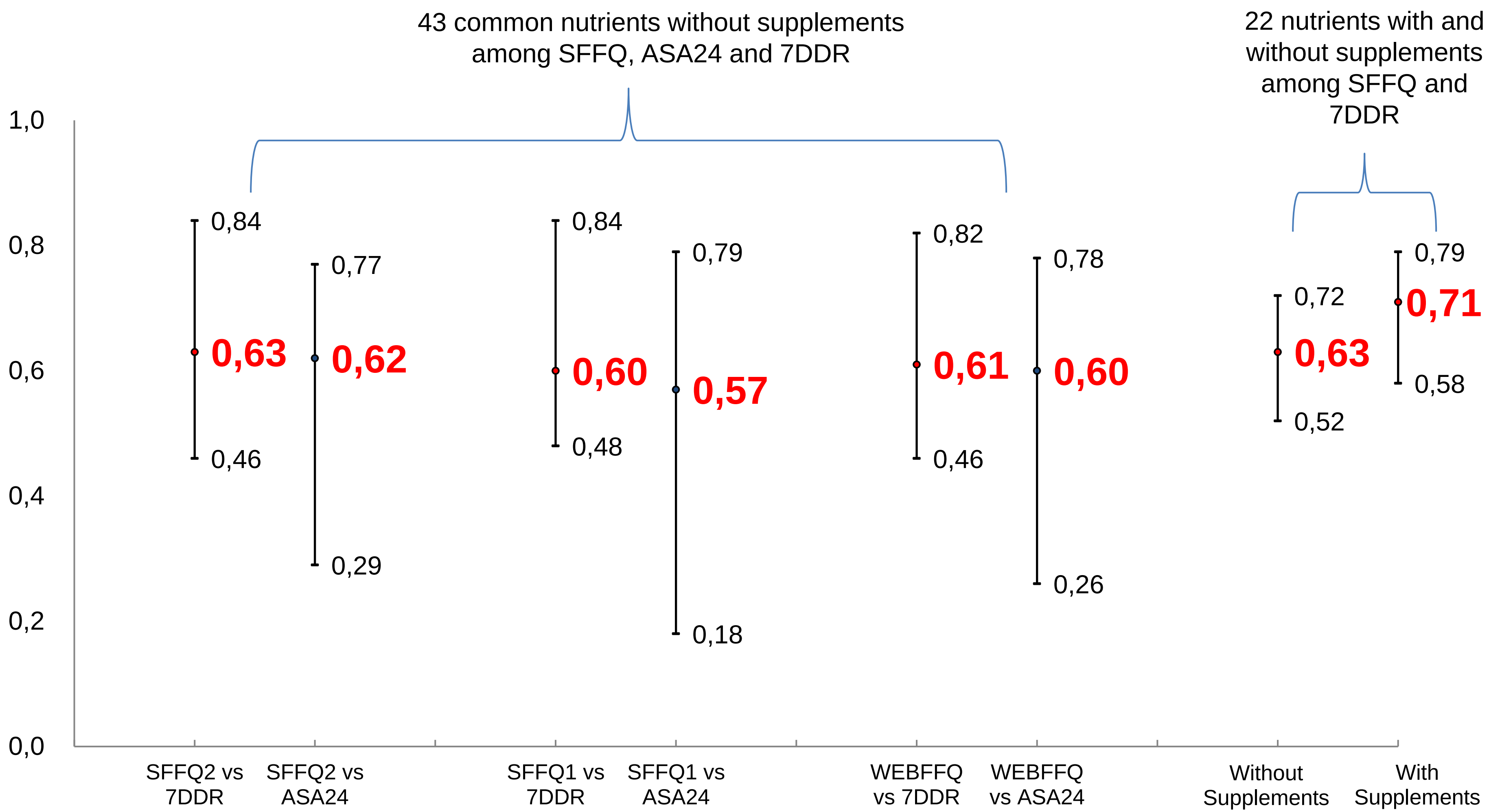


Yuan C et al., Am J Epidemiol 2017



(Yuan C et al., Am J Epidemiol 2017; Al-Shaar L, Am J Epidemiol, 2021)

Overall validity of SFFQ2, SFFQ1, WebFFQ
<u>De-attenuated r</u> (N = 632 women in NHS and NHS II)



*50 additional common nutrients between SFFQ2 & 7DDR: mean r=0.56

(Yuan C et al., Am J Epidemiol 2017; Al-Shaar L, Am J Epidemiol, 2021)

Relative Validity of Dietary Assessment Methods: Design

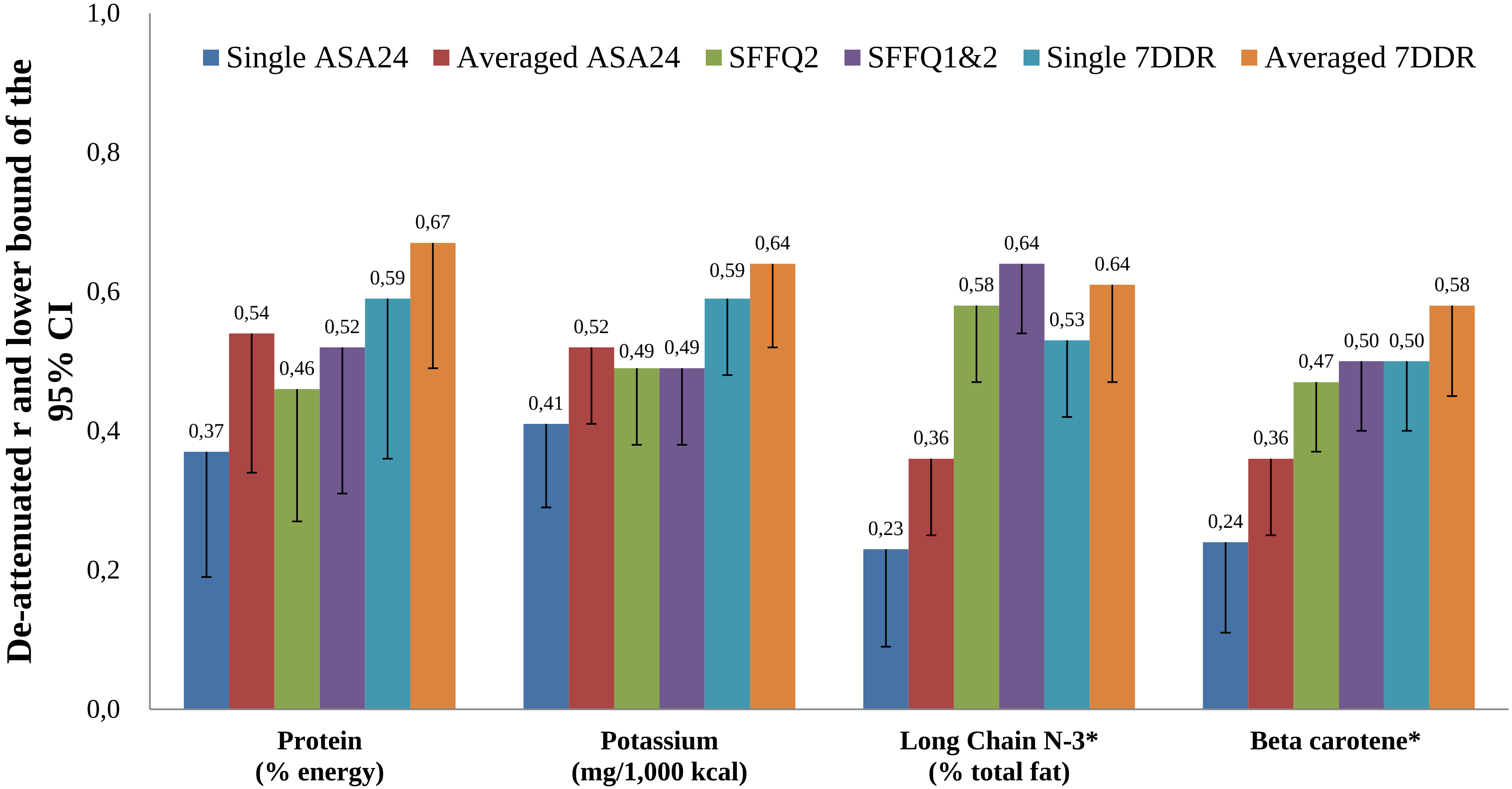
(N = 600+ women in Nurses' Health Studies)

- 24-hour recall (1 day)
- 24-hour recall (3-4 days)
- FFQ (1)
- FFQ (average of 2)
- 7-day diet record (1)
- 7-day diet record (2)

Biomarker

(2, averaged, de-attenuated)

Deattenuated Spearman correlation coefficients (and lower bound of the 95% CI) between diet assessed by FFQ's, 24-hour recalls, and 1-week diet records and biomarkers of diet (n = 627 U.S. female nurses aged 45-80 years)



***Subgroups of women who didn't take supplements for this nutrient (N= 363 for long-chain N-3 fatty acids, and 335 for beta-carotene)**

(Yuan C et al. Am J Epidemiol 2018)

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Correlations comparing FFQ with diet records

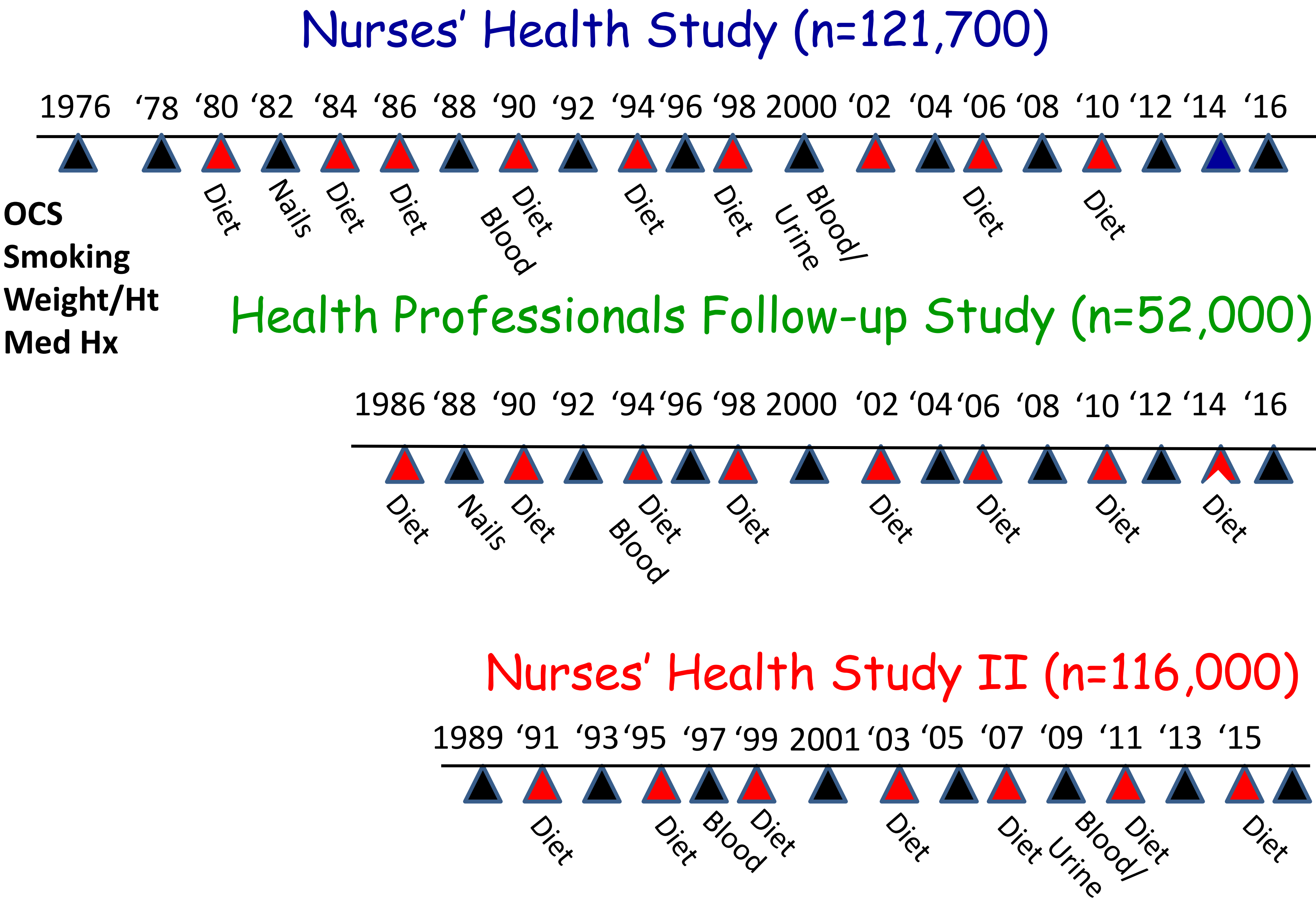
TABLE 1. **Comparison of mean daily intakes of 122 food items estimated by two administrations of a FFQ (Q1 & Q2) and by two 1-week diet records (DRs) among 127 Boston-area male cohort members of the Health Professionals' Follow-up Study**

Food Item	Serving Size	*No. of Servings/Day* Q1	Q2	DR	*Observed Correlations* Q1 vs Q2	DR vs Q1	DR vs Q2	σ_w^2/σ_b^2	*Deattenuated Correlations** DR vs Q2 (95% CI)
Dairy Foods									
Skim, lowfat milk	8 fl oz	0.53	0.56	0.42	.77	.72	.82	0.28	**.88 (0.79,0.92)**
Whole milk	8 fl oz	0.15	0.10	0.17	.75	.58	.59	0.55	**.67 (0.51,0.78)**
Cream	1 tb	0.22	0.23	0.46	.60	.41	.57	0.93	**.69 (0.50,0.81)**
Sour cream	1 tb	0.04	0.06	0.10	.55	.36	.41	2.61	**.63 (0.30,0.82)**
Nondairy coffee whitener	1 tsp	0.18	0.12	0.16	.66	.63	.70	0.29	**.75 (0.64,0.83)**
Sherbet, ice milk	1 cup	0.05	0.05	0.03	.43	.35	.50	3.77	**.85 (0.00,0.99)**
Ice cream	1 cup	0.17	0.22	0.17	.49	.49	.48	2.27	**.71 (0.38,0.88)**
Yogurt	1 cup	0.13	0.14	0.07	.74	.69	.76	0.51	**.86 (0.74,0.92)**
Cottage, ricotta cheese	½ cup	0.08	0.08	0.08	.69	.34	.28	4.84	**.52 (0.07,0.79)**
Cream cheese	1 oz	0.08	0.10	0.09	.67	.50	.51	2.26	**.75 (0.40,0.91)**
Other cheese	1 oz 1 slice	0.39	0.36	0.64	.48	.48	.41	1.70	**.56 (0.31,0.73)**
Margarine	1 pat	0.63	0.74	0.87	.62	.61	.50	0.55	**.57 (0.40,0.70)**
Butter	**1 pat**	**0.32**	**0.36**	**0.74**	**.73**	**.55**	**.53**	**1.86**	**.74 (0.45,0.89)**

Salvini S et al. Int J Epidemiol, 1989

Pearson correlation coefficients (deattenuated) for macronutrient intakes assessed by FFQs and the average intakes by 1980 and 1986 diet records

	1980 FFQ vs. average diet records	1984 FFO vs. average diet records	1986 FFQ vs. average diet records	1980 and 1986 ave. FFQs vs. average diet records	1980, 1984, 1986 FFQs vs. average diet records
Total fat	0.44 (0.57)	0.47 (0.61)	0.62 (0.81)	0.61 (0.79)	0.64 (0.83)
Saturated Fat	0.50 (0.70)	0.49 (0.68)	0.64 (0.90)	0.66 (0.92)	0.68 (0.95)
Choles-terol	0.52 (0.69)	0.61 (0.82)	0.58 (0.78)	0.60 (0.80)	0.67 (0.90)
Protein	0.39 (0.48)	0.38 (0.46)	0.50 (0.61)	0.53 (0.65)	0.56 (0.68)
Carbo-hydrates	0.37 (0.43)	0.59 (0.68)	0.69 (0.79)	0.63 (0.72)	0.68 (0.78)
Mean	**0.44 (0.57)**	**0.51 (0.65)**	**0.61 (0.78)**	**0.61 (0.78)**	**0.65 (0.83)**



Investigators: Frank Speizer, Bernie Rosner, Meir Stampfer, David Hunter, JoAnn Manson, Eric Rimm, Edward Giovannucci, Alberto Ascherio, Gary Curhan, Michelle Holmes, Frank Hu, Heather Eliassen, Lorelei Mucci, Jae Hee Kang, **Jo**rge Chavarro, Molin Wang, Kana Wu, Andrew Chan, Daniel Wang, Qi Sun

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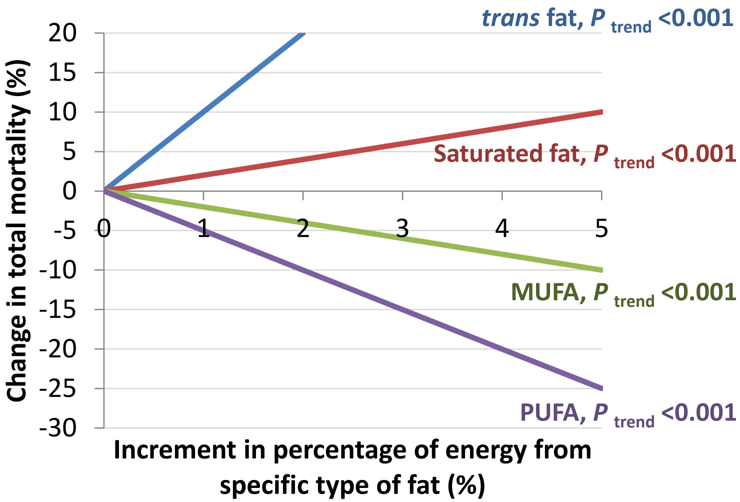
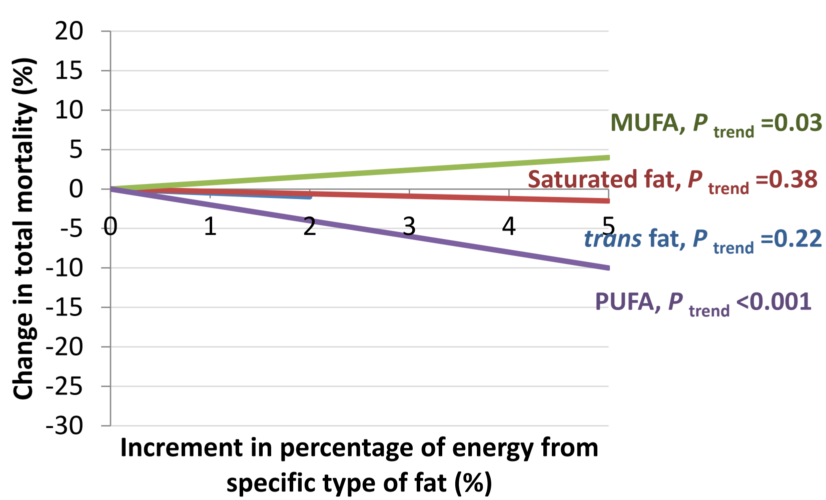
Types of dietary fat and total mortality



Cumulative Average



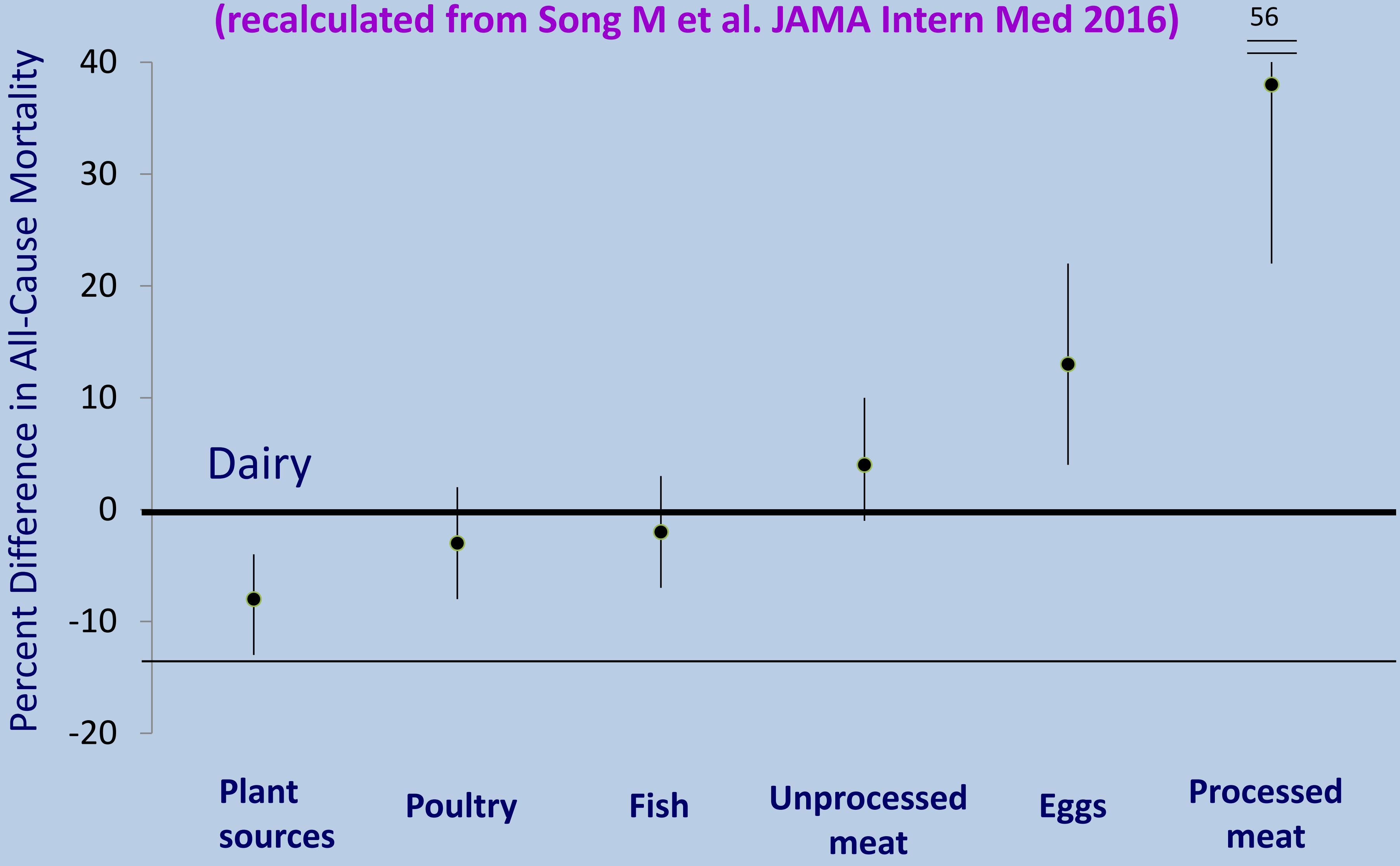
Baseline Only

Multivariable-adjusted substitution model, comparison nutrient is total carbohydrate
Data source: Nurses' Health Study (1980-2012) and Health Professionals Follow-Up Study (1986-2012)

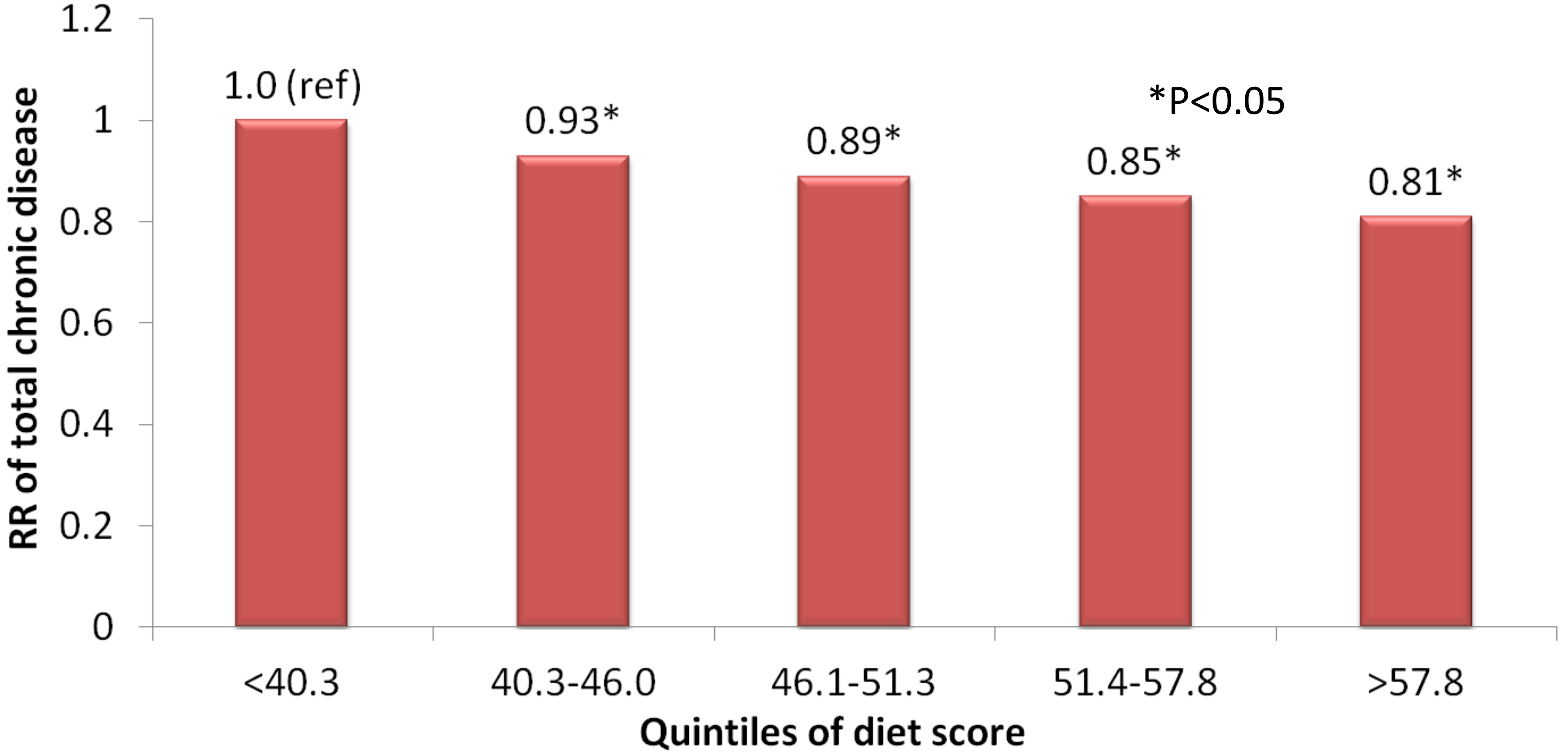
(Wang D et al. JAMA Int Med. 2016)

Differences in all-cause mortality for major protein sources vs dairy (for 3% of energy from protein)

(recalculated from Song M et al. JAMA Intern Med 2016)



Higher scores on the AHEI-2010 was associated with lower risk of total chronic disease

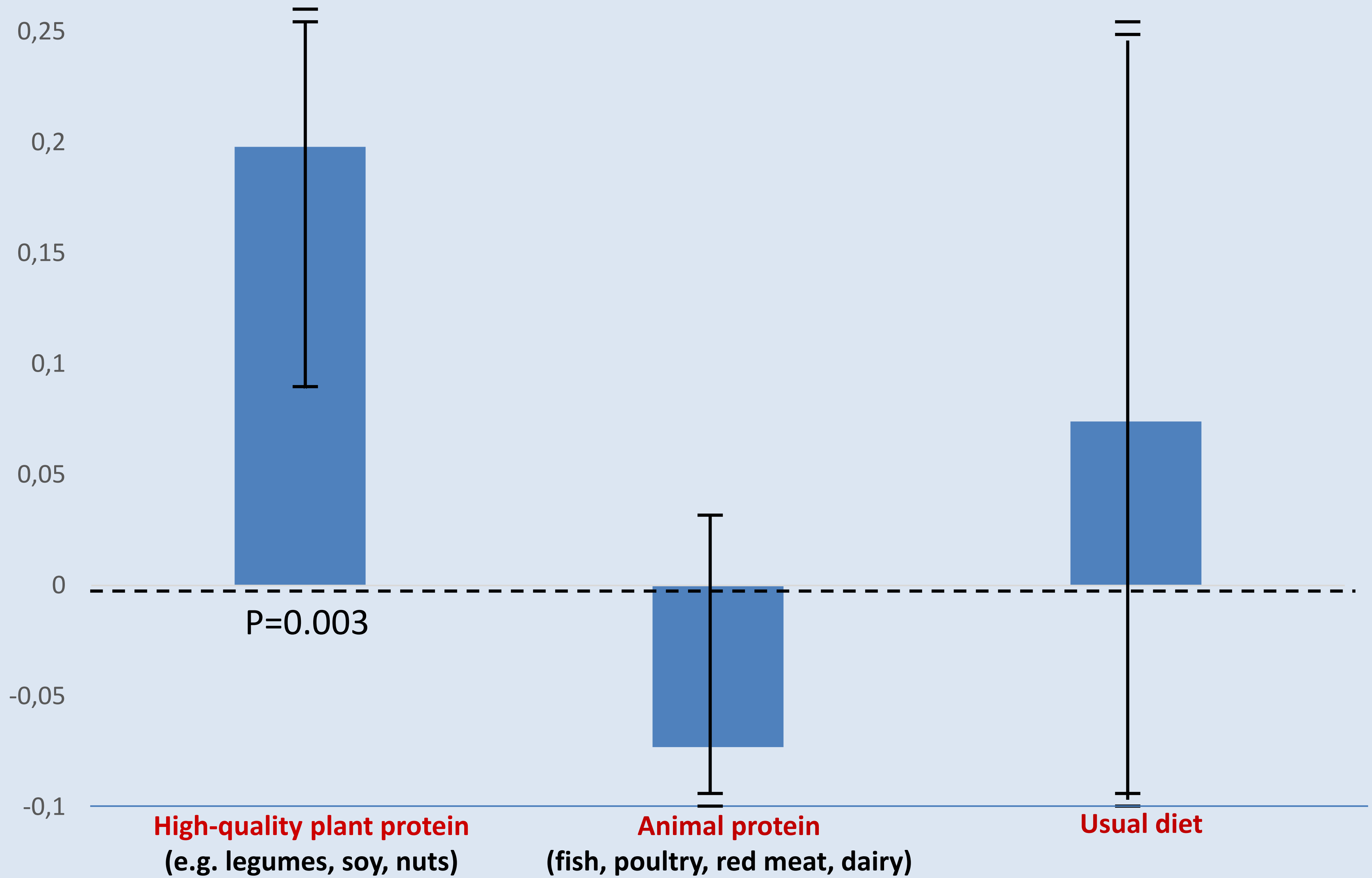


Age, total energy, smoking status, BMI, aspirin use, physical activity, vitamin E supplementation, family history of MI, and cancer, history of hypertension and high cholesterol and use of hormone therapy (in women)

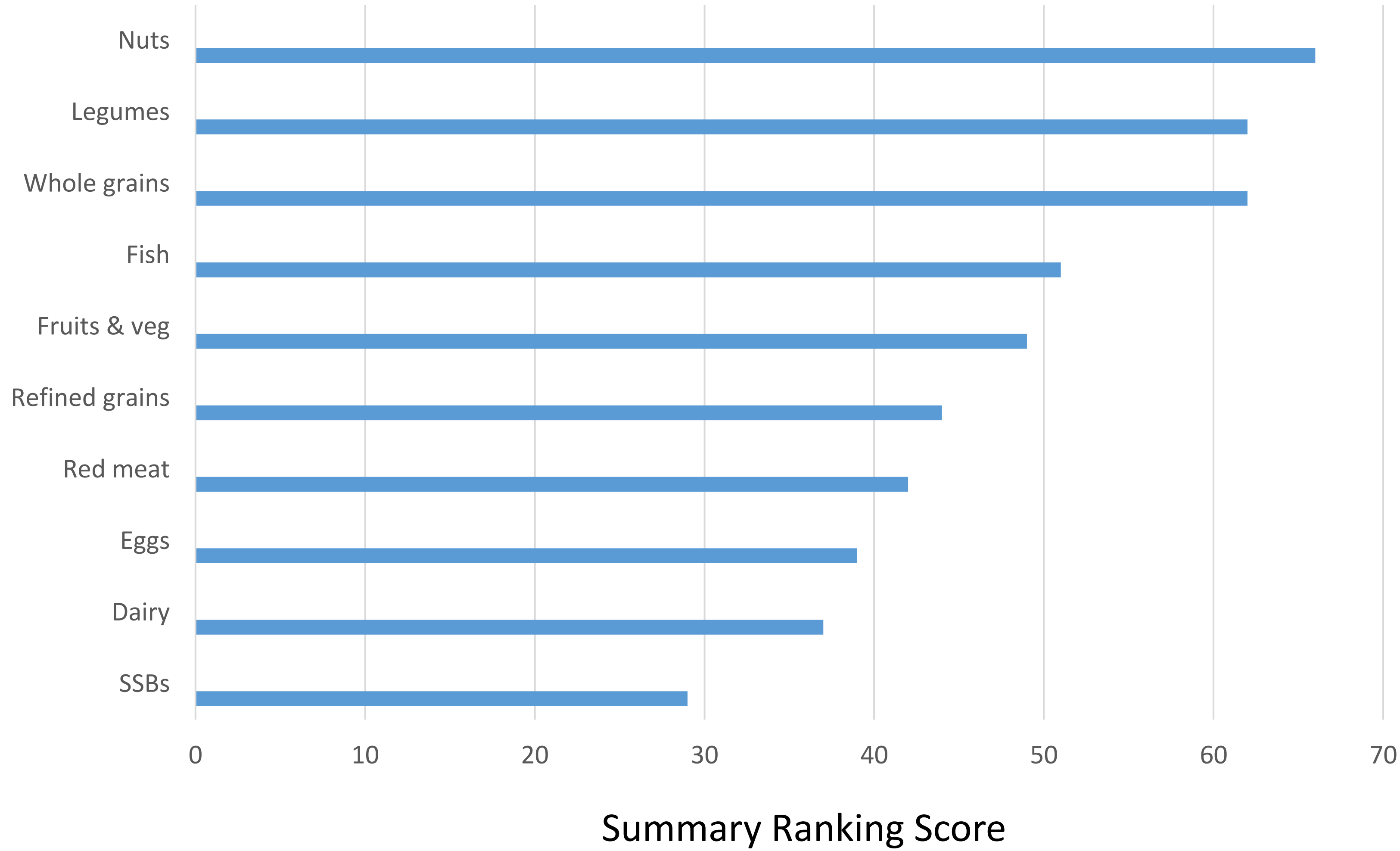
Chiuve, J Nutr, 2012

Meta-analysis assessing the effects of red meat on LDL cholesterol (mmol/L) from RCTs by type of comparison diet

(Guasch-Ferre M et al. Circulation 2019)



Network meta-analysis of 66 randomized trials of food group effects on risk factors for cardiometabolic disease
(LDL-C, TG, TC, HDL-C, FG, HbA1c, HOMA-IR, SBP, DBP, CRP)



(Schwingschakl L, Am J Clin Nutr 2017)

Table. Dietary Factors and Cardiometabolic Outcomes With Probable or Convincing Evidence of Associations[a]

Dietary factor	Cardiovascular outcome	Metabolic outcome
Protective association		
Fruits[b]	CVD, CHD, stroke, ischemic stroke, hemorrhagic stroke	NA
Vegetables[c]	CVD, CHD, stroke, ischemic stroke	NA
Nuts or seeds	CVD, CHD	NA
Whole grains	CVD, CHD, ischemic stroke	Diabetes
Fish or seafood[d]	CHD, CHD in patients with diabetes, MI, stroke	NA
Yogurt	NA	Diabetes
Chocolate	CVD, CHD, MI, stroke, hemorrhagic stroke	NA
Milk	Stroke	NA
Tea	Stroke	NA
Dietary fiber	CVD, CHD, stroke	Diabetes
Cereal fiber	NA	Diabetes
Fruit fiber	Stroke	NA
Vegetable fiber	Stroke	NA
PUFA replacing carbohydrate	CHD	Diabetes
PUFA replacing SFA	CHD	NA
Potassium	Stroke	NA

Miller V et al. JAMA Network Open. 2022;5(2):e2146705. doi:10.1001/jamanetworkopen.2021.46705

Table. Dietary Factors and Cardiometabolic Outcomes With Probable or Convincing Evidence of Associations[a]

Dietary factor	Cardiovascular outcome	Metabolic outcome
Harmful association		
Potatoes	NA	Diabetes
Red meats, unprocessed[e]	CVD, CHD, stroke	Diabetes
Processed meats[f]	CVD, CHD, stroke, ischemic stroke	Diabetes
SSBs[g]	CVD, CHD, ischemic stroke	Diabetes, high BMI
Glycemic index	CHD	Diabetes
Glycemic load	CHD	Diabetes
Trans-fatty acid	CVD	NA
Total protein	NA	Diabetes
Animal protein	NA	Diabetes
Sodium	Stroke, SBP	NA

Miller V et al. JAMA Network Open. 2022;5(2):e2146705. doi:10.1001/jamanetworkopen.2021.46705

Limitations of Biomarkers

- May not be sensitive to intake
- May not be time-integrated
- Expensive
- Markers not available for many nutrients
- Few cohorts have multiple blood samples
- Few cohorts have 24-hour urines, fewer have repeated 24-hour urines.

Application of Food-specific Biomarkers

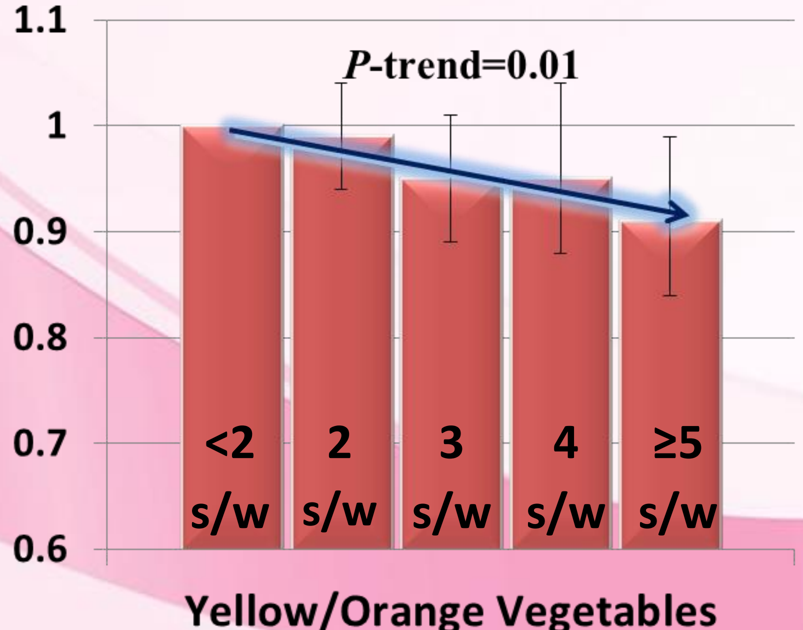
Examples: fish (N-3 fatty acids), citrus fruit (proline-betaine), pepper (pepperine), dairy fat (odd chain saturated fatty acids), soy (genistein)

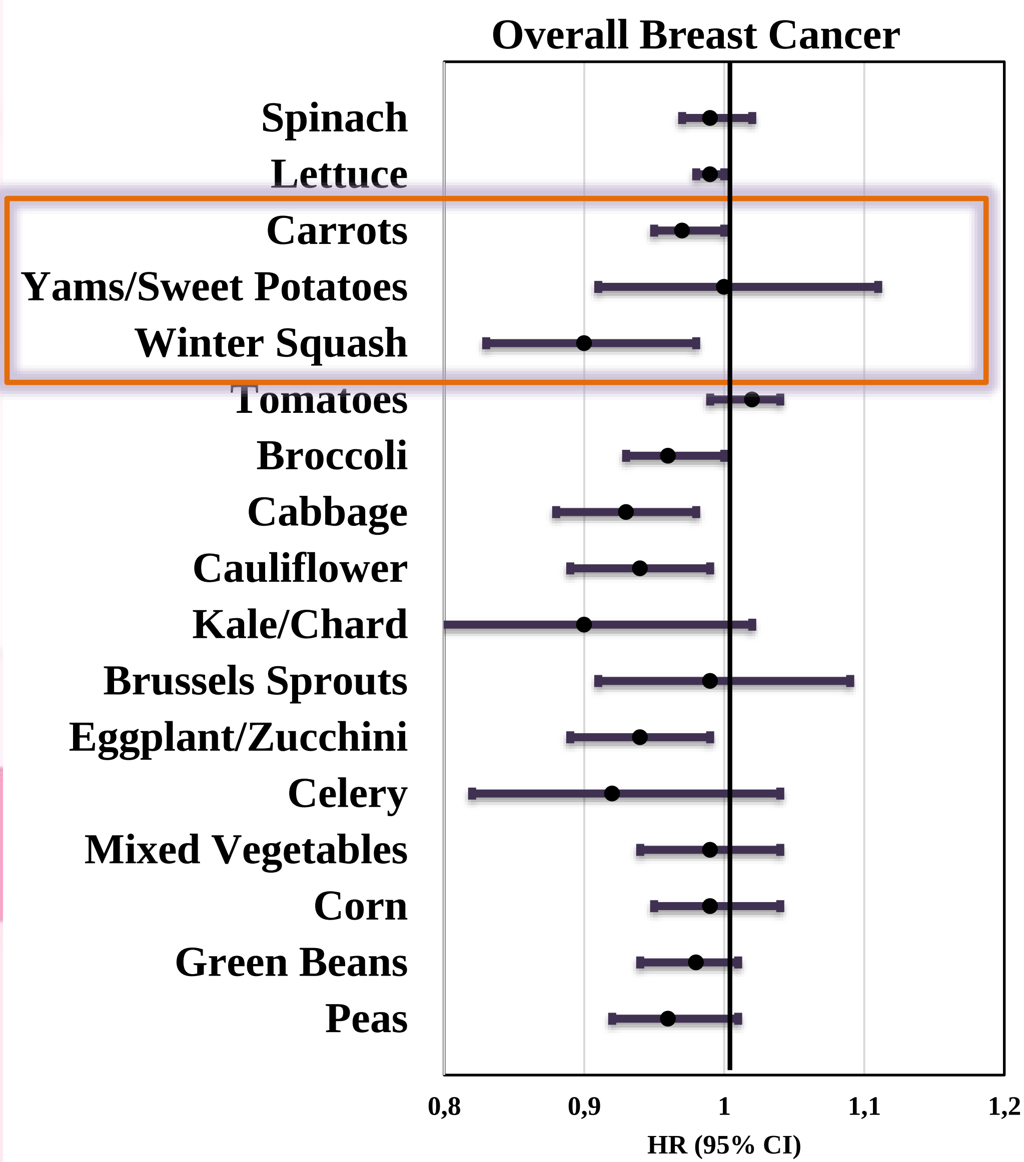
Validity and relative validity—within-person variation, comparisons with diet records or feeding studies

Potential role in validation studies

Use in combination with intake data (e.g, plasma carotenoid levels and carrot intake)

Consumption of Yellow/Orange Vegetables and Breast Cancer Incidence

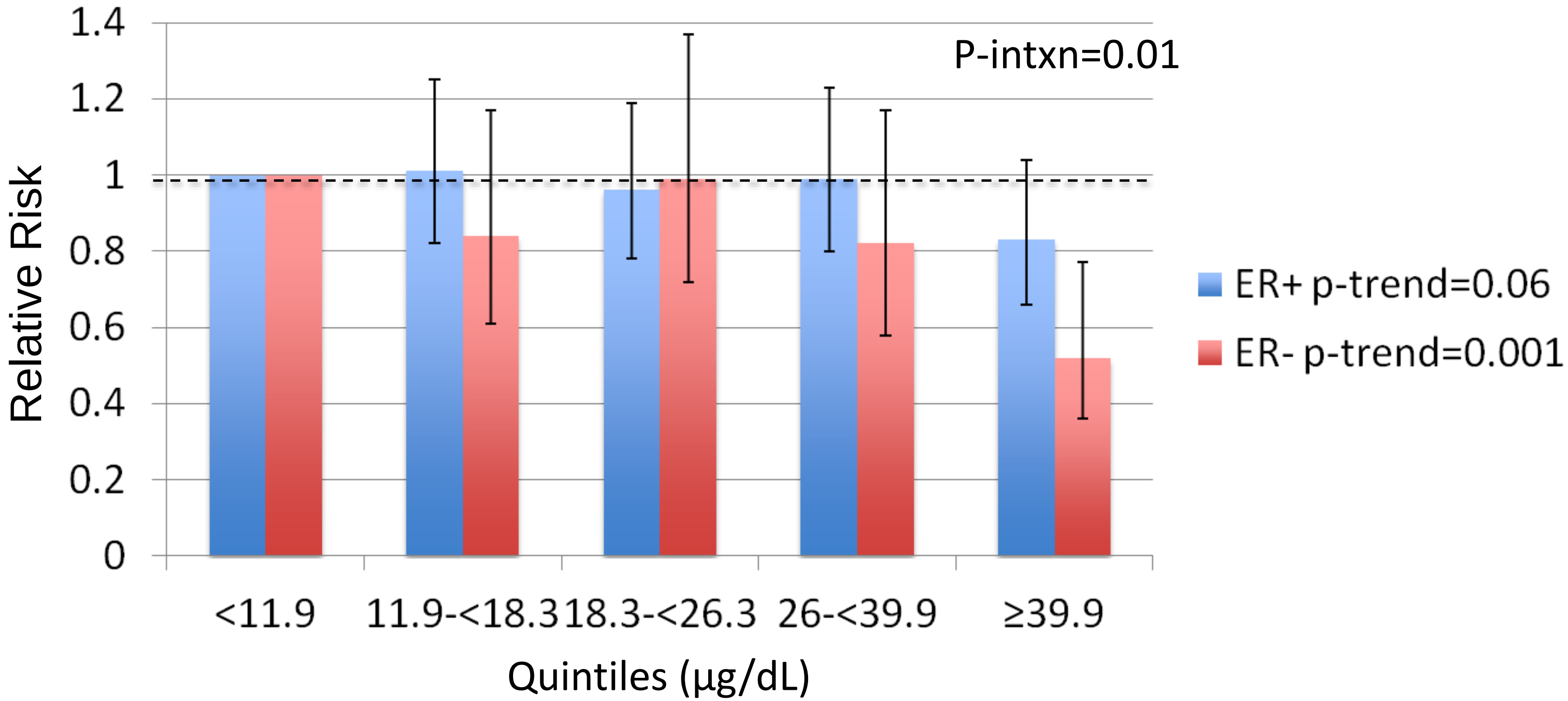




(Farvid MS et al., Int J Cancer 2019)

0.387

Plasma β-carotene and risk of breast cancer in pooled cohorts (ER+ vs ER-)

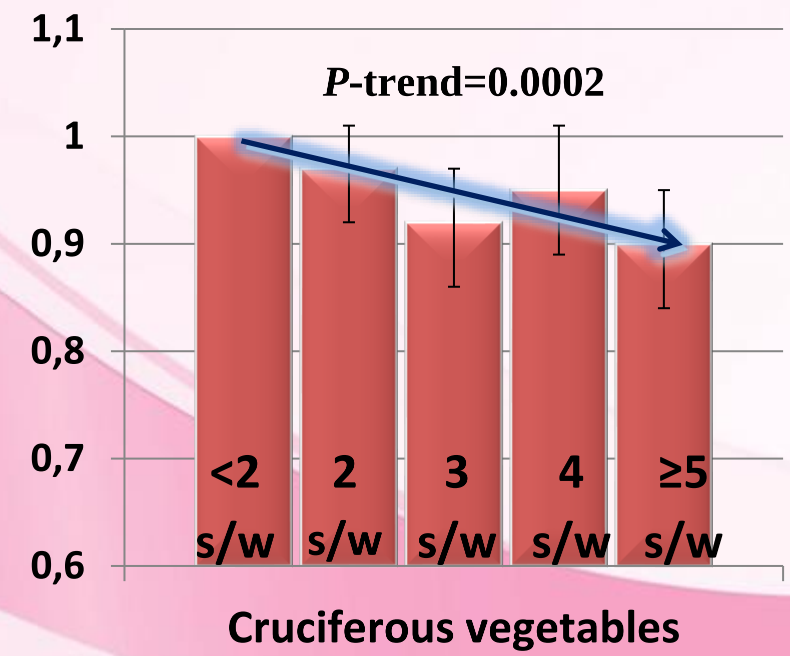


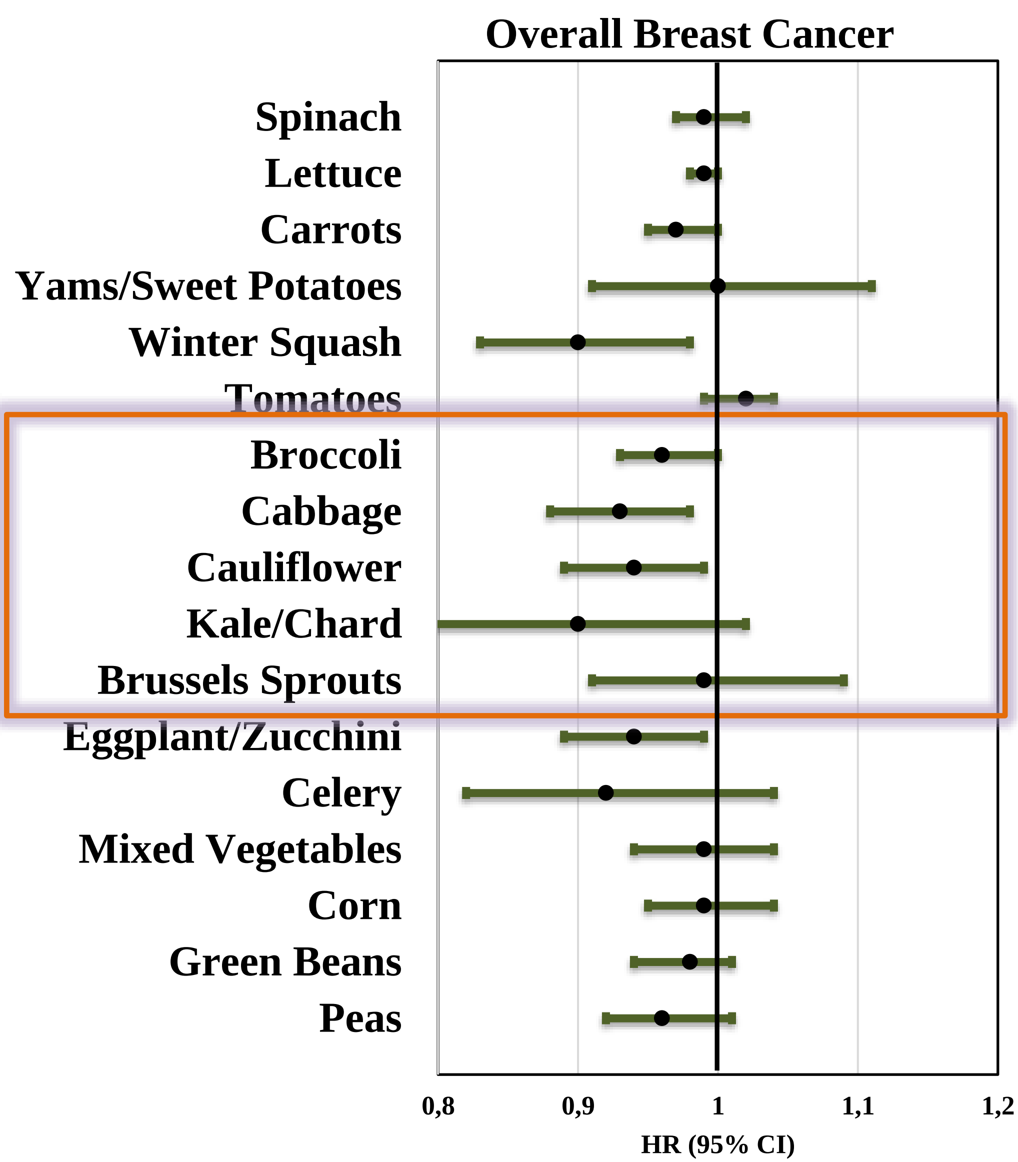
(Eliassen AH et al. JNCI 2012)

0.336

Consumption of Cruciferous Vegetables and Breast Cancer Incidence (32 years of follow-up)

(n=182,000/ 11,000 cases)





(Farvid M et al., unpublished)

0.389

Intakes of fruits and vegetables (per 3 servings/week) and risk of pancreatic cancer in pooled analysis of 14 cohort studies

Fruits	*MV RR (95% CI)*	*Vegetables*	*MV RR (95% CI)*
Apples, pears & applesauce	0.98 (0.94-1.03)	Broccoli	0.98 (0.89-1.08)
Bananas	1.02 (0.95-1.08)	Brussel sprouts	1.26 (1.03-1.54)
Cantaloupe	1.04 (0.87-1.25)	Cabbage	1.03 (0.94-1.14)
Grapefruit	0.97 (0.91-1.03)	Carrots	0.99 (0.92-1.07)
Oranges	0.99 (0.93-1.06)	Cauliflower	1.02 (0.78-1.33)
Peaches	1.06 (0.99-1.13)	Corn	0.97 (0.79-1.19)
Strawberries	1.13 (1.01-1.27)	Green pepper	1.15 (1.01-1.30)
Fruit juice	1.03 (1.00-1.05)	Lettuce, salad	1.03 (1.00-1.07)
		Peas, lima beans	0.95 (0.80-1.14)
		Spinach	1.06 (0.97-1.16)
		String beans	1.00 (0.89-1.13)
		Tomatoes, tomato juice	1.05 (1.01-1.09)
		Yams	0.85 (0.61-1.18)

(Koushik A et al. AJE, 2012)

1.085

Acrylamide Hemoglobin Adducts as a Biomarker

(Wilson K, et al.)

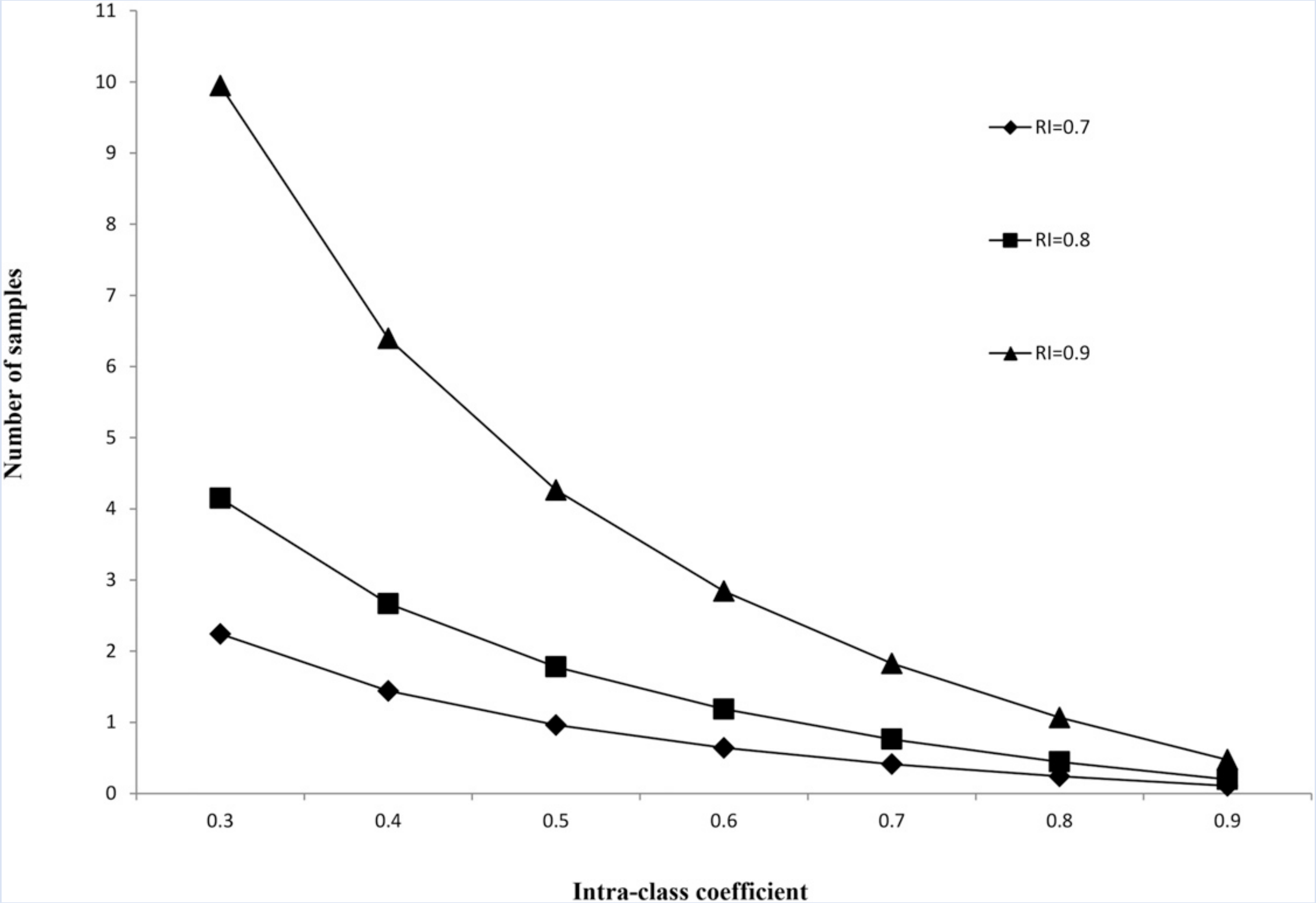
Correlation with calculated intake, adjusted for within-person variation in biomarker = 0.34 (CI: 0.23 – 0.45)

Correlation for reproducibility of biomarker = 0.77 in blood samples collected 1 to 3 years apart

Limitations of RCTs for Prevention

- Appropriate time of initiation is uncertain
- Necessary duration is uncertain
- Adherence and “drop-ins”
- Supplements do not represent dietary range

Number of samples needed to achieve a given reliability index by a range of intraclass correlation coefficients. RI, reliability index



(Sun Q et al. Am J Clin Nutr, 2017)

Summary of food-based dietary assessment

- No single approach exists for assessing health effects of specific foods
- Best evidence will often derive from prospective cohort studies of diet combined with short term trials using intermediate risk factors as outcomes
- Biomarkers alone with rarely be sufficient, but they can play a supporting role