

Sugar & Disease: A Sixty Year Saga (1954 – 2014)

Jim Mann



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for Human Nutrition



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NEW ZEALAND



THE VIPEHOLM DENTAL CARIES STUDY

**The Effect of Different Levels of Carbohydrate Intake on Caries Activity
in 436 Individuals Observed for Five Years ¹**

**BENGT E. GUSTAFSSON, M.D., CARL-ERIK QUENSEL, PH.D.,
LISA SWENANDER LANKE, M.D., CLAES LUNDQVIST, M.D. L.D.S. D.D.S.,
HANS GRAHNÉN, L.D.S., BO ERIK BONOW, L.D.S., BO KRASSE, L.D.S.**

Acta Odontol Scand; 1954

1960s

Sugar related to:

- Obesity
- Cardiovascular disease
- Diabetes

PURE WHITE AND DEADLY **John Yudkin**



The Problem of Sugar

A  Original

1960s, early 1970s, Sugar & Diabetes, Obesity & Lipids

Confusion reigns supreme

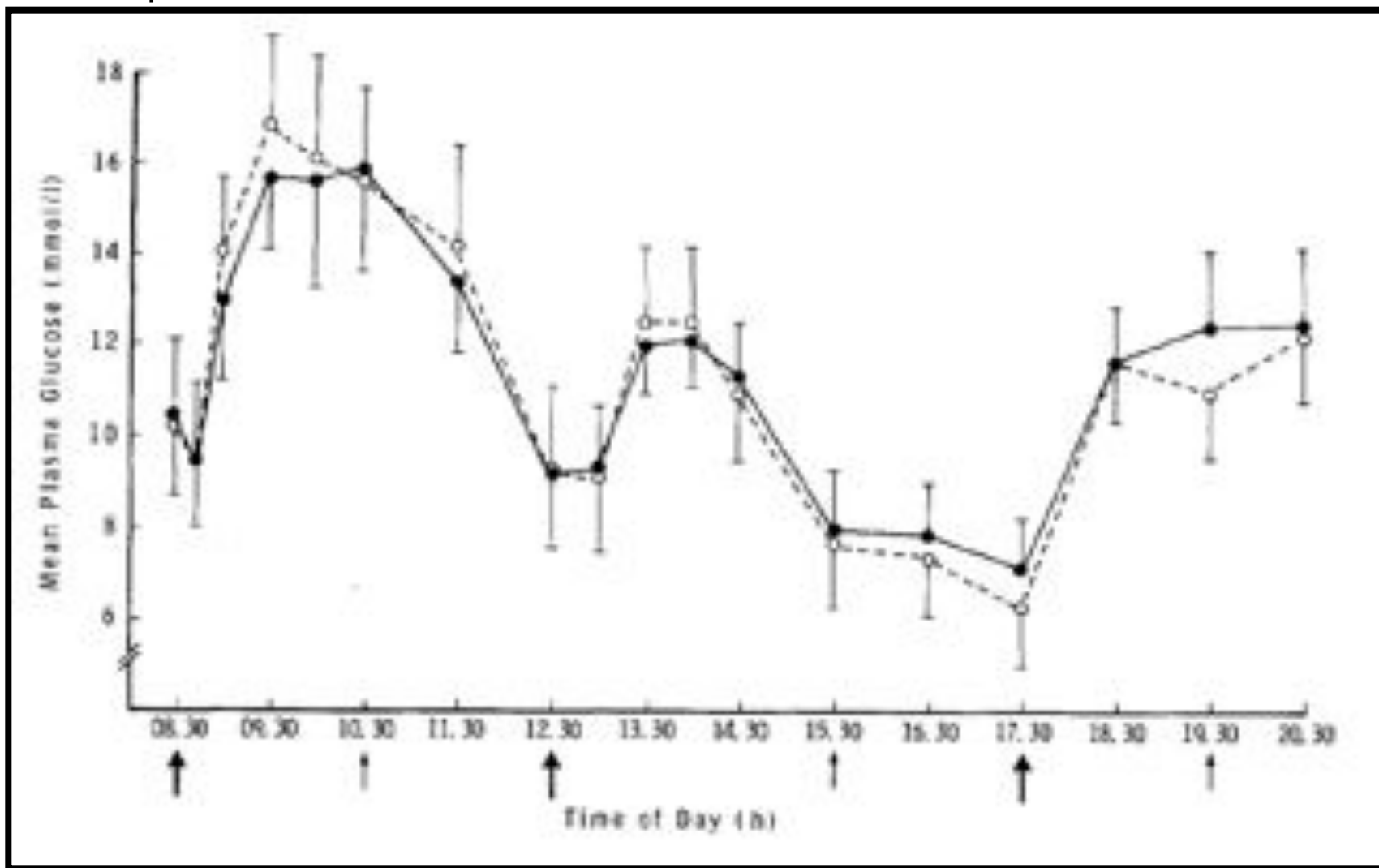
- Epidemiological studies flawed: *international comparisons, casecontrol & cross sectional studies*
- Dietary intervention studies in animals & humans equally flawed:
almost all involved exceptionally high intakes of sucrose, no attempt to control weight changes
- Free living individuals who restricted sugar lost weight & reduced triglycerides.
[Mann et al, Lancet 1970]
- Sucrose restriction with no weight loss appears to be hypertriglyceridaemic only when consumed in large amounts & when dietary fat is predominantly saturated
[Mann et al, BJN, 1972, Mann et al, Clin Sci, 1973]
- A small number of hypertriglyceridaemic people may be sucrose sensitive.
[Mann et al, Proc.Nutr Soc, 1974]

Sucrose in the diet of diabetic patients – just another carbohydrate?

D. B. Peterson¹, J. Lambert¹, S. Gerring¹, P. Darling¹, R. D. Carter¹, R. Jelfs¹ and J. I. Mann^{1, 2}

Peterson et al, Diabetologia (1986) 29: 216-220

Mean (\pm SEM) diurnal plasma glucose values during profiles for 12 Type 1 diabetic patients



Simple Sugars and Diabetes

J. I. Mann

Radcliffe Infirmary, Oxford and John Radcliffe Hospital, Oxford OX3 9DU, UK

Diabetic Medicine, 1987

Sugars in the aetiology of diabetes:

‘.....many of the papers claiming to show an effect of sugar in the aetiology of NIDDM have major flaws and in summary it may be concluded that the evidence in favour of such an association is extremely weak. There is no evidence relating monosaccharides, other disaccharides or indeed any other carbohydrate-containing foods to the aetiology of NIDDM.....’

Mann J, Diabetic Medicine, 1987

Medium term studies:

'It seems likely that for many diabetic patients permitting a modest amount of sucrose may enhance palatability and this may aid long-term compliance to a high fibre/low fat diet.'

Further long-term studies of sucrose and fructose feeding are urgently needed. For the present it would seem reasonable to permit the use of sucrose in moderate quantities (up to 50 g/day) provided that an isocaloric quantity of carbohydrate is removed from the calculated daily energy requirement.

The replacement carbohydrate should be taken from the high glycaemic index carbohydrate already in the diet and low glycaemic index foods should not be reduced.'





✓	Low in fat
✓	High in fibre
✓	High in carbohydrate
✓	No artificial colours

Nutrition Information (Average)

Servings per package - 1

Average serving size - 90g (1 Slice†)

	Quantity Per Serving	Quantity Per 100g
Energy	1230 kJ	1360 kJ
Protein	6.1 g	6.8 g
Fat		
- Total	1.6 g	1.8 g
- Saturated	0.5 g	0.6 g
Carbohydrate		
- Total	60.5 g	67.2 g
- Sugars	29.2 g	32.4 g
Dietary Fibre	4.4 g	4.9 g
Sodium	135 mg	150 mg
Potassium	374mg	415 mg

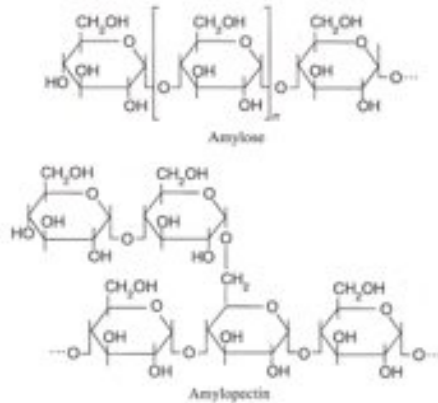
† Weight of slice is approximate and is only to be used as a guide. If you have any specific dietary requirements please weigh your serving.

Carbohydrates in human nutrition

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FAO
FOOD AND
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PAPER

66



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the
United
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Rome, 14 – 18 April 1997

The Consultation recommends.....

‘That excess energy intake in any form will cause body fat accumulation, so that excess consumption of low fat foods, while not as obesity-producing as excess consumption of high fat products, will lead to obesity if energy expenditure is not increased.

Excessive intakes of sugars which compromise micronutrient density should be avoided. There is no evidence of a direct involvement of sucrose, other sugars and starch in the etiology of lifestyle-related diseases.’

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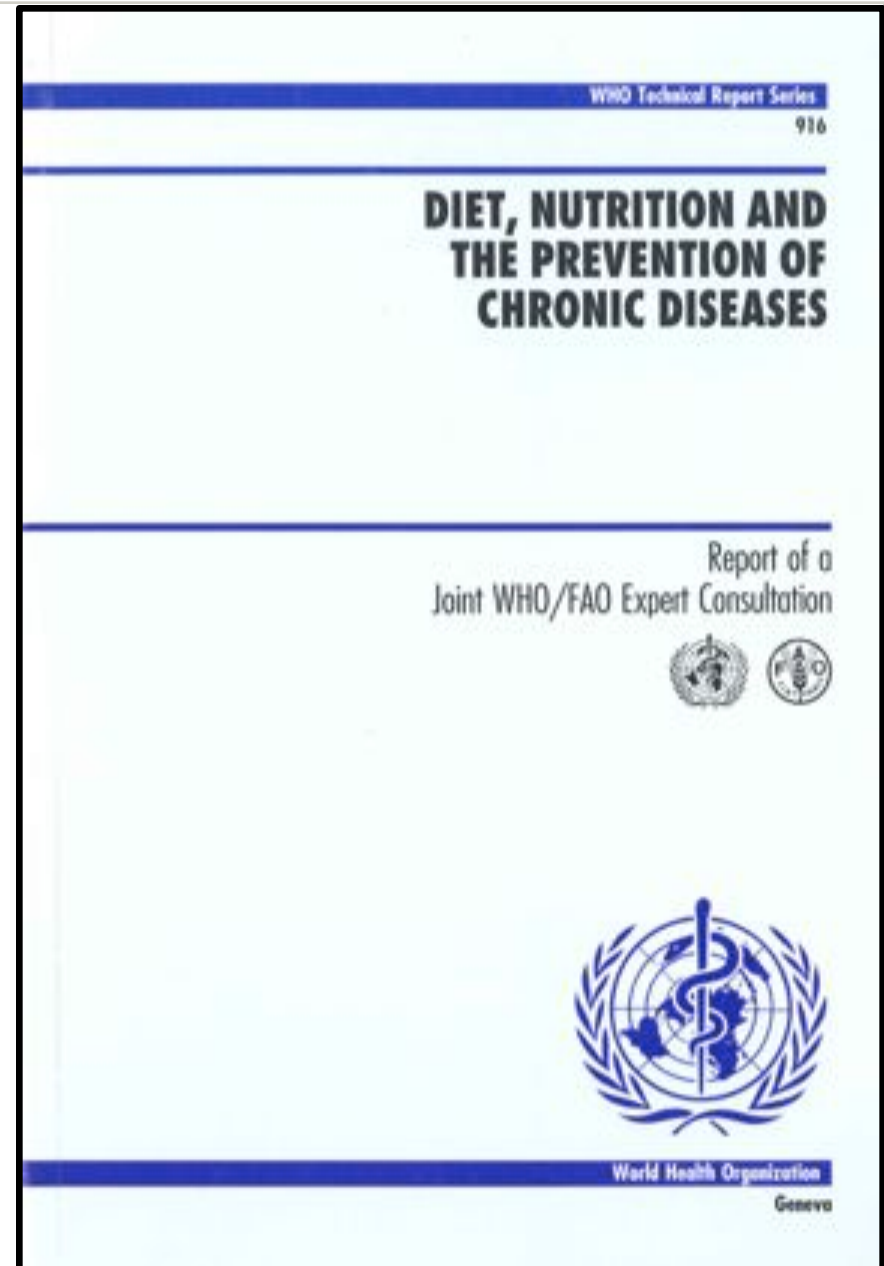
The trouble with sugar



WHO Technical Report (TR 916)

Free sugars: <10% TE

Total CHO: 50 – 75% TE



Sugar industry threatens to scupper WHO

Sarah Boseley, health editor

The Guardian, Monday 21 April 2003 09.33 BST

The sugar industry in the US is threatening to bring the World Health Organisation to its knees by demanding that Congress end its funding unless the WHO scraps guidelines on healthy eating, due to be published on Wednesday.

The threat is being described by WHO insiders as tantamount to blackmail and worse than any pressure exerted by the tobacco lobby.

In a letter to Gro Harlem Brundtland, the WHO's director general, the Sugar Association says it will "exercise every avenue available to expose the dubious nature" of the WHO's report on diet and nutrition, including challenging its \$406m (£260m) funding from the US.

The industry is furious at the guidelines, which say that sugar should account for no more than 10% of a healthy diet. It claims that the review by international experts which decided on the 10% limit is scientifically flawed, insisting that other evidence indicates that a quarter of our food and drink intake can safely consist of sugar.



INSTITUTE OF MEDICINE

OF THE NATIONAL ACADEMIES

2002

Added sugars should comprise no more
than 25% total calories

SCIENTIFIC OPINION

Scientific Opinion on Dietary Reference Values for carbohydrates and dietary fibre¹

EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA)^{2, 3}

European Food Safety Authority (EFSA), Parma, Italy

EFSA (February 2010)

- Frequent consumption of sugar containing foods **CAN** increase risk of dental caries.
- **SOME** evidence that sugar sweetened beverages **MIGHT** contribute to weight gain.
- **SOME** evidence that high intakes (>20 %TE) of sugars **MAY** increase TG and cholesterol concentration and that 20 – 25% E **MIGHT** adversely affect glucose and insulin response.

BUT

- The available data are not sufficient to set an upper limit for intake of added sugars

WHO Nutrition Guidance Expert Advisory Group (NUGAG)



Definition of 'Sugars'

Total sugars	All monosaccharides & disaccharides, other than polyols
Added sugars	<p>Sugars added to foods & beverages during processing or home preparation. Would include honey, molasses, fruit juice concentrates, brown sugar, corn sweetener, sucrose, lactose, glucose, high fructose corn syrup, malt syrups</p> <p><u>BUT</u> Fruit, fresh fruit, fruit pulp, tinned fruit, dried fruit, fruit concentrate (< 2x concentration) (CIP suggests these are not added sugars)</p>
Free sugars	All mono- & disaccharides added to foods by manufacturer, cook & consumer, plus sugars naturally present in honey, syrup & fruit juices

GRADE Process for Developing Guidelines

First steps:

1. Select panel, conflict of interests
-

2. Formulate structured questions

P Population, participants
I Intervention (s)
C Comparison (s)
O Outcome (s)
T Time-frame

3. Agree process

Preparation steps:

1. Systematic literature review
 2. Prepare evidence profiles
-

Final steps:

GRADE Evidence & Determine Strength of Recommendations.

(BMJ, 2004;328: 1494-96)

Quality of evidence	Study design	Lower if...	Higher if...
High (<i>further research is very unlikely to change our confidence in the estimate of effect</i>)	Randomised trial	Study imitations	Large effect (R.R. 0.5) Very large effect (e.g. RR 0.2)
Moderate (<i>further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate</i>)		Inconsistency	Evidence of dose-response gradient
Low (<i>further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate</i>)	Observational study	Indirectness	All plausible confounding would reduce a demonstrated effect
Very low (<i>any estimate of effect is very uncertain</i>)		Imprecision	
		Publication bias	

RESEARCH

Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies

OPEN ACCESS

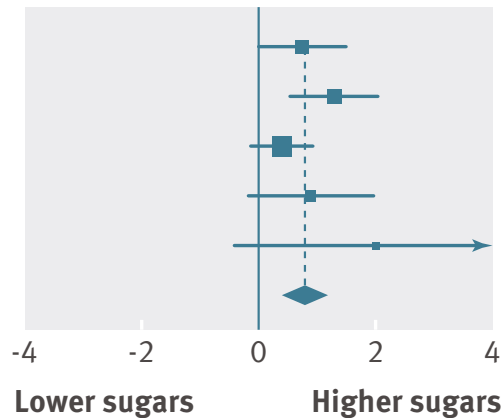
Lisa Te Morenga *research fellow*^{1,2}, Simonette Mallard *research assistant*¹, Jim Mann *professor*^{1,2,3}

¹Departments of Human Nutrition and Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand ; ²Riddet Institute, University of Otago;

³Edgar National Centre for Diabetes and Obesity Research, University of Otago

Reduced versus usual sugars in adults

Study	Mean difference	Standard error	Mean difference (95% CI)	Weight (%)	Mean difference (95% CI)
Gatenby 1997	0.75	0.39		22.5	0.75 (-0.02 to 1.52)
Mann 1972	1.30	0.38		23.3	1.30 (0.55 to 2.05)
Palneau 2008	0.40	0.27		38.4	0.40 (-0.13 to 0.93)
Saris 2000	0.90	0.54		13.0	0.90 (-0.16 to 1.96)
Smith 1996	1.99	1.23		2.8	1.99 (-0.42 to 4.40)
Total (95% CI)				100.0	0.80 (0.39 to 1.21)



Test for heterogeneity: $\tau^2=0.04$,

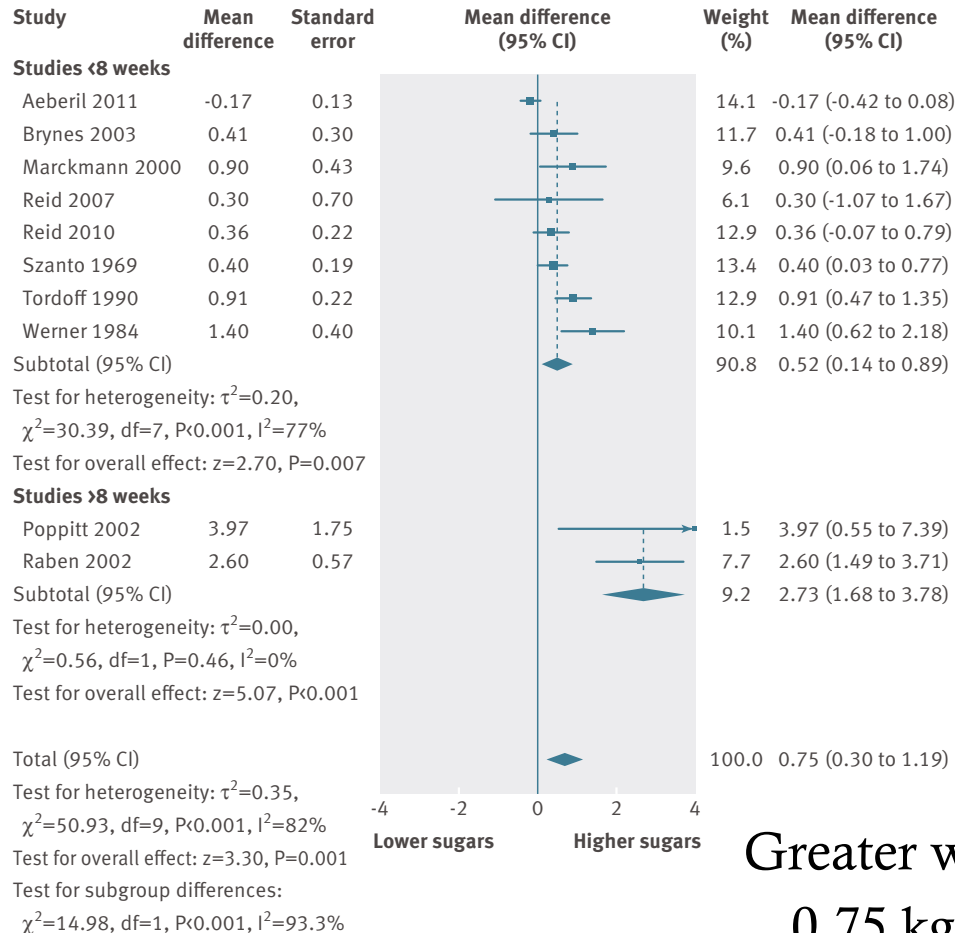
$\chi^2=4.85$, $df=4$, $P=0.30$, $I^2=17\%$

Test for overall effect: $z=3.85$, $P<0.001$

Greater weight in the usual/higher sugars group

0.8 kg (95%CI: 0.39, 1.21); $p < 0.001$

Increased versus usual sugars in adults

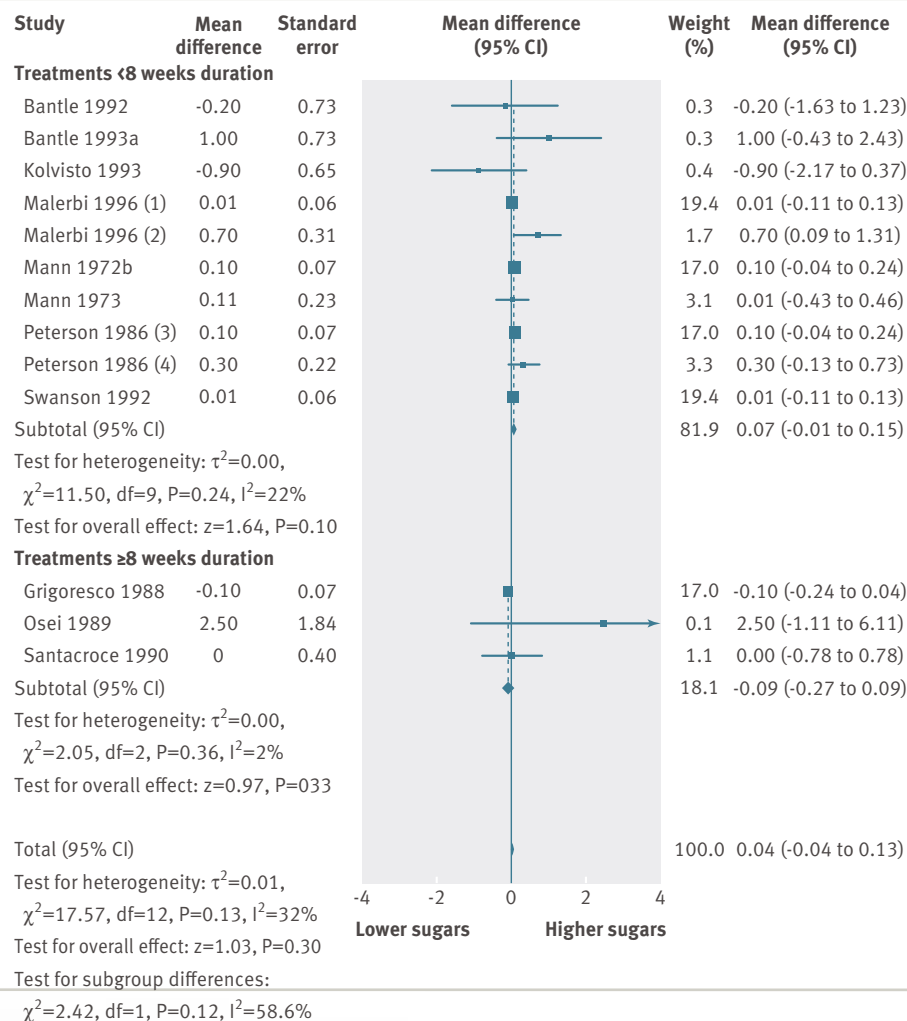


Shorter studies
0.52 kg (95%CI: 0.14, 0.89);
 $p = 0.007$

Longer studies
2.73 kg (95%CI: 1.68, 3.78);
 $p < 0.001$

Greater weight gain with increased sugars
0.75 kg (95%CI: 0.30, 1.19); $p < 0.001$

Higher versus lower sugars in adults (isoenergetic comparisons)



No evidence of an
effect of sugars *per se*

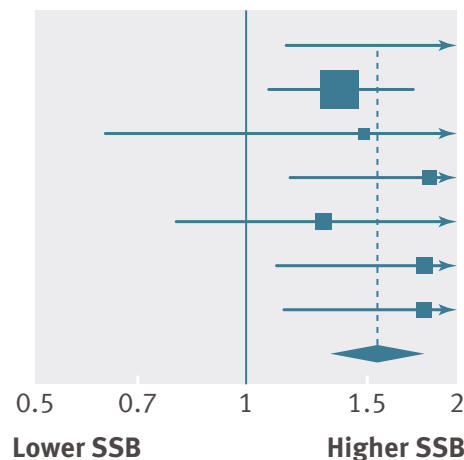
Overall
0.04 kg (95%CI: -0.04, 0.13);
P =0.3

Higher versus lower sugars (SSBs) in children (cohort studies)

Study	Log (odds ratio)	Standard error	Odds ratio (95% CI)	Weight (%)	Odds ratio (95% CI)
Dubols 2007 (1)	0.77	0.32		6.3	2.16 (1.15 to 4.07)
Lim 2009 (2)	0.31	0.12		44.5	1.37 (1.08 to 1.74)
Ludwig 2001 (3)	0.39	0.44		3.5	1.48 (0.63 to 3.47)
Weijts 2011 (4)	0.61	0.24		11.8	1.84 (1.16 to 2.92)
Welsh 2005 (5)	0.26	0.25		10.7	1.30 (0.80 to 2.11)
Welsh 2005 (6)	0.59	0.24		11.2	1.80 (1.12 to 2.89)
Welsh 2005 (7)	0.59	0.23		12.1	1.80 (1.14 to 2.84)
Total (95% CI)				100.0	1.55 (1.32 to 1.82)

Test for heterogeneity: $\tau^2=0.00$,
 $\chi^2=3.93$, $df=6$, $P=0.69$, $I^2=0\%$

Test for overall effect: $z=5.42$, $P<0.001$



1.55 (95%CI: 1.32, 1.82);
p , 0.001

- (1) OR for incident obesity in frequent versus infrequent consumers of SSB between meals
- (2) OR for incident overweight per daily serve SSB (8 oz)
- (3) OR for incident obesity per daily serve SSB
- (4) OR for incident overweight per approximate daily serve SSB (5% energy from beverage sugar)
- (5) OR for incident overweight in normal weight children who consumed >1 serve/d SSB versus <1 serve SSB/d
- (6) OR for remaining overweight in overweight children who consumed >1 serve/d SSB versus <1 serve SSB/d
- (7) OR for incident overweight in children at risk of overweight who consumed >1 serve/d SSB versus <1 serve SSB/d

Table 1: GRADE summary of findings table for the reduction in free sugars in adults

Question: What is the effect of a reduction in free sugars intake in adults

Settings: General adult population.

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary sugar reduction	Control	Absolute (95% CI)		
Q1: What is the effect of a reduction in free sugars intake on body weight in adults											
5	Randomised trials	Serious	No serious inconsistency	No serious indirectness	No serious imprecision	Potential publication bias ²	397	414	MD 0.80 lower (0.39 to 1.21 lower)	⊕⊕⊕ MODERATE	IMPORTANT

Te Morenga et al, BMJ 2013

Effect on Caries of Restricting Sugars Intake: Systematic Review to Inform WHO Guidelines

P.J. Moynihan and S.A.M. Kelly

J DENT RES published online 9 December 2013

DOI: 10.1177/0022034513508954

The online version of this article can be found at:

<http://jdr.sagepub.com/content/early/2013/10/23/0022034513508954>

Draft WHO guidelines on free sugars released for public consultation:

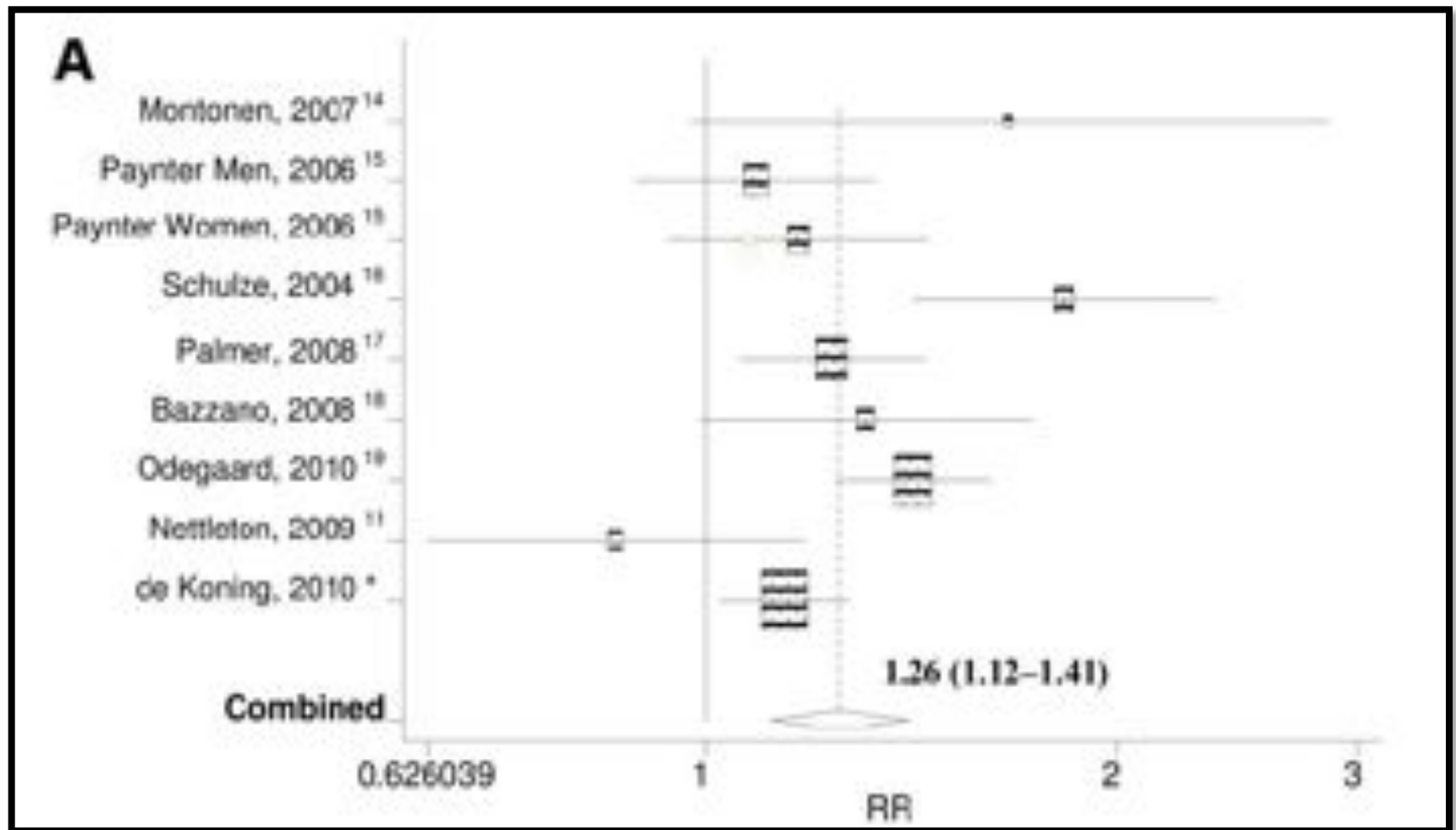
5 March 2014

- WHO recommends reduced intake of free sugars throughout the life-course (***strong recommendation***) *
- In both adults and children, WHO recommends that intake of free sugars not exceed 10% of total energy (***strong recommendation***) *
- WHO suggests further reduction to below 5% of total energy (***conditional recommendation***) * *

* *Recommendations should be adopted as policy*

* * *Recommendations should be debated and considered as policy*

Forest plot of studies evaluating SSB consumption & risk of type 2 diabetes



Malik at al, Diabetes Care (2010) 33: 2477-83



Research

Original Investigation

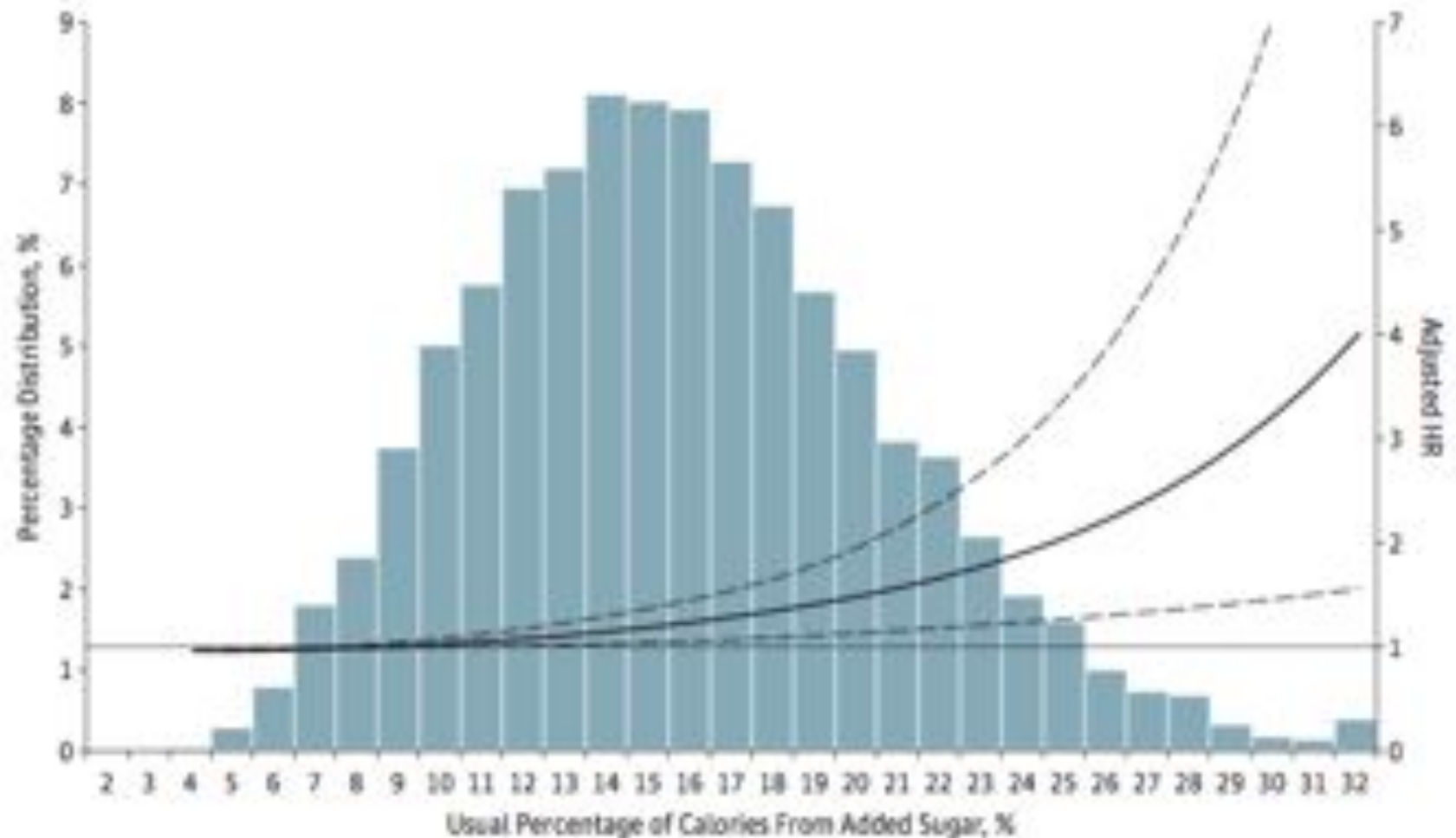
Added Sugar Intake and Cardiovascular Diseases Mortality Among US Adults

Quanhe Yang, PhD; Zefeng Zhang, MD, PhD; Edward W. Gregg, PhD; W. Dana Flanders, MD, ScD;
Robert Merritt, MA; Frank B. Hu, MD, PhD

CONCLUSIONS AND RELEVANCE Most US adults consume more added sugar than is recommended for a healthy diet. We observed a significant relationship between added sugar consumption and increased risk for CVD mortality.

JAMA Intern Med. Published online February 3 2014

Figure 1. Adjusted Hazard Ratio (HR) of the Usual Percentage of Calories From Added Sugar for Cardiovascular Disease Mortality Among US Adults 20 Years or Older: National Health and Nutrition Examination Survey Linked Mortality Files, 1988-2006

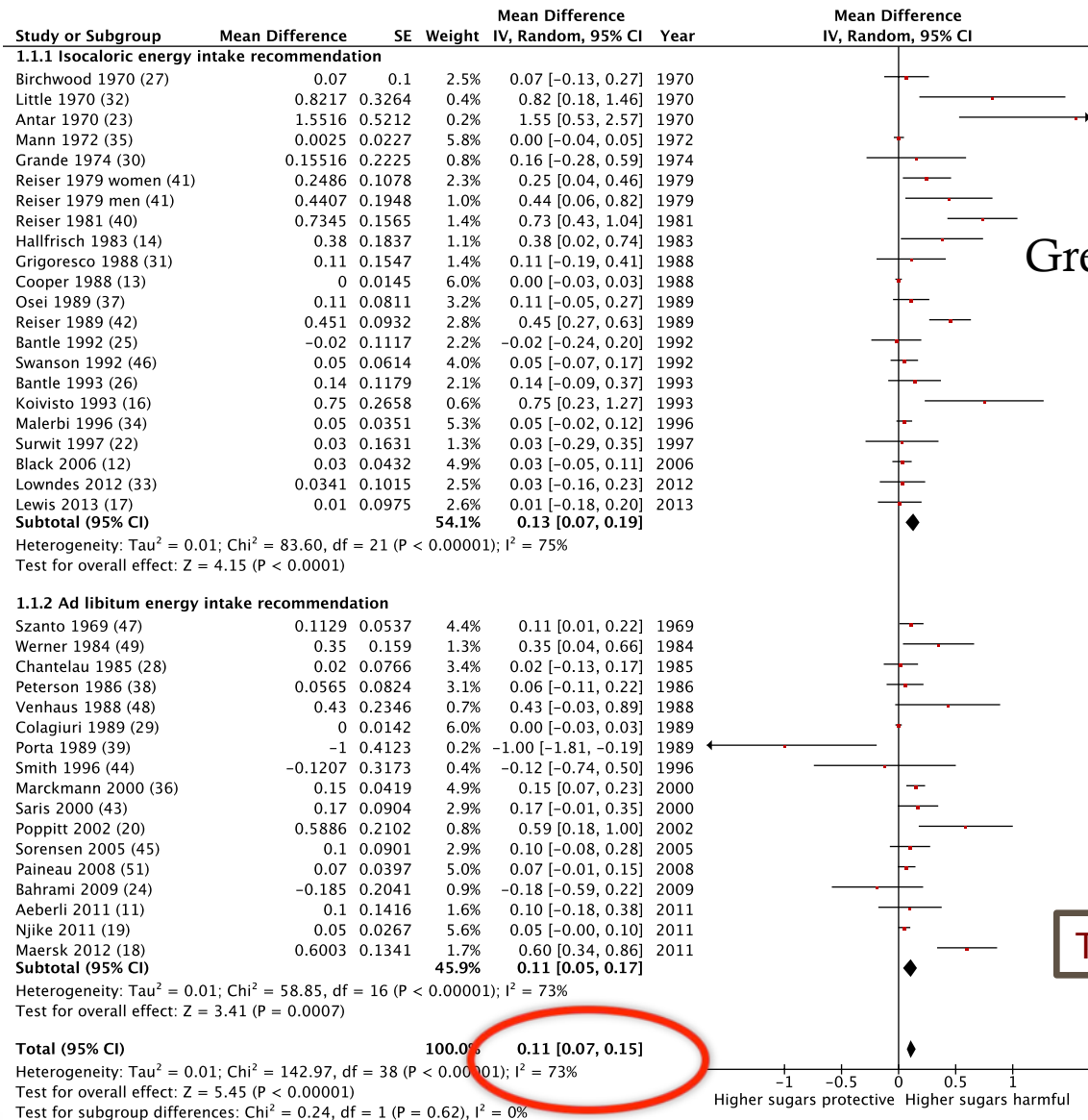


AJCN. First published ahead of print May 7, 2014 as doi: 10.3945/ajcn.113.081521.

Dietary sugars and cardiometabolic risk: systematic review and meta-analyses of randomized controlled trials of the effects on blood pressure and lipids¹⁻³

Lisa A Te Morenga, Alex J Howatson, Rhiannon M Jones, and Jim Mann

Effect of sugars on triglyceride

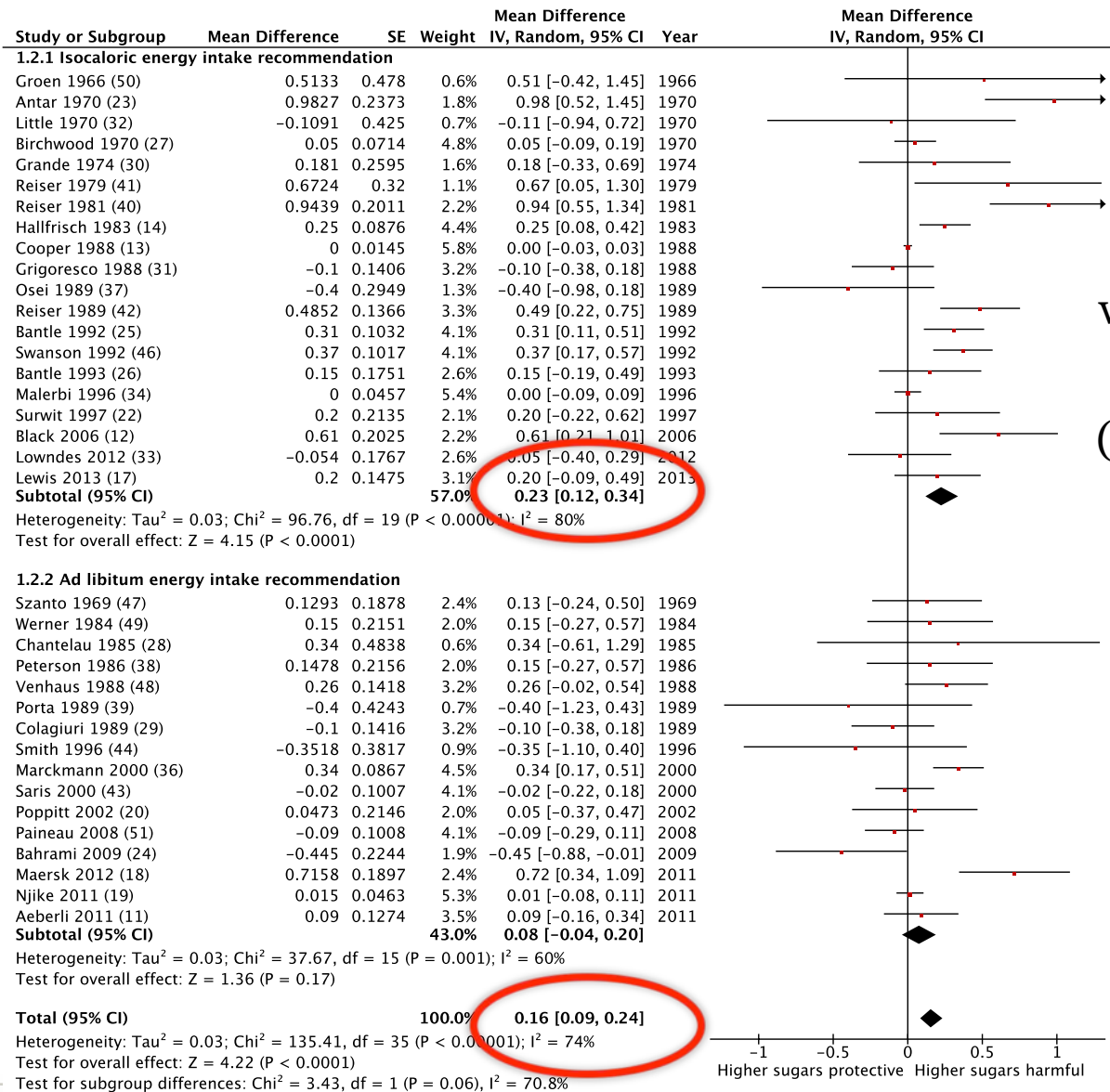


Greater TAG with increased
sugars
+0.11 mmol/l
(95%CI: 0.07 to 0.15)
 $p < 0.00001$

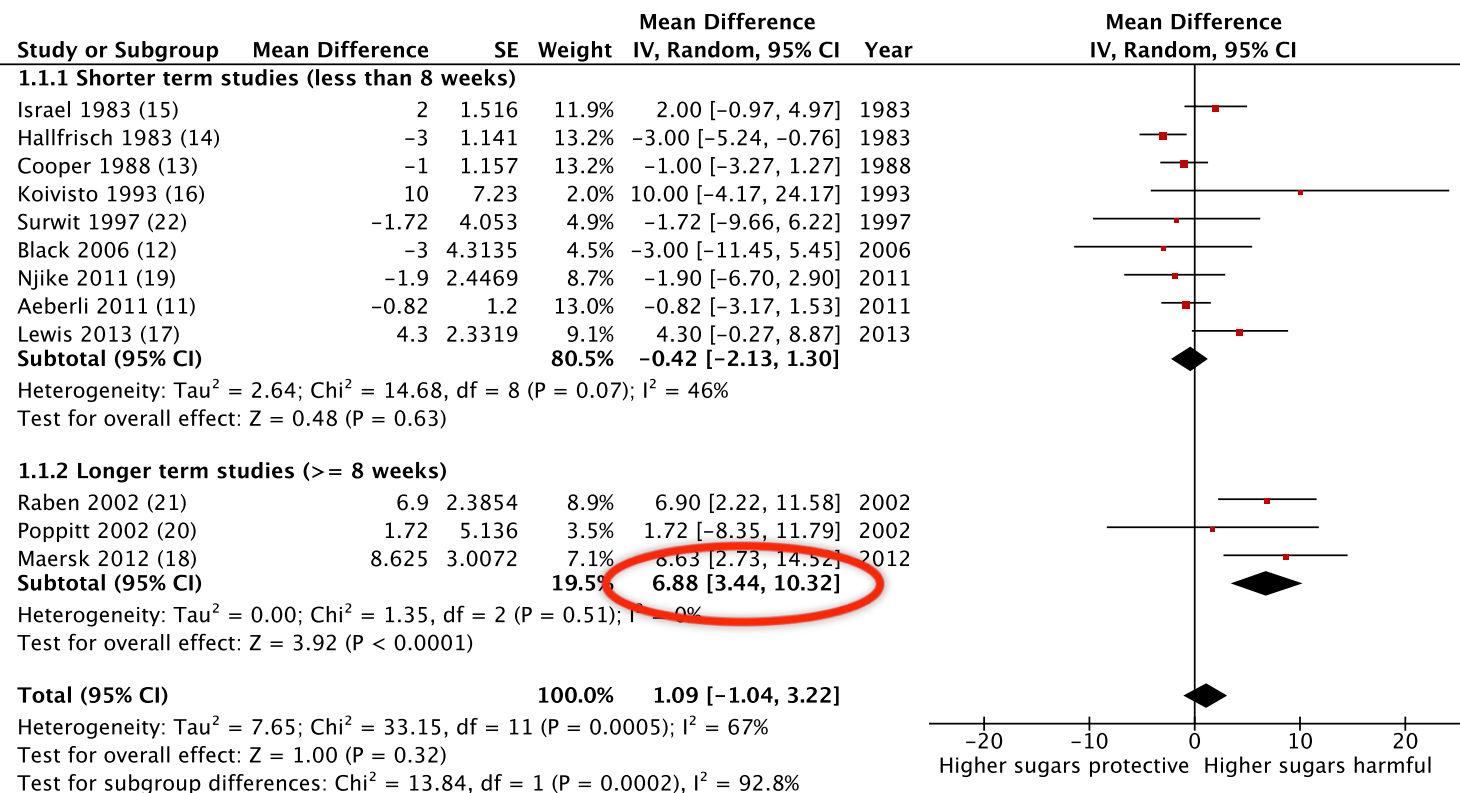
Te Morenga et al, AJCN,

Higher sugars protective Higher sugars harmful

Effect of sugars on total cholesterol



Effect of sugars on systolic blood pressure



Greater SBP with increased sugars in longer-term trials only
 +6.9 mm Hg (95%CI: 3.4 to 10.3), $P < 0.0001$

Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans

Kimber L. Stanhope,^{1,2} Jean Marc Schwarz,^{3,4} Nancy L. Keim,⁵ Steven C. Griffen,⁶ Andrew A. Bremer,⁷ James L. Graham,^{1,2} Bonnie Hatcher,² Chad L. Cox,² Artem Dyachenko,³ Wei Zhang,⁶ John P. McGahan,⁸ Anthony Seibert,⁸ Ronald M. Krauss,⁹ Sally Chiu,⁹ Ernst J. Schaefer,¹⁰ Masumi Ai,¹⁰ Seiko Otokozaawa,¹⁰ Katsuyuki Nakajima,^{10,11} Takamitsu Nakano,¹¹ Carine Beynen,¹² Marc K. Hellerstein,^{12,13} Lars Berglund,^{6,14} and Peter J. Havel^{1,2}

J. Clin. Invest. 2009; 119: 1322-1334

Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study¹⁻³

Maria Maersk, Anita Belza, Hans Stødkilde-Jørgensen, Steffen Ringgaard, Elizaveta Chabanova, Henrik Thomsen, Steen B Pedersen, Arne Astrup, and Bjørn Richelsen

AJCN 2012

Recommendations relating to sugars:

- Adoption of term '**FREE SUGARS**'
- Limit FREE SUGARS to no more than 10%TE at individual level to achieve a population average of around 5% TE
- Consumption of sugar sweetened beverages to be minimised in adults and children

Recommendations relating to sugar based on:

- Sugar sweetened beverages increase risk of weight gain & diabetes
- Sugars and dental disease
- Increase in energy intake associated with sugars intake in ad libitum diets

10% energy from sugar (50g)

