”Low-calorie sweeteners – a place in a healthy diet?

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International Sweeteners Association - Conference 2014
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Content

Low-calorie sweeteners – a place in a healthy diet?

1. Introduction
2. Appetite
3. Body weight and fat mass
4. Risk for diabetes and CV diseases
5. Conclusions

(This presentation is not a formal review, but includes relevant examples from the literature)

1. Introduction

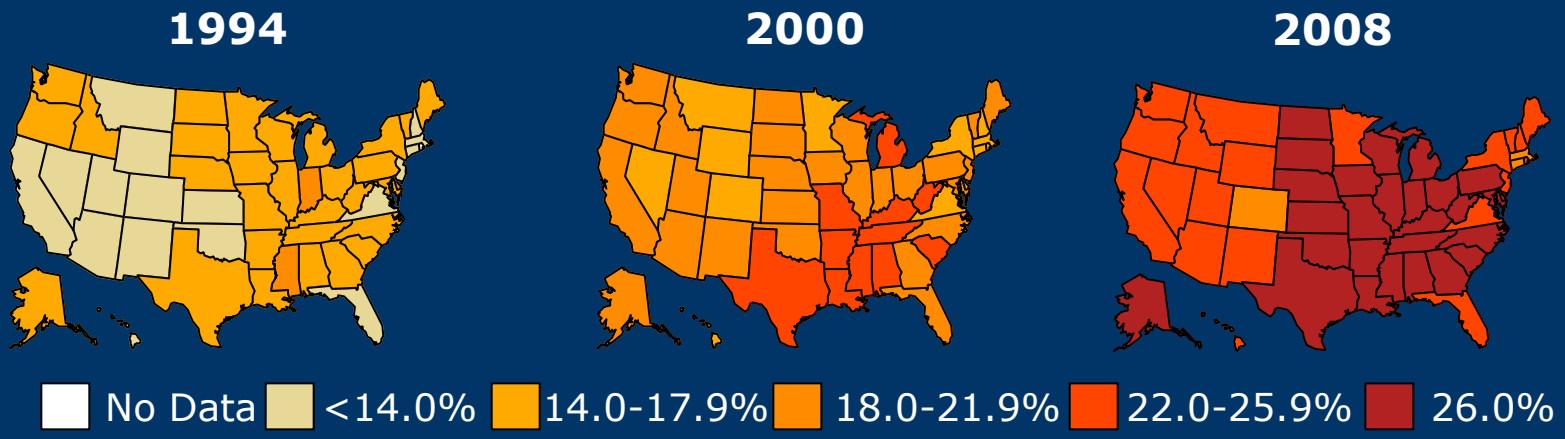
- Prevalence of obesity still increasing.
- Type-2 diabetes increases exponentially with increased obesity -> diabesity
- 50% of individuals with type-2 diabetes are obese and nearly 90% are overweight
- Around 31 mio people in Europe need treatment for diabetes
- By 2020 prevalence of pre-diabetes and diabetes in the USA will be around 50% !
- Most serious consequence of diabetes: a 3-4 times increased risk of cardiovascular diseases
- Even a 5-10% weight loss can prevent or delay progression to type-2 diabetes

- 1 in 5 children in the WHO European region is overweight.

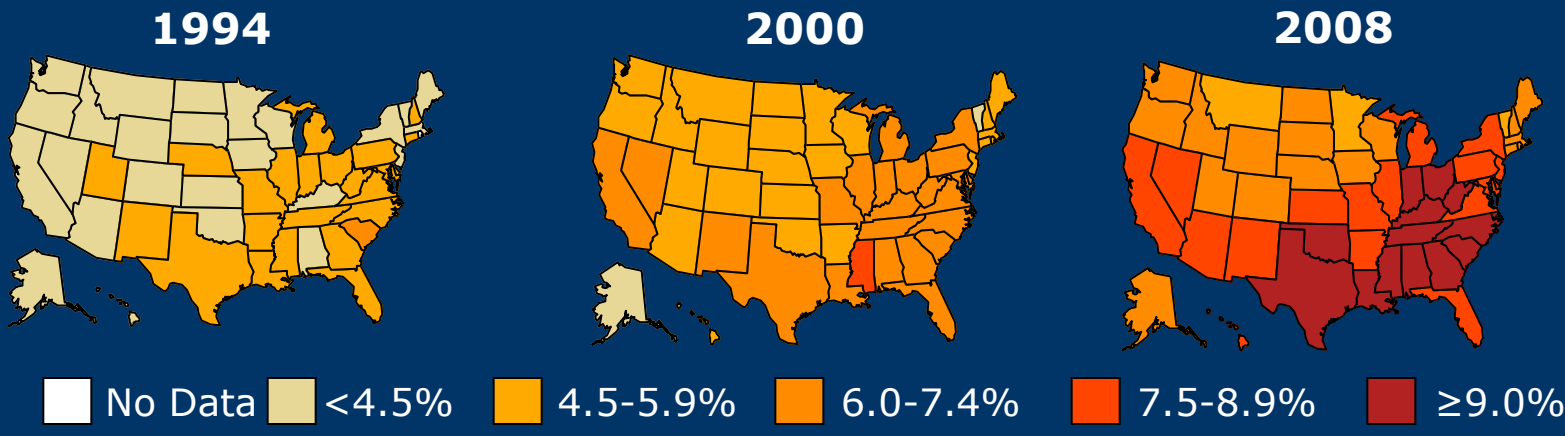
Garber, Diabetes, Obesity and Metabolism 2012;14:399-408

Percentage of U.S. Adults who were Obese or had diagnosed Diabetes

Obesity (BMI ≥30 kg/m²)



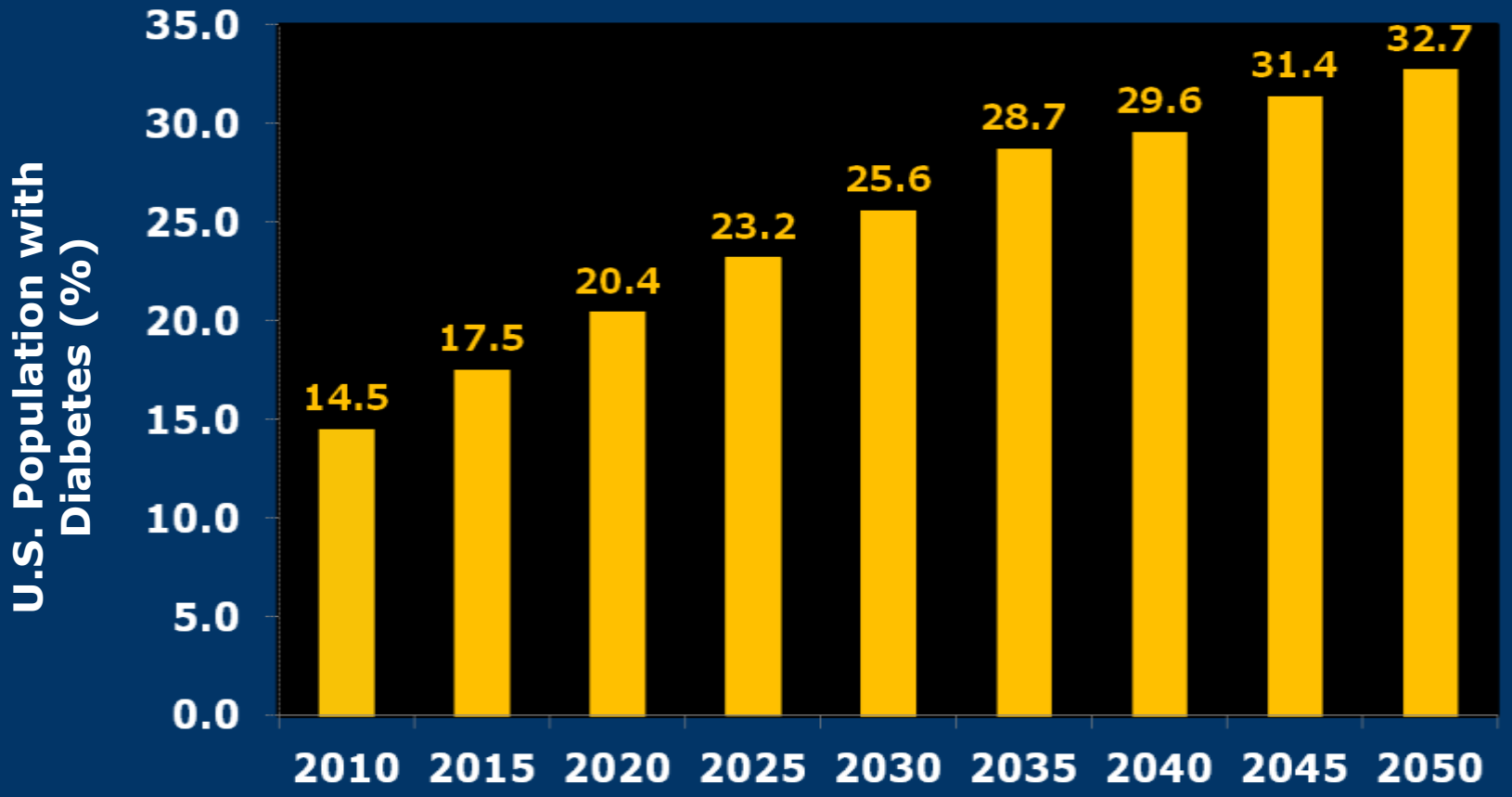
Diabetes



American Diabetes Association.

Centers for Disease Control and Prevention: National Diabetes Surveillance System. Available online at: http://apps.nccd.cdc.gov/DDTSTRS/default.aspx. Accessed 10/3/2011.

Projecting the Future Diabetes Population: The Imperative for Change



American Diabetes Association.

Boyle JP, et al. *Popul Health Metr*. 2010;8(29):1-12.

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Hunger and satiety

Satiety hierarchy: Protein > carbohydrate > fat (> alcohol?)

Hunger and satiety influenced by:

- Sensorical factors:
  - View, smell, taste
- Physiological signals from the intestine, blood, depots, brain:
  - Blood glucose
  - Glycogen stores/Fat stores
  - Oxidation of macronutrients
  - Hormones:
    Insulin, GLP-1, CCK, PPY, leptin, ghrelin, etc

Will low-calorie sweeteners make you fat?

Sucrose ↓

Carbohydrate intake ↓

Fat/carbohydrate ratio ↑

Sweenetes ↑, but no calories

Hunger ↑

Compensation?

Increased energy intake?

Sukkerindholdet i en *Pepsi*® svarer til 18 sukkerknalde, mens der ikke er tilsat sukker i *Pepsi Light*®.

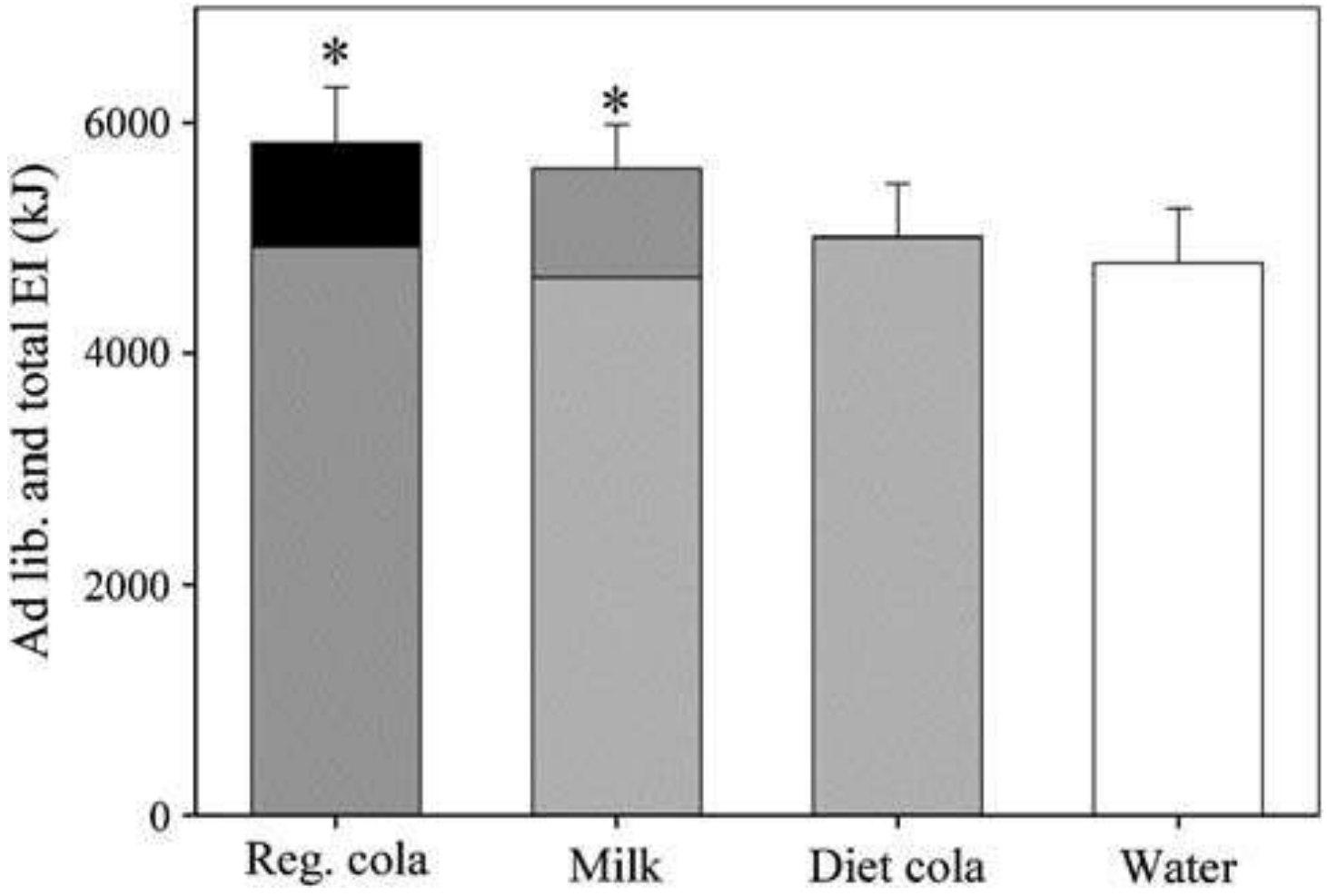
Possible mechanisms for compensation after low-calorie sweeteners:

- Over-stimulating taste receptors and increase cravings for sweetness?
- Provoking hunger and causing overeating?
- Not promoting satiety and therefore compensatory eating occurs at the next meal?

➢ These mechanisms considered, but rejected again
(Mattes and Popkin 2009, Raben & Richelsen 2012).

➢ No studies the past > 25 y have confirmed the earlier suggestions

<u>Decreased</u> ad libitum energy intake after intake of diet cola vs regular cola



(Maersk et al Eur J Clin Nutr 2012)

Short-term studies interesting from a mechanistic point of view.

However, longer-term studies needed to look at effects on

body weight, fat mass

and

risk factors for diabetes and

cardiovascular disease

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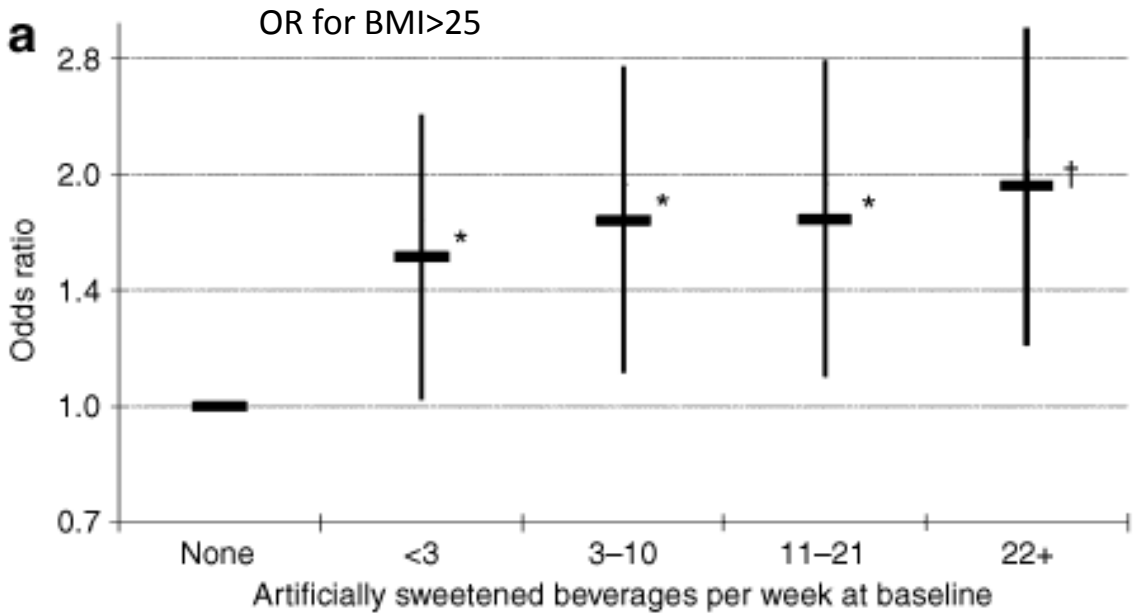
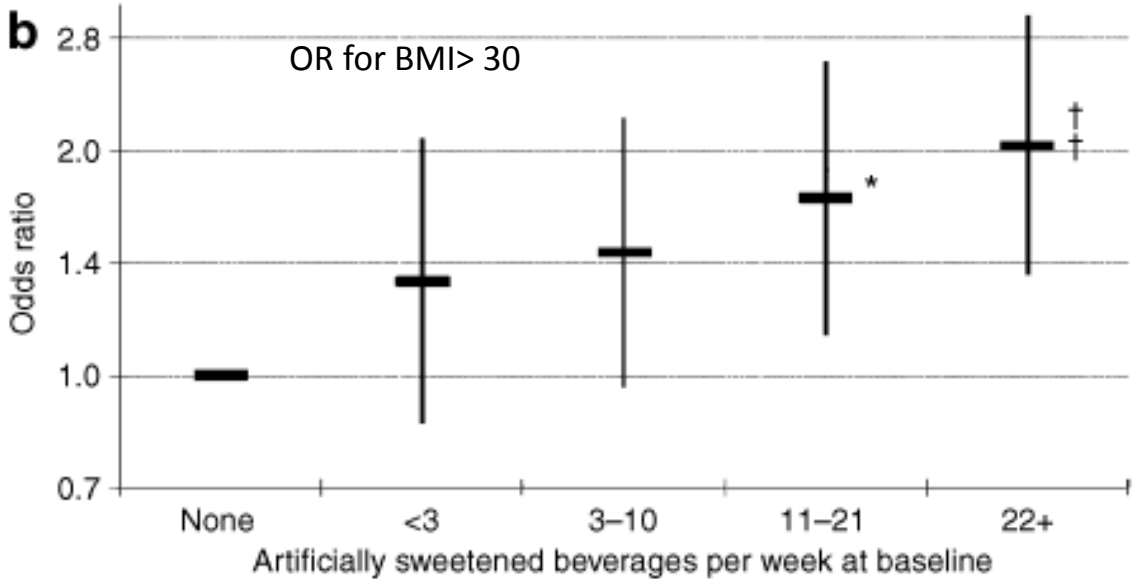
Low calorie-sweetened beverage use and long-term weight gain. Fueling the Obesity Epidemic?

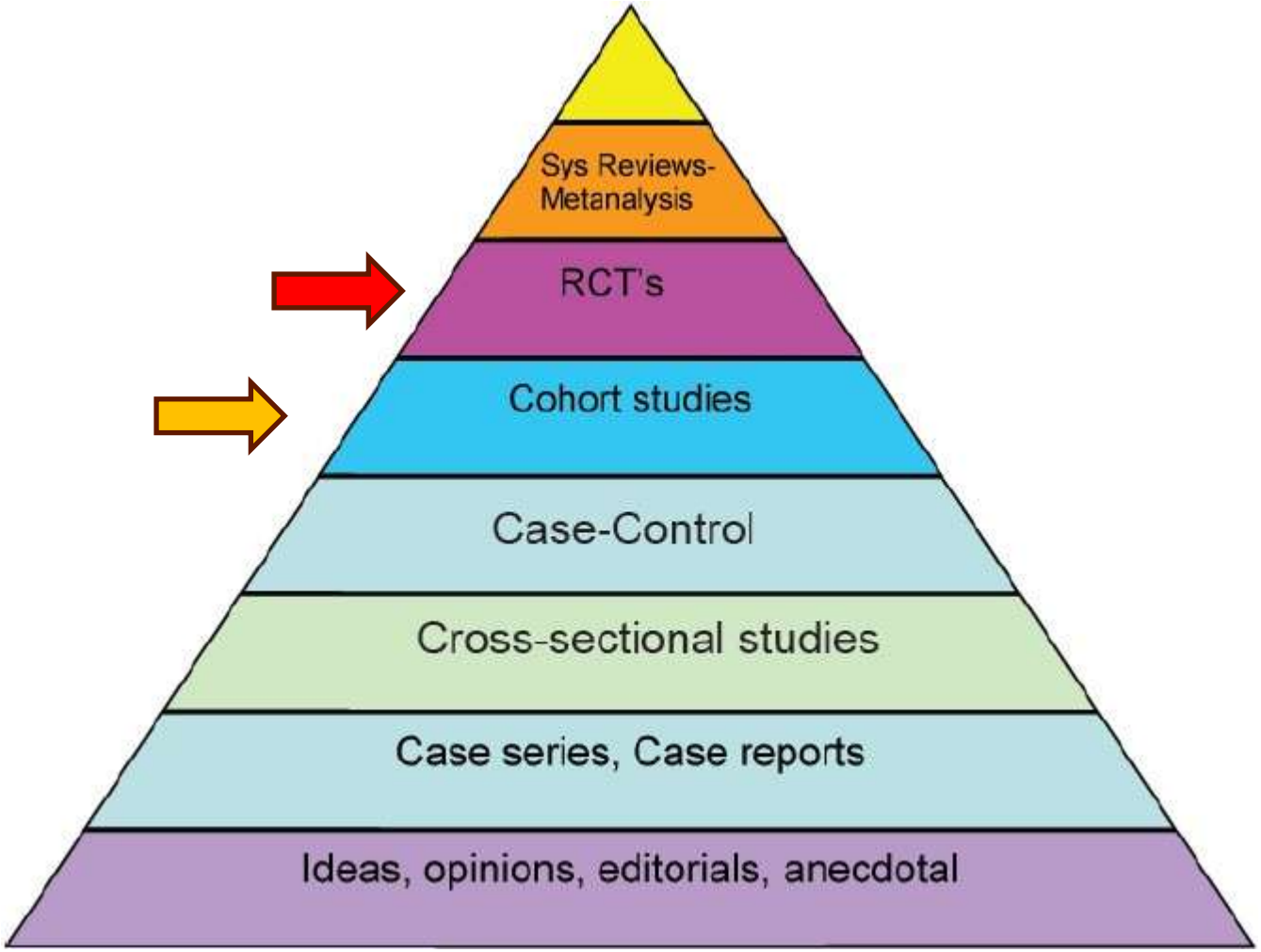




OR for overweight and obesity by 7-8-year follow-up.

Obesity 2008;16:1894

Evidence hierarchy for studies:



10 wks study with supplements and *ad libitum* intake

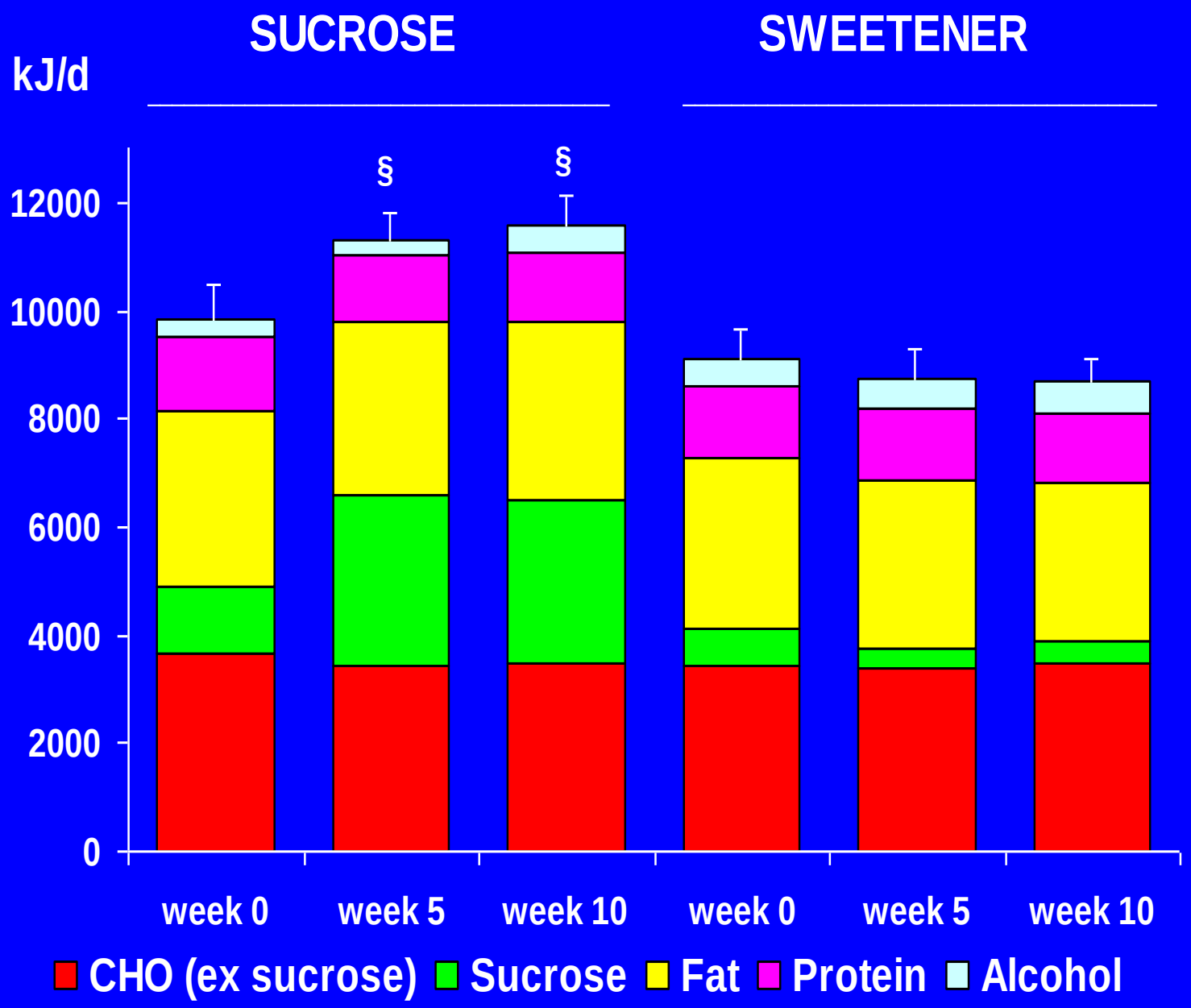
Supplements of drinks and food - average intake in week 10:

	SUCROSE	SWEETENER[a]
Carbohydrate (g/d)	176 ± 3 §	31 ± 3
Sucrose (g/d)	151 ± 3 §	0 ± 0
Dietary fiber (g/d)	3 ± 1 §	5 ± 1
Fat (g/d)	8 ± 0	9 ± 0
Protein (g/d)	9 ± 0	9 ± 0
Total energy (kJ)	3349 ± 66§	963 ± 44
Amount (g/d)	1621 ± 43	1564 ± 48

N=43 overweight. Parallel design. Data are means ± SEM. Between groups: §: p<0.0001.

a: 54% aspartame, 22% acesulfame K, 23% cyclamate, 1% saccharin.

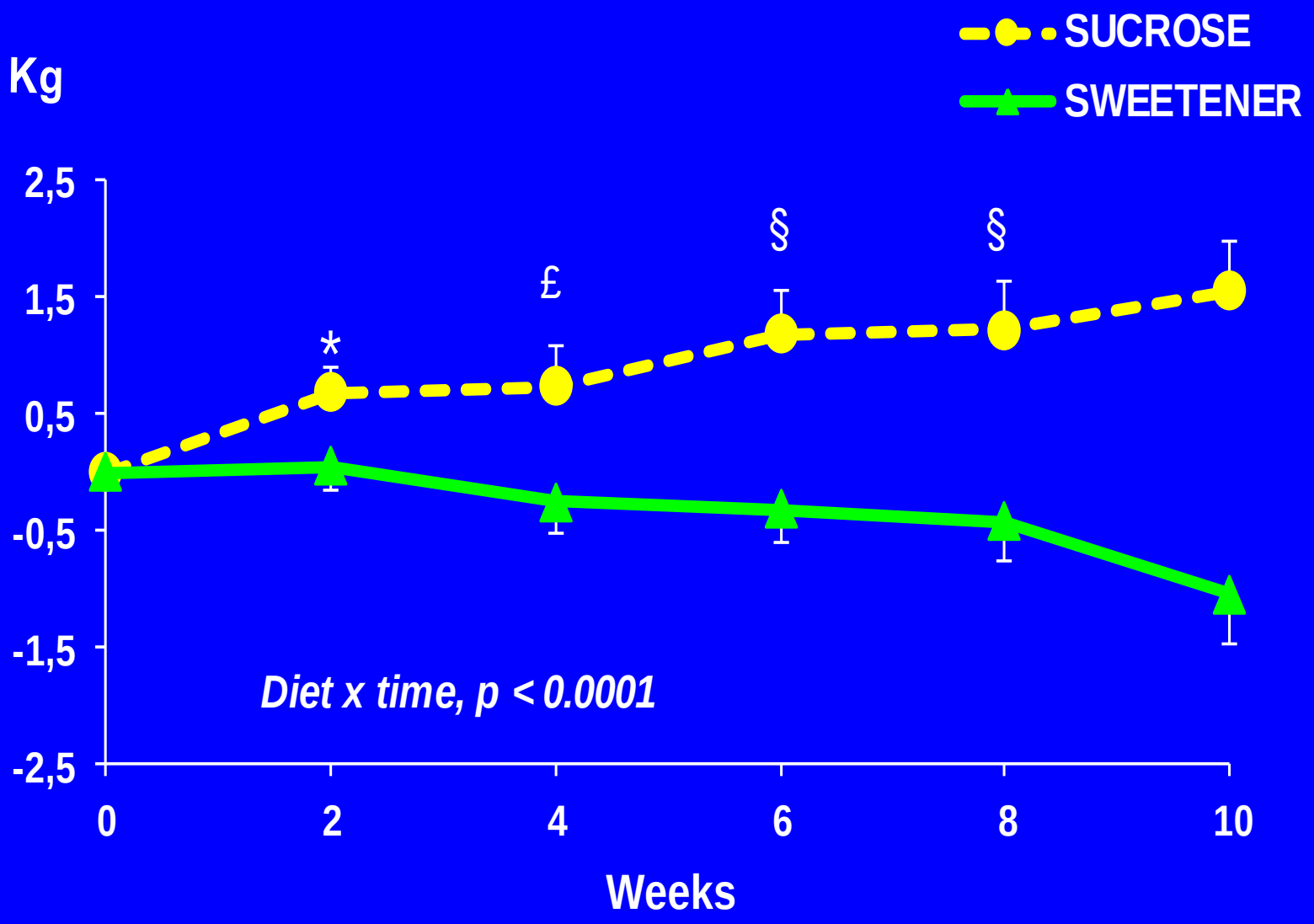
Raben et al AJCN 2002



Means ± SEM. §: p<0.0001 vs Ei on SWEETENER.

Raben et al AJCN 2002

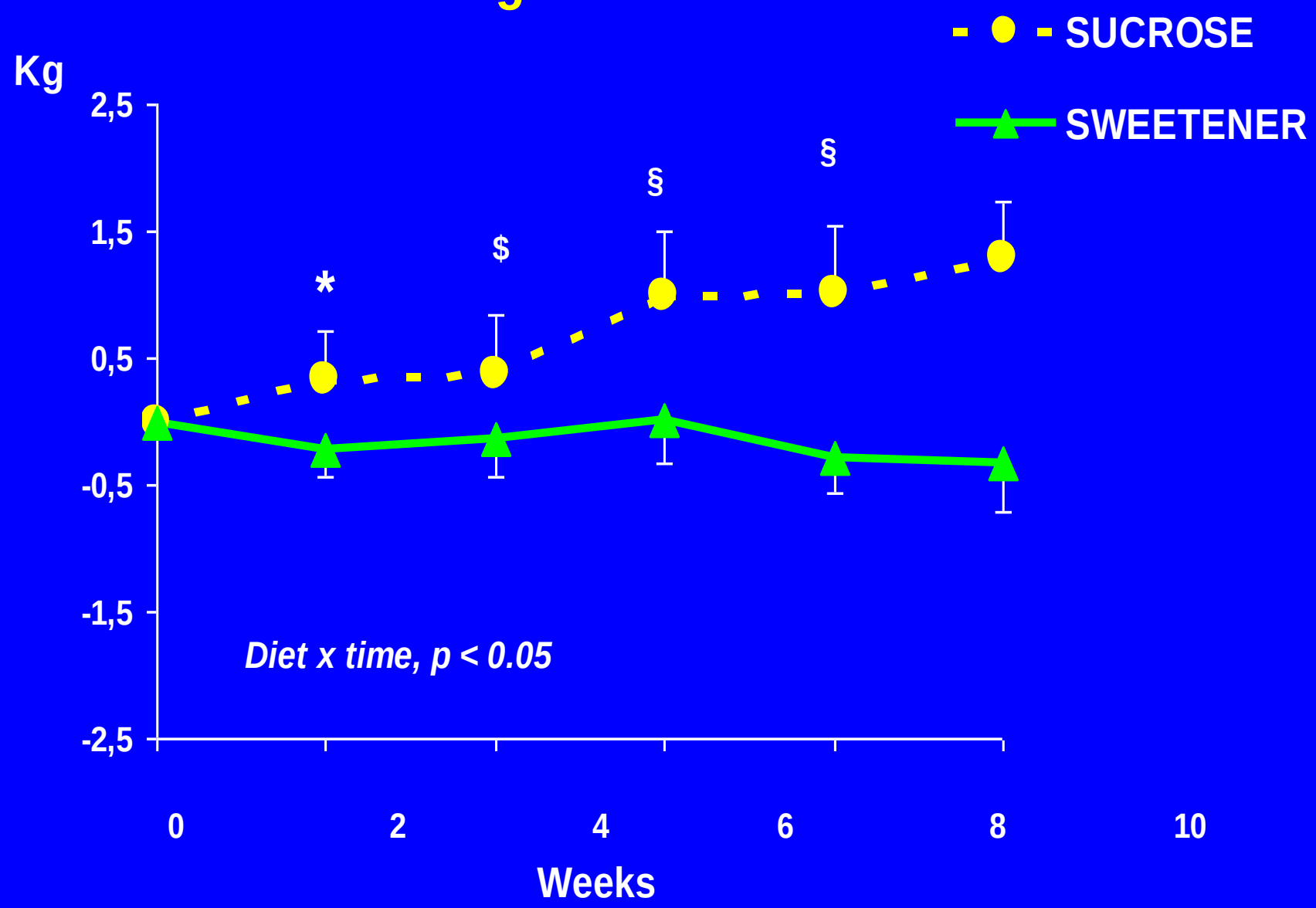
Weight changes after 10 weeks ad lib diet



Means ± SEM. *: p<0.05. $: p<0.01. £: p<0.001. §: p<0.0001.

Raben et al AJCN 2002

Changes in fat mass



Means ± SEM. *: p<0.05. $: p<0.01. £: p<0.001. §: p<0.0001.

Raben et al AJCN 2002

18-m study, children

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

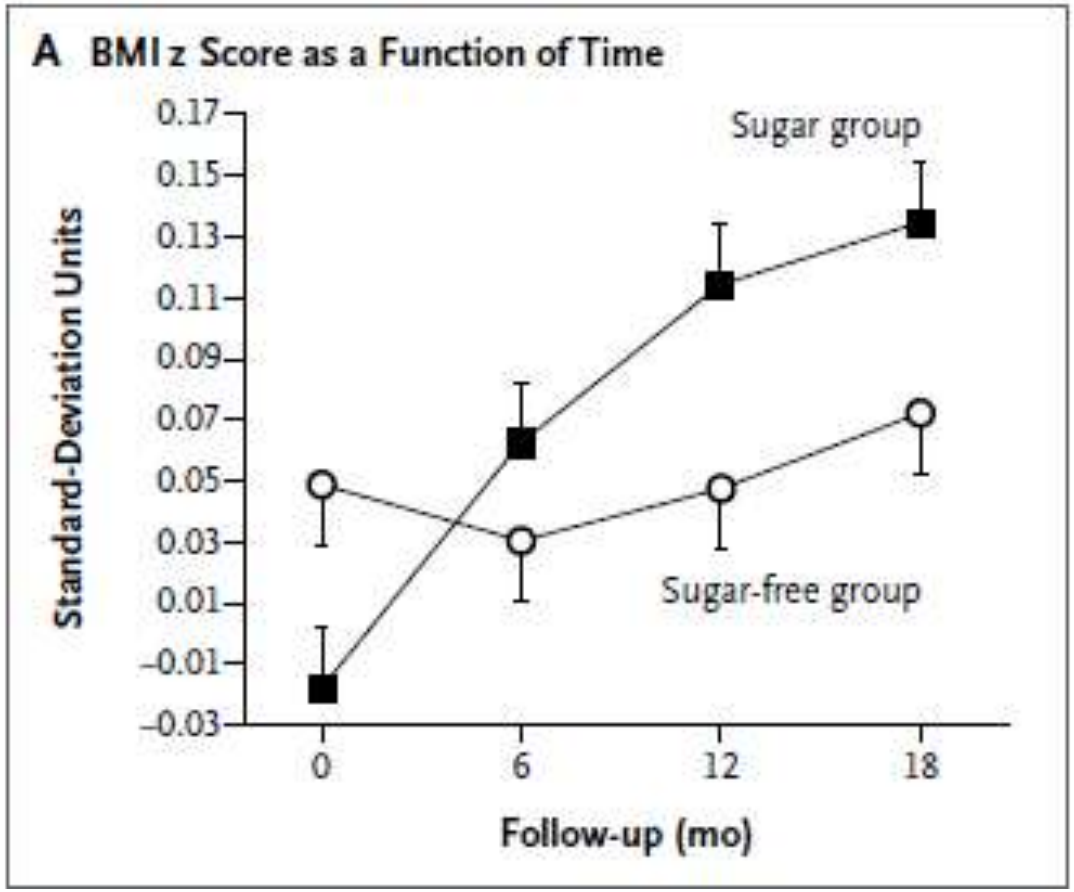
A Trial of Sugar-free or Sugar-Sweetened Beverages and Body Weight in Children

Janne C. de Ruyter, M.Sc., Margreet R. Olthof, Ph.D., Jacob C. Seidell, Ph.D., and Martijn B. Katan, Ph.D.

METHODS

We conducted an 18-month trial involving 641 primarily normal-weight children from 4 years 10 months to 11 years 11 months of age. Participants were randomly assigned to receive 250 ml (8 oz) per day of a sugar-free, artificially sweetened beverage (sugar-free group) or a similar sugar-containing beverage that provided 104 kcal (sugar group). Beverages were distributed through schools. At 18 months, 26% of the children had stopped consuming the beverages; the data from children who did not complete the study were imputed.

This article was published on September 21, 2012, at NEJM.org.

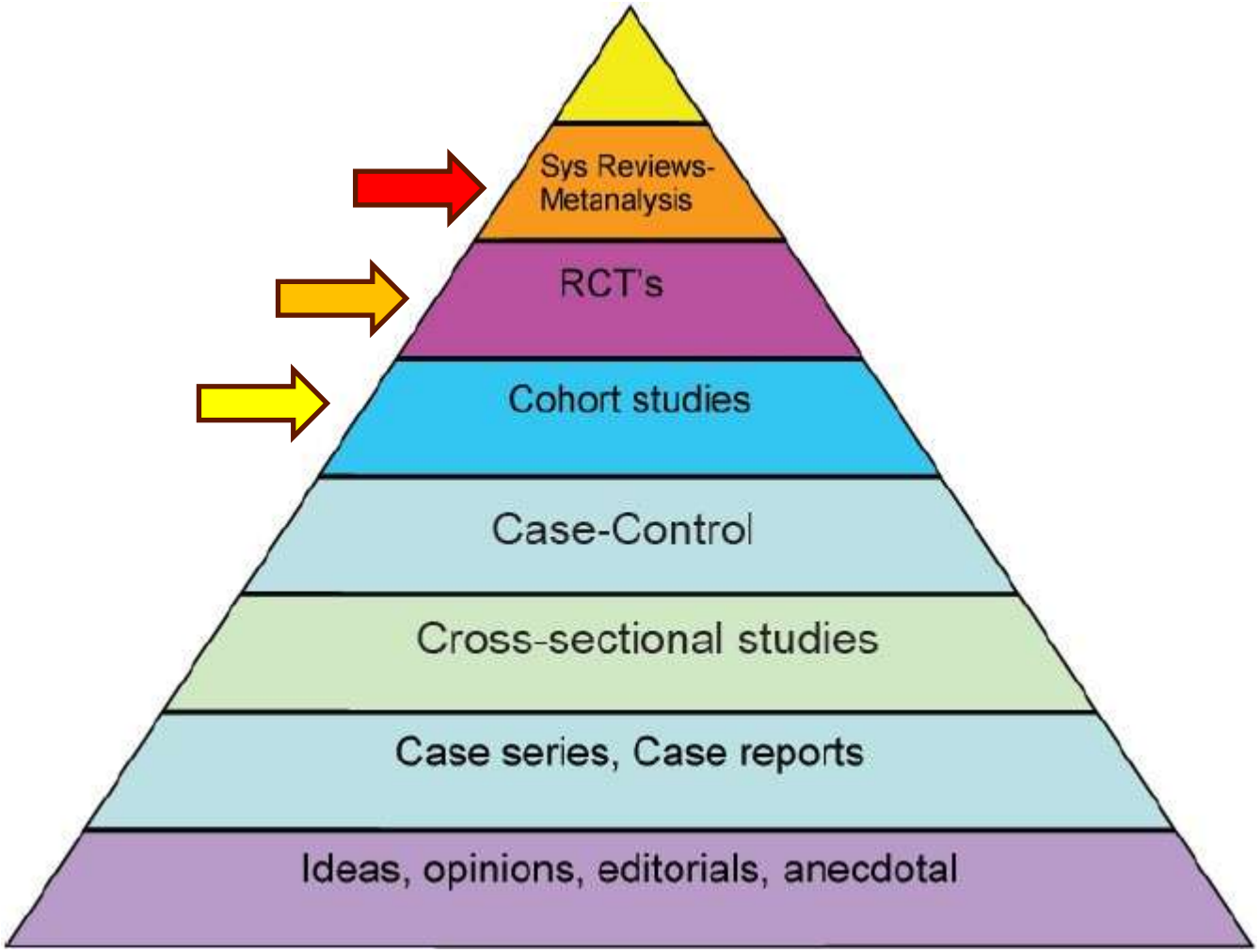


CONCLUSIONS

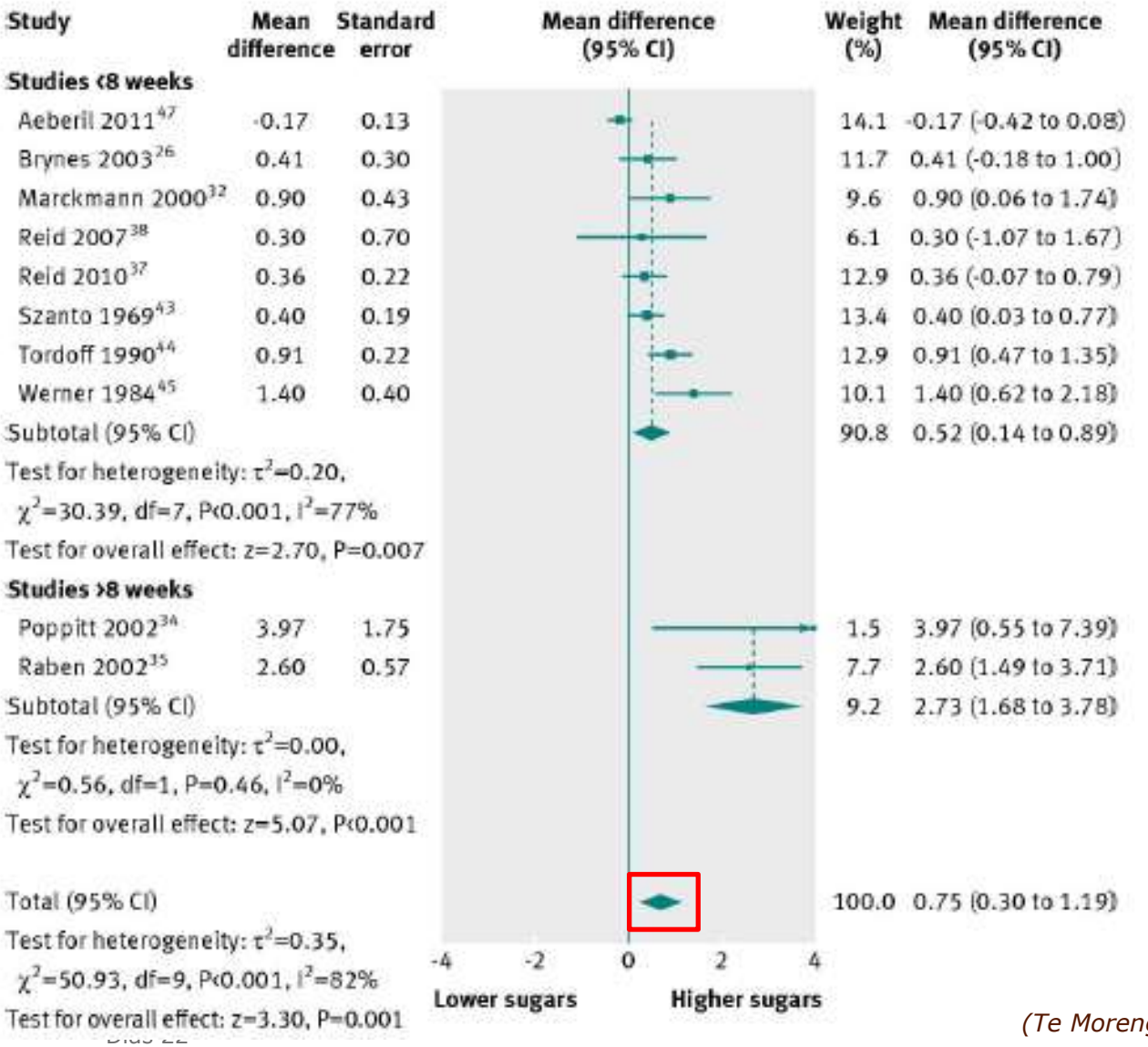
Masked replacement of sugar-containing beverages with noncaloric beverages reduced weight gain and fat accumulation in normal-weight children.

(De Reyter et al NEJM 2012)

Evidence hierarchy for studies:



Increasing sugar intake increases body weight - Adults

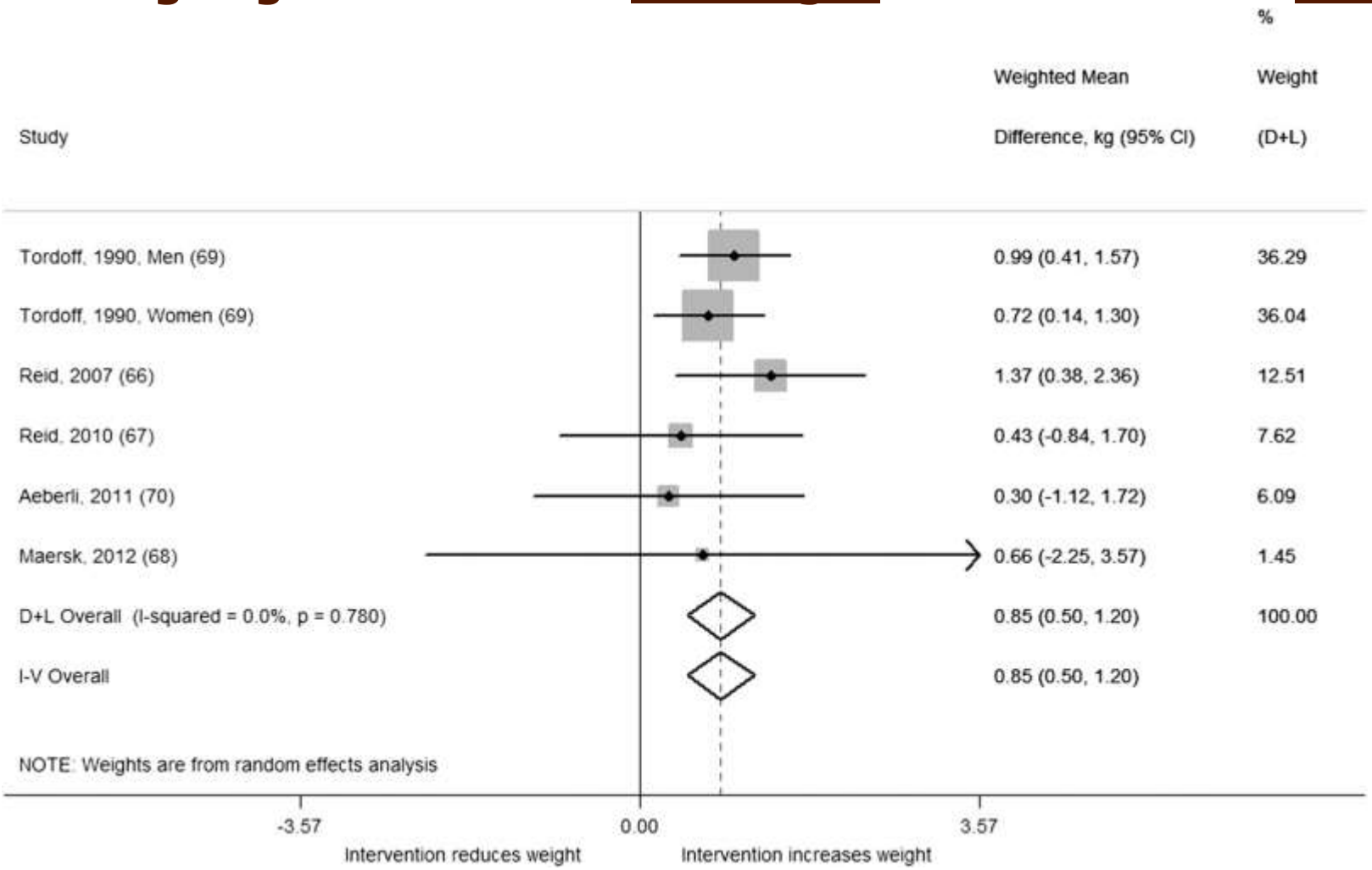


Pooled effects for differences in BW (kg) for studies comparing increased intake (higher sugars) with usual intake (lower sugars).

BW was increased in higher sugar groups

(Te Morenga et al BMJ Jan 2013)

Increasing sugar-sweetened beverages increases BW in adults



Weighted mean differences (95% CI) in weight change (kg) between the intervention and control regimens from **randomized controlled trials** in adults. Interventions evaluated the effect of **adding** sugar-sweetened beverages

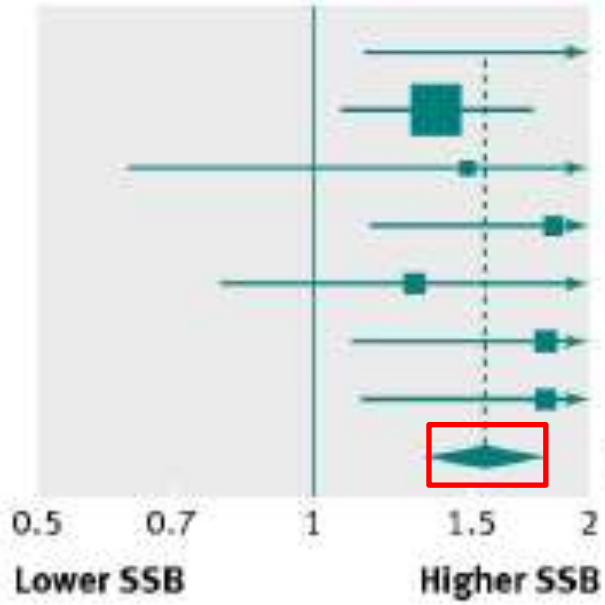
(Malik et al Am J Clin Nutr 2013)

Increasing intake of sugar-sweetened beverages increases overweight/obesity in children

Study	Log (odds ratio)	Standard error	Weight (%)	Odds ratio (95% CI)
Dubois 2007 (1)[94]	0.77	0.32	6.3	2.16 (1.15 to 4.07)
Lim 2009 (2)[97]	0.31	0.12	44.5	1.37 (1.08 to 1.74)
Ludwig 2001 (3)[95]	0.39	0.44	3.5	1.48 (0.63 to 3.47)
Weijs 2011 (4)[80]	0.61	0.24	11.8	1.84 (1.16 to 2.92)
Welsh 2005 (5)[96]	0.26	0.25	10.7	1.30 (0.80 to 2.11)
Welsh 2005 (6)[96]	0.59	0.24	11.2	1.80 (1.12 to 2.89)
Welsh 2005 (7)[96]	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, $I^2=0\%$

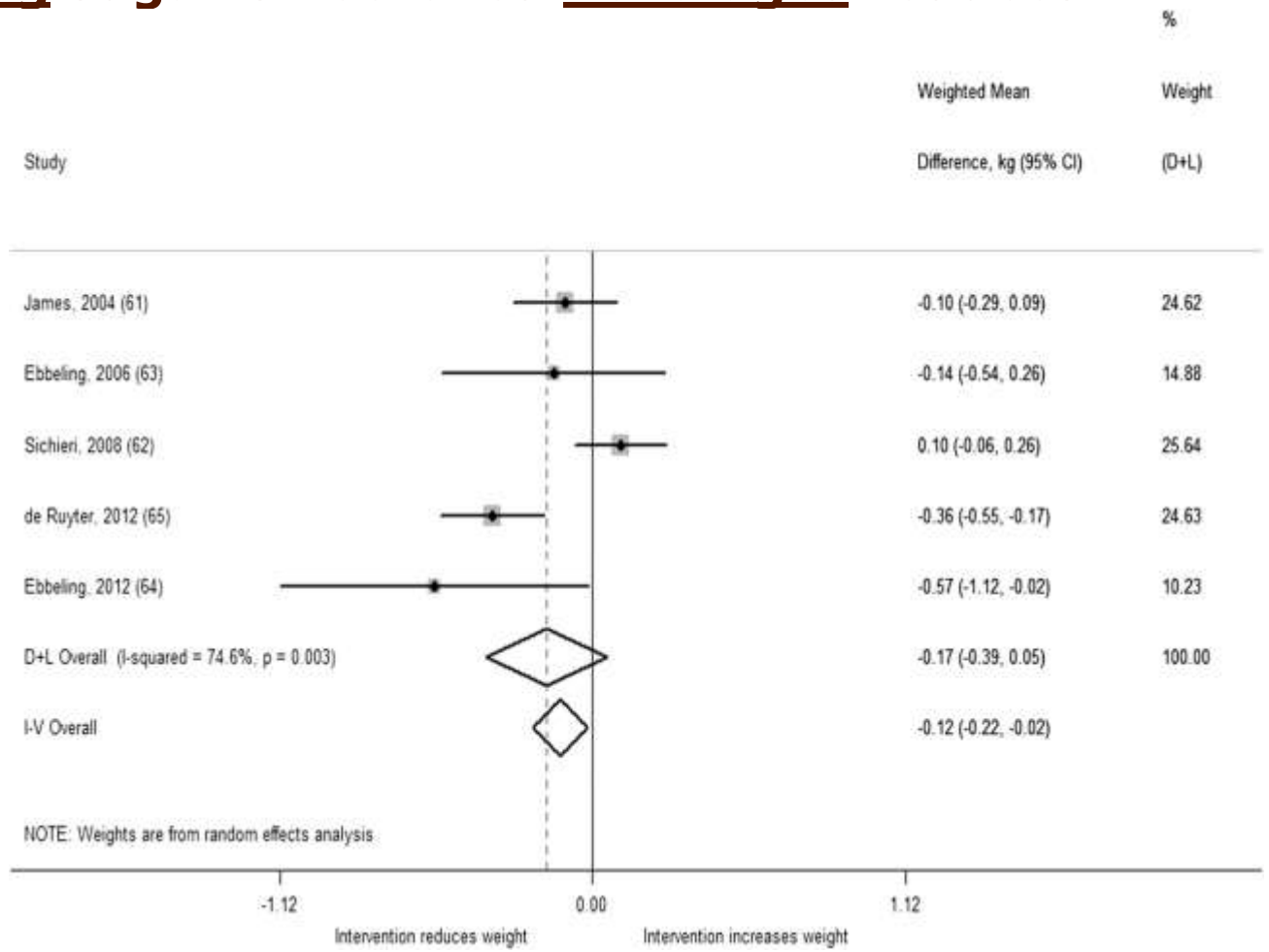
Test for overall effect: z=5.42, P<0.001



- Higher odds ratio of overweight or obesity at follow-up in children consuming one or more servings of sugar sweetened beverages at baseline compared with children consuming none or very little at baseline.

Te Morenga et al BMJ Jan 2013

Reducing sugar-sweetened beverages reduces BMI in children



Weighted mean differences in BMI change (95% CI) between the intervention and control regimens from **randomized controlled trials** in children. Interventions evaluated the effect of **reducing** sugar-sweetened beverages.

(Malik et al Am J Clin Nutr 2013)

Intake of soft drinks and overweight reduced in children in California

"Political measures may have changed the consumption of sugar-sweetened drinks in the population!"

	2003	2005	2007	
	16.4%	11.0%	5.0%	
	15.7%	13.3%	11.2%	
	22.5%	16.0%	9.9%	
	13.5%	14.3%	11.1%	
	35.7%	30.6%	25.7%	
	12.4%	14.2%	13.3%	

Shi & Meijgaard, Int J Gen Med. 2010; 3: 221–224.

Editorial, NEJM, 21-Sep-2012 (S Caprio):

Sugar intake from sugar-sweetened beverages approaches **15% of the daily caloric intake** in several population groups in the US.

Sugar-sweetened beverages are marketed extensively to **children and adolescents**.

Large increases in consumption of sugar-sweetened beverages have occurred among **black and Mexican-American youth**, who are at higher risk for obesity and the development of **type 2 diabetes** than white counterparts.

Editorial, NEJM, Sep-2012 (S. Caprio)

In relation to publication of several studies on sucrose-rich drinks in adults and children:

"These randomized, controlled studies — in particular, the study by de Ruyter et al. — provide a ….

strong impetus to develop recommendations
and policy decisions to
limit consumption of sugar-sweetened beverages,

especially those served at low cost and in excessive portions, to attempt to reverse the increase in childhood obesity….. "

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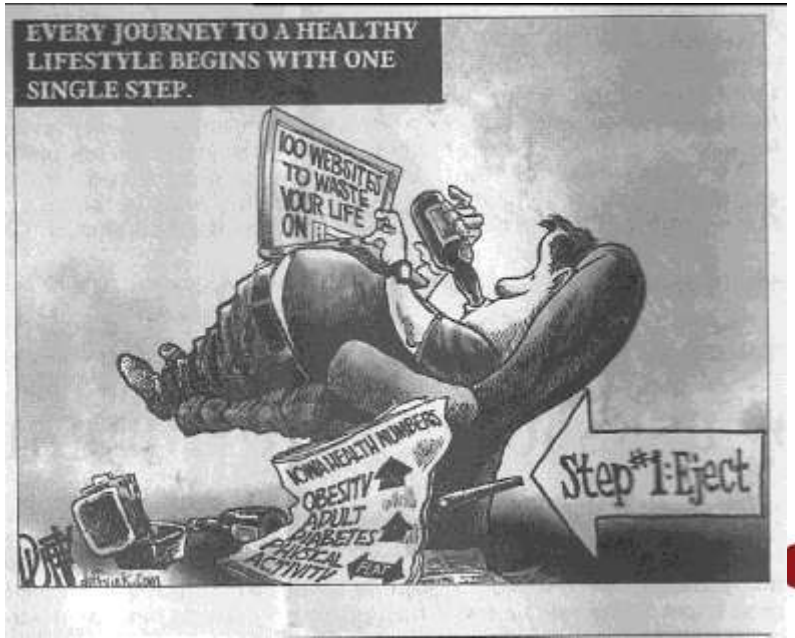


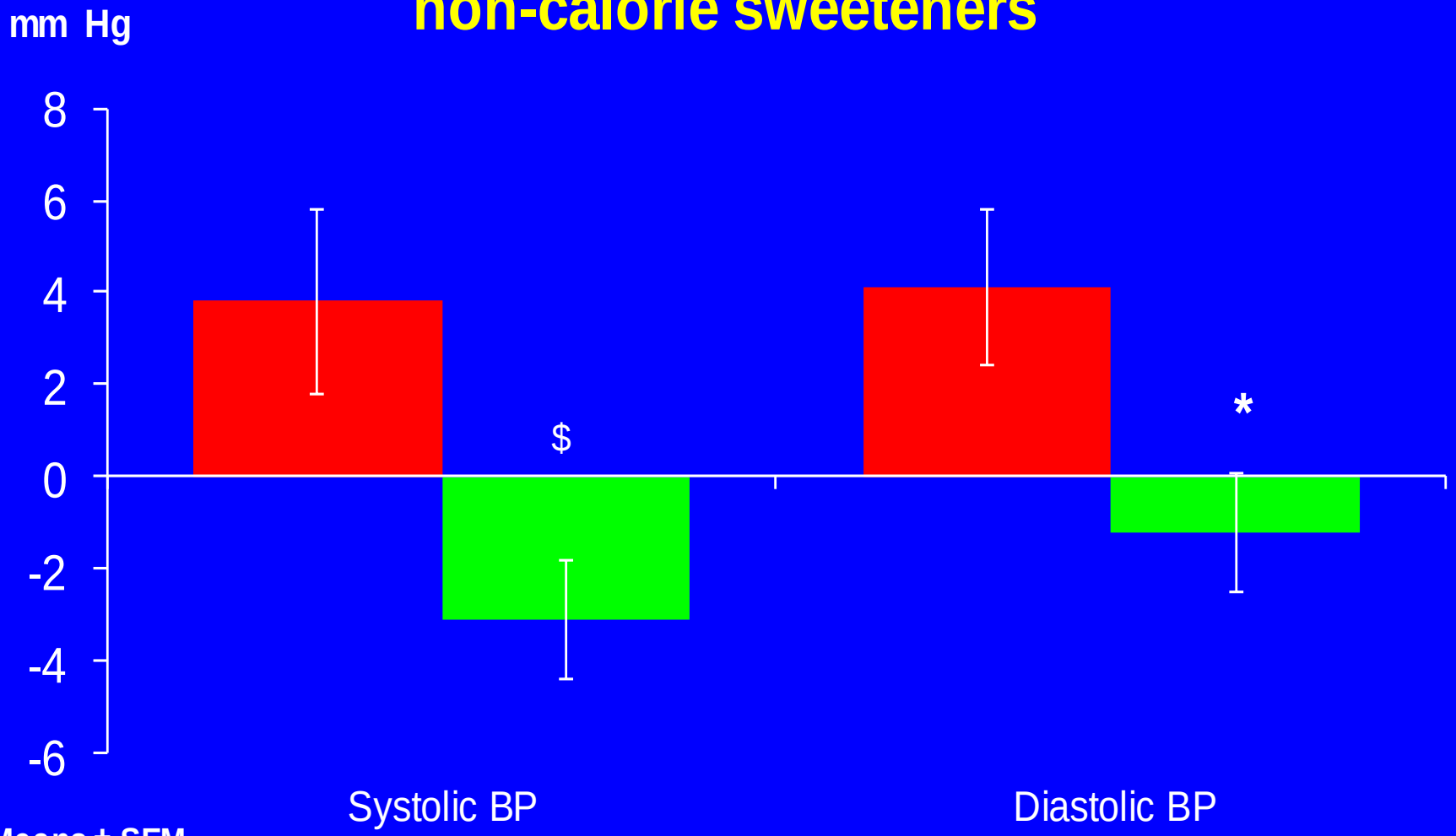
Sugar vs low-calorie sweetened soft drinks, obesity and the metabolic syndrome
Observational studies

- Positive associations between sugar-sweetened soft drinks obesity, type-2 diabetes, and cardiovascular disease
- (*Nurses Health Study, Am J Clin Nutr 2006;84:274 & JAMA 2004;292:927)*

- Positive associations between low-calorie sweetened soft drinks, obesity, metabolic syndrome, and Type-2 diabetes
- *(Nettleton et al Diabetes Care 2009, Fagherazzi et al Am J Clin Nutr 2013)*

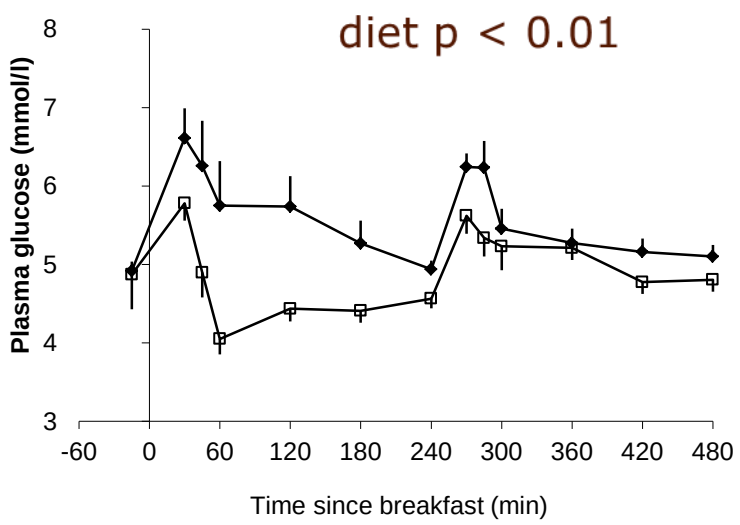
- Careful with findings from observational studies due to "Spurious associations" or "reverse causality"
- *(Mackenzie, Ann Epidemiol 2006).*

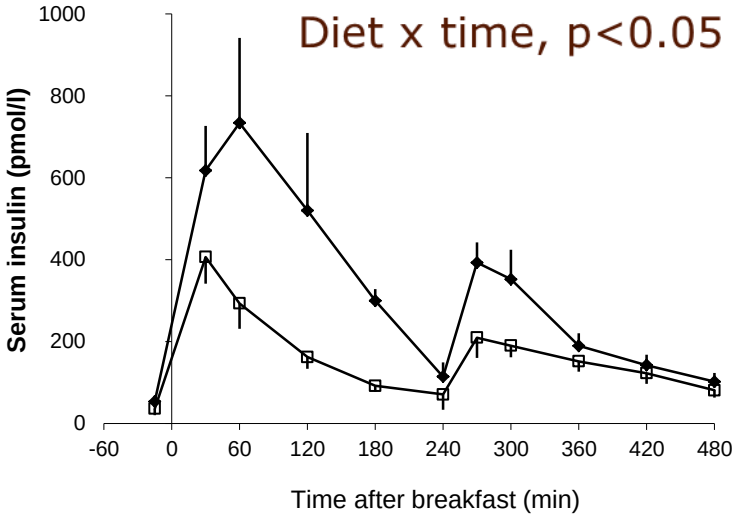
Blood pressure decreased after 10 wks' on non-calorie sweeteners

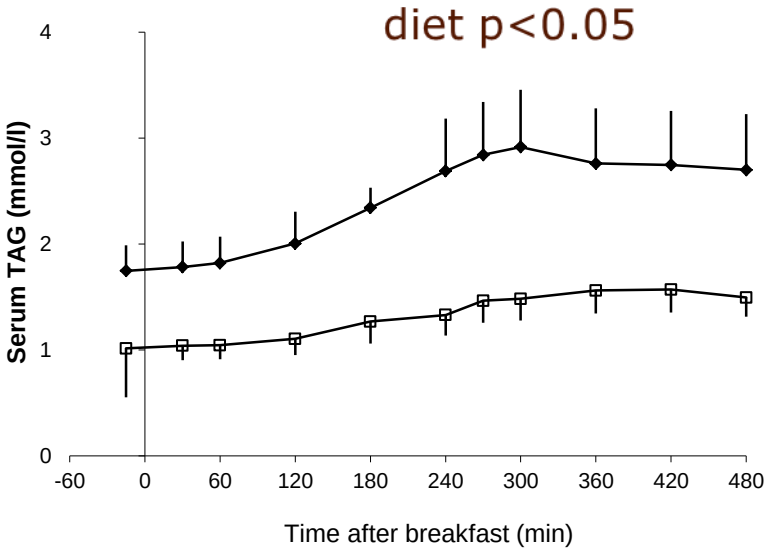


Raben et al AJCN 2002

Postprandial glucose, insulin and triglycerides increase after 10 wks' sucrose compared with low-calorie sweeteners







Adjusting for differences in Δ-BW & fasting values (wk 10): Postprandial glucose and insulin still higher.

Adjusting further for differences in energy and sucrose intake: Postprandial insulin still higher on the sucrose-rich diet.

Mean +/- SEM

Raben et al FNR 2011

Sugar-sweetened drink increases blood lipids and liver, muscle, and visceral fat compared with low-calorie sweetened drink, milk or water

6-mo randomized intervention study:

Four different beverages were ingested daily for 6 months:

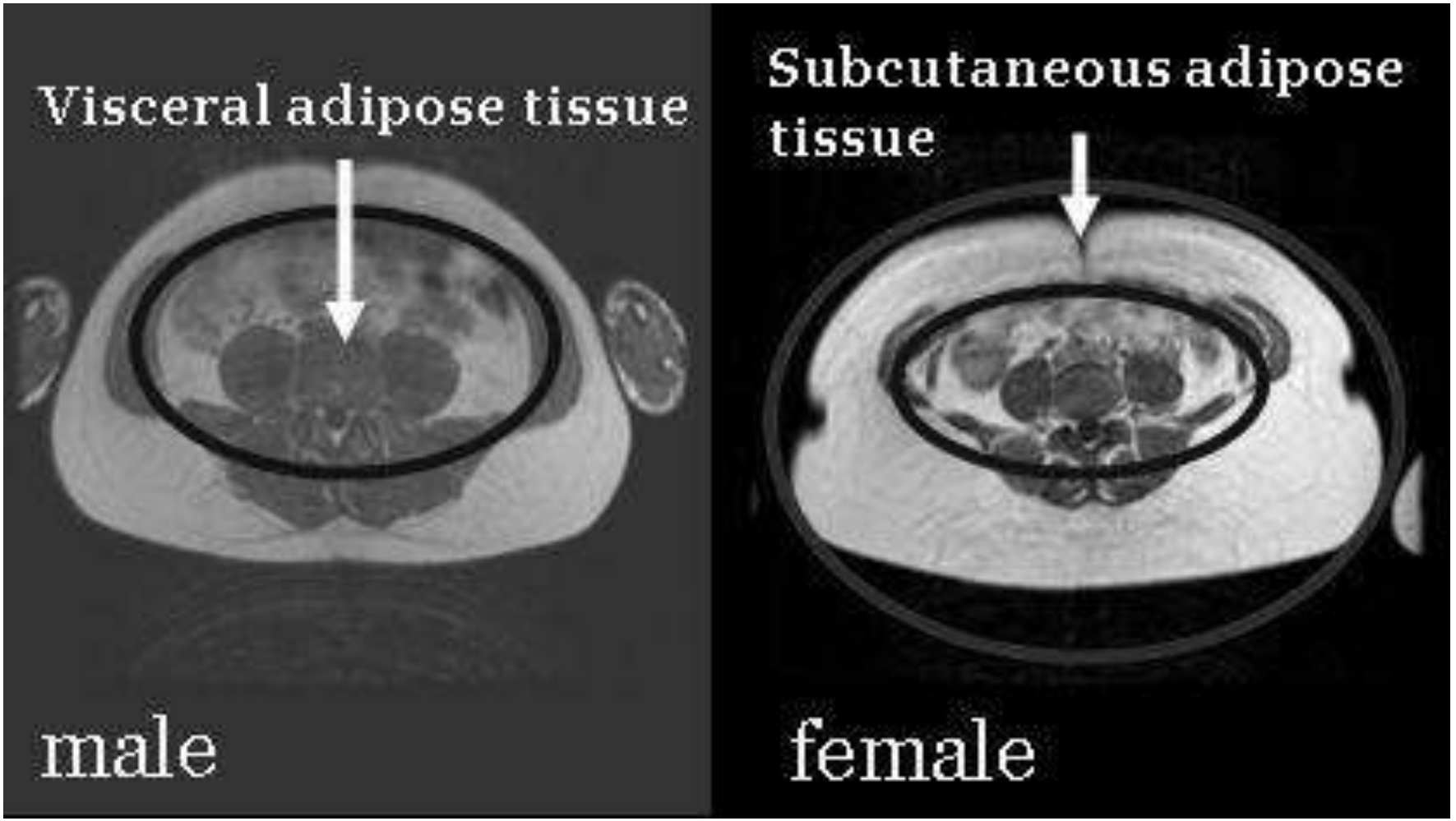
1. 1 liter sucrose sweetened soda (Coca Cola)
2. 1 liter skimmed milk (isocaloric with 1)
3. 1 liter aspartame sweetened (Diet Cola)
4. 1 liter water (control)

by overweight - obese individuals

Investigations:
Body composition (DXA), visceral fat (MR), liver- and muscle fat (MRI-spectroscopy)
Metabolic factors: blood lipids, insulin/HOMA, inflammatory markers

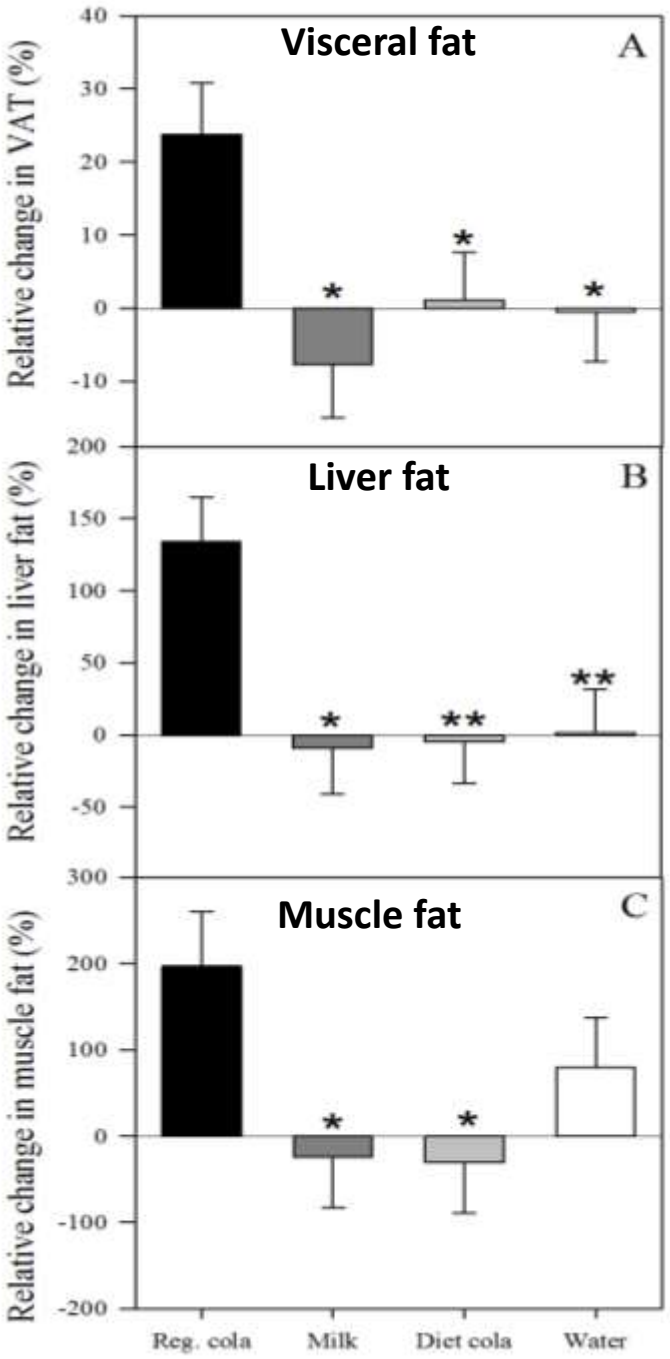
(Maersk et al. Am J Clin Nutr 2012)

MR-scan to determine fat in the abdomen (visceral) and under the skin (subcutane)



Relative changes in ectopic fat accumulation

(from baseline to 6 mo)



ANOVA:

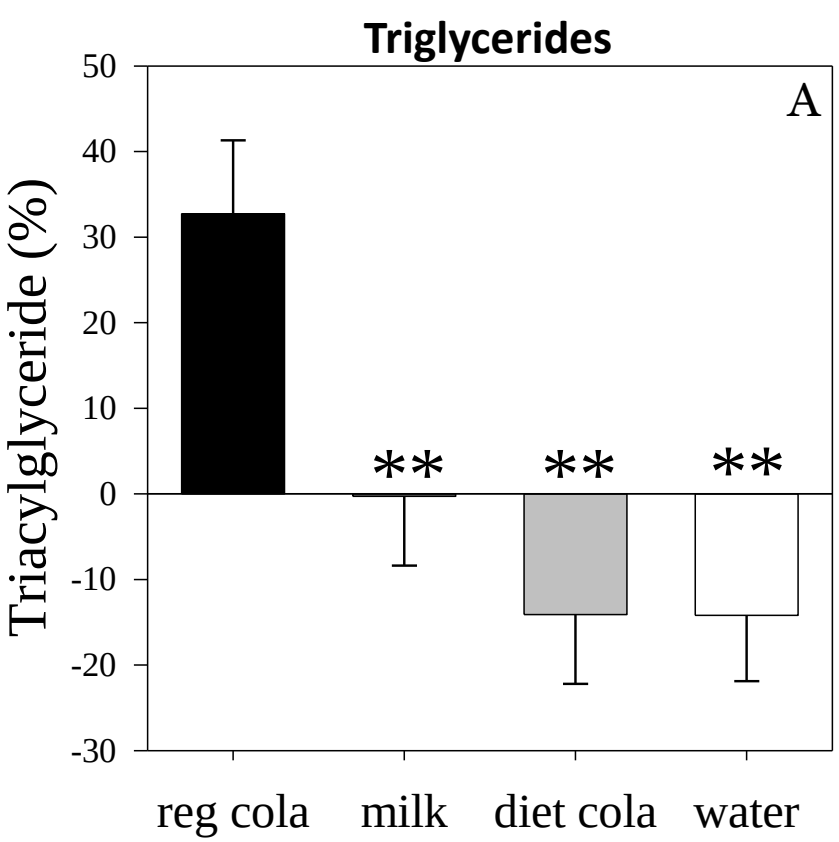
P<0.05

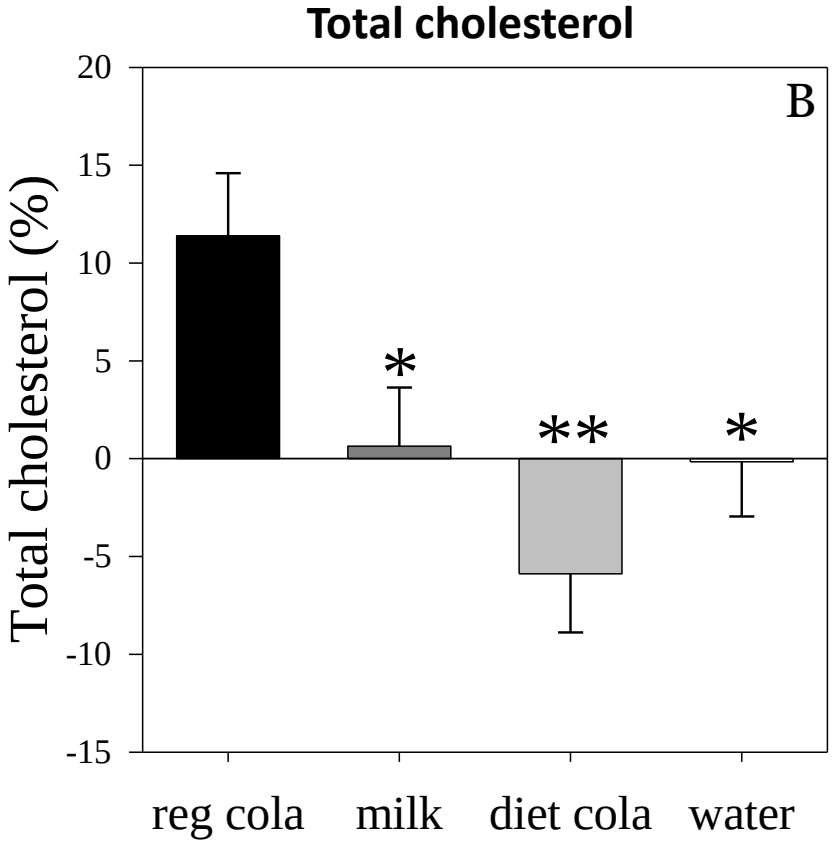
P<0.01

P<0.05

(Maersk et al Am J Clin Nutr 2012)

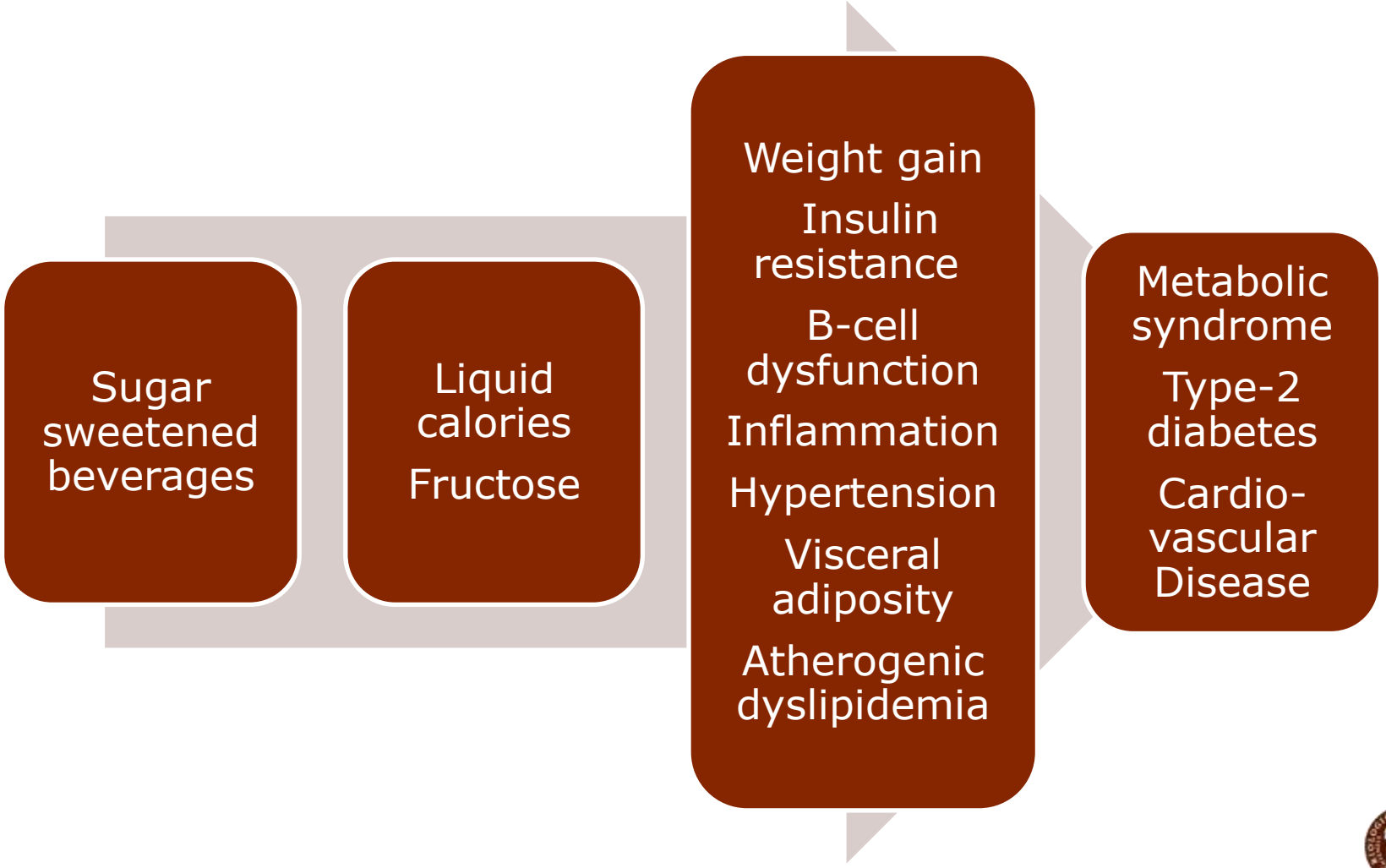
Effects of the beverages on blood lipids





(Maersk et al Am J Clin Nutr 2012)

Mechanisms


Sugar sweetened beverages
Liquid calories
Fructose
Weight gain
Insulin resistance
B-cell dysfunction
Inflammation
Hypertension
Visceral adiposity
Atherogenic dyslipidemia
Metabolic syndrome
Type-2 diabetes
Cardio-vascular Disease

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Conclusions

- Relatively large intake of sugars, especially in the form of liquid sugar, can result in increased energy intake and body weight.
- Sucrose and fructose intake have been linked to development of lipid dysregulation, visceral adiposity, hypertension, inflammation, metabolic syndrome, type-2 diabetes, and coronary heart disease.
- Data from recent longer-term intervention studies point towards a beneficial effect of low calorie sweeteners on energy intake, body weight, liver fat, fasting and postprandial glycemia, insulinemia, and lipidemia compared with sugars.
- Low-calorie sweeteners, especially in beverages, can be a useful aid to maintain reduced energy intake and body weight and decrease risk of type-2 diabetes and CVD compared to sugars.
- Concerning beverages, low-calorie sweeteners is from a metabolically point of view a more healthy choice than sugar, but water is still a neutral and healthy choice.

Thank you for your attention !

Extra...

Safety concerns – Aspartame

EFSA - European Food Safety Authority - completed full risk assessment on aspartame and concluded that it is safe at current levels of exposure (Dec 2013)

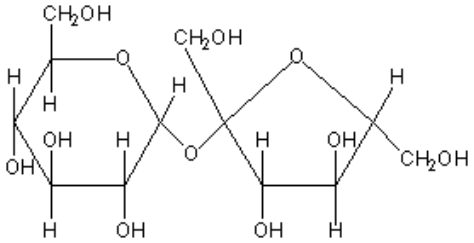
- Aspartame: Sweetener authorised as food additive in the EU.
- Aspartame rapidly and completely hydrolysed in the gastrointestinal tract to phenylalanine, aspartic acid and methanol.
- Panel Conclusion: Aspartame not of safety concern at current exposure or at acceptable daily intake, ADI, 40 mg/kg bw/day.
- Therefore, no reason to revise ADI of aspartame.
- Current exposures to aspartame - and its degradation product DKP (5-benzyl-3,6-dioxo-2-piperazine acetic acid) – are below their respective ADIs.
- The ADI is not applicable to PKU patients

EFSA Journal 2013;11(12):3496

Taste - Sweetness

- Sugar tasted by sugar receptors in mouth and stomach. Possibly also taste receptors in the intestine!

- Sweetness of a carbohydrate measured relatively to sucrose (saccharose or table sugar) - set at 100



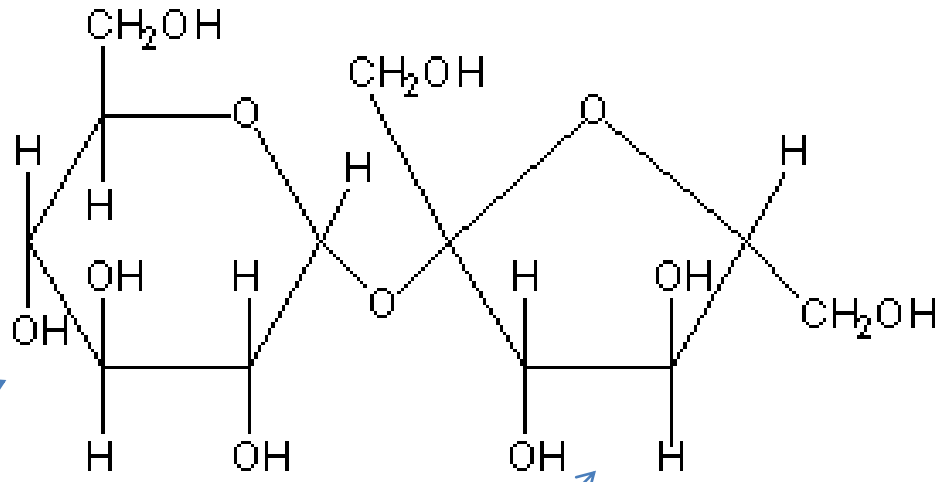
- Fructose: Sweetness of 173
- High-Fructose Corn Syrop (HFCS): 120

- Aspartame: 200 times sweeter than sucrose

- Dried leaves from *Stevia rebaudiana* relative sweetness 200-300 that of sucrose

- Amount of non-caloric sweeteners needed to obtain sweet taste very small compared with sucrose

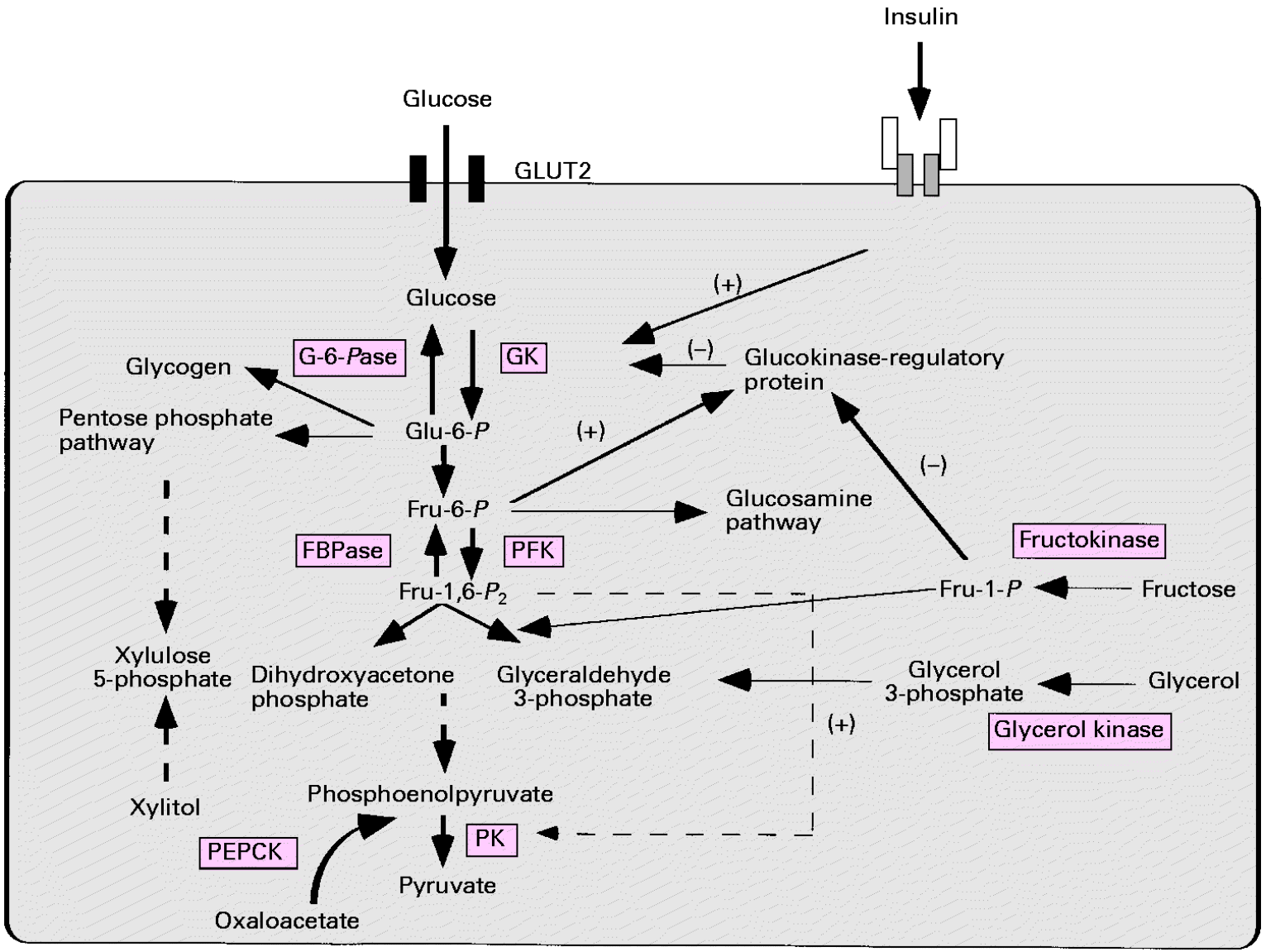
Sucrose



Glucose

FRUCTOSE

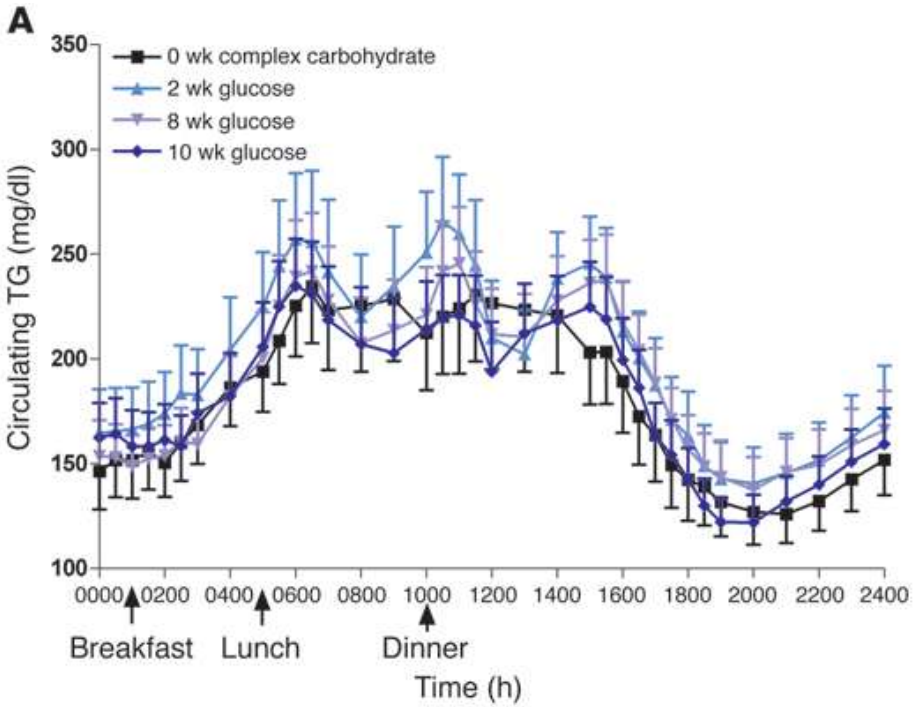
Carbohydrate metabolism and regulation in the liver

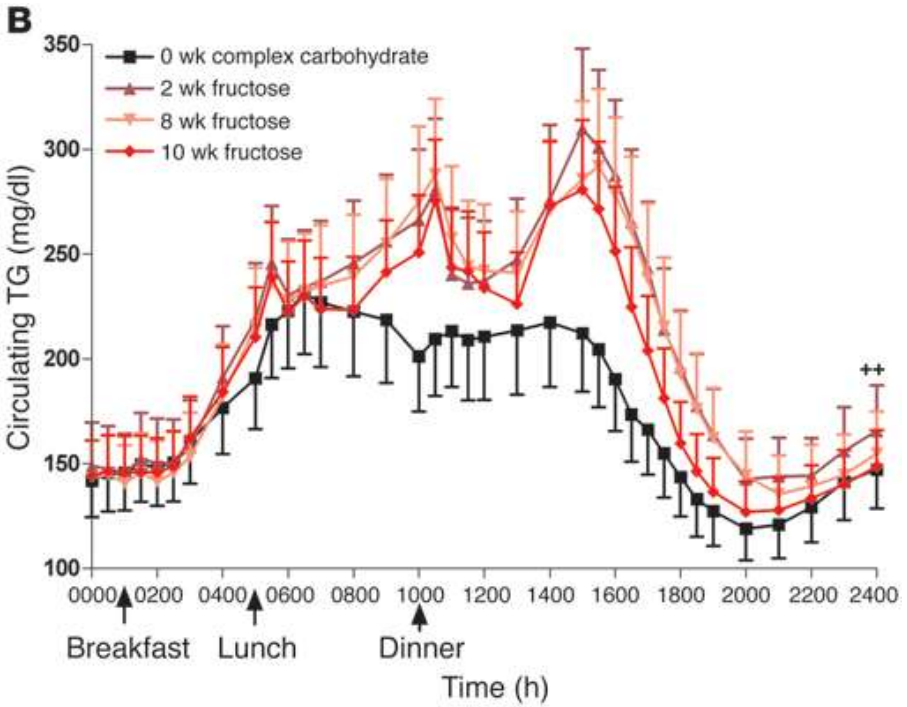


24-hour circulating triglyceride concentrations increased after fructose (B) compared with glucose (A) before and after 2, 8, and 10 weeks

Glucose

Fructose





J Clin Invest 2009;119:1322

Intake of added sugars should be kept below 10 E%.

- Limitation of the intake of added sugars from particularly sugar-sweetened beverages and sugar-rich foods is recommended in order to reduce the risk for type 2 diabetes, weight gain and dental caries.

- A limitation of the intake of added sugars is also necessary to ensure an adequate intake of essential nutrients and dietary fibre, especially in children and adults with a low energy intake.

Relative Risk of Type 2 Diabetes According to Frequencies of Sugar-Sweetened Beverage Consumption in 91 249 Women.

Table 3. Relative Risk of Type 2 Diabetes According to Frequencies of Sugar-Sweetened Beverage Consumption in 91 249 Women

	Sugar-Sweetened Soft Drink Intake				*P* Value for Trend
	<1/mo	1-4/mo	2-6/wk	≥1/d	
All sugar-sweetened soft drinks					
Cases	368	163	95	115	
Person-years	381 275	188 501	80 086	66 438	
Age-adjusted RR (95% CI)	1.00	0.93 (0.78-1.12)	1.32 (1.06-1.66)	1.98 (1.60-2.44)	<.001
Multivariate-adjusted RR (95% CI)*	1.00	1.06 (0.87-1.28)	1.49 (1.16-1.91)	1.83 (1.42-2.36)	<.001
Sugar-sweetened cola					
Cases	403	142	96	100	
Person-years	420 598	166 656	75 778	53 267	
Age-adjusted RR (95% CI)	1.00	0.92 (0.76-1.12)	1.44 (1.16-1.81)	2.14 (1.72-2.67)	<.001
Multivariate-adjusted RR (95% CI)*	1.00	0.99 (0.80-1.23)	1.56 (1.21-2.02)	1.87 (1.43-2.45)	<.001
Fruit punch					
Cases	589	85	38	29	
Person-years	525 780	124 932	45 958	19 630	
Age-adjusted RR (95% CI)	1.00	0.95 (0.73-1.24)	1.24 (0.86-1.77)	2.31 (1.55-3.45)	<.001
Multivariate-adjusted RR (95% CI)*	1.00	0.90 (0.68-1.18)	1.15 (0.79-1.66)	2.00 (1.33-3.03)	.001

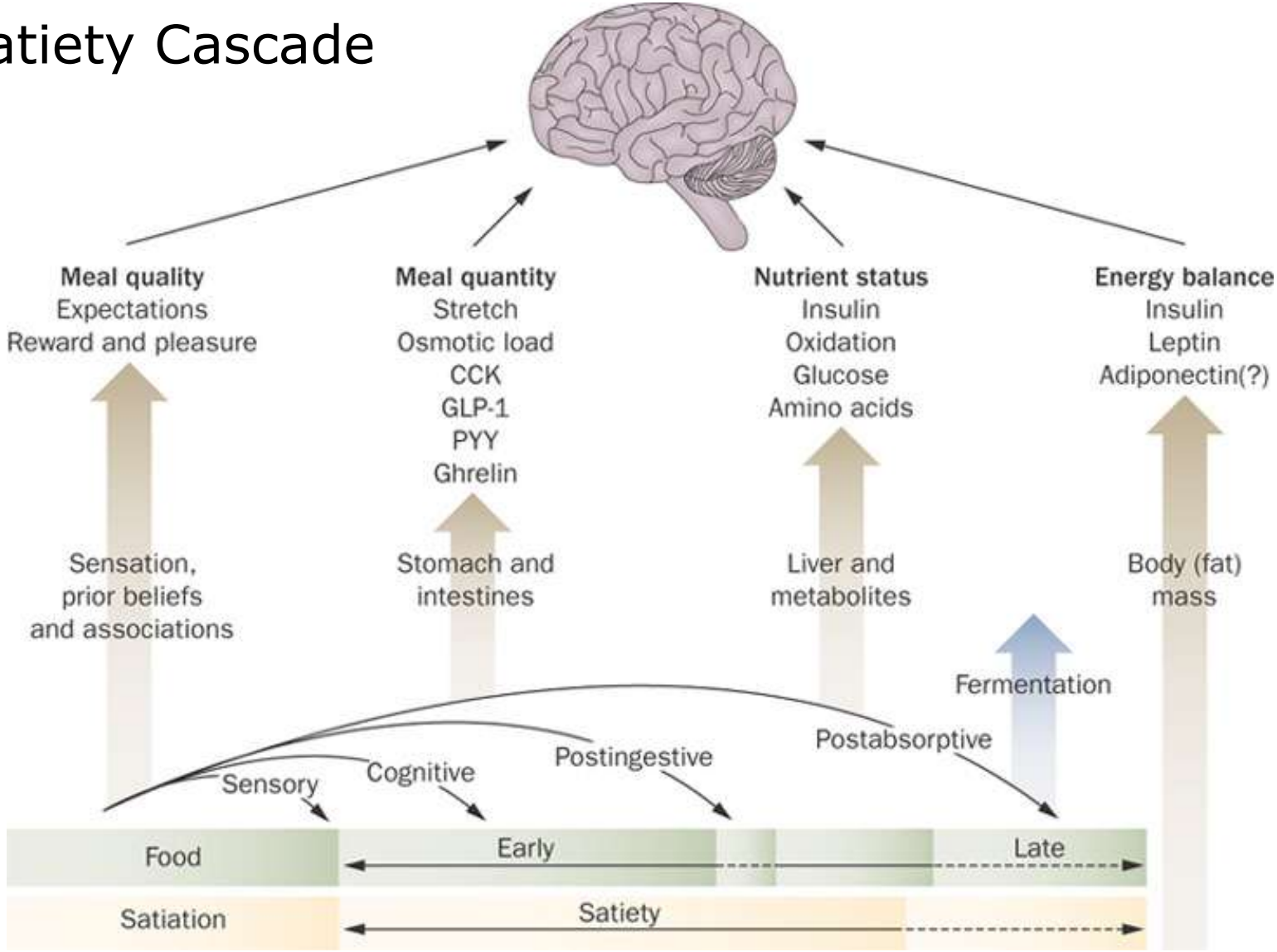
SSSD

Abbreviations: CI, confidence interval; RR, relative risk.

*Relative risks are adjusted for age; alcohol intake (0, 0.1-4.9, 5.0-9.9, or ≥10 g/d); physical activity (quintiles); family history of diabetes; smoking (never, past, or current); pos menopausal hormone use (never or ever); oral contraceptive use (never, past, or current); intake (quintiles) of cereal fiber, magnesium, *trans*-fat, and ratio of polyunsaturated t saturated fat; and consumption of sugar-sweetened soft drinks, diet soft drinks, fruit juice, and fruit punch (other than the main exposure, depending on model).

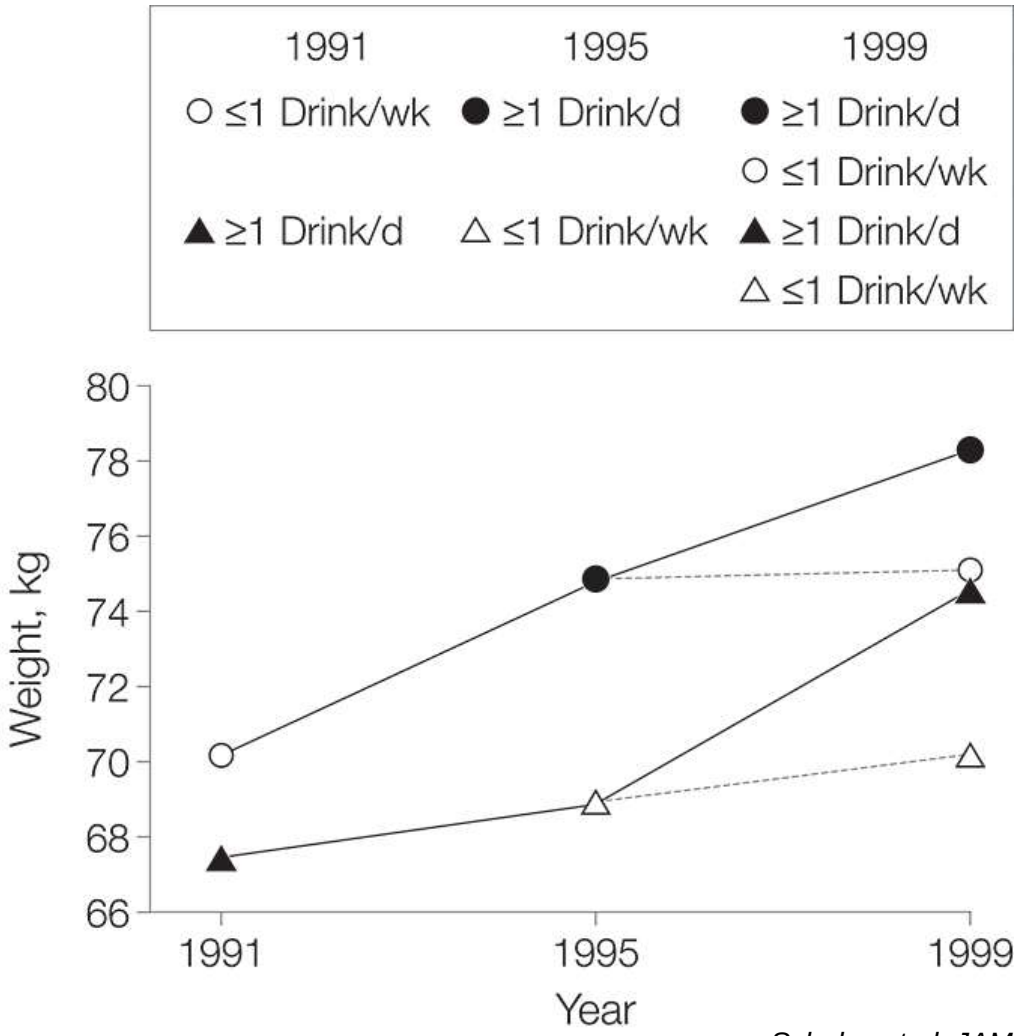
Schulze, M. B. et al. JAMA 2004;292:927-934

Satiety Cascade



(Blundell)

Mean body weight in 1991, 1995, and 1999 according to trends in Sugar-Sweetened Soft Drink Consumption in 1969, Women Who Changed Consumption From 1991 to 1995 and either changed or maintained Level of Consumption Until 1999.
Low and high intakes were defined as 1 drink or less per wk and 1 drink or more per d, resp.



Schulze,et al. JAMA 2004;292:927-934