Original Articles/นิพนธ์ต้นฉบับ

Sugar-sweetened Beverage Intake and Diabetes Risk: A systematic review and meta-analysis

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Abtract

Background: The consumption of sugar-sweetened beverages has been increasing continuously worldwide. Drinking sugar-sweetened beverages has been suspected to be a risk factor of developing diabetes mellitus but results from previous were conflicting. Therefore, we performed a systematic review and meta-analysis aiming to estimate the effect size of sugar-sweetened beverages on the risk of developing diabetes mellitus.

Methods: Medline and Scopus databases were comprehensively searched for relevant studies. Two reviewers selected studies based on titles and abstracts. Observational studies published in English were selected, if they met all of these following criteria: 1) considered sugar-sweetened beverages as an interested risk factor, 2) measured the outcomes as having or not having diabetes mellitus, 3) provided adequate data for pooling the effect size. Odds ratios or relative risks of having type 2 diabetes mellitus of each study were pooled by using random effect model, if heterogeneity between studies presents. If not, the fixed effect model with inverse variance method was used. Sources of heterogeneity were assessed by fitting co-variables (such as age of patient, study design, assessment method) one by one in meta-regression.

Results: Eight out of 1439 studies were finally eligible in our review. Compared with never or seldom drinking, drinking sugar-sweetened beverages equal or more than one serving per week significantly increased risk of having diabetes mellitus with pooled odds ratio of 1.30 (95% CI: 1.05, 1.62). Pooling odds ratio adjusted with body mass index still showed the significant risk effect of drinking sugar-sweetened beverages equal or more than one serving per week with pooled adjusted odds ratio of 1.25 (95% CI: 1.19, 1.31).

Conclusion: Results from our study suggested that drinking sugar-sweetened beverages equal or more than one serving per week significantly increased risk of having diabetes mellitus. This risk effect still persisted even after adjusting the effect of body mass index.

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Background and Rationale

Nowadays, the intake of added sugars has been increasing with comprising of 15.8% of total energy intake in American population. The largest source of these added sugars is sugar-sweetened beverages which account for 47% of total added sugars in diet[1]. The sugar-sweetened beverages provide high energy which has 150 kcal for a 12 oz serving and drinking 12 oz of sugar-sweetened beverages per day can lead to a weight gain of 6.75 kg in 1 year[2]. Therefore, sugar-sweetened beverages have been believed to be the cause of obesity and related health outcomes. This belief leads to the prohibition of sugar-sweetened beverages sales in many countries in USA and Western Europe[3]. However, at the present time, there has not had sufficient evidence to support the negative effect of sugar-sweetened beverages on the health outcomes. Thus, actions taken to decrease sugar-sweetened beverages consumption may not warrant the benefit for the public health. Although, there have been a number of reviews[4-6] and meta-analyses[3,7,8] of sugar-sweetened beverages and health outcomes such as obesity, diabetes mellitus, most of them are not systematic reviews and the methodological quality of previous reviews are still poor9. Therefore, we would like to perform the systematic review and meta-analysis of sugar-sweetened beverages on type 2 diabetes mellitus risk.

Objectives

- To systematically review the effect of sugar-sweetened beverages on risk of type 2 diabetes mellitus
- To pool the effect size of sugar-sweetened beverages on risk of type 2 diabetes mellitus

Methods

Search strategy

Two databases (Medline and Scorpus) were searched for relevant studies published from year 1949 to present. Search terms and search strategies of these two databases are described as follows:

For Medline:

("soft drink*"[All Fields] OR "sweetened beverage*"[All Fields] OR "soda"[All Fields]) AND ("diabetes mellitus"[All Fields] OR "obesity"[All Fields] OR "overweight"[All Fields] OR "weight gain"[All Fields] OR "metabolic syndrome"[All Fields] OR "cardiovascular disease"[All Fields] OR "myocardial infarction"[All Fields] OR "stroke"[All Fields] OR "cerebrovascular"[All Fields] OR ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields])) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang]))

For Scorpus:

(((TITLE-ABS-KEY("soda")) OR (TITLE-ABS-KEY-AUTH("soft drink*")) OR (TITLE-ABS-KEY-AUTH("sweetened beverage*")))) AND (((TITLE-ABS-KEY-AUTH("stroke")) OR (TITLE-ABS-KEY-AUTH ("cerebrovascular")) OR (TITLE-ABS-KEY-AUTH(cancer)) OR (((TITLE-ABS-KEY-AUTH("diabetes mellitus")) OR (TITLE-ABS-KEY-AUTH("obesity")) OR(TITLE-ABS-KEY-AUTH("overweight")) OR (TITLE-ABS-KEY-AUTH ("weight gain")) OR (TITLE-ABS-KEY-AUTH("metabolic syndrome")) OR (TITLE-ABS-KEY-AUTH("weight gain")) OR (TITLE-ABS-KEY-AUTH("cardiovascular disease")) OR (TITLE-ABS-KEY-AUTH("myocardial infarction")))))) AND (LIMIT-TO(LANGUAGE, "English") OR LIMIT-TO(LANGUAGE,"Spanish") OR LIMIT-TO(LANGUAGE, "English") ORLIMIT-TO(LANGUAGE, "Spanish"))

Reference lists of included studies and previous systematic reviews were also explored for relevant studies.

Study selection

Two reviewers selected studies based on titles and abstracts. If the decision could not be made, full articles were retrieved. Agreement and disagreement of selecting studies among two reviewers were assessed using kappa statistic. Disagreement between two reviewers were resolved by consensus and discussion with third party.

Inclusion criteria

Observational studies (such as case-control or cohort study), or experimental studies published in English or Spanish were selected, if they met all of these following criteria:

1. Study that considered soft drinks or other sugar sweetened beverages as an interested risk factor
2. Study that measured the outcomes as having or not having type 2 DM
3. Study that provided adequate data for extraction and pooling such as mean and standard deviation for continuous outcomes and frequency or number of patients in each group for binary outcomes

Data extraction

Demographic data of patients (such as age, sex, activity level), type of sugar-sweetened beverages (such as carbonated soft drinks, fruit juices or other sugar-sweetened beverages), study design, study setting, and method to assess soft drink intake (such as self-reports, or observations) were extracted independently by two reviewers using standardized data extraction form. Disagreement between two reviewers was discussed with the third party.

The outcomes

The outcome of interests was risk of type 2 DM. The patient were diagnosed with type 2 DM if their fasting blood sugar is higher than 126 mg/dl or HbA1C was higher than 6.5%.

Statistical analysis

Odds ratios or relative risks of type 2 diabetes mellitus of each study were pooled by using random effect model, if heterogeneity between studies presented. If not, the fixed effect model with inverse variance method was used. Sources of heterogeneity were assessed by fitting co-variables (such as age of patient, study design, assessment method) one by one in meta-regression. All statistical analyses were performed using STATA soft ware program version 12.

Results

Fifthteen studies were eligible for reviewing full papers of diabetic outcomes. Four studies10-13 were excluded because they did not concern soft drinks as the interested risk factors and one study14 was ineligible because the outcome of that study was not diabetes mellitus. Two studies[15,16] had insufficient data for pooling and then were excluded from the review. Thus, eight studies[17-24] were finally eligible in our review.

Baseline characteristics of included studies were described in table 1. The designs of most studies were cohort, except one study was cross-sectional[22]. Six studies were conducted in USA, while one study[22] was conducted in Finland and only one study[19] was done in Asian country. Mean age of study's participants ranged from 31 to 62 years and mean body

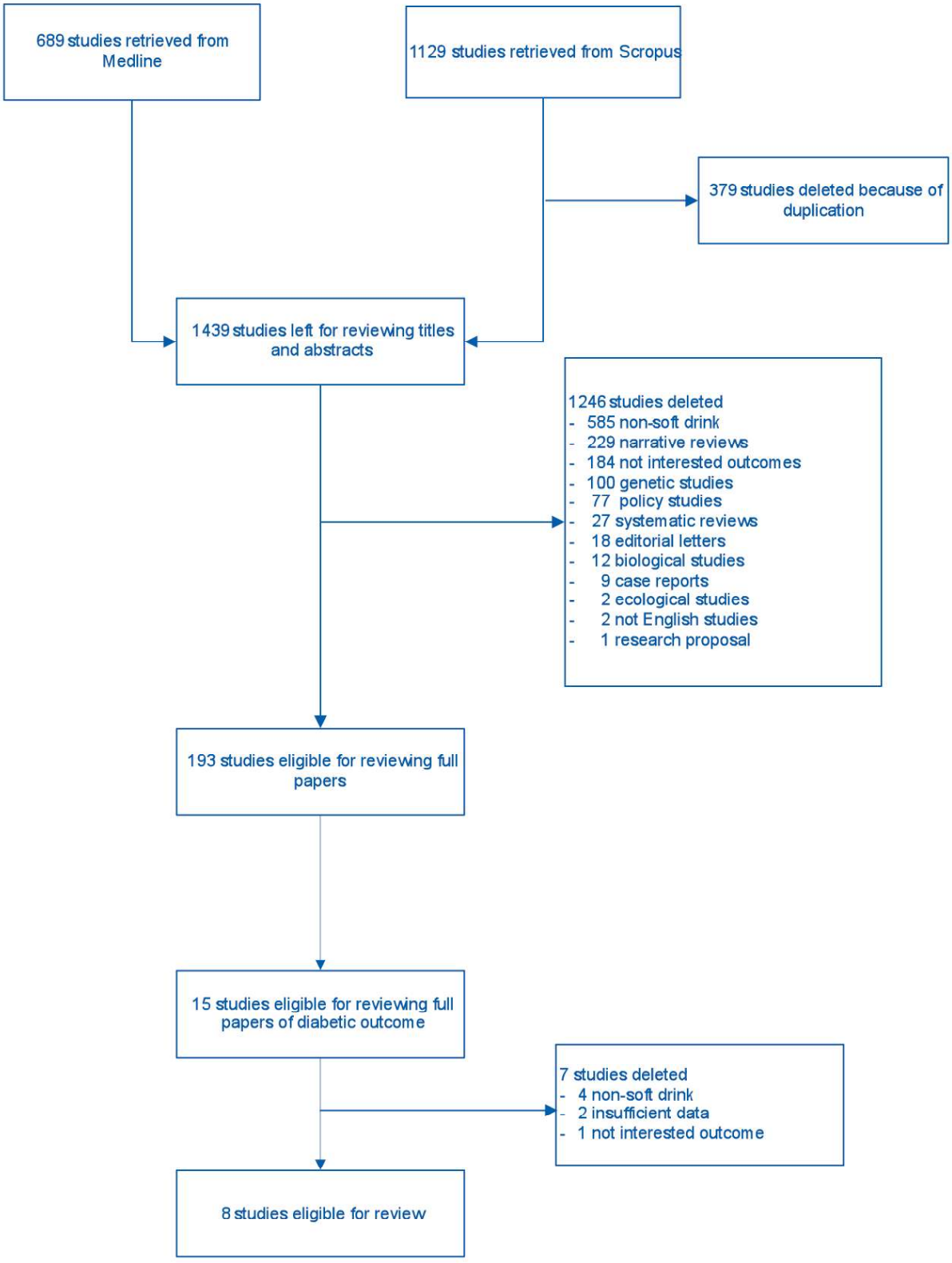

Figure 1. *Flow chart of selecting studies*

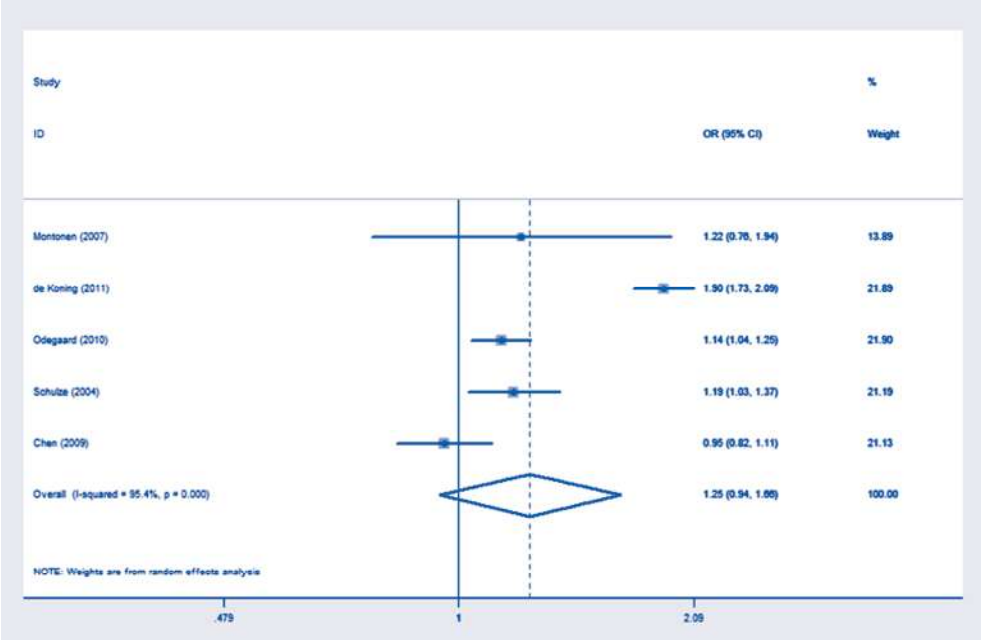

Figure 2. *Pooled odds ratio of drinking soft drink ≥1 serving/month vs non or seldom drinking*

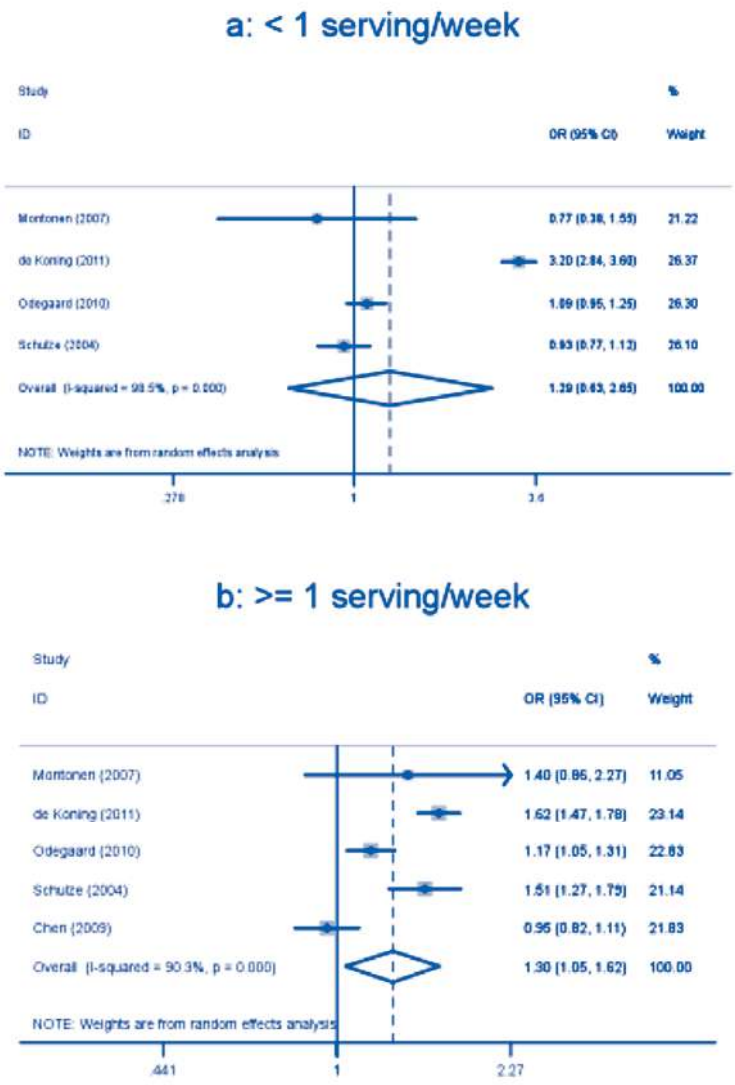

Figure 3. *Poole odds ratio of drinking soft drink according to dose intake*

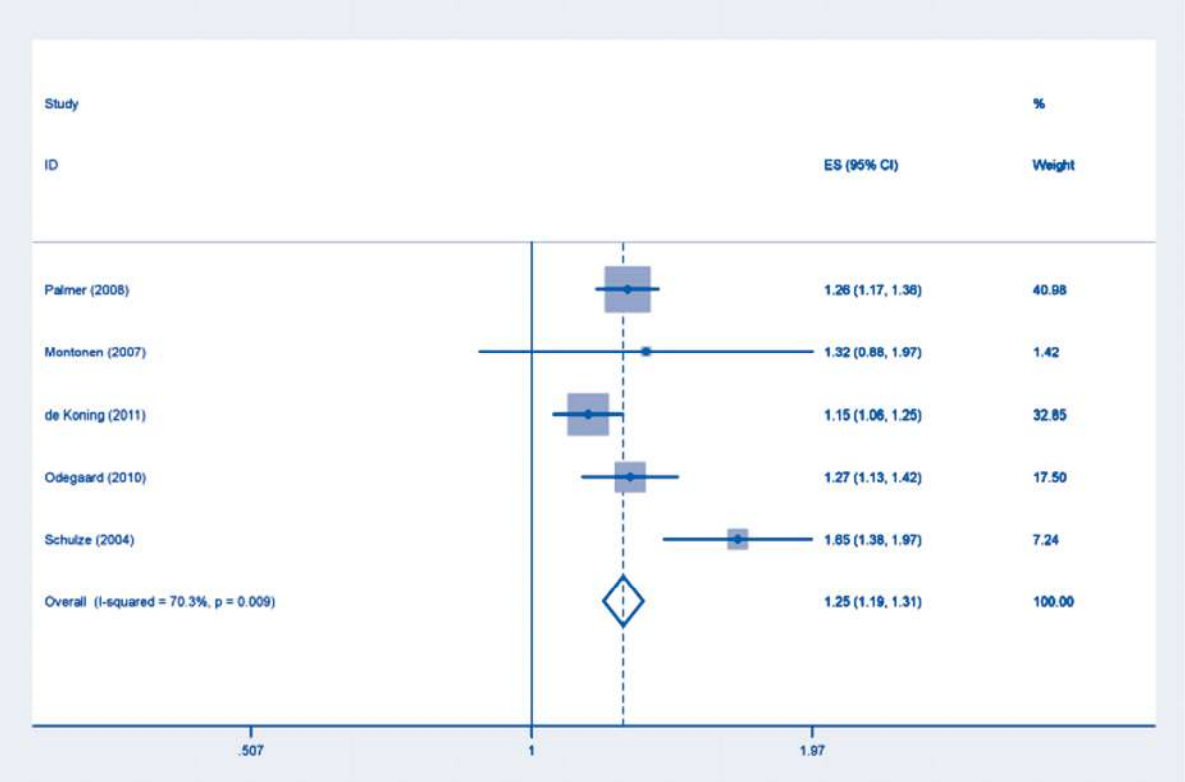

Figure 4. *Pooled adjusted odds ratio of drinking soft drink*

mass index were varied from 23 to 28 kg/m^2. Three studies were done in only female population, while one study was conducted in only male population. Percentage of smoking in study's participant was ranged from 8.8 to 32.5%.

Sugar-sweetened beverages

Drinking sugar-sweetened beverages ≥1 serving per month vs never or seldom drinking

For seven studies that measured the effect of sugar-sweetened beverages on diabetic risk, six studies[13,17-19,22,24] reported the crude odds ratio, while one study[20] reported only adjusted odds ratio of drinking sugar-sweetened beverages and diabetes risk and thus was excluded for pooling the crude effect size. The reference groups in most of the included six studies were classified as never drinking or drinking sugar-sweetened beverages less than one serving per month, except one study[24] that defined the reference group as drinking sugar-sweetened beverages less than one cup per day. Thus, this study was excluded from pooling. The odds ratios (OR) of five studies were presented in table 2. Compared with never or seldom drinking, drinking soft drink equal or more than one serving per month increased 25% risk of developing diabetes mellitus with the pooled odds ratio equal to 1.25 (95% CI: 0.94, 1.66) (see figure 2 and table 2). However, this effect did not reach statistical significance.

Dose response relationship

For exploring the effect of dose response relationship, we divided the category of drinking sugar-sweetened beverages into three categories (i.e., category 1 = never or seldom drinking, category 2 = drinking equal or more than one serving per month but less than one serving per week, category 3 = drinking equal or more than one serving per week). Compared with never or seldom drinking, the risk of de-

Table 1. Baseline characteristics of included studies

Author	Year	Study design	Setting	Age (year)	BMI	% smoking	Sex (% male)	No. of DM	No. of non DM
Schulze[21]	2004	Cohort	USA	36.2 (4.6)	24.4 (5)	10.3	0	741	90508
Paynter[24]	2006	Cohort	USA	54	27.2	NA	NA	1437	10767
Palmer[20]	2008	Cohort	USA	38.5	27.6	15.9	0	2713	41347
Montonen[22]	2007	Cross-sectional	Finland	51.9 (8.0)	26.5 (4.0)	32.5	53.1	177	4127
De Koning[18]	2011	Cohort	USA	NA	25.5 (3.3)	9.3	100	2680	37709
Odegaard[19]	2010	Cohort	Singapore	55.2	23.0	27.1	57.2	2273	41307
Chen[17]	2009	Cohort	USA	31.5 (3.3)	23.4	8.8	0	760	12715
Nettleton[23]	2009	Cohort	USA	61.7 (10.5)	27.9 (5.4)	14.3	47.4	413	4598

Table 2. Pooled OR of regular and non-regular drinking soft drink

Author	Year	Drinking ≥ 1 serving/month		Drinking < 1 serving/month		Odds ratio (95% CI)
		DM	Non-DM	DM	Non-DM	
Montonen[22]	2007	66	1553	25	716	1.22 (0.76, 1.95)
De Koning[18]	2011	2094	24620	586	13089	1.90 (1.73, 2.09)
Odegaard[19]	2010	658	10862	1615	30445	1.14 (1.04, 1.25)
Schulze[21]	2004	373	41673	368	48835	1.19 (1.03, 1.37)
Chen[17]	2009	437	7454	323	5261	0.96 (0.82, 1.11)
Pooled OR						1.25 (0.94, 1.66)

veloping diabetes mellitus minimally increased when the amount of drinking sugar-sweetened beverages increased. The pooled OR of category 2 is equal to 1.29 (95% CI: 0.63, 2.65) (see figure 3a), while pooled OR of category 3 is equal 1.30 (95% CI: 1.05, 1.62) (see figure 3b). However, only pooled OR of category 3 reaches statistical significance that means drinking sugar-sweetened beverages equal or more than one serving per week significantly increased 30% risk of developing diabetes mellitus, when compared with never or seldom drinking.

Pooled adjusted odds ratio

Since drinking sugar-sweetened beverages is related with increasing weight and obesity which are the risk factors of diabetes mellitus, the risk effect of drinking sugar-sweetened beverages found in our review may be confounded with obesity and overweight. Thus in order to eliminate the confounding effect of obesity and overweight, we pooled the odds ratios that adjusted for body mass index. Five studies reported the odds ratios adjusted for body mass index. Due to the lack of significant effect of drinking soft drink equal or more than one serving per month but less than one serving per week on diabetes risk only the odds ratio of drinking soft drink equal or more than one serving per week were pooled.

Pooling adjusted odds ratio from the five studies[18-22] showed the significant risk effect of drinking sugar-sweetened beverages equal or more than one serving per week on developing diabetes mellitus with pooled OR = 1.25 (95% CI: 1.19, 1.31) (see figure 4). However the effect of drinking sugar-sweetened beverages modestly decreased when adjusted with body mass index. The pooled adjusted OR still reaches statistical significance that means drinking sugar-sweetened beverages is independently associated with diabetes mellitus.

Discussion

Our study found that drinking sugar-sweetened beverages equal or more than one serving per week significantly increased risk of diabetes around 30%, when compared to never or seldom drinking. Drinking sugar-sweetened beverages equal or more than one serving per month but less than 1 serving per week also increased risk of diabetes around 29%, when compared to never or seldom drinking, but this risk effect did not reach statistical significance.

Results of our study is consistent with the results from previous meta-analysis[8] that found a significant association between sugar-sweetened beverages consumption and risk of type 2 diabetes. This study compared extreme quartiles of sugar-sweetened beverages intake, none or <1 serving/month with ≥1 or 2 servings/day and showed the pooled relative risk of 1.26 (95% CI: 1.12-1.41). In addition, results from large prospective cohort studies also showed the significant risk effect of sugar-sweetened beverages intake on diabetes risk. Results from the E3N study[25], including 66,118 women with 1,369 incidences of diabetes, found that women reporting consumption > 359 ml of sugar-sweetened beverages/week were significantly higher risk of developing diabetes than non-consuming women with hazard ratio of 1.34 (95% CI: 1.05, 1.71). Moreover, results from European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct study[26] also demonstrated the higher risk of diabetes in sugar-sweetened soft drink consumption than non-consumption. All of these findings confirm the hazard of regular sugar-sweetened beverages intake on the probability of developing diabetes in the future.

However, the effect of sugar-sweetened beverages on diabetes risk may be mediated through obesity. Sugar-sweetened beverages have high added sugar content that leads to positive energy balance and weight gain. Findings from well-conducted cohort studies show the consistent positive associations between sugar-sweetened beverage intake and weight gain and obesity in both children and adults[27]. However, sugar-sweetened beverages usually added sucrose (50% glucose and 50% fructose) combined with high-fructose corn syrup. These kinds of carbohydrate are rapidly absorbed and then raise blood glucose and insulin concentrations rapidly and dramatically[28]. Thus, sugar-sweetened beverages are considered as a one kind of diet with high glycemic index and contribute to a high dietary glycemic load. High glycemic index diets can induce glucose intolerance and insulin resistance. In addition, these diets can increase level of inflammatory biomarkers such as C-reactive protein, which are link to type 2 diabetes risk. Therefore, apart from risk mediated through obesity, sugar-sweetened beverages intake is independently associated with diabetes mellitus. This independent association is approved by our analysis that pooling the adjusted OR with body mass index. Pooled adjusted odds ratio also showed the signifi-

cant risk effect of sugar-sweetened beverage intake on diabetes risk with pooled OR = 1.25 (95% CI: 1.19, 1.31).

In conclusion, our study showed the significant risk effect of sugar-sweetened beverage intake on diabetes risk even adjusted for obesity effect.

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