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The Effect of Dairy Products Subgroups Consumption on the Risk of Diabetes: A Systematic Review and Meta-Analysis

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Abstract

Context: There is no global consensus on the issue that what dairy subgroups can affect diabetes; thus, this meta-analysis aims to shed light on this matter.
Evidence Acquisition: Main electronic databases such as Web of Science, Scopus, Science Direct, and PubMed, updated to March 2016, were investigated. All original articles from Prospective Cohort and Case-Cohort studies examining the relationship between dairy products subgroups consumption and the risk of diabetes were brought under consideration without any restrictions on age, gender, language, race, and publication year. To validate this study, the STROBE checklist was used. The indices of relative risk and rate ratio were reported using Random Effect Model.
Results: Out of 1391 articles, 13 (covering 421,421 people) were introduced to the current meta-analysis. The findings showed that the consumption of yoghurt and cream has preventive effects on the risk of diabetes: Yogurt: relative risk = 0.74 (95% CI: 0.65, 0.84), rate ratio = 0.66 (95% CI: 0.63, 0.70); Cream: rate ratio = 0.86 (95% CI: 0.82, 0.91). Although the relative risk index showed that milk consumption diminishes the risk of diabetes by 11%, this relationship was not statistically significant: Milk: relative risk = 0.89 (95% CI: 0.82, 0.97), rate ratio = 1.07 (95% CI: 0.93, 1.24). This study also indicated that intake of low-fat milk, ice cream, and cheese has no impact on the incidence of diabetes: Cheese: relative risk = 0.92 (95% CI: 0.82, 1.04), rate ratio = 1.04 (95% CI: 0.93, 1.16); Low-fat milk: rate ratio = 0.93 (95% CI: 0.76, 1.14); Ice cream: rate ratio = 1.05 (95% CI: 0.93, 1.18).
Conclusions: Due to the scarcity of studies related to some dairy subgroups, it is not possible to make a final judgment about their effects on the risk of diabetes; therefore, more studies need to be conducted on this issue.

Keywords: Dairy Products, Diabetes Mellitus Type 2, Cohort Studies, Meta-Analysis

1. Context

Diabetes is a metabolic disease and a major health problem (1). Nowadays, this latent disease is warningly breaking out around the world (2). According to the projection of world health organization (WHO), there will have been 300 million diabetics by 2025 (3). Diabetes foments macro- and micro-vascular disorders culminating in early morbidity or mortality (4). These factors incur enormous health costs on people, health experts, and health systems. Considering this issue, it is necessary to come up with preventive strategies against diabetes (5).

Recent studies have shown that changes in the diet can prevent diabetes or postpone its incidence (6). The Finnish diabetes prevention study (DPS) was the first randomized trail research which showed relative risk reduction can get to 60% via diet consultation and doing physical exercises. Nowadays, other studies in various countries on different ethnic groups have also affirmed this result indicating that this risk reduction could be in fluctuation between 30 and 60% (7).

The main on the dietary list is dairy products; however, there have been some contradictory results. Some studies showed that dairy products, because of having whey and fatty acids, can preclude this disease (8), but other researches made it evident that dairies play no role in regard to diabetic issues (9).

Seemingly, the main reason for this difference is some componential parts of dairy products which can change the influence pattern of diaries on diabetes (6). Some recent studies in Europe about the relationship of dairy products subgroup and risk of diabetes yielded different results: fermented dairy, especially yoghurt, have protective effects against diabetes, while milk or cheese consumption is unrelated to diabetes (10, 11). Other studies showed that cheese protects against diabetes, but milk does not (10, 12). As it is not really clear that which dairy subgroups affect diabetes, it seems necessary to carry out a systematic review and meta-analysis to shed light on this matter.

Searching through databases of PubMed (February1992 to March2016), Science Direct (April 1870 to December 2015), Scopus (May 1986 to March 2016), and Web of Science (April 1870 to March 2016) was done by means of keywords ("dairy" OR "milk" OR "cheese" OR "butter" OR "cream" OR "yogurt" OR "yoghurt" AND "NIDDM" OR "T2DM" OR "diabetes" AND "follow-up" OR "cohort" OR "observational"). To achieve more texts, we took advantage of cited studies and also initiated contacts with the authors of similar papers.

1.1. Criteria for Including Study

All original articles from Prospective Cohort and Case-Cohort studies examining the relationship between the consumption of dairy products subgroups and the risk of diabetes regardless of limitations in age, gender, language, race, and publication year were brought under consideration. Those researches examining the relationship between dairies consumption and death were excluded. In addition, out of multiple publications based on the same population studies, just those were included that had more dairy products subgroups. Just, standard healthy people were qualified to enter this study, thus those who suffered from diabetes in baseline population were excluded from the study. Our main focus was on dairy products and their effects on the risk of diabetes.

1.2. Data Collection and Validity Assessment

Two researchers (M. KH and Z.Ch), independently, took the responsibility of choosing the articles to evaluate the validity of them; when a difference in opinions occurred, the difference would be settled by consulting a third researcher (M. R). The authors' names, the journals' names, and their findings were not blind to the mentioned researchers. The inter-authors reliability based on kappa statistics was 83%.

The extracted variables to analyze the data contained corresponding author's surname, title of the study, publication year, the setting of the study, people's age at the beginning of the study, people's gender, population of interest, the period of following-up, type of dairies, the diabetes cases, the potentially exposed people to diabetes, and the number-time of those exposed to diabetes.

To evaluate the validity of studies, seven items on the STROBE checklist were selected: careful reference to the framework of the study, following-up period, inclusion and exclusion criteria, definition of corollaries and the relevant criteria, definition of exposure and its measurement method, number of included and excluded people at each stage, and population of interest. The studies in compliance with all seven items on the STROBE checklist were classified as high-quality studies, and those complying with six items were of middle quality. The studies that did not conform to two or more items on STROBE checklist were classified as low-quality studies.

1.3. Measures of Exposure Effect

In order to show the relationships, the indices of relative risk and rate ratio were utilized with a confidence interval of 95%. In this study, relative risk was defined as the risk-rate of diabetes in people with the highest rate of consumption of dairy products in proportion to the risk-rate of diabetes in those with the lowest rate of consumption of dairy products; rate ratio was defined as diabetes cases by the years one was exposed to the risk of diabetes among people with the highest rate of consumption of dairy products in proportion to diabetes cases by the years one was exposed to the risk of diabetes among people with the lowest rate of consumption of dairy products.

1.4. Statistical Analysis

Meta-analysis was performed to obtain summary measure with 95% confidence interval (CI). Stata 11 (StataCorp, College Station, TX, USA) was employed for data analysis. The results were reported via random effect models.

1.5. Heterogeneity, Publication Bias and Sensitivity Analyses

To assess the data heterogeneity in statistical terms, the chi2 (χ^2) test was used, and to evaluate heterogeneity quantitatively, I^2 statistical test came to use. These tests were interpreted in terms of Higgins classification: 25% for low heterogeneity, 50% for middle heterogeneity, and 75% for high heterogeneity. Funnel figure was used to investigate the publication bias, and Begg's test and Egger's test were utilized to measure it statistically. Sensitivity analysis was used in order to exclude any study which would make a remarkable difference in the estimation of the current study compared to when that study was not included (Figure 1).

2. Results

2.1. Study Selection and its Characteristics

After 1391 article being studied, 448 of them were excluded because of repetitiveness; the remaining 943

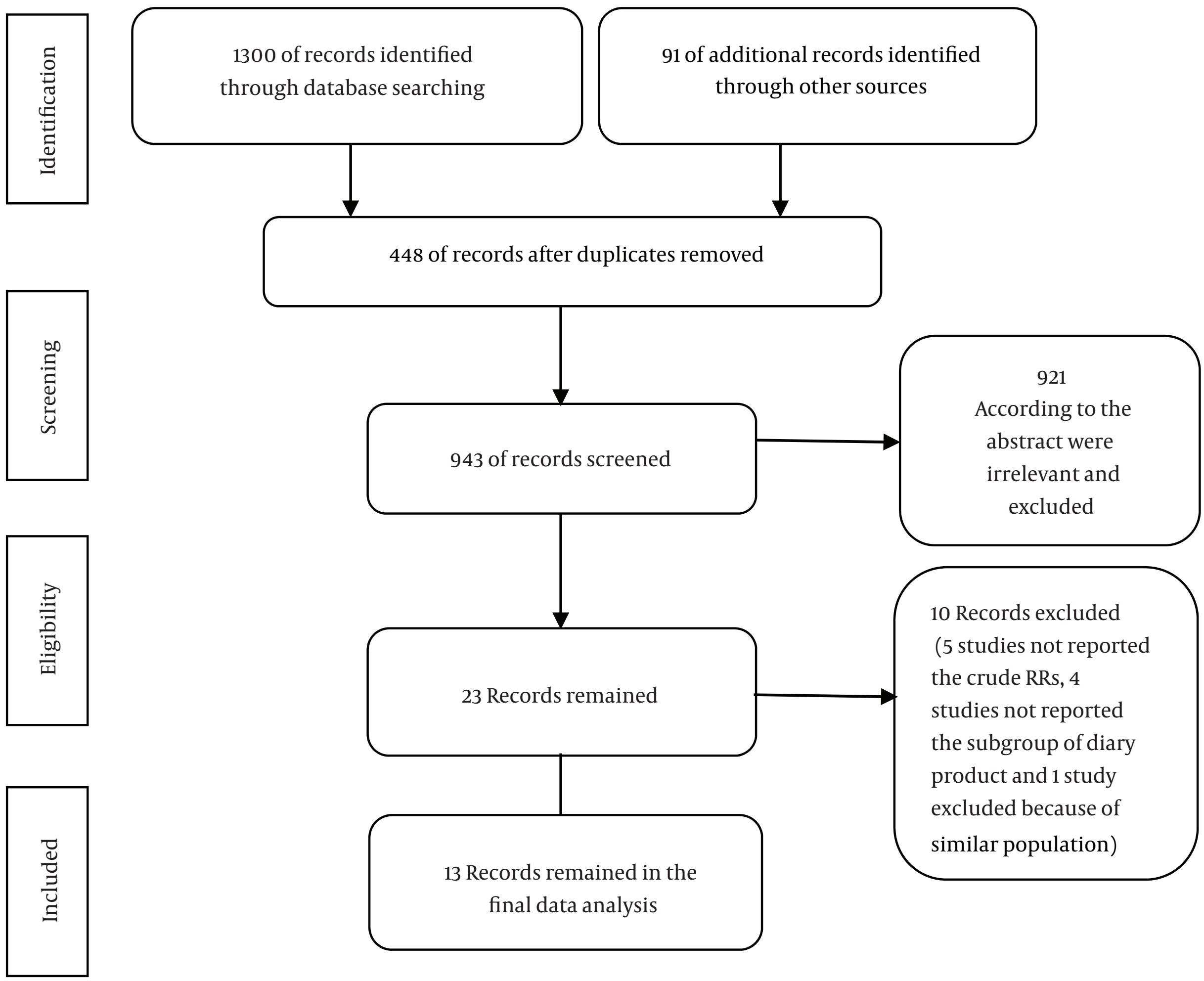

Figure 1. Flowchart of Selection of Studies in the Meta Analysis

underwent through summing-up study that showed 23 full-text studies met the inclusion criteria for this meta-analysis study. 5 studies were excluded because they reported adjusted indices (10, 13-16), and 4 others, due to reporting just the total dairy (17-20). Additionally, out of two publications with similar populations (21, 22), the one with more dairy products subgroups (22) was selected. Thus, 13 publications entered this meta-analytical study (460,421 people). To estimate the dairy products in 13 populations, FFQ questionnaire was used, but as to two populations (11, 23), the 7-day food diary was utilized. The features of the studies are shown in Table 1.

2.2. Risk of Bias

We classified the cohort studies based on the seven selected items of the recommended checklist of STROBE into high-quality, intermediate-quality, and low-quality. In this study, all of articles were classified as high-quality.

2.3. Effect of Exposure

Two indices, i.e. relative risk and rate ratio, were used to show the effects of milk, low-fat milk, yogurt, cheese, ice cream, and cream on type II diabetes. Our study, using both indices, showed that yogurt consumption has a preventive impact on diabetes by decreasing its risk by 26% - 34%. Yogurt: relative risk = 0.74 (95% CI: 0.65, 0.84), rate ratio = 0.66 (95% CI: 0.63, 0.70).

This amount of decrease was up to 14% for the consumption of cream: rate ratio = 0.86 (95% CI 0.82, 0.91). Though the relative risk index showed that milk diminishes the incidence of diabetes by 11%, this relationship was not significant with rate ratio index.

Milk: relative risk = 0.89 (95% CI: 0.82, 0.97), rate ratio = 1.07 (95% CI: 0.93, 1.24). This study also made it known that the intake of low-fat milk, ice cream, and cheese has no effect on diabetes. Cheese: relative risk = 0.92 (95% CI: 0.82, 1.04), rate ratio = 1.04 (95% CI: 0.93, 1.16). Low fat milk: rate ratio = 0.93 (95% CI: 0.76, 1.14). Ice cream: rate ratio = 1.05 (95% CI: 0.93, 1.18).

2.4. Heterogeneity

Heterogeneity was appraised via χ^2 test and I^2 statistics (Figures 2 and 3). There has been homogeneity of P = 0.51 for milk, P = 0.30 for cheese, and P = 0.08 for yogurt in estimating the relative risk in the study, while in measuring the rate ratio in regard to milk, there has been some heterogeneity (I^2 = 93.1%), dropping to 74.3% after the exclusion of study 24 (24). In a similar vein, studies showed a high heterogeneity (I^2 = 98.1%) as to yogurt, which shrank to zero after the exclusion of Choi et al. study (25). Meta-regression could not be carried out to detect the reason for heterogeneity because there were not enough studies in all three groups.

2.5. Sensitivity Analysis

The analysis of sensitivity in calculating the relative risk showed that the overall estimation of studies does not change considerably when each study is excluded (relative risk was in fluctuation between 0.86 and 0.90; relative risk in yogurt was fluctuating between 0.69 and 0.76; and relative risk in cheese was ranging from 0.82 to 0.93). Similarly, the rate ratio changed from 0.97 to 1.06 for cheese, from 0.84 to 1.06 for low-fat milk, from 0.85 to 0.88 for cream, and from 0.99 to 1.07 for ice cream. The sensitivity analysis, in the current paper, regarding the rate ratio of yogurt indicated that the overall figure related to 5 studies amounted to 1 (95% CI: 0.66 - 1.51); with the exclusion of Choi et al. study (25), which had the greatest effect on this estimation, this figure, considering 4 remained studies, changed to 0.66 (95% CI: 0.63 - 0.70). On the other hand, the rate ratio for milk was 0.88, which increased up to 1.07 after the exclusion of Villegas et al. study (26) as the most remarkable study affecting the estimation.

2.6. Publication Bias

To show publication bias, funnel plots, Begg's, and Egger's statistical tests were used. The obtained graphs are shown in Figure 4. The insignificance of statistical tests shows the lack of publication bias.

3. Discussion

We carried out the current study because similar previous studies (6, 8, 31) had major limitations. Earlier studies reported biased pooled relative risk of diary consumption on diabetes, since they had used the adjusted RRs. In the primary studies, the adjusting factors are very different, which makes RRs integrated due to biased summary measures.

The results of the current paper showed that yogurt, cream, and milk consumption had a preventive effect on diabetes risk; while there was not any meaningful relationship between low-fat milk, ice cream, and cheese consumption and diabetes. Dose-response meta-analysis conducted in 2016 indicated that there was no relation between milk, low-fat milk, cream, and cheese consumption and diabetes, whereas ice cream decreased the risk of diabetes by 19%. In this research, it was also affirmed that there was a meaningful, nonlinear relationship between yogurt intake and diabetes: as reported 80 g/d intake of yogurt lowers the risk of diabetes by 14%; any more intake (> 80 g/d) would have no effect on the more reduction of the risk (32). Another meta-analysis (2011) on 7 cohort studies delineated that there existed no meaningful relationship between milk and diabetes, but yogurt had protective effects against diabetes [0.83 (%95 CI: 0.74 - 0.93)] (6).

Cohort studies of dairies subgroups yielded disparate results. For instance, a study in Spain mentioned that yogurt consumption decreases diabetes risk by 40% (2), or a study in 2014 conducted on 3 cohorts showed that the consumption of 28 g/d yogurt, curtailed the risk of diabetes by 17% (24), while, in two other cohorts, there was not any significant relationship between yogurt consumption and diabetes (9, 28). It merits mention that there are copious researches on the consumption of probiotic yogurt, mostly unanimously saying that probiotic yogurt intake decreases the blood glucose. A randomized clinical performance study in 2012 showed that the consumption of probiotic yogurt decreases significantly fasting blood glucose ($P < 0.01$) and hemoglobin A1C ($P < 0.05$) compared to the control group (i.e. those consuming conventional yogurt) (33). It seems if a conventional yogurt is consumed in lieu of probiotic one, it can, more confidently, be said that yogurt protects body against diabetes. A Chinese study on the middle-aged and the elderly indicated that there is no relation between milk and diabetes (12); in addition, a research in London obtained similar results (9), as well as there was not found any connection between milk and diabetes in a Japanese study (28).Generally speaking, dairy products have instrumental effects on weight control in the following ways: (1) decreasing fatty substances, (2) decreasing lipogenesis and increasing lipolysis, and (3) increasing fat

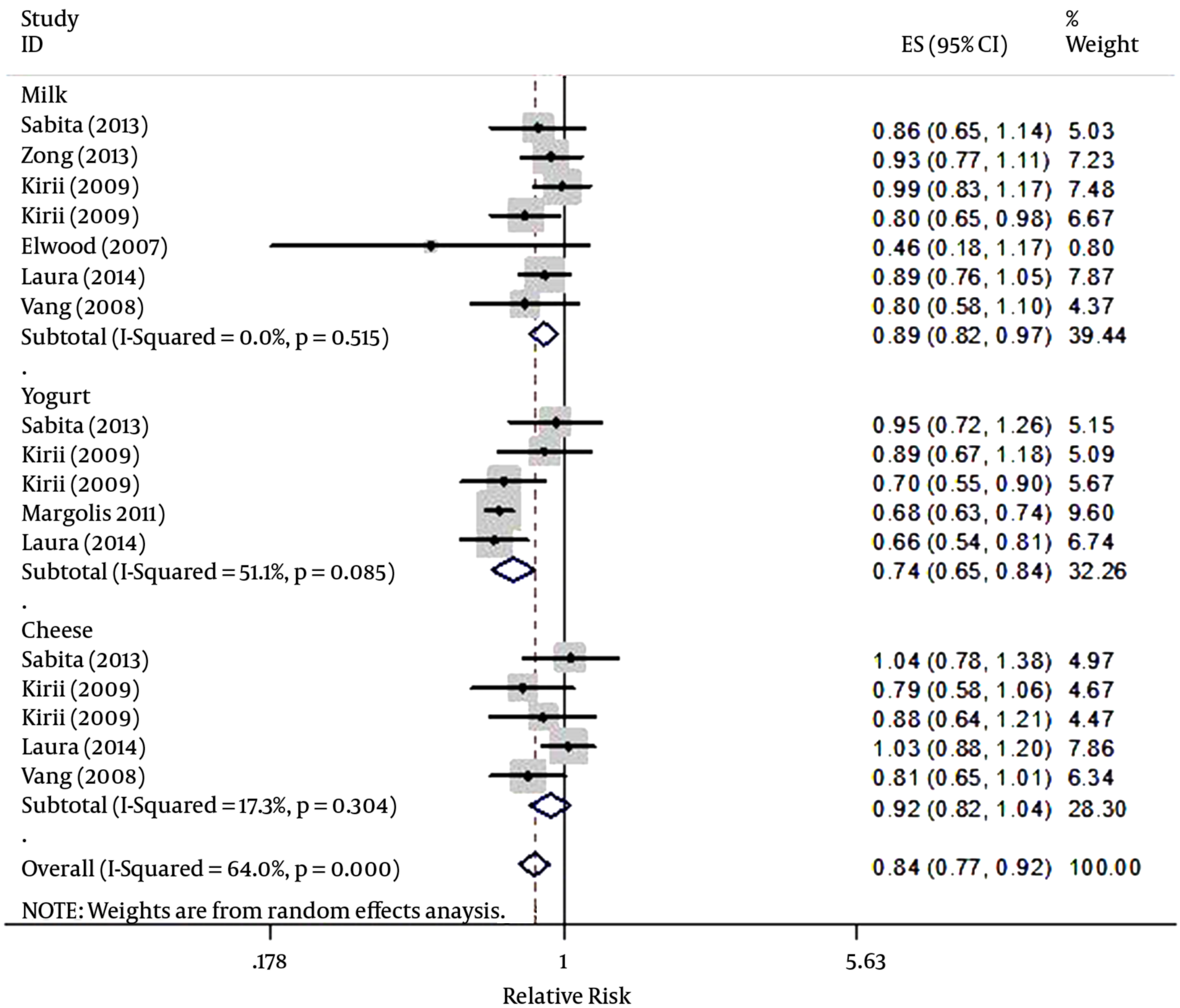

Figure 2. Forest Plot of Relative Risk by Dairy Products Subgroups Consumption and the Risk of Diabetes Mellitus (Highest Versus Lowest Intake)

oxidation; additionally, dairies play an important role in glucose metabolism, because they contain calcium and vitamin D, as calcium affects glucose metabolism via: (1) regulating insulin-mediated intracellular processes, (2) secretory function of pancreatic b-cells, and (3) phosphorylating insulin receptors, while vitamin D acts via the following mechanisms: (1) direct effect on insulin secretion by binding to vitamin D receptors in pancreatic b-cells, (2) indirect effect via the regulation of extracellular calcium, and (3) protection against systemic inflammation (34). The differences among studies could stem from different populations, ethnicities, and populations of interest. The reported indices in previous studies are adjusted with respect to influencing variables, but the indices in this paper are unadjusted and unmarked.

3.1. Limitations

Most studies on the effect of butter on diabetes reported just the adjusted relative risk index; the more information was needed to calculate the unadjusted index, in spite of initiating contacts with the authors; thus, it was not possible to examine the relationship between butter and diabetes. Although cohort studies are beneficial, they are susceptible to many errors, such as confounding, selection bias, and information bias. Thus, it seems better to assess the association between dairy products and risk of diabetes mellitus (T2DM) in a strong, exact study such as clinical trials.

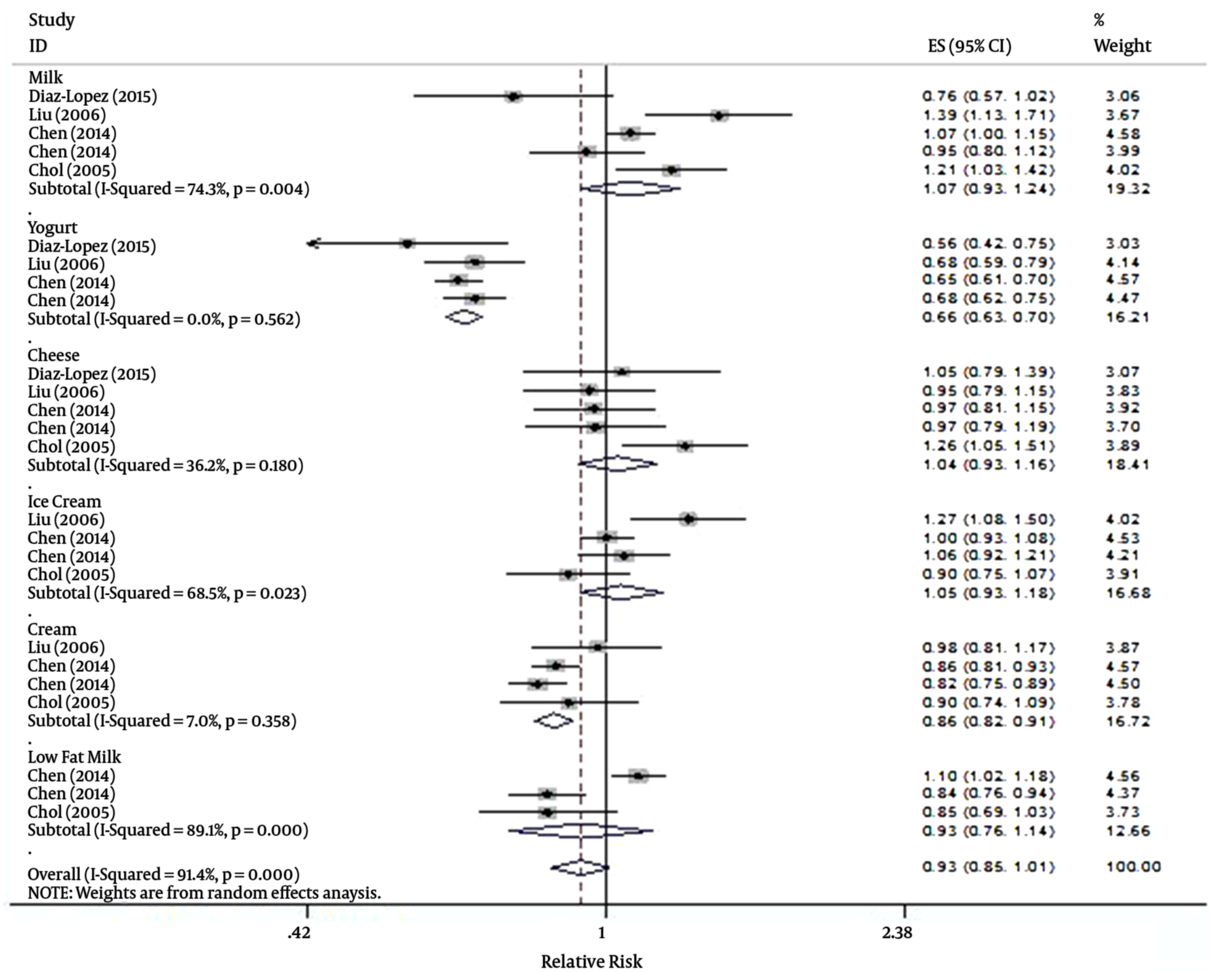

Figure 3. Forest Plot of Rate Ratio by Dairy Products Subgroups Consumption and the Risk of Diabetes Mellitus (Highest Versus Lowest Intake)

3.2. Conclusion

It can be generally declared that dairy products have protective effects against diabetes; anyhow, the current meta-analysis, due to shortage of studies on some subgroups, cannot confidently claim which subgroup affects the risk of diabetes. Consequently, this study calls for more studies and researches on this subject.

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Footnote

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Table 1. Characteristics of the Cohort Studies by Dairy Products Subgroups Consumption and the Risk of Diabetes Mellitus (T2DM)

First Author/ Publication Year	Study, Country	Age	Sex	Subject	Case	Follow-Up (Years)	Quality Score	Exposure	Relative Risk (95% CI)	Rate Ratio (95% CI)
Soedamah-Muthu,2013 (9)	Population Whitehall II/ London	56	Both	4186	273	10	Moderate	Milk; yogurt; cheese	0.86 (0.65 - 1.14) 0.95 (0.72 - 1.26) 1.04 (0.78 - 1.38)	-
Diaz-Lopez, 2015 (2)	Population; PREDIMED Study/ Spain	55 - 80	Both	3454	270	4.1	High	Milk; yogurt; cheese	-	0.76 (0.57 - 1.02); 0.56 (0.42 - 0.75); 1.05 (0.79 - 1.39)
Zong, 2013 (12)	Population; Nutrition And Health Of older Population In China/China	50 - 70	Both	2091	507	6	High	Milk	0.93 (0.77-1.11)	-
Liu, 2006 (27)	WHS(USA)	55	Female	37183	1603	10	High	Milk, yogurt, cheese, ice cream, cream	-	1.39 (1.13 - 1.71), 0.68 (0.59 - 9.79), 0.95 (0.79 - 1.15), 1.27 (1.08 - 1.50), 0.98 (0.81 - 1.17)
Kirii, 2009 (28)	Japan Public Health Center-Based Prospective Study /Japan	40 - 59	Male; female	25877; 33919	634; 480	5, 5	High, high	Milk, yogurt, cheese, milk, yogurt, cheese,	0.99 (0.83 - 1.17), 0.89 (0.67 - 1.18), 0.79 (0.58 - 1.06), 0.80 (0.65 - 0.98), 0.70 (0.55 - 0.90), 0.88 (0.64 - 1.27)	-
Chen, 2014 (22)	NHS/USA	30 - 55	Female	67138	7841	30	Moderate	Milk, low-fat milk, cheese, yogurt, ice cream, cream	-	1.07 (1 - 1.15), 1.10 (1.02 - 1.18), 0.97 (0.81 - 1.15), 0.65 (0.61 - 0.70), 1 (0.93 - 1.08), 0.86 (0.81 - 0.93)
Chen, 2014 (22)	NHS II/USA	25 - 42	Female	85884	3951	16	Moderate	Milk, low-fat milk, cheese, yogurt, ice cream, cream	-	0.95 (0.80 - 1.12), 0.84 (0.76 - 0.94), 0.97 (0.79 - 1.19), 0.68 (0.62 - 0.75), 1.06 (0.92 - 1.21), 0.82 (0.75 - 0.89)
Margolis, 2011 (29)	WHI-OS/USA	50 - 79	Female	82076	3946	7.9	High	Yogurt	0.68 (0.63 - 0.74)	-
Villegas, 2009 (26)	SWHS/ china	40 - 70	Female	64191	2270	6.9	High	Milk	-	0.29 (0.20 - 0.40)
Elwood, 2007 (23)	the Caerphilly prospective study/UK	45 - 59	Male	640	41	20	High	Milk	0.46 (0.18 - 1.17)	-
Laura, 2014 (11)	EPIC-Norfolk /UK	40 - 79	Both	4127	753	11	High	Milk, yogurt, cheese	0.89 (0.76 - 1.05), 0.66 (0.54 - 0.81), 1.03 (0.88 - 1.20)	-
Choi, 2005 (25)	Health Professionals/USA	40 - 75	Male	41254	1243	12	High	Milk, low-fat milk, yogurt, cheese, ice cream, cream	-	1.21 (1.03 - 1.42), 0.85 (0.69 - 1.03), 6.56 (4.81 - 8.94), 1.26 (1.05 - 1.51), 0.90 (0.75 - 1.07), 0.90 (0.74 - 1.09)
Vang, 2008 (30)	AMS and AHS/USA	45 - 88	Both	8401	543	17	High	Milk; cheese	0.80 (0.58 - 1.10); 0.81 (0.65 - 1.01)	-

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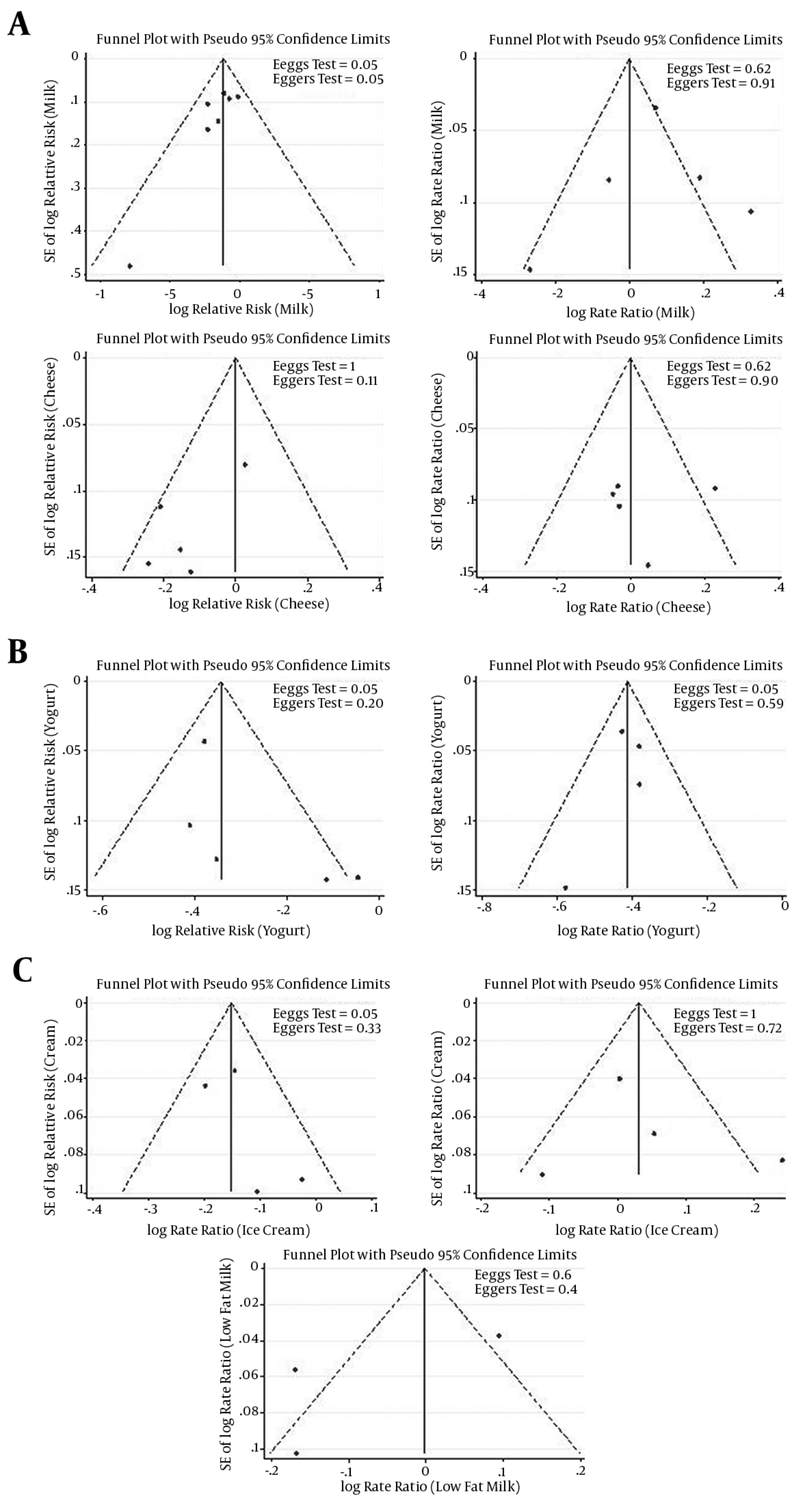

Figure 4. Funnel Plots for the Analysis of Dairy Products Subgroup Consumption and the Risk of Diabetes Mellitus