

Dairy Products Consumption and Risk of Type 2 Diabetes: A Systematic Review and Meta-Analysis of Prospective Cohort Studies

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Abstract

Context: The relationship between dairy products consumption and the incidence of diabetes is investigated in various studies leading to contradictory results; therefore, the current meta-analytical study aimed at shedding light on the matter and estimating the potentiality of diabetes resulting from consuming dairy products.

Evidence Acquisition: The study used some reliable electronic databases such as Web of Science, Scopus, Science Direct, and PubMed revised to March 2016. All original articles from prospective cohort and case-cohort studies examining the relationship between dairy products consumption and the risk of diabetes were considered without any restrictions on age, gender, language, race, and publication year. To assess the quality of the study, the STROBE (strengthening the reporting of observational studies in epidemiology) checklist was employed. The indices of relative risk and rate ratio were reported using the random effect model.

Results: Out of 1391 articles, 14 studies (covering 458,082 subjects) were included in the current meta-analysis. The findings showed that consuming dairy products prevents diabetes: total dairy decreases the risk of diabetes by 8% to 12% (relative risk = 0.88 (95%CI: 0.80, 0.96), rate ratio = 0.92 (95%CI: 0.88, 0.97)). The decrease adds up from 11% to 19% in the case of consuming low-fat dairy (relative risk = 0.81 (95%CI: 0.68, 0.96); rate ratio = 0.89 (95%CI: 0.85, 0.93)). In spite of the fact that high-fat dairy diminishes the risk of diabetes, the relationship is not statistically significant (relative risk = 0.98 (95%CI: 0.78, 1.24); rate ratio = 1.01 (95%CI: 0.96, 1.06)).

Conclusions: The current study indicated that the consumption of total dairy and low-fat dairy had a preventive impact on the incidence of diabetes; therefore, it seems that drawing up some plans in this regard decreases the risk of the disease.

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

1. Context

Ancient Egyptians identified diabetes for the first time in 1500 BCE as a rare disease marked by excessive urination (1). Nowadays, diabetes is the most common metabolic disease with an incidence of 2.8% in the year 2000; if this situation persists, the incidence is expected to rise to 4.4% in the year 2030 (2). Currently, 382 million people are afflicted with diabetes worldwide and it is predicted that this number is 552 million people in 2030 (3, 4). Diabetes is one of the disasters of the current century, responsible for the death of 9 million people a year and 9% of total global death cases (5).

Diabetes causes other complications such as cardiovascular diseases, cerebrovascular problems, circumferential vessels, retinopathy, neuropathy, diabetic legs, amputation, and depression (6). Diabetes, similar to other chronic

diseases, challenges the patient to difficulties such as pressures of controlling the disease, following the treatment plans, costly, complex care, visiting the doctor frequently, undergoing different tests, anxiety about the future state of the disease, increasing the risk of disease for children, problems in social and familial relationships, sexual deficiencies, occupational disorders, and some other similar disruptions in the life (7).

Considering the aforementioned issues, it is highly essential to monitor preventive factors to minimize the incidence rate of diabetes. Seemingly, changing lifestyle and observing diets can prevent the occurrence of this disease (8). One special diet-related issue given undivided attention by researchers is the consumption of dairy products, because dairy products are full of proteins, vitamins A, D, and B12, phylloquinone, menaquinone, and riboflavin. These products are also rich in minerals; e.g., calcium,

potassium, and magnesium; however, dairy products also have saturated fats which raise cholesterol (9). These issues lead the researches to come up with different results.

Some scholars believe that dairy products have protective effects against diabetes (10, 11), whereas futuristic researches in 2013 mentioned that dairies have no effect on diabetes (12, 13).

Thus, it seems necessary to conduct a meta-analysis study, as there is no consensus of opinion on the relationship between dairy products consumption and the risk of diabetes. The current paper aimed at reaching a unique result by studying and summarizing the previous relevant studies.

2. Evidence Acquisition

2.1. Search Strategy

The current paper searched through databases of PubMed (February 1992 to March 2016), Science Direct (April 1870 to December 2015), Scopus (May 1986 to March 2016), and Web of Science (April 1870 to March 2016); the searching method used the 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 get more contexts, authors took advantage of reference studies and initiated contacts with the authors. The grey literatures were searched using Google Scholar as well.

2.2. Inclusion Criteria

All original articles from prospective cohort and case-cohort studies on the relationship between the consumption of dairy products and the risk of diabetes were considered regardless of limitations in age, gender, language, race, and publication year. Out of multiple publications focusing the same population studies, just the ones with longer following-up periods were included. The study solely authorized the inclusion of healthy people; therefore, the ones with diabetes in baseline population were excluded from the study. Additionally, the articles which focused on just one type of dairies or covered the relationship between dairy products consumption and rate of death from diabetes were excluded. The study defined the exposure to all dairy products and the outcome of the study was the incidence of diabetes.

2.3. Data Collection and Validity Assessment

Two researchers, independently, took the responsibility of selecting the articles and assessing their validities; different opinions between the researchers were settled by consulting a third researcher. The current study applied

blinding and task separation to the study selection. The inter-authors reliability based on kappa statistics was 81%.

The extracted variables to analyze the date comprised corresponding author's surname, title of the study, publication year, the place where the study was carried out, subjects' age at the baseline, subjects' gender, target population, follow-up period, type of dairies, and the diabetes cases.

To evaluate the quality of the studies, 7 items on the STROBE (strengthening the reporting of observational studies in epidemiology) checklist were selected: meticulous references based on the framework of the study, following-up period, inclusion and exclusion criteria, definition of corollaries and criteria, identification and measuring methods of corollaries and criteria, definition of exposure and its measurement method, number of included and excluded people at each stage, and the target population of the study. The studies in compliance with all 7 items on the STROBE checklist were classified as high-quality studies; those observing 6 items were of medium-quality. The studies that did not conform to 2 or more items on STROBE checklist were classified as low-quality studies.

2.4. Measures of Exposure Effect and Data Analysis

Pooled measures were calculated as the inverse variance-weighted mean of the logarithm of rate ratio (RR) and heterogeneity ratio (HR) with 95% confidence interval (CI) to assess the strength of association. In the current study, relative risk was defined as the risk of diseases in people with the highest rate of consumption of dairy products compared to the risk of diseases in people with the lowest rate of dairy products consumption; rate ratio was defined as diabetes cases, by the years one, exposed to the risk of diabetes in people with the highest rate of dairy products consumption in proportion to diabetes cases, by the years one, exposed to the risk of diabetes in people with the lowest rate of consumption of dairy products. The data was analyzed using Stata 11, and results were reported via random effect models.

2.5. Heterogeneity, Publication Bias, and Sensitivity Analysis

To assess the data heterogeneity in statistical terms, the Chi-square (χ^2) test was used, and to evaluate heterogeneity quantitatively, I² statistical test came into use. This test was interpreted in terms of the Higgins classification: 25% for low heterogeneity, 50% for medium heterogeneity, and 75% for high heterogeneity. The funnel plot was used to investigate the publication bias, and the Begg and the Egger tests were utilized to measure it statistically. Sensitivity analysis was applied to leave out any studies which would make a remarkable difference in the estimation of

the current study compared to the time the study was not included.

3. Results

Based on the search and study of 1391 articles, 448 were excluded because of duplication; considering the thorough summing-up of the remaining 943 articles, full text of 22 studies met the inclusion criteria of the current meta-analysis; 3 (14-16) studies were left out again as they focused on just one type of dairy products, and 5 others (17-21) were excluded because they reported adjusted indices and did not have access to the required information to calculate the raw index. In addition, out of 2 publications with similar populations (22, 23), the 1 with the shorter follow-up period (22) was excluded. Thus, 13 publications were included in the current study, although 1 publication (23) just extracted the information of 2 other studies. Finally, the details of 14 populations, viz. 458,082 people, were enrolled in the current meta-analysis. Figure 1 displays the method of selection in the current study.

To estimate the dairy products in 12 populations, the food frequency questionnaire (FFQ) was used, but as to one population (24), a questionnaire covering socioeconomic, lifestyle, and dietary factors was utilized. The other remaining population (9) used a 7-day diary; 9 studies were classed as high-quality ones, and 5 as the middle-quality ones. Some other features of these publications are shown in Table 1.

3.1. Effect of Exposure

Two indices of relative risk and rate ratio were used to show the effects of total dairy, low-fat dairy, and high-fat dairy on the risk of diabetes. In the current study, using both indices revealed that dairy products consumption had a preventive impact on the risk of diabetes. It decreased the risk of diabetes by 8% to 12% (total dairy: relative risk = 0.88 (95%CI: 0.80, 0.96); rate ratio = 0.92 (95% CI: 0.88, 0.97)). The rate was 11% to 19%, while consuming low-fat dairy (relative risk = 0.81 (95% CI: 0.68, 0.96); rate ratio = 0.89 (95% CI: 0.85, 0.93)). Despite the fact that high-fat dairy curtails the risk of diabetes, this relationship was not statistically significant according to the results of the current study (relative risk = 0.98 (95%CI: 0.78, 1.24); rate ratio = 1.01 (95%CI: 0.96, 1.06)).

3.2. Heterogeneity

Heterogeneity was assessed via the Chi-square test and I^2 statistics (Figures 2 and 3). There was homogeneity in estimating the relative risk of total and high-fat dairy studies,

while in low-fat dairy studies there was an average heterogeneity ($I^2 = 65.6\%$). By the estimation of RR in total dairy studies, the heterogeneity was 94.9%, dropping to 80.5% after the exclusion of Chio study (28): this change indicated that the study played a major role in heterogeneity. The heterogeneity figures of the studies on low-fat and high-fat dairies were 78.3% and 68.5%, respectively. Meta-regression could not be carried out to detect the reason for heterogeneity as there was lack of enough studies in all 3 groups.

3.3. Sensitivity Analysis

The sensitivity analysis in calculating the relative risk showed that the general estimation of studies did not change considerably when each study was excluded (the relative risk in total dairy was fluctuated from 0.86 to 0.89; the relative risk in low-fat dairy was fluctuated from 0.76 to 0.86; and the relative risk in high-fat dairy was fluctuated from 0.85 to 1). The sensitivity analysis in the current study, regarding the RR of total dairy indicated that the overall figure out of 8 studies was 0.89 (10, 23-25, 27, 28); with the exclusion of Chio study (28), which had the greatest effect on this estimation, the RR figure changed to 0.92 (0.88, 0.97). On the contrary, there was no remarkable change by one-by-one exclusion of studies related to low-fat and high-fat dairy (RR in low-fat dairy ranged from 0.80 to 0.86; RR in high-fat dairy ranged from 0.97 to 1).

3.4. Publication Bias

To show publication bias, funnel plots, the Begg and the Egger statistical tests were used. The graphs of the included studies are depicted in Figure 4. There were no publication bias (statistical tests were insignificant for both relative risk and RR; except for the relative risk of total dairy, which was meaningful).

4. Discussion

In the current meta-analysis study, authors assessed the role of dairy products consumption in the risk of type 2 diabetes (T2D); therefore, the study combined the results of many cohort studies which assessed this association. The current study assessed the effect of 3 types of dairy products on the risk of T2D, including low-fat dairy, high-fat dairy, and total dairy. As a result of the current study, a significant association was observed between the higher consumption of dairy products and the lower risk of T2D. In addition, a protective association was indicated between the consumption of low-fat dairy and T2D, but the relationship between the consumption of high-fat dairy and risk of T2D was insignificant.

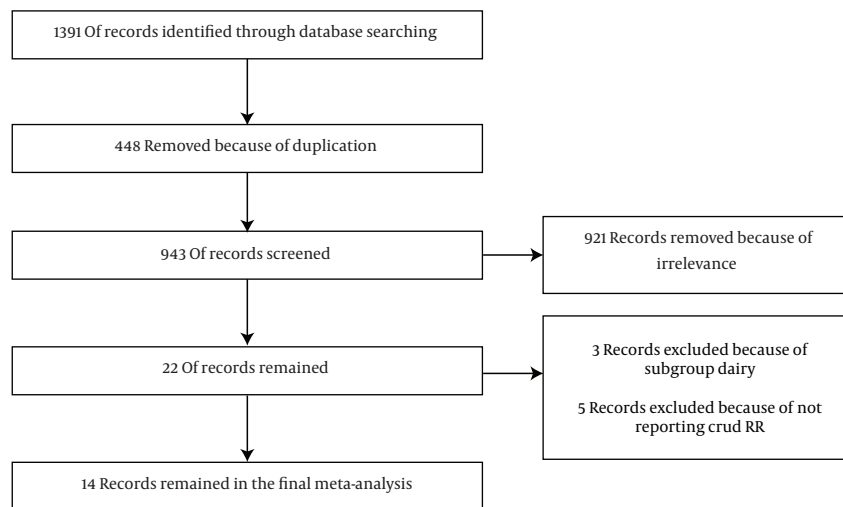


Figure 1. Flowchart of Selection of Studies in the Current Meta-Analysis

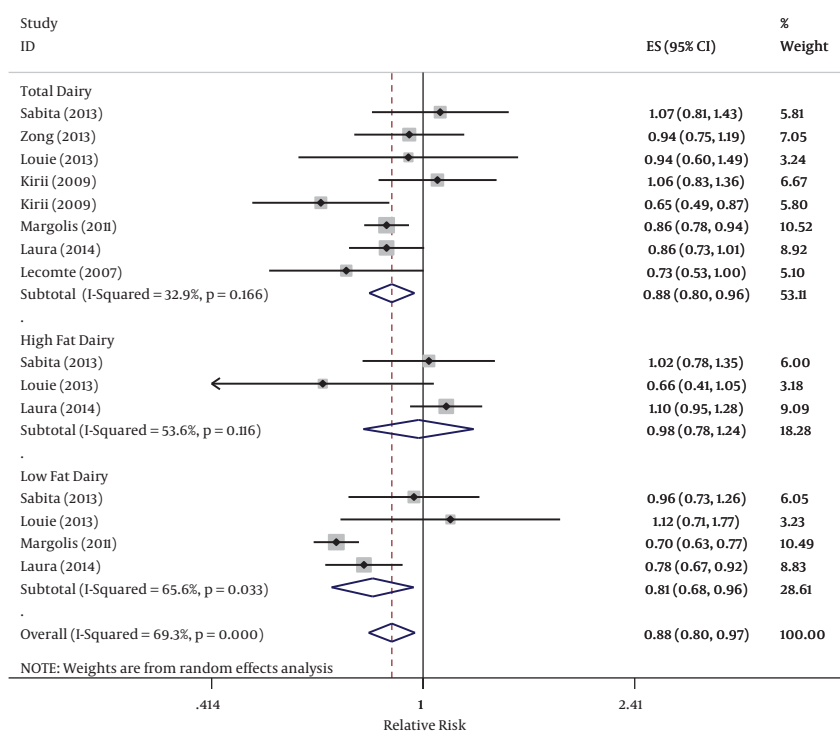


Figure 2. Forest Plot of the Relative risks for the Total, Low-Fat, and High-Fat Dairies Intake and T2DM (Highest Versus Lowest Intake)

A meta-analysis and published literature suggested a marginally lower risk of T2D with a higher dairy consumption and a consistent inverse relationship between the dairy products consumption and T2D risk (25). Another meta-analysis estimated that the use of dairy products can

reduce the risk of T2D by 7% to 14% (30, 31). The results were consistent with 2 previous meta-analyses of cohort studies on dairy products and type 2 diabetes, finding inverse associations (30, 32). Aune et al., carried out a systematic review covering the intake of dairies and the risk of type 2 di-

Table 1. Characteristics of Cohort Studies on Dairy Products Intake and Type 2 Diabetes Mellitus

First Author/ Publication Year	Study/Country	Age	Gender	Subject	Case	Follow-up, y	Exposure	Relative Risk (95% CI)	Rate Ratio (95% CI)
Soedamah- Muthu, 2013 (13)	Population Whitehall II/ London/UK	56	Both	4186	273	10	Total dairy	1.07 (0.81 - 1.43)	
							Low-fat dairy	0.96 (0.73 - 1.26)	
							High-fat dairy	1.02 (0.78 - 1.35)	
Diaz-Lopez, 2015 (10)	Population PREDIMED Study/Spain	55 - 80	Both	3454	270	4.1	Total dairy		0.69 (0.52 - 0.91)
							Low-fat dairy		0.64 (0.48 - 0.85)
							Whole-fat dairy		0.83 (0.62 - 1.11)
Zong, 2013 (11)	Population Nutrition and Health of Aging Population in China/China	50 - 70	Both	2091	507	6	Total dairy	0.94 (0.60 - 1.49)	
Louie, 2013 (12)	BMES/Australia	49	Both	1824	145	10	Total dairy	0.94 (0.60 - 1.49)	
							Low-fat dairy	1.12 (0.71 - 1.77)	
							Medium-fat dairy	0.66 (0.41 - 1.05)	
Liu, 2006 (25)	WHS (USA)	55	Female	37183	1603	10	Total dairy		0.88 (0.76 - 1.03)
							Low-fat dairy		0.78 (0.67 - 0.91)
							High-fat dairy		1.25 (1.06 - 1.46)
Kirii, 2009 (2)	Japan Public Health Center-a prospective study /Japan	40 - 59	Male	25877	634	5	Total dairy	1.06 (0.83 - 1.36)	
			Female	33919	480	5	Total dairy	0.65 (0.49 - 0.87)	
Chen, 2014 (23)	NHS/USA	30 - 55	Female	67138	7841	30	Total dairy		0.97 (0.91 - 1.04)
							Low-fat dairy		0.96 (0.90 - 1.03)
							High-fat dairy		0.98 (0.91 - 1.05)
Chen, 2014 (23)	NHS II/USA	25 - 42	Female	85884	3951	16	Total dairy		0.80 (0.72 - 0.89)
							Low-fat dairy		0.81 (0.73 - 0.90)
							High-fat dairy		0.93 (0.84 - 1.03)
Margolis, 2011 (26)	WHI-OS/USA	50 - 79	Female	82076	3946	7.9	Total dairy	0.86 (0.73 - 1.01)	
							Low-fat dairy	0.70 (0.63 - 0.77)	
Van Dam, 2006 (27)	Black Females' Health Study of Boston University and Howard University/USA	21 - 69	Female	41186	1964	8	Total dairy		1.01 (0.83 - 1.23)
							Low-fat dairy		1 (0.88 - 1.14)
							High-fat dairy		1.09 (0.95 - 1.26)
O'Connor, 2014 (9)	EPIC-Norfolk /UK	40-79	Both	4127	753	11	Total dairy	0.86 (0.73 - 1.01)	
							Low-fat dairy	0.78 (0.67 - 0.92)	
							High-fat dairy	1.1 (0.95 - 1.28)	
Choi, 2005 (28)	Health Professionals/USA	40 - 75	Male	41254	1243	12	Total dairy		0.16 (0.12 - 0.22)
							Low-fat dairy		0.75 (0.62 - 0.89)
							High-fat dairy		1.18 (0.99 - 1.40)
Ericson, 2012 (24)	MDC/Sweden	45 - 74	Male	10550	837	12	Total dairy		1.29 (1.05 - 1.58)
			Female	16590	836		Total dairy		0.81 (0.65 - 1)
Lecomte, 2007 (29)	NA/France	20-60	Male	743	127	5	Total dairy	0.73 (0.53 - 1)	

abetes. They used 17 cohort studies in their meta-analysis and suggested that the intake of dairy products, low-fat dairy products and cheese, had inverse relationship with the risk of type 2 diabetes as these products can decrease the risk of morbidity and the development of T2DM (30). In a meta-analysis by Tong et al., on cohort studies, an inverse association was found between the intake of dairy products, especially low-fat dairy, and T2DM. The association indicated a beneficial effect of dairy consumption on

the prevention of T2DM development (32). In a systematic review and meta-analysis accomplished by Gao et al., it was concluded that the intake of dairy products, such as low-fat dairy or other products, may contribute to the prevention of T2DM (3). In the study by Diaz-Lopez et al., the results showed a healthy dietary pattern, including the consumption of dairy products, particularly yoghurt, may have protective effects against T2D, especially in older adults (10). Several potential mechanisms could explain an inverse as-

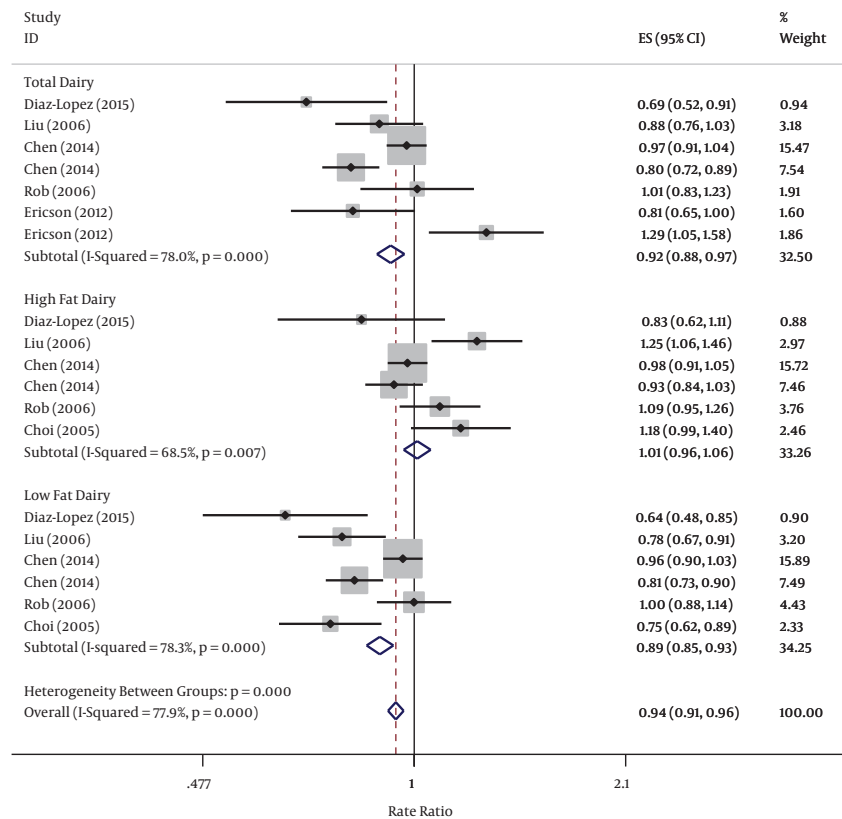


Figure 3. Forest Plot of the Rate Ratio for Total, Low-Fat, and High-Fat Dairies Intake and T2DM (Highest Versus Lowest Intake)

sociation between dairy products consumption and T2D. Dairy products are an important source of dietary calcium, vitamin D, proteins, and magnesium. Lactose and dairy proteins probably have a favorable impact on metabolic factors such as body weight, hypertension, and glucose homeostasis (23). The inverse associations between dairy product intake and risk of some chronic diseases were well proven (33). It was shown, in both animal experiments and human studies, that calcium increases insulin secretion and is essential for the insulin-responsive tissue such as skeletal muscles and adipose tissue; it may reduce insulin resistance (34). In addition, some dairy products, especially low-fat products, may be fortified with vitamin D and is associated with reduced insulin resistance and diabetes risk (35, 36); it happens by influencing the insulin secretion and reducing the insulin resistance (34).

Advantages: 1) Previous studies presented information on biased pooled relative risk of dairy consumption regarding the diabetes; that is because they had used the adjusted RR. Since in primary studies the adjusted factors differ remarkably, these RRs are integrated according to biased summary measures, but the crud relative risks and RR

were pooled in the current study. 2) Reported pooled risks in the current study were based on the relative risk and RR.

Disadvantages: 1) Despite many advantages of the current study, cohort studies are very likely to have errors, such as complexity, selection bias, and information bias. Therefore, it is better to conduct clinical trials to examine the relationship between dairy products and diabetes. 2) The number of studies carried out in this field is low; therefore, further studies should be conducted to fill the gap. 3) The evaluated relationship may lack reality, as it is influenced by different confounding variables.

4.1. Conclusions

The current study indicated that consumption of total dairy and low-fat dairy had a preventive impact on the incidence of diabetes; therefore, it seems that drawing up some plans in this regard can decrease the risk of the disease.

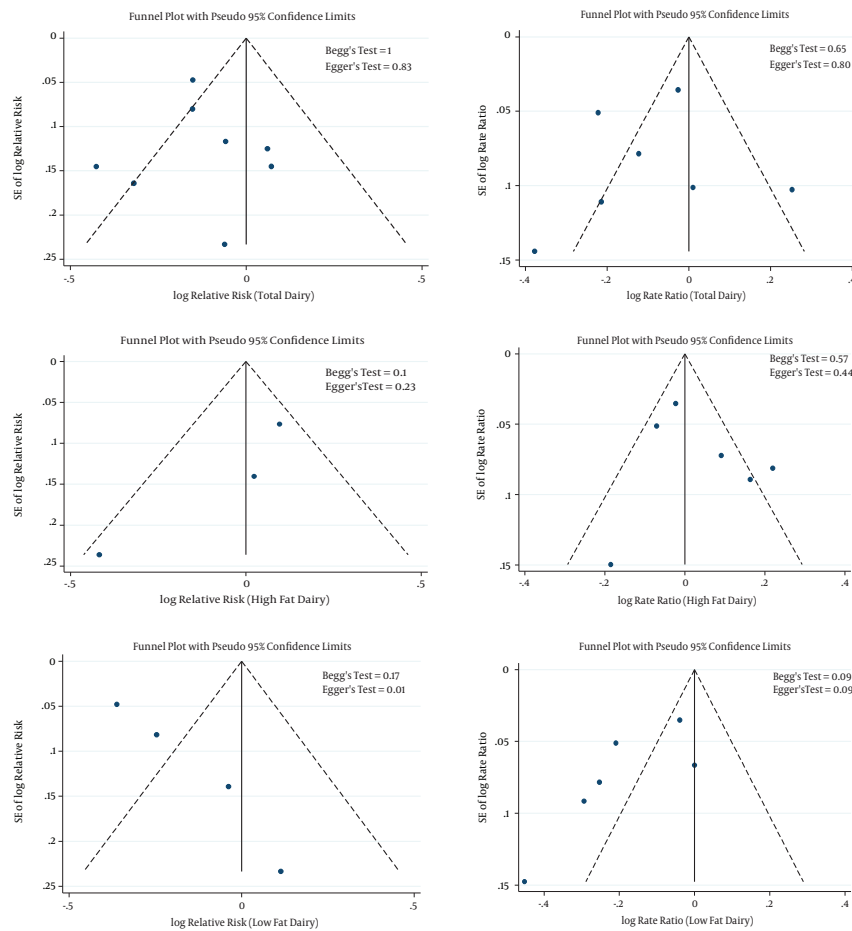


Figure 4. Funnel Plots for the analysis of Total, Low-Fat, and High-Fat Dairies and T2DM

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Footnote

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