REVIEW

Saturated Fatty Acid Intake and Risk of Type 2 Diabetes: An Updated Systematic Review and Dose–Response Meta-Analysis of Cohort Studies

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ABSTRACT

This systematic review and meta-analysis was conducted to pool findings of cohort studies that investigated hazards of type 2 diabetes mellitus (T2DM) in relation to intakes of SFAs. A systematic search was conducted in the PubMed, Scopus, and Embase databases up to June 2021 to find eligible studies. Review articles or commentaries, clinical trials, cross-sectional studies, studies on gestational or type 1 diabetes patients, animal studies, articles with no access to full-texts, articles published in non-English languages, and articles with missing critical data needed for the systematic review were excluded from the meta-analysis. A random-effects model was used to combine study-specific results. Thirteen cohort studies with 361,686 participants and 11,865 T2DM events were included. Dietary total SFA intake, as well as dietary palmitic acid (PA) or stearic acid (SA) were not associated with risk of T2DM when the highest was compared with the lowest intake category (HR = 0.99; 95% CI: 0.91, 1.09; $n = 13$ for total SFAs; HR = 0.96; 95% CI: 0.79, 1.15; $n = 4$ for PA; and HR = 1.08; 95% CI: 0.79, 1.49; $n = 4$ for SA). However, the risk of T2DM decreased by 11% in the highest compared with the lowest category of dietary lauric acid (HR = 0.89; 95% CI: 0.82, 0.97; $n = 2$), and by 17% in the highest compared with lowest category of dietary myristic acid (MA) (HR = 0.83; 95% CI: 0.74, 0.92; $n = 3$). There was evidence of publication bias among studies on dietary total SFAs and T2DM. Our results indicated no significant association between dietary total SFA and risk of T2DM. However, dietary intake of MA was negatively associated with developing T2DM. *Adv Nutr* 2022;13:2125–2135.

Statement of significance: The prior published meta-analysis in this field investigated the association between dietary total SFAs and risk of T2DM; no systematic review and meta-analysis has been conducted for the association between individual SFAs (lauric acid, myristic acid, palmitic acid, and stearic acid) and risk of T2DM. Moreover, dose–response associations of SFAs and T2DM remained undetermined. The results of our meta-analysis showed negative associations between dietary intake of LA and MA and risk of T2DM.

Keywords: saturated fats, diabetes mellitus, lauric acid, myristic acid, palmitic acid, stearic acid

Introduction

Although dietary guidelines generally recommend reducing total fat and SFA intakes (1), controversy still surrounds the diabetogenic effect of SFAs. Some of the experimental studies support the notion that dietary fats, and SFAs in particular, are associated with the development of insulin resistance and type 2 diabetes mellitus (T2DM) (2–5). On the other hand, the majority of more recent cohort studies have indicated no association between dietary SFAs and the incidence of T2DM (6–9). In the case of dietary SFAs with different chain lengths [i.e., lauric acid (LA), myristic acid (MA), palmitic acid (PA), stearic acid (SA)], the results are inconclusive. Whereas there was no significant association between intake of SFAs and T2DM in some studies (5, 7, 9, 10), a significant negative association was reported for LA and MA (6, 8), and a significant positive association was reported for SA (11). Due

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Supplemental Figures 1–5 and Supplemental Tables 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances/.

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Abbreviations used: LA, lauric acid; MA, myristic acid; PA, palmitic acid; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial; ROBINS-E, Cochrane Risk of Bias in Non-Randomized Studies of Exposures tool; SA, stearic acid; T2DM, type 2 diabetes mellitus.

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to these challenges, dietary recommendations to limit SFAs for T2DM prevention might need re-evaluation.

Although a prior meta-analysis investigated the association between dietary total SFAs and T2DM incidence (12), no systematic review and meta-analysis has been conducted for the association between individual SFAs (LA, PA, MA, and SA) and risk of T2DM. Moreover, dose–response associations of SFAs and T2DM have remained undetermined.

Therefore, this study aimed to conduct an updated systematic review and a dose–response meta-analysis of cohort studies to test the linear and potential nonlinear dose–response associations between intakes of total SFAs, LA, MA, PA, and SA and the risk of T2DM. Further subgroup analyses were also conducted to clarify the possible effects of confounding factors.

Methods

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement as guidance for reporting this systematic review (13). We also followed the 12-item PRISMA extension for writing the abstract (14).

Search strategy

We searched all English-language papers in PubMed, Scopus, and Embase databases, using appropriate keywords, according to the following search formula: (“diabetes”[Title] OR “diabetes mellitus”[Title] OR “type 2 diabetes”[Title] OR “dysglycemia”[Title] OR “diabetic”[Title] OR “NIDDM”[Title] OR ((“non-insulin”[Title] OR “noninsulin”[Title]) AND “depend”[Title])) AND (“fatty acid”[Title] OR “dietary fat”[Title] OR “saturated fat”[Title] OR “butyric acid”[Title] OR “butanoic acid”[Title] OR “caproic acid”[Title] OR “hexanoic acid”[Title] OR “caprylic acid”[Title] OR “octanoic acid”[Title] OR “decanoic acid”[Title] OR “capric acid”[Title] OR “lauric acid”[Title] OR “octadecanoic acid”[Title] OR “myristic acid”[Title] OR “tetradecanoic acid”[Title] OR “palmitic acid”[Title] OR “hexadecanoic acid”[Title] OR “stearic acid”[Title] OR “carbohydrate-restricted”[Title]). Evidence not published in commercial or academic publications (gray literature) were also searched using Google Scholar. We checked the reference lists from reviews and original studies investigating the potential association between dietary SFAs and T2DM, to find other relevant articles that might have been missed in our searches.

Eligibility and study selection

Two authors (ZG and ZB) reviewed the title and abstract of all obtained articles. The exclusion criteria for study selection were: *1*) articles published in non-English languages; *2*) review articles or commentaries; *3*) study designs other than cohort studies including clinical trials and cross-sectional studies; *4*) studies on gestational or type 1 diabetes patients; *5*) animal studies; *6*) articles with no access to full texts; and *7*) articles with missing critical data needed for the systematic review. Studies that reported dose of SFA and adjusted effect sizes across categories of exposures; and provided the numbers of participants or person-years and events across categories were included for dose–response meta-analysis. Included studies were published between 1992 and 2020.

Study eligibility was assessed based on initial inclusion and exclusion criteria; final relevant full-text articles were included in the meta-analysis and retrieved for data extraction (**Figure 1**).

Quality assessment for each study was conducted using the Cochrane Risk of Bias in Non-Randomized Studies of Exposures (ROBINS-E) tool (15) (**Supplemental Table 1**). The tool includes 7 domains of bias: confounding bias, selection of participants bias, exposure assessment bias, misclassification of exposures, missing data bias, measurement of outcomes, and selective reporting of the results. Disagreements were solved by consulting the principal investigator (PM).

Data extraction

Data extraction was conducted by the first author (ZG) and double-checked by the last author (PM) to ensure that all data were extracted correctly. The following variables were extracted from eligible studies: the first author’s name, publication year, country, sex of participants, follow-up duration, exposure, categories of exposure, number of participants and cases per category, the dose of SFAs, LA, MA, PA, and SA intake per category, risk estimates expressed as HRs, RRs, or ORs with corresponding 95% CIs per category, and confounding factors in the multivariable analysis (**Supplemental Table 2**). For all meta-analyses, we used the maximally adjusted effect sizes reported in primary studies.

Data synthesis and statistical analysis

Due to the high heterogeneity observed between studies in our meta-analysis ($>50\%$) and considering the potential for high variation within and between the observational studies, we performed random-effects meta-analyses to calculate summary HRs and 95% CIs for a 1% increase in the percentage of fat intake from total energy (16). The reported RRs were considered equal to HRs (17). We conducted linear dose–response meta-analyses using the method of Greenland and Longnecker (18). For this method, the distribution of events and participants or person-years and adjusted risk estimates across categories of SFAs were needed. When studies reported the ranges of exposure categories, instead of the direct median of each category, we estimated approximate medians by the midpoint between the lower and upper limit. For open categories, we assumed the same range as the adjunct category. If a study did not report the numbers of participants or person-years in each category, if the exposures were defined as quantiles, the distribution of participants and person-years was estimated by dividing the total number of participants or person-years by the number of categories (19). If the dietary SFA intake was reported as grams per day, we converted them to energy percentage. For

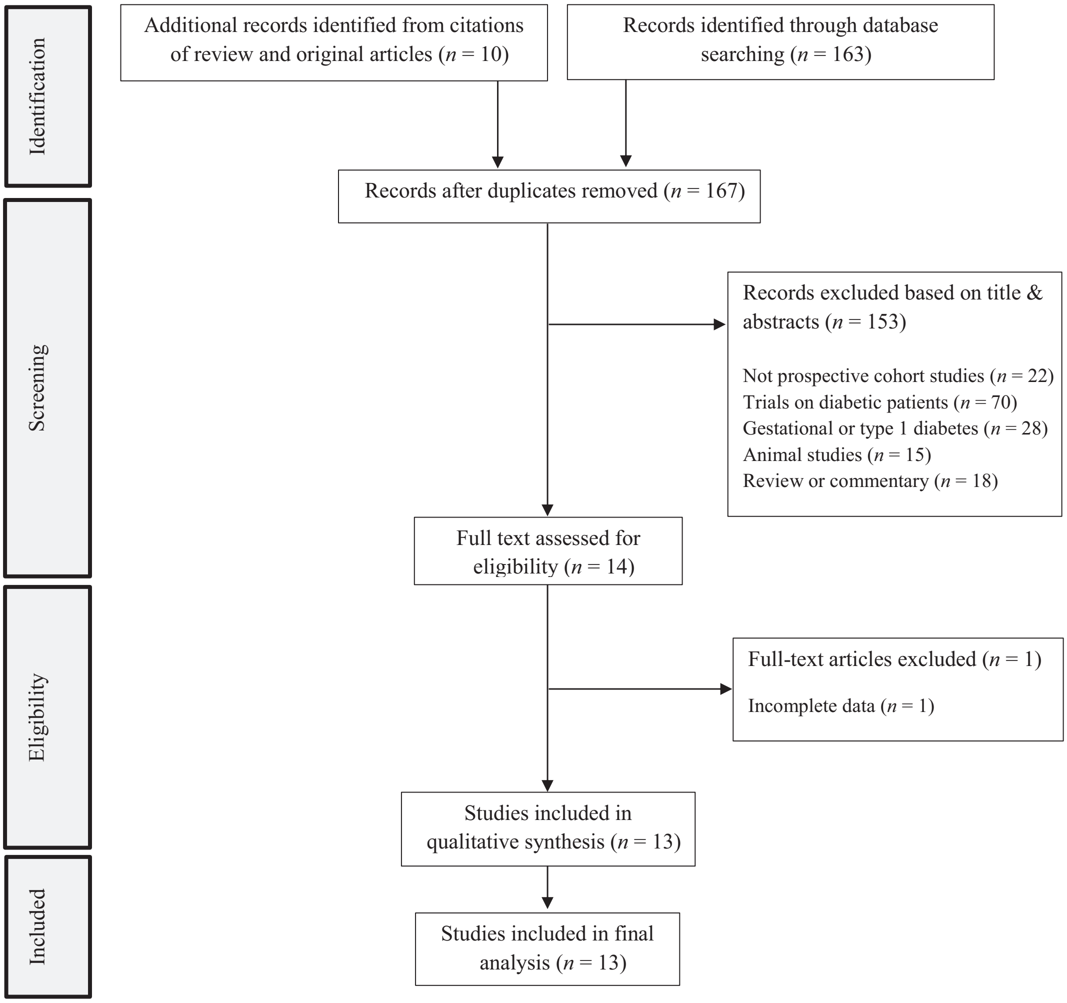

FIGURE 1 Flow chart of the literature search.

the 1 study (20) that did not consider the lowest category as a reference, the effect size was recalculated, assuming the lowest category as reference, using the method suggested by Hamling et al. (21).

We performed subgroup analyses by sex, geographical location, follow-up duration, number of participants, exposure assessment method, study quality, and adjustment for main confounders. Also, sensitivity analyses were conducted to evaluate the potential influence of each study on the results by re-estimating the HRs after excluding 1 study at a time. We evaluated between-study heterogeneity by using the I^2 statistic (specific categories such as low = 25%, moderate = 50%, and high = 75%) (22). Publication bias was assessed using funnel plots and Egger regression test asymmetry (23) if sufficient studies existed ($n \geq 10$) (24).

Moreover, we performed a $P_{\text{nonlinearity}}$ r dose–response meta-analysis, using the Wald test, to determine whether there was departure from linearity, and to test the potential nonlinear association between dietary SFAs and risk of T2DM (25). For the nonlinear dose–response meta-analysis, we modeled curvilinear dose–response associations using a 1-stage weighted mixed-effects meta-analysis (26). The exposures were modeled using restricted cubic splines (27): a spline function set of smoothly joined curves that curve at knots. The knots were based upon Harrell's recommended percentiles for 3 knots at 10th, 50th, and 90th percentiles (27). The correlation within each category of published RRs was taken into account, and the study-specific estimates were combined by using a 1-stage weighted mixed-effects meta-analysis (26, 28). This method estimates the study-specific slope lines and combines them to obtain an overall average slope in a single stage (18, 25).

Finally, we repeated meta-analyses with the inclusion of 1 unpublished dataset in the full data (**Supplemental Figures 1–4**).

All analyses were conducted with Stata software, version 16 (Stata Corp). $P < 0.05$ was considered statistically significant.

Results

After removing duplicates, 167 publications were found through database searching. We reviewed the titles and

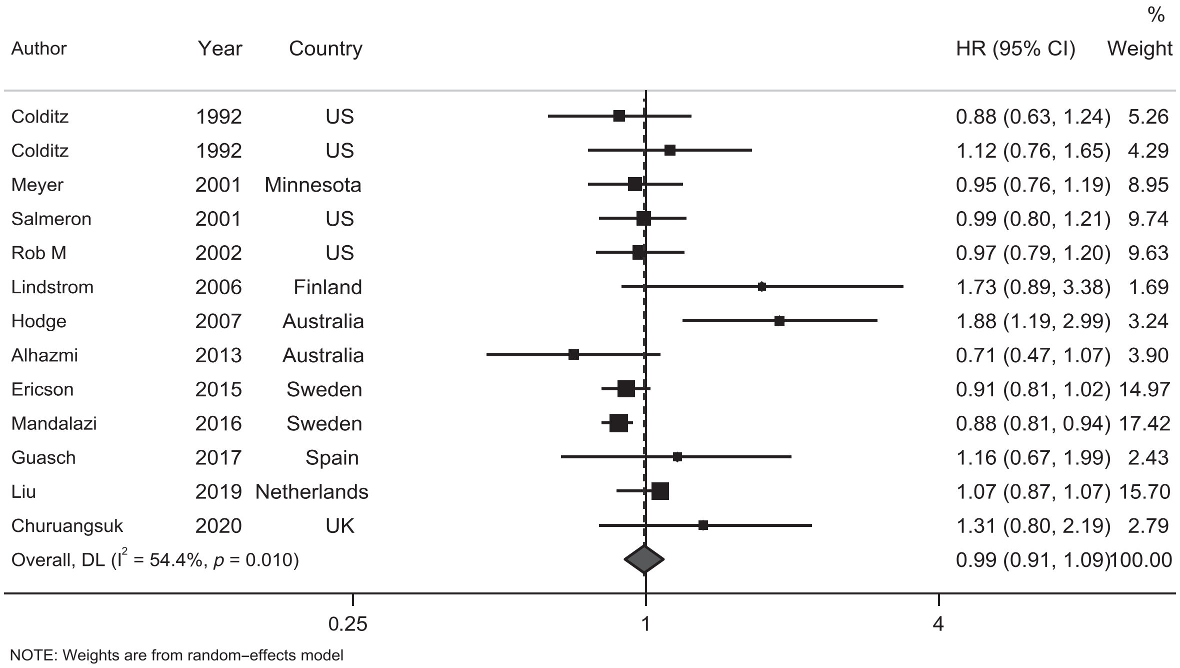

FIGURE 2 Forest plot of cohort studies showing weighted mean differences in risk of type 2 diabetes between highest vs. lowest category of total saturated fat intake, for all eligible studies. Analysis was conducted using a random-effects model. DL, DerSimonian & Laird.

abstracts of all articles, and 153 were removed. The full texts of the remaining studies were assessed for eligibility, and 1 study was excluded. Ultimately, 13 prospective cohort studies with 361,686 participants and 11,865 T2DM events were included in the final meta-analysis (5–11, 20, 29–33).

Characteristics of included studies

Of the 13 studies, 6 were from Europe, 5 from the United States and 2 from Australia. Follow-up durations were between 4 and 17 y (median follow-up duration was 8.0 y, with IQR = 5.1–13.0 y). Of the 13 studies, 12 studies reported the risk of T2DM for total dietary SFAs (5–11, 20, 29–31, 33), 2 studies reported the risk for dietary LA (6, 8), 3 studies for MA (6, 8, 32), 4 studies for PA (6, 8, 11, 32), and 4 studies for SA (6, 8, 11, 32). Four studies included only women (9, 10, 30, 33), 1 study included only men (5), and another 9 studies included both men and women (6–8, 11, 20, 29, 31, 32). T2DM diagnosis was based on self-report in 5 studies (6, 9, 30, 33, 34); however, 8 studies confirmed self-reports of T2DM by assessing the glucose concentrations in blood samples. The general characteristics of the included studies are presented in Supplemental Table 2.

Quality assessment of included studies, using the ROBINS-E tool, revealed that 9 studies were at serious risk of bias, and 5 studies had moderate risk of bias (Supplemental Table 1). Mostly, the high risk of bias was due to not controlling confounders, selection bias due to the selection of participants into the study, or bias due to changes in exposure during follow-up that were not measured.

Total saturated fats

Figure 2 summarizes the results of the meta-analysis for total dietary SFAs as a risk factor for T2DM. Dietary SFA intake was not associated with risk of T2DM when the highest was compared with the lowest intake category (HR: 0.99; 95% CI: 0.91, 1.09; $n = 13$), with high heterogeneity ($I^2 = 54.4\%$; $P_{\text{heterogeneity}} = 0.010$). In sensitivity analysis, summary results did not change when each study was sequentially excluded from main analysis (HRs = 0.96–1.01). In the subgroup analyses, we observed no significant differences in meta-analysis results between the categories of studies based on sex, geographical location, follow-up duration, diabetes diagnostic method, number of participants, study quality, and main adjustments (**Table 1**).

The linear dose–response meta-analysis of the main 13 studies showed no linear association between increasing intake of SFAs and T2DM risk (HR: 0.93; 95% CI: 0.84, 1.03). From 13 cohort studies regarding the association between total SFAs and T2DM risk, 7 studies (5–7, 9, 31, 33, 34) reported sufficient data for the nonlinear dose–response analyses. There was no evidence of a U- or J-shaped association between total SFA intake and risk of T2DM ($P_{\text{nonlinearity}} = 0.153$; $n = 7$; **Figure 3**). **Supplemental Figure 5** presents the results for publication bias. Overall, there was evidence of publication bias with the Egger test ($P = 0.032$).

Individual SFAs

Figure 4 summarizes the results of the meta-analysis for dietary LA, MA, PA, and SA regarding T2DM. Risk of T2DM decreased by 11% in the highest compared with

TABLE 1 Subgroup analyses of total saturated fat intakes (energy percentage) and risk of type 2 diabetes

Characteristics	n	HR (95% CI)	I^2, %	P-heterogeneity	P-interaction[1]
All studies	13	0.99 (0.90, 1.09)	54.4	0.010	
Sex					0.513
Women	5	0.95 (0.83, 1.07)	0	0.564	
Men	1	0.97 (0.79, 1.20)	—		
Men and women	7	1.06 (0.91, 1.22)	74.2	0.001	
Geographical region					0.584
United States	5	0.97 (0.87, 1.09)	0	0.922	
Europe	6	1.05 (0.88, 1.25)	72.1	0.006	
Oceania	2	1.15 (0.44, 2.98)	89.5	0.002	
Follow-up duration, y					0.175
<10	7	1.15 (0.89, 1.49)	55.5	0.036	
>10	6	0.95 (0.88, 1.03)	54.4	0.085	
Diabetes diagnosis method					0.075
Self-report	6	0.93 (0.85, 1.01)	0	0.676	
Blood sampling	7	1.09 (0.93, 1.29)	73.4	0.001	
Number of participants					0.160
<10,000	5	1.26 (0.86, 1.84)	64.2	0.025	
>10,000	8	0.95 (0.89, 1.02)	34	0.157	
Study bias					0.055
Moderate	5	1.07 (0.98, 1.17)	0	0.519	
Serious	8	0.94 (0.85, 1.04)	47.5	0.064	
Main confounders adjustments					0.681
Yes	9	0.97 (0.90, 1.06)	46.8	0.058	
No	4	1.06 (0.73, 1.53)	72	0.013	

[1] P-interaction (or P-between) refers to the significance of the difference between subgroups.

lowest category of dietary LA (HR: 0.89; 95% CI: 0.82, 0.97; $n = 2$), with no evidence of heterogeneity ($I^2 = 37.8\%$; $P_{\text{heterogeneity}} = 0.205$). Dietary MA intake was associated with a 17% lower risk of T2DM when the highest was compared with the lowest intake category (HR: 0.83; 95% CI: 0.74, 0.92; $n = 3$), with no evidence of heterogeneity ($I^2 = 0\%$; $P_{\text{heterogeneity}} = 0.522$). The risk of T2DM was not associated with categories of PA (HR: 0.96; 95% CI: 0.79, 1.15;

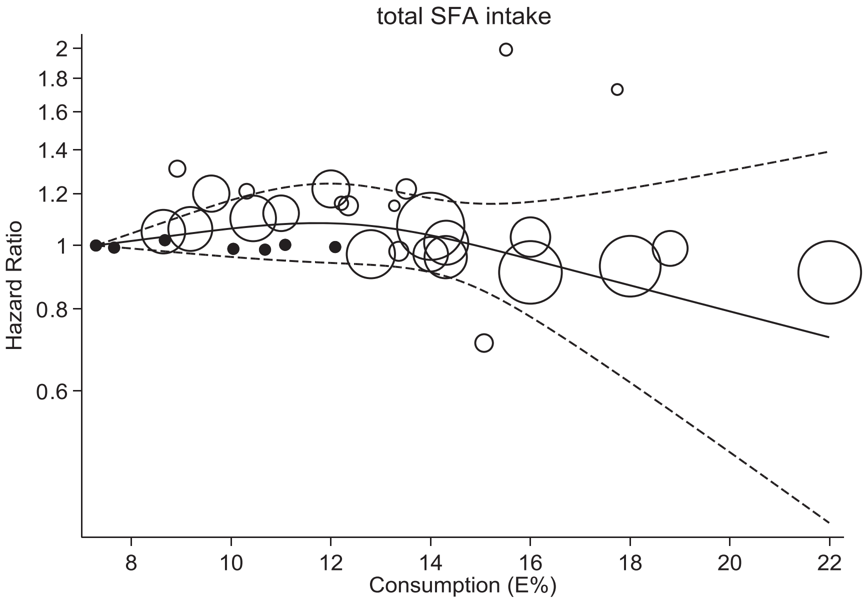

FIGURE 3 Dose–response association between dietary total saturated fat and risk of type 2 diabetes. The solid line and the dashed lines represent the estimated HRs and 95% CIs, respectively. The solid circles and the open circles represent the reference categories and other categories of dietary saturated fats intake, respectively. E%, percentage from total energy intake.

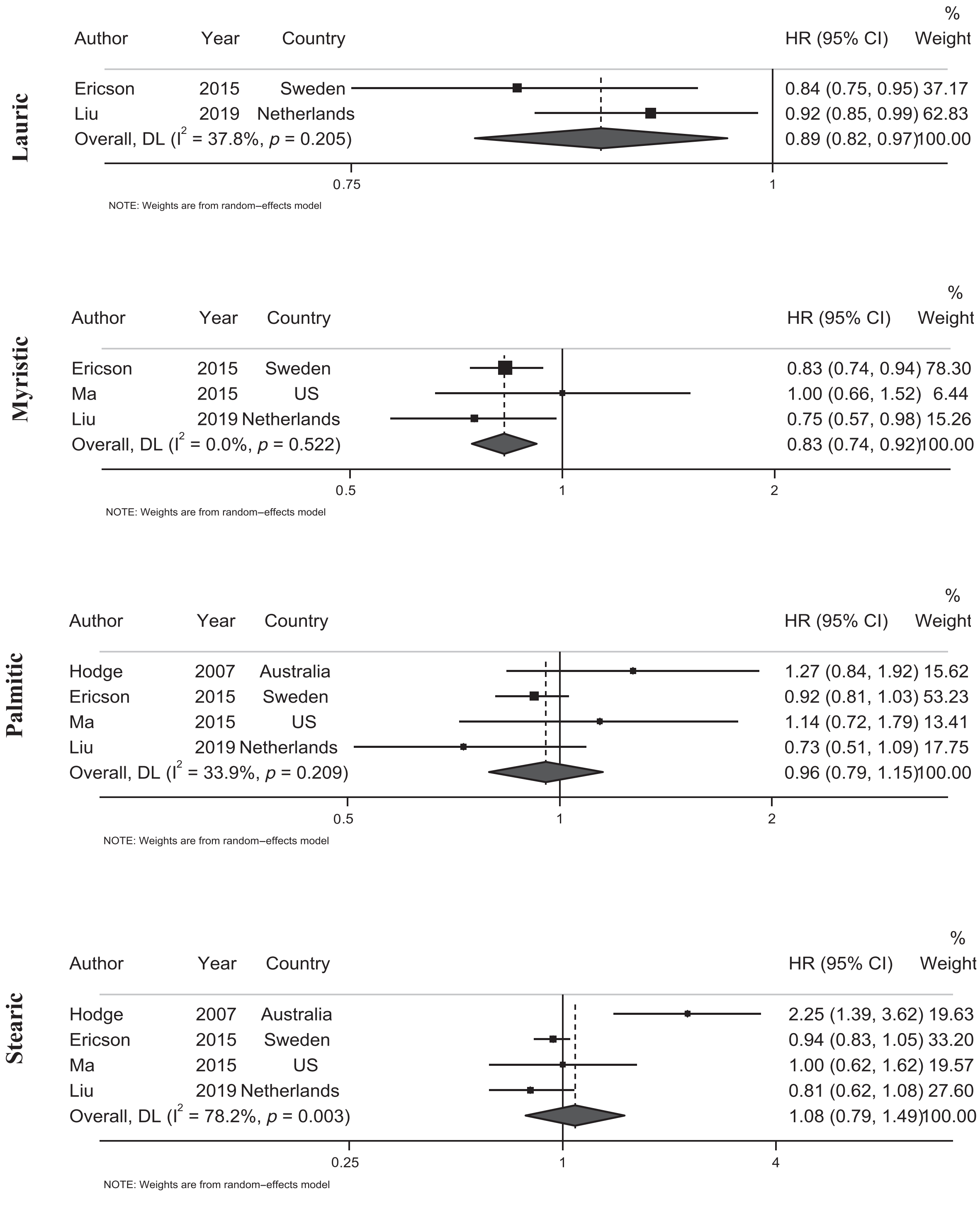

FIGURE 4 Forest plot of cohort studies showing weighted mean differences in risk of type 2 diabetes between highest vs. lowest categories of different saturated fatty acids intake. Analysis was conducted using a random-effects model. DL, DerSimonian & Laird.

I^2 = 33.9%; n = 4), or SA (HR: 1.08; 95% CI: 0.79, 1.49; I^2 = 78.2%; n = 4).

The linear dose–response meta-analysis of the association between dietary MA intake and risk of T2DM showed a 12% lower risk of T2DM with each 1% increase in MA intake (HR: 0.88; 95% CI: 0.82, 0.95). However, there was no evidence that increased intakes of PA and SA were associated with risk of T2DM (HR: 0.82; 95% CI: 0.63, 1.06 for PA; and HR: 0.75; 95% CI: 0.42, 1.36 for SA). Furthermore, there was no evidence of a U- or J-shaped association between each SFA intake and risk of T2DM ($P_{\text{nonlinearity}}$ for MA = 0.395; $P_{\text{nonlinearity}}$ for PA = 0.549; $P_{\text{nonlinearity}}$ for SA = 0.795;

Figure 5). Potential publication bias was not assessed ($n < 10$). We could not assess the dose–response association between LA and risk of T2DM, because only 1 study reported sufficient data for the dose–response analysis of LA and risk of T2DM.

We repeated the meta-analyses after inclusion of 1 unpublished dataset (Supplemental Figures 1–4). As with the analysis excluding the unpublished data, those including the unpublished results showed no significant associations between total SFAs, PA, and SA and risk of T2DM, whereas higher intakes of LA and MA were associated with lower risks of T2DM (published articles only: HR: 0.89; 95% CI: 0.82, 0.97, $n = 2$ for LA; HR: 0.83; 95% CI: 0.74, 0.92, $n = 3$ for MA; adding unpublished data: HR: 0.90; 95% CI: 0.84, 0.96; $n = 3$ for LA; HR: 0.85; 95% CI: 0.75, 0.96; $n = 4$ for MA). Because the unpublished data had sufficient data regarding dose–response analyses, we repeated dose–response meta-analyses for total SFAs, and all 4 individual SFAs. There was a 20% lower risk of T2DM with each 1% increase in LA intake (HR: 0.80; 95% CI: 0.70, 0.92). However, there was no evidence that increasing intakes of total SFAs, MA, PA, and SA were associated with risk of T2DM.

Discussion

In the present systematic review and dose–response meta-analysis, we pooled current data from available prospective cohort studies to present a relatively broad overview of the association between dietary SFAs, LA, MA, PA, and SA and risk of T2DM. Our findings showed no significant association between dietary SFA intake and the risk of developing T2DM; however, medium-chain SFAs (LA and MA) exerted protective association against the development of T2DM.

The lack of association between dietary total SFA intakes and risk of T2DM is consistent with findings from previous meta-analyses of cross-sectional studies (12, 35, 36). In a meta-analysis of randomized controlled feeding trials estimating the effects of isocaloric replacements between macronutrients, there was no significant change in fasting glucose concentration by replacing 5% energy from carbohydrate with SFAs (+0.02 mmol/L; 95% CI = −0.01, +0.04; n trials = 99) (37).

The included studies were heterogeneous; this high heterogeneity can be explained by differences in follow-up duration of studies or number of participants, varying population groups, or differences in dietary sources of SFAs that each population consumed. Processed and red meats, as the major sources of SFAs in the European and American populations' diet, were associated with a higher risk of T2DM (38, 39). In contrast, total dairy products, low-fat dairy products, and cheese, which are also primary sources of SFAs, had an inverse association with the risk of T2DM (40). Intakes of dairy products (3 servings/d) in the context of a healthy diet could reduce the risk of T2DM (41).

Recently, particular attention has focused on the effects of dairy products on cardiometabolic health. Randomized controlled trials (RCTs) have supported the hypothesis that a complex food matrix such as milk, cheese, or yogurt can ameliorate the potential adverse effects of SFAs on metabolic health (42). More RCTs with a large sample and long follow-up duration are needed to fully determine the effects of dairy products and other sources of SFAs on cardiometabolic outcomes.

The potential effects of dietary SFAs on insulin sensitivity are under debate. Reducing dietary SFAs in subjects with metabolic syndrome did not affect insulin sensitivity (43). An SFA-rich diet induced whole-body insulin resistance after a 24-h period (44). Replacement of a MUFA-rich diet with an SFA-rich diet had favorable effects on insulin sensitivity (45).

In contrast to the epidemiological findings, experimental studies and high-fat-diet–induced animal models of T2DM and insulin resistance mostly support diabetogenic effects of dietary fats, and SFAs in particular (46–48). The result of an animal study that tested the impact of SFAs with different chain lengths on insulin resistance is notable. It reported that animals fed a high-fat obesogenic diet with high amounts of medium-chain SFAs, particularly LA, had greater insulin sensitivity compared with animals fed an obesogenic diet with high concentrations of long-chain SFAs, although both obesogenic groups still had greater insulin resistance than a control group fed a normal-fat diet (49).

In vitro studies suggested that exposure of cultured muscle cells to SFAs, specially PA, can induce insulin resistance due to their proinflammatory properties and induction of cytokines, such as TNFα, in blood or tissues, activation of cell stress pathways, elevation of SFA metabolites (such as ceramides), inhibition of the phosphorylation cascade downstream of the insulin receptor, and insulin-induced glucose uptake (50–53). Also, an animal study showed that the markers of adipose tissue inflammation and systemic insulin resistance were lower in mice fed a high-LA diet, compared with mice fed a high-PA diet (54). However, the studies revealed that some potential confounders in experimental conditions, such as SFA-solubilizing agents, might affect interpretation of the effects of SFAs on inflammation and other cellular responses, so re-evaluation of the results of the culture studies seems essential (52). However, because T2DM is a multifactorial and multistage metabolic disorder, misclassification and missing actual cases have been suggested as a reason for reduced magnitude of the RR for dietary fat intakes in population-based cohorts (55). Different case definitions (e.g., hyperinsulinemia with normal glucose tolerance compared with established T2DM) could be responsible for inconsistent findings of epidemiological studies (55). Therefore, the case definition might need to consider the T2DM stage because a large number of steps are involved in the progression of T2DM where nutrient influences might occur (55). The variables included in multiple regression analyses could be a source of diverse findings of population-based studies; overadjustment for confounders modifying the potential association between dietary fats and T2DM risk (e.g., genetic susceptibility and physical activity) could underestimate the strength of the fat-T2DM associations (55). On the other hand, the divergent results could be real because the association of dietary fat

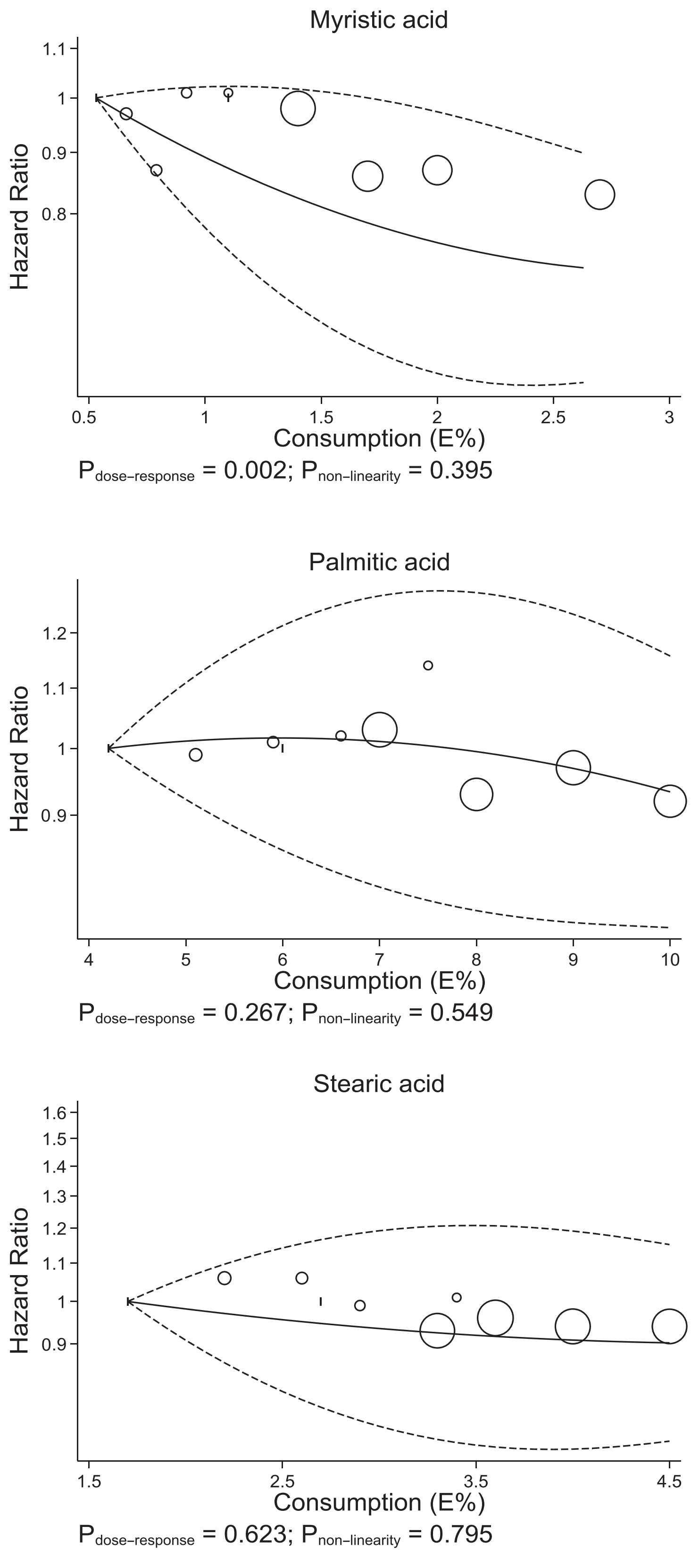

FIGURE 5 Dose–response association between different saturated fatty acids and risk of type 2 diabetes. The solid lines and the dashed lines represent the estimated HRs and 95% CIs, respectively. The circles represent the categories of dietary saturated fatty acids. E%, percentage from total energy intake.

and T2DM might vary with population characteristics, such as age, BMI, and physical activity, that are associated with insulin sensitivity (5). Notably, the high-fat diets used to induce T2DM and insulin resistance in animal models are usually composed of 45% fats (approximately one-third SFAs and two-thirds unsaturated fats) (47), which differs from the high-fat diets prescribed in human studies to induce metabolic alterations.

To the best of our knowledge, this is the first meta-analysis of prospective cohort studies examining the associations of individual SFAs with different chain lengths (LA, MA, PA, and SA) with risk of T2DM. We found that higher dietary intake of SFAs with medium chain lengths (LA and MA) might have a protective association with the risk of T2DM, whereas there was no significant association between SFAs with longer chain lengths (PA and SA) and T2DM.

One remarkable finding of our meta-analysis was that each 1% increase in energy intake from MA was associated with a 12% lower risk of T2DM. However, due to the limited number of studies with sufficient data for the dose–response analysis of LA and risk of T2DM ($n = 1$), we could not assess the dose–response association between LA and risk of T2DM. Two large prospective cohort studies indicated that higher dietary intake of LA was associated with significantly lower risk of T2DM (6, 8). There are limited data regarding the association of LA intake and T2DM, although the effect of coconut oil, as a rich source of LA (56), has been examined in a number of studies. An RCT conducted in 48 subjects with metabolic syndrome reported that subjects who consumed 30 mL virgin coconut oil for 4 wk had a significantly lower concentration of fasting blood sugar, compared with the control group (56). Also, a case report of a 66-y-old man with T2DM who had insulin treatment, found that he began experiencing hypoglycemia within 1–2 d of starting the coconut oil supplementation (57). On the other hand, a protective association between dietary MA and T2DM was reported by most of the previous studies (6, 8, 58, 59). This finding is largely consistent with studies that examined circulating concentration of MA, which could more accurately reflect its concentrations from both dietary intake and endogenous synthesis (11, 60).

To sum up, considering the null association between dietary total SFAs and risk of T2DM and the protective association between dietary SFAs with medium-chain lengths and T2DM observed in this meta-analysis and previous studies, and given the importance of early prevention strategies for reducing the risk of T2DM, it seems necessary to reconsider the dietary recommendations regarding limitation of SFAs to prevent hyperglycemia and instead emphasize the types and quality of fats consumed within the context of a healthy dietary pattern.

Strengths and limitations

To the best of our knowledge, this is the first study that provides a comprehensive review and dose–response meta-analysis of the association between dietary SFAs with different chain lengths and the risk of T2DM. Also, dose–response associations of SFAs and T2DM have not been investigated before. However, our study has some limitations. The high level of heterogeneity among the studies can be attributed to the diversity of populations, their different cultural and genetic backgrounds, geographical variation, and different follow-up durations. However, we tried to detect potential sources of heterogeneity of the studies by conducting subgroup analyses. Moreover, we did not assess the dose–response association between LA and risk of T2DM, because only 1 study reported sufficient data for such analysis.

We had some limitations for selecting the eligible studies because we searched only for English-language databases. Due to the limited number of included studies, publication bias could only be assessed for total SFAs; there was evidence of publication bias, which can lead to downgrading of evidence. The number of studies in each subgroup was also limited, especially for studies with men participants and studies in Oceania, which could affect the results of the subgroup analysis. Also, all of the included studies relied on questionnaires to estimate typical fat intake, which is a significant source of measurement errors in estimating food and nutrient intakes. It should be noted that SFAs are consumed as components of foods and meals and they are not eaten in pure form, and composition of fatty acids, particularly from animal sources like dairy and beef, can vary greatly with management conditions such as breed and food source. Further, well-designed prospective cohort studies and clinical trials with appropriate controlling for potential confounders and validated dietary intakes with nutrient concentrations in blood and tissues are needed.

Conclusions

In conclusion, this study supports the null association between dietary total SFAs and risk of T2DM. However, dietary LA and MA seem to have a protective association with developing T2DM.

Acknowledgments

The authors' responsibilities were as follows—ZG: designed the study; ZG, ZB: collected data; ZG, PM: analyzed data; ZG: wrote the manuscript; ZB: corrected the manuscript; and all authors: read and approved the final manuscript.

Data Availability

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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