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A global analysis of dairy consumption and incident cardiovascular disease

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The role of dairy products in cardiovascular disease (CVD) prevention remains controversial. This study investigates the association between dairy consumption and CVD incidence using data from the China Kadoorie Biobank and the UK Biobank, complemented by an updated meta-analysis. Among Chinese participants, regular dairy consumption (primarily whole milk) is associated with a 9% increased risk of coronary heart disease (CHD) and a 6% reduced risk of stroke compared to non-consumers. Among British participants, total dairy consumption is linked to lower risks of CVD, CHD, and ischemic stroke, with cheese and semi-skimmed/skimmed milk contributing to reduced CVD risk. Meta-analysis reveals that total dairy consumption is associated with a 3.7% reduced risk of CVD and a 6% reduced risk of stroke. Notably, inverse associations with CVD incidence are observed for cheese and low-fat dairy products. Current evidence suggests that dairy consumption, particularly cheese, may have protective effects against CVD and stroke.

Cardiovascular disease (CVD) is the largest contributor to death globally[1]. Adopting healthy dietary patterns is one of the cornerstones of primary prevention of CVD. Thereinto, although dairy consumption features in many dietary guidelines, its role in a heart-healthy diet remains highly debated[2]. Dairy products contain various beneficial nutrients, including high biological value protein, milk fat globule phospholipids, and vitamins and minerals that could improve CVD risk factors[3–6], whereas saturated fats[7] and multiple anabolic hormones might adversely affect the health benefit, such as IGF-1[8,9]. Previous prospective studies linking dairy consumption with CVD outcomes have yielded conflicting results. Some cohort studies reported a protective relationship between dairy consumption and CVD outcomes[10–14], whereas others showed no significant associations[15–18] or even positive associations[19,20]. Meta-analyses also yielded inconsistent conclusions on associations of dairy intake with coronary heart disease (CHD) and stroke risk[21,22]. Notably, heterogeneity between included studies was considerable and the overall quality of the evidence was low to moderate.

Prevailing recommendations advocate low-fat or non-fat dairy over whole-fat dairy[23]. However, scientific evidence for this recommendation was scant and inconsistent[21]. Importantly, different subtypes of dairy products may confer divergent health effects after processing. Fermented milk products such as yogurt contain probiotics that can favorably regulate gut microbiome[24], whereas cheese is rich in sodium which may elevate blood pressure when consumed in excessive amounts[25]. Nonetheless, cheese is also a fermented food that can contain vitamin K2[26], high levels of milk fat globule membrane[27], as well as probiotics[28]. Furthermore, previous epidemiological studies were largely conducted in Western countries, where the consumption level of dairy products especially cheese is high and usually correlated with a higher socioeconomic position[29,30]. In Asia where strokes are more common than CHD, only a few studies demonstrated an inverse association of dairy consumption with stroke[10,31]. Overall, evidence from large cohort studies in both Western and non-Western countries is needed to make global policy recommendations.

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To address the above-mentioned gaps in knowledge, we followed 0.9 million individuals from the UK Biobank (UKB) study and the China Kadoorie Biobank (CKB) study to evaluate the associations of dairy product consumption with incident CVD, CHD, and stroke. We also performed an updated systematic review of the literature and meta-analysis of dairy product intake and incident CVD risk which included our findings to address the role of dairy consumption in CVD prevention and improve dietary guidelines.

In this study, we demonstrate that total dairy consumption is inversely associated with the overall risk of CVD and stroke. Higher intake of dairy products is significantly linked to a reduced risk of stroke in the Chinese population, while it is associated with a lower risk of CVD, CHD, and ischemic stroke in the British population. When examining specific dairy subtypes, cheese, and low-fat dairy products emerge as potentially protective and may be recommended for CVD prevention.

Results

Cohort analyses

During a follow-up of 4,190,676 person-years in CKB and 4,736,113 person-years in UKB, we documented 66,132 CVD cases in CKB and 32,822 CVD cases in UKB. In CKB, participants who consumed dairy products more frequently tended to be women, higher-educated, high-income class, urban residents and vitamin and mineral supplements users, have diabetes and family history of CVD, and consume fruits and eggs more frequently (Supplementary Data 1). In UKB, individuals with higher total dairy consumption were more likely to exercise, be more educated, take vitamin and mineral supplements, and consume oily fish and fruits more frequently, whereas they drank alcohol less frequently and had a lower hypertension prevalence (Supplementary Data 2). Characteristics of participants by cheese consumption (the main subtype of dairy in UKB) and milk types in UKB are shown in Supplementary Data 3 and 4.

Compared to non/rare consumers, those who consumed at least 4 times/week of dairy had no significant association with CVD after the multivariable adjustment in CKB (HR 1.00, 95% CI 0.97–1.03, *P*-trend = 0.470). Regular dairy consumption was related to a 9% higher risk of CHD (HR 1.09, 95% CI 1.05–1.13, *P*-trend < 0.001) but a 6% lower risk of stroke (HR 0.94, 95% CI 0.91–0.97, *P*-trend = 0.005), especially hemorrhagic stroke (HR 0.76, 95% CI 0.69–0.83, P-trend<0.001) (Table 1). Similar associations of CVD, CHD, and stroke were detected for the long-term usual dairy intakes (per 50 g/d increment) (Supplementary Data 5). In UKB, total dairy intake was inversely associated with incident CVD (HR 0.93, 95% CI 0.88–0.98, *P*-trend = 0.004), CHD (HR 0.93, 95% CI 0.88–0.99, *P*-trend = 0.014), and ischemic stroke (HR 0.86, 95% CI 0.75–0.99, *P*-trend = 0.036) (Table 2).

For individual dairy products, cheese (46.49%) and yogurt (35.69%) were the majority (Supplementary Fig. 1a). Cheese consumption was associated with lower CVD and CHD risk. The HRs (95% CIs) comparing the frequency at least 7 times/week of cheese with less than 2 times/week were 0.88 (0.83–0.94) for CVD, 0.88 (0.82–0.94) for CHD, and 0.97 (0.85–1.11) for stroke in the fully adjusted model (Supplementary Data 6), which was similar to the results from 24-h dietary recalls (Supplementary Data 7). For subtypes of cheese, the proportions of each subtype are shown in Supplementary Fig. 1b and we found both hard cheese and fresh cheese (>0.5 serving/d) were associated with a lower risk of CVD and CHD (Supplementary Data 8–10). Considering the fat content of cheese, a protective association with CVD and CHD was found for high-fat cheese (>0.5 serving/d) while low-fat cheese was negatively associated with stroke incidence, especially ischemic stroke (Supplementary Data 11 and 12). Milk consumption (>0 to 0.5 serving/d) was associated with a lower risk of hemorrhagic stroke (HR 0.43, 95% CI 0.21–0.87), and yogurt consumption (>0.5 serving/d) was related to decreased ischemic stroke risk (HR 0.86, 95% CI 0.77–0.98), compared with non-consumers (Supplementary Data 13 and 14). No significant relationships were detected for ice cream consumption (Supplementary Data 15). Regarding different types of milk, compared with participants who never or rarely drank milk, both semi-skimmed and skimmed milk consumers had decreased CVD risk (semi-skimmed: HR 0.92, 95% CI 0.87–0.98; skimmed: HR 0.91, 95% CI 0.86–0.97) and stroke risk (semi-skimmed: HR 0.80, 95% CI 0.71–0.90; skimmed: HR 0.76, 95% CI 0.66–0.86). Attentionally, the association of whole milk (HR: 0.93, 95% CI: 0.87–1.00) with CVD incidence was marginally inverse (Supplementary Data 16).

Results for subgroup analyses in CKB and UKB were shown in Supplementary Data 17–20. Notably, the inverse associations between dairy consumption and the risks of CVD and stroke were observed exclusively in men, not women (*P*-interaction < 0.001), and in individuals with hypertension, but not in those without hypertension (*P*-interaction < 0.001), in the CKB (Supplementary Data 17). The inverse association of dairy consumption and CVD risk was detected in current smokers but not in non-smokers (*P*-interaction = 0.007) in UKB (Supplementary Data 18). Moreover, our results did not alter substantially in sensitivity analyses (Supplementary Data 21-24). In hypothetical substitution analyses, no significant associations were found in UKB. In CKB, replacing 50 g/d of eggs with an equivalent amount of dairy products was associated with an 11% higher risk of CVD, a 13% higher risk of CHD, and a 9% higher risk of stroke. In addition, substituting dairy products for fish or soybeans was associated with a 4% increase in CHD risk, whereas replacing red meat or soybeans with dairy products was associated with a 2% or 3% reduction in stroke risk, respectively (Supplementary Fig. 2).

Systematic review and meta-analysis

Overall, 30 publications from 25 prospective cohorts and our results from CKB and UKB were kept in our final meta-analysis (Supplementary Fig. 3, Supplementary Data 25 and 26). During a range of 5.5 to 30.0 follow-up years, 73,193 CVD cases were documented among 1,288,420 participants from 30 countries or territories around the world in the previous studies (30 studies) (Supplementary Data 27).

In the meta-analysis of previously published studies, a marginal inverse association was identified between total dairy intake and incident cardiovascular disease (CVD) (RR, 0.963; 95% CI, 0.926–1.001; $n = 24$ risk estimates). When the results from the CKB and UKB studies were incorporated, the 95% CI of the summary RR narrowed to 0.963 (0.932–0.995) (Fig. 1). Each serving/day increment of total dairy products was related to a 2% lower CVD risk (RR 0.98, 95% CI 0.96–0.99, $P < 0.001$, $n = 17$ risk estimates) (Supplementary Fig. 4). A similar inverse relationship for CVD was also shown in nonlinear analysis (*P*-nonlinear = 0.002, $n = 12$ studies, Supplementary Fig. 5). For subtypes of CVD, the meta-analysis showed dairy consumption had an inverse relationship with total stroke risk (RR 0.94, 95% CI 0.90–0.98, 14 risk estimates, $I^2 = 61.8\%$) but a null association with CHD risk (RR 0.98, 95% CI 0.93–1.02, 19 risk estimates, $I^2 = 70.5\%$, Fig. 1).

For major subtypes of dairy products, high intake of fermented dairy products, especially cheese, had a protective association with CVD risk (RR for fermented dairy 0.96, 95% CI: 0.94–0.98, $n = 24$ risk estimates; RR for cheese 0.94, 95% CI: 0.91–0.97, $n = 20$ risk estimates), but not yogurt (RR 0.99, 95% CI 0.93–1.06, $n = 14$ risk estimates) or milk (RR 1.00, 95% CI 0.97–1.04, $n = 21$ risk estimates) (Fig. 2 and Supplementary Fig. 6). Cheese intake was also associated with a decreased risk of CHD and stroke (Supplementary Figs. 7 and 8). Considering the content of fat, consumption of low-fat dairy products was significantly related to lower total CVD (RR: 0.96, 95% CI: 0.92–0.99, $n = 20$ risk estimates) and stroke risk (RR: 0.90, 95% CI: 0.84–0.98, $n = 9$ risk estimates) (Fig. 3 and Supplementary Fig. 9). Consumption of high-fat dairy products (including high-fat milk, high-fat yogurt, high-fat cheese, and cream or butter) was not associated

Table 1 | Hazard ratios (95% confidence intervals) for incident cardiovascular disease according to categories of dairy consumption in China Kadoorie Biobank

	Frequency of dairy consumption				*P* trend
	Never/rarely	Monthly	1–3 d/wk	Regularly (≥4 d/wk)	
CVD					
No of cases (%)	42,641 (12.6)	7830 (14.5)	5788 (14.1)	9873 (18.1)	
Person-years	2,939,269	450,552	343,795	457,060	
Model 1[a]	1 (Reference)	1.21 (1.18–1.24)	1.26 (1.23–1.30)	1.33 (1.30–1.36)	<0.001
Model 2[b]	1 (Reference)	1.00 (0.98–1.03)	0.98 (0.95–1.01)	0.94 (0.92–0.97)	<0.001
Model 3[c]	1 (Reference)	1.01 (0.99–1.04)	1.00 (0.97–1.03)	0.96 (0.93–0.98)	0.007
Model 4[d]	1 (Reference)	1.03 (1.00–1.05)	1.03 (1.00–1.06)	1.00 (0.97–1.03)	0.470
CHD					
No of cases (%)	21,129 (6.3)	4032 (7.5)	3264 (8.0)	6051 (11.1)	
Person-years	3,006,398	463,388	352,952	471,541	
Model 1[a]	1 (Reference)	1.24 (1.20–1.28)	1.41 (1.36–1.46)	1.61 (1.57–1.66)	<0.001
Model 2[b]	1 (Reference)	1.03 (1.00–1.07)	1.03 (0.99–1.07)	1.04 (1.00–1.07)	0.023
Model 3[c]	1 (Reference)	1.04 (1.00–1.08)	1.05 (1.01–1.09)	1.05 (1.01–1.09)	0.002
Model 4[d]	1 (Reference)	1.05 (1.02–1.09)	1.07 (1.03–1.12)	1.09 (1.05–1.13)	<0.001
Stroke					
No of cases (%)	25,708 (7.6)	4732 (8.8)	3338 (8.1)	5450 (10.0)	
Person-years	2,999,803	461,574	353,514	475,204	
Model 1[a]	1 (Reference)	1.20 (1.17–1.24)	1.20 (1.16–1.24)	1.17 (1.13–1.20)	<0.001
Model 2[b]	1 (Reference)	0.98 (0.95–1.01)	0.96 (0.92–0.99)	0.88 (0.85–0.91)	<0.001
Model 3[c]	1 (Reference)	0.99 (0.96–1.02)	0.98 (0.94–1.02)	0.89 (0.86–0.92)	<0.001
Model 4[d]	1 (Reference)	1.01 (0.98–1.04)	1.01 (0.97–1.05)	0.94 (0.91–0.97)	0.005
Hemorrhagic stroke					
No of cases (%)	6128 (1.8)	825 (1.5)	410 (1.0)	552 (1.0)	
Person-years	3,065,433	475,123	363,921	492,972	
Model 1[a]	1 (Reference)	0.86 (0.80–0.92)	0.60 (0.55–0.67)	0.48 (0.44–0.52)	<0.001
Model 2[b]	1 (Reference)	0.89 (0.83–0.96)	0.83 (0.75–0.92)	0.66 (0.60–0.72)	<0.001
Model 3[c]	1 (Reference)	0.92 (0.85–0.99)	0.87 (0.78–0.96)	0.69 (0.63–0.76)	<0.001
Model 4[d]	1 (Reference)	0.95 (0.88–1.02)	0.92 (0.83–1.02)	0.76 (0.69–0.83)	<0.001
Ischemic stroke					
No of cases (%)	20,256 (6.0)	4008 (7.4)	2992 (7.3)	4966 (9.1)	
Person-years	3,010,375	463,106	354,354	476,285	
Model 1[a]	1 (Reference)	1.30 (1.25–1.34)	1.37 (1.31–1.42)	1.35 (1.31–1.40)	<0.001
Model 2[b]	1 (Reference)	0.99 (0.96–1.03)	0.98 (0.94–1.02)	0.90 (0.87–0.93)	<0.001
Model 3[c]	1 (Reference)	1.00 (0.97–1.04)	1.00 (0.96–1.04)	0.91 (0.88–0.95)	<0.001
Model 4[d]	1 (Reference)	1.02 (0.98–1.05)	1.03 (0.98–1.07)	0.96 (0.92–0.99)	0.090

Multi-variable Cox proportional hazard model was used. All statistical tests were two-sided.

[a]Model 1 was adjusted for age and sex.

[b]Model 2 was further adjusted for study area (10 regions), survey season, education (no formal school, primary school, middle or high school, or college and above), income (in yuan/year; <5000, 5000–9999, 10,000–19,999, 20,000–34,999, or ≥35,000), physical activity (in MET-h/wk; quartiles), smoking (never/occasionally, former, or current smoker), alcohol drinking (never/occasionally, former, or current drinker), family history of CVD (yes or no), aspirin use (yes or no), vitamins use (yes or no) and minerals use (yes or no).

[c]Model 3 was further adjusted for body mass index (in kg/m^2; <18.5, 18.5–23.9, 24–27.9, or ≥28), history of hypertension (yes or no), and diabetes (yes or no).

[d]Model 4 was further adjusted for red meat, fish, poultry, eggs, fruits (never/rarely, monthly, 1–3 days/week, or regularly), and vegetables (daily or less than daily).

with CVD risk (RR: 0.97, 95% CI: 0.93–1.01, $n = 21$ risk estimates) but inversely associated with CHD risk (RR: 0.96, 95% CI: 0.93–0.99, $n = 14$ risk estimates) (Fig. 3 and Supplementary Fig. 10). For subtypes of stroke, milk consumption was related to a higher risk of hemorrhagic stroke (RR 1.08, 95% CI 1.01–1.17, $n = 5$ risk estimates) and a decreased ischemic stroke risk was detected for total dairy (RR 0.92, 95% CI 0.86–0.99, $n = 7$ risk estimates) and cheese consumption (RR 0.91, 95% CI 0.85–0.97, $n = 4$ risk estimates) (Supplementary Figs. 11–14).

For total dairy consumption, we observed considerable heterogeneity across the studies ($I^2 = 66.1\%$) but did not find any publication bias (Fig. 1 and Supplementary Figs. 15–19). No significant heterogeneity was found in the predefined subgroup (sex, follow-up duration, region, Newcastle-Ottawa Scale score, etc.) meta-regressions (Supplementary Data 28), indicating the source of heterogeneity mainly comes from subtypes of dairy. No single study disproportionately caused the heterogeneity (Supplementary Fig. 20). Results of influence analysis for subtypes of dairy and subtypes of CVD are shown in Supplementary Figs. 21–30. If no significant heterogeneity was found across the studies for specific meta-analyses, we also conducted a fixed effects model to calculate summary HRs and 95% CIs which showed similar results (Supplementary Data 29). Results of the GRADE confidence in the estimates of associations are presented in Supplementary Data 30, indicating overall evidence of very low to moderate quality.

Table 2 | Hazard ratios (95% confidence intervals) for incident cardiovascular disease according to categories of dairy consumption in UK Biobank

	Dairy consumption				*P* trend
	0 serving/d	≤0.5 serving/d	0.5–1.0 serving/d	>1 serving/d	
N	33,803	34,858	54,276	60,509	
CVD					
No of cases (%)	2448 (7.2)	2292 (6.6)	3497 (6.4)	3895 (6.4)	
Person-years	373,622.5	390,329.4	606,703.7	678,468.8	
Model 1[a]	1 [Reference]	0.87 (0.83–0.93)	0.86 (0.81–0.90)	0.84 (0.80–0.88)	<0.001
Model 2[b]	1 [Reference]	0.93 (0.88–0.99)	0.91 (0.86–0.96)	0.90 (0.86–0.95)	<0.001
Model 3[c]	1 [Reference]	0.95 (0.90–1.01)	0.92 (0.88–0.97)	0.92 (0.87–0.97)	<0.001
Model 4[d]	1 [Reference]	0.96 (0.90–1.01)	0.93 (0.88–0.98)	0.93 (0.88–0.98)	0.004
CHD					
No of cases (%)	2042 (6.0)	1906 (5.5)	2912 (5.4)	3228 (5.3)	
Person-years	375,317.5	391,952.6	609,158.4	681,277.5	
Model 1[a]	1 [Reference]	0.87 (0.82–0.93)	0.86 (0.81–0.91)	0.84 (0.80–0.89)	<0.001
Model 2[b]	1 [Reference]	0.94 (0.88–1.00)	0.92 (0.87–0.97)	0.91 (0.86–0.96)	<0.001
Model 3[c]	1 [Reference]	0.96 (0.90–1.02)	0.93 (0.88–0.99)	0.92 (0.87–0.98)	0.005
Model 4[d]	1 [Reference]	0.96 (0.90–1.02)	0.94 (0.89–0.99)	0.93 (0.88–0.99)	0.014
Stroke					
No of cases (%)	499 (1.5)	457 (1.3)	698 (1.3)	802 (1.3)	
Person-years	384,114.7	399,863.2	621,356.8	694,107.5	
Model 1[a]	1 [Reference]	0.84 (0.74–0.96)	0.82 (0.73–0.92)	0.83 (0.74–0.93)	0.003
Model 2[b]	1 [Reference]	0.89 (0.78–1.01)	0.86 (0.77–0.97)	0.87 (0.78–0.98)	0.027
Model 3[c]	1 [Reference]	0.90 (0.79–1.02)	0.87 (0.78–0.98)	0.89 (0.79–0.99)	0.051
Model 4[d]	1 [Reference]	0.91 (0.80–1.03)	0.88 (0.78–0.99)	0.90 (0.80–1.01)	0.084
Hemorrhagic stroke					
No of cases (%)	81 (0.2)	73 (0.2)	106 (0.2)	138 (0.2)	
Person-years	385,796.5	401,501.5	623,807.9	696,931.7	
Model 1[a]	1 [Reference]	0.82 (0.60–1.13)	0.76 (0.57–1.02)	0.87 (0.66–1.14)	0.369
Model 2[b]	1 [Reference]	0.85 (0.62–1.17)	0.79 (0.59–1.05)	0.89 (0.67–1.17)	0.464
Model 3[c]	1 [Reference]	0.86 (0.62–1.18)	0.79 (0.59–1.06)	0.90 (0.68–1.19)	0.521
Model 4[d]	1 [Reference]	0.86 (0.63–1.19)	0.80 (0.60–1.07)	0.91 (0.69–1.20)	0.555
Ischemic stroke					
No of cases (%)	338 (1.0)	307 (0.9)	472 (0.9)	512 (0.9)	
Person-years	384,882.6	400,535.3	622,373.4	695,336.2	
Model 1[a]	1 [Reference]	0.84 (0.72–0.98)	0.82 (0.71–0.94)	0.78 (0.68–0.89)	<0.001
Model 2[b]	1 [Reference]	0.89 (0.77–1.04)	0.87 (0.75–1.00)	0.83 (0.72–0.95)	0.010
Model 3[c]	1 [Reference]	0.91 (0.78–1.06)	0.88 (0.76–1.01)	0.85 (0.74–0.98)	0.023
Model 4[d]	1 [Reference]	0.92 (0.78–1.07)	0.89 (0.77–1.02)	0.86 (0.75–0.99)	0.036

Multi-variable Cox proportional hazard model was used. All statistical tests were two-sided.

[a]Model 1 was adjusted for age (continues) and sex (male or female).

[b]Model 2 was additionally adjusted for centers (22 categories), survey season (spring, summer, autumn, or winter), education (college or university degree, vocational qualifications, optional national exams at ages 17–18 years, national exams at age 16 years, others, or missing), household income (<£18,000, £18,000–£30,999, £31,000–£51,999, £52,000–£100,000, >£100,000, or missing), physical activity (MET-h/wk, quartiles), smoking (never, former, current, or missing), alcohol drinking (never or special occasions only, 1 or 2 times/week, 3 or 4 times/week, ≥5 times/week, or missing), family history of CVD (yes or no), aspirin use (yes or no), vitamins use (yes or no) and minerals use (yes or no).

[c]Model 3 was further adjusted for body mass index (in kg/m^2; <18.5, 18.5–25, 25–30), history of hypertension (yes or no), and diabetes (yes or no).

[d]Model 4 was further adjusted for red meat, poultry (times/week; <2, 2–4, >4), processed red meat, oily fish, non-oily fish (times/week; <1, 1, ≥2), vegetables (servings/day; <1/, 1-3, ≥3), fruits (servings/day; <2, 2–4, ≥4), and eggs (yes or no).

Discussion

In both UKB and CKB studies, dairy consumption was overall associated with a lower risk of stroke. Further analysis of dairy subtypes in UKB revealed that cheese and skimmed/semi-skimmed milk consumption were inversely associated with CVD risk. The updated meta-analysis overall supported that dairy consumption, especially cheese and low-fat dairy consumption, was beneficial for CVD prevention among the general population.

Our finding of the inverse association of dairy consumption with stroke risk was consistent with a recent meta-analysis showing a 1-serving/d increase in total dairy consumption was significantly related to a 4% decreased stroke risk[22]. Although dairy products are major sources of saturated fatty acids (SFA) (about 65% of total fats), which has been shown to increase low-density lipoprotein (LDL) cholesterol levels, emerging evidence suggests that a low LDL cholesterol level (<70 mg/dL) was a risk factor for hemorrhagic stroke[32,33]. A meta-analysis summarizing data from 462,268 participants showed a dose-response relation of dietary SFA intake with lower stroke risk, especially intracranial hemorrhage risk[34]. Congruously, we found that total dairy consumption (mainly fresh milk/

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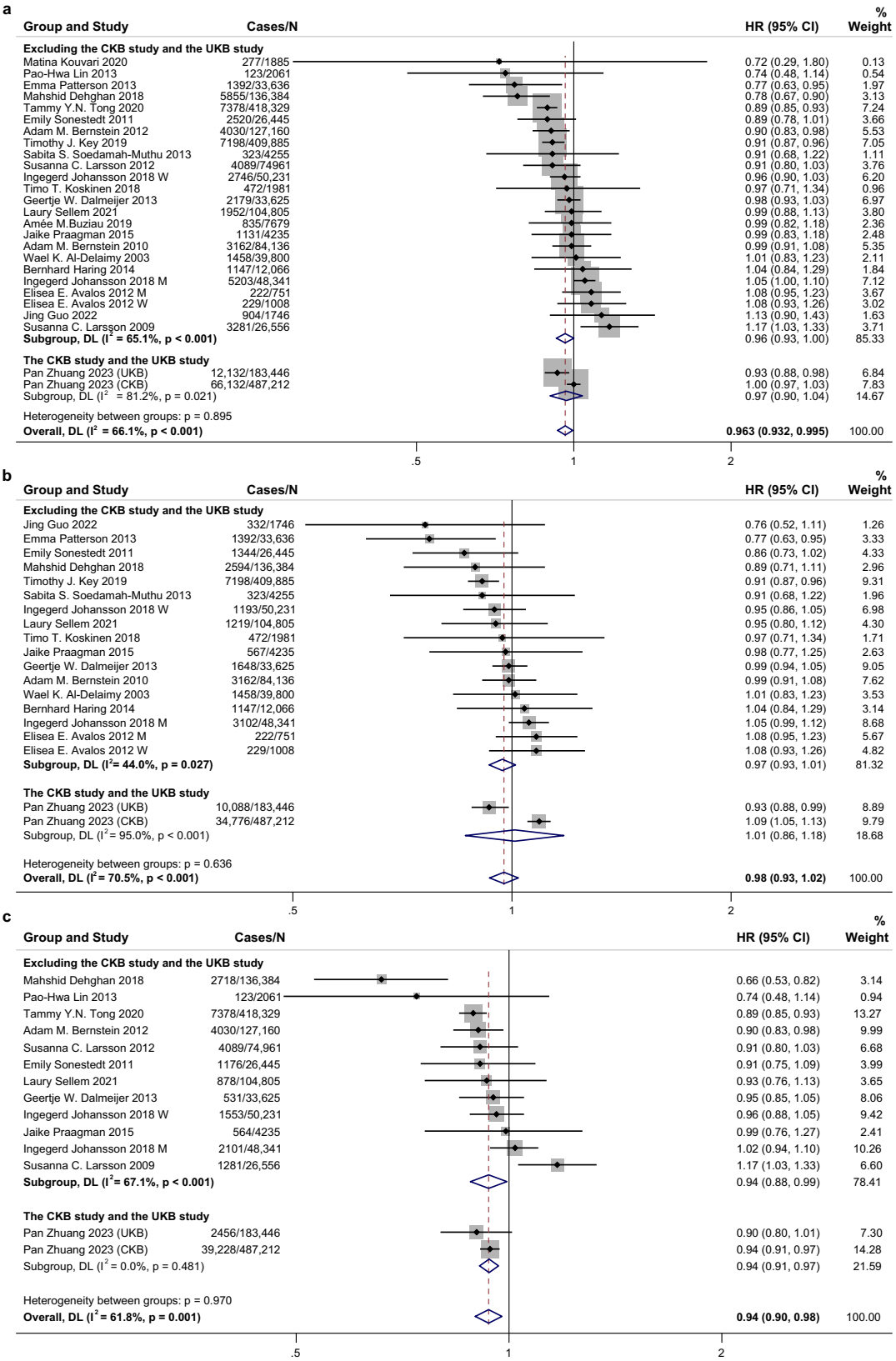

liquid whole milk in China)[35,36] was related to lower hemorrhagic stroke risk in CKB. Importantly, despite a high content of even-chain SFAs, dairy fats also consist of medium-chain (9.8%) and odd-chain (31.9%) SFAs[37], which may improve insulin sensitivity[38], Besides, dairy products also contain potentially beneficial natural trans fats, unsaturated fats, specific amino acids, branched-chain fats, vitamins K1 and K2, and calcium[39]. Thus, given the complex food matrix of dairy products, their health impact cannot be fully accounted for by the presumed effect of SFAs. In addition, meta-analyses of randomized controlled trials demonstrated that fermented milk or dairy foods enriched with probiotics could reduce blood pressure[40,41], which also partially explains the protective association for stroke,

Fig. 1 | Associations of dairy consumption with cardiovascular disease, coronary heart disease, and stroke risk for high compared with low category of intake using random effects meta-analysis. a Cardiovascular disease. **b** Coronary heart disease. **c** Stroke. Meta-analysis pooling of aggregate data used the random-effects inverse-variance model with DerSimonian-Laird estimate of tau². Data are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Squares represent study-specific HRs. Horizontal lines denote 95% CIs. Gray square areas are proportional to the individual study weight for the overall meta-analysis. The red dotted line represents risk ratio of pooled meta-analysis. The blue hollow diamonds represent the results of the meta-analysis for each group, with the center indicating the risk ratio and the width representing the 95% CI. I^2 refers to the proportion of heterogeneity among studies. All statistical tests were two-sided. M, men; W, women; CKB, China Kadoorie Biobank; UKB, UK Biobank. Source data are provided as a Source Data file.

including a lower ischemic stroke risk for dairy in UKB and our meta-analysis.

With regard to CHD, we found great heterogeneity between UKB and CKB studies, which was also shown in our further updated meta-analysis (I^2 = 68.6%). This heterogeneity could be attributed to several factors. First, the difference in dairy intake levels between the two cohorts is notable. The average intake of total dairy products in the UKB was more than four times higher than in the CKB[42]. It is plausible that the cardiometabolic benefits of dairy consumption may require a relatively high level of intake. Second, genetic differences between the populations may play a role. Chinese populations have a higher prevalence of lactose intolerance compared to European populations[43], which could influence the metabolic outcomes associated with dairy consumption and potentially contribute to the observed differences in CHD risk. Importantly, our further analyses suggest that the discrepancy between the studies may be largely attributable to the consumption of different subtypes of dairy products. Notably, cheese consumption ranked highest among dairy products in the UK, whereas liquid whole milk was the predominant dairy product in China[35,36]. The protective relationship was mainly driven by cheese intake in the UKB study, which was further supported by our updated meta-analysis. Consistently, a meta-analysis of 15 prospective studies demonstrated that cheese consumption was related to reduced risk of CHD (RR [95% CI] for high vs. low consumption 0.86 [0.77–0.96]), stroke, and total CVD[44]. Another meta-analysis also showed a protective relationship of fermented dairy products with CVD risk and such a protective association was detected for cheese but not yogurt[21]. Compared with these two meta-studies, our meta-analysis incorporated data from 11 additional studies, significantly increasing the sample size and further reinforcing the robustness of the protective association between cheese consumption and CVD risk. Although cheese, especially hard cheese, is rich in salt, saturated fat, and calories, we still detected protective relationships for hard cheese and high-fat cheese in UKB. Potential mechanisms that underpin the relationship may be related to the high content of calcium, which may benefit cardiovascular health by limiting the absorption of SFAs and cholesterol[45] and regulating the cell membrane potentials of the myocardium[46]. Cheese also contains a high amount of conjugated linoleic acid that has been evidenced to inhibit the progression or induce the regression of atherosclerosis through modulating monocyte/macrophage function[47]. In addition, the fermentation of dairy produces beneficial vitamin K_2 that has been linked with a lower CHD risk[48]. Microorganisms or probiotics from fermented dairy could modulate the gut microbiota composition, inhibit the reabsorption of bile acid, and produce beneficial short-chain fatty acids[49]. A recent meta-analysis of 39 trials demonstrated that probiotic fermented milk products reduced serum total cholesterol and LDL cholesterol levels[50]. However, our results of the updated meta-analysis and other meta-analyses found little benefit of yogurt consumption on CVD risk[21,51], which could be due to the commonly added sugars or artificial sweeteners that might counteract the health benefit[52]. Sweetened or flavored yogurts are classified as ultra-processed foods, which have been linked to an increased risk of CVD[53,54]. It is also possible that the consumption of yogurt is too low to detect a benefit, especially in older cohorts.

Pertaining to milk consumption, mixed results have been reported from prospective studies[21,22]. A meta-analysis of cohort studies reported that milk intake was associated with a 4% (1%–5%) higher CHD mortality[55], which was congruent with our finding of a positive relation with CHD risk in CKB where liquid whole milk was the major dairy product[35,36]. In addition to the long even-chain SFAs elevating LDL cholesterol, a high D-galactose intake from non-fermented milk might also adversely affect lipid metabolism. A trial in nonobese men demonstrated that galactose ingestion within a high-fat beverage exacerbated postprandial lipemia and increased plasma lactate concentrations compared with glucose[56]. Compared to cheese, milk generally contains higher concentrations of D-galactose[57,58]. D-galactose has been widely used to establish an experimental model for premature aging by inducing oxidative stress and chronic inflammation[59,60], which is also involved in the pathogenesis of CVD. Results from 2 large Swedish cohorts showed positive relations of milk intake with oxidative stress and inflammation markers while negative associations were observed for fermented milk products[61]. Altogether, individual dairy products have divergent associations with CVD risk, which seemed to be the major reason for the discrepant results for CHD observed in CKB and UKB and also for the great heterogeneity between studies in our meta-analysis. Therefore, our study provides compelling evidence to highlight the importance of focusing on specific types of dairy products among which cheese may be a beneficial choice for the primary prevention of CVD.

Although prevailing dietary recommendations advocate consuming low-fat or non-fat dairy products over high-fat dairy/whole milk, previous evidence from meta-analyses showed no significant relationship of low-fat dairy consumption with CVD or CHD risk[21,22]. Our meta-analysis showed inverse relationships of low-fat dairy consumption with CVD and stroke risk, supporting the protective role of low-fat dairy in CVD prevention. Nonetheless, we observed an inverse but non-significant association between high-fat dairy consumption and CVD, characterized by slightly wider confidence intervals. In addition, a significant inverse relationship with CHD risk was identified, which may be driven by high-fat cheese consumption. In a meta-analysis of 20 trials, both low-fat and high-fat dairy consumption increased body weight but had neutral effects on other cardiometabolic indicators, including waist circumference, fasting glucose, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, blood pressure, and C-reactive protein (CRP)[62]. Overall, current evidence suggests low-fat dairy may be beneficial for CVD whereas specific subtypes of high-fat dairy such as cheese could also be protective. More large studies are needed to compare low-fat with high-fat dairy on long-term CVD outcomes.

The differing outcomes of substitution analyses between CKB and UKB may be attributed to differences in national dietary patterns and the metabolic profiles of their respective populations[63]. Research has indicated that egg consumption could confer health benefits in Asian populations[64]. A previous cohort study within the CKB cohort found that daily egg consumption (up to <1 egg/day) was associated with an 18% reduction in CVD mortality and a 26% lower risk of hemorrhagic stroke[65]. Our substitution model results aligned with these findings, suggesting that egg consumption may offer more significant cardioprotective benefits than dairy products among the Chinese population. In contrast, the UKB substitution analysis showed a null association, indicating that the cardiometabolic impacts of other protein sources were comparable to those of dairy products in the UK.

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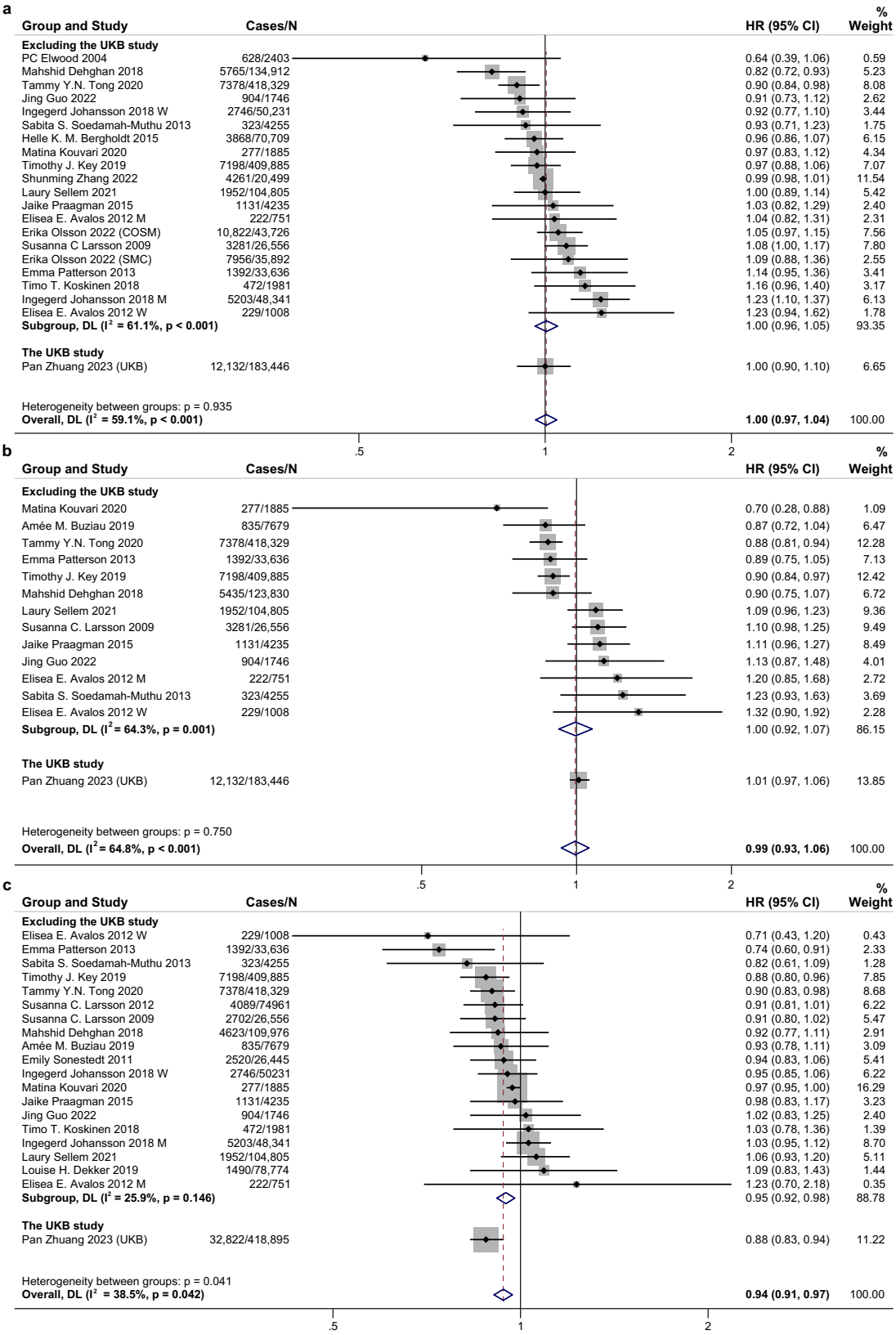

This is consistent with findings from a previous study in the US, which showed that replacing dairy products with other protein sources did not significantly affect CHD risk[66].

The inverse association between total dairy intake and the risk of CVD and stroke was observed among individuals with hypertension but not among those without hypertension in the CKB study. Hypertension is a well-established risk factor for CVD, making those with high blood pressure more susceptible to cardiovascular damage[67]. As a result, the potential protective effects of dairy intake, such as improved blood pressure regulation, may have a more pronounced impact on reducing CVD and stroke risk in hypertensive individuals compared with those without hypertension. Interestingly,

Fig. 2 | Associations of milk, yogurt, cheese consumption with cardiovascular disease risk for high compared with low category of intake using random effects meta-analysis. a Milk. **b** Yogurt. **c** Cheese. Meta-analysis pooling of aggregate data used the random-effects inverse-variance model with DerSimonian-Laird estimate of tau^2. Data are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Squares represent study-specific HRs. Horizontal lines denote 95% CIs. Gray square areas are proportional to the individual study weight for the overall meta-analysis. The red dotted line represents risk ratio of pooled meta-analysis. The blue hollow diamonds represent the results of the meta-analysis for each group, with the center indicating the risk ratio and the width representing the 95% CI. I^2 refers to the proportion of heterogeneity among studies. All statistical tests were two-sided. M, men; W, women; CKB, China Kadoorie Biobank; UKB, UK Biobank. Source data are provided as a Source Data file.

the significant inverse associations of dairy consumption with the risk of CVD and stroke were more evident among men than women in the CKB study. This disparity may be due to differences in how men and women metabolize nutrients, influenced by hormonal variations[68], which can affect the impact of dairy intake on stroke risk. In addition, men typically have higher baseline blood pressure levels, which might make them more responsive to the protective effects of dairy against stroke. Furthermore, the inverse association between cheese intake and CVD risk was significant only among participants without diabetes in UKB. This could be attributed to the altered lipid metabolism and insulin resistance commonly seen in individuals with diabetes[69], potentially diminishing the cardiovascular benefits of cheese. Further research is necessary to elucidate the significant interactions observed in our subgroup analyses.

This analysis has important strengths, including the large sample size, long follow-up duration, and the design of using data from two large cohorts in the UK and China, which enable us to directly compare the results from Western vs. Eastern countries. Finally, the updated meta-analysis provides a comprehensive overview of the evidence. Potential limitations also deserve attention. First, measurement errors by FFQs are inevitable in epidemiological studies. However, such errors tend to attenuate findings toward the null because of the prospective analysis. Although absolute dairy intake was not estimated in CKB and UKB at baseline, consumption frequency is rather useful in categorizing individuals on the basis of relative intakes. Second, unmeasured or residual confounding cannot be fully ruled out despite our full adjustment for multiple risk factors. Specifically, higher dairy consumption seemed to be indicative of a higher socioeconomic status. Nonetheless, our results were consistent among both individuals with higher and lower income, indicating the documented associations of dairy were independent of socioeconomic status. Third, dairy consumption was assessed only once at baseline in the CKB study and only a small proportion of participants completed all five 24-hour dietary recalls in the UKB. As a result, dietary changes during the follow-up period could potentially weaken the observed associations. However, we estimated the long-term usual intake of dairy by incorporating data from dietary resurveys in the CKB and included participants with at least two 24-hour dietary recalls in UKB in sensitivity analyses, which yielded similar results. In addition, consistent findings were observed even with a shorter follow-up duration of 5 years, suggesting that the lack of repeated measurements is unlikely to have significantly impacted our findings. Nonetheless, further studies incorporating repeated measures of dairy intake are encouraged to validate these results. Fourth, no apparent 'ceiling' effect was observed in our dose-response analysis, likely due to the limited number of studies with a broad range of dairy consumption. Additional studies encompassing a wider spectrum of intake levels are needed to fully explore this relationship. Last, we could not further analyze dairy subtypes separately in CKB, and butter was also not assessed in both CKB and UKB due to the lack of available data at baseline, which could have provided more implications.

The results from our two large cohort studies and updated meta-analysis show that dairy consumption is associated with a lower risk of stroke and total CVD overall while relationships for subtypes of dairy products differ. Cheese consumption, but not milk and yogurt, was inversely associated with CVD risk. Low-fat dairy consumption was inversely related to CVD and stroke risk. Our findings provide useful clinical evidence to support the beneficial role of dairy consumption in the primary prevention of CVD. Additional clinical trials are necessary to validate the distinct cardiometabolic effects of various subtypes of dairy products.

Methods

Study design

The CKB study received ethical approval from the Oxford University Tropical Research Ethics Committee, the Chinese Centre for Disease Control and Prevention (CDC) Ethical Review Committee, and the local CDC of each study area. The UK Biobank received ethical approval from the research ethics committee (REC reference for UK Biobank 11/NW/0382).

CKB is one of the largest cohort studies that recruited over 500,000 adults from ten geographically diverse areas across China during 2004–2008[70]. All participants gave written informed consent. For this analysis, participants with a history of CVD or cancer were excluded at baseline, which resulted in a sample of 487,212 individuals in the CKB.

UKB is also a large prospective study of more than 500,000 people who were aged 37–73 years recruited from one of 22 assessment centers across the UK between 2007 and 2010 [71]. Among 502,476 participants, we excluded participants with a history of CVD or cancer at baseline and participants who withdrew during the follow-up (data cannot be used). Furthermore, we excluded persons without data on cheese consumption frequency from the food frequency questionnaire (FFQ) or those without information about 24 h dietary recalls. Finally, 418,895 individuals in the UKB remained in the final analytical samples for cheese consumption and 183 446 individuals remained for individual dairy products. The detailed flow chart is shown in Supplementary Fig. 31.

Dietary assessments

In the CKB, participants were asked about the consumption frequency of 12 major food groups, including total dairy products over the preceding year by a qualitative FFQ. The adjusted Spearman coefficients of dairy consumption frequency were 0.4 for reproducibility and 0.5 for validity, comparing two FFQs conducted in the second and third surveys with the baseline FFQ, which implicated good performance of the FFQ[72]. Subtypes of dairy products were not included in the baseline FFQ and thus were not analyzed in CKB. The long-term usual amount of consumption for each category of food consumption variable was estimated according to the previously published method using the data of two resurveys in the CKB[73]. The daily energy intake at baseline was also estimated[74].

In the UKB, participants completed a touch-screen short dietary questionnaire that consisted of 29 diet questions over the past 12 months, including frequency of cheese intake (0, <1, 1, 2 to 4, 5 to 6, ≥7 times a week) and type of milk (never/rarely have milk, full, semi-skimmed, skimmed cream, soya milk, other) in which they could select multiple types of milk they drank. Soya milk was excluded from the analysis as it is made from soybeans. Besides, participants were invited to complete a 24 h dietary questionnaire that inquired about the consumption of nearly 200 foods and drinks including various dairy products (milk, cheese, yogurt, and ice cream). Five separate occasions

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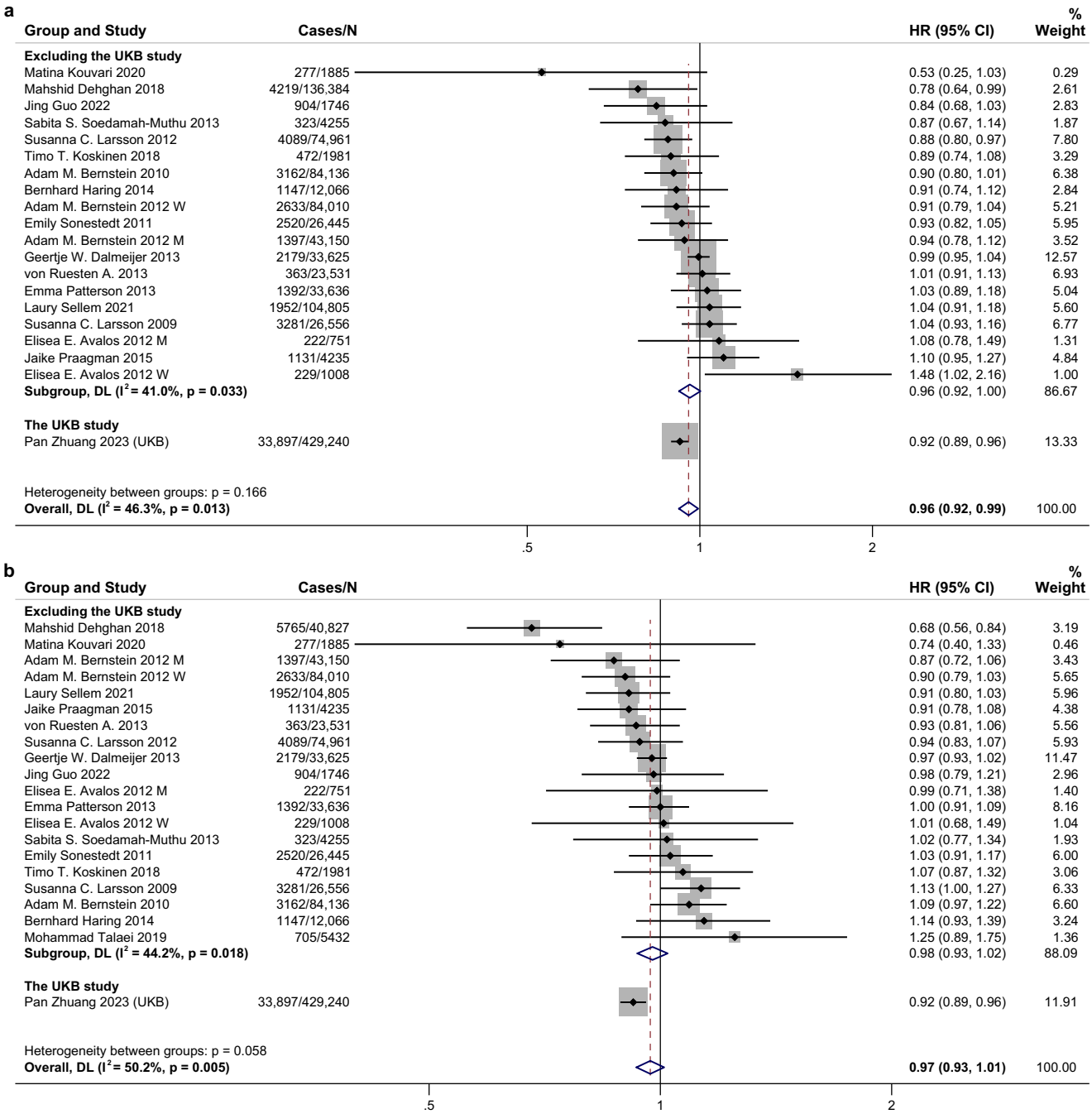

Fig. 3 | Associations of low-fat and high-fat dairy consumption with cardiovascular disease risk for high compared with low category of intake using random effects meta-analysis. a Low-fat dairy. **b** High-fat dairy. Meta-analysis pooling of aggregate data used the random-effects inverse-variance model with DerSimonian-Laird estimate of tau^2. Data are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Squares represent study-specific HRs. Horizontal lines denote 95% CIs. Gray square areas are proportional to the individual study weight for the overall meta-analysis. The red dotted line represents risk ratio of pooled meta-analysis. All statistical tests were two-sided. The blue hollow diamonds represent the results of the meta-analysis for each group, with the center indicating the risk ratio and the width representing the 95% CI. I^2 refers to the proportion of heterogeneity among studies. M, men; W, women; CKB, China Kadoorie Biobank; UKB, UK Biobank. Source data are provided as a Source Data file.

of 24 h dietary recalls were conducted during 2011–2012 to provide an average measure for individuals (repeated measurement per person). A total of 183,446 participants with at least one 24 h dietary recall were included in the study. The number of 24 h dietary records provided by these participants is detailed in Supplementary Data 31. The consistency between dietary touch-screen questionnaires and online 24 h dietary assessments has been reported before[75]. The Spearman coefficients of cheese intake frequency between baseline and resurveys during follow-up are higher than 0.5 Supplementary Data 32. The Oxford WebQ used in online 24 h dietary recalls performed well across key nutrients which were validated using objective urine biomarkers[76].

Ascertainment of incident cardiovascular disease

Detailed information used to define incident CVD cases including fatal or non-fatal CHD and stroke is presented in Supplementary Data 33. Incident cases of CVD were identified by using linkages with disease

registries, national health insurance claim databases, and the local disease surveillance points system death registries by reviewing residential records and/or by visits to local communities for those uninsured participants in CKB to minimize any underreporting cases[70]. The records of CHD and stroke cases were retrieved and reviewed by qualified cardiovascular specialists blinded to the information of patients since 2014[77]. In UKB, information on the CVD cases of all participants was obtained from cumulative hospital inpatient records, death certificates in the national death registries, and self-reports from interviews during follow-up. The high accuracy of this approach has been reported before[78,79]. All events were ascertained using the International Classification of Diseases, 10th Revision (ICD–10).

Statistical analysis

The main exposures of interest were the frequency of total dairy consumption in CKB and the frequency of cheese intake (<2, 2 to 4, 5 to 6, or ≥7 times a week), milk type, and total dairy consumption in UKB. In UKB, the frequency of cheese intake and milk type were collected by the touch-screen questionnaire, while the total dairy consumption was the sum of all types of milk, yogurt, cheese, and ice cream collected by 24 h diet recalls. The intakes of dairy products (0, ≤0.5, 0.5 to 1, or >1 serving per day), milk, yogurt, ice cream, and cheese (0, ≤0.5, or >0.5 serving per day) were categorized into predefined categories based on consumption distributions.

The person-year was calculated from the date of entry to the time of CVD diagnosis, lost to follow-up, death, or the end date of follow-up (December 31, 2016, for CKB, and 31 December 2020 for UKB), whichever occurred earlier. Only 1.2% of individuals in CKB and 0.3% in UKB were lost to follow-up and censored in analyses. Cox proportional hazards regression model was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of CVD risk for total or each type of dairy product consumption after checking the violation of the proportional hazard assumption. To control known and potential confounders, multivariable models were sequentially adjusted for age, sex, race, study area (for CKB)/assessment centers (for UKB), body mass index (BMI), education level, household income, Townsend deprivation index (TDI, only in UKB), smoking status, alcohol drinking, physical activity, history of hypertension, history of diabetes, family history of CVD, use of vitamins, minerals, and aspirin, and consumption frequency of red meat, processed red meat (only in UKB), fish, oily fish (only in UKB), non-oily fish (only in UKB), poultry, vegetables, fruits, and eggs (all categories of consumption). The sex information was obtained from the central registry at recruitment in the UKB, while it was collected from the baseline questionnaire in the CKB. Dairy in the final model is compared against carbohydrate-rich foods (grains, starches, sugars) as the implicit substitution. All missing data were coded as an independent category if necessary. The linear trend was tested by fitting the ordinal dairy variables as continuous variables in the models.

As dairy products are one of the major sources of dietary protein, we used substitution analysis to estimate the theoretical effect on CVD risk of substituting one serving of dairy products for an equivalent serving of other common alternative protein sources, including red/processed meat, fish, poultry, eggs, and soybean/legumes[13]. We further examined whether the documented associations varied by subgroups according to baseline characteristics which were important covariates based on previous studies (Supplementary Data 26), including age, sex, BMI, household income, smoking status, alcohol intake frequency, physical activity, diet quality, hypertension, diabetes, and family history of CVD. P interaction was calculated by adding a cross-product term for the baseline stratifying variable with dairy as an ordinal variable in the model. Besides, we conducted several sensitivity analyses. First, we adjusted a healthy diet score[80,81] to evaluate the influence of the overall diet quality. Second, lipid-lowering drugs or antihypertensive medications were further adjusted in the model. Third, we further adjusted for total energy intake to assess whether the relationship between dairy consumption and CVD development was independent of the amount of energy provided. Fourth, we further excluded incident CVD cases within the first 2 years of follow-up or participants with extreme BMIs (<18.5 or >40 kg/m^2). Finally, participants were censored at a 5 y follow-up. In addition, in CKB analysis, we used a multivariable Cox frailty model with random intercepts to account for center clustering (10 regions). In UKB analysis, we further adjusted for salt added to food to see whether the main findings altered. Individuals with at least two 24 h dietary records were included to better represent their usual diet.

All statistical analyses were conducted with SAS 9.4 (SAS Institute, Cary, NC, USA) and a two-sided $P < 0.05$ was considered statistically significant.

Meta-analysis

We performed a systematic review and updated meta-analysis including UKB and CKB studies as well as previous prospective cohort studies which explored the relationship of dairy product intake with CVD risk in the general population. Supplementary Data 34 shows the search strategy. Additional details of the meta-analysis are provided in Supplementary Methods.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The data supporting the findings from this study are available within the manuscript and its supplementary information. Source data are provided with this paper. The research has been conducted using the UK Biobank resource (https://www.ukbiobank.ac.uk) under application number 47365 and China Kadoorie Biobank resource (https://www.ckbiobank.org/) under application number DAR-2020-00282. The data for this research obtained from the above Biobank resources are publicly available to approved researchers for health-related research. Source data are provided with this paper.

Code availability

The analysis code used in this study is available from the corresponding author upon appropriate request.

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Author contributions

J.J.J., and Y.Z. conceived and designed the study. P.Z., J.J.J., X.H.L., Y.L., and Y.A. did the data cleaning, analysis, and interpretation. P.Z. and X.H.L. wrote the manuscript and provided statistical expertize and assistance. P.Z., X.H.L., Y.L., Y.A., Y.Q.W., H.Y., X.Z.W., L.G.Z., D.H.M., Y.M.T., X.M.Y., F.Z., A.L.W., Y.Z., and J.J.J. contributed to the interpretation of the data and critical revision of the manuscript for important intellectual content and approved the final draft. P.Z., J.J.J., and Y.Z. were involved in data acquisition. Y.Z. is the guarantor. Y.Z. and J.J.J. had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

Competing interests

The authors declare no competing interests.

Additional information

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