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EDITORIAL

Are dairy products the answer to metabolic dysfunction-associated fatty liver disease?

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Metabolic dysfunction-associated fatty liver disease (MAFLD), previously known as non-alcoholic fatty liver disease, is currently the most common chronic liver disease and a leading cause of cirrhosis and hepatocellular carcinoma worldwide [1]. MAFLD is strongly associated with obesity, diabetes and the metabolic syndrome. Not surprisingly, lifestyle intervention in terms of diet and physical activity has been shown to reduce hepatic steatosis. When weight reduction through lifestyle changes exceeds 5–10% of the baseline body weight, steatohepatitis and fibrosis can also improve. However, lifestyle intervention is difficult to maintain, with most people regaining weight to different extents after a period of weight reduction [2]. It is also culture specific. For example, the European guidelines recommend the Mediterranean diet as the preferred diet in patients with MAFLD. However, the Mediterranean diet may be inaccessible or too expensive in some countries. Moreover, it is important to remember that unlike other chronic liver diseases, the majority of patients with MAFLD are not seen by hepatologists but primary care physicians, endocrinologists and cardiologists [3]. Therefore, a simple but effective lifestyle message for patients with MAFLD, healthcare providers and the public is of vital importance.

In this issue of *Hepatology International*, Xu et al. conducted a population-based study with a sample size of 36,122 participants aged 20–74 years, excluding those with excessive alcohol consumption, to investigate the association between dairy product intake and MAFLD in the Chinese population [4]. Dietary information was collected via a food frequency questionnaire, and MAFLD diagnosis was established through ultrasonography. The study design incorporated a follow-up analysis to assess the incidence of MAFLD over time. In addition, stratified analysis was employed to explore the associations between dairy intake and MAFLD risk within specific subgroups. This approach involved categorizing the study population into subgroups based on key characteristics, such as age, sex, or the presence of conditions like hypertension, to gain deeper insights into the associations within distinct subpopulations.

The authors found a significant association between dairy intake and the prevalence and incidence of MAFLD. In the baseline analysis, a negative correlation was observed between dairy intake and the prevalence of MAFLD. Specifically, participants who consumed more than seven servings of dairy products per week were less likely to have MAFLD than those who consumed no dairy products (odds ratio 0.91, 95% CI 0.84–0.98).

Moreover, the follow-up analysis demonstrated a significant inverse relationship between the incidence of MAFLD and dairy intake. Participants with higher dairy intake were less likely to develop incident MAFLD (> 7 vs 0 servings/week, hazard ratio = 0.89, 95% CI 0.81–0.98). This inverse association was observed not only for total-dairy intake but also for milk and yogurt intake. Further stratified analysis indicated that the inverse association between total-dairy intake and MAFLD risk was particularly pronounced among individuals without hypertension.

However, when investigating the reversal of MAFLD among participants with the disease at baseline, no significant association was found between MAFLD reversal and total-dairy intake, milk intake, or yogurt intake. The hazard ratios for MAFLD recovery did not reach statistical significance for both high dairy intake (> seven servings/week) and an increase in dairy intake per serving/day. Nevertheless, stratified analysis revealed a positive association between

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Table 1 Studies on the association between dairy product consumption and metabolic dysfunction-associated fatty liver disease

Study	*N*	Setting	Diagnosis of MAFLD	Key findings
Zhang 2020 [5]	24,389	General population	Ultrasound scan	Higher yogurt consumption was inversely associated with the prevalence of newly diagnosed MAFLD
Charatcharoenwitthaya 2021 [6]	252	General population	Vibration-controlled transient elastography	A high intake of full-fat dairy products was inversely associated with the development of MAFLD
Lee 2021 [7]	5171	General population	NAFLD liver fat score	Higher dairy protein intake was significantly and inversely associated with the risk of incident MAFLD in men and women aged ≥ 50 years. Consumption of milk and other dairy products helped prevent the development of MAFLD
Keshavarz 2022 [8]	7540	General population	Fatty liver index	Higher milk consumption was inversely associated with fatty liver index, but there was not any significant association between other types of dairy products and MAFLD
Sun 2022 [9]	11,888	General population	Ultrasound scan	Higher dairy intake was inversely correlated to the incidence of MAFLD
Xu 2024 [4]	36,122	General population	Ultrasound scan	A dairy intake of more than one serving per day was inversely associated with the incidence and prevalence of MAFLD, but the total-dairy intake did not have significant association in MAFLD reversal

MAFLD, metabolic dysfunction-associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease

MAFLD recovery and dairy intake (> 0–2 servings/week) among individuals aged < 55 years and non-menopausal females.

Thus, the study suggests that consuming more than one serving of dairy products per day is associated with a lower prevalence and incidence of MAFLD in the Chinese population. However, total-dairy intake did not demonstrate a significant association with the reversal of MAFLD. It is important to note that variations in the associations were observed based on age, sex, and the presence of hypertension.

Similar to the study by Xu et al., several published studies found that a high intake of dairy product, milk, or yogurt was inversely associated with the development of MAFLD (Table 1) [5–9]. Compared with the other studies, the one by Xu et al. had the biggest sample size and adopted a longitudinal design. The use of abdominal ultrasonography also avoided the inclusion of metabolic factors in the diagnosis of hepatic steatosis as in some serum scores.

Does it mean we should now recommend all patients with MAFLD or even everyone to consume more dairy products? The existing studies, including the one by Xu et al., are all observational studies and retrospective in nature. Selection bias, recall bias, confounding and reverse causality might all be at play. Besides, lifestyle is complicated. A person who consumes more dairy product may also have concurrent differences in diet, alcohol consumption and physical activity, and many of these factors may not be easy to dissect.

That being said, perfection is the enemy of the good. As it is unlikely that investigators will conduct randomized controlled trials to test the therapeutic effect of dairy products with the same scientific vigor as drug trials for metabolic dysfunction-associated steatohepatitis, we should make the most out of observational data to come out with least biased recommendations. According to the Bradford Hill criteria for causality [10], a causal relationship can be inferred if the followings are met: strong association (modest for dairy product), consistency across studies (fulfilled), specificity for the population and disease (not quite), temporality (confirmed in the longitudinal data), dose–response effect (probably), biologic plausibility (yes), coherence (yes), supported by experimental data (some), and analogy (probably).

In recent years, there has also been much interest in the development of data-driven models for causal inference. Among them, the structural causal model framework and the potential outcome framework are relatively popular, and different models can be used in the same study to interrogate the data and come up with more robust conclusions.

In conclusion, the interesting study by Xu et al. suggests another lifestyle advice we may offer to people with or at risk of MAFLD. Meanwhile, other important lifestyle elements such as low-sugar consumption and physical activity should not be neglected. We also encourage investigators to interrogate data rigorously using contemporary statistical- and machine-learning models.

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Declarations

Conflict of interest Vincent Wong served as a consultant or advisory board member for AbbVie, Boehringer Ingelheim, Echosens, Gilead Sciences, Intercept, Inventiva, Novo Nordisk, Pfizer, Sagimet Biosciences, TARGET PharmaSolutions, and Visirna; and a speaker for Abbott, AbbVie, Gilead Sciences, Novo Nordisk, and Unilab. He has received a research grant from Gilead Sciences, and is a co-founder of Illuminatio Medical Technology. Kristopher Lau reports no conflicts of interest.

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