

Dairy products: good or bad for cardiometabolic disease?^{1,2}

D Ian Givens

Two studies are published in the current issue of the Journal (1, 2) that tackle in different ways the considerable challenge of understanding the relation between dairy product consumption and cardiometabolic health. One study (1) reports on the cross-sectional association between dairy food intake and estimates of glycemic status in a large Brazilian cohort (10,010 after excluding those with diabetes and other chronic diseases). The other study (2) reports on a randomized controlled trial (RCT) that examines the effects of milk proteins on postprandial lipemia. These studies raise a number of issues concerning the study of dairy foods and health.

There is a long-held, technically correct, view that evidence from cohort studies, and particularly those of a cross-sectional nature, is much weaker than that from an RCT. In truth, both are valuable and often complementary. Prospective cohort studies, in particular, although giving only statistical associations, have the big advantage of large populations and real disease events as the outcome measures; whereas RCTs can probe more deeply into mechanisms, they often rely on a limited number of markers of disease risk, which can vary considerably in their predictive power. The second study in this issue (2), an RCT in abdominally obese subjects, is concerned with the effect of dairy proteins and fatty acids on postprandial lipemia. The choice of these subjects is interesting, because although it is universally agreed that obesity should be reduced, this is likely to be a largely unfulfilled aspiration and it is therefore vital to understand cardiometabolic responses to diet in those who are obese. The study by Drehmer et al. (1) reported that greater dairy intake, especially of fermented dairy products, was associated with improved glucose homeostasis/insulin sensitivity, which, interestingly, was independent of obesity status. These findings are broadly in accord with findings in other individual cohort studies (3) and in a meta-analysis of these studies examining the risk of type 2 diabetes (4); although the latter reported a greater benefit of low-fat dairy products, Drehmer et al. (1) did not. The meta-analysis (4) also reported a greater effect of fermented dairy foods (e.g., yogurt, cheese) than nonfermented dairy foods, which is in agreement with other studies (e.g., reference 5).

There has been much focus and concern about the role of dairy products as major dietary sources of SFAs, and it is interesting that Drehmer et al. (1) suggested that myristic acid (14:0) in dairy foods may play a part in improving glucose homeostasis. This appears to be in contradiction to the findings of the EPIC (European Prospective Investigation into Cancer and Nutrition)–InterAct

case-cohort study (6), which showed a positive relation between myristic acid [and palmitic acid (16:0), stearic acid (18:0)] concentration in plasma phospholipids and diabetes risk, although, interestingly, concentrations of odd-numbered [pentadecanoic acid (15:0), heptadecanoic acid (17:0)] and long-chain [eicosanoic acid (20:0)–tetracosanoic acid (24:0)] SFAs were associated with reduced risk. Other prospective studies (e.g., reference 7) showed plasma phospholipid *trans*-palmitoleic acid (*trans*-16:1n-7) concentration to be associated with lower incident type 2 diabetes (*P*-trend = 0.02), but it remains unclear if *trans*-palmitoleic acid and the odd-numbered and long-chain SFAs are mechanistically involved in diabetes reduction or simply markers of dairy food intake. It is also noteworthy and concerning that the E3N-EPIC study found a significant (*P*-trend = 0.002) positive relation between plasma phospholipid *trans*-palmitoleic acid and risk of breast cancer (8).

The RCT by Bohl et al. (2) studied the effects of milk proteins on postprandial lipemia, a somewhat understudied state considering the fact that currently most people in Western societies are in the postprandial state for up to 18 h/d. This study compared the effects of whey protein and casein with or without medium-chain SFAs in butter. Broadly, they showed that the postprandial apolipoprotein B-48 response to a high-fat meal was significantly reduced after consumption of 60 g whey protein but not after casein consumption and was independent of medium-chain SFAs. Other studies showed whey proteins to have an insulinotropic effect most probably related to branched-chain amino acids and specifically leucine. The reduced apolipoprotein B-48 response to whey protein is indicative of a reduced number of chylomicron particles, which may provide reduced cardiovascular disease (CVD) risk, although whether long-term daily consumption of 60 g whey protein as used in this study is likely to be achieved by free-living individuals may be questionable. Nevertheless, the study highlights the important role that milk proteins play in chronic disease prevention. Although there is also evidence that milk proteins play a key role in blood pressure control (9), it was also shown that whey protein but not casein can reduce vascular stiffness, an emerging CVD risk factor (10).

¹ From the Food Production and Quality Division, Faculty of Life Sciences, University of Reading, Reading, United Kingdom.

² Address correspondence to DI Givens, Food Production and Quality Division, Faculty of Life Sciences, University of Reading, Earley Gate, Reading RG6 6AR, United Kingdom. E-mail: d.i.givens@reading.ac.uk.

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These various studies highlight several areas of considerable uncertainty, including the following: 1) what constitutes a high- and low-fat dairy product and do they possess different risks/benefits for disease, 2) why do fermented products appear to impart greater benefit, 3) what are the differential effects of different SFAs/*trans* fatty acids, and 4) what study designs are needed to truly understand the cardiometabolic response to dairy product consumption? It can be stated with some confidence that not all dairy SFAs are equal in relation to CVD risk and indeed evidence is increasing that the risk may be small or nonexistent (11), and that the role of milk proteins in reducing cardiometabolic risk is likely to be substantial. Studies into the impact of dairy products on cardiometabolic risk therefore need to be more holistic in nature rather than concentrating on dairy lipids and proteins independent of each other.

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REFERENCES

- Drehmer M, Pereira MA, Schmidt MI, Molina MDCB, Alvim S, Lotufo PA, Duncan BB. Associations of dairy intake with glycemia and insulinemia, independent of obesity, in Brazilian adults: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *Am J Clin Nutr* 2015;101:775–82.
- Bohl M, Bjørnshave A, Rasmussen KV, Schioldan AG, Amer B, Larsen MK, Dalsgaard TK, Holst JJ, Herrmann A, O'Neill S, et al. Dairy proteins, dairy lipids, and postprandial lipemia in persons with abdominal obesity (DairyHealth): a 12-wk, randomized, parallel-controlled, double-blinded, diet intervention study. *Am J Clin Nutr* 2015;101:870–8.
- Elwood PC, Pickering JE, Givens DI, Gallacher J. The consumption of milk and dairy foods and the incidence of vascular disease and diabetes: an overview of the evidence. *Lipids* 2010;45:925–39.
- Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Am J Clin Nutr* 2013;98:1066–83.
- Sluijjs I, Forouhi NG, Beulens JW, van der Schouw YT, Agnoli C, Arriola L, Balkau B, Barricarte A, Boeing H, Bas Bueno-de-Mesquita H, et al. The amount and type of dairy product intake and incident type 2 diabetes: results from the EPIC-InterAct Study. *Am J Clin Nutr* 2012;96:382–90.
- Forouhi NG, Koulman A, Sharp SJ, Fumiaki I, Kröger J, Schulze MB, Crowe FL, Huerta JM, Guevara M, Beulens JWJ, et al. Differences in the prospective association between individual plasma phospholipid saturated fatty acids and incident type 2 diabetes: the EPIC-InterAct case-cohort study. *Lancet Diabetes Endocrinol* 2014;2:810–8.
- Mozaffarian D, de Oliveira Otto MC, Lemaitre RN, Fretts AM, Hotamisligil G, Tsai M, Siscovick DS, Nettleton JA. *trans*-Palmitoleic acid, other dairy fat biomarkers, and incident diabetes: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* 2013;97:854–61.
- Chajès V, Thiébaud ACM, Rotival M, Gauthier E, Maillard V, Boutron-Ruault M-C, Joulin V, Lenoir GM, Clavel-Chapelon F. Association between serum trans-monounsaturated fatty acids and breast cancer risk in the E3N-EPIC study. *Am J Epidemiol* 2008;167:1312–20.
- Fekete AA, Givens DI, Lovegrove JA. Casein-derived lactotripeptides reduce systolic and diastolic blood pressure in a meta-analysis of randomised clinical trials. *Nutrients* 2015;7:659–81.
- Pal S, Ellis V. The chronic effects of whey proteins on blood pressure, vascular function and inflammatory markers in overweight individuals. *Obesity (Silver Spring)* 2010;18:1354–9.
- Astrup A. A changing view on SFAs and dairy: from enemy to friend. *Am J Clin Nutr* 2014;100:1407–8.

