

Highlights

- The milk matrix describes the unique structure of milk, its components, and how they interact, and how this impacts potential health effects upon consumption.
- Scientific evidence shows either neutral or beneficial associations between milk consumption and cardiometabolic health.
- The mechanisms underlying the effects of milk consumption on bone health are not fully understood, but experts believe the milk matrix exerts a positive effect on bone that goes beyond calcium intake.
- A decreased risk of colorectal cancer has been observed with increased consumption of milk, attributed to factors such as improved calcium absorption.

Factsheet series summary

Nowadays, nutrition research focuses on the holistic impact of whole foods on health. This entails the recognition that a food's impact is shaped by the interaction of its components and structure, going beyond the sum of its individual nutrients (i.e., food matrix effect). This factsheet series delves into the emerging body of research on the dairy matrix, reshaping current nutritional and health perspectives. Dairy foods have different matrices that result in distinct matrix effects.

What is the milk matrix?

Milk is an emulsion that consists of droplets of fat suspended in an aqueous phase containing proteins, lactose and numerous vitamins and minerals. The milk lipids are part of the milk fat globules that are surrounded by a trilayer structure, i.e., the milk fat globule membrane (MFGM), of which the more prominent components are proteins and polar lipids with potential bioactive functions (Lopez et al., 2015).

The milk matrix concept describes the unique structure of milk, its nutrient and non-nutrient components, and how they interact, that ultimately impact milk digestion, nutrient absorption, and physiological functions important for health (International Dairy Federation, 2023; Unger et al., 2023).

Milk matrix health effects

Research consistently indicates that the health effects of milk, as a whole, differ from the effects of its individual nutrients.

Cardiometabolic health

The latest scientific evidence, based on systematic reviews and meta-analyses of prospective cohort studies, shows neutral or beneficial associations between total milk consumption and cardiovascular (CV) and metabolic health outcomes (see Table 1). These studies showed that intake of total whole-fat dairy (including milk) is not associated with CV risk factors in accordance with a recent systematic review on markers of cardiometabolic health (Kiesswetter et al., 2023). It is important to highlight that most of the scientific research has grouped dairy products together, therefore showing the effects of total dairy (using various definitions), which makes comparisons on associations of dairy with chronic disease complex. Interestingly, Engel et al. (2018) showed that whole milk consumption did not negatively impact body lipids compared to fat-free milk, suggesting that saturated fat embedded in the milk matrix does not seem to affect health outcomes differently than low-fat milk.

Several studies have consistently shown inverse associations between total milk consumption and risk of developing metabolic syndrome (MetS), hypertension and stroke (Bhavadharini et al., 2020; Chen et al., 2021; Feng et al., 2022; Heidari et al., 2021). Overall, the positive benefits of milk consumption have been attributed to the milk matrix, postulating interactions between calcium, phosphorus, potassium, bioactive peptides, and the MFGM (Torres-Gonzalez & Rice Bradley, 2023).

As shown in Table 1, consumption of milk has been associated with neutral risk of developing type 2 diabetes (T2D). Nevertheless, a recent large Australian cohort study, with 12 years of follow-up investigating risk of prediabetes, showed protective associations for whole milk, whereas neutral associations were seen for low-fat dairy (Slurink et al., 2023). A theoretical population attributable risk analysis to estimate the burden of disease from low dairy intake showed that consumption of milk was associated with decreased risk of T2D (Cohen et al., 2022). Milk has been shown to provide limited glycemic responses while delivering high levels of carbohydrates through factors like controlled gastric emptying rate and sugar absorption, and increased insulin release (Shkembi & Huppertz, 2023a).

The Prospective Urban Rural Epidemiology (PURE) study, which was a large prospective study of 136 384 individuals from 21 countries on 5 continents who were followed for 9 years, found that milk consumption was inversely associated with all-cause mortality and major CV diseases events (Dehghan et al., 2018). Additional results from the PURE study looking at dairy foods and MetS, incidence of T2D and hypertension found that consumption of dairy foods -especially whole milk dairy foods- was associated with lower risk of MetS and lower incidence of T2D and hypertension (Bhavadharini et al., 2020). More recently, a study analyzing data from several regions across the world, involving 245 000 people from 80 countries, found that a diet that includes higher amounts of whole-fat dairy (including milk) is associated with lower risk of CV disease, heart attack, stroke, and mortality (Mente et al., 2023).



Table 1. Milk consumption and cardiometabolic health outcomes in dose-response meta-analyses of cohort studies.

Study	Stroke	Type 2 Diabetes	Coronary heart disease	Hypertension	Overweight or obesity
Feng et al. (2022)		Neutral		Beneficial	Beneficial
Chen et al. (2021)	Beneficial		Neutral	Neutral	
(Heidari et al., 2021)				Beneficial	
Soedamah-Muthu and De Goede (2018)	Beneficial	Neutral	Neutral		

Beneficial refers to a statistically significant reduced risk. Neutral refers to no statistically significant effect – neither beneficial nor harmful. Grey cells indicate the parameter was not assessed.

Bone and musculoskeletal health

The mechanisms underlying the effects of milk consumption on bone health are not fully understood, but researchers believe that the dairy matrix exerts an effect on bone that goes beyond calcium (Geiker et al., 2020). In a follow-up study for 32 years of two US cohorts of 80 600 women and 43 306 men over 50 years, each serving of milk per day was associated with a significant 8% lower risk of hip fracture in men and women combined (Feskanich et al., 2018). A recent meta-analysis of cohort studies found reductions in the risk of hip fracture with milk consumption only among American adults, but not among Scandinavian adults, possibly because milk products are more commonly fortified with vitamin D in the American population (Geiker et al., 2020).

In comparison with other sources of calcium, several foods of plant origin contain high calcium levels but its absorption is adversely affected by the presence and interactions of anti-nutritional factors contained in the food matrix, such as oxalates and phytates (Shkembi & Huppertz, 2021). It is thought that the unique molecular structure of calcium in milk (i.e., calcium phosphate nanoclusters of the casein micelles) allows a higher delivery of its stable and bioavailable form (Lenton et al., 2015) with the help of other nutrients such as vitamin D, K_2 and high-quality protein.

Moreover, milk consumption has been associated with a positive impact on dental health related to various aspects, e.g., the presence of high levels of calcium and phosphate, its buffering capacity, and the specific phosphorylated sequences in the main milk proteins (Shkembi & Huppertz, 2023b). Interestingly and emphasizing the importance of the food matrix, soy beverage with added calcium did not show the same enamel mineralisation effect as milk (Shen et al., 2019).

Colorectal cancer

As part of the 2019 Global Burden of Disease study, a systematic analysis of data from 204 countries (1990-2019) estimated the incidence, mortality, and disability-adjusted life years (DALYs) linked to colorectal cancer (Sharma et al., 2022). Globally, the main contributors to colorectal cancer DALYs were a diet low in milk (15.6%), smoking (13.3%), and a diet low in calcium (12.9%).

Recent systematic reviews and meta-analyses found consistent neutral or beneficial decreases in the risk of colorectal cancer (CRC) in those who consumed more dairy products and milk (Alegria-Lertxundi et al., 2022; Barrubés et al., 2018; Jin et al., 2020). The World Cancer Research Fund report concludes that the observed inverse associations between intake of dairy products and CRC development have been largely attributed to "their high calcium content. In addition to calcium,



lactic acid-producing bacteria may also protect against CRC, while the casein and lactose in milk may increase calcium bioavailability" (World Cancer Research Fund, 2018).

Conclusions

The evidence of milk consumption consistently shows either neutral or beneficial health effects. However, more research is needed to understand the individual health effects of the milk type, including differentiating the impact of low-fat versus whole milk. Researchers will continue to explore the milk matrix more in-depth, including the mechanisms and pathways through which the different milk components work together and impact health, based on an evaluation of the health effects of the entire milk matrix, not just single nutrients. Shifting the focus from nutrient-based policy recommendations to a more comprehensive dietary pattern-based approach may be more beneficial for health and may, in turn, encourage consumers to make the right food-based dietary choices.

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References

- Alegria-Lertxundi, I., Bujanda, L., & Arroyo-Izaga, M. (2022). Role of Dairy Foods, Fish, White Meat, and Eggs in the Prevention of Colorectal Cancer: A Systematic Review of Observational Studies in 2018-2022. *Nutrients*, 14(16). <u>https://doi.org/10.3390/nu14163430</u>
- Barrubés, L., Babio, N., Mena-Sánchez, G., Toledo, E., Ramírez-Sabio, J. B., Estruch, R., Ros, E., Fitó, M., Arós, F., Fiol, M., Santos-Lozano, J. M., Serra-Majem, L., Pintó, X., Martínez-González, M. Á., Sorlí, J. V., Basora, J., & Salas-Salvadó, J. (2018). Dairy product consumption and risk of colorectal cancer in an older mediterranean population at high cardiovascular risk. *International Journal of Cancer*, 143(6), 1356-1366. <u>https://doi.org/10.1002/ijc.31540</u>
- Bhavadharini, B., Dehghan, M., Mente, A., Rangarajan, S., Sheridan, P., Mohan, V., Iqbal, R., Gupta, R., Lear, S., Wentzel-Viljoen, E., Avezum, A., Lopez-Jaramillo, P., Mony, P., Varma, R. P., Kumar, R., Chifamba, J., Alhabib, K. F., Mohammadifard, N., Oguz, A., Lanas, F., Rozanska, D., Bostrom, K. B., Yusoff, K., Tsolkile, L. P., Dans, A., Yusufali, A., Orlandini, A., Poirier, P., Khatib, R., Hu, B., Wei, L., Yin, L., Deeraili, A., Yeates, K., Yusuf, R., Ismail, N., Mozaffarian, D., Teo, K., Anand, S. S., & Yusuf, S. (2020). Association of dairy consumption with metabolic syndrome, hypertension and diabetes in 147812 individuals from 21 countries. *BMJ Open Diabetes Research & Care*, 8(1), e000826. https://doi.org/10.1136/bmjdrc-2019-000826
- Chen, Z., Ahmed, M., Ha, V., Jefferson, K., Malik, V., Ribeiro, P. A. B., Zuchinali, P., & Drouin-Chartier, J. P. (2021). Dairy Product Consumption and Cardiovascular Health: a Systematic Review and Meta-Analysis of Prospective Cohort Studies. *Adv Nutr*, 13(2), 439-454. <u>https://doi.org/10.1093/advances/nmab118</u>
- Cohen, S. S., Bylsma, L. C., Movva, N., & Alexander, D. D. (2022). Theoretical attributable risk analysis and Disability Adjusted Life Years (DALYs) based on increased dairy consumption. *BMC public health*, 22(1), 1625. <u>https://doi.org/10.1186/s12889-022-14042-7</u>
- Dehghan, M., Mente, A., Rangarajan, S., Sheridan, P., Mohan, V., Iqbal, R., Gupta, R., Lear, S., Wentzel-Viljoen, E., & Avezum, A. (2018). Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *The Lancet*, 392(10161), 2288-2297. https://doi.org/10.1016/S0140-6736(18)31812-9
- Feng, Y., Zhao, Y., Liu, J., Huang, Z., Yang, X., Qin, P., Chen, C., Luo, X., Li, Y., Wu, Y., Li, X., Huang, H., Hu, F., Hu, D., Liu, Y., & Zhang, M. (2022). Consumption of Dairy Products and the Risk of Overweight or Obesity, Hypertension, and Type 2 Diabetes Mellitus:
 A Dose–Response Meta-Analysis and Systematic Review of Cohort Studies. *Advances in Nutrition*, *13*(6), 2165-2179. <u>https://doi.org/10.1093/ADVANCES/NMAC096</u>
- Feskanich, D., Meyer, H. E., Fung, T. T., Bischoff-Ferrari, H. A., & Willett, W. C. (2018). Milk and other dairy foods and risk of hip fracture in men and women. Osteoporos Int, 29(2), 385-396. <u>https://doi.org/10.1007/s00198-017-4285-8</u>
- Geiker, N. R. W., Mølgaard, C., Iuliano, S., Rizzoli, R., Manios, Y., van Loon, L. J. C., Lecerf, J. M., Moschonis, G., Reginster, J. Y., Givens, I., & Astrup, A. (2020). Impact of whole dairy matrix on musculoskeletal health and aging-current knowledge and research gaps. *Osteoporos Int*, 31(4), 601-615. <u>https://doi.org/10.1007/s00198-019-05229-7</u>



- Heidari, Z., Rashidi Pour Fard, N., Clark, C. C. T., & Haghighatdoost, F. (2021). Dairy products consumption and the risk of hypertension in adults: An updated systematic review and dose–response meta-analysis of prospective cohort studies. *Nutrition, Metabolism and Cardiovascular Diseases*, *31*(7), 1962-1975. https://doi.org/10.1016/j.numecd.2021.02.033
- International Dairy Federation. (2023). *Dairy matrix: Understanding its impact on the health effects of dairy foods* (Factsheet of the IDF N° 27/2023). <u>https://doi.org/10.56169/DEIX9744</u>
- Jin, S., Kim, Y., & Je, Y. (2020). Dairy Consumption and Risks of Colorectal Cancer Incidence and Mortality: A Meta-analysis of Prospective Cohort Studies. *Cancer Epidemiology, Biomarkers & Prevention*, 29(11), 2309-2322. <u>https://doi.org/10.1158/1055-9965.Epi-20-0127</u>
- Kiesswetter, E., Stadelmaier, J., Petropoulou, M., Morze, J., Grummich, K., Roux, I., Lay, R., Himmelsbach, L., Kussmann, M., Roeger, C., Rubach, M., Hauner, H., & Schwingshackl, L. (2023). Effects of Dairy Intake on Markers of Cardiometabolic Health in Adults: A Systematic Review with Network Meta-Analysis. *Advances in Nutrition*, 14(3), 438-450. <u>https://doi.org/10.1016/j.advnut.2023.03.004</u>
- Lenton, S., Nylander, T., Teixeira, S. C. M., & Holt, C. (2015). A review of the biology of calcium phosphate sequestration with special reference to milk. *Dairy Science & Technology*, *95*(1), 3-14. <u>https://doi.org/10.1007/s13594-014-0177-2</u>
- Mente, A., Dehghan, M., Rangarajan, S., O'Donnell, M., Hu, W., Dagenais, G., Wielgosz, A., A. Lear, S., Wei, L., Diaz, R., Avezum, A., Lopez-Jaramillo, P., Lanas, F., Swaminathan, S., Kaur, M., Vijayakumar, K., Mohan, V., Gupta, R., Szuba, A., Iqbal, R., Yusuf, R., Mohammadifard, N., Khatib, R., Nasir, N. M., Karsidag, K., Rosengren, A., Yusufali, A., Wentzel-Viljoen, E., Chifamba, J., Dans, A., Alhabib, K. F., Yeates, K., Teo, K., Gerstein, H. C., & Yusuf, S. (2023). Diet, cardiovascular disease, and mortality in 80 countries. *European Heart Journal*, 44(28), 2560-2579. https://doi.org/10.1093/eurheartj/ehad269
- Sharma, R., Abbasi-Kangevari, M., Abd-Rabu, R., Abidi, H., Abu-Gharbieh, E., Acuna, J. M., Adhikari, S., Advani, S. M., Afzal, M. S., Aghaie Meybodi, M., Ahinkorah, B. O., Ahmad, S., Ahmadi, A., Ahmadi, S., Ahmed, H., Ahmed, L. A., Ahmed, M. B., Al Hamad, H., Alahdab, F., . . . Zoladl, M. (2022). Global, regional, and national burden of colorectal cancer and its risk factors, 1990 2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Gastroenterology & Hepatology*, *7*(7), 627-647. https://doi.org/10.1016/S2468-1253(22)00044-9
- Shen, P., Walker, G. D., Yuan, Y., Reynolds, C., Stanton, D. P., Fernando, J. R., & Reynolds, E. C. (2019). Effects of soy and bovine milk beverages on enamel mineral content in a randomized, double-blind in situ clinical study. *Journal of Dentistry*, 88, 103160. <u>https://doi.org/10.1016/j.jdent.2019.06.007</u>
- Shkembi, B., & Huppertz, T. (2021). Calcium Absorption from Food Products: Food Matrix Effects. Nutrients 2022, Vol. 14, Page 180, 14(1), 180-180. <u>https://doi.org/10.3390/NU14010180</u>
- Shkembi, B., & Huppertz, T. (2023a). Glycemic Responses of Milk and Plant-Based Drinks: Food Matrix Effects. *Foods*, 12(3), 453. <u>https://doi.org/10.3390/foods12030453</u>



- Shkembi, B., & Huppertz, T. (2023b). Impact of Dairy Products and Plant-Based Alternatives on Dental Health: Food Matrix Effects. *Nutrients*, *15*(6). <u>https://doi.org/10.3390/nu15061469</u>
- Slurink, I. A. L., Chen, L., Magliano, D. J., Kupper, N., Smeets, T., & Soedamah-Muthu, S. S. (2023). Dairy Product Consumption and Incident Prediabetes in the Australian Diabetes, Obesity, and Lifestyle Study With 12 Years of Follow-Up. *The Journal of Nutrition*, 153(6), 1742-1752. <u>https://doi.org/10.1016/j.tjnut.2023.03.032</u>
- Soedamah-Muthu, S. S., & De Goede, J. (2018). Dairy consumption and cardiometabolic diseases: systematic review and updated meta-analyses of prospective cohort studies. *Current Nutrition Reports*, 7, 171-182. <u>https://doi.org/10.1007/s13668-018-0253-y</u>
- Torres-Gonzalez, M., & Rice Bradley, B. H. (2023). Whole-milk dairy foods: biological mechanisms underlying beneficial effects on risk markers for cardiometabolic health. *Advances in Nutrition*. <u>https://doi.org/10.1016/j.advnut.2023.09.001</u>
- Unger, A. L., Astrup, A., Feeney, E. L., Holscher, H. D., Gerstein, D. E., Torres-Gonzalez, M., & Brown, K. (2023). Harnessing the Magic of the Dairy Matrix for Next-Level Health Solutions: A Summary of a Symposium Presented at Nutrition 2022. *Current Developments in Nutrition*, 7(7), 100105. <u>https://doi.org/10.1016/j.cdnut.2023.100105</u>

