

REVIEW ARTICLE

Edward W. Campion, M.D., *Editor*

Milk and Health

Walter C. Willett, M.D., Dr.P.H., and David S. Ludwig, M.D., Ph.D.

From the Departments of Nutrition (W.C.W., D.S.L.) and Epidemiology (W.C.W.), Harvard T.H. Chan School of Public Health; Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School (W.C.W.); the Department of Pediatrics, Harvard Medical School (D.S.L.); and the New Balance Foundation Obesity Prevention Center, Boston Children's Hospital (D.S.L.) — all in Boston.

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MILK PRODUCTS FROM COWS AND OTHER NONHUMAN MAMMALS ARE major components of traditional Western diets, especially in cold climates. The recommended intake of milk or equivalent portions of cheese, yogurt, or other dairy products in the United States is three 8-oz (237 ml) servings per day for adults and children 9 years of age or older, an amount that is substantially higher than the current average intake among adults of 1.6 servings per day.¹ The recommended intake amount has been justified to meet nutritional requirements for calcium and reduce the risk of bone fractures. However, the health benefit of a high intake of milk products has not been established, and concerns exist about the risks of possible adverse health outcomes. Therefore, the role of dairy consumption in human nutrition and disease prevention warrants careful assessment.

COMPOSITION OF DAIRY PRODUCTS

Because the natural function of milk is to nourish and promote the growth of young mammals, it contains all essential nutrients as well as multiple anabolic hormones (Table 1).³⁻⁶ To increase milk production, cows have been bred to produce higher levels of insulin-like growth factor I (IGF-I),⁷ and they are pregnant for most of the time they are milked,⁸ which greatly increases levels of progesterone, estrogens, and other hormones in milk.⁹

Milk processing has many potential health implications. Pasteurization reduces transmission of brucellosis, tuberculosis, and other pathogens. Fermentation to produce aged cheese, yogurt, kefir, and other products denatures peptide hormones, alters protein antigens, reduces lactose content, and affects bacterial composition.¹⁰ Fractionation yields butter, reduced-fat products, and whey protein, and fortification with vitamins A and D can supplement diets.

GROWTH AND DEVELOPMENT

If breast milk is not available, cow's milk (as the basis of infant formula for children younger than 1 year of age) can add important nutritional value during early childhood. However, normal growth and development can be obtained throughout childhood without dairy products if attention is given to diet quality,¹¹ including the use of supplemental B₁₂ in diets that include few animal products and vitamin D to compensate for low sun exposure.

Even with adequate overall nutrition, milk consumption augments longitudinal growth and attained height.¹²⁻¹⁴ Whether this growth-promoting effect is caused by specific amino acids, anabolic hormones, or other factors is not clear. Cow's milk contains substantial amounts of the branched-chain amino acids leucine, isoleucine, and valine, which are key to protein quality. Consumption of these amino acids by humans increases plasma concentrations of IGF-I, which mediates

growth hormone action,¹⁵⁻²⁰ and leucine specifically activates the mammalian target of rapamycin (mTOR) pathway, which promotes cell replication and inhibits apoptosis.²¹ However, the health consequences of accelerated growth and greater adult height are complex. Tall stature is associated with lower risks of cardiovascular disease²² but with higher risks of many cancers,²³ hip fractures,²⁴ and pulmonary emboli.²²

BONE HEALTH AND FRACTURE RISK

A central rationale for high lifelong milk consumption has been to meet calcium requirements for bone health (Table 2).²⁶ Paradoxically, countries with the highest intakes of milk and calcium tend to have the highest rates of hip fractures (Fig. 1).^{30,31} Although this correlation may not be causal and might be due to confounding by factors such as vitamin D status and ethnicity, low dairy consumption is clearly compatible with low rates of hip fracture.

The basis for the U.S. recommendations for milk consumption derives from studies assessing the balance of calcium intake and excretion in just 155 adults in whom the estimated calcium intake needed to maintain balance was 741 mg per day.^{25,32} Beyond small size, these balance studies have other serious limitations, including short duration (2 to 3 weeks) and high habitual calcium intakes. By contrast, the estimated balance was attained at approximately 200 mg of dietary calcium per day among Peruvian men with low habitual calcium intake,³³ a finding consistent with the ability of the body to greatly

Table 1. Nutrient Composition of Human and Cow's Milk and Cheese.*

| Component | Human Milk | Whole-Fat Cow's Milk | Fat-Free Cow's Milk | Cheddar Cheese† |
|-------------------|------------|----------------------|---------------------|-----------------|
| | | | | |
| No. of kcal | 172 | 149 | 83 | 149 |
| Protein — g | 2.5 | 7.7 | 8.2 | 8.4 |
| Total fat — g | 10.8 | 7.9 | 0.2 | 12.3 |
| Saturated fat — g | 4.9 | 4.6 | 0.1 | 7.0 |
| Carbohydrate — g | 16.9 | 11.7 | 12.1 | 1.1 |
| Calcium — mg | 78.7 | 276.0 | 298.0 | 262.0 |
| Potassium — mg | 125.0 | 322.0 | 381.0 | 28.0 |
| Phosphorus — mg | 34.4 | 205.0 | 246.0 | 167.9 |

* Values are from the U.S. Department of Agriculture.²

† The amount of cheese (37 g) is isocaloric with 237 ml of whole milk.

upregulate absorption when dietary calcium is low. In randomized trials that used bone mineral density as a surrogate for fracture risk, calcium supplements of 1000 to 2000 mg per day resulted in 1 to 3% greater bone mineral density than placebo. If sustained, this small divergence could be important. However, after 1 year, the rate of change in bone mineral density among late perimenopausal and postmenopausal women equaled that of placebo³⁴; with discontinuation of supplementation, the small difference in bone mineral density is lost.³⁵ Because of this transient phenomenon, trials lasting 1 year or less can be misleading,³⁴ and the 2-to-3-week balance studies used to establish calcium requirements have limited relevance to fracture risk.³³ We therefore think that cross-sectional studies can pro-

Table 2. Suggested Calcium Intake Amounts, According to the United States, United Kingdom, and World Health Organization, by Age.

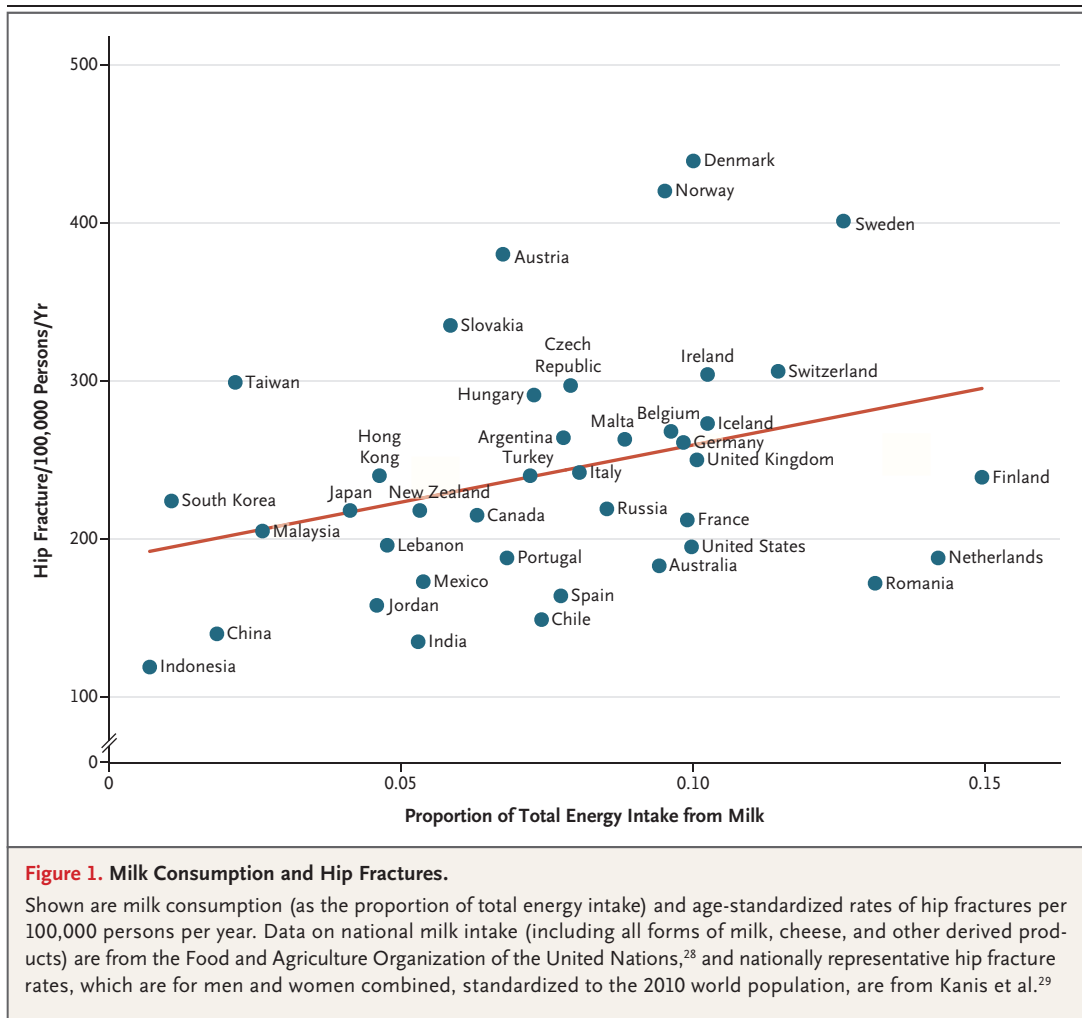
| Source | Age Group | | | | | | |
|-----------------|---------------------------|-----------|--------------------------------|--|-------------|-----------------------|------|
| | 0 to 1 yr | 1 to 3 yr | 4 to 18 yr | 19 to 50 yr | 51 to 70 yr | >70 yr | |
| | <i>milligrams per day</i> | | | | | | |
| United States* | — | 700 | 1000 (4–8 yr) | 1300 (9–18 yr) | 1000 | 1000 (M), 1200 (F) | 1200 |
| United Kingdom† | 525 | 350 | 450 (4–6 yr), 550 (7–10 yr) | 1000 (11–18 yr, M), 800 (11–18 yr, F) | 700‡ | 700 | |
| WHO§ | — | — | — | | 500 | 500 | 500 |

* Data are from the Institute of Medicine.²⁵ F denotes female, and M male.

† Data are from the Committee on Medical Aspects of Food and Nutrition Policy, U.K. Department of Health.²⁶

‡ Intake during lactation is recommended to be increased by 550 mg per day.²⁶

§ Data are from the World Health Organization (WHO) Report of a Joint WHO/FAO Expert Consultation.²⁷



vide additional useful information on steady-state bone mineral density. Among nearly 10,000 men and women representative of the U.S. population, calcium intake was unrelated to bone mineral density at the hip.³⁶

In a meta-analysis of prospective studies, total calcium intakes ranging from less than 555 mg per day to more than 1100 mg per day were unrelated to the risk of hip fracture.³⁷ In other meta-analyses of prospective studies, milk intake (ranging from fewer than 1.5 servings per week to 30 or more servings per week) or total dairy food consumption was unrelated to the risk of hip fracture in men or women.³⁸⁻⁴⁰ Both positive and inverse associations have been observed in subsequent studies^{41,42}; the overall evidence does not support a benefit of higher dairy consumption for prevention of hip fractures.

Clinical trials examining calcium supple-

ments and the risk of fractures are complicated to interpret because most supplements included both calcium and vitamin D; studies of calcium alone are limited in size, number, and duration. In a meta-analysis of five trials in which a total of 6740 patients with a total of 814 nonvertebral fractures received either calcium-only supplements or placebo,³⁷ no significant benefit from calcium was seen in reducing the number of all nonvertebral fractures (relative risk, 0.92; 95% confidence interval [CI], 0.81 to 1.05), and the risk of hip fracture was greater among persons who received calcium supplements than among those who received placebo (relative risk, 1.64; 95% CI, 1.02 to 2.64).

Estimation of calcium requirements for children is problematic because a positive balance is needed for growth, and recommendations reflect this uncertainty. In the United States, the recom-

mended daily allowance of calcium is 1000 mg per day for children 4 to 8 years of age, whereas in the United Kingdom 450 to 550 mg per day is considered adequate (Table 2). Among girls in the early stages of puberty, calcium balance was positive even with an intake of less than 400 mg per day,⁴³ and among children 4 to 8 years of age, calcium intake was uncorrelated with bone mineral density.⁴⁴ Studies of calcium or dairy supplementation and bone mineral density in children show the same transient phenomenon observed in adults. Although with supplementation a small increase — or no increase — in bone mineral density is observed,⁴⁵ increases do not persist after discontinuation,⁴⁶⁻⁴⁹ thus providing no evidence that high calcium intake is needed during childhood to serve as a “bank” for calcium throughout life. In a randomized trial, consumption of three additional servings of milk or equivalent dairy foods per day for 18 months by girls and boys in early stages of puberty who had calcium intakes below 800 mg per day had no effect on bone mineralization.⁵⁰ These findings suggest a fairly low threshold for calcium intake, above which higher intake has little additional effect on bone mineralization. Although concern has been raised about the effects on calcium balance of the high phosphorous content of cow’s milk (Table 1), in a large cross-sectional study in the United States, phosphorus intake tended to be positively associated with bone mineral density.⁵¹

Because milk increases attained height, and taller height is strongly related to fractures of the hip and other bones,²⁴ high milk consumption during adolescence was examined in relation to the risk of hip fractures later in life in two large cohorts.⁵² Among men, milk intake during adolescence was linearly associated with a 9% greater risk of hip fracture later in life for every additional glass consumed per day. No association with the risk of hip fracture was seen among women. Thus, existing data do not support high intakes of milk during adolescence for prevention of fractures later in life and suggest that such intakes may contribute to the high incidence of fractures in countries with the greatest milk consumption.

BODY WEIGHT AND OBESITY

Although milk has been widely promoted as beneficial for weight control, in a meta-analysis

of 29 randomized trials, no overall effects of milk or other dairy foods on body weight were seen.⁵³ Among men and women in three large cohorts,⁵⁴ changes in consumption of whole milk, low-fat milk, and cheese had no clear associations with weight change, whereas yogurt consumption was associated with less weight gain. As one of the only commonly consumed sources of probiotics in modern Western diets, freshly fermented dairy products such as yogurt may protect against obesity and confer other health benefits resulting from their effects on the gut microbiome.⁵⁵⁻⁵⁸ However, confounding by the generally healthier lifestyles of people who consume yogurt cannot be excluded.

Studies of milk consumption and body weight in children are few and are subject to confounding and reverse causation. Among 12,829 adolescents followed for 3 years, intake of low-fat milk was positively associated with gain in body-mass index (BMI, the weight in kilograms divided by the square of the height in meters), but intakes of full-fat milk and dairy fat were not; the weight gain associated with low-fat milk was accounted for by higher energy intake.⁵⁹ Similarly, in three cohorts of young children, consumption of full-fat or 2%-fat milk was associated with lower BMI or lower risk of obesity than was consumption of low-fat or skim milk.⁶⁰⁻⁶² In one study, no overall association between milk and percent body fat was observed.⁶³

Few randomized, controlled trials of milk consumption have been conducted among children or adolescents. In a 1976 study in the United Kingdom, 581 elementary-school children living in a low-income area were randomly assigned to receive either school lunch with milk (about 7 oz, presumably of whole milk) or lunch without milk. After 21 months, no significant difference in weight was seen, although children in the group that received milk had modestly increased height.⁶⁴ In subsequent smaller, randomized trials published since 2008 that enrolled overweight or normal-weight children, consumption of low-fat milk did not reduce body weight more than consumption of sugar-sweetened beverages, fruit juice, or water.⁶⁵⁻⁶⁸ In a recent trial designed to examine the effects of dairy calcium, 274 adolescent girls with BMIs ranging from the 50th to the 98th percentile were randomly assigned either to a group that received an intervention that substantially in-

creased their consumption of low-fat dairy products (from 0.6 servings per day to 3.2 servings per day) or to a control group in which consumption was to remain constant (and increased only from 0.6 servings per day to 0.7 servings per day). Contrary to the hypothesis, no effect on amounts of body fat was reported after 1 year.⁶⁹

Overall, the findings of prospective cohort studies and randomized trials do not show clear effects of milk intake on body weight in children or adults. Contrary to U.S. Department of Agriculture (USDA) advice to choose reduced-fat dairy, low-fat milk does not appear to have advantages over whole milk for weight control — and in children, available evidence suggests greater long-term weight gain with reduced-fat milk than with full-fat milk. Regular consumption of yogurt may result in less weight gain, and this possibility warrants further study in appropriately controlled trials to minimize confounding.

BLOOD PRESSURE, LIPIDS, AND CARDIOVASCULAR DISEASE

The relatively high potassium content of milk has led to the suggestion that greater milk intake may reduce blood pressure. The Dietary Approaches to Stop Hypertension (DASH) diet, which includes low-fat dairy foods, reduces blood pressure, but the specific contribution of milk is unclear because the diet is low in sodium and high in fruits and vegetables. Randomized trials of low-fat milk have shown inconsistent results with respect to reduction of blood pressure.^{15,70,71} It is important to note that the effect of milk in such trials often depends on the comparison beverages or foods. If milk replaces sugar-sweetened beverages or other refined carbohydrates, outcomes will probably be beneficial,^{72,73} but results may differ if milk replaces nuts, legumes, or whole fruits.

Prevailing recommendations also advocate consumption of reduced-fat dairy products instead of full-fat alternatives because saturated fat (about 65% of dairy fats is saturated fat²) increases low-density lipoprotein (LDL) cholesterol, and increased LDL cholesterol is an established risk factor for coronary heart disease. However, the reported effects of saturated fat depend on the comparison source of calories.⁷⁴

Replacement of saturated fat with most carbohydrates, as encouraged for many years by USDA dietary guidelines, lowers LDL cholesterol; however, high-density lipoprotein (HDL) cholesterol and LDL cholesterol particle sizes also decrease, and levels of triglycerides and inflammatory factors increase.^{75,76} Alternatively, replacement of saturated fat with unsaturated fats has similar benefits on LDL cholesterol but without the adverse effects.^{76,77}

In prospective cohort studies, neither whole milk nor low-fat milk has been clearly associated with the incidence of, or mortality associated with, coronary heart disease or stroke.⁷⁸ As with studies of blood lipids, the association of milk with the risk of cardiovascular disease depends on the comparison foods. In most cohort studies, no specific comparison was made; by default, the comparison was everything else in the diet — typically large amounts of refined grains, potato products, sugar, and meat. In a large cohort of women, full-fat and low-fat dairy products had similar relationships to coronary heart disease risk; both were associated with a lower risk than that associated with same number of servings of red meat but with a higher risk than was seen with the same number of servings of fish or nuts.⁷⁹ A similar pattern of risk of stroke was seen among men and women.⁸⁰ Likewise, dairy fat per se was associated with a higher risk of cardiovascular disease than was polyunsaturated or vegetable fat.⁸¹ For persons living in low-income countries where diets are very high in starch, moderate intake of dairy foods may reduce cardiovascular disease by providing nutritional value and reducing glycemic load.⁸²

DIABETES

Cow's milk has been hypothesized to be a cause of type 1 diabetes owing to cross-reactivity between dairy proteins and pancreatic islet cells.⁸³ However, in a randomized trial, children weaned to hydrolyzed protein instead of cow's milk did not have fewer autoantibodies to beta cells after 7 years than children who drank cow's milk,⁸⁴ and the relationship of milk intake to the risk of type 1 diabetes remains unclear.

Intake of dairy products has been associated with a modestly lower risk of type 2 diabetes in some cohort studies.⁸⁵ However, in large meta-

analyses, dairy consumption was not associated with⁸⁶ — or was only weakly associated with⁸⁷ — lower risk. Furthermore, a genetic marker for lactose tolerance, and thus higher milk intake, was not related to diabetes risk.⁸⁸ In a substitution analysis, the risk of diabetes was lower with milk consumption than with consumption of sugar-sweetened beverages or fruit juices but higher with milk consumption than with coffee consumption.⁸⁹

CANCER

In international comparisons, consumption of dairy products is strongly correlated with rates of breast cancer, prostate cancer, and other cancers.^{9,90} The effects of milk consumption on plasma IGF-I,^{20,91} which predicts increased risks of prostate and breast cancers,⁹² provides a plausible mechanism. In prospective cohort studies, milk consumption is most consistently associated with a greater risk of prostate cancer,^{23,93} especially aggressive or fatal forms, but not with a greater risk of breast cancer.²³ Total dairy intake has been associated with a greater risk of endometrial cancer, particularly among postmenopausal women who are not receiving hormone therapy, a finding possibly related to the sex-hormone content of dairy products.⁹⁴ Consumption of dairy products or lactose has been hypothesized to increase the risk of ovarian cancer, but no relation was seen in a pooled analysis.⁹⁵ In contrast, in meta-analyses and pooled analyses of primary data,^{96,97} milk consumption was inversely associated with the risk of colorectal cancer, potentially owing to its high calcium content.²³ A major limitation of the existing literature is that almost all prospective studies have been initiated among persons in midlife or later, whereas many cancer risk factors operate in childhood or early adult life.⁹⁸ In one study of diets in adolescents, milk intake was shown to be unrelated to a future risk of breast cancer.⁹⁹

ALLERGIES AND INTOLERANCE

Allergy to cow's milk proteins may affect up to 4% of infants and cause considerable nutritional problems.¹⁰⁰ Scattered reports suggest that milk consumption may exacerbate atopic tendencies,

conferring a predisposition to asthma, eczema, and food allergies.^{100,101} Over a period of 10 years, infants with a family history of atopy who were randomly assigned to receive hydrolyzed protein formula had a lower risk of any allergic disease and of eczema than did infants who were randomly assigned to receive cow's milk.¹⁰² In a double-blind crossover study of children with intolerance to cow's milk, 44 of 65 children had a reduction in symptoms (including resolution of anal fissures) when they consumed soy milk, whereas there was no reduction in symptoms among children in the group that received cow's milk.¹⁰³ Beyond childhood, cow's milk may precipitate asthmatic exacerbations¹⁰⁴ and related conditions.¹⁰⁵ In addition, lactose intolerance limits consumption of milk worldwide.

TOTAL MORTALITY

In a meta-analysis that included 29 cohort studies, intakes of milk (total, high-fat, and low-fat) or total intakes of dairy foods were not associated with overall mortality.⁷⁸ In a recent analysis of three large cohorts with more than 30 years of follow-up, whole milk was associated with higher total mortality, but consumption of low-fat milk and cheese was not.¹⁰⁶ However, when major protein sources were compared, consumption of dairy foods was associated with lower mortality than consumption of processed red meat and eggs, with similar mortality to consumption of unprocessed red meat, poultry, and fish, and with significantly higher mortality than consumption of plant-based sources of protein¹⁰⁷ (Fig. 2).

ORGANIC AND GRASS-FED PRODUCTION

Consumption of organic milk instead of conventionally produced milk has been promoted because of concern about the use of recombinant bovine somatotropin and the presence of residues of pesticides and antibiotics in conventionally produced milk and because of the expectation that organic milk has better nutritional composition. Although milk from cows treated with bovine somatotropin contains elevated IGF-I levels,¹⁰⁸ no long-term studies have compared milk from cows treated with bovine somatotro-

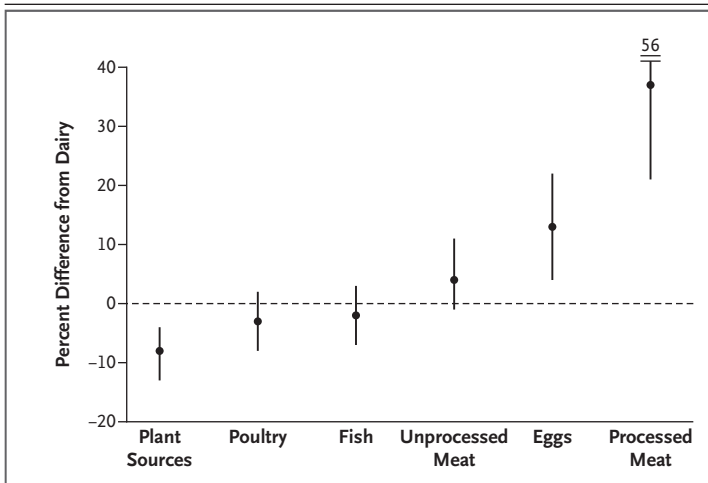


Figure 2. All-Cause Mortality Associated with Protein Sources.

Shown are the percent differences in all-cause mortality between dairy foods and other major protein sources. The dashed line at 0 is the reference value for mortality associated with dairy as a protein source. Comparisons are for 3% of energy from protein from each source; for milk, this corresponds to approximately 500 g or two 8-oz glasses. Data are from Song et al.,¹⁰⁷ recalculated to use dairy foods as the comparison, and are based on up to 32 years of follow-up of 131,342 men and women. Associations are adjusted for major lifestyle, dietary, and other risk factors for cardiovascular disease and cancer.

pin with milk from untreated cows with respect to health outcomes in humans. After extensive reviews, Canada and the European Union banned the sale of milk from cows treated with bovine somatotropin — not because of human health issues, but because of animal welfare issues, including increased mastitis, foot problems, and reduced fertility in treated cows.^{108,109}

Organic milk may have slightly higher amounts of n-3 polyunsaturated fatty acids¹¹⁰ and beta carotene¹¹¹ than conventional milk — a consequence of grass-feeding, not of its organic status. The sex-hormone content of milk is increased if cows are milked while they are pregnant, but this practice appears to be widespread among both conventional and organic milk producers.

ENVIRONMENTAL EFFECTS

Foods may influence health both directly and indirectly through the environmental effects of their production.¹¹² The effects of dairy production, particularly industrial-scale production, on greenhouse gas production and climate change,

water use and pollution, and antibiotic resistance are large¹¹³⁻¹¹⁶ — potentially 5 to 10 times greater per unit of protein than the effects from production of soy foods, other legumes, and most grains.¹¹⁷ Thus, the environmental implications of doubling production to meet current U.S. dietary guidelines likewise would be large — massive, if applied worldwide, including low-income countries with low intakes of dairy.¹¹⁸ Conversely, limiting dairy production could make a major contribution toward reaching international greenhouse-gas targets.¹¹⁹

CONCLUSIONS

Cow's milk includes a complex combination of macronutrients, micronutrients, and growth-promoting factors that can contribute to human nutrition; however, all these nutrients can be obtained from other sources (as has been the case in many traditional societies with historically low intakes of dairy products). For adults, the overall evidence does not support high dairy consumption for reduction of fractures, which has been a primary justification for current U.S. recommendations. Moreover, total dairy consumption has not been clearly related to weight control or to risks of diabetes and cardiovascular disease. High consumption of dairy foods is likely to increase the risks of prostate cancer and possibly endometrial cancer but reduce the risk of colorectal cancer. It is important to note that the reported health effects of dairy foods depend strongly on the specific foods or beverages to which they are compared; for many outcomes, dairy foods compare favorably with processed red meat or sugar-sweetened beverages but less favorably with plant-protein sources such as nuts. Furthermore, no clear benefit of consuming reduced-fat dairy over whole dairy products has been established.

The effects on children of consumption of cow's milk are less clear because of children's greater nutritional requirements for growth, and data are more limited. If mother's milk is not available, cow's milk may provide a valuable substitute in early childhood. Milk promotes growth velocity and greater attained height, which confer both risks and benefits. The high nutrient density of milk can be particularly beneficial in regions where overall diet quality and

energy intake are compromised. However, in populations with generally adequate nutrition, high consumption of milk may increase the risk of fractures later in life, and the association of greater height with the risk of cancer remains a concern.

In our opinion, the current recommendation to greatly increase consumption of dairy foods to 3 or more servings per day does not appear to be justified. The optimal intake of milk for an individual person will depend on overall diet quality. If diet quality is low, especially for children in low-income environments, dairy foods can improve nutrition, whereas if diet quality is high, increased intake is unlikely to provide substantial benefits, and harms are possible. When consumption of milk is low, the two nutrients of primary concern, calcium and vitamin D (which is of particular concern at higher latitudes),¹²⁰

can be obtained from other foods or supplements without the potential negative consequences of dairy foods. For calcium, alternative dietary sources include kale, broccoli, tofu, nuts, beans, and fortified orange juice^{11,121}; for vitamin D, supplements can provide adequate intake at far lower cost than fortified milk. Pending additional research, guidelines for milk and equivalent dairy foods ideally should designate an acceptable intake (such as 0 to 2 servings per day for adults), deemphasize reduced-fat milk as preferable to whole milk, and discourage consumption of sugar-sweetened dairy foods in populations with high rates of overweight and obesity.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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REFERENCES

- Department of Agriculture, Department of Health and Human Services. Scientific report of the Dietary Guidelines Advisory Committee. Washington, DC: Government Printing Office, 2015.
- Department of Agriculture, Agricultural Research Service. FoodData Central (<https://fdc.nal.usda.gov/index.html>).
- Adebamowo CA, Spiegelman D, Danby FW, Frazier AL, Willett WC, Holmes MD. High school dietary dairy intake and teenage acne. *J Am Acad Dermatol* 2005; 52:207-14.
- Maruyama K, Oshima T, Ohshima K. Exposure to exogenous estrogen through intake of commercial milk produced from pregnant cows. *Pediatr Int* 2010;52:33-8.
- Hartman S, Lacorn H, Steinhart H. Natural occurrence of steroid hormones in food. *Food Chem* 1998;62:7-20.
- Darling JA, Laing AH, Harkness RA. A survey of the steroids in cows' milk. *J Endocrinol* 1974;62:291-7.
- Echternkamp SE, Aad PY, Eborn DR, Spicer LJ. Increased abundance of aromatase and follicle stimulating hormone receptor mRNA and decreased insulin-like growth factor-2 receptor mRNA in small ovarian follicles of cattle selected for twin births. *J Anim Sci* 2012;90:2193-200.
- Managing cow lactation cycles. The Cattle Site. May 18, 2015 (<http://www.thecattlesite.com/articles/4248/managing-cow-lactation-cycles/>).
- Ganmaa D, Sato A. The possible role of female sex hormones in milk from pregnant cows in the development of breast, ovarian and corpus uteri cancers. *Med Hypotheses* 2005;65:1028-37.
- Fernández M, Hudson JA, Korpela R, de los Reyes-Gavilán CG. Impact on human health of microorganisms present in fermented dairy products: an overview. *Biomed Res Int* 2015;2015:412714.
- Messina V, Mangels AR. Considerations in planning vegan diets: children. *J Am Diet Assoc* 2001;101:661-9.
- de Beer H. Dairy products and physical stature: a systematic review and meta-analysis of controlled trials. *Econ Hum Biol* 2012;10:299-309.
- Berkey CS, Colditz GA, Rockett HR, Frazier AL, Willett WC. Dairy consumption and female height growth: prospective cohort study. *Cancer Epidemiol Biomarkers Prev* 2009;18:1881-7.
- Olsen SF, Halldorsson TI, Willett WC, et al. Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study. *Am J Clin Nutr* 2007;86:1104-10.
- Barr SI, McCarron DA, Heaney RP, et al. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults. *J Am Diet Assoc* 2000;100:810-7.
- Cadogan J, Eastell R, Jones N, Barker ME. Milk intake and bone mineral acquisition in adolescent girls: randomised, controlled intervention trial. *BMJ* 1997; 315:1255-60.
- Zhu K, Du X, Cowell CT, et al. Effects of school milk intervention on cortical bone accretion and indicators relevant to bone metabolism in Chinese girls aged 10-12 y in Beijing. *Am J Clin Nutr* 2005;81: 1168-75.
- Rich-Edwards JW, Ganmaa D, Pollak MN, et al. Milk consumption and the prepubertal somatotrophic axis. *Nutr J* 2007;6: 28.
- FAO/WHO/UNU ad hoc Expert Consultation on Energy and Protein Requirements. Energy and protein requirements: report of a joint FAO/WHO/UNU expert consultation. WHO technical report no. 724. Geneva: World Health Organization, 1985.
- Harrison S, Lennon R, Holly J, et al. Does milk intake promote prostate cancer initiation or progression via effects on insulin-like growth factors (IGFs)? A systematic review and meta-analysis. *Cancer Causes Control* 2017;28:497-528.
- Melnik BC. Milk — a nutrient system of mammalian evolution promoting mTORC1-dependent translation. *Int J Mol Sci* 2015;16:17048-87.
- Emerging Risk Factors Collaboration. Adult height and the risk of cause-specific death and vascular morbidity in 1 million people: individual participant meta-analysis. *Int J Epidemiol* 2012;41:1419-33.
- World Cancer Research Fund, American Institute for Cancer Research. Second expert report: food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington, DC: AICR, 2007.
- Hemenway D, Azrael DR, Rimm EB, Feskanich D, Willett WC. Risk factors for hip fracture in US men aged 40 through 75 years. *Am J Public Health* 1994;84: 1843-5.
- Institute of Medicine. Dietary reference intakes for calcium and vitamin D.

- Washington, DC: National Academy of Sciences, 2010.
26. Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food and Nutrition Policy. Nutrition and bone health with particular reference to calcium and vitamin D: report of the Subgroup on Bone Health. London: The Stationery Office, U.K. Department of Health, 1998.
 27. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO/FAO expert consultation (report 916). Geneva: World Health Organization, 2003.
 28. New food balances (preliminary data). New York: Food and Agriculture Organization of the United Nations (<http://www.fao.org/faostat/en/#data/FBS>).
 29. Kanis JA, Odén A, McCloskey EV, et al. A systematic review of hip fracture incidence and probability of fracture worldwide. *Osteoporos Int* 2012;23:2239-56.
 30. Hegsted DM. Calcium and osteoporosis. *J Nutr* 1986;116:2316-9.
 31. Hegsted DM. Fractures, calcium, and the modern diet. *Am J Clin Nutr* 2001;74:571-3.
 32. Hunt CD, Johnson LK. Calcium requirements: new estimations for men and women by cross-sectional statistical analyses of calcium balance data from metabolic studies. *Am J Clin Nutr* 2007;86:1054-63.
 33. Hegsted DM, Moscoso I, Collazos C. A study of the minimum calcium requirements of adult men. *J Nutr* 1952;46:181-201.
 34. Elders PJ, Lips P, Netelenbos JC, et al. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 1994;9:963-70.
 35. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of withdrawal of calcium and vitamin D supplements on bone mass in elderly men and women. *Am J Clin Nutr* 2000;72:745-50.
 36. Bischoff-Ferrari HA, Kiel DP, Dawson-Hughes B, et al. Dietary calcium and serum 25-hydroxyvitamin D status in relation to BMD among U.S. adults. *J Bone Miner Res* 2009;24:935-42.
 37. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr* 2007;86:1780-90.
 38. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. Milk intake and risk of hip fracture in men and women: a meta-analysis of prospective cohort studies. *J Bone Miner Res* 2011;26:833-9.
 39. Bian S, Hu J, Zhang K, Wang Y, Yu M, Ma J. Dairy product consumption and risk of hip fracture: a systematic review and meta-analysis. *BMC Public Health* 2018;18:165.
 40. Matía-Martín P, Torrego-Ellacuría M, Larrad-Sainz A, Fernández-Pérez C, Cuesta-Triana F, Rubio-Herrera MÁ. Effects of milk and dairy products on the prevention of osteoporosis and osteoporotic fractures in Europeans and Non-Hispanic whites from North America: a systematic review and updated meta-analysis. *Adv Nutr* 2019;10:Suppl_2:S120-S143.
 41. Feskanich D, Meyer HE, Fung TT, Bischoff-Ferrari HA, Willett WC. Milk and other dairy foods and risk of hip fracture in men and women. *Osteoporos Int* 2018;29:385-96.
 42. Holvik K, Meyer HE, Laake I, Feskanich D, Omsland TK, Sjøgaard AJ. Milk drinking and risk of hip fracture: the Norwegian Epidemiologic Osteoporosis Studies (NOREPOS). *Br J Nutr* 2018 December 27 (Epub ahead of print).
 43. Abrams SA, Griffin IJ, Hicks PD, Gunn SK. Pubertal girls only partially adapt to low dietary calcium intakes. *J Bone Miner Res* 2004;19:759-63.
 44. Abrams SA, Chen Z, Hawthorne KM. Magnesium metabolism in 4-year-old to 8-year-old children. *J Bone Miner Res* 2014;29:118-22.
 45. Winzenberg TM, Shaw K, Fryer J, Jones G. Calcium supplementation for improving bone mineral density in children. *Cochrane Database Syst Rev* 2006;2:CD005119.
 46. Merrilees MJ, Smart EJ, Gilchrist NL, et al. Effects of dairy food supplements on bone mineral density in teenage girls. *Eur J Nutr* 2000;39:256-62.
 47. Lee WT, Leung SS, Leung DM, Cheng JC. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. *Am J Clin Nutr* 1996;64:71-7.
 48. Lee WT, Leung SS, Leung DM, et al. Bone mineral acquisition in low calcium intake children following the withdrawal of calcium supplement. *Acta Paediatr* 1997;86:570-6.
 49. Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. *J Bone Miner Res* 1997;12:676-82.
 50. Vogel KA, Martin BR, McCabe LD, et al. The effect of dairy intake on bone mass and body composition in early pubertal girls and boys: a randomized controlled trial. *Am J Clin Nutr* 2017;105:1214-29.
 51. Lee AW, Cho SS. Association between phosphorus intake and bone health in the NHANES population. *Nutr J* 2015;14:28.
 52. Feskanich D, Bischoff-Ferrari HA, Frazier AL, Willett WC. Milk consumption during teenage years and risk of hip fractures in older adults. *JAMA Pediatr* 2014;168:54-60.
 53. Chen M, Pan A, Malik VS, Hu FB. Effects of dairy intake on body weight and fat: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2012;96:735-47.
 54. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med* 2011;364:2392-404.
 55. Le Chatelier E, Nielsen T, Qin J, et al. Richness of human gut microbiome correlates with metabolic markers. *Nature* 2013;500:541-6.
 56. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature* 2006;444:1022-3.
 57. Ridaura VK, Faith JJ, Rey FE, et al. Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science* 2013;341:1241214.
 58. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 2006;444:1027-31.
 59. Berkey CS, Rockett HRH, Willett WC, Colditz GA. Milk, dairy fat, dietary calcium, and weight gain: a longitudinal study of adolescents. *Arch Pediatr Adolesc Med* 2005;159:543-50.
 60. Scharf RJ, Demmer RT, DeBoer MD. Longitudinal evaluation of milk type consumed and weight status in preschoolers. *Arch Dis Child* 2013;98:335-40.
 61. Huh SY, Rifas-Shiman SL, Rich-Edwards JW, Taveras EM, Gillman MW. Prospective association between milk intake and adiposity in preschool-aged children. *J Am Diet Assoc* 2010;110:563-70.
 62. Barba G, Troiano E, Russo P, Venezia A, Siani A. Inverse association between body mass and frequency of milk consumption in children. *Br J Nutr* 2005;93:15-9.
 63. Noel SE, Ness AR, Northstone K, Emmett P, Newby PK. Milk intakes are not associated with percent body fat in children from ages 10 to 13 years. *J Nutr* 2011;141:2035-41.
 64. Baker IA, Elwood PC, Hughes J, Jones M, Moore F, Sweetnam PM. A randomised controlled trial of the effect of the provision of free school milk on the growth of children. *J Epidemiol Community Health* 1980;34:31-4.
 65. St-Onge MP, Goree LL, Gower B. High-milk supplementation with healthy diet counseling does not affect weight loss but ameliorates insulin action compared with low-milk supplementation in overweight children. *J Nutr* 2009;139:933-8.
 66. Albala C, Ebbeling CB, Cifuentes M, Lera L, Bustos N, Ludwig DS. Effects of replacing the habitual consumption of sugar-sweetened beverages with milk in

- Chilean children. *Am J Clin Nutr* 2008;88:605-11.
67. Lambourne K, Washburn RA, Lee J, et al. A 6-month trial of resistance training with milk supplementation in adolescents: effects on body composition. *Int J Sport Nutr Exerc Metab* 2013;23:344-56.
68. Arnberg K, Mølgaard C, Michaelsen KF, Jensen SM, Trolle E, Larnkjær A. Skim milk, whey, and casein increase body weight and whey and casein increase the plasma C-peptide concentration in overweight adolescents. *J Nutr* 2012;142:2083-90.
69. Lappe JM, McMahon DJ, Laughlin A, et al. The effect of increasing dairy calcium intake of adolescent girls on changes in body fat and weight. *Am J Clin Nutr* 2017;105:1046-53.
70. Maki KC, Rains TM, Schild AL, et al. Effects of low-fat dairy intake on blood pressure, endothelial function, and lipoprotein lipids in subjects with prehypertension or stage 1 hypertension. *Vasc Health Risk Manag* 2013;9:369-79.
71. van Meijl LE, Mensink RP. Low-fat dairy consumption reduces systolic blood pressure, but does not improve other metabolic risk parameters in overweight and obese subjects. *Nutr Metab Cardiovasc Dis* 2011;21:355-61.
72. Cohen L, Curhan G, Forman J. Association of sweetened beverage intake with incident hypertension. *J Gen Intern Med* 2012;27:1127-34.
73. Appel LJ, Sacks FM, Carey VJ, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *JAMA* 2005;294:2455-64.
74. Willett WC, Stampfer M. Diet and coronary heart disease. In: Willett WC, ed. *Nutritional epidemiology*. 3rd ed. New York: Oxford University Press, 2013:426-7.
75. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* 2003;77:1146-55.
76. Astrup A, Dyerberg J, Elwood P, et al. The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010? *Am J Clin Nutr* 2011;93:684-8.
77. Brassard D, Tessier-Grenier M, Allaire J, et al. Comparison of the impact of SFAs from cheese and butter on cardiometabolic risk factors: a randomized controlled trial. *Am J Clin Nutr* 2017;105:800-9.
78. Guo J, Astrup A, Lovegrove JA, Gijsbers L, Givens DI, Soedamah-Muthu SS. Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. *Eur J Epidemiol* 2017;32:269-87.
79. Bernstein AM, Sun Q, Hu FB, Stampfer MJ, Manson JE, Willett WC. Major dietary protein sources and risk of coronary heart disease in women. *Circulation* 2010;122:876-83.
80. Bernstein AM, Pan A, Rexrode KM, et al. Dietary protein sources and the risk of stroke in men and women. *Stroke* 2012;43:637-44.
81. Chen M, Li Y, Sun Q, et al. Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults. *Am J Clin Nutr* 2016;104:1209-17.
82. Dehghan M, Mente A, Rangarajan S, et al. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *Lancet* 2018;392:2288-97.
83. Knip M, Simell O. Environmental triggers of type 1 diabetes. *Cold Spring Harb Perspect Med* 2012;2(7):a007690.
84. Knip M, Åkerblom HK, Becker D, et al. Hydrolyzed infant formula and early β -cell autoimmunity: a randomized clinical trial. *JAMA* 2014;311:2279-87.
85. 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.
86. Chen M, Sun Q, Giovannucci E, et al. Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *BMC Med* 2014;12:215.
87. Gijsbers L, Ding EL, Malik VS, de Goede J, Geleijnse JM, Soedamah-Muthu SS. Consumption of dairy foods and diabetes incidence: a dose-response meta-analysis of observational studies. *Am J Clin Nutr* 2016;103:1111-24.
88. Bergholdt HK, Nordestgaard BG, Ellervik C. Milk intake is not associated with low risk of diabetes or overweight-obesity: a Mendelian randomization study in 97,811 Danish individuals. *Am J Clin Nutr* 2015;102:487-96.
89. Pan A, Malik VS, Schulze MB, Manson JE, Willett WC, Hu FB. Plain-water intake and risk of type 2 diabetes in young and middle-aged women. *Am J Clin Nutr* 2012;95:1454-60.
90. Ganmaa D, Li XM, Wang J, Qin LQ, Wang PY, Sato A. Incidence and mortality of testicular and prostatic cancers in relation to world dietary practices. *Int J Cancer* 2002;98:262-7.
91. Qin LQ, He K, Xu JY. Milk consumption and circulating insulin-like growth factor-I level: a systematic literature review. *Int J Food Sci Nutr* 2009;60:Suppl 7:330-40.
92. Shi R, Yu H, McLarty J, Glass J. IGF-I and breast cancer: a meta-analysis. *Int J Cancer* 2004;111:418-23.
93. Aune D, Navarro Rosenblatt DA, Chan DS, et al. Dairy products, calcium, and prostate cancer risk: a systematic review and meta-analysis of cohort studies. *Am J Clin Nutr* 2015;101:87-117.
94. Ganmaa D, Cui X, Feskanich D, Hankinson SE, Willett WC. Milk, dairy intake and risk of endometrial cancer: a 26-year follow-up. *Int J Cancer* 2012;130:2664-71.
95. Genkinger JM, Hunter DJ, Spiegelman D, et al. Dairy products and ovarian cancer: a pooled analysis of 12 cohort studies. *Cancer Epidemiol Biomarkers Prev* 2006;15:364-72.
96. Aune D, Lau R, Chan DS, et al. Dairy products and colorectal cancer risk: a systematic review and meta-analysis of cohort studies. *Ann Oncol* 2012;23:37-45.
97. Cho E, Smith-Warner SA, Spiegelman D, et al. Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. *J Natl Cancer Inst* 2004;96:1015-22.
98. Mahabir S, Aagaard K, Anderson LM, et al. Challenges and opportunities in research on early-life events/exposures and cancer development later in life. *Cancer Causes Control* 2012;23:983-90.
99. Linos E, Willett WC, Cho E, Frazier L. Adolescent diet in relation to breast cancer risk among premenopausal women. *Cancer Epidemiol Biomarkers Prev* 2010;19:689-96.
100. Sackesen C, Assa'ad A, Baena-Cagnani C, et al. Cow's milk allergy as a global challenge. *Curr Opin Allergy Clin Immunol* 2011;11:243-8.
101. Murray MG, Kanuga J, Yee E, Bahna SL. Milk-induced wheezing in children with asthma. *Allergol Immunopathol (Madr)* 2013;41:310-4.
102. von Berg A, Filipiak-Pittroff B, Krämer U, et al. Allergies in high-risk schoolchildren after early intervention with cow's milk protein hydrolysates: 10-year results from the German Infant Nutritional Intervention (GINI) study. *J Allergy Clin Immunol* 2013;131:1565-73.
103. Iacono G, Cavataio F, Montalto G, et al. Intolerance of cow's milk and chronic constipation in children. *N Engl J Med* 1998;339:1100-4.
104. Pelikan Z. Asthmatic response to milk ingestion challenge in adults: a comparison of the open and double-blind challenges. *Int Arch Allergy Immunol* 2013;161:163-73.
105. Olivier CE, Lorena SL, Pavan CR, et al. Is it just lactose intolerance? *Allergy Asthma Proc* 2012;33:432-6.
106. Ding M, Li J, Qi L, et al. Associations of dairy intake with risk of mortality in women and men: three prospective cohort studies. *BMJ* 2019;367:l6204.
107. Song M, Fung TT, Hu FB, et al. Association of animal and plant protein intake with all-cause and cause-specific mortality. *JAMA Intern Med* 2016;176:1453-63.

108. Scientific Committee on Animal Health and Animal Welfare. Report on animal welfare aspects of the use of bovine somatotrophin. March 10, 1999 (https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scab_out21_en.pdf).
109. Canada rejects bovine growth hormone. January 19, 1999 (<http://www.ipsnews.net/1999/01/environment-canada-rejects-bovine-growth-hormone/>).
110. Benbrook CM, Butler G, Latif MA, Leifert C, Davis DR. Organic production enhances milk nutritional quality by shifting fatty acid composition: a United States-wide, 18-month study. *PLoS One* 2013;8(12):e82429.
111. Smith-Spangler C, Brandeau ML, Hunter GE, et al. Are organic foods safer or healthier than conventional alternatives? A systematic review. *Ann Intern Med* 2012;157:348-66.
112. Willett W, Rockström J, Loken B, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019;393:447-92.
113. Organisation for Economic Co-Operation and Development. The dairy sector, agriculture, trade and the environment. Paris: OECD Publishing, 2004.
114. Pimental D, Pimental MH. Livestock production and energy use. In: Pimental D, Pimental MH, eds. Food, energy, and society. 3rd ed. Boca Raton, FL: CRC Press, 2011:67-76.
115. Garnett T. Where are the best opportunities for reducing greenhouse gas emissions in the food system (including the food chain)? *Food Policy* 2011;36:Suppl:S23-S32.
116. Springmann M, Clark M, Mason-D'Croz D, et al. Options for keeping the food system within environmental limits. *Nature* 2018;562:519-25.
117. Gonzales AD, Frostell B, Carlsson-Kanyama A. Protein efficiency per unit energy and per unit greenhouse gas emissions: Potential contribution of diet choices to climate change mitigation. *Food Policy* 2011;36:562-70.
118. Gerosa S, Skoet J. Milk availability: trend in production and demand and future outlook. Rome: Food and Agriculture Organization of the United Nations, 2012.
119. Goodland R. A fresh look at livestock greenhouse gas emissions and mitigation potential in Europe. *Glob Chang Biol* 2014;20:2042-4.
120. Scientific Advisory Committee on Nutrition. Vitamin D and health. July 2016 (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/537616/SACN_Vitamin_D_and_Health_report.pdf).
121. American Dietetic Association, Dietitians of Canada. Position of the American Dietetic Association and Dietitians of Canada: vegetarian diets. *Can J Diet Pract Res* 2003;64:62-81.

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