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Nutrition and health aspects of milk and dairy products and their ingredients

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Abstract

At approximately 190 g/day, current consumption of milk and dairy products in Germany is lower than recommended by the German Nutrition Society. Milk and dairy products are good sources of a range of essential nutrients. One of their main characteristics is the unique composition of the milk fat. Research is currently focusing on the effects of specific fatty acids, the influence of animal feed on the fatty acid pattern, and the health implications of bacteria and their metabolites in fermented dairy products.

Epidemiological data suggest that the consumption of milk and dairy products is associated with a lower risk of a range of diseases. Diseases which are likely to occur less frequently in the case of normal consumption compared to low or no consumption include cardiovascular diseases (CVD), stroke, hypertension, type 2 diabetes mellitus, and colorectal cancer. The consumption of milk and dairy products was associated with higher bone mineral density and better bone metabolism markers. An elevated risk of prostate cancer was observed in the case of very high consumption (more than 1.2 L of milk or 140 g of hard cheese per day). Overall, milk and dairy products significantly contribute to a disease-preventing, plant-based diet.

Keywords: milk, dairy products, health, prevention, risks, systematic review

Preface

The association between the consumption of milk and dairy products and possible health effects can be investigated at various levels: at the level of milk-specific constituents (e.g. saturated fatty acids), at the level of product categories (e.g. milk, yogurt, cheese, as full-fat or low-fat products), or at the level of specific dietary patterns (e.g. the Mediterranean diet). This narrative, non-systematic review is mainly based on meta-analyses and systematic reviews from 2010 on, which evaluated randomized, controlled intervention studies and observational studies. Studies from before

2010 were only taken into account if more recent studies did not exist. The observation studies were mainly prospective cohort studies. Some associations were also studied in subgroups of larger cohort studies, in the form of (prospective) case-cohort studies, or in the form of nested casecontrol studies.

Health significance of milk constituents

Milk fat

The fat globules in milk consist of a triglyceride core (average diameter $3-5 \ \mu m$), which is surrounded by a trilayer membrane (a monolayer plus a bilayer) composed of proteins and phospholipids (milk fat globule membrane, MFGM). This membrane gives the fat globules emulsion stability in the aqueous phase of the milk, and protects against lipolysis. Triglycerides account for around 98% of total fat. The fat phase also contains cholesterol, phospholipids, cerebrosides and other lipids. Milk fat consists of about 400 different fatty acids. For major groups and important individual fatty acids see • Table 1. It is rich in saturated fatty acids (SFA), which make up about 70% of total fatty acids, but it is low in polyunsaturated fatty acids. A characteristic specific to milk is the presence of (saturated) short-chain fatty acids (SCFA) and medium-chain fatty acids (MCFA) of C4:0 to C10:0. Unsaturated fatty acids present in the green feed are partially reduced by the rumen flora. The rumen flora also produces

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trans-fatty acids (TFA), which make up about 1.5 to 6% of the milk fat. Other characteristic minor fatty acids are odd-chain fatty acids such as C15:0 and C17:0, branchedchain fatty acids, conjugated linoleic acid (CLA) cis9, trans11-CLA, trans16:1n-7, and phytic acid, which are all derived from the metabolism of rumen microorganisms. Milk fat is viewed negatively due to its high proportion of SFA [1]. Compared to monounsaturated or polyunsaturated fatty acids, SFA increased plasma cholesterol concentration in humans. This in turn is a risk factor for cardiovascular diseases (CVD) [2]. CVD include coronary heart disease (CHD), circulatory disorders, and stroke. Therefore, milk fat is seen as a risk factor for CVD [1]. More recent studies, which evaluated SFA as a component of complex foods (milk, dairy products) resulted in a more differentiated evaluation [3-6].

Milk fat and plasma cholesterol

Milk fat is usually equated with butter. Most of the intervention studies on milk fat have been conducted using butter, and the conclusions have been applied to milk and dairy products. In fact, butter consumption increased plasma cholesterol concentration, but not only LDL but also HDL cholesterol was increased. Therefore, the total/HDL cholesterol ratio remained mostly unchanged [7]. Obviously, not only fatty acids, but also other components of milk, such as minerals, have a role to play. This explains why the fat in cheese had a lesser hypercholesterolemic effect than the same amount of fat from butter [7, 8]. Fermented milk products (like yogurt) [9-11] and phospholipids in the MFGM [12, 13] reduced total cholesterol and LDL cholesterol, compared to non-fermented milk products. Within the SFA group, stearic acid [14] and MCFA [15] did not increase cholesterol concentration.

Milk fat exhibits a moderate hypercholesterolemic effect, which is modified by other components of milk.

Milk-typical trans fatty acids (TFA)

TFAs are unsaturated fatty acids with at least one double bond in the trans-configuration. The Food and Drug Administration and the Codex Alimentarius Commission use the term TFA only for fatty acids with non-conjugated double bonds, with at least one of these double bonds being in the trans-configuration. According to this definition, cis9,trans11-CLA is not a TFA. Elevated risk of CHD and CVD in the case of high TFA intake is likely attributable to various mechanisms, such as the elevation of LDL cholesterol and lipoprotein(a) and the reduction in HDL cholesterol concentrations, proinflammatory effects, and impaired vascular elasticity [16]. TFA are present in industrially-produced partially hydrogenated fats, i.e. mainly in partially hydrogenated vegetable oils (iTFA i stands for industrially produced), as well as in ruminant fats, i.e. in milk fat and ruminant meat (rTFA - r stands for ruminant). There are many positional isomers. Among the iTFA, the main positional isomers are elaidic acid (trans9-18:1) and trans10-C18:1. Vaccenic acid (trans11-C18:1) predominates in the rTFA, accounting for up to 70% of rTFA. The trans9/trans11 index can be used to draw approximate conclusions about the origin of the TFA in a food [17]. Total TFA intake in Germany is moderate - on average 1.94 g/day (0.77 energy percent [en%]), with up to 80% of this being rTFA. In contrast, TFA intake in the USA from 1999 to 2002 was still 6.1 g/day (2.5 en%) on average, with around 80% of this being iTFA [17]

Intervention studies have shown that higher intake of rTFA in milk fat does not increase total/HDL cholesterol or LDL/HDL cholesterol ratios [18]. According to a further meta-analysis, higher intake of rTFA (in part, however, calculated on the basis of the CLA intake) and iTFA increased total cholesterol and LDL cholesterol, as well as the ratios to the same extent [19]. When consumed in amounts < 1 en%, neither rTFA nor iTFA exhibited any effect [19].

The latest meta-analysis found that higher intake of iTFA significantly increased the risk of death due to CHD (RR 1.18) and the risk of CHD-associated events and illnesses (RR 1.42). The same was true for total TFA intake (CHD mortality RR 1.28, CHD-associated events and illnesses 1.21). However, higher intake of rTFA alone did not affect the risk (CHD mortality RR 1.01, total CHD RR 0.93) [20]. Higher intake of rTFA, calculated on the basis of the biomarker trans16:1n-7 in the plasma, was associated with a lower risk of type 2 diabetes mellitus (RR 0.58), whereas higher total TFA intake tended to increase risk (RR 1.10) [20].

It remains unclear whether rTFA and iTFA should be viewed equally negatively. Vaccenic acid, which is the predominant fatty acid in rTFA, is metabolized differently from elaidic acid [16]. In addition, in the body it is partially transformed into cis9, trans11-CLA [16] and into trans16:1n-7 [21], which both show favorable metabolic properties. Irrespective of this aspect, the general consensus is that the relatively low intake of rTFA makes adverse metabolic effects unlikely [16]. In the concentrations found in milk fat, rTFAs do not increase the risk of CVD.

Milk fat-specific fatty acids as biomarkers

Milk fat contains minor fatty acids whose concentrations in the plasma phospholipids and in erythrocytes are used as biomarkers for the consumption of milk and dairy products/milk fat. These include the odd-chain fatty acids C15:0 and C17:0 [22, 23] and trans-16:1n-7 (also written as trans9-16:1) [23-25]. However, trans-16:1n-7 [21], as well as C15:0 and C17:0 [26] are also endogenously synthesized to a small extent.

According to a meta-analysis [27] and an individual study [22], a higher

Fatty acids	biodynamic/ organic	conventional		
saturated	69.4	69.4		
short and medium-chain (C4:0-C10:0)	7.9	7.7		
C12:0 and C14:0	14.6	15.1		
C16:0	30.2	30.1		
C18:0	9.4	9.3		
odd chain (C15:0 and C17:0)	1,9	1.7		
odd chain, branched-chain	4.0	3.6		
monounsaturated	26.4	27.0		
oleic acid (C18:1n-9)	18.8	19.6		
polyunsaturated, omega-6	2.1	2.2		
arachidonic acid (C20:4n-6)	0.06	0.08		
polyunsaturated, omega-3	1.4	1.0		
α-linoleic acid (C18:3n-3)	0.89	0.58		
eicosapentaenoic acid (C20:5n-3) and docosahexaenoic acid (C22:6n-3)	0.20	0.14		
trans fatty acids (trans-18:1)	3.6	3.2		
vaccenic acid (trans11-18:1)	2.0	1.5		
conjugated linoleic acids (CLA)	1.4	1.1		
cis9,trans11-CLA	1.04	0.87		

Tab. 1: Influence of feed given to cows on the fatty acid pattern of milk (g/100 g milk fat) (adapted acc. to [31])

Mean values from 35 and 36 pooled samples from southern German farms, all seasons

concentration of C17:0 (but not C15:0) in the plasma phospholipids is associated with a lower risk of CVD. Another meta-analysis, with a partially different selection of individual studies, observed no lower risk for C15:0 and C17:0 [20]. Furthermore, in a total of four US cohorts, higher concentrations of trans-16:1n-7 in plasma phospholipids [22, 24], and in total plasma and erythrocytes [25] were associated with a lower risk of type 2 diabetes mellitus. This was also the case for C15:0 and C17:0 in the EPIC-InterAct case-cohort study (EPIC = European Prospective Investigation Into Cancer) [28]. There was no association between the concentration of the three biomarkers and the risk of stroke [23].

A higher concentration of trans-16:1n-7 in phospholipids was associated with lower cholesterol [24] and triglyceride concentrations in plasma [22, 24]. In women in the EPIC Potsdam cohort, a higher concentration of C15:0 and C17:0 in erythrocytes was associated with lower concentrations of triglycerides and higher concentrations of HDL cholesterol [29].

Concentrations of minor fatty acids in plasma or in erythrocytes are suitable biomarkers for the consumption of milk and dairy products. Whether it is these minor fatty acids themselves, or the intake of milk and dairy products indicated by their concentration that are responsible for the aforementioned health effects is unclear.

Other potentially bioactive lipids

A meta-analysis demonstrated that MCFA and MCT (i.e. triglycerides with MCFA) significantly reduce body weight and, in particular, body fat mass (subcutaneous fatty tissue and abdominal fatty tissue) compared to the usual fatty acids (mainly C18, e.g. stearic acid, oleic acid, linoleic acid) [15].

There has been little research on the role of phospholipids in MFGM. Butter is low in MFGM, while cream and buttermilk have high concentrations of predominantly intact MFGM. In intervention studies, both buttermilk compared to a macro-/ micronutrient matched control drink [12] and cream compared to butterfat (same fat content) [13], led to lower concentrations of total cholesterol and LDL cholesterol [12, 13] as well as lower concentrations of triglycerides in the plasma [12]. Phytic acid, a saturated fatty acid (C20:0) with 4 methyl side chains, is derived from phytol, the side chain of the chlorophyll molecule. Phytol is released from the chlorophyll in green feed during microbial fermentation in the rumen. Phytic acid may influence energy metabolism, lipid metabolism, and glucose metabolism [30]. However, no studies in humans regarding this have been carried out. There is no information about the health significance of branched-chain fatty acids in humans. Milk fat and MFGM contain potentially bioactive components.

The influence of animal feeding regimes on the fatty acid pattern

Pasture and green feeding is obligatory in organic livestock farming. Organic dairy products have a higher concentration of a-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid, total omega-3 fatty acids, cis9, trans11-CLA, trans-16:1n-7 and vaccenic acid in milk fat compared to conventional products [31] (Table 1). Even in conventional livestock farming, the concentration of these fatty acids increases with a higher proportion of green feed instead of concentrate feed, which mainly increases milk yield [31]. In four out of eight human intervention studies on the effects of milk and dairy products with a fatty acid pattern modified by green feeding instead of a typical pattern, total and LDL cholesterol was reduced [32]. Furthermore, the daily consumption

of 90 g of cheese with a modified fatty acid pattern increased the proportion of cis9,trans11-CLA, α -linoleic acid and eicosapentaenoic acid in the plasma fatty acids. Total, LDL and HDL cholesterol were reduced, while the total/HDL cholesterol ratio remained unchanged [33]. However, as yet there have been no human studies that could answer the question of whether long-term consumption of milk fat with such a modified fatty acid pattern could have an additional health benefit.

The fatty acid pattern can be modified by adjusting the feed given to the cows. The possible health significance of such a modification must be investigated further.

Milk protein

Cow's milk protein is composed of 80% caseins and 20% whey proteins. Caseins are phosphoproteins that bind part of the calcium in the milk. In the cheese-making process caseins are precipitated by acid or rennet and coagulate. Whey proteins, however, remain in the liquid fraction called whey. Milk proteins, and especially whey proteins, are among the proteins with the highest biological value, alongside egg white protein.

Whey proteins have a higher proportion of indispensable amino acids than caseins. In addition to the amino acid pattern of the proteins, the kinetics of their digestion and thus their absorption also influence the utilization of amino acids in the metabolism [34]. Caseins are precipitated (coagulated) in the stomach by the stomach acid, which means they are digested more slowly than whey proteins, and breakdown products take longer to appear in the blood. Digestion produces peptides, including some with known biological activity [35]. For peptides that originate from milk, some of the effects that are currently being discussed include anti-microbial, anti-hypertensive, cholesterollowering, mineral-binding, and opioid effects [36].

Milk protein and blood pressure

A meta-analysis of the effect of casein-derived lactotripeptides isoleucine-proline-proline (IPP) and valine-proline-proline (VPP) was based on 30 intervention studies, predominantly in hypertensive individuals [37]. This meta-analysis confirmed that such peptides reduce systolic and diastolic blood pressure. The effect was stronger in Asians than in Europeans [37]. The intake of intact milk proteins also reduced blood pressure [38].

The beneficial effect of milk proteins (and especially milk peptides) on blood pressure has been demonstrated in many studies. Peptides may originate from fermentation within the milk product itself, or they can be released from milk proteins during digestion.

Milk protein and height

Insulin-like Growth Factor-1 (IGF-1) is a peptide hormone that is mainly synthesized in the liver and is bound to various binding proteins in the blood. It is also found in traces in milk and other animal-derived foods. IGF-1 is important for growth and development. Due to its proliferative and antiapoptotic effects, it may be procarcinogenic [39]. Bovine and human IGF-1 have an identical amino acid sequence. However, in the only study with cow's milk that has been conducted in humans to date, no intact cow's milk-derived IGF-1 could be detected in the blood [40]. Dairy products such as cheese and yogurt contain much less IGF-1 than milk because the fermentation and resultant acidification reduce IGF-1 concentration.

The findings of NHANES (National Health And Nutrition Examination Survey, USA) demonstrated that the consumption of milk moderately promotes longitudinal growth. However, this only applied during a specific time window: it was true for infants (aged 2-5 years) and adolescents (aged 12-17), which is to say that it applied during periods of rapid longitudinal growth [41]. A meta-analysis calculated that the

additional height was 0.4 cm/year for every 245 mL of milk consumed per day [42]. It is possible that IGF-1 is responsible for this effect [39].

In intervention studies that were mainly conducted in children, milk consumption moderately increased the concentration of endogenous IGF-1 in the plasma [43]. Intervention studies [44] and cohort studies [45, 46] conducted in adults confirmed this effect for milk and cheese [45] and milk protein [44, 46]. In addition to proteins, minerals (especially calcium, magnesium, potassium, and phosphorus) and vitamin B₂ appear to increase IGF-1 concentration [45].

Milk moderately stimulates longitudinal growth, which is mainly attributable to the stimulation of the body's endogenous IGF-1 synthesis by milk proteins, rather than the low concentration of IGF-1 in milk.

Milk protein: bone mass and bone strength

Bone (which is made up of 25–30% organic substance and 50% inorganic substance) is a living tissue. It has a fibrous matrix, consisting mainly of collagen, which is hardened by minerals (calcium, phosphorus, and others). What determines bone strength is bone mass (measured as bone mineral content [BMC, g] or bone mineral density [BMD, g/cm² or g/cm³] and structure, i.e. microarchitecture. An adequate protein intake is essential for the formation and maintenance of the organic bone matrix.

Whether milk proteins improve bone strength is a controversial issue [47, 48]. This is because they contain phosphoproteins and sulfur-containing amino acids (methionine and cysteine), whose metabolic end products (phosphoric and sulphuric acid residues) need to be eliminated as fixed acids via the kidney, which increases the acid load in the body. It is hypothesized that the increased excretion of calcium via urine and the pH reduction of the urine demineralize bones. A high protein intake does indeed reduce calcium absorption in the kidney, thus increasing the excretion of calcium in urine [47, 48]. However, it also increases calcium absorption in the intestine [47, 48] and reduces calcium excretion via the feces [48]. Therefore, in the case of adequate calcium intake [49] and normal kidney function [44] the acid load caused by milk proteins does not pose a problem.

Dietary proteins also benefit the bones and skeleton by stimulating IGF-1 synthesis and (in the case of an intake < 800 mg/day), by stimulating intestinal calcium absorption and reducing the concentration of parathyroid hormone [49]. Via these mechanisms, dietary proteins also have the potential to prevent or minimize the loss of bone mass that is usually associated with weight loss [44].

According to a meta-analysis, a higher protein intake (no differentiation according to protein source) increased the bone mineral density of the lumbar spine, but not of the total hip, or the total body [50]. In a cohort of older men, a higher intake of milk proteins was associated with a higher bone mineral density, but this was not the case for plant proteins [51]. However, the effects of milk proteins cannot be separated from the foods from which they are derived (milk and dairy products). Other constituents [52] and perhaps even dietary patterns [53] could also modulate effects of dietary proteins. Dietary proteins, including milk proteins, may have a beneficial effect on bone mineral density and bone strength - most likely in combination with other food components.

Milk protein and muscle protein synthesis

Protein intake in Germany is high [54]. Since protein synthesis becomes less efficient with age, it is currently being discussed whether elderly people have a higher protein requirement [55].¹ Among older people, maintaining the musculature is particularly important because sarcopenia (loss of muscle mass and function) increases the risk of falls, thus increasing the fracture risk. Strong muscles may also benefit the skeleton [49].

The amino acid pattern and the kinetics of digestion and absorption are crucial factors in the stimulation of muscle protein synthesis [55]. Whey proteins are also rich in leucine. Branched-chain amino acids such as leucine stimulate protein synthesis via various signaling pathways, including the mammalian target of Rapamycin complex-1 (mTORC-1) [56].

Compared to soy proteins and especially caseins, whey proteins are fast proteins meaning that leucine and other indispensable amino acids quickly appear in the blood after intake. Therefore, whey proteins stimulated acute muscle protein synthesis more strongly than other proteins [34]. In intervention studies, milk, and especially whey proteins, increased lean body mass (i.e. muscle mass) more than soy protein [55]. Resistance training increased the effect further [34, 55]. According to a meta-analysis, whey proteins, mainly consumed as a supplement, increased lean body mass among people aged 18-72 years when combined with resistance training [57].

Milk proteins have a high biological value. In light of the fact that a large variety of foods, and therefore a large variety of nutrients is available, this is not a compelling argument either in favor of or against the intake of milk protein. However, it does make them a valuable source of protein for elderly, hospitalized and/or malnourished persons.

Lactose and lactose intolerance

Lactose is a disaccharide. In the small intestine, the enzyme lactase (lactase-phloricin hydrolase) cleaves it into the monosaccharides glucose and galactose. Hydrolysis of lactose is slow compared to other disaccharides. In about 65% of the world's population, the activity of lactase in the mucosa of the small intestine drops considerably between the ages of 2 and 5 years [58]. Individuals

with reduced lactase activity either no longer can digest lactose at all or not completely (lactose malabsorption).

If lactose reaches the large intestine due to incomplete cleavage in the small intestine, it is utilized by bacteria present in the large intestine. This causes the formation of metabolites, including short-chain fatty acids (SCFA) and gases such as hydrogen and methane. In combination with the osmosis-controlled influx of water (due to lactose, carbohydrate monomers, SCFA), the gases can cause flatulence, diarrhea, and lower abdominal pain (lactose intolerance). In Germany, around 15% of the population are lactose malabsorbers [59], and about 50% of these malabsorbers experience symptoms after consuming lactose, making them lactose intolerant. Most lactose malabsorbers can tolerate 12 g of lactose, which corresponds to 250 mL of milk, without any problems [60]. Conversely, many persons who perceive intolerance symptoms after consuming milk are in fact able to digest lactose normally [61]. Whether fermentation of lactose that has reached the large intestine causes complaints depends on various factors. These include:

- The composition and metabolic activities of the intestinal microbiota
- The intestinal wall's capacity to absorb the SCFA produced (acetic acid, propionic acid, and butyric acid) and thus remove them from the intestinal lumen
- The person's perception of symptoms and pain, as well as other psychological factors [62].

In addition to its function as a carbohydrate and source of energy, lactose also appears to promote the absorption of calcium and other minerals such as phosphorus, magnesium, manganese, and zinc [63]. Lactose is a source of energy and enhances the absorption of minerals.

¹ The Protein Paradox": p. M90 in this issue

Minerals

The importance of milk and dairy products as sources of calcium is undisputed. Milk contains calcium and phosphorus in a physiologically favorable ratio (Ca: Pi 1.3:1) [64]. An appropriate Pi intake also improves renal calcium reabsorption, thus improving calcium balance [64]. Calcium from milk or rather the sum of the minerals contained in milk also reduced the absorption of fat (from milk and dairy products) and thus increased fat excretion in feces [65]. Consumption of milk fat plus milk minerals reduced plasma and LDL cholesterol compared to pure milk fat [66]. Intake of milk and (milk) minerals such as calcium, magnesium, potassium, and phosphorus correlated positively with the IGF-1 concentration in the blood [45].

The minerals in milk, especially calcium, promote bone health and moderately reduce fat absorption.

Constituents of fermented dairy products

The fermented dairy products consumed most are yogurt products (particularly mild yogurt) and mixed dairy products made from them. Others include soured milk products such as soured milk and kefir, and cheese. During the microbial fermentation of lactose, organic acids (lactic acid, citric acid, acetic acid, propionic acid and so on) and free fatty acids are formed in the dairy product. At the same time, the numbers of the lactose-fermenting microorganisms naturally present in milk or added as starter cultures increase. Bioactive peptides can originate from caseins and whey proteins [36].

Consumption of yogurt improved lactose intolerance in lactose malabsorbers and persons with lactose intolerance [67], and also improved the absorption of minerals [67]. According to three meta-analyses, higher consumption of fermented dairy products (yogurt-type pro-

ducts) compared to non-fermented dairy products or those fermented with other cultures reduced the concentration of total and LDL cholesterol [9-11]. The effect was stronger in people with hypercholesterolemia [10, 11] and also increased with increasing length of treatment [10]. Lb. acidophilus was particularly effective [10, 11]. Body Mass Index, abdominal circumference, and the inflammatory marker CRP (C-reactive protein) were also reduced [10, 11]. It remains unclear whether the acidic pH value, the remaining lactose, the yogurt bacteria themselves, the metabolites formed during fermentation, or a combination of these factors are what caused these effects.

Fermentation increases the shelf life of milk and also affects its consistency and taste. Living bacteria and/or their metabolic end products in the fermented milk products may have special health effects.

Milk consumption and disease risks

This chapter deals with the associations between (higher) consumption of milk and dairy products and the risk of various diseases, conside-shows the results of the meta-ana-provides a general assessment. Studying the nutrition-related physiological effects and health effects of complex foods and dietary patterns is challenging for several reasons. One reason is the often extraordinarily high variation in the composition and structure of products which are (or must be) put in the same category. This applies in particular to cheese, which ranges from fresh cheese (quark) to long ripened hard cheeses aged several months. Then there are also differences in quality, which result from differences in manufacturing processes and/or different storage conditions. Furthermore, consumption habits differ between countries. Consumption habits have also changed considerably in the last decades. In Europe, yogurt and cheese make up a large and growing proportion of total milk and dairy consumption, while in the USA, their proportion is far lower. In Europe, yogurt accounts for up to 32% of total dairy consumption, but in the USA it only accounts for 5% on average [67]. In the USA, low-fat or fat-free milk and dairy products are preferred. There, milk fat is predominantly consumed in confections such as ice cream and "frozen yogurt", or in cheese used as a pizza topping [3]. There is an additional difficulty in that people who are on the whole better informed and try to follow a healthy lifestyle in accordance with recommendations often also prefer low-fat milk and dairy products. In addition, total consumption of milk and dairy products in Scandinavian countries and in the Netherlands is much higher than in Germany, France, Italy, and the USA. All of these factors may have influenced the results of the cohort studies. These aspects are taken into account to varying extents in meta-analyses.

The food matrix appears to have an impact on the effects of individual nutrients [52]. This could also apply to the background diet, and therefore also to the dietary pattern [53]. Currently, it is not possible to conduct a differentiated evaluation of the health effects of full-fat milk and low-fat milk, or of the products derived from them. However, it appears that the characteristics of various product categories (milk, fermented products, cheese) may be more important than the fat content [4]. There is little evidence that full-fat products are associated with health risks compared to low-fat products [3, 5-7].

Stroke, coronary heart disease (CHD), cardiovascular diseases (CVD)

High intake of SFA is a risk factor for the development of CVD [1].

Total milk and c	otal milk and dairy products Milk and dairy products, low-fat		Milk and dairy products, full-fat			Milk, if applicable low-/full-fat					
Consumption	n	RR	Consumption	n	RR	Consumption	n	RR	Consumption	n	RR
Stroke											
h/n	18	0.88*	h/l	8	0.91*	h/l	8	0.96	h/l	3	1.02
h/n	12	0.87*	h/l	6	0.93*	h/l	4	0.95	-	-	-
200 g/day	9	0.99	200 g/day	7	0.97*	200 g/day	6	0.96*	200 g/day	4	0.96/1.04*
h/n	7	0.91*	h/l	3	0.90*	h/l	3	0.91*	h/l	7	0.90
Coronary heart	disease	(CHD)									
200 g/day	4	1.02	200 g/day	3	0.93	200 g/day	4	1.04	200g/day	6	1.00
h/n	12	0.94	h/l	8	1.02	h/l	7	1.08	-	-	-
h/n	7	0.91	h/l	4	0.90*	h/l	4	1.05	h/l	6	1.05
HK Cardiovascu	lar disea	ase (CVD)									
h/n	9	0.88*	-	-	-	-	-	-	-	-	-
h/n	4	0.88	-	-	-	-	-	-	h/l	4	0.94
-	-	-	-	-	-	-	-	-	200g/day	4	0.94*
Metabolic syndi	rome										
h/n	7	0.86*	-	-	_	-	-	_	h/l	3	0.75*
Hypertension											
h/n	5	0.87*	h/l	4	0,84*	h/l	4	1.00	-	-	-
200 g/day	9	0.97*	200 g/day	6	0.96*	200 g/day	6	0.99	200g/day	7	0.96*
Type 2 diabetes	mellitu	s									
h/n	6	0.86*	h/l	3	0.82*	h/l	3	1.00	h/l	5	0.95
200 g/day	13	0.94*	200 g/day	8	0.88*	200 g/day	8	0.95	200g/day	3/3	0.83*/1.27
400 g/day	12	0.93*	200 g/day	9	0.91*	200 g/day	9	0.98	200 g/day	7	0.87
1 Portion/day	14	0.98	-	-	-	-	-	-	-	-	-
200 g/day	16	0.97*	200 g/day	13	0.96(*)	200 g/day	13	0.98	200 g/day	7/9	1.01/0.99
Breast cancer											
h/n	10	0.85*	h/l	4	0.84*	h/l	4	0.99	h/l	5/8	0,93*/0,98
Prostate cancer											
h/n	15	1.09*	-	-	-	-	-	-	h/l	6/8	1,14*/0,92*
Colorectal cance	er										
h/n	12	0.81*	h/l	2	0.97	h/l	3	0.74	h/l	10	0.83*
-	-	-	-	-	-	-	-	-	h/l	17	0.85*

Tab. 2: Effects of milk and dairy products on disease risks – meta-analysis of prospective cohort studies¹

¹ GAO et al. 2013 also includes a case control study;

FM = fermented milk; h/l = highest vs. lowest consumption category; n = number of individual studies/comparisons; RR = relative risk *Change is statistically significant; (*) only trend (p = 0.07)

Cheese			Yogurt/fermei	nted mi	Meta-analysis	
Consumption	n	RR	Consumption	n	RR	
h/l	6	0.94	h/l (FM)	3	0.80*	Hu et al. 2014 [68]
h/l	4	0.91*	h/l	3	0.98	QIN et al. 2015 [69]
40g/day	7	0.97	100g/day	3	1.02	DE GOEDE et al. 2016 [70]
h/l	4	0.87*	-	-	-	Alexander et al. 2016 [71]
-	-	_	-	_	-	Soedamah-Muthu et al. 2011 [72]
h/l	7	0.84*	h/l	5	1.06	QIN et al. 2015 [69]
h/l	5	0.82*	h/l	4	1.08	Alexander et al. 2016 [71]
-	-	-	-	-	-	QIN et al. 2015 [69]
h/l	3	0.89	h/l	3	0.93	ALEXANDER et al. 2016 [71]
-	-	-	-	-	-	Soedamaн-Митни et al. 2011 [72]
-	-	-	-	-	-	CHEN et al. 2015 [76]
h/l	4	1.00	_	-	-	RALSTON et al. 2012 [93]
30 g/day	8	1.00	50g/day	5	0.99	Soedamah-Muthu et al. 2012 [94]
-	-	-	h/l	4	0.83*	TONG et al. 2011 [101]
30g/day	7	0.80*	50g/day	7	0.91*	GAO et al. 2013 [97]
50g/day	8	0.92*	200 g/day	7	0.78	AUNE et al. 2013 [98]
-	-	-	1 Portion/day	9	0.82*	Снем et al. 2014 [100]
10g/day	12	1.00	80g/day	11	0.86*	GIJSBERS et al. 2016 [99]
-	-	-	-	-	-	Dong et al. 2011 [110]
h/l	11	1.07*	h/l	6	1.12	AUNE et al. 2015 [111]
h/l	7	0.94	h/l (FM)	4	0.93	AUNE et al. 2012 [107]
h/l	7	1.11	h/l (FM)	7	1.01	Ralston et al. 2014 [106]

According to this statement, in the past, the consumption of full-fat milk and dairy products was believed to bear an elevated risk of CVD. Four meta-analyses on the effects of milk and dairy products on the risk of stroke, with in part differing inclusion criteria, found a lower risk in the case of higher consumption of low-fat dairy (sum of low-fat milk and dairy products) [68-71], and partially also in the case of higher consumption of full-fat dairy [69, 71], as well as cheese [69, 71] and yogurt [68]. The risk was lowest in the case of a daily intake of 200 mL of milk [68] or 125 g milk and 25 g cheese [70]. The effect was stronger in Asia than in Europe [68, 70], where average consumption is higher (median milk intake 38 g/ day compared to 266 g/day) [70]. The consumption of full-fat milk was found to be associated with a higher risk in one meta-analysis [70] (Table 2).

Three meta-analyses on the effects of the consumption of milk and dairy products on the risk of CHD found no association between risk and consumption of milk [71, 72], or of total dairy [69, 71, 72]. There was, however, an inverse association with cheese intake [69, 71] (\bullet Table 2).

Three meta-analyses on the effects of the consumption of milk and dairy products on the risk of CVD found a lower risk associated with higher consumption of milk [72], of total dairy [69], or respective trends [71] (• Table 2). A potential extra benefit of fermented products is being discussed [9].

Higher consumption of milk and dairy products correlates with a reduced risk of stroke, but this is not the case for CHD. There may be an inverse association with CVD.

Metabolic syndrome (MetS) and associated risk markers

MetS is a clustering of at least three of the five following medical conditions: disturbed lipid metabolism (low HDL cholesterol, high fasting

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Disease	Association
stroke	\checkmark
coronary heart disease (CHD)	\leftrightarrow
cardiovascular disease (CVD)	\checkmark
metabolic syndrome	\checkmark
overweight/obesity	\leftrightarrow
hypertension	$\downarrow\downarrow$
type 2 diabetes mellitus	$\downarrow \downarrow$
cancer	colorectal $\psi \psi$, breast ψ , stomach ψ , prostate \uparrow , other organs $\leftarrow \rightarrow$
fractures: bone mineral content, bone density, bone markers	\leftrightarrow

 Tab. 3: Association between the consumption of milk and dairy products and risk of diseases (meta-analysis of observation studies)

 $\uparrow \uparrow / \downarrow \downarrow$ likely increases/decreases; \uparrow / \downarrow potentially increases/decreases; $\leftarrow \rightarrow$ no association

triglycerides), hypertension, overweight (most pronounced in the abdomen), and type 2 diabetes mellitus. Insulin resistance is a key phenomenon in this condition. Overweight usually occurs at the beginning of disease development. The incidence of the MetS results in a disproportionately increased CVD risk [73].

According to systematic reviews the majority of observational studies found that consumption of milk and dairy products has a favorable impact, or at least no adverse impact on the development of MetS [74, 75]. According to a meta-analysis, higher consumption of milk and of total dairy was associated with a lower risk [76] (Table 2). With each additional serving per day, the risk was 6% lower [76]. In adolescents, case-control studies found a favorable association between the consumption of milk and dairy products and abdominal circumference and skin fold thickness [77], as well as cardiovascular risk scores [77, 78]. But the latter finding was only a trend for male adolescents [77].

A meta-analysis of intervention studies lasting on average six months found that low-fat or full-fat dairy had no effect on MetS risk markers, namely on abdominal circumference, fasting glucose, insulin resistance, LDL and HDL cholesterol, blood pressure, or the inflammatory marker CRP, but body weight was slightly increased [79]. However, in the case of longer duration, (≥ 3 months), according to this meta-analysis [79] and a systematic review [80], insulin resistance was mostly decreased. In another systematic review, the (usually increased) concentration of biomarkers of inflammation in overweight or obese people remained unchanged or was reduced [81].

Higher consumption of milk and dairy products appears to be associated with a lower risk of MetS.

Overweight/obesity

The number of obese people worldwide has almost doubled since 1980. Obesity has now also become a serious health problem in many developing countries [82].

A meta-analysis of cohort studies found no effect for low-fat and fullfat dairy in adults [83]. A systematic review evaluated the available data as inconsistent [84]. However, yogurt consumption was found to have an inverse association with weight increase, and higher cheese consumption showed a positive association [83]. Another meta-analysis found that total dairy intake was associated with a non-linear risk reduction, i.e. an inverse association that was reduced with increasing consumption [85]. In a US cohort, after an observation period of 11 years, 45% of the women (\geq 45 years old) who were of normal weight at the beginning of the study had become either overweight or obese. Higher consumption of fullfat dairy, but not of low-fat dairy, reduced the risk of weight gain [86].

According to a meta-analysis, higher consumption of dairy in children was associated with a lower risk of overweight and obesity. With each additional serving per day, the risk was 13% lower [87]. Another study found a non-linear risk reduction [85]. According to a systematic review, dairy had no effect in children of pre-school and school age, but in adolescents (12–19 years old) they had a moderately favorable effect [88].

Meta-analyses of intervention studies have shown that higher consumption of dairy - without energy restriction, which is to say ad libitum - does not significantly reduce, or can even slightly increase body weight and body fat [79, 89, 90]. Full-fat dairy and low-fat dairy showed no different effects in this regard [79]. However, in the case of concomitant energy restriction [89-92], body weight and body fat mass were moderately reduced. Endurance training during the intervention strengthened this beneficial effect [91] (◆ Table 4).

Even though it remains unclear if there is an inverse association between the consumption of milk and dairy products and overweight/obesity and/or weight stability, a detrimental effect appears unlikely. There is no evidence that lowfat dairy products are advantageous in this regard.

Hypertension

About a third of the adult population in industrialized western coun-

Energy restriction	Duration (months)	Products	Body weight (kg)	n	Body fat (kg)	n	Meta-analysis
no	5–12	nd	+0.33	5	-0.16	4	Approcess et al. 2012 [20]
yes		nd	-1.29*	10	-1.11*	9	ABARGOUEI et al. 2012 [89]
no	1–36	nd	+0.39*	13	-0.12	8	Curry et al. 2012 [00]
yes		nd	-0.79	16	-0.94*	15	CHEN EL al. 2012 [90]
yes	1–12	nd	-1.16*	16	-1.49*	14	STONEHOUSE et al. 2016 [91]
no	1–36	low-fat	+0.82*	8	nm.		Proverse et al. 2012 [70]
no		full-fat	+0.41*	10	nm.		DENATAR et al. 2015 [79]
yes/no	3–24	nd	-0.06	31	-0.32	21	
yes		nd	-0.32	19	-0.96	13	BOOTH et al. 2015 [92]

Tab. 4: Changes in body weight and body fat in adults due to higher consumption of milk and dairy products (meta-analysis of intervention studies)

* Change is statistically significant

n = number of studies included; nd = not defined, i.e. not specified; nm. = not measured

tries has high blood pressure [93]. Two meta-analyses [93, 94] found that higher consumption of total dairy, as well as higher consumption of low-fat dairy was associated with a lower risk of hypertension. Full-fat dairy and cheese [93, 94] or yogurt [94] had no effect (
 Table 2). It is possible that the salt in the cheese counteracted the protective effects of other constituents. In the Framingham cohort, in persons who were normotensive at baseline, higher intakes of total dairy, lowfat dairy, yogurt, and fermented dairy products during the 15-year follow-up were associated with risk reduction [95].

According to a meta-analysis of 14 intervention studies lasting 1 to 6 months conducted in hypertensive and pre-hypertensive persons, the consumption of (probiotic) fermented milk compared to non-fermented milk (control) decreased blood pressure. In Japan, the effects were more pronounced than in Europe [96]. *Higher consumption of milk and dairy products, including dairy products fermented with special cultures is cor-*

fermented with special cultures, is correlated with reduced blood pressure. Low-fat products are particularly effective in this regard.

Type 2 diabetes mellitus

The prevalence of type 2 diabetes mellitus is markedly increasing in many regions of the world. Several meta-analyses of cohort studies showed a lower risk of type 2 diabetes mellitus with higher consumption of total dairy, low-fat dairy, yogurt [97-101] and partially also cheese [97, 98] (* Table 2). In the EPIC-InterAct case-cohort study, higher consumption of cheese plus yogurt (fermented products) was associated with a lower risk of type 2 diabetes mellitus. However, this did not apply to total dairy. The results varied widely between the individual countries [102]. However, when the consumption of milk and dairy products in this cohort was estimated based on C15:0 and C17:0 as biomarkers, an inverse association was found both overall and in each individual country [28]. The differing results could be due to limited accuracy of dietary intake assessment. Plasma fatty acids can be measured more precisely, but their concentrations are partially dependent on endogenous regulation [26]. Nonlinear inverse associations were observed for total dairy and for some of the product categories, which means that risk reduction became less with increasing consumption [97, 98]. Furthermore, the effects were stronger in Asia than in Europe, with overall consumption being lower in Asia [99].

Higher consumption of milk and dairy products is associated with a lower risk of type 2 diabetes mellitus.

Cancer

The development of cancer is a complex, multifactorial, long-term process. This makes it particularly difficult to detect causal relationships. The German Nutrition Society and the World Cancer Research Fund (WCRF) systematically update the literature on the association between nutrition and the risk of various types of cancer, namely breast cancer, colorectal cancer, stomach cancer, prostate cancer, bladder cancer, ovarian cancer, uterine cancer, and testicular cancer. The Nutrition Report 2016 of the German Nutrition Society and the WCRF evaluations from 2011 [103] and 2014 [104, 105] assessed the potential risk from milk and dairy products, with the same conclusions.

Current meta-analyses [106, 107]

(Table 2) and findings from the EPIC cohort [108] showed a lower risk of colorectal cancer in the case of higher consumption of total dairy [107] and milk alone [106, 107]. In the EPIC cohort full-fat and low-fat dairy had the same effects [108]. The consumption of yogurt and cheese was associated with a lower risk [108]. The inverse association is largely attributed to the calcium contained in milk and dairy products [108, 109]. According to the metaanalysis, each additional 300 mg/ day of calcium (corresponding to approximately 250 mL of milk, 200 g of yogurt, or 30 g of hard cheese), reduces the risk by 8% [109]. According to a meta-analysis, the risk of breast cancer was lower in the case of higher consumption of total dairy , as well as low-fat dairy and low-fat milk [110] (
 Table 2).

The most recent meta-analysis showed that risk of prostate cancer increases with higher consumption of total dairy, as well as of low-fat milk, cheese, and calcium derived from foods (RR 1.05 per 400 mg/ day). In the case of full-fat milk, there was a lower risk [111] (• Table 2). This meta-analysis is the basis for the evaluation of the WCRF [105].

Both this meta-analysis and the Nutrition Report 2016 state that the evidence of an increased risk of prostate cancer due to milk and dairy products is "possible". The WCRF report considers the evidence that high calcium intake (with primary sources being milk and dairy products) can increase risk "limited". Increased risk was only observed at a total calcium intake of more than 1.2 g/day [105]. This corresponds to a daily consumption of 1 L of milk or 110 g of hard cheese.

For all other types of cancer, higher dairy consumption was not found to have an effect.

Milk and dairy products may reduce the risk of colorectal cancer and breast cancer, whereas higher consumption of milk and dairy products (and therefore calcium) may increase the risk of prostate cancer.

Bone mass, bone strength, and osteoporosis

Osteoporosis (bone loss) is characterized by an imbalance between bone building and bone breakdown, reduced bone mass, and deterioration in the bone microarchitecture, which causes increased susceptibility to fractures. Adequate calcium supply is essential throughout life: it is needed to build bone mass until the third decade of life, and in the following decades it is needed to maintain bone mass and delay bone loss. Milk and dairy products are important sources of calcium. Dietary proteins and vitamin D, as well as body weight and physical activity also play an important role in the development or prevention of osteoporosis [56, 112].

According to a systematic review [112] and a meta-analysis [113], bone mineral content and density were higher in children and adolescents who consumed more milk. In women, low milk intake in adolescence led to low values in adulthood [114]. In individual studies, higher intake of milk protein (and therefore of milk and dairy products) in older people was associated with higher bone mineral density [51], and the diet pattern "low-fat milk" was associated with higher bone mineral density in the femoral neck (but not in other places) compared to the "red meat" pattern and the "processed foods" pattern [115]. In adults, higher consumption of dairy improved bone metabolism markers [112].

The influence on risk of fracture is unclear. A meta-analysis [116] and a systematic review [117] found no association between the consumption of milk [116, 117] or the consumption of dairy [117] and the risk of hip fracture. However, in individual studies, fewer hip fractures were recorded in older men with higher milk (protein) intake [51], as well as in postmenopausal women who had a high milk intake during adolescence [114], and in older persons who consumed \geq 1 servings of milk a week (threshold value) [118]. Cohort studies mostly focused on hip fractures, although fractures of the spine occur more frequently and usually earlier in the osteoporosis development. In individual studies, there was an inverse association between milk (protein) intake and the total number of osteoporosis-associated low-trauma fractures among older men [51]. Vegans with a very low calcium intake (< 525 mg/day) had a higher risk of fracture (all types, proportion of hip fractures < 3%) than lacto vegetarians or vegans with higher calcium intake [119]. The possible role of favorable dietary patterns for reducing the risk of fracture is an additional aspect to consider [53].

According to a systematic review [117], in intervention studies, a higher calcium intake via supplements did reduce the number of vertebral fractures and total fractures, but it did not reduce the number of hip and forearm fractures.

Many more factors influence the risk of fracture. Thus 60-80% of a person's maximum bone mass is determined by genetic factors [112]. In addition, there are individual factors such as body height and weight, muscle mass, and physical activity (which improves coordination of movement), life expectancy (the risk of falling increases with increasing age) and the geographical location of a country (endogenous vitamin D synthesis). In older women in industrialized countries, up to 86% of bone fractures (excluding those of the spine) are caused by falls [120]. Beyond that Asians have a different skeletal geometry than Caucasians, which reduces the risk of hip fractures, but increases the risk of vertebral fractures [121]. African-Americans have a higher bone mineral density than Caucasians. Their bones also have a more favorable microarchitecture. Both of these characteristics reduce the risk of fracture under otherwise identical baseline conditions [122].

Higher consumption of milk and dairy products when young improves bone

mineral content and density. The association between the consumption of milk and dairy products and risk of fracture needs to be investigated further.

Milk and dairy products as components of a healthy dietary pattern

The first DASH study was published in 1997. DASH stands for Dietary Approaches to Stop Hypertension. The study looked for ways to reduce blood pressure through diet-based treatment. It turned out that a diet with plenty of fruit, vegetables, and wholegrain products reduces blood pressure. An even greater reduction in blood pressure (-11%) was achieved with 2-3 additional servings daily of low-fat dairy foods (the DASH diet).

Meta-analyses of intervention studies confirmed the beneficial effect of this diet on blood pressure [123, 124], insulin resistance [125], as well as total and LDL cholesterol [124]. Meta-analyses of cohort studies have shown that the DASH diet is associated with a lower risk of CVD [126, 127], type 2 diabetes mellitus, and cancer [127]. A DASH diet with full-fat dairy foods reduced blood pressure and total cholesterol to the same extent [128], and according to a cohort study, was also associated with a lower risk of MetS [129]. Study participants with risk factors, such as hypertension, benefited from a DASH diet even more than subjects without risk factors

[123–125]. The 2015 scientific report of the Dietary Guidelines Advisory Committee for the USA listed the DASH diet among the "healthy" diets [130].

Dairy consumption in Germany and its assessment

In Germany, the consumption of fresh milk products (milk, buttermilk and others, yogurt) has remained relatively stable since the 1980s at around 80 kg/person/ year, while cheese consumption has increased [131]. According to results of the German National Food Consumption Study II, adults (15-80 years old) consume an average of 192/190 g (m/f) of milk and dairy products per day [54]. Of these, 51% are milk and mixed milk products, 30% are yogurt, and 19% are cheese and quark [54]. Daily consumption is therefore somewhat lower than recommended by the German Nutrition Society (200-250 g milk and dairy products and 50-60 g cheese). For girls and boys between 9 and 13 years of age, the DONALD study (Dortmund Nutritional and Anthropometric Longitudinally Designed) calculated a total consumption of 304 g/ day and 391 g/day respectively. Within these product categories shifts occurred from 1986 to 2001. Consumption of milk decreased, whereas consumption of yogurt and cheese increased [132].

The protective effects of milk consumption have already been

observed at intake levels that are in line with or even below the current recommendations of the German Nutrition Society. Several studies observed a plateau in the doseresponse relationship. Consequently, at the population level, there is no need to increase intake beyond the recommendations. Restricting consumption is not desirable, as milk and dairy products are a valuable source of calcium, among other things. The findings of the DASH studies highlight the fact that milk and dairy products are a beneficial component of a disease-preventing, plant-based diet.

References online: → www.ernaehrungs-umschau.de

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Conflict of Interest

Dr. PFEUFFER received honorarium for two lectures given at advanced training events held by the Bavarian Dairy Association (*Bayerische Milchwirtschaft e. V.*). Beyond that, the authors declare no conflict of interest.

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