MILK Symposium review: the importance of milk and dairy foods in the diets of infants, adolescents, pregnant women, adults, and the elderly

Article

Accepted Version

Givens, I. (2020) MILK Symposium review: the importance of milk and dairy foods in the diets of infants, adolescents, pregnant women, adults, and the elderly. Journal of Dairy Science, 103 (11). pp. 9681-9699. ISSN 1525-3198 doi: https://doi.org/10.3168/jds.2020-18296 Available at https://centaur.reading.ac.uk/94534/

Published version at: https://doi.org/10.3168/jds.2020-18296

To link to this article DOI: http://dx.doi.org/10.3168/jds.2020-18296

Publisher: American Dairy Science Association

Invited Review: The importance of milk and dairy foods in the diets of infants, adolescents, pregnant females, adults and the elderly.

Running head: Dairy foods in the diet at key life stages

D. I. Givens

Institute for Food, Nutrition and Health, University of Reading, Reading RG6 6AR, United Kingdom**.** Email: d.i.givens@reading.ac.uk

Interpretive summary

There is now increasing evidence that diets in early life can influence health throughout later life. Milk and dairy foods are important sources of certain nutrients and have functional effects particularly important at certain life stages. This paper examines some of the key nutrition issues during childhood, adolescence, pregnancy, middle and older age and discusses where dairy foods can be helpful. As an example, these foods can aid bone development in childhood and adolescence, maintain adequate iodine status during pregnancy and reduce muscle loss by the elderly.

ABSTRACT

Despite an ongoing increase in life expectancy, it is not always accompanied by an increase in healthy lifespan. There is increasing evidence that dietary exposure in early life can substantially impact on chronic disease risk in later life. Milk and dairy foods are important suppliers of a range of key nutrients with some being particularly important at certain life stages. It is now recognized that milk protein can stimulate insulin-like growth factor-1 (IGF-1) essential for longitudinal bone growth and bone mass acquisition in young children, thus reducing the risk of stunting. Low milk consumption during adolescence, particularly by females, may contribute to sub-optimal intake of calcium, magnesium, iodine, and other important nutrients. Given the generally low vitamin D status of European populations, this may have already impacted bone development and any resulting reduced bone strength may become a big issue when they are much older. A sub-optimal iodine status of many young females has already been reported together with several observational studies showing an association between sub-optimal iodine status during pregnancy and reduced cognitive development by the offspring. There is now good evidence that consumption of milk/dairy foods does not lead to an increased risk of cardiovascular diseases and type 2 diabetes. Indeed some negative associations are seen, notably that between yogurt consumption and type 2 diabetes, which should be researched with urgency. Greater emphasis should be placed on reducing malnutrition in the elderly and on dietary approaches to reduce their loss of muscle mass, its functionality and bone strength. Whey protein has been shown to be particularly effective for reducing muscle loss and this needs development to provide simple dietary regimes for the elderly to follow. There is an ongoing, often too simplistic debate about the relative value of animal vs. plant food sources for protein in particular. It is important that judgements on the replacement of dairy products with those from plants also include the

evidence on relative functionality which is not expressed in simple nutrient content (e.g. hypotensive and muscle synthesis stimulation effects). Only by considering such functionality will a true comparison be achieved.

Key words: Milk, dairy, life stage, chronic disease

INTRODUCTION

In its recent review of world health statistics, the World Health Organization (WHO, 2019) reports that global life expectancy has continued to increase, on average by 5.5 years from 2000 to 2016, although healthy life expectancy increased by only 4.8 years. There are however great discrepancies, notably that life expectancy at birth being over 18 years shorter in low income countries than in high-income countries, with a sizable proportion of the difference being related to preventable health issues. Moreover, childhood obesity continues to increase across the world but most notably in Europe and North America.

In the United Kingdom (UK), life expectancy doubled over the last 200 years and is now higher than 80 years (Roser, 2017) with an even greater population growth rate among those aged 85 years and over. Aging brings with it some important nutrition-health challenges such as increased risk of bone breakages and sarcopenia and those linked to lower absorption of vitamin B_{12} and efficiency of vitamin D synthesis. Gullberg et al. (1997) estimated the total worldwide number of hip fractures to be around 1.26 million in 1990 and they predicted this would increase to 2.6 and 4.5 million by 2025 and 2050 respectively. In support of this, Hernlund et al. (2013) reported that the frequency of osteoporotic fracture has increased in many parts of the world and proposed that in the European Union (EU), the prevalence will double by 2035. It is therefore of considerable concern that in the UK at least, milk consumption in teenage years has now reduced, particularly in females, such that considerable sub-optimal intakes of calcium, iodine and other key nutrients are apparent.

Sarcopenia is an age-related progressive loss of muscle mass and strength. The meta-analysis of Shafiee et al. (2017) reported that the overall prevalence of sarcopenia was 10% in males and females but it was higher in non-Asian than Asian countries. There are many effects of sarcopenia including reduced muscle strength and mass leading to increased risk of falls and related bone breakages which can have major negative impacts on quality of life and independence. It is also now appreciated that both reduced muscle mass and reduced mobility can increase the risk of type 2 diabetes which further reduces healthy and quality lifespan (Hunter et al., 2019).

In middle and later life cardiovascular diseases (CVD) remain a major cause of death and morbidity in the EU and worldwide even though prevention and treatment programs have brought major benefits (Wilkins et al., 2017). While CVD related mortality has declined in most of Europe, there remain some 49 million people living with CVD in the EU which represents a major healthcare cost (Wilkins et al., 2017). Of related concern is the substantial rise in the prevalence of type 2 diabetes related in good part to increased obesity. Recent data from Diabetes UK (2019) indicate that about 10% of people over 40 years of age now have type 2 diabetes with some 4.7 million cases of all types of diabetes (~90% type 2). It is predicted that by 2030 the number of cases will have reached 5.5 million.

Diet is a key risk modifying factor for chronic diseases and this must be used appropriately throughout the various life stages, not least because reducing risk in early life can have benefits in later life. The intention of this review to focus on key life stage issues where milk/dairy components can play a substantial role in reducing chronic disease risk. This predominantly relates to high income countries although some reference is made to low income countries where relevant.

MILK IN CHILDHOOD

Milk and growth

The benefits of milk in a child's diets have been known for many years. For example in 1926, a report produced by the UK Medical Research Council showed that giving an additional 568 mL/day (d) of milk to boys in a children's residential home led to a marked increase in growth (Corry Mann, 1926). Subsequently, UK nutrition policy encouraged milk drinking for children. In recent years there has been an increased focus on the importance of nutrition during childhood as there is increasing evidence that diets during this period can influence health in later life. It is well recognized that undernutrition in childhood can lead to a marked reduction in linear growth (stunting), increased risk of slower short-term cognitive development and in adulthood of hyperglycemia, hypertension, elevated blood lipids and obesity (de Onis and Branca, 2016). Despite recent worldwide improvements, Semali et al. (2015) noted that stunting in sub-Saharan African children remains at about 40 % and some countries have an even higher prevalence. Recently, Leroy and Frongillo (2019) confirmed that childhood stunting remains a major health concern in many parts of the world. They also proposed that the conventional focus on linear growth reduction and stunting is not always the most cost-efficient way to improve the well-being of children.

Nevertheless, a range of studies over a substantial time period have shown milk to be a key food for reducing stunting in children. In the mid-1970s a randomized controlled trial (RCT) was started to evaluate the effect of milk provision at school on child growth (Baker et al., 1980). Some 600 children aged 7 and 8 years in families in South Wales, UK with 4 or more children were chosen from schools in areas with a high socioeconomic deprivation. The selected children were on average 2.5 cm shorter and 1.5 kg lighter than the average for the area, and for height, they were representative of the lowest 20% of children throughout the whole region. The children in the treatment group were given 190 mL of milk every school day. After 2 school years, these children were significantly taller and heavier (both $P<0.01$) than those in the control group although the increases were very small (0.28 cm taller and 0.13 kg heavier). In addition, there was significantly increased growth in children from families in the highest social classes compared with those in the lowest. More recently, Michaelsen (2013) emphasized that milk has a specific growth promoting effect in children, an effect which is seen in both developing and developed countries, indicating an effect even when energy and nutrient intakes are apparently adequate. In a recent study in Bangladeshi children from households with milk producing cows, Choudhury and Headey (2018) found that these children had increased height-for-age Z scores (+0.52 standard deviations) in the crucial 6 to 23 month growth phase compared with control children from households with non-milk producing animals, an effect apparently not confounded by family socio-economic status. However, it was also found that children aged 0–11 months from treatment households were 21.7% less likely to be breastfed than children from control households, suggesting that ready access to dairy milk substantially reduces the incentive for mothers to breastfeed. Reduced availability of breast milk will be a considerable disadvantage for the very young child with the increased acute risk of gastrointestinal infections and infant morbidity and mortality.

The effect of milk on linear growth is now thought to be primarily mediated through the stimulation of IGF-1 by milk proteins, in particular by casein (Hoppe et al., 2009). IGF-1 is essential for longitudinal bone growth, skeletal maturation, and bone mass acquisition during childhood and maintenance of bone matrix in adult life (Locatelli et al., 2014), with regulation of bone length associated with changes in chondrocytes of the proliferative and hypertrophic zones of the growth plate (Yakar et al., 2018). It is of note that Wan et al. (2017) showed that activation of peroxisome proliferator-activated receptor gamma (PPARγ) is also involved in the regulation of hepatic IGF-1 secretion and gene expression in response to dietary protein, thus providing a possible explanation whereby dietary protein and related amino acids stimulate hepatic secretion of IGF-1.

Milk, obesity and future health

The general rise in childhood obesity in many parts of the world is a major concern. At least 60% of children that are overweight before puberty will remain overweight in early adulthood (Nittari et al., 2019) with the increased risk of CVD (Steinberger et al., 2016) and type 2 diabetes. It is therefore of considerable interest that dairy consumption is inversely and longitudinally associated with childhood obesity and overweight (Lu et al., 2016; Dougkas et al., 2019). There are concerns however, about the so-called 'early protein hypothesis' with consistent evidence that the use of infant formulae with higher protein contents than human milk throughout the first year of life leads to greater abdominal fat mass in children from 2 to 6 years old. This is likely to be related to higher circulating IGF-1 and insulin (Totzauer et al., 2018). Insulin in particular is known to promote adipose tissue deposition and this is a key component of the early development of insulin resistance. Thus in many Western populations there may be a need to moderate the use of the high protein formula milks in early life.

Milk and bone health

It is now recognized that sub-optimal vitamin D status in children and adults is prevalent in many parts of the world. Holick (2010) proposed this to be a pandemic of '*a forgotten hormone important for health*'. Cashman et al. (2016) confirmed that within Europe, the prevalence of vitamin D deficiency represented a major health risk which required a major public health initiative. More recently Jazayeri et al. (2018) reported that the prevalence of vitamin D deficiency in Iranian children is very high.

A 2-year intervention study with 757 Chinese females initially aged 10 years compared those who consumed on school days, 330 mL of calcium-fortified milk with or without a vitamin D_3 supplement (5 or 8 µg). Over the intervention period, mean calcium intake was 649, 661, and 457 mg/d for the milk, milk plus vitamin D, and control groups, respectively. Milk consumption with or without added vitamin D, led to a significantly greater rate of height increase, body weight, total bone mineral mass, and bone mineral density (BMD). The subjects who also received vitamin D relative to those receiving just milk showed significantly greater increases in (size-adjusted) total-body bone mineral content (2·4 *v.* 1·2%) and BMD (5·5 *v.* 3·2%.) (Du et al., 2004).

A study in the United States of America (US) with children aged 4-8 years (Abrams et al., 2014) found that calcium intake, when not substantially deficient, was not highly related to bone mineral status and that a supplement of 25 µg/d of vitamin D in these children did not influence calcium absorption or bone mineral status. Intake of magnesium and the amount absorbed were however key predictors of BMD and bone mineral content. The authors propose that this study is evidence that magnesium should be more considered as an important nutrient in relation to bone development. The extent to which these findings can be extended to other populations is at present uncertain, but milk and dairy products are important sources of magnesium for children (15-25% of intake in UK; Roberts et al.,2018) and are especially important during the phase of rapid bone growth in late childhood/early adolescence. It is also of note that low serum magnesium concentrations in males aged 42-61 years were associated with increased risk of bone fracture in the Japanese Kuopio Ischemic Heart Disease prospective study (Kunutsor et al., 2017).

It has been known for a long time that low vitamin D status in children could lead to the development of rickets and consequent increased risk of osteoporosis in later life. As noted by Holick (2010), at the start of the 20th century some 80% of children in North America and Europe suffered from rickets. Subsequently the occurrence of rickets declined markedly as a result of vitamin D fortification in some countries of foods including milk, and the policy of providing cod liver oil to children, and by the late 1930s rickets was essentially eradicated. It is therefore of considerable concern that cases of rickets are again increasing in the US (Thacher et al., 2013) and worldwide (Prentice, 2013). In the UK, Goldacre et al. (2014) reported that in England, the need for hospital treatment for rickets was at the highest level seen in the last 50 years.

Many, but not all new cases of rickets are the result of sub-optimal vitamin D status with some cases implicating sub-optimal calcium intake. Milk is of course an excellent dietary source of calcium and as noted above, milk proteins, especially casein, provide an anabolic stimulus for bone development (Hoppe et al., 2009). Although milk is not a naturally rich source of vitamin D, it is an excellent medium for vitamin D fortification. Vitamin D fortification of milk has been a policy in the US and Canada for a long time but in Europe such a policy for liquid milk is limited to Finland although Sweden and Norway do fortify some dairy products (Itkonen et al., 2018). Itkonen et al. (2018) also concluded that countries that have a national vitamin D fortification of milk policy, dairy foods do make a substantial contribution to vitamin D intake whereas in those with no such policy or with only a few dairy foods fortified, the contribution is low. Given the evolving picture on rickets, considerably more attention should be focused on the importance of vitamin D fortification of milk. There is also concern about the increasingly popular plant-based milk alternative drinks especially when used to replace milk for young children (Scholz-Ahrens et al., 2019). Many contain very little protein, have lower micronutrient concentrations than milk (Bath et al., 2017) and there have been cases where young children have become seriously ill as a result of consuming such milk alternatives (e.g. Fourreau et al., 2013; Le Louer et al., 2014).

Hypersensitivity to milk and dairy foods

There are 2 main types of hypersensitivities (often called intolerances) relating to dairy food consumption i.e. cow's milk protein allergy (CMPA) and lactose intolerance. These are 2 very different conditions that require medical diagnosis to avoid unnecessary or inappropriate removal of cow's milk from a child's diet which is a major event that can have significant nutritional consequences.

CMPA is an adverse immune response to proteins in cow's milk with β-lactoglobulin and αs1-casein (both absent in human milk) often being quoted as the 2 key allergenic proteins (Pastuszka et al., 2016) although many other milk proteins can be involved. CMPA is usually recognized as 2 sub-types, the IgE-mediated rapid onset and non-IgE-mediated delayed onset variants (Vojdani et al., 2018) with anaphylaxis and related death being possible in severe cases of the rapid onset sub-type (Turner et al., 2015). CMPA is the most common type of food allergy and usually affects very young children although a high proportion are in remission by the age of 3 years (Host and Halken, 2014). The increased prevalence of CMPA has been suggested to be the result of increased use of cow's milk as a substitute for human milk (Rangel et al., 2016) although the recent study of Munblit et al. (2020) reports that identification and management of symptoms as CMPA is often not evidence-based suggesting that there may be considerable over-diagnosis.

Lactose intolerance is a non-allergic hypersensitivity that results from a reduced ability to digest lactose. Intestinal digestion and absorption of lactose requires the enzyme lactase and deficiency or insufficiency of lactase leads to malabsorption of lactose and subsequent digestive upset. The ability or otherwise to synthesize lactase is genetically determined. For a full and up to date review of lactose intolerance and CPMA the reader is referred to Miles (2020).

MILK IN ADOLESCENCE

Adolescence and dietary change

Adolescence is the life period (10-19 years, WHO, 1999) involving hormonal changes, rapid growth and sexual maturation. There are also changing dietary habits, new motivations and challenges, some persisting into adulthood (Forbes and Dahl, 2010). The age of puberty onset has reduced substantially over the last 100 years; currently the UK average age for males and females is 12 and 11 years respectively (NHS, 2019).

In the UK, data from the National Diet and Nutrition Survey covering the period 2008/09-2011/12 (Bates et al., 2014) identify that adolescent females in particular, have considerably lower milk consumption than those under 11 years of age while older age groups have somewhat higher intakes (Figure 1). A similar picture has been seen in the more recent National Diet and Nutrition Survey covering a longer period 2014/15 to 2015/16 (Roberts et al., 2018) and this will have contributed substantially to the lower intakes of some key nutrients by adolescent females (Table 1).

The reasons for the lower intakes of milk by adolescent females are not known with certainty. However, poor complexion or weight gain during adolescence is often attributed to milk consumption. The recent large meta-analysis of RCT on the association between milk/dairy consumption and body composition in children and adolescents (n=2844; 6-18 years old) does not support the fattening belief, the primary finding being that consumption of milk/dairy foods is more likely to produce a lean body phenotype (Kang et al., 2019).

The very low intakes of magnesium by UK adolescent females are worrying given the evidence concerning the possible key association between magnesium status and bone mineral status (Abrams et al., 2014; Kunutsor et al., 2017) summarized above. Larson et al. (2009) noted that US National Survey longitudinal data suggest that only 53% of young males and 21% of young females (19 to 30 years) have calcium intakes that meet recommendations. They also showed that in the Eating Among Teens (EAT) study both male and female adolescents recorded significant reductions in calcium intake and dairy food (main reduction was in milk) consumption from baseline (mean age of 15.9 years) to early adulthood (mean age 20.5 years). The mean daily reduction in calcium intake was 153 mg and 194 mg for females and males respectively (both about -15%). It was also seen that greater availability of milk at mealtimes, a liking for milk and peer support for healthy eating at baseline were associated with smaller reductions in calcium intake (Larson et al., 2009). Given the coexistence of suboptimal vitamin D status, the above data give rise to considerable concern.

Milk and bonetrophic nutrients

The US National Osteoporosis Foundation's position paper concerning peak bone mass development (Weaver et al., 2016) emphasized that bone mineral accretion rate becomes rapid around the time of puberty and reaches its peak a little after achieving maximum height gain. Weaver et al. (2016) indicated that for children of European ancestry, maximum bone mineral accretion rate occurs at age of 12.5 ± 0.90 years for females and 14.1 ± 0.95 years for males. They emphasized that sub-optimal bone mineral accretion in teenage years increases the risk of osteoporotic fractures in later life, particularly for post-menopausal females. This is supported by the study of Black et al. (2002) which found that male and female New Zealand children with a long history of avoiding milk had poor bone health with small bones, low areal BMD and volumetric bone mineral apparent density, and a high prevalence of bone fractures. Also, Kalkwarf et al. (2003) used data from 3251 white females in the US National Health and Nutrition Examination Survey and reported that milk consumption in childhood and adolescence was positively associated with bone mass in later life and negatively associated with osteoporotic fracture after 50 years of age. It is of interest that the association between milk intake in childhood and fracture rate was higher than for milk consumption during the period of adolescence. This issue was also raised by Feskanich et al. (2014) who, in an analysis of post-menopausal females in the Nurses' Health Study, found no association between hip fractures and milk consumption in teenage years. They queried whether data for milk consumption during pre-teenage years would have been more helpful since females reach maximum height about 2 years sooner than males and are younger at the start of puberty when bone mineralization doubles (Feskanich et al., 2014). There must also be a question about the quality of recall of diet data from adulthood back to adolescence and childhood.

More recently the study by Ma et al. (2014) reported that in Chinese adolescents (12-14 years of age), females in the high-calcium intake group (mean 1243 mg/d) had greater increases in BMD of the femoral neck relative to those in the low-calcium intake group (mean 706 mg/d) over the 12 month intervention period. A similar effect was observed in males. They proposed that to increase bone mineral mass, calcium supplementation is more effective in early than late puberty and that additionally, children should be encouraged to increase their weight-bearing exercise which enhances the effect of dietary calcium.

The strength of evidence for effects of milk/bonetrophic nutrients on bone development in adolescents is fairly strong but there remains more uncertainty about the effect on bone health in middle and later life following long term exposure to diets low or devoid of milk/dairy. Also, a recent systematic review and meta-analysis of the associations between vegan and vegetarian diets and bone health gives further evidence on the chronic effect of diets containing low or zero milk and dairy products (Iguacel et al., 2018). Twenty studies of adequate quality were included in the meta-analysis of Iguacel et al. (2018) which included 37,134 participants of which 33,131 had data on fracture rate and 4003 data on BMD. Overall, compared with omnivores, vegetarians and vegans had significantly lower BMD at the femoral neck, lumbar spine and whole body, with vegans generally exhibiting lower BMD than vegetarians (Table 2). Vegans also had a higher relative risk (RR) for fracture rate (RR: 1.44; 95% confidence interval (CI) 1.047-1.977) particularly in subjects aged over 50 years. These findings highlight the absolute need for careful, detailed and long-term planning of vegetarian and vegan diets in order reduce the risk of negative effects on bone health.

A very recent review on milk and bone health (Batty and Bionaz, 2019) has provided some new thinking on the mechanisms concerning the role of milk in bone development including the possible role of micro-RNA (miRNA) contained in milk. While there appears to be considerable, but building evidence that endogenous miRNA is involved in regulation of osteoblastic differentiation and other pathways relevant to bone development in adolescents, there remains uncertainly about the effect of miRNA provided by the diet in the form of exosomes. Zempleni (2017) has shown that exosomes are absorbed and can accumulate in peripheral tissues but the functionality of their miRNA is unclear. At present the possible involvement of milk-derived exosomes/miRNA in bone development and maintenance remains speculative and is clearly a target for further research.

MILK AND PREGNANCY

Iodine status during pregnancy

In the UK and many other countries milk and milk products are the biggest dietary source of iodine by a considerable margin. The recent UK National Diet and Nutrition Survey (Year 8, 20114/15-15/16; Roberts et al., 2018) reports that milk and milk products contribute 40% and 34% of dietary iodine intake for 11-18 years and 19-64 years age groups respectively, with liquid milk being the primary dairy source. Fish are the next largest contributor to dietary intake at 10% for both age groups. Interestingly, milk and dairy products were also shown to be the most important determinant of iodine status in US adult (≥ 20 years) males and females, despite the availability of iodized salt (Lee et al., 2016).

Until fairly recently it was believed that the UK population was of adequate iodine status. However, a study which measured iodine concentrations of urine from UK schoolgirls showed 51% of them to be mildly iodine deficient (Vanderpump et al., 2011). As noted earlier, 27% of adolescent females (11-18 years) have iodine intakes below the Lower Reference Nutrient Intake (70 µg/d), while the mean value for females 19-64 years is 15% (Roberts et al., 2018; Table 1) but given the milk intake values in Figure 1, females of childbearing age are likely to exceed this value substantially. Of particular concern are the results from a study in a large UK cohort of pregnant females which showed consistent mild-to-moderate iodine deficiency (Bath et al., 2014) with similar findings in pregnant Norwegian females (Brantsæter et al., 2013). Bath and Rayman (2015) reviewed the then current evidence on the iodine status of pregnant females in the UK and the risks to child development after birth (as discussed below) associated with below optimum status. They concluded that a substantial proportion of UK pregnant and non-pregnant women were iodine deficient. The WHO database on iodine deficiency (WHO, 2020) highlights that large parts of the world are affected with substantial parts of Africa and Asia having mild or moderate deficiency. Example studies include one from Tanzania that reported an unacceptably high prevalence of iodine deficiency among pregnant females (Abdalla et al., 2017) and a recent assessment on the iodine status of teenage females on the island of Ireland (Mullan et al., 2019) showed that this population were at ‘the low end of sufficiency’ which clearly has implications for their future progression into pregnancy and for child development after birth (as discussed below).

Bath and Rayman (2015) also discussed the potentially contributing fact that UK recommendation for iodine intake of 140µg/d for adults (Department of Health, 1991) is not only lower than WHO et al. (2007) recommends for non-pregnant/non-lactating adults and adolescents (>12 years of age) (150µg/d) but it does not increase during pregnancy (or lactation) whereas WHO et al. (2007) recommends an increase to 250µg/d. There are clear needs for a greater iodine intake during pregnancy including the demands associated with substantially increased maternal thyroid hormone production in early pregnancy and later for the fetus when it is able to synthesize thyroid hormones (Bath and Rayman, 2015).

It is concerning to note that that there are now a number of studies from several countries including Spain (Costeira et al., 2011), The Netherlands (van Mil et al., 2012), Australia (Hynes et al., 2013) and the UK (Bath et al., 2013) that have found a significant association between low maternal iodine status in early pregnancy and poorer cognitive performance/neurological development in the children. A systematic review and meta-analysis found that low maternal iodine status was associated with 6.9 to 10.2 lower IQ points in children <5 years of age (Bougma et al., 2013). They concluded that independent of study type, low iodine status had a major effect on mental development. It is also worth recording that Businge et al. (2019) reported that although sub-clinical hypothyroidism during pregnancy is one of the key risk factors for pre-eclampsia, the connection between sub-optimal iodine status and pre-eclampsia remains uncertain. Given the risks associated with pre-eclampsia, Businge et al. (2019) proposed that a systematic review and meta-analysis on the subject should be undertaken.

Given the potentially serious implications of sub-optimal iodine status on child development, there is a clear need for more precise RCT to give more definitive evidence on the need for supplementary iodine during pregnancy to avoid impaired neurological development of the offspring. Such studies would no doubt raise important ethical considerations, but it is interesting to note that in the study of Bath et al. (2014), only females consuming more than 280 ml of milk/d had achieved adequate iodine status and a recent RCT in low-moderate (<250 mL/d) milk consuming females showed that increasing consumption to 459 mL/d (3L/week) of semi-skimmed (fat reduced) milk significantly increased their iodine status (O'Kane et al., 2018). The volume of milk needed to achieve an adequate iodine intake will clearly depend on its iodine concentration which can be substantially variable.

Factors affecting the iodine concentration in milk

Survey studies on UK milk iodine concentrations (Food Standards Agency, 2008) do not suggest that milk iodine concentration has declined but they do show that milk produced in the summer has on average, a 50% lower iodine concentration than winter milk. Moreover, 4 UK studies (Food Standards Agency, 2008; Bath et al., 2012; Payling et al., 2015; Stevenson et al., 2018) and the meta-analysis of Średnicka-Tober et al. (2016) all reported that milk from organic dairy systems had significantly lower iodine concentrations than from conventional systems. The interacting involvement of season and production system on milk iodine concentration can be seen in Figure 2 from Stevenson et al. (2018). The review of Flachowsky et al. (2014) confirms that the iodine intake by the dairy cow has the primary influence on milk iodine concentration. Since most iodine is provided to the cow by concentrate feeds, this would explain the lower values reported in milk in the summer and from organic systems, since the animals in both situations are likely to be provided with less concentrate feeds. The effect of iodine supplements (30 or 70 mg/d) to dairy cows were compared to a control (0 mg/d). Iodine concentration increased ~2 fold in the milk of the supplemented animals compared with the non-supplemented animals. No difference was seen between the 30 and 70 mg/d doses

(O’Brien et al., 2013). It is important to note that the iodine concentrations in milk from the iodine-supplemented diets were much higher (up to 1034 µg/kg) than is desirable for processing into infant formula products. As the authors point out, the supplemented diets did not contain more iodine than the maximum prescribed in the present EU legislation (5 mg iodine/kg diet at 12% moisture; European Commission, 2005). O’Brien et al. (2013) also showed that the use of iodine-containing teat disinfection products both pre- and post-milking increased milk iodine concentration ($P < 0.001$**)** at all of the dietary iodine supplementation amounts. This and a number of additional factors which influence milk iodine concentration are extensively reviewed by Flachowsky et al. (2014).

Overall, knowledge on the relationship between iodine in the dairy cow diet and milk iodine concentration, together with other factors, provides a means to produce milk with the required iodine concentration for consumption by adults but avoiding concentrations too high for children.

MILK IN ADULTHOOD

Milk consumption and body composition

The prevalence of overweight and obesity (body mass index (BMI) of 30 kg/m^2 or more) continues to rise worldwide. OECD (2017) reports that since the 1990s overweight and obesity rates have increased substantially in England, Mexico and the US although the increase has been somewhat slower in the other 7 OECD countries for which data are available. It was also noted that in 2015, 19.5% of adults in OECD countries were obese but this was highly variable with for example <6% in Korea and Japan but up to >30% in Hungary, New Zealand, Mexico and the US.

Obesity is a major risk factor for chronic diseases, particularly diabetes, CVD, stroke and some cancers. The association between obesity/overweight and type 2 diabetes is particularly critical, accounting for up to some 70-90% of the risk for type 2 diabetes (Hu et al., 2001; Gatineau et al., 2014), although there remains some uncertainty why some obese subjects do not develop type 2 diabetes (Abdullah et al., 2010).

It is not the intention of this paper to review in detail all the evidence on the association between milk/dairy and obesity. There is however, a large amount of evidence from observational, cross-sectional, and prospective studies which is consistent with a negative association between dairy consumption and both body weight and central obesity (Dougkas et al., 2011). The review of Kratz et al. (2013), using observational and RCT evidence, found that in 11 out of 16 studies, high-fat dairy consumption was inversely associated with measures of adiposity whereas the association between high-fat dairy and metabolic health was either inverse or had no association. The recent report on middle-aged males (at baseline) in the Caerphilly Prospective Cohort showed no association between milk consumption and BMI, but higher cheese consumption was associated with lower BMI at the 5-year follow-up ($P=0.013$) (Guo et al., 2018).

Many RCT have evaluated the association between dairy consumption and body weight and fat mass, but the majority have been small and of limited duration and although some have included energy restriction, others have focused on weight maintenance with the overall findings being difficult to interpret. Nevertheless, a meta-analysis of 29 RCT of varied designs showed that while the inclusion of dairy foods in weight maintenance diets is not associated with weight loss or weight gain, there were weight loss benefits from the combination of these foods and energy-restricted diets (Chen et al., 2012).

Milk consumption, stroke, cardiovascular and metabolic diseases

It is interesting to note that while in most high income countries the prevalence of death from CVD has reduced considerably over recent decades, it is concerning that recent data from the US indicate a levelling off of the decline, thought probably a result of increasing obesity and related type 2 diabetes (Zia et al., 2018). These data highlight the risk of complacency and the continued need for the management of lifestyle including diet. In this regard and as noted above, the impact of dairy foods in the diet is poorly understood by many in the general population.

Evidence from prospective studies. Many prospective studies have investigated the association between milk and dairy product consumption and cardiometabolic diseases (CMD, includes CVD, stroke and type 2 diabetes). Data from prospective cohort studies are usually regarded as providing poorer evidence than that from RCT since they only estimate risk and cannot prove cause and effect, but they do have the advantage of looking at chronic effects and use hard disease data outcomes. Another limitation of this type of study is the presence of variables (confounders) which are beyond the control of the researchers (e.g. some subjects may be smokers, some will not) but which can influence the variables being studied (e.g. the effect of cheese consumption on the risk of CVD) leading to results which do not represent the actual association. This is normally dealt with by including the confounder in the statistical model used so that as far as is possible its effect is removed, however there often remains some residual confounding not accounted for. Long-term RCT using hard disease endpoints would be impractical, very costly and likely with high subject dropout rates with the result that most RCT are relatively short term and use markers of disease risk such as low density lipoprotein cholesterol (LDL-C) as primary outcome measures. Meta-analysis of prospective data is a valuable tool for investigating the overall associations between dairy food consumption and CMD risk, although there is a concern that in many studies these foods are poorly defined, especially their fat content, which limits assessment of any differential effects.

While there have been several other meta-analyses published over recent times, a series of dose-response meta-analyses was published in 2016/17 examining the association between dairy food consumption and type 2 diabetes (Gijsbers et al., 2016), stroke (de Goede et al., 2016), and CVD and all-cause mortality (Guo et al., 2017). The availability of new data has allowed key components of these meta-analyses to be updated (Soedamah-Muthu and de Goede, 2018) and the outline results are presented in Table 3.

Overall, these prospective studies show no increase in risk of coronary heart disease (CHD) and stroke per 200g increase in total dairy and milk. Interestingly, milk and yogurt consumption was associated with a substantially reduced risk of stroke and type 2 diabetes respectively. The reduced risk of type 2 diabetes associated with yogurt consumption is also highlighted in the recent review of evidence of Guo et al. (2019). There are few studies which have looked into the association between butter consumption and CMD although the dose-response meta-analysis of Pimpin et al. (2016) showed no significant association between butter consumption and all-cause mortality, CVD, CHD specifically, or stroke, although there was a significant negative association with type 2 diabetes. This meta-analysis involved only a few cohorts for CVD (*n*=4), CHD (*n*=3), stroke (*n*=3) although 11 cohorts were judged to be suitable for inclusion for type 2 diabetes. More recently, Griffin and Lovegrove (2018) raised the possibility that increased high density lipoprotein-mediated cholesterol efflux capacity compensates for the adverse effect of saturated fatty acids (SFA) in butter in raising blood LDL-C.

The Prospective Urban Rural Epidemiology (PURE) study recently published its results (Dehghan et al., 2018). PURE is a multinational cohort study of 136,384 subjects aged 35-70 years from 21 countries (6, 11, 4 low, middle and high income respectively) across 5 continents, which examined the association between consumption of dairy foods (total and milk, yogurt, and cheese) with mortality and CVD. Higher intake of total dairy foods (>2 servings/d vs. none) was associated with a lower risk of non-CVD mortality (hazard ratio (HR) 0.86, 95% CI 0.72-1.02**;** P_{trend} = 0.046), CVD mortality (HR 0.77, 95% CI 0·58-1·01; P_{trend} = 0·029), major CVD events (HR 0.78, 0.67-0.90; P_{trend} = 0·0001), and stroke (HR 0.66, 0.53-0·82; P_{trend} = 0·0003). Greater consumption of milk and yogurt, but not cheese, was associated with a lower risk of the combination of mortality or major CVD events. Although the results from PURE are largely in agreement with earlier studies and meta-analyses, it is believed to be the first study of its kind to involve such large and diverse cohorts of subjects with substantial variation in habitual dairy and other dietary component intake between regions and countries.

Overall, the findings from meta-analyses of prospective cohort studies provide no evidence of an increased risk of CMD associated with increased consumption of dairy foods despite most of these foods making a major contribution to SFA intake. These findings may seem counterintuitive in view well-established link between LDL-C and CVD. There is however emerging evidence which goes some way to explaining these relationships, including differential effects of different SFA and the food matrix influences (Thorning et al., 2017; Astrup et al., 2019).

A number of prospective studies have also examined the association between milk/dairy intake and blood pressure. For example, findings from the Caerphilly Prospective Study indicate that after a 22.8 year follow-up, men who consumed >586 mL/d of milk had a mean lower systolic blood pressure of 10.4 mmHg, compared with non-milk consumers ($P_{trend} = 0.033$) (Livingstone et al., 2013).

Evidence from randomized controlled trials. The American Heart Association recently reported that in 2015 the proportion of US adults ≥18 years of age with diagnosed hypertension was 29.7% (age adjusted) although there was considerable variability with equivalent values ranging from 24.2% for Minnesota to 39.9% for Mississippi (Benjamin et al., 2018). Data from 2016 in England indicate that 28 % of adults had diagnosed hypertension (National Statistics, 2017a). In addition, there are substantial numbers of individuals with undiagnosed hypertension. Hypertension is one of the major risk factors for CVD and for stroke in particular.

There is now good evidence that the proteins in milk and milk derived products have beneficial hypotensive effects, particularly whey proteins. This has been shown in vitro (Giromini et al., 2017) and in vivo. An 8-week RCT (Fekete et al., 2016) found that whey protein isolate (2 x 28g/d) had a larger hypotensive effect than casein with effects seen on both central and peripheral blood pressures. Whey protein was also shown to have a greater effect than casein in an acute setting (Fekete et al., 2018). A number of mechanisms by which milk and its components could lower blood pressure have been proposed including the effects of dairy nutrients, in particular calcium, potassium and magnesium (Kris-Etherton et al., 2009), and the effect of milk protein-derived peptides (Fekete et al., 2013). A number of peptides released during digestion of casein and whey proteins possess hypotensive activity through inhibiting the action of the angiotensin-1-converting enzyme that would normally increase the production of angiotensin-2 which has a vasoconstricting effect leading to increased blood pressure (FitzGerald and Meisel, 2000; Giromini et al., 2019). Other effects of milk protein-derived peptides may be important such as binding with opioid receptors thus increasing nitric oxide production which mediates arterial tone and thus reduces blood pressure (Kris-Etherton et al., 2009).

Recent work on hemodynamics has shown that arterial stiffness, especially of the central large vessels, is a valuable predictor of future CVD events (Cockcroft and Wilkinson, 2000). Milk and dairy consumption have been shown to be associated with reduced arterial stiffness. Livingstone et al. (2013), working with the Caerphilly Prospective Study, showed, it is believed for the first time in a longitudinal study, that augmentation index (an indirect measure of arterial stiffness) was 1.9% lower in subjects with the highest dairy product consumption (not including butter) compared with the lowest ($P_{trend} = 0.021$) after a mean follow up period of 22.8 years. A similar effect was seen in a cross-sectional study that showed a negative association between milk/dairy consumption and pulse wave velocity (another indirect measure of arterial stiffness, Crichton et al., 2012). More recently, the specific effect of milk proteins together with exercise has been shown to reduce arterial stiffness in pre-hypertensive and hypertensive young females (Figueroa et al., 2014). Whey protein and casein both significantly ($P< 0.05$) reduced arterial stiffness as indicated by reduced augmentation index by about 9.2% and 8.1%, respectively and reduced pulse wave velocity by 57 cm/s and 53 cm/s, respectively compared with no changes in the control group.

Food matrix effects of dairy products on blood lipids. New evidence on the food matrix goes a considerable way to explaining the lack of effect of dairy SFA on CVD risk. This topic has been extensively discussed recently by Astrup et al. (2019) and will not be fully repeated here, but aspects of food matrix effects are worthy of mention.

Traditionally, nutritional evaluation of foods and diets and their links with the health/disease of the consumer has normally been assessed on separate considerations of food components, notably protein, fat, carbohydrates and micronutrients. For some dairy foods there is now good evidence that this approach is not appropriate and indeed may mislead since the modifying effects of the so-called food matrix needs to be considered. This subject was extensively reviewed by an expert working party jointly established by the Universities of Copenhagen and Reading and the outcome has been published (Thorning et al., 2017).

A good illustration of the differential matrix effects on blood lipids of SFA from hard cheese and butter is reported in the RCT of Hjerpsted et al. (2011). This involved two 6-week crossover periods with 49 males and females replacing part of their habitual dietary fat with 13% of energy from cheese or butter (both providing 80 g/d and 36 g/d of total fat and SFA, respectively). Crucially, the cheese and butter diets provided 1192 g and 417 g of calcium/d, respectively. Compared with baseline, cheese did not increase blood total cholesterol or LDL-C whereas the butter diet increased both of these ($P<0.001$, 0.05 respectively). The cheese diet led to a 5.7 and 6.9 % lower total cholesterol or LDL-C concentrations respectively, than the butter diet ($P< 0.0001$). The recently published and rather unique study of Feeney et al. (2018) attempted to explore the matrix effect in a stepwise-response fashion. The study was a 6-week randomized parallel design where subjects consumed 40 g of dairy fat/d in macronutrient-matched food matrices as either 1) 120 g full-fat cheddar cheese, 2) 120 g reduced-fat cheddar cheese plus 31 g of butter, or 3) 49 g butter plus 30 g calcium caseinate and 500 mg of calcium as $CaCO_3$. The blood lipid responses are summarized in Table 4 but the results did indeed show a stepwise-matrix effect with significantly lower post-intervention total cholesterol and LDL-C concentrations seen when all of the dairy fat was provided by the cheese.

Several mechanisms have been proposed as being responsible for the benefits of the so-called matrix effect and these are reviewed in detail by Thorning et al. (2017). In brief, most studies involving hard cheese result in increased fecal fat and calcium excretion which, in part at least, seems to be the result of a saponification reaction in the gut between calcium and fatty acids leading to largely indigestible soaps. There is also evidence that fecal bile acid excretion is increased due to adsorption on amorphous calcium phosphate formed from dietary calcium and phosphorus. This reduces the enterohepatic recycling of bile acids thus increasing bile acid and fat excretion. Since the liver synthesizes bile acids from cholesterol, reduced bile acid recycling may also lead to reduced circulating cholesterol. There is also evidence of a role for the milk fat globule membrane apparently protecting fat from digestion. A good example of this is in the study of Rosqvist et al. (2015).

These studies clearly confirm that the effect of dairy foods on CVD risk factors, primarily blood lipids, are influenced by the food matrix, even when compared with foods providing the same amount of dairy fat and SFA. However, most of the evidence available relates to hard cheese vs. butter and as proposed by Thorning et al. (2017), more research is required to more fully understand food matrix effects on health and how these relate to specific dairy foods and methods of processing and cooking.

MILK AND DAIRY PRODUCTS FOR THE ELDERLY

Dairy proteins and sarcopenia

Sarcopenia: the condition. Sarcopenia is a condition characterized by a mainly chronic ongoing loss of muscle mass and muscle strength with advancing age (Cruz-Jentoft et al., 2019). It is therefore a condition of particular importance in the elderly (though not exclusively) with an increasing prevalence mainly associated with the increasing age of populations worldwide. Sarcopenia can have far reaching consequences since, for example, it reduces bone protection increasing the risk of breakage in a fall leading to reduced mobility, disability and lower quality of life. A less well known outcome of reduced muscle mass and possibly associated reduced exercise ability is the increased risk of metabolic diseases, type 2 diabetes in particular (Hunter et al., 2019).

Based on general population studies, Shafiee et al. (2017) published a meta-analysis on the prevalence of sarcopenia worldwide involving a total 58,404 generally healthy subjects >60 years of age. This study showed a mean prevalence of 10% in both males and females, with a higher value in non-Asian than Asian populations with the non-Asian values (~20%) being about double those of Asians when Bio-electrical Impedance Analysis was used to estimate muscle mass.

The role of dietary proteins for reducing sarcopenia. Consumption of protein and resistance exercise are both known to provide an anabolic stimulus for skeletal muscle protein synthesis and there has been considerable debate about the amounts and the relative timing of protein consumption and exercise needed to stimulate muscle protein synthesis in the elderly. In the UK, the Reference Nutrient Intake for protein is equivalent to 0.75g/kg body weight, slightly less than the Recommended Dietary Allowance (RDA) of 0.8 g/kg body weight proposed for males and non-pregnant and non-lactating females >18 years of age by the FAO/WHO/UNU (2007). These recommendations take no account of specific age or health status and Lonnie et al. (2018) have discussed and highlighted the relevance of new recommendations suggesting protein requirements of 1.0-1.2, 1.2-1.5 and 2.0 g/kg body weight respectively for people >65 years, for those with acute/chronic illnesses and those with severe illness or malnutrition respectively. The review of Lonnie et al. (2018) cites work which confirms that intake of protein in accordance with the RDA has led to deleterious health outcomes including a 14-week RCT in subjects aged between 55 and 77 years who consumed the FAO/WHO/UNU RDA of 0.8 g protein/kg bodyweight which led to a reduced mid-thigh muscle area and other characteristics suggesting the protein intake was below requirement (Campbell et al., 2001). This is concerning since in the UK the latest National Diet and Nutrition Survey (Roberts et al., 2108) indicates a mean protein intake of 75.8 g/d (males) and 60.5 g/d (females) 65+ years old, which with a mean bodyweights for this age group of 85.8 kg (males) and 71.5 kg (females) (National Statistics, 2017b), equates to 0.88 and 0.85 g protein/kg bodyweight for males and females respectively.

Overall, there is considerable agreement of the benefits from increasing protein intake to 1.0 g/kg body weight or higher by the elderly, yet there have been concerns that the strong satiating effect of protein may limit total food and energy intake. In addition there have been concerns that higher protein intake may adversely affect individuals with chronic kidney disease which may be undiagnosed. The meta-analysis of Devries et al. (2018a) compared the effect of low (mean 0.93g/kg body weight per day) vs high (mean 1.81 g/kg body weight per day) protein diets and showed no effect on kidney function in subjects with normal function and in those with type 2 diabetes who would have a greater risk of chronic kidney disease. Nevertheless, it is probably wise for the elderly to have regular tests of kidney function irrespective of diet.

Type of dietary proteins for reducing sarcopenia. There has been considerable research on the relative anabolic effects of specific protein types. Wall et al. (2014) concluded that proteins such a whey protein which are rapidly digested and absorbed lead to greater muscle protein synthesis than from slower digested proteins like casein and those in soya. They also note that even when casein is hydrolyzed to increase digestion rate, the muscle protein response is still smaller than from equivalent amounts of whey protein. This is primarily attributed to the higher leucine content of whey protein, the specific effect of leucine having also been seen in studies using leucine supplements (Wall et al., 2013; Devries et al., 2018b). The effect of leucine is complex. It is an important activator of the mammalian target of rapamycin (mTOR) a nutrient-sensing signaling pathway in skeletal muscle. In addition, leucine is insulinotrophic and the additional insulin enhances muscle protein synthesis (Paddon-Jones and Rasmussen, 2009). There is evidence however, that consumption of 40g of casein before sleep increases muscle protein synthesis rates during overnight sleep in older males (Kouw et al., 2017). This is potentially important as overnight is generally a period of negative whole body protein net balance.

A number of studies have compared the relative value of plant proteins compared with whey protein. The study of Yang et al. (2012) compared the response in myofibrillar protein fractional synthetic rate (FSR) in rested elderly males resulting from 0, 20 or 40g of either whey protein or soya protein. Myofibrillar FSR did not respond to consumption of 40g soya protein compared with 20g, but it responded essentially in a linear fashion to increased whey protein. A similar differential effect was seen when the protein supplements were given post-exercise.

Magnesium and sarcopenia. As with the influence of magnesium intake on bone mineralization noted earlier, there is also increasing evidence of an association between magnesium and preservation of skeletal muscle. With a large cohort of 156,575 males and females aged 39-72 years, Welch et al. (2017) examined cross-sectional associations between magnesium intake and skeletal muscle mass (as fat-free mass % body mass (FFM%)) and grip strength. They showed positive associations between quintiles of magnesium intake and FFM% (P trend < 0.001) and grip strength (P trend <0.001). The association with grip strength was greater in older (60 years of age or older) than younger males although the opposite was the case for females.

Despite being a cross-sectional study, it was, according to the authors, the largest population to date used to study the association between magnesium intake and direct measures of skeletal muscle. Milk and milk products are important sources of magnesium contributing some 13% to diets of the elderly (Roberts et al., 2018) and in the US it was reported that consuming the recommended quantities of dairy would significantly reduce the prevalence of low magnesium intake (Quann et al., 2015). Erem et al. (2019) highlighted that magnesium intake is particularly low in the elderly US population which is similar to the UK where 25% of individuals 75 years old and above consume less than the Lower Reference Nutrient Intake. Clearly more work on this is needed but this study adds to increasing importance of magnesium in muscle and bone health.

Dairy foods and bone fragility

Type of dairy foods. Unlike the situation with the young, the effect of dairy foods on bone strength in the elderly is less clear. A meta-analysis of 6 cohorts reported a 17% increased risk of hip fracture in males and females who consumed less than 1 glass of milk per day although the change was not significant (Kanis et al., 2005) and a later meta-analysis including a further 6 cohorts found no association between milk consumption and hip fracture risk (Bischoff-Ferrari et al., 2011). More recently, data from the Framingham Original Cohort (mean age at baseline 75 years) showed that higher milk and milk+yogurt+cheese intakes were associated with higher lumber spine BMD (P=0.011, 0.005) and higher milk+yogurt+cheese intakes protected against trochanter BMD loss (P=0.009) over 4 years. In all cases, the significant beneficial associations were only seen in subjects that were vitamin D supplement users (Sahni et al., 2014). The results from a Swedish female cohort indicated a significant 9% increased risk of hip fracture per glass of milk per day while no effect was seen in a male cohort (Michaëlsson et al., 2014). The reasons for the positive associations in the females are unclear.

More recently, the analysis of 2 US cohorts containing 80,600 post-menopausal females and 43,306 males greater than 50 years of age at baseline that were followed up for 32 years reported that for females and males combined, each serving of milk/d was associated with a 8% lower risk of hip fracture (RR 0.92, 95% CI 0.87-0·97) compared with those that consumed less than 1 serving per week (Feskanich et al., 2018). The authors suggested that a major strength of the study was that multiple measures of milk and dairy food intake were made over the 32 years of follow-up allowing long term mean intakes to be estimated. Calcium, vitamin D and protein from non-dairy and dairy sources did not influence the association between milk and fracture risk in this study although a recent meta-analysis of 20 studies showed that a dietary pattern classified as ‘milk/dairy’ led to the greatest reduction in risk of low BMD compared with patterns classified as ‘healthy’ and ‘meat/Western’ and the effect remained significant in older females (Fabiani et al., 2019).

Ong et al. (2019) conducted a systematic review on fermented milk products (yogurt and cheese) and bone health in post-menopausal women. The analysis included RCT, prospective cohorts and case-control studies. Overall, only increased yogurt consumption was associated with a reduced risk of hip fracture when compared with little or no intake. The evidence for cheese was limited and suggests that further work to understand the effect of yogurt is needed.

Magnesium and bone health. The possibly important role of dietary magnesium for bone development in young people was discussed earlier but there is now some evidence of a similar benefit in later life. The review of Erem et al. (2019) highlights that the risk of osteoporosis in older people can result from low intake of magnesium which gives rise to excess calcium release from bone and increased excretion which increases bone fragility and hence a higher risk of bone fractures. Also, high intakes of calcium can lead to lower retention of magnesium and Erem et al. (2019) suggest that the optimal dietary ratio of calcium:magnesium is between 2.0:1.0 and 2.8:1.0 but in many current US diets the ratio above 3.0:1.0.

There is an obvious need to further explore the role of magnesium and its interaction with calcium and vitamin D in relation to bone strength in the elderly. Dairy products are a good source of calcium and for many an important source of magnesium along with vitamin D when fortification is practiced.

CONCLUSIONS

Despite a favorable ongoing increase in life expectancy, an increase in healthy lifespan is not assured and indeed some of the health issues in aging populations arise because of longer life. Moreover, there is now increasing evidence that diets in early life can influence health in older life stages. There is good evidence that milk and dairy foods are important sources of nutrients some of which are particularly important at certain life stages. The concentration of some nutrients, notably iodine, are also dependent in the diet of the milk producing animal, a good example of an early stage in the food chain having an influence on nutrient intake. The reduced milk consumption, notably by adolescence females, is a major worry since it may have already had an impact on bone development such that reduced bone strength may become evident when they are much older. Despite being counterintuitive to many, there is now consistent evidence that consumption of milk/dairy foods does not increase the risk of CMD, indeed a number of significant negative associations with risk of this group of diseases have been reported. The negative and positive associations of yogurt with type 2 diabetes and bone strength respectively are particularly interesting given the rapid rise in prevalence of type 2 diabetes and bone weakness and these should be researched with urgency to identify the mechanisms involved and to develop yogurt with targeted efficacy. Much greater effort is also needed to reduce malnutrition in the elderly and to reduce the loss of muscle mass, bone strength and functionality and this seems to provide good opportunities for dairy products to play a key role. There is of course an ongoing debate about the relative sustainability of animal vs. plant food sources. While it makes sense to examine this tradeoff, it is important that judgements on the replacement of dairy products with those from plants include evidence on relative functionality (e.g. hypotensive and muscle protein synthesis stimulation effects) and not only on simple comparisons of nutrient content (Grant and Hicks, 2018). Interestingly, a very recent, detailed modelling of the relationship between diet and health care costs concludes that adoption of a dietary pattern with increased dairy consumption by US adults would have the potential to save billions of dollars (Scrafford et al., 2020).

ACKNOWLEDGMENTS

This paper is based on an invited contribution to the symposium on ‘Improving Milk Production, Quality, and Safety in Developing Countries’ hosted by the Feed the Future Innovation Lab for Livestock Systems (FFILLS) of the University of Florida, at the American Dairy Science Association’s annual meeting in Cincinnati, Ohio on June 23-26, 2019. I am most grateful to Dr Adegbola Adesogan, Director of FFILLS for his invitation and support to attend the event.

REFERENCES

Abdalla, H. M., J. E. Ntwenya, E. Paul, M. Huang, and S. Vuai. 2017. Socio-economic and spatial correlates of subclinical iodine deficiency among pregnant women age 15–49 years in Tanzania. BMC Nutrition 3:47.

Abdullah, A., A. Peeters, M. de Courten, and J. Stoelwinder. 2010. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res. Clin. Pract. 89:309-319. https://doi.org/10.1016/j.diabres.2010.04.012

Abrams, S. A., Z. Chen, and K. M. Hawthorne. 2014. Magnesium metabolism in 4-year-old to 8-year-old children. J. Bone Miner. Res. 29:118–122. https://doi.org/10.1002/jbmr.2021

Astrup, A., H. C. S. Bertram, J.-P. Bonjour, L .C. P. de Groot, M. C. de Oliveira Otto, E. L. Feeney, M. L. Garg, D. I. Givens, F. J. Kok, R. M. Krauss, B. Lamarche, J.-M. Lecerf, P. Legrand, M. McKinley, R. Micha, M.-C. Michalski, D. Mozaffarian, and S. S. Soedamah-Muthu. 2019. WHO draft guidelines on dietary saturated and trans fatty acids: time for a new approach? BMJ. 365:l4137. https://doi.org/10.1136/bmj.l4137

Baker, I. A., P. C. Elwood, J. Hughes, M. Jones, F. Moore, and P. Sweetnam. 1980. A randomised controlled trial of the effect of the provision of free school milk on the growth of children. J. Epidemiol. Community Health. 34:31-34. https://doi.org/10.1136/jech.34.1.31

Bates, B., A. Lennox, A. Prentice, C. Bates, P. Page, S. Nicholson, and G. Swan. 2014. *National Diet and Nutrition Survey, Results from Years 1-4 (combined) of the Rolling Programme (2008/2009-2011/12).* A survey carried out on behalf of Public Health England and the Food Standards Agency, London, UK.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/594361/NDNS_Y1_to_4_UK_report_full_text_revised_February_2017.pdf

Bath, S. C., S. Button, and M. P. Rayman, 2012. Iodine concentration of organic and conventional milk: implications for iodine intake. Br. J. Nutr. 107:935-940. https://doi.org/10.1017/S0007114511003059

Bath, S. C., M. P. Rayman, C. D.Steer, J. Golding, and P. Emmett, 2013. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). The Lancet. 382:331-337.

Bath, S. C., A. Walter, A. Taylor, J. Wright, and M. P. Rayman, 2014. Iodine deficiency in pregnant women living in the South East of the UK: the influence of diet and nutritional supplements on iodine status. Br. J. Nutr. 111:1622-1631.

Bath, S. C., and M. P. Rayman, 2015. A review of the iodine status of UK pregnant women and its implications for the offspring. Environ. Geochem. Health. 27:619-629.

Bath, S. C., S. Hill, H. G. Infante, S. Elghul, C. J. Nezianya, and M. P. Rayman. 2017. Iodine concentration of milk-alternative drinks available in the UK in comparison to cows' milk. Br. J. Nutr. 118: 525–532.

Batty, B. S., and M. Bionaz, 2019. The milk behind the moustache: A review of milk and bone biology. J. Dairy Sci. 102:7608-7617.

Benjamin, E. J. et al. (+50 authors), 2018. Heart Disease and Stroke Statistics-2018 Update. Circulation. 137:e67–e492

Bischoff-Ferrari, H. A., B. Dawson-Hughes, J. A. Baron, J. A. Kanis, E. J. Orav, H. B. Staehelin, P. Kiel, P. Burckhardt, J. Henschkowski, D. Spiegelman, R. Li, J. B. Wong, D. Feskanich, and W. C. Willett. 2011. Milk intake and risk of hip fracture in men and women; a meta-analysis of prospective cohort studies. J. Bone Miner. Res. 26: 833-839.

Black, R. E., S. M. Williams, I. E. Jones, and A. Goulding. 2002. Children who avoid drinking cow milk have low dietary calcium intakes and poor bone health. Am. J. Clin. Nutr. 76:675–680.

Bougma, K., F. E. Aboud, K. B. Harding, and G. S. Marquis. 2013. Iodine and mental development of children 5 years old and under: A systematic review and meta-analysis. Nutrients. 5:1384-1416.

Brantsæter, A. L., M. H. Abe, M. Haugen, and H. M. Meltzer. 2013. Risk of suboptimal iodine intake in pregnant Norwegian women. Nutrients 5:424-440.

Businge, C. B., N. Madini, B. Longo-Mbenza, and A. P. Kengne. 2019. Insufficient iodine nutrition status and the risk of pre-eclampsia: a protocol for systematic review and meta-analysis. BMJ Open. 9:e025573.

Campbell, W. W., T. A. Trappe, R. R. Wolfe, and W. J. Evans. 2001. The recommended dietary allowance for protein may not be adequate for older people to maintain skeletal muscle. J. Gerontol. A Biol. Sci. Med. Sci. 56:M373–M380.

Cashman, K. D., K. G. Dowling, Z. Skrabáková, M. Gonzalez-Gross, J. Valtueña, S. De Henauw, L. Moreno, C. T. Damsgaard, K. F. Michaelsen, C. Mølgaard, R. Jorde, G. Grimnes, G. Moschonis, C. Mavrogianni, Y. Manios, M. Thamm, G. B. M. Mensink, M. Rabenberg, M. A. Busch, L. Cox, S. Meadows, G. Goldberg, A. Prentice, J. M. Dekker, G. Nijpels, S. Pilz, K. M. Swart, N. M. van Schoor, P. Lips, G. Eiriksdottir, V. Gudnason, M. F. Cotch, S. Koskinen, C. Lamberg-Allardt, R. A. Durazo-Arvizu, C. T. Sempos, and M. Kiely. 2016. Vitamin D deficiency in Europe: pandemic? Am. J. Clin. Nutr. 103:1033–1044.

Chen, M., A. Pan, V. S. Malik, and F. B. Hu. 2012. Effects of dairy intake on body weight and fat: A meta-analysis of randomized controlled trials. Am. J. Clin. Nutr. 96:735–747.

Cockcroft, J. R., and I. B. Wilkinson. 2000. Large arterial stiffness: an important therapeutic target. J. Hum. Hypertens.14:533-535.

Corry Mann, H. C. 1926. Diets for boys during the school age. Medical Research Council Special Report Series No. 105. HMSO: London.

Crichton, G. E., M. F. Elias, G. A. Dore, A. P Abhayaratna, and M. A. Robbins. 2012. Relations between dairy food intake and arterial stiffness. Hypertension. 59:1044-1051.

Costeira, M. J., P. Oliveira, N. C. Santos, S. Ares, B. Saenz-Rico, G. M. de Escobar, and J. A. Palha. 2011. Psychomotor development of children from iodine-deficient region. J. Pediatr. 159:447-453.

Cruz-Jentoft, A. J., G. Bahat, J. Bauer, Y. Boirie, O. Bruyère, T. Cederholm, C. Cooper, F. Landi, Y. Rolland, A. A. Sayer, S. M. Schneider, C. C. Sieber, E. Topinkova, M. Vandewoude, M. Visser, M. Zamboni, Writing Group for the European Working Group on

Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. 2019. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 48:16-31.

Choudhury, S., and D. D. Headey. 2018. Household dairy production and child growth: Evidence from Bangladesh. Econ. Hum. Biol. 30:150–161. https://doi.org/10.1016/j.ehb.2018.07.001

de Goede, J., S. S. Soedamah-Muthu, A. Pan, L. Gijsbers, and J. M. Geleijnse. 2016. Dairy Consumption and Risk of Stroke: A Systematic Review and Updated Dose–Response Meta-Analysis of Prospective Cohort Studies. J. Am. Heart Assoc. 5:e002787.

Dehghan, M., A. Mente, S. Rangarajan, P. Sheridan, V. Mohan, R. Iqbal, R. Gupta, S. Lear, E. Wentzel-Viljoen, A. Avezum, P. Lopez-Jaramillo, P. Mony, R. P. Varma, R. Kumar, J. Chifamba, K. F. Alhabib, N. Mohammadifard, A. Oguz, F. Lanas, D. Rozanska, K. B. Bostrom, K. Yusoff, L. P. Tsolkile, A. Dans, A. Yusufali, A. Orlandini, P. Poirier, R. Khatib, B. Hu, L. Wei, L. Yin, A. Deeraili, K. Yeates, R. Yusuf, N. Ismail, D. Mozaffarian, K. Teo, S. S. Anan, and S. Yusuf on behalf of the Prospective Urban Rural Epidemiology (PURE) study investigators. 2018. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. The Lancet. 392:10161, 2288-2297. http://dx.doi.org/10.1016/S0140-6736(18)31812-9

de Onis, M., and F. Branca. 2016. Childhood stunting: a global perspective. Matern. Child Nutr. 12 (Suppl. 1):12–26.

Department of Health. 1991. Dietary Reference Values, A Guide. London: HMSO 51pp.

Devries, M. C., A. Sithamparapillai, K. S. Brimble, L. Banfield, R. W. Morton, and S. M. Phillips. 2018a. Changes in kidney function do not differ between healthy adults consuming higher compared with lower- or normal-protein diets: A systematic review and meta-analysis. J. Nutr. 148:1760–1775.

Devries, M. C., C. McGlory, D. R. Bolster, A. Kamil, M. Rahn, L. Harkness, S. K. Baker, and S. M. Phillips. 2018b. Leucine, not total protein, content of a supplement is the primary determinant of muscle protein anabolic responses in healthy older women. J. Nutr.148:1088–1095.

Diabetes UK. 2019. Number of people with diabetes reaches 4.7 million. Available at: https://www.diabetes.org.uk/about_us/news/new-stats-people-living-with-diabetes

Dougkas, A., C. K. Reynolds, D. I. Givens, P. C. Elwood, and A. M. Minihane. 2011. Associations between dairy consumption and body weight: A review of the evidence and underlying mechanisms. Nutr. Res. Rev. 24:72–95.

Dougkas, A., S. Barr, S. Reddy, and C. D. Summerbell. 2019. A critical review of the role of milk and other dairy products in the development of obesity in children and adolescents. Nutr. Res. Rev. 32:106-127.

Du, X., K. Zhu, A. Trube, Q. Zhang, G. Ma, X. Hu, D.R. Fraser, and H. Greenfield. 2004. School-milk intervention trial enhances growth and bone mineral accretion in Chinese girls aged 10–12 years in Beijing. Br. J. Nutr. 92:159-168.

Erem, S., A. Atfi, and M. S. Razzaque. 2019. Anabolic effects of vitamin D and magnesium in aging bone. J. Steroid Biochem. Mol. Biol. 193: 105400.

European Commission. 2005. Council Regulation (EC) No 1459/2005 of 08 September 2005 amending the condition of authorization of a number of feed additives belonging to the group of trace elements. Official Journal of the European Union. L 233:8-10.

Fabiani, R., G. Naldini, and M. Chiavarini. 2019. Dietary patterns in relation to low bone mineral density and fracture risk: A systematic review and meta-analysis. Adv. Nutr. 10: 219-236.

FAO/WHO/UNU. 2007. Protein and amino acid requirements in human nutrition. Report of a joint FAO/WHO/UNU expert consultation (WHO Technical Report Series 935), 265pp.

Feeney, E. L., R. Barron, V. Dible, Z. Hamilton, Y. Power, L. Tanner, C. Flynn, P. Bouchier, T. Beresford, N. Noronha, and E. R. Gibney. 2018. Dairy matrix effects: response to consumption of dairy fat differs when eaten within the cheese matrix-a randomized controlled trial. Am J Clin. Nutr. 108:1-8.

Fekete, Á. A., D. I. Givens, and J. A. Lovegrove. 2013. The impact of milk proteins and peptides on blood pressure and vascular function: a review of evidence from human intervention studies. Nutr. Res. Rev. 26:177-190.

Fekete, Á. A., C. Giromini, Y. Chatzidiakou, D. I. Givens, and J. A. Lovegrove. 2016. Whey protein lowers blood pressure and improves endothelial function and lipid biomarkers in adults with prehypertension and mild hypertension: results from the chronic Whey2Go randomized controlled trial. Am. J. Clin. Nutr. 104:1534-154.

Fekete, Á. A., C. Giromini, Y. Chatzidiakou, D. I. Givens, and J. A. Lovegrove. 2018. Whey protein lowers systolic blood pressure and Ca-caseinate reduces serum TAG after a high-fat meal in mildly hypertensive adults. Sci. Rep. 8:5026.

Feskanich, D., H. A. Bischoff-Ferrari, L. Frazier, and W. C. Willett. 2014. Milk consumption during teenage years and risk of hip fractures in older adults. JAMA Pediatr. 168:54-60.

Feskanich, D, H. E. Meyer, T. T. Fung, H. A. Bischoff-Ferrari, and W. C. Willett. 2018. Milk and other dairy foods and risk of hip fracture in men and women. Osteoporos. Int. 29: 385-396. https://doi.org/10.1007/s00198-017-4285-8

Figueroa, A., A. Wong, A. Kinsey, R. Kalfon, W. Eddy, and M. J. Ormsbee. 2014. Effects of milk proteins and combined exercise training on aortic hemodynamics and arterial stiffness in young obese women with high blood pressure Am. J. Hypertens. 27:338-344.

FitzGerald, R. J., and H. Meisel. 2000. Milk protein-derived peptide inhibitors of angiotensin-1-converting enzyme. Br. J. Nutr. 84: Suppl. 1, S33-S37.

Flachowsky, G., K. Franke, U. Meyer, M. Leiterer, and F. Schöne. 2014. Influencing factors on iodine content of cow milk. Eur. J. Nutr. 53: 351-365. https://link.springer.com/article/10.1007/s00394-013-0597-4

Food Standards Agency. 2008. *Retail Survey of Iodine in UK Produced Dairy Foods, FSIS 02/08.* London: Food Standards Agency.

Forbes, E. E., and R. E. Dahl. 2010. Pubertal development and behavior: Hormonal activation of social and motivational tendencies. Brain Cogn. 72:66-72.

Fourreau, D., N. Peretti, B. Hengy, Y. Gillet, S. Courtil-Teyssedre, L. Hess, I. Loras-Duclaux, N. Caron, C. Didier. F. Cour-Andlauer, S. Heissat, A. Lachaux, and É. Javouhey. 2013. Complications carentielles suite à l'utilisation de laits végéaux, chez des nourrissons de deux mois et demi à 14 mois (quatre cas). Presse Med. 42:e37-43. doi: 10.1016/j.lpm.2012.05.029

Gatineau, M., C. Hancock, N. Holman, H. Outhwaite, L. Oldridge, C. Anna, and L. Ells. 2014. Adult Obesity and Type 2 diabetes. PHE publications gateway number: 2014211. Public Health England, London. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/338934/Adult_obesity_and_type_2_diabetes_.pdf

Gijsbers, L., E. L. Ding, V. S. Malik, J. de Goede, J. M. Geleijnse, and S. S. Soedamah-Muthu. 2016. Consumption of dairy foods and diabetes incidence: a dose-response meta-analysis of observational studies. Am. J. Clin. Nutr. 103:1111-1124.

Giromini, C., Á. A. Fekete, D. I. Givens, A. Baldi, and J. A. Lovegrove. 2017. A comparison of the in vitro angiotensin-converting enzyme inhibitory capacity of dairy and plant protein supplements. Nutrients 9:1352.

Giromini, C., J. A. Lovegrove, D. I. Givens, R. Rebucci, L. Pinotti, E. Maffioli, G. Tedeschi, and A. Baldi. 2019. In vitro digested milk proteins: evaluation of angiotensin-converting enzyme inhibitory and antioxidant activities, peptidomic profile and mucin gene expression in HT29-MTX cells. J. Dairy Sci. in press.

Goldacre, M., N. Hall, and D. G. R.Yeates. 2014. Hospitalisation for children with rickets in England: a historical perspective. The Lancet 383:597-598.

Grant, C. A., and A. L. Hicks. 2018. Comparative life cycle assessment of milk and plant-based alternatives. Environ. Eng. Sci. 35: 1235-1247.

Griffin, B. A. and J. A. Lovegrove. 2018. Butter increases HDL functional capacity: Is this compensation for its adverse effect on serum LDL cholesterol? J. Nutr. 148: 1069-1070.

Gullberg, B., O. Johnell, and J. A. Kanis. 1997. World-wide projections for hip fracture. Osteoporosis Int. 7:407-413. https://link.springer.com/article/10.1007/PL00004148

Guo, J., A. Dougkas, P. C. Elwood, and D. I. Givens. 2018. Dairy foods and body mass index over 10-Year: Evidence from the Caerphilly prospective cohort study. Nutrients 10:1515.

Guo, J., A. Astrup, J. A. Lovegrove, L. Gijsbers, D. I. Givens, and S. S. Soedamah-Muthu. 2017. Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Eur. J. Epidemiol. 32:269–287.

Guo, J., D. I. Givens, A. Astrup, S. J. L. Bakker, G. H. Goossens, M. Kratz, A. Marette, H. Pijl, and S. S. Soedamah-Muthu. 2019. The impact of dairy products in the development of type 2 diabetes: where does the evidence stand in 2019? Advances in Nutrition. Published on line ahead of print, available at: https://doi.org/10.1093/advances/nmz050

Hernlund, E., A. Svedbom, M. Ivergård, J. Compston, C. Cooper, J. Stenmark, E. V. McCloskey, B. Jönsson, and J. A. Kanis. 2013. Osteoporosis in the European Union: medical management, epidemiology and economic burden. Arch. Osteoporos. 8:136.

Hjerpsted, J., E. Leedo, and T. Tholstrup. 2011. Cheese intake in large amounts lowers LDL-cholesterol concentrations compared with butter intake of equal fat content. Am. J. Clin. Nutr. 94:1479–1484.

Holick, M. F. 2010. The vitamin D deficiency pandemic: a forgotten hormone important for life. Public Health Rev. 32:267-283

Host, A., and S. Halken. 2014. Cow's milk allergy: where have we come from and where are we going? Endocr. Metab. Immune Disord. Drug Targets. 14:2-8.

Hoppe, C., C. Mølgaard, C. Dalum, A. Vaag, and K. F. Michaelsen. 2009. Differential effects of casein versus whey on fasting plasma levels of insulin, IGF-1 and IGF-1/IGFBP-3: results from a randomized 7-day supplementation study in pre-pubertal boys. Eur. J. Clin. Nutr. 63: 1076–1083.

Hu, F. B., J. E. Manson, M. J. Stampfer, G. Colditz, S. Liu, C. G. Solomon, and W. C. Willett. 2001. Diet, lifestyle and the rise of type 2 diabetes in women. N. Engl. J. Med. 345:790–797.

Hunter, G. R., H. Singh, S. J. Carter, D. R. Bryan, and G. Fisher. 2019. Sarcopenia and its implications for metabolic health. J. Obes. 2019: Article ID 8031705. https://doi.org/10.1155/2019/8031705

Hynes, K. L., P. Otahal, I. Hay, and J. R. Burgess. 2013. Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort. J. Clin. Endocrinol. Metab. 98: 1954-1962.

Itkonen, S. T., M. Erkkola, and C. J. E. Lamberg-Allardt. 2018. Vitamin D fortification of fluid milk products and their contribution to vitamin D intake and vitamin D status in observational studies – a review. Nutrients 10:1054. doi: 10.3390/nu10081054.

Iguacel, I., M. L. Miquel-Berges, A. Gómez-Bruton, L. A. Moreno, and C. Julián. 2018. Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis. Nutr. Rev. 77: 1-18.

Jazayeri, M., Y. Moradi, A. Rasti, M. Nakhjavani, M. Kamali, and H. R. Baradaran. 2018. Prevalence of vitamin D deficiency in healthy Iranian children: a systematic review and meta-analysis. Med. J. Islam Repub. 32:83. Iran doi: 10.14196/mjiri.32.83. eCollection 2018.

Kanis. J. A., H. Johansson, A. Oden, C. De Laet, O. Johnell, J. A. Eisman, E. McCloskey, D. Mellstrom, H. Pols, J. Reeve, A. Silman, and A. A. Tenenhouse. 2005. Meta-analysis of milk intake and fracture risk: low utility for case finding. Osteoporos. Int. 16: 799-804.

Kalkwarf, H. J., J. C. Khoury, and B. P. Lanphear. 2003. Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women. Am. J. Clin. Nutr. 77: 257-265.

Kang, K., O. F. Sotunde, and H. A. Weiler. 2019. Effects of milk and milk product consumption on growth among children and adolescents aged 6-18 years: A meta-analysis of randomized controlled trials. Adv. Nutr. 10:250-261.

Kouw, I. W. K., A. M. Holwerda, J. Trommelen, I. F. Kramer, J. Bastiaanse, S. L. Halson, W. K. W. H. Wodzig, L. B. Verdijk, and L. J. C. van Loon. 2017. Protein ingestion before sleep increases overnight muscle protein synthesis rates in healthy older men: A randomized controlled trial. J. Nutr. 147:2252-2261.

Kratz, M., T. Baars, and S. Guyenet. 2013. The relationship between high-fat dairy consumption and obesity, cardiovascular, and metabolic disease. Eur. J. Nutr. 52:1-24.

Kris-Etherton, P. M., J. A. Grieger, H. F. Hilpert, and S. G. West. 2009. Milk products, dietary patterns and blood pressure management. J. Am. Coll. Nutr. 28: Suppl 1:103S-119S.

Kunutsor, S. K., M. R. Whitehouse, A. W. Blom, and J. A. Laukkanen. 2017. Low serum magnesium levels are associated with increased risk of fractures: a long-term prospective cohort study. Eur. J. Epidemiol. 32:593-603.

Larson, N. I., D. Neumark-Sztainer, L. Harnack, M. Wall, M. Story, and M. E. Eisenberg. 2009. Calcium and dairy intake: Longitudinal trends during the transition to young adulthood and correlates of calcium intake. J. Nutr. Educ. Behav. 41:254-260.

Le Louer, B., J. Lemale, K. Garcette, C. Orzechowski, A. Chalvon, J.-P.Girardet, and P. Tounian. 2014. Conséquences nutritionnelles de l'utilisation de boissons végétales inadaptées chez les nourrissons de moins d'un an. Arch Pediatrie 21:483-488.

Lee, K. W., D. Shin, M. S. Cho, and W. O. Song. 2016. Food group intakes as determinants of iodine status among us adult population. Nutrients 8:325.

Leroy, J. L., and E. A. Frongillo. 2019. Perspective: What does stunting really mean? A critical review of the evidence. Adv. Nutr. 10:196-204.

Livingstone, K. M., J. A. Lovegrove, J. R. Cockcroft, P. C. Elwood, J. E. Pickering, and D. I. Givens. 2013. Does dairy food intake predict arterial stiffness and blood pressure in men? Evidence from the Caerphilly Prospective Study. Hypertension 61:42-47.

Locatelli, V., and V. E. Bianchi. 2014. Effect of GH/IGF-1 on bone metabolism and osteoporosis. Int. J. Endocrinol. 2014: Article ID 235060.

Lonnie, M., E. Hooker, J. M. Brunstrom, B. M. Corfe, M. A. Green, A. W. Watson, E. A. Williams, E. J. Stevenson, S. Penson, and A. M. Johnstone. 2018. Protein for Life: Review of optimal protein intake, sustainable dietary sources and the effect on appetite in ageing adults. Nutrients 10:360.

Lu, L., P. Xun, Y. Wan, K. He, and W. Cai. 2016. Long-term association between dairy consumption and risk of childhood obesity: a systematic review and meta-analysis of prospective cohort studies. Eur. J. Clin. Nutr. 70:414-423.

Ma, X., Z. Huang, X. Yang, and Y. Su. 2014. Calcium supplementation and bone mineral accretion in Chinese adolescents aged 12–14 years: a 12-month, dose-response, randomised intervention trial. Br. J. Nutr. 112:1510-1520.

Michaelsen, K. F. 2013. Cow's milk in the prevention and treatment of stunting and wasting. Food Nutr. Bull. 34:249-251.

Michaëlsson, K., A. Wolk, S. Langenskiöld, S. Basu, E. W. Lemming, H. Melhus, and L. Byberg. 2014. Milk intake and risk of mortality and fractures in women and men: cohort studies. BMJ 349:g6205.

Miles, E. A. 2020. Adverse reactions to cow's milk. Pages 271-297 in Milk and Dairy Foods: Their Functionality in Human Health and Disease. D. I. Givens, ed. Elsevier, Cambridge, MA 02139, United States.

Mullen, K., L. Hamill, K. Doolan, I. Young, P. Smyth, A. Flynn, J. Walton, A. A. Meharg, M. Carey, C. McKernan, M. Bell, N. Black, U. Graham, D. McCance, C. McHugh, P. McMullan, S. McQuaid, A. O'Loughlin, A. Tuthill, S. C. Bath, M. Rayman, and J. V. Woodside. 2019. Iodine status of teenage girls on the island of Ireland. Eur. J. Nutr. Epub ahead of print at: https://doi.org/10.1007/s00394-019-02037-x.

Munblit, D., M. R. Perkin, D. J. Palmer, K. J. Allen, and R. J. Boyle. 2020. Assessment of evidence about common infant symptoms and cow's milk allergy. JAMA Pediatr. Published online April 13, 2020. doi:10.1001/jamapediatrics.2020.0153

National Statistics. 2017a. Health Survey for England 2016, Summary of Key Findings. Government Statistical Service, available at: https://files.digital.nhs.uk/pdf/s/q/hse2016-summary.pdf

National Statistics. 2017b. Health Survey for England 2016, Adult Health Trends. Government Statistical Service, available at: http://healthsurvey.hscic.gov.uk/media/63757/HSE2016-Adult-trends.pdf

NHS. 2019. Stages of puberty. Available at: https://www.nhs.uk/live-well/sexual-health/stages-of-puberty-what-happens-to-boys-and-girls/

Nittari, G., S. Scuri, F. Petrelli, I. Pirillo, N. M. di Luca, and I. Grappasonni. 2019. Fighting obesity in children from European World Health Organization member states. Epidemiological data, medical-social aspects, and prevention programs. Clin. Ter. 170:e223-230.

http://www.clinicaterapeutica.it/ojs/index.php/ClinicaTerapeutica/article/view/427/169

O'Brien, B., D. Gleeson, and K. Jordan. 2013. Iodine concentrations in milk. Irish J. Agr. Food Res. 52:209-216.

OECD. 2017. Obesity Update. Available at: www.oecd.org/health/obesity-update.htm

O'Kane, S. M., L. K. Pourshahidi, M. S. Mulhern, J. J. Strain, E. M. Mackle, D. Koca, L. Schomburg, S. Hill, J. O'Reilly, D. Kmiotek, C. Deitrich, S. C. Bath, and A. J. Yeates. 2018. Cow milk consumption increases iodine status in women of childbearing age in a randomized controlled trial. J. Nutr. 148:401-408. https://doi.org/10.1093/jn/nxx043

Ong, A. M., K. Kang, H. A. Weiler, and S. N. Morin. 2019. Fermented milk products and bone health in postmenopausal women: A systematic review of randomized controlled trials, prospective cohorts, and case-control studies. Adv. Nutr. 00: 1-15. https://doi.org/10.1093/advances/nmz108

Paddon-Jones, D, and B. B. Rasmussen. 2009. Dietary protein recommendations and the prevention of sarcopenia: Protein, amino acid metabolism and therapy. Curr. Opin. Clin. Nutr. Metab. Care 12:86-90.

Pastuszka, R., J. Barłowska, and Z. Litwińczuk. 2016. Allergenicity of milk of different animal species in relation to human milk. Postepy Hig. Med. Dosw. 70:1451-1459.

Payling, L. M., D. T. Juniper, C. Drake, C. Rymer, and D. I. Givens. 2015. Effect of milk type and processing on iodine concentration of organic and conventional winter milk at retail: implications for nutrition. Food Chem. 178:327-330.

Pimpin, L., J. H. Y. Wu, H. Haskelberg, L. Del Gobbo, and D. Mozaffarian. 2016. Is butter back? A systematic review and meta-analysis of butter consumption and risk of cardiovascular disease, diabetes, and total mortality. PLoS ONE 11:e0158118.

Prentice, A. 2013. Nutritional rickets around the world. J. Steroid Biochem. 136:201-206.

Quann, E. E., V. L. Fulgoni 111, and N. Auestad. 2015. Consuming the daily recommended amounts of dairy products would reduce the prevalence of inadequate micronutrient intakes in the United States: diet modeling study based on NHANES 2007-2010. Nutr. J. 14: 90.

Rangel, A. H. do N., D. C. Sales, S. A. Urbano, J. G. B. Galvão Júnior, J. C. de Andrade Neto, and C. de S. Macêdo. 2016. Lactose intolerance and cow's milk protein allergy. Food Sci. Technol. (Campinas).36 April/June Epub: https://doi.org/10.1590/1678-457X.0019

Roberts, C., T. Steer, N. Maplethorpe, L. Cox, S. Meadows, S. Nicholson, P. Page, and G. Swan. 2018. National Diet and Nutrition Survey. Results from Years 7-8 (combined) of the Rolling Programme (2014/15 to 2015/16). PHE Publication gateway number: 2017851 Public Health England, London.

Roser, M. 2017. Life Expectancy. Retrieved on 5 June 2017 from https://ourworldindata.org/life-expectancy/

Rosqvist, F., A. Smedman, H. Lindmark-Mansson, M. Paulsson, P. Petrus, S. Straniero, M. Rudling, I. Dahlman, and U. Risérus. 2015. Potential role of milk fat globule membrane in modulating plasma lipoproteins, gene expression, and cholesterol metabolism in humans: a randomized study. Am. J. Clin. Nutr. 102: 20-30.

Sahni S., K. M. Mangano, D. P. Kiel, K. I. Tucker, and M. T. Hannan. 2017. Dairy intake is protective against bone loss in older vitamin D supplement users: The Framingham Study. J. Nutr. 147, 645-652.

Scrafford, C. G., X. Bi, J. K. Multani, M. M. Murphy, J. K. Schmier, and L. M. Barraj. 2020. Health care costs and savings associated with increased dairy consumption among adults in the United States. Nutrients 12: 233. doi:10.3390/nu12010233

Schoz-Ahrens, K. E., F. Ahrens, and C. A. Barth. 2019. Nutritional and health attributes of milk and milk imitations. Eur. J. Clin. Nutr. Epub ahead of print: https://doi.org/10.1007/s00394-019-01936-3.

Semali, I. A., A. Tengia-Kessy, E. J. Mmbaga, and G. Leyna. 2015. Prevalence and determinants of stunting in under-five children in central Tanzania: remaining threats to achieving Millennium Development Goal 4. BMC Public Health 15:1153. https://dx.doi.org/10.1186%2Fs12889-015-2507-6

Shafiee, G., A. Keshtkar, A. Soltani, Z. Ahadi, B. Larijani, and R. Heshmat. 2017. Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies. J. Diabetes Nutr. Metab. Dis. 16:21.

Średnicka-Tober, D., M. Barański, C. J. Seal, R. Sanderson, C. Benbrook, H. Steinshamn, J. Gromadzka-Ostrowska, E. Rembiałkowska, K. Skwarło-Sońta, M. Eyre, G. Cozzi, M. K. Larsen, T. Jordon, U. Niggli, T. Sakowski, P. C. Calder, G. C. Burdge, S. Sotiraki, A. Stefanakis, S. Stergiadis, H. Yolcu, E. Chatzidimitriou, G. Butler, G. Stewart, and C. Leifert.

2016. Higher PUFA and n-3 PUFA, conjugated linoleic acid, α-tocopherol and iron, but lower iodine and selenium concentrations in organic milk: a systematic literature review and meta- and redundancy analyses. Br. J. Nutr. 115:1043-1060.

Soedamah-Muthu, S. S., and J. de Goede. 2018. Dairy consumption and cardiometabolic diseases: systematic review and updated meta-analyses of prospective cohort studies. Curr. Nutr. Rep. 7:171-172.

Steinberger, J., S. R. Daniels, N. Hagberg, C. R. Isasi, A. S. Kelly, D. Lloyd-Jones, R. R. Pate, C. Pratt, C. M. Shay, J. A. Towbin, E. Urbina, L. V. Van Horn, and J. P. Zachariah. 2016. Cardiovascular health promotion in children: challenges and opportunities for 2020 and beyond. Circulation 134:e236–e255.

Stevenson, M. C., C. Drake, and D. I. Givens. 2018. Further studies on the iodine concentration of conventional, organic and UHT semi-skimmed milk at retail in the UK. Food Chem. 239: 551-555.

Thacher, T. D., P. R. Fischer, P. J. Tebben, R. J. Singh, S. S. Cha, J. A. Maxson, and B. P. Yawn. 2013. Increasing incidence of nutritional rickets: A population-based study in Olmsted County, Minnesota. Mayo Clin. Proc. 88:176-183.

Thorning, T. K., H. C. Bertram, J.-P. Bonjour, L. de Groot, D. Dupont, E. Feeney, R. Ipsen, J.-M. Lecerf, A. Mackie, M. C. McKinley, M.-C. Michalski, D. Rémond, U. Risérus, S. Soedamah-Muthu, T. Tholstrup, C. Weaver, A. Astrup, and D. I. Givens. 2017. Whole dairy matrix or single nutrients in assessment of health effects: current evidence and knowledge gaps. Am. J. Clin. Nutr. 105:1033-1045.

Totzauer, M., V. Luque, J. Escribano, R. Closa-Monasterolo, E. Verduci, A. ReDionigi, J. Hoyos, J.-P. Langhendries, D. Gruszfeld, P. Socha, B. Koletzko, and V. Grote. 2018. Effect of lower versus higher protein content in infant formula through the first year on body composition from 1 to 6 years: follow-up of a randomized clinical trial. Obesity 26: 1203–1210.

Turner, P. J., M. H. Gowland, V. Sharma, D. Ierodiakonou, N. Harper, T. Garcez, R. Pumphrey, and R. J. Boyle. 2015. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: An analysis of United Kingdom national anaphylaxis data, 1992-2012. J. Allergy Clin. Immunol. 135:956-963.

van Mil, N. H., H. Tiemeier, J. J. Bongers-Schokking, A. Ghassabian, A. Hofman, H. Hooijkaas, V. W. V. Jaddoe, S. M. de Muinck Keizer-Schrama, E. A. P. Steegers, T. J. Visser, W. Visser, H. A. Ross, F. C. Verhulst, Y. B. de Rijke, R. P. M. Steegers-Theunissen. 2012. Low urinary iodine excretion during early pregnancy is associated with alterations in executive functioning in children. J. Nutr. 142:2167-2174. https://doi.org/10.3945/jn.112.161950

Vanderpump, M. P. J., J. H. Lazarus, P. P. Smyth, P. Laurberg, R. L. Holder, K. Boelaert, and J. A. Franklyn. 2011. Iodine status of UK schoolgirls: a cross-sectional survey. The Lancet 377, 2007-2012.

Vojdani, A., C. Turnpaugh, and E. Vojdani. 2018. Immune reactivity against a variety of mammalian milks and plant-based milk substitutes. J. Dairy Res. 85:358–365.

Wan, X., S. Wang, J. Xu, L. Zhuang, K. Xing, M. Zhang, X. Zhu, L. Wang, P. Gao, Q. Xi1, J. Sun, Y. Zhang, T. Li, G. Shu, and Q. Jiang. 2017. Dietary protein-induced hepatic IGF-1 secretion mediated by PPARγ activation. PLoS ONE 12:e0173174.

Wall, B., H. Hamer, A. de Lange, A. Kiskini, B. B. Groen, J. M. Senden, A. P. Gijsen, L. B. Verdijk, and L. J. van Loon. 2013. Leucine co-ingestion improves post-prandial muscle protein accretion in elderly men. Clin. Nutr. 32:412-419.

Wall, B. T., N. M. Cermak, and L. J. C. van Loon. 2014. Dietary protein considerations to support active aging. Sports Med. 44 (Suppl 2):S185-S194.

Weaver, C. M., C. M. Gordon, K. F. Janz, H. J. Kalkwarf, J. M. Lappe, R. Lewis, M. O'Karma, T. C. Wallace, and B. S. Zemel. 2016. The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. Osteoporosis Int. 27:1281-1386.

Welch, A. A., J. Skinner and M. Hickson. 2017. Dietary magnesium may be protective for aging of bone and skeletal muscle in middle and younger older mem and women. Nutrients 9: 1189.

WHO. 1999. Technical Report Series 886. Programming for adolescent health and development, Geneva, World Health Organization. https://www.who.int/maternal_child_adolescent/documents/trs_886/en/

WHO Secretariat, M. Andersson, B. de Benoist, F. Delange, and J. Zupan. 2007. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the technical consultation. Public Health Nutr. 10:1606–1611. https://doi.org/10.1017/S1368980007361004

WHO. 2019. World health statistics 2019: monitoring health for the SDGs, sustainable development goals. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO.

WHO. 2020. Vitamin and Mineral Nutrition Information System (VMNIS), Database on Iodine Deficiency. https://www.who.int/vmnis/database/iodine/en/ Accessed 26 April 2020.

Wilkins, E., L. Wilson, K. Wickramasinghe, P. Bhatnagar, J. Leal, R. Luengo-Fernandez, R. Burns, M. Rayner, and N. Townsend. 2017. European Cardiovascular Disease Statistics 2017. European Heart Network, Brussels, Belgium. http://www.ehnheart.org/cvd-statistics/cvd-statistics-2017.html

Yakar S., H. Werner, and C. J. Rosen. 2018. 40 Years of IGF1. Insulin-like growth factors: actions on the skeleton. J. Mol. Endocrinol. 61:T115-T137. https://dx.doi.org/10.1530%2FJME-17-0298

Yang, Y., T. A. Churchward-Venne, N. A. Burd, L. Breen, M. A. Tarnopolsky, and S. M. Phillips. 2012. Myofibrillar protein synthesis following ingestion of soy protein isolate at rest and after resistance exercise in elderly men. Nutr. Metab. 9:57. https://doi.org/10.1186/1743-7075-9-57

Zia, A., H. U. Siddiqui, H. Mohiuddin, and S. Gul. 2018. Levelling-off of declining trend of cardiovascular disease-related mortality in the USA: the challenge to rein in obesity and diabetes epidemic. Cardiovascular Endocrinology & Metabolism 7:54-55.

Zempleni, J. 2017. Milk exosomes: beyond dietary microRNAs. Genes Nutr. 12:12. https://doi.org/10.1186/s12263-017-0562-6

Table 1. Percentage of 3 UK population groups with micronutrient intakes less than the Lower Reference Nutrient Intake (LRNI) and percentage achievement of the Reference Nutrient Intake (RNI) for vitamin D (Adapted from data in Roberts et al., 2018).

	% with intakes less than the LRNI for:						% RNI
Population	Iron	Calcium	Magnesium	Zinc	Selenium	Iodine	Vitamin D
Males 11-18 years	12	11	27	18	26	14	20
Females 11-18 years	54	22	50	27	45	27	17
Females 19-64 years	27	11	11	8	47	15	21

Table 2. Effects of vegetarian and vegan relative to omnivore diets on bone mineral density (BMD) at the lumbar spine, femoral neck and of whole body. (Adapted from data in Iguacel et al., 2018).

BMD comparison	Mean difference in BMD[3] (g/cm^2)	95% CI[1]	*P*[2]
At the lumbar spine			
Vegetarians + vegans vs. omnivores	-0.032	-0.048, -0.015	<0.05
Vegetarian vs. omnivores	-0.023	-0.035, -0.010	<0.05
Vegans vs. omnivores	-0.070	-0.116, -0.025	<0.05
At the femoral neck			
Vegetarians + vegans vs. omnivores	-0.037	-0.054, -0.020	<0.05
Vegetarian vs. omnivores	-0.025	-0.038, -0.012	<0.05
Vegans vs. omnivores	-0.055	-0.090, -0.021	<0.05
Whole body			
Vegetarians + vegans vs. omnivores	-0.048	-0.080, -0.016	<0.05
Vegetarian vs. omnivores	-0.035	-0.093, 0.022	NS[4]
Vegans vs. omnivores	-0.059	-0.106, -0.012	<0.05

[1]CI, confidence interval, [2]for test if difference was >0, [3]comapred with omnivores, [4]NS, not significant (P>0.05)

Table 3. Dose-response meta-analyses examining the relative risk (RR) of cardiometabolic diseases in relation to consumption of dairy foods (Adapted from data in Soedamah-Muthu and de Goede, 2018).

Disease outcome	Dairy food[1]	RR (95% CI[2])	*P*
Diabetes mellitus	Total dairy	0.97 (0.95-1.00)	NS
	Low fat dairy	0.96 (0.92-1.00)	NS
	Yogurt	0.94 (0.91-0.97)	<0.05
CHD[3]	Total dairy	1.00 (0.98-1.03)	NS
	Milk	1.01 (0.97-1.04)	NS
Stroke	Total dairy	0.98 (0.96-1.01)	NS
	Low fat dairy	0.97 (0.95-0.99)	<0.05
	Full fat dairy	0.96 (0.93-0.99)	<0.05
	Milk	0.92 (0.88-0.97)	<0.05

[1] per increment of 200g/d except yogurt 100g/d, [2] Confidence interval, [3] Coronary heart disease

Table 4. Changes in blood lipids from baseline to end of 6 weeks intervention when 40 g/d of dairy fat were provided in 3 types of dairy products (Adapted from data in Feeney et al., 2018).

	Treatment			
Blood lipid (mmol/L)	T1[1]	T2	T3	*P*[2]
Total cholesterol	-0.52	-0.37	-0.15	0.033
HDL-cholesterol	0	-0.07	+0.05	0.284
LDL-cholesterol	-0.45	-0.27	-0.14	0.016
Triacylglycerols	-0.15	-0.05	-0.12	0.386

[1] T1, 120g Cheddar cheese, T2, 120g low fat Cheddar cheese + 21g butter, T3, 49g butter + 30g calcium caseinate + 500mg calcium (as $CaCO_3$)

[2] for differences between treatments, for controlling factors included in model see original paper