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The effects of dairy consumption on body composition and bone properties in youth: a systematic review

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Abbreviations:

BMD: Bone Mineral Density,

BMC: Bone Mineral Content,

BMI: Body Mass Index,

BTMs: Bone Turnover Markers,

Ca: Calcium,

DXA: Dual-energy X-ray absorptiometry,

F: Females,

FM: Fat Mass,

FFQ: food frequency questionnaire,

IGF-1: Insulin growth factor 1

LBM: Lean Body Mass

M: Males

PA: physical activity,

PTH: parathyroid hormone,

pQCT: peripheral quantitative computer tomography,

RCTs: Randomized Controlled Trials

SPA: single photon absorptiometry

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ABSTRACT

Background: According to previous reviews, there is no clear evidence about the effects of dairy consumption on body composition and bone properties in pediatric populations. There is a need for further assessment of existing findings and methodological quality of studies prior to summarize the evidence.

Objective: To assess the quality, methodologies and substantive findings of randomized controlled trials (RCTs) examining the effects of dairy consumption on body size, body composition and bone properties in children and adolescents. Methods: After searching Pub Med and Google scholar up to December 2016, 15 RCTs were retained and included in this systematic review for further analysis. The quality of the included studies was assessed via the Jadad scale; detailed methodological and statistical characteristics were evaluated and the main findings were summarized.

Results: The effects of dairy consumption were found significant for bone structure, and non significant for body size and composition. 8 of the 11 RCTs assessing bone found significant effects ($p<0.05$) for bone mineral content (BMC) and bone mineral density (BMD), with an average 8% increase in BMD after 16-months of dairy consumption. Conversely, significant effects ($p<0.05$) were found only in 2 of the 14 RCTs focusing on body size, i.e. height and weight, and in only 1 of the 11 RCTs focusing on body composition, i.e. lean mass.

Conclusions: The systematic consumption of dairy products may benefit bone structure and development, but it does not appear to affect body composition or body size in children and adolescents. Based on the Jadad scale, the methodological quality of the 15 RCTs was rated as good overall. However, there were methodological disparities and limitations that may have led

to non significant results, particularly for body size and composition. Future RCTs designed to address these limitations are warranted.

Key words: dairy consumption, exercise, body composition, bone turnover, children.

INTRODUCTION

Over the years there has been an increased interest in the effects of dairy on body composition and bone development in humans. The results of the 4 following reviews, however, are inconclusive for body composition possibly due to methodological limitations of the included studies referring, for example, to study design, experimental power, compliance etc. In Barr's review (1), which assessed 30 randomized controlled trials (RCTs) using dairy products or calcium supplementation as the dietary intervention, only 3 RCTs focused on children (girls) and found non-significant effects of dairy consumption on body composition. Their non significant findings were attributed to inappropriate study designs, inadequate experimental power, and the possible increase in energy intake with increased dairy consumption. Huang et al. (2) reviewed 5 observational studies and 10 RCTs examining the effects of dairy intake and calcium supplementation on body composition in children. 3of the 5observational studies reported significant effects of dairy and/or calcium intake on body composition. However, none of the 10 RCTs (3 RCTs used dairy products and 7 RCTs used calcium supplementation) showed significant effects, mainly due to dietary report problems, lack of compliance monitoring, and the confounding effects of other dietary variables (such as energy intake). A later review by Lanou & Barnard (3) found similar insignificant effects of dairy consumption on body composition. It assessed 49 RCTs, 18 of which were in children and adolescents, with only 5 of them using dairy foods as opposed to calcium supplements. Finally, a recent systematic review and meta-analysis of 36 observational studies and 4 RCTs showed modest effects of dairy intake on body composition (adiposity) in adolescents but not in children (4).

The existing evidence for the positive effects of dairy consumption on bones in children and adolescents is more conclusive, even though many of the relevant studies are methodologically disparate. Early RCTs showed significant positive effects of dairy products (e.g., milk) on bone related variables (e.g., bone mineral density [BMD] and bone mineral content [BMC]) in pediatric populations (e.g., 5-7). Similarly, the longitudinal study by Fiorito et al. (8) found calcium intake (especially from dairy foods) to have beneficial effects on BMC in young girls. However, the review of Lanou et al. (9) proposed that the existing evidence does not support the nutritional guidelines suggesting increased calcium/dairy intake for enhancing bone mineralization in children and adolescents. Lanou et al. (9) assessed 58 studies (22 cross-sectional, 13 retrospective, 10 longitudinal, and 13 RCTs) examining the effects of dairy product consumption or calcium supplementation on bone health in children and young adults. 12 out of 13 RCTs had a minimum one-year treatment, and 9 RCTs examined the effects of calcium supplementation. Only 3 of these 12 RCTs examined the effects of dairy products either in combination with calcium supplements (in 1RCT by Matkovic et al., 1990) (10) or not (in 2 RCTs by Cadogan et al., 1997 and Chan et al., 1995, respectively) (5, 6). Further, 27 out of 37 studies in this review, that used dairy or dietary calcium intake and managed to control for weight, pubertal status and exercise in children and young adults, showed no relationship between dietary calcium or dairy intake and bone. As a result, the authors suggested the revision of the pediatric recommendations on calcium and dairy intake due to the marginal effects on bone (9, 11). In contrast, a later meta-analysis found that the increased consumption of dietary calcium, via dairy products or supplements with and without vitamin D, significantly increased total body and lumbar spine BMC in children with low baseline calcium intake (12). From the 21 RCTs assessed in this meta-analysis, only 4 studies though used dairy, mainly milk. As stated by Huncharek et al. (12), the heterogeneity of the participants' diet and calcium intake (low, near normal or normal intake) might have affected the findings of this meta-analysis. The same study design limitation may also apply to the findings and conclusions of the previous reviews by Lanou et al. (9, 11).

As mentioned in some previous relevant reviews (1, 13), there is a need for assessing the methodological quality of the studies prior to summarizing the evidence. In fact, using only RCTs for assessing whether an experimental treatment is effective, or not, may be more appropriate (14). Therefore, the purpose of this review was to examine the potential impact of dairy consumption on body size and composition, and on bone in children and adolescents using exclusively RCTs. Additionally, this review assessed the quality of the methodologies and summarized the findings of the included RCTs.

METHODS

Search and selection criteria - strategy

Two databases (PubMed and Google Scholar) were electronically searched for studies suitable for this review up to December 2016. The search terms included different combinations of relevant key words, namely dairy (consumption), body composition, bone, children, adolescents, pediatric population.

The inclusion criteria were as follows: articles written in English; RCTs; pediatric population (<18 years old); males or females, or both sexes; intervention including dairy products; outcomes relevant to anthropometrics (e.g., height, weight, BMI), body composition (e.g., lean body mass [LBM], fat mass [FM]), and bone measurements (e.g., BMD, BMC, and bone turnover markers [BTMs]).

First, the titles of all the studies found in the databases were read and their relevance to the topic of the review was assessed. Then the abstracts and the full texts of the relevant studies were read in order to check whether all inclusion criteria were met. Lastly, the references of the relevant studies as well as of previous systematic reviews and meta-analyses were checked to locate additional studies.

Data extraction and management

Each study that met all of the inclusion criteria was subjected to the systematic extraction of a number of key design, methodological, and statistical characteristics (Tables 1 and 2). The methodological and statistical characteristics included sample size estimation/power calculation (yes or no, and if yes the % of power), adjustment of confounding effects (yes or no, and if yes the variables/covariates), control group (yes or no), dropouts (number of participants, %), calculation of effect size and confidence interval CI (yes or no), diet/exercise assessment (method of assessment), limitations and recommendations (if stated which or not stated) (Table 1).The design-specific characteristics were: i) sample size (N after dropout), and participants' gender (males M, females F), age (mean/range years), country, weight profile (e.g., normal weight, overweight or obese), and health status (healthy or not); ii) study duration (weeks, months, years), iii) intervention: diet (dairy/calcium intake), and exercise (type, frequency, duration, intensity); iv) measurements/variables (assessment tool); and v) main findings (anthropometrics, body composition, and bone properties) (Table 2).

Quality assessment: Jadad scale

The quality of the included studies was assessed via the Jadad scale (15). This scale has been used extensively in previous systematic reviews in various clinical areas, as for example in obesity (16-18), due to its efficiency in assessing the methodological quality of RCTs (19). The scale includes seven items leading to a 5-point scoring system that assesses the methodological quality of RCTs according to criteria relevant to randomization, blinding, and dropouts. Specifically, five questions are positively scored by adding one point each for the “yes” answers or zero for the “no” answers, while the other two questions are negatively scored by either subtracting one point for a positive answer or giving a zero for a negative answer (scores -1, -2: bad quality, scores 0, 1: poor quality, scores 2, 3: good quality, score 4: very good quality, score 5: excellent quality).

Included and excluded studies

A total of 15 studies met all the inclusion criteria and included in this systematic review (Tables 1 and 2). Studies that did not meet all of the inclusion criteria were excluded from further analysis as for example, the study by Bonjour et al. (20), where participants were given a variety of other calcium enriched foods, e.g., cakes, biscuits, along with dairy. Another example of an excluded study was by Matkovic et al. (21), where the study design for examining the effects of dairy consumption was not suitable (two designs were used in this study: an observational for the assessment of the effects of high calcium diet with dairy, while an RCT for the effects of calcium supplements).

RESULTS

Assessing the quality of the included studies (Jadad scale)

Most of the included studies were rated as good quality. 8 studies (6, 22-26, 29, 31) had a score of 2, and 5 studies (5, 7, 10, 28, 32) had a score of 3. Only two studies (27, 30) had a score of 1, indicating poorer quality. However, it has been previously demonstrated in one systematic review (17) that the methodological quality of studies can be underestimated by 1-2 points using the Jadad scale. Specifically, items 3 and 4 of this scale refer to blindness, which is not always applicable to the type of research that assesses nutritional and exercise interventions. Overall, the design quality of the 15 included RCTs was assessed as satisfactory for the purpose of this review.

Methodological and Statistical Characteristics

The methodological and statistical characteristics of the included studies are summarized in Table 1. Power analyses to estimate sample size were performed in seven studies. Specifically, four studies (10, 23-24, 29) used a power of 80%, 2 studies (7, 32) used a power of 90%, and 1 study (28) used a power of 95%. A control group was implemented in all studies except in the study of St-Onge et al. (31). 14 of the 15 reviewed studies reported dropouts. Dropouts were in average 13.3% and ranged between 2.4% (5) and 32.1% (30).

Adjustments for confounding factors (puberty, age, gender, body and bone size, baseline weight, energy, protein and calcium intake, physical activity [PA]) were made in 7studies (5, 22, 23, 25, 29, 31, 32). Effect size was not estimated and presented in any of the 15studies, and confidence intervals were reported in 4 studies (5, 25, 26, 32). Dietary intake was assessed with food records (3, 7 or 9 days, two to nine times during the study) in 10 studies (5-7, 10, 22, 23, 25, 27, 28, 32). In addition, 24 hour, 3 day and 7 day recalls were used in 3 studies (26, 30, 31), a food frequency questionnaire (FFQ) for nutritional or calcium intake was used in 5 studies (6, 7, 24, 29, 30), and a daily record of dairy products consumption was used in 6 studies (7, 22, 24-27). 8 out of the 15 included studies (6, 7, 22, 24-27, 30) used more than one nutritional assessment tool (e.g., FFQ and 24 hour recalls in one study, 30). PA was assessed in 11 of the 15 included studies (5-7, 22, 23, 25, 26, 28, 30-32) mainly via questionnaires (only one study used accelerometers, 23).

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Methodological limitations were stated in 5 studies (22, 23, 28, 29, 31). The main limitations were convenient and too small sample sizes, short study duration, recall bias in food records and PA questionnaires, reliance on self-report for dietary assessment, and questionnaire based estimation of energy assessment. Recommendations for future research were stated in 5 studies (10, 23, 29, 31, 32). The recommendations were larger sample sizes, matching of participants for skeletal age, bone mass and calcium intake, to use participants with calcium deficiency, to increase calcium intake, and use energy reducing diets.

Participant Characteristics

The final samples sizes (N, after dropouts) ranged from 28 to 698 participants (mean N = 135). 10 studies used less than 100 participants and 5 studies used 123 to 698 participants. In total, 2032 children and adolescents participated in the 15 studies included in this review. The sample comprised of females only in 7 studies (N=1157), males only in 1 study (N=28), and both sexes in 7 studies (N=857). The age of the participants ranged from 4.8 to 17 years, with over half of the studies (8 studies) including participants that were 10 years old or younger. Participants were described as overweight/obese in 4 studies (23, 28, 29, 31), and of normal weight in 1 study (22). In the remaining 10 studies, no data were reported about participants' weight classification; however, based on the reported anthropometric data, these participants, on average, can be considered normal weight. With the exception of one study (30), the health status of the participants was not stated; participants were reported as healthy in the other 14 included studies. The studies were undertaken in several countries including USA (6 studies), New Zealand (2 studies), China (2 studies) and the UK, Iran, Germany, Chile and Finland (1 study each) (Table 2).

Duration and Intervention (dairy, exercise/physical activity)

Study duration ranged from 3 weeks to 3 years; specifically, from 3 to 16 weeks in 4 studies, from 1 to 2 years in 8 studies, and greater than 2.5 years in 3 studies. Twelve studies had only an intervention period (3 weeks to 2 years) while the remaining 3 studies also included a follow-up period (from 1 to 2.5 years) (Table 2).

The dairy intervention involved the intake of milk in various quantities/servings in most of the studies. As shown in Table 1, 9 studies (5, 10, 23-27, 29, 31) used only milk as the dairy product in their interventions. The milk differed in terms of fat percentage (from 0% fat to full fat milk) and in the daily amount required to be consumed (from 236 ml to 900 ml). However, in 2 of these studies (24, 25), the intervention involved milk powder (enriched with calcium) of different amounts (80 gr in one study [24], and either 40 or 80 gr in another study [25]). The rest of the studies (6, 7, 22, 28, 30, 32) used other dairy products (i.e., yogurt and cheese) as well, along with milk in their intervention. With the exception of 2 studies (25, 32), all other studies reported participants' dietary calcium intake being between 650 mg/day (26) and 2076 mg/day (24), and in average 1330 mg/day with the dairy intervention. Volek et al. (27) was the only study where 12 weeks of milk consumption (3 servings/day, 708 ml of 1% milk, 1723 mg calcium/day) was combined with resistance training (1 hour x 3 times/week).

Measurements variables

Four main variables were measured in the 15 studies reviewed (Table 1) including: i) body size (height, sitting height, weight, waist & hip circumference-ratio, and BMI); ii) body composition (mainly LBM and FM) assessed by dual energy X-ray absorptiometry (DXA) in 9 studies (5-7, 22, 24, 25, 27, 29, 32), magnetic resonance imaging (MRI) in 1 study (31), and bioelectrical impendence analysis (BIA) in 1 study (28); iii) bone properties, mainly BMC and

BMD of total body and of different body sites, assessed by DXA in 9 studies (5-7, 24-27, 29, 32); peripheral quantitative computed tomography (pQCT) along with DXA in 1 study (32), and single/dual photo absorptiometry (SPA/DPA) in 2 studies (10, 30); and iv) biochemical markers (hormones, BTMs).

MAIN FINDINGS

From the 14 studies (5-7, 10, 22-32) assessing body size, only 2 studies found significant effects ($p<0.05$). Specifically, the study of Du et al. (26) found a significant increase ($p<0.05$) in height, sitting height, and weight in Chinese, 10 years old girls, after 2 years of dairy intervention. In contrast, the study of Albala et al. (29) examined the effects of 16 weeks dairy intervention in 8 to 10 years old overweight/obese boys and girls in Chile and found a significant increase in height for boys only. The same study by Albala et al. (29) was the only study from the 11 studies assessing as well body composition (5-7, 22, 24, 25, 27-29, 31, 32) that found a significant increase in LBM in both boys and girls. (Table 2). In fact, this study was the only study out of the 3 studies (23, 28, 31) examining the effects of dairy on body size and composition in overweight/obese boys and girls that found significant effects (Table 2).

From the 11 studies (5-7, 10, 24-27, 29, 30, 32) assessing bone mainly in normal weight boys and girls, 8 studies (5-7, 25-27, 30, 32) reported significant positive effects on BMD and BMC for total body and/or specific body sites (e.g., lumbar spine). Five of these studies (5, 26, 27, 30, 32) showed a significant increase in total body BMD ranging from 2.5% (after a 12-week intervention with dairy and 3 1-hour resistance exercise sessions per week) (27) to 13.4% (after a 1-year intervention) (30). Further, the other 2 of these 5 studies with 18-month intervention (5) and 2-year intervention (32) found 9.6% and 10.4% change in total body BMD, respectively, while 1 study with 2-year intervention (26) found a 3.2% increase in BMD after adjusting for size.

Biochemical markers, including hormones (e.g., parathyroid hormone [PTH], 25-OH vitamin D), BTMs including markers of bone formation (e.g., osteocalcin and bone specific alkaline phosphatase) and bone resorption markers (e.g., urinary calcium/creatinine ratio), and in a few cases inflammatory markers (C-reactive protein, leptin), were assessed in 8 studies (5-7, 26, 28, 30-32) (Table 1). Specifically, BTMs were assessed in 6 studies (5-7, 26, 30, 32) showing insignificant results in 4studies (5, 6, 30, 32) while some significant changes showed in only 2 studies (7, 26). Non-significant effects were also reported for the other biochemical markers with the exception of a significant increase in insulin growth factor-1 (IGF-1) in dairy group that was found in 1 study (5).

DISCUSSION

This review examined the outcomes of dairy consumption interventions in children and adolescents. Overall, the findings suggest positive effects of dairy consumption on bone properties with 8 of the 11 studies showing significant increases in BMC and BMD (total body and different sites). Specifically, the combined results of 5 of these studies show an average increase of about 8% in BMD after an average 16 months of dairy consumption (milk, yogurt, cheese) with calcium intakes of about 1000 mg/day. These 5 studies assessed BMD in boys and girls, 10 to 17 years old, mainly of normal weight and health status, and from different countries (e.g., USA, UK, and China). Some of these studies were included in previous reviews by Lanou et al. (9) and Huncharek et al. (12).

The positive effects of dairy consumption on bone related variables (BMD, BMC) can be attributed to significant increases in dietary calcium intake, with the latter being significantly higher in the dairy group compared to the control group in most of the included studies. For example, in the study by Chan et al. (6) the control group had a daily calcium intake of 728 mg compared to 1461 mg in the dairy group. However, significant treatment effects were also reported by Cheng et al (32) despite there being a non-significant difference in dietary calcium intake between the dairy (cheese) group and the calcium supplement (calcium carbonate tablets) group. Thus, the positive effects of dairy product consumption on bone might be better explained by the improved absorption of calcium from dairy due to the presence of lactose, casein phoshopeptides or vitamin D in dairy products (33).

There are various nutritional components found in dairy products that can affect bone structure and physiology. For example, calcium and protein can affect bone mineralization (through the formation of hydroxyapatite crystals) and collagen formation, respectively (34). According to a review by Tang et al. (35), experimental and observational studies have shown beneficial effects of high protein intake on bone health versus an increased risk of fracture with inadequate protein intake. In addition, the high calcium and vitamin D intake achieved via dairy products can lead to decreased circulating PTH, decreased bone turnover and increased bone mass (34). Specifically, PTH increases when blood calcium levels are low (i.e. due to low dietary calcium). This causes calcium to be released from the bones leading to bone resorption and eventually a reduction in BMD. The latter has been negatively correlated with the levels of serum PTH in adolescent males and females in the RCT by Renner et al. (30), who examined the effects of calcium intake through milk and milk products on BMD.

It is noteworthy that 4 of the studies (5, 6, 26, 32) reporting significant effects of dairy consumption on BMC and BMD did not also show significant effects on BTMs. One reason for this may relate to the relatively long duration (more than 1 year) of these RCTs. BTMs can respond to treatment quicker than BMD, so these can be better used in clinical trials measuring acute and shorter term effects (<6 months) of different treatment modalities such as diet and exercise (36-38). Another possible reason may be the relative difficulty in evaluating the magnitudes of changes in BTMs, as they are affected by a variety of factors such as puberty, growth, hormones, nutrition, exercise, circadian rhythm and sensitivity and specificity of assays (39).

In relation to body size and composition, there are few possible mechanisms through which the consumption of dairy products may have positive effects. First, a calcium and vitamin D interaction can affect adipocyte lipogenesis and lipolysis, as well as fat oxidation (40-42). Second, calcium can help decrease fat absorption and increase fat excretion (43). Third, calcium can help to regulate appetite and food-fat intake (44). A fourth mechanism may be related to the beneficial effects of various nutritional components found in dairy products such as branched chain amino acids (45) and medium chain triglycerides (46).

Despite the aforementioned mechanisms, dairy consumption did not show significant effects on body size and composition in most of the included RCTs. Specifically, only 2 (26, 29) of the 14 studies showed significant effects on height and weight, and only 1 (29) of the 11 studies that examined body composition found a significant increase in LBM. Specifically, Albala et al. (2008), who examined the effects of replacing the habitual consumption of sugar-sweetened beverages with milk for 16 weeks in Chilean overweight/obese boys and girls, could not show significant effects in body fat despite the significant increase in LBM. According to the authors, either the short duration of the intervention or the replacement of one energy-containing beverage for another affecting the energy reduction in participants diets, was the reason for not showing significant effects on body fat.

Certain design and methodological limitations of the included studies (Table 2) can explain, in part, why most of the effects, especially on body size and composition, were not significant. Some of these limitations have been previously mentioned (1-3). For example, most of the RCTs did not estimate sample size nor did they consider the experimental power required for detecting a significant effect. Thus, their sample size was relatively small, possibly explaining the non-significant findings.

As previously mentioned by Huang et al. (2), the lack of compliance monitoring in the RCTs can be another important reason for not finding significant effects. Most of the included studies did not report the compliance of their participants to the dairy intervention. On the other hand, compliance was relatively high (>80%) in the few studies where compliance was reported (e.g., 99% and 100% in studies 8 and 9, respectively). The assessment of dietary intake by using self-reporting methods, such as food records or recall, is another methodological weakness, which has been highlighted as a potential reason for not finding significant effects on FM in three studies (22, 28, 29).

The potential confounding effects of decisive factors such as energy intake, physical activity and puberty were not addressed in most of the relevant studies, and, as mentioned in previous reviews, may have affected the findings (2, 4, 13). For example, except for the study of Lappe et al (22), energy intake was not statistically controlled for in all other RCTs, and this might have obscured the effects of dairy on body composition. In addition, healthy eating or energy restriction was not necessarily recommended and not followed by participants in any of these RCTs assessing the effects of dairy consumption on body composition. As a result, this may be the main reason for not finding significant effects of increased dairy consumption on body composition. In keeping with this trend, Weaver et al. (23) suggested that areas of future research should include energy-reducing diets along with an increased dairy intake to adequately assess these effects. Other confounding factors, such as gender, puberty, and physical activity level, were controlled for in seven studies (5, 22, 25, 26, 29, 31, 32) but not all of the RCTs, which add to the limited acceptability of the composite results.

Even though most of the included studies scored quite well on the Jadad scale, future RCTs should address these methodological limitations in order to clarify both the statistical and the substantive significance of the findings. On the other hand, there is potential to improve the intervention models. For example, it has been previously suggested (23) that dietary interventions of higher calcium intake combined with energy restriction should be used in future RCTs, especially with overweight/obese participants. Thus, dairy consumption should be combined with healthy eating advice as well as exercise, in order to achieve a modest energy deficit or a stimulus for body composition change in a pediatric population. Indeed, exercise should be included in any intervention assessing the effects of dairy consumption on bone, as for example, in one of the included studies by Volek et al (27). As referred above, this study with 12 weeks dairy intervention (3 servings of milk per day) combined with resistance exercise (3 times per week) found significant effects in total body BMD even in relatively short period of time.

The present systematic review has two distinct advantages compared to previous relevant reviews: the exclusive use of RCTs, and the use of a standardized tool (Jadad scale) for the assessment of the methodological quality of the included studies. The Jadad scale has shown the best validity and reliability among other relevant scales assessing RCTs in health research (47). In addition, most of the methodological and statistical criteria used in this review were in accordance with the criteria proposed in AMSTAR, a reliable and valid tool for assessing the quality of systematic reviews (48, 49). Based on the 11 questions of this tool, the current systematic review took a score of 6, which is satisfactory considering that 30 randomly selected systematic reviews had scores between 3 and 10 (49). However, the present systematic review also has limitations. Our search was limited to two databases and included only studies published in English. Therefore, future systematic reviews on this topic may extend their search to more databases and potentially other languages.

The significance of this review relates to the importance of providing solid evidence about the role of dairy consumption on body size, body composition and bone properties in children and adolescents. In conclusion, it appears that dairy consumption has overall positive effects on bone structure and development in children and adolescents, but there is not enough evidence to support the beneficial role of dairy consumption on body size and composition in this population. Further research (mainly RCTs) overcoming the above limitations is needed to provide clear evidence on this critical issue.

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Table 1. Methodological and statistical characteristics of RCTs examining the effects of dairy on body size, body composition and bone in a pediatric population.

Studies (#/ Reference)	Sample size estimation- Power Calculation	Control group	Dropouts #, %	Adjustment for confounding	Effect size / Confidence Intervals	Diet, PA Assessment (Method)	Limitations	Recommendations
Lappe et al., 2004 (22)	No	Yes	4, 6.3 %	Yes (baseline weight, energy & protein intake)	No / No	Diet: 3 day food records (8 times), & daily checklist with calcium rich foods. PA: questionnaire	Pilot study, small sample size, self-report of dietary intake.	Not stated
Weaver et al., 2011 (23)	Yes (80 % power)	Yes	4, 9.5 %	Yes (sex)	No / No	Diet: 9 day food records (9 times), monitor of dietary intake at each meal by camp counsellors. PA: accelerometer	Convenient & relatively small sample, short-term study.	Intervention with higher calcium intake & energy reducing diets.
Chan et al., 1995 (6)	No	Yes	2, 4.2 %	No	No / No	Diet: 3 day food records (4 times) & FFQ. PA: questionnaire	Not stated	Not stated
Cadogan et al., 1997 (5)	No	Yes	2, 2.4 %	Yes (pubertal status)	No / Yes	Diet: 7 day food records with weighted method (2 times) & 4 days food records (5 times). PA: questionnaire	Not stated	Not stated
Merrilees et al., 2000 (7)	No	Yes	22, 21 %	No	No / No	Diet: 3 day food records, calcium FFQ, dairy products compliance questionnaire (5 times). PA: questionnaire	Not stated	Not stated
Gibbons et al., 2004 (24)	Yes (80 % power)	Yes	31, 20 %	No	No / No	Diet: calcium FFQ (5 times) and daily (milk product consumption) compliance check list.	Not stated	Not stated
Matkovic et	Yes	Yes	3, 9.6 %	No	No /	Diet: 3 day food records	Not stated	Larger samples,

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Studies (#/ Reference)	**Sample size estimation-Power Calculation**	**Control group**	**Dropouts #, %**	**Adjustment for confounding**	**Effect size / Confidence Intervals**	**Diet, PA Assessment (Method)**	**Limitations**	**Recommendations**
al., 1990 (10)	(80 % power)				No	(5 times)		matching of participants for skeletal age, bone mass and calcium intake.
Lau et al., 2004 (25)	No	Yes	20, 5.8 %	Yes (gender, baseline dietary calcium & protein intake, physical activity, puberty: Tanner stage)	No/ Yes	Diet: 3 day food records (3 times) and daily record of milk product consumption. PA: questionnaire	Not stated	Not stated
Du et al., 2004 (26)	No	Yes	59, 7.8 %	Yes (body and bone size e.g. height, weight, and puberty)	No / Yes	Diet: 7 day recall once & 3 day recall (4 times) and daily record of milk product consumption. PA: questionnaire	Not stated	Not stated
Volek et al., 2003 (27)	Yes	Yes	Not stated	No	No / No	Diet: 7 day food records (3 times) and daily record of milk product consumption.	Not stated	Not stated
Kelishadi et al., 2009 (28)	Yes (95 % power)	Yes	25, 25 %	No	No / No	Diet: 3 day food records (7 times) PA: questionnaire	Bias in recording food intake and answering PA questionnaire, estimation of energy expenditure with questionnaire, DXA for measuring body fat instead of using the gold standard method of underwater weighing.	Not stated

Studies (#/ Reference)	**Sample size estimation-Power Calculation**	**Control group**	**Dropouts #, %**	**Adjustment for confounding**	**Effect size / Confidence Intervals**	**Diet, PA Assessment (Method)**	**Limitations**	**Recommendations**
Albala et al., 2008 (29)	Yes (80 %)	Yes	5, 5.1 %	Yes (age, sex)	No / No	Diet: FFQ (2 times)	Small sample size & short intervention period, reliance on self-report for dietary assessment.	Larger samples
Renner et al., 1998 (30)	No	Yes	61, 32.1 %	No	No / No	Diet: FFQ & 24-hour food recall (once) PA: questionnaire	Not stated	Not stated
St-Onge, et al., 2009 (31)	No	No	16, 26.2 %	Yes (gender, race, age)	No / No	Diet: 24-hour food recall (7 times) PA: report of participation via recall method	Small sample size, short duration, possibly participants in different pubertal stage.	Longer duration of intervention.
Cheng et al., 2005 (32)	Yes (90 %)	Yes	22, 11.3 %	Yes (baseline puberty Tanner stage)	No / Yes	Diet: 3 day food records PA: questionnaire	Not stated	Future studies with calcium deficient participants.

DXA: Dual-energy X-ray absorptiometry, FFQ: food frequency questionnaire, PA: physical activity.

Table 2. RCTs on the effects of dairy with or without exercise on body size, body composition and bone properties in a pediatric population.

Studies	Participants				Study Duration	Intervention		Measurements - Variables (Assessment tool)	Main findings
	N*	Sex / Age†	Country	Weight		Diet (Dairy)	Exercise		
Lappe et al., 2004 (22)	59	F / 9.5, 9.1-9.9	USA	Normal weight	2 years	Ca rich foods (mainly dairy), average intake: 1656 mg Ca / day.	No	Height, weight, BMI, LBM & FM (DXA).	Non significant effects ($p>0.05$).
Weaver et al., 2011 (23)	38	F, M / 12-15	USA	Overweight, Obese (≥85 percentile of BMI for age)	3 weeks	Dairy (2 servings of chocolate milk/day) average intake: 1461 mg Ca / day (controlled diet)	No	Weight loss	Non significant effects ($p>0.05$).
Chan et al., 1995 (6)	46	F / 11, 9-13	USA	Not stated (possibly normal weight ‡)	1 year	Dairy (milk, cheese, yogurt), average intake: 1437 mg Ca / day.	No	Height, weight, LBM & FM (DXA), BMC, BMD of different sites (e.g. lumbar spine) (DXA), Serum calcium, magnesium, phosphate, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, albumin, Serum alkaline phosphatase, Urinary hydroxyproline, calcium/creatinine ratio).	Body size and composition: non significant effects ($p>0.05$). Significant increase in lumbar spine BMD (22.8 ± 6.9 %) & total body BMC (14.2 ± 7.0 %) ($p<0.001$). Biochemical markers: non significant effects ($p>0.05$).
Cadogan et al., 1997 (5)	80	F / 12.2, 11.8-12.5	UK	Not stated (possibly normal weight ‡)	18 months	Dairy (whole or reduced fat 568 ml milk, average	No	Height, weight, BMI, LBM & FM (DXA), Total body BMC & BMD (DXA),	Body size and composition: non significant effects ($p>0.05$)

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Studies	Participants				Study Duration	Intervention		Measurements - Variables (Assessment tool)	Main findings
	N*	Sex / Age†	Country	Weight		Diet (Dairy)	Exercise		
						consumption 486 ml / day), average intake: 1125 mg Ca / day.		Serum PTH, oestradiol, IGF-1, osteocalcin, urine N-telopeptide of type I collagen and Deoxypiridinoline cross link.	Significant increase in BMC (27 %, p = 0.009) & BMD (9.6 %, p = 0.0017). Significant increase in IGF-1 (p = 0.02).
Merrilees et al., 2000 (7)	73	F / 15-16	New Zealand	Not stated (possibly normal weight ‡)	3 years (1 interve-ntion & 2 follow-up)	Dairy (e.g. milk), average intake: 1160 mg Ca / day.	No	Height, weight, LBM & FM (DXA), Bones: BMC & BMD (total body & different sites) (DXA), Biochemical (bone) markers: (urine hydroxyproline, creatinine, calcium and sodium excretion, calcium/ creatinine & hydroxyproline/creatinine ratios).	Body size and composition: non significant effects (p>0.05). Significant increase in BMD of trochanter (4.6 %), lumbar spine (1.5 %) & femoral neck (4.8 %) after 1 year, and in BMC of trochanter after 2 years (p<0.05). Significant increase in creatinine (p<0.05).
Gibbons et al., 2004 (24)	123	F, M / 9.4, 8-10	New Zealand	Not stated (possibly normal weight ‡)	30 months (18 inter-vention, 12 follow-up)	Dairy (80gr milk powder), average intake: about 2076 mg Ca / day (1200 mg from milk & 876 mg from diet).	No	Height, weight, LBM & FM (DXA), BMC & BMD (total body & different sites: hip & spine) (DXA).	Non significant effects (p>0.05).

Studies	Participants				Study Duration	Intervention		Measurements - Variables (Assessment tool)	Main findings
	N*	Sex / Age†	Country	Weight		Diet (Dairy)	Exercise		
Matkovic et al., 1990 (10)	28	F/ 14	USA	Not stated (possibly normal weight ‡)	2 years	Dairy (900 ml milk 2 % fat / day), average intake: 1383.5 Ca mg / day.	No	Height, weight, Bone size, mass, BMD (single-SPA and dual-photo absorptiometry-DPA).	Non significant effects ($p>0.05$).
Lau et al., 2004 (25)	324	F, M / 10, 9-10	China	Not stated (possibly normal weight‡) /	18 months	Dairy (milk powder enriched with Ca: 1 group with 40 gr, 650 mg Ca / day, and 1 group with 80 gr, 1300 mg Ca /day).	No	Height, weight, LBM, FM (DXA), BMD g/cm^2 (total body and different sites: hip and spine) (DXA).	Body size and Composition: non significant effects ($p>0.05$). Significant effects (higher in 80gr group: 7.4% ± 0.4% vs 6.3% ± 0.4% in control group for hip BMD, 8.4% ± 0.5% vs 7.0% ± 0.5% in control group for spine BMD, lower in 40 gr group: 3.1% ± 0.3% vs 2.4% ± 0.2% in control group for total BMD) ($p<0.05$).
Du et al., 2004 (26)	698	F / 10, 9.7-10.4	China	Not stated (possibly normal weight ‡)	2 years	Dairy (milk fortified with Ca with or without Vit.D, average intake 144 ml / day), average intake: 650 mg Ca, 3.3 μg Vit.D / day.	No	Height, sitting height, weight, BMI, BMC, BMD (DXA), Plasma 25(OH)D, serum PTH, plasma & urine calcium, urine calcium/creatinine ratio.	Significant increase in height (0.6 %), sitting height (0.8 %), weight (2.9 %) ($p<0.05$). Significant increase in (size-adjusted) total body BMC (1.2%) and BMD (3.2 %), (more effects with the fortified milk with calcium & Vit. D), ($p<0.05$).

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Studies	Participants				Study Duration	Intervention		Measurements - Variables (Assessment tool)	Main findings
	N*	Sex / Age†	Country	Weight		Diet (Dairy)	Exercise		
									Significant increase in plasma 25(OH)D & urinary Ca in group consuming milk fortified with Ca & vit.D ($p<0.05$).
Volek et al., 2003 (27)	28	M / 14.3, 13-17	USA	Not stated (possibly normal weight ‡)	12 weeks	Dairy (3 servings, 708 ml of 1% milk / day), average intake: 1723 mg Ca.	Resi-stance training (1hour x 3 times / week)	Height, weight, LBM & FM (DXA), BMC & BMD (total body & different sites) (DXA).	Body size and composition: non significant effects ($p>0.05$). Significant effect (2.49 % increase) in total body BMD (0.028 g / cm^2 vs 0.014 g/cm^2 in treatment and control group, respectively) ($p<0.05$).
Kelishadi et al., 2009 (28)	95	F, M / 5.6, 4.8-6.2	Iran	Obese (≥95[th] percentile of BMI for age)	36 months (6 inter-vention, 30 follow-up)	Dairy (milk, cheese, yogurt rich diet), average intake: about 850 mg Ca/day)	No	Height, weight, waist circumference, BMI, body fat (BIA), C-reactive protein CRP.	Non significant effects ($p<0.05$). However, small increase in BMI, waist circumference in dairy group at follow up.
Albala et al., 2008 (29)	93	F, M / 8-10	Chile	Overweight-obese (≥ 85 percentile of BMI for age) Healthy	16 weeks	Dairy (3 servings, 600 ml of 1.5% milk / day), average intake: about 1650 Ca mg / day.	No	Height, weight, BMI, LBM & FM (DXA), Bone mass (DXA).	Significant increase in height only in boys ($p<0.05$). Significant increase in LBM (3.72%; 0.92 ± 0.10kg vs 0.62 ± 0.11kg) ($p=0.04$). Non significant effects in bone mass ($p>0.05$).
Renner et al., 1998 (30)	129	F, M / 15-16	Germany	Not stated	1 year	Dairy (milk, cheese, yogurt, low fat or not), average intake:	No	BMD (SPA), Serum follicular stimulating hormone (FSH), luteinizing hormone (LH) PTH, Ca,	Significant increase (13.4 %) in BMD in dairy group (0.053 vs 0.036 g / cm^2) ($p<0.05$),

Studies	Participants				Study Duration	Intervention		Measurements - Variables (Assessment tool)	Main findings
	N*	Sex / Age†	Country	Weight		Diet (Dairy)	Exercise		
						1400 Ca mg / day (1150 mg from dairy and 250 mg from other foods).		osteocalcin, alkaline phosphatase, Urine pyridine derivatives: pyridinoline and deoxypyridinoline.	Higher decrease in levels of PTH, alkaline phosphatase and osteocalcin in intervention group.
St-Onge, et al., 2009 (31)	45	F, M / 9.4, 8–10	USA	Overweight, Obese (≥85 percentile of BMI for age	16 weeks	Dairy (0-1% milk, high milk group with 944 ml / day & low milk group with 236 ml / day).	No	Height, weight, waist & hip circumferences- ratio, BMI, total adipose tissue, subcutaneous adipose tissue, visceral adipose tissue, intermuscular adipose tissue, and muscle mass (MRI), Serum leptin.	Non significant effects ($p<0.05$).
Cheng et al., 2005 (32)	173	F / 10-12	Finland	Not stated (possibly underweight, normal weight & overweight-obese ‡)	2 years	Dairy (mainly low fat cheese), average intake: 1413 mg Ca / day.	No	Height, weight, BMI, LBM & FM (DXA), BMC, areal & volumetric BMD (total body & different sites e.g. spine), cortical thickness of tibia etc (DXA, pQCT), Serum PTH, vit.D, leptin, BTMs, urine Ca.	Body size and composition: non significant effects ($p>0.05$). Significant increase in areal BMD (total body, 10.4% ± 0.5% g /cm^3) & cortical thickness of tibia (37.1% ± 1.3 % mm) ($p<0.05$). Biochemical markers: non significant effects ($p>0.05$).

*Sample after dropout (except study 10 that dropout is not stated), †Sex: Males (M), Females (F), Age (years) mean, range (in two studies: Cadogan et al., 1997, and Kelishadi et al., 2009, range calculated: minimum age = mean age - SD, maximum age = mean + SD), ‡ Based on BMI percentiles for the participants' (mean or range) age (BMI was calculated from the provided height & weight mean values in case that it was not available). BMI: Body Mass Index, BTMs: Bone Turnover Markers, Ca: Calcium, DXA: Dual-energy X-ray absorptiometry, F: Females, FM: Fat Mass, LBM: Lean Body Mass, M: Males, PTH: parathyroid hormone, pQCT: peripheral quantitative computer tomography, SPA: single photon absorptiometry.

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