1   **The effects of dairy consumption on body composition and bone properties in**

2   **youth: a systematic review**

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8   **Running title:** Dairy Interventions in Youth

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Abbreviations:

23   BMD: Bone Mineral Density,

24   BMC: Bone Mineral Content,

25   BMI: Body Mass Index,

26   BTMs: Bone Turnover Markers,

27   Ca: Calcium,

28   DXA: Dual-energy X-ray absorptiometry,

29   F: Females,

30   FM: Fat Mass,

31   FFQ: food frequency questionnaire,

32   IGF-1: Insulin growth factor 1

33   LBM: Lean Body Mass

34   M: Males

35   PA: physical activity,

36   PTH: parathyroid hormone,

37   pQCT: peripheral quantitative computer tomography,

38   RCTs: Randomized Controlled Trials

39   SPA: single photon absorptiometry

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43   **Tables:** 2

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45   **No conflicts of interest**

46 **ABSTRACT**

47 Background: According to previous reviews, there is no clear evidence about the effects of dairy

48 consumption on body composition and bone properties in pediatric populations. There is a need

49 for further assessment of existing findings and methodological quality of studies prior to

50 summarize the evidence.

51 Objective: To assess the quality, methodologies and substantive findings of randomized

52 controlled trials (RCTs) examining the effects of dairy consumption on body size, body

53 composition and bone properties in children and adolescents. Methods: After searching Pub Med

54 and Google scholar up to December 2016, 15 RCTs were retained and included in this systematic

55 review for further analysis. The quality of the included studies was assessed via the Jadad scale;

56 detailed methodological and statistical characteristics were evaluated and the main findings were

57 summarized.

58 Results: The effects of dairy consumption were found significant for bone structure, and non

59 significant for body size and composition. 8 of the 11 RCTs assessing bone found significant

60 effects ($p<0.05$) for bone mineral content (BMC) and bone mineral density (BMD), with an

61 average 8% increase in BMD after 16-months of dairy consumption. Conversely, significant

62 effects ($p<0.05$) were found only in 2 of the 14 RCTs focusing on body size, i.e. height and

63 weight, and in only 1 of the 11 RCTs focusing on body composition, i.e. lean mass.

64 Conclusions: The systematic consumption of dairy products may benefit bone structure and

65 development, but it does not appear to affect body composition or body size in children and

66 adolescents. Based on the Jadad scale, the methodological quality of the 15 RCTs was rated as

67 good overall. However, there were methodological disparities and limitations that may have led

68   to non significant results, particularly for body size and composition. Future RCTs designed to

69   address these limitations are warranted.

70

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

72

73 **INTRODUCTION**

74   Over the years there has been an increased interest in the effects of dairy on body

75 composition and bone development in humans. The results of the 4 following reviews, however,

76 are inconclusive for body composition possibly due to methodological limitations of the included

77 studies referring, for example, to study design, experimental power, compliance etc. In Barr's

78 review (1), which assessed 30 randomized controlled trials (RCTs) using dairy products or

79 calcium supplementation as the dietary intervention, only 3 RCTs focused on children (girls) and

80 found non-significant effects of dairy consumption on body composition. Their non significant

81 findings were attributed to inappropriate study designs, inadequate experimental power, and the

82 possible increase in energy intake with increased dairy consumption. Huang et al. (2) reviewed 5

83 observational studies and 10 RCTs examining the effects of dairy intake and calcium

84 supplementation on body composition in children. 3of the 5observational studies reported

85 significant effects of dairy and/or calcium intake on body composition. However, none of the 10

86 RCTs (3 RCTs used dairy products and 7 RCTs used calcium supplementation) showed

87 significant effects, mainly due to dietary report problems, lack of compliance monitoring, and the

88 confounding effects of other dietary variables (such as energy intake). A later review by Lanou

89 & Barnard (3) found similar insignificant effects of dairy consumption on body composition. It

90 assessed 49 RCTs, 18 of which were in children and adolescents, with only 5 of them using dairy

91 foods as opposed to calcium supplements. Finally, a recent systematic review and meta-analysis

92 of 36 observational studies and 4 RCTs showed modest effects of dairy intake on body

93 composition (adiposity) in adolescents but not in children (4).

94   The existing evidence for the positive effects of dairy consumption on bones in children

95 and adolescents is more conclusive, even though many of the relevant studies are

96 methodologically disparate. Early RCTs showed significant positive effects of dairy products

97 (e.g., milk) on bone related variables (e.g., bone mineral density [BMD] and bone mineral

98 content [BMC]) in pediatric populations (e.g., 5-7). Similarly, the longitudinal study by Fiorito et

99 al. (8) found calcium intake (especially from dairy foods) to have beneficial effects on BMC in

100 young girls. However, the review of Lanou et al. (9) proposed that the existing evidence does

101 not support the nutritional guidelines suggesting increased calcium/dairy intake for enhancing

102 bone mineralization in children and adolescents. Lanou et al. (9) assessed 58 studies (22 cross-

103 sectional, 13 retrospective, 10 longitudinal, and 13 RCTs) examining the effects of dairy product

104 consumption or calcium supplementation on bone health in children and young adults. 12 out of

105 13 RCTs had a minimum one-year treatment, and 9 RCTs examined the effects of calcium

106 supplementation. Only 3 of these 12 RCTs examined the effects of dairy products either in

107 combination with calcium supplements (in 1RCT by Matkovic et al., 1990) (10) or not (in 2

108 RCTs by Cadogan et al., 1997 and Chan et al., 1995, respectively) (5, 6). Further, 27 out of 37

109 studies in this review, that used dairy or dietary calcium intake and managed to control for

110 weight, pubertal status and exercise in children and young adults, showed no relationship

111 between dietary calcium or dairy intake and bone. As a result, the authors suggested the revision

112 of the pediatric recommendations on calcium and dairy intake due to the marginal effects on

113 bone (9, 11). In contrast, a later meta-analysis found that the increased consumption of dietary

114 calcium, via dairy products or supplements with and without vitamin D, significantly increased

115 total body and lumbar spine BMC in children with low baseline calcium intake (12). From the 21

116 RCTs assessed in this meta-analysis, only 4 studies though used dairy, mainly milk. As stated by

117 Huncharek et al. (12), the heterogeneity of the participants' diet and calcium intake (low, near

118 normal or normal intake) might have affected the findings of this meta-analysis. The same study

119   design limitation may also apply to the findings and conclusions of the previous reviews by

120   Lanou et al. (9, 11).

121   As mentioned in some previous relevant reviews (1, 13), there is a need for assessing the

122   methodological quality of the studies prior to summarizing the evidence. In fact, using only

123   RCTs for assessing whether an experimental treatment is effective, or not, may be more

124   appropriate (14). Therefore, the purpose of this review was to examine the potential impact of

125   dairy consumption on body size and composition, and on bone in children and adolescents using

126   exclusively RCTs. Additionally, this review assessed the quality of the methodologies and

127   summarized the findings of the included RCTs.

METHODS

128

Search and selection criteria - strategy

129

130   Two databases (PubMed and Google Scholar) were electronically searched for studies

131   suitable for this review up to December 2016. The search terms included different combinations

132   of relevant key words, namely dairy (consumption), body composition, bone, children,

133   adolescents, pediatric population.

134   The inclusion criteria were as follows: articles written in English; RCTs; pediatric

135   population (<18 years old); males or females, or both sexes; intervention including dairy

136   products; outcomes relevant to anthropometrics (e.g., height, weight, BMI), body composition

137   (e.g., lean body mass [LBM], fat mass [FM]), and bone measurements (e.g., BMD, BMC, and

138   bone turnover markers [BTMs]).

139   First, the titles of all the studies found in the databases were read and their relevance to

140   the topic of the review was assessed. Then the abstracts and the full texts of the relevant studies

141   were read in order to check whether all inclusion criteria were met. Lastly, the references of the

142   relevant studies as well as of previous systematic reviews and meta-analyses were checked to

143   locate additional studies.

144   **Data extraction and management**

145   Each study that met all of the inclusion criteria was subjected to the systematic extraction

146   of a number of key design, methodological, and statistical characteristics (Tables 1 and 2). The

147   methodological and statistical characteristics included sample size estimation/power calculation

148   (yes or no, and if yes the % of power), adjustment of confounding effects (yes or no, and if yes

149   the variables/covariates), control group (yes or no), dropouts (number of participants, %),

150   calculation of effect size and confidence interval CI (yes or no), diet/exercise assessment

151   (method of assessment), limitations and recommendations (if stated which or not stated) (Table

152   1).The design-specific characteristics were: i) sample size (N after dropout), and participants'

153   gender (males M, females F), age (mean/range years), country, weight profile (e.g., normal

154   weight, overweight or obese), and health status (healthy or not); ii) study duration (weeks,

155   months, years), iii) intervention: diet (dairy/calcium intake), and exercise (type, frequency,

156   duration, intensity); iv) measurements/variables (assessment tool); and v) main findings

157   (anthropometrics, body composition, and bone properties) (Table 2).

158   **Quality assessment: Jadad scale**

159   The quality of the included studies was assessed via the Jadad scale (15). This scale has

160   been used extensively in previous systematic reviews in various clinical areas, as for example in

161   obesity (16-18), due to its efficiency in assessing the methodological quality of RCTs (19). The

162   scale includes seven items leading to a 5-point scoring system that assesses the methodological

163 quality of RCTs according to criteria relevant to randomization, blinding, and dropouts.

164 Specifically, five questions are positively scored by adding one point each for the "yes" answers

165 or zero for the "no" answers, while the other two questions are negatively scored by either

166 subtracting one point for a positive answer or giving a zero for a negative answer (scores -1, -2:

167 bad quality, scores 0, 1: poor quality, scores 2, 3: good quality, score 4: very good quality, score

168 5: excellent quality).

169 **Included and excluded studies**

170 A total of 15 studies met all the inclusion criteria and included in this systematic review

171 (Tables 1 and 2). Studies that did not meet all of the inclusion criteria were excluded from

172 further analysis as for example, the study by Bonjour et al. (20), where participants were given a

173 variety of other calcium enriched foods, e.g., cakes, biscuits, along with dairy. Another example

174 of an excluded study was by Matkovic et al. (21), where the study design for examining the

175 effects of dairy consumption was not suitable (two designs were used in this study: an

176 observational for the assessment of the effects of high calcium diet with dairy, while an RCT for

177 the effects of calcium supplements).

178 **RESULTS**

179 **Assessing the quality of the included studies (Jadad scale)**

180 Most of the included studies were rated as good quality. 8 studies (6, 22-26, 29, 31) had a

181 score of 2, and 5 studies (5, 7, 10, 28, 32) had a score of 3. Only two studies (27, 30) had a score

182 of 1, indicating poorer quality. However, it has been previously demonstrated in one systematic

183 review (17) that the methodological quality of studies can be underestimated by 1-2 points using

184 the Jadad scale. Specifically, items 3 and 4 of this scale refer to blindness, which is not always

185 applicable to the type of research that assesses nutritional and exercise interventions. Overall, the

186 design quality of the 15 included RCTs was assessed as satisfactory for the purpose of this

187 review.

Methodological and Statistical Characteristics

189 The methodological and statistical characteristics of the included studies are summarized

190 in Table 1. Power analyses to estimate sample size were performed in seven studies. Specifically,

191 four studies (10, 23-24, 29) used a power of 80%, 2 studies (7, 32) used a power of 90%, and 1

192 study (28) used a power of 95%. A control group was implemented in all studies except in the

193 study of St-Onge et al. (31). 14 of the 15 reviewed studies reported dropouts. Dropouts were in

194 average 13.3% and ranged between 2.4% (5) and 32.1% (30).

195 Adjustments for confounding factors (puberty, age, gender, body and bone size, baseline

196 weight, energy, protein and calcium intake, physical activity [PA]) were made in 7studies (5, 22,

197 23, 25, 29, 31, 32). Effect size was not estimated and presented in any of the 15studies, and

198 confidence intervals were reported in 4 studies (5, 25, 26, 32). Dietary intake was assessed with

199 food records (3, 7 or 9 days, two to nine times during the study) in 10 studies (5-7, 10, 22, 23, 25,

200 27, 28, 32). In addition, 24 hour, 3 day and 7 day recalls were used in 3 studies (26, 30, 31), a

201 food frequency questionnaire (FFQ) for nutritional or calcium intake was used in 5 studies (6, 7,

202 24, 29, 30), and a daily record of dairy products consumption was used in 6 studies (7, 22, 24-

203 27). 8 out of the 15 included studies (6, 7, 22, 24-27, 30) used more than one nutritional

204 assessment tool (e.g., FFQ and 24 hour recalls in one study, 30). PA was assessed in 11 of the 15

205 included studies (5-7, 22, 23, 25, 26, 28, 30-32) mainly via questionnaires (only one study used

206 accelerometers, 23).

207   Methodological limitations were stated in 5 studies (22, 23, 28, 29, 31). The main

208   limitations were convenient and too small sample sizes, short study duration, recall bias in food

209   records and PA questionnaires, reliance on self-report for dietary assessment, and questionnaire

210   based estimation of energy assessment. Recommendations for future research were stated in 5

211   studies (10, 23, 29, 31, 32). The recommendations were larger sample sizes, matching of

212   participants for skeletal age, bone mass and calcium intake, to use participants with calcium

213   deficiency, to increase calcium intake, and use energy reducing diets.

214   **Participant Characteristics**

215   The final samples sizes (N, after dropouts) ranged from 28 to 698 participants (mean N =

216   135). 10 studies used less than 100 participants and 5 studies used 123 to 698 participants. In

217   total, 2032 children and adolescents participated in the 15 studies included in this review. The

218   sample comprised of females only in 7 studies (N=1157), males only in 1 study (N=28), and both

219   sexes in 7 studies (N=857). The age of the participants ranged from 4.8 to 17 years, with over

220   half of the studies (8 studies) including participants that were 10 years old or younger.

221   Participants were described as overweight/obese in 4 studies (23, 28, 29, 31), and of normal

222   weight in 1 study (22). In the remaining 10 studies, no data were reported about participants'

223   weight classification; however, based on the reported anthropometric data, these participants, on

224   average, can be considered normal weight. With the exception of one study (30), the health status

225   of the participants was not stated; participants were reported as healthy in the other 14 included

226   studies. The studies were undertaken in several countries including USA (6 studies), New

227   Zealand (2 studies), China (2 studies) and the UK, Iran, Germany, Chile and Finland (1 study

228   each) (Table 2).

229   **Duration and Intervention (dairy, exercise/physical activity)**

230   Study duration ranged from 3 weeks to 3 years; specifically, from 3 to 16 weeks in 4

231   studies, from 1 to 2 years in 8 studies, and greater than 2.5 years in 3 studies. Twelve studies had

232   only an intervention period (3 weeks to 2 years) while the remaining 3 studies also included a

233   follow-up period (from 1 to 2.5 years) (Table 2).

234   The dairy intervention involved the intake of milk in various quantities/servings in most

235   of the studies. As shown in Table 1, 9 studies (5, 10, 23-27, 29, 31) used only milk as the dairy

236   product in their interventions. The milk differed in terms of fat percentage (from 0% fat to full

237   fat milk) and in the daily amount required to be consumed (from 236 ml to 900 ml). However, in

238   2 of these studies (24, 25), the intervention involved milk powder (enriched with calcium) of

239   different amounts (80 gr in one study [24], and either 40 or 80 gr in another study [25]). The rest of

240   the studies (6, 7, 22, 28, 30, 32) used other dairy products (i.e., yogurt and cheese) as well, along

241   with milk in their intervention. With the exception of 2 studies (25, 32), all other studies reported

242   participants' dietary calcium intake being between 650 mg/day (26) and 2076 mg/day (24), and

243   in average 1330 mg/day with the dairy intervention. Volek et al. (27) was the only study where

244   12 weeks of milk consumption (3 servings/day, 708 ml of 1% milk, 1723 mg calcium/day) was

245   combined with resistance training (1 hour x 3 times/week).

246   **Measurements variables**

247   Four main variables were measured in the 15 studies reviewed (Table 1) including: i)

248   body size (height, sitting height, weight, waist & hip circumference-ratio, and BMI); ii) body

249   composition (mainly LBM and FM) assessed by dual energy X-ray absorptiometry (DXA) in 9

250   studies (5-7, 22, 24, 25, 27, 29, 32), magnetic resonance imaging (MRI) in 1 study (31), and

251   bioelectrical impendence analysis (BIA) in 1 study (28); iii) bone properties, mainly BMC and

252   BMD of total body and of different body sites, assessed by DXA in 9 studies (5-7, 24-27, 29,

253   32); peripheral quantitative computed tomography (pQCT) along with DXA in 1 study (32), and

254   single/dual photo absorptiometry (SPA/DPA) in 2 studies (10, 30); and iv) biochemical markers

255   (hormones, BTMs).

256   **MAIN FINDINGS**

257   From the 14 studies (5-7, 10, 22-32) assessing body size, only 2 studies found significant

258   effects ($p<0.05$). Specifically, the study of Du et al. (26) found a significant increase ($p<0.05$) in

259   height, sitting height, and weight in Chinese, 10 years old girls, after 2 years of dairy

260   intervention. In contrast, the study of Albala et al. (29) examined the effects of 16 weeks dairy

261   intervention in 8 to 10 years old overweight/obese boys and girls in Chile and found a significant

262   increase in height for boys only. The same study by Albala et al. (29) was the only study from

263   the 11 studies assessing as well body composition (5-7, 22, 24, 25, 27-29, 31, 32) that found a

264   significant increase in LBM in both boys and girls. (Table 2). In fact, this study was the only

265   study out of the 3 studies (23, 28, 31) examining the effects of dairy on body size and

266   composition in overweight/obese boys and girls that found significant effects (Table 2).

267   From the 11 studies (5-7, 10, 24-27, 29, 30, 32) assessing bone mainly in normal weight

268   boys and girls, 8 studies (5-7, 25-27, 30, 32) reported significant positive effects on BMD and

269   BMC for total body and/or specific body sites (e.g., lumbar spine). Five of these studies (5, 26,

270   27, 30, 32) showed a significant increase in total body BMD ranging from 2.5% (after a 12-week

271   intervention with dairy and 3 1-hour resistance exercise sessions per week) (27) to 13.4% (after a

272   1-year intervention) (30). Further, the other 2 of these 5 studies with 18-month intervention (5)

273   and 2-year intervention (32) found 9.6% and 10.4% change in total body BMD, respectively,

274   while 1 study with 2-year intervention (26) found a 3.2% increase in BMD after adjusting for

275   size.

276   Biochemical markers, including hormones (e.g., parathyroid hormone [PTH], 25-OH

277   vitamin D), BTMs including markers of bone formation (e.g., osteocalcin and bone specific

278   alkaline phosphatase) and bone resorption markers (e.g., urinary calcium/creatinine ratio), and in

279   a few cases inflammatory markers (C-reactive protein, leptin), were assessed in 8 studies (5-7,

280   26, 28, 30-32) (Table 1). Specifically, BTMs were assessed in 6 studies (5-7, 26, 30, 32) showing

281   insignificant results in 4studies (5, 6, 30, 32) while some significant changes showed in only 2

282   studies (7, 26). Non-significant effects were also reported for the other biochemical markers with

283   the exception of a significant increase in insulin growth factor-1 (IGF-1) in dairy group that was

284   found in 1 study (5).

285   **DISCUSSION**

286   This review examined the outcomes of dairy consumption interventions in children and

287   adolescents. Overall, the findings suggest positive effects of dairy consumption on bone

288   properties with 8 of the 11 studies showing significant increases in BMC and BMD (total body

289   and different sites). Specifically, the combined results of 5 of these studies show an average

290   increase of about 8% in BMD after an average 16 months of dairy consumption (milk, yogurt,

291   cheese) with calcium intakes of about 1000 mg/day. These 5 studies assessed BMD in boys and

292   girls, 10 to 17 years old, mainly of normal weight and health status, and from different countries

293   (e.g., USA, UK, and China). Some of these studies were included in previous reviews by Lanou

294   et al. (9) and Huncharek et al. (12).

295   The positive effects of dairy consumption on bone related variables (BMD, BMC) can be

296   attributed to significant increases in dietary calcium intake, with the latter being significantly

297 higher in the dairy group compared to the control group in most of the included studies. For

298 example, in the study by Chan et al. (6) the control group had a daily calcium intake of 728 mg

299 compared to 1461 mg in the dairy group. However, significant treatment effects were also

300 reported by Cheng et al (32) despite there being a non-significant difference in dietary calcium

301 intake between the dairy (cheese) group and the calcium supplement (calcium carbonate tablets)

302 group. Thus, the positive effects of dairy product consumption on bone might be better explained

303 by the improved absorption of calcium from dairy due to the presence of lactose, casein

304 phoshopeptides or vitamin D in dairy products (33).

305   There are various nutritional components found in dairy products that can affect bone

306 structure and physiology. For example, calcium and protein can affect bone mineralization

307 (through the formation of hydroxyapatite crystals) and collagen formation, respectively (34).

308 According to a review by Tang et al. (35), experimental and observational studies have shown

309 beneficial effects of high protein intake on bone health versus an increased risk of fracture with

310 inadequate protein intake. In addition, the high calcium and vitamin D intake achieved via dairy

311 products can lead to decreased circulating PTH, decreased bone turnover and increased bone

312 mass (34). Specifically, PTH increases when blood calcium levels are low (i.e. due to low dietary

313 calcium). This causes calcium to be released from the bones leading to bone resorption and

314 eventually a reduction in BMD. The latter has been negatively correlated with the levels of

315 serum PTH in adolescent males and females in the RCT by Renner et al. (30), who examined the

316 effects of calcium intake through milk and milk products on BMD.

317   It is noteworthy that 4 of the studies (5, 6, 26, 32) reporting significant effects of dairy

318 consumption on BMC and BMD did not also show significant effects on BTMs. One reason for

319 this may relate to the relatively long duration (more than 1 year) of these RCTs. BTMs can

320 respond to treatment quicker than BMD, so these can be better used in clinical trials measuring

321 acute and shorter term effects (<6 months) of different treatment modalities such as diet and

322 exercise (36-38). Another possible reason may be the relative difficulty in evaluating the

323 magnitudes of changes in BTMs, as they are affected by a variety of factors such as puberty,

324 growth, hormones, nutrition, exercise, circadian rhythm and sensitivity and specificity of assays

325 (39).

326   In relation to body size and composition, there are few possible mechanisms through

327 which the consumption of dairy products may have positive effects. First, a calcium and vitamin

328 D interaction can affect adipocyte lipogenesis and lipolysis, as well as fat oxidation (40-42).

329 Second, calcium can help decrease fat absorption and increase fat excretion (43). Third, calcium

330 can help to regulate appetite and food-fat intake (44). A fourth mechanism may be related to the

331 beneficial effects of various nutritional components found in dairy products such as branched

332 chain amino acids (45) and medium chain triglycerides (46).

333   Despite the aforementioned mechanisms, dairy consumption did not show significant

334 effects on body size and composition in most of the included RCTs. Specifically, only 2 (26, 29)

335 of the 14 studies showed significant effects on height and weight, and only 1 (29) of the 11

336 studies that examined body composition found a significant increase in LBM. Specifically,

337 Albala et al. (2008), who examined the effects of replacing the habitual consumption of sugar-

338 sweetened beverages with milk for 16 weeks in Chilean overweight/obese boys and girls, could

339 not show significant effects in body fat despite the significant increase in LBM. According to the

340 authors, either the short duration of the intervention or the replacement of one energy-containing

341 beverage for another affecting the energy reduction in participants diets, was the reason for not

342 showing significant effects on body fat.

343   Certain design and methodological limitations of the included studies (Table 2) can

344   explain, in part, why most of the effects, especially on body size and composition, were not

345   significant. Some of these limitations have been previously mentioned (1-3). For example, most

346   of the RCTs did not estimate sample size nor did they consider the experimental power required

347   for detecting a significant effect. Thus, their sample size was relatively small, possibly

348   explaining the non-significant findings.

349   As previously mentioned by Huang et al. (2), the lack of compliance monitoring in the

350   RCTs can be another important reason for not finding significant effects. Most of the included

351   studies did not report the compliance of their participants to the dairy intervention. On the other

352   hand, compliance was relatively high (>80%) in the few studies where compliance was reported

353   (e.g., 99% and 100% in studies 8 and 9, respectively). The assessment of dietary intake by using

354   self-reporting methods, such as food records or recall, is another methodological weakness,

355   which has been highlighted as a potential reason for not finding significant effects on FM in

356   three studies (22, 28, 29).

357   The potential confounding effects of decisive factors such as energy intake, physical

358   activity and puberty were not addressed in most of the relevant studies, and, as mentioned in

359   previous reviews, may have affected the findings (2, 4, 13). For example, except for the study of

360   Lappe et al (22), energy intake was not statistically controlled for in all other RCTs, and this

361   might have obscured the effects of dairy on body composition. In addition, healthy eating or

362   energy restriction was not necessarily recommended and not followed by participants in any of

363   these RCTs assessing the effects of dairy consumption on body composition. As a result, this

364   may be the main reason for not finding significant effects of increased dairy consumption on

365   body composition. In keeping with this trend, Weaver et al. (23) suggested that areas of future

366   research should include energy-reducing diets along with an increased dairy intake to adequately

367   assess these effects. Other confounding factors, such as gender, puberty, and physical activity

368   level, were controlled for in seven studies (5, 22, 25, 26, 29, 31, 32) but not all of the RCTs,

369   which add to the limited acceptability of the composite results.

370   Even though most of the included studies scored quite well on the Jadad scale, future

371   RCTs should address these methodological limitations in order to clarify both the statistical and

372   the substantive significance of the findings. On the other hand, there is potential to improve the

373   intervention models. For example, it has been previously suggested (23) that dietary

374   interventions of higher calcium intake combined with energy restriction should be used in future

375   RCTs, especially with overweight/obese participants. Thus, dairy consumption should be

376   combined with healthy eating advice as well as exercise, in order to achieve a modest energy

377   deficit or a stimulus for body composition change in a pediatric population. Indeed, exercise

378   should be included in any intervention assessing the effects of dairy consumption on bone, as for

379   example, in one of the included studies by Volek et al (27). As referred above, this study with 12

380   weeks dairy intervention (3 servings of milk per day) combined with resistance exercise (3 times

381   per week) found significant effects in total body BMD even in relatively short period of time.

382   The present systematic review has two distinct advantages compared to previous relevant

383   reviews: the exclusive use of RCTs, and the use of a standardized tool (Jadad scale) for the

384   assessment of the methodological quality of the included studies. The Jadad scale has shown the

385   best validity and reliability among other relevant scales assessing RCTs in health research (47).

386   In addition, most of the methodological and statistical criteria used in this review were in

387   accordance with the criteria proposed in AMSTAR, a reliable and valid tool for assessing the

388   quality of systematic reviews (48, 49). Based on the 11 questions of this tool, the current

389   systematic review took a score of 6, which is satisfactory considering that 30 randomly selected

390   systematic reviews had scores between 3 and 10 (49). However, the present systematic review

391   also has limitations. Our search was limited to two databases and included only studies published

392   in English. Therefore, future systematic reviews on this topic may extend their search to more

393   databases and potentially other languages.

394   The significance of this review relates to the importance of providing solid evidence

395   about the role of dairy consumption on body size, body composition and bone properties in

396   children and adolescents. In conclusion, it appears that dairy consumption has overall positive

397   effects on bone structure and development in children and adolescents, but there is not enough

398   evidence to support the beneficial role of dairy consumption on body size and composition in

399   this population. Further research (mainly RCTs) overcoming the above limitations is needed to

400   provide clear evidence on this critical issue.

401

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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,

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)

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 intervention & 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 intervention, 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).

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.	Resistance 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 (≥95th percentile of BMI for age)	36 months (6 intervention, 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.