Supplement Article

Dairy products, yogurt consumption, and cardiometabolic risk in children and adolescents

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The high prevalence of obesity in children is a global health issue. Obesity in children and adolescents can result in hypertension, dyslipidemia, chronic inflammation, and hyperinsulinemia, increasing the risk of death, as children grow into adulthood, and raising public health concerns. Type 2 diabetes in children and adolescents is a cardiovascular disease (CVD) risk factor. Dairy consumption may have a protective effect against the development of CVD, but there is scarce evidence of this in children and adolescents. Within the Healthy Lifestyle in Europe by Nutrition in Adolescence, the objective of this study was to investigate the relationship between dairy consumption and CVD risk factors in a sample of adolescents (aged 12.5–17.5 years) from 8 European cities. Overall, dairy products emerged as the food group that best identified adolescents at low CVD risk. Higher consumption of milk and yogurt and of milk- and yogurt-based beverages was associated with lower body fat, lower risk for CVD, and higher cardiorespiratory fitness.

INTRODUCTION

Obesity is an excess of body fat. In practice, methods to define or measure excess body fat in children and adolescents have limitations.[1] Children grow at different rates at different times, making obesity in children and adolescents difficult to define.[2] In addition, the definitions of overweight and obesity in children differ among epidemiological studies, hindering comparisons with cross-sectional prevalence data.[1] Despite its limitations, the body mass index (BMI) is the most widely used index to assess excess body fat in epidemiological studies. In developed countries, obesity prevalence steadily increased until around the year 2000; currently, it appears to have stabilized or even decreased in some countries.[3,4] A growing number of developing countries are affected by the double burden of malnutrition in which undernutrition and overnutrition (overweight and obesity) coexist in the same communities and families.[5]

As with adults, obesity in children and adolescents can result in hypertension, dyslipidemia, chronic inflammation, and hyperinsulinemia, increasing the risk of death, as children grow into adulthood, and raising public health concerns.[6] This clustering of cardiovascular disease (CVD) risk factors, known as the insulin resistance syndrome (metabolic syndrome), has been recognized in early life.[7] A decade ago, type 2 diabetes accounted for <3% of all new cases of diabetes in adolescents; today, type 2 diabetes accounts for approximately 45% of new cases.[8] Some studies have suggested that dairy consumption and its contribution to calcium intake may have a protective effect against the development of CVD.[9] However, dairy fat is often also portrayed as a negative component of milk and dairy products,[10] and some research has

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suggested an increased risk of obesity with frequent dairy consumption.[11] There is a lack of consistent evidence of the effect that dairy consumption has on obesity and CVD risk in adults. The consumption of yogurt and other dairy products in observational studies is associated with a reduced risk of weight gain and obesity, as well as of CVD, and these findings are, in part, supported by randomized trials.[12,13] There is an even greater lack of data to address this possible association in children and adolescents. The aim of the present review is to address the available information on the association between dairy products intake, especially yogurt intake, and cardiometabolic risk factors in children and adolescents, focusing on results from adolescents who participated in the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study.[14]

DAIRY CONSUMPTION, OBESITY, AND CARDIOMETABOLIC RISK IN CHILDREN AND ADOLESCENTS

The Committee on Nutrition of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition reviewed the literature and, in 2011, concluded that "available evidence does not allow recommendations on the role of calcium or dairy products in the development of obesity."[15] In a more recent review that focused specifically on children and adolescents,[16] it was found that 34 of 35 observational and intervention studies reported null or inverse associations between dairy intake and BMI, body fat, or energy balance. Four of 5 randomized control trials (RCTs) that were included in the review showed no positive associations between dairy intake and measures of adiposity, while 1 trial showed an inverse association. Twenty-three of the 35 studies included in the review analyzed data collected in the United States. The authors concluded that despite concerns that energy provided by dairy products may contribute to childhood obesity, the evidence overwhelmingly supports a null or inverse association between milk or dairy product intake and indicators of adiposity.[16]

Dairy products have also been shown to have antihypertensive effects as the result of the unique proteins and peptides they contain (angiotensin-converting enzyme [ACE] inhibitory peptides).[17,18] Two prospective cohort studies found that children who consume more dairy products early in life (age range, 18–59 months) have lower blood pressure in middle childhood and early adolescence.[19,20] Milk fat increases high-density lipoproteins,[21] which are thought to be protective against CVDs, and some of the saturated fats present in milk fat have a neutral effect on low-density lipoproteins,[22] which constitute a recognized risk factor.

FINDINGS OF THE HEALTHY LIFESTYLE IN EUROPE BY NUTRITION IN ADOLESCENTS STUDY

Within the HELENA study, the current analysis of data was undertaken to investigate the relationship between dairy consumption and CVD risk factors in a sample of adolescents (age range, 12.5–17.5 years) from 8 European cities (Athens, Greece; Dortmund, Germany; Ghent, Belgium; Lille, France; Rome, Italy; Stockholm, Sweden; Vienna, Austria; and Zaragoza, Spain). The cross-sectional HELENA study was conducted between 2006 and 2007.[14] Measurements were obtained for diet, waist circumference, skin-fold thicknesses (biceps, triceps, subscapular, suprailiac), systolic blood pressure, insulin resistance, triglycerides, total cholesterol/high-density lipoprotein ratio, and cardiorespiratory fitness for a subset (511) of 3528 adolescents. Approximately half of the subset was composed of males. Due to the lack of appropriate criteria to define the metabolic syndrome in children and adolescents, it has been suggested that clustering CVD risk factors may be an adequate measure of cardiovascular health. Individual, sex-specific z-scores of CVD risk factors, considering systolic blood pressure, sum of 4 skin-fold thicknesses (bicipital, tricipital, subscapular, and suprailiac), serum triglyceride concentrations, total cholesterol to HDL-cholesterol ratio, Homeostatic Model Assessment index, and cardiorespiratory fitness, were summed to compute sex-specific clustered CVD risk scores.[23] Cardiorespiratory fitness was multiplied by -1 to indicate higher CVD risk with increasing value. The lower the score, the better the overall CVD risk factor profile. Because this was a multicenter study, both intra- and interobserver reliability of anthropometric measurements were assessed and found to be 95% and 90%, respectively.[24]

Dietary intakes were assessed using the validated HELENA dietary assessment tool (DIAT),[25] which includes two 24-hour recalls (1 weekday and 1 weekend day). The participants' usual consumption of food groups was estimated using the multiple source method.[26] The adolescents completed the 24-hour recall twice (time-span of 2 weeks) during school time; at both times, trained staff, including a dietitian, were present. The HELENA-DIAT incorporated special techniques to support and enhance respondents' memory, which allowed a more detailed description and quantification of the dishes/foods consumed. HELENA-DIAT was validated in European adolescents[25] ($r_s = 0.86$–0.91, for all nutrients and energy intake). The "milk" food group included both milk and buttermilk, and the "yogurt and milk- and yogurt-based beverages" group included yogurt, yogurt- and milk-based beverages such as chocolate milk and probiotic beverages, and "fromage blanc."[14] Cheese and milk-based desserts were considered as 2 separate food groups due to their differing nutrient composition. No distinctions regarding the fat content in any of the 2 food groups was made.

Concerning confounding variables, in brief, socioeconomic status was estimated by means of the family affluence scale, which is based on the concept of material conditions in the family including car ownership, bedroom occupancy, home computers, and internet access. The average time engaged in 2 sedentary behaviors (TV viewing and playing video games) was estimated by means of a self-administered questionnaire. Uniaxial accelerometers (Actigraph MTI, model GT1M, Manufacturing Technology Inc., Fort Walton Beach, FL, USA) were used to objectively measure physical activity. At least 3 days of recording, with a minimum of 8 hours of registration per day, was set as an inclusion criterion. Time spent at moderate-to-vigorous physical activity (>3 metabolic equivalents) was calculated through the following cutoff point: 2000 counts per minute for moderate-to-vigorous physical activity.

In comparison to the rest of the food groups, milk, yogurt, and milk- and yogurt-based beverages accounted for greater variability for most CVD risk factors in both male and female adolescents.[14] Multiple linear regressions were performed to examine the association of individual CVD risk factors and CVD risk score (dependent variables) with dairy consumption (independent variables). Confounders adjusted for in the analyses included the following: socioeconomic status, pubertal maturity, moderate-to-vigorous physical activity, sedentary behavior, and daily energy intakes. In agreement with data from other studies that reported an inverse association between dairy consumption and waist circumference in adolescents,[27,28] waist circumference for both adolescent boys and adolescent girls was significantly greater among those in tertile 1 of total dairy consumption compared with those in tertile 3. In adolescent girls, greater consumption of yogurt was associated with a lower z-score for waist circumference. The association was greater among adolescent girls for both waist circumference and skin-fold thicknesses when the milk group was added to yogurt and yogurt-based beverages. A positive association between consumption of foods in the yogurt group and cardiorespiratory fitness was also observed among adolescent girls. Among adolescent boys, there was an inverse association between overall dairy consumption and both the sum of skin-fold thickness measurements and cardiorespiratory fitness.

In addition to previously published findings,[8] additional analyses were performed on 1422 adolescents (44.95% male) aged 12.5–17.5 years, focusing on body composition, with complete measurements for waist circumference, skin-fold thicknesses, and two 24-hour dietary recalls (S. Bel-Serrat and L. A. Moreno, unpublished data). Greater overall dairy consumption was associated with lower BMI, reduced skin-fold thicknesses, and smaller waist circumference (Figures 1–3). Pubertal maturity, study center, socioeconomic status, sedentary behavior, physical activity, and daily energy intake were confounders that were corrected for in the analyses.

Overall, dairy emerged as the food group that best identified adolescents at low CVD risk. Higher consumption of milk, yogurt, and milk- and yogurt-based beverages was associated with lower body fat and higher cardiorespiratory fitness. Despite its contributions to nutrient intake and evidence suggesting that intake may help reduce the risk of overweight and obesity along with other CVD risk factors, consumption of milk and dairy products by children and adolescents has decreased in many countries in recent decades.[16] A substantial proportion of children and adolescents now fail to meet even minimum recommendations for intake of dairy foods, and consumption tends to decrease with age through childhood and early adolescence.

Discrepant results among studies[10] could be due to differences in dietary assessment methods and the food items/groups considered in every study. In a systematic review of the association between dairy intake and adiposity in children and adolescents, 36 relevant studies were identified.[13] Sufficient data for effect size estimation and inclusion in the metaanalyses were obtained from 22 studies. In the reviewed studies that contained data on adolescents, 9 were cross-sectional, 4 were longitudinal, and 2 were RCTs. To assess dietary intake in the cross-sectional studies, 6 used the 24-hour recall method, 2 used a food frequency questionnaire, and 1 used dietary records; 3 longitudinal studies used a food frequency questionnaire and 1 used dietary records. Concerning the exposure, 8 considered milk alone and the remaining 7 considered dairy products in general.

Possible mechanisms

Several potential mechanisms have been suggested to explain the association between dairy consumption and indicators of body composition and reduced risk of CVD in humans. One mechanism may be the shift in food consumption patterns observed in children in recent decades. The Bogalusa Heart Study[29] revealed a significant decrease in the amount of milk consumed by US children, whereas the amounts of beverages and fruit/fruit juices consumed increased significantly. The decrease in milk consumption, concomitant with the increased consumption of sugar-sweetened beverages,

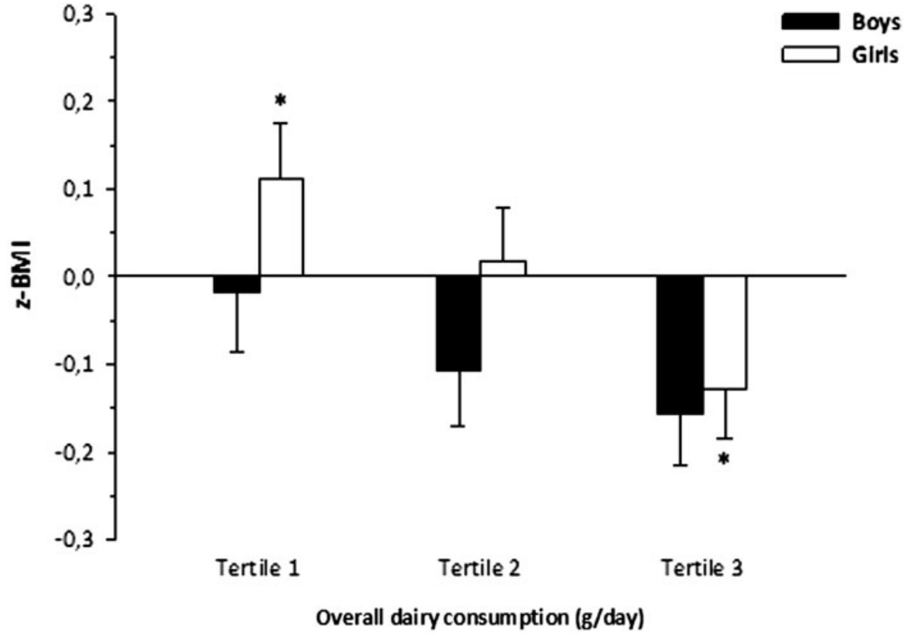

Figure 1 **Relationship between body mass index *z*-score and dairy consumption (g/day) in adolescent (12.5–17.5 years) boys and girls from 8 European cities participating in the Healthy Lifestyle in Europe by Nutrition in Adolescence Study.** Dairy consumption was divided into tertiles of consumption. Data are expressed as mean ± standard error. Asterisk indicates differences between tertiles of intake at $P < 0.05$. *Abbreviation*: BMI, body mass index.

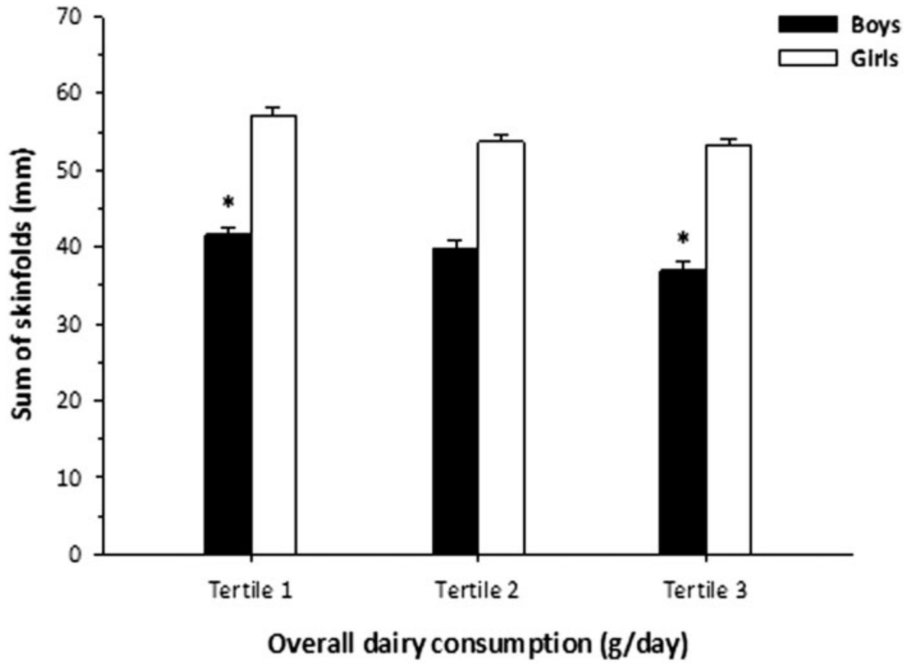

Figure 2 **Relationship between sum of skin-fold thicknesses (mm) and dairy consumption (g/day) in adolescent (12.5–17.5 years) boys and girls from 8 European cities participating in the Healthy Lifestyle in Europe by Nutrition in Adolescence Study.** Dairy consumption was divided into tertiles of consumption. Data are expressed as mean ± standard error. Asterisk indicates differences between tertiles of consumption at $P < 0.05$.

may be responsible, in part, for the hypothesized inverse relationship between dairy intake and obesity in both children and adolescents.[30] According to Huang et al.,[30] 3 energy-dependent effects have been hypothesized to occur when milk is replaced with sugar-sweetened beverages: 1) increased energy intake by consuming more calories per common serving and due to the typically larger serving sizes of these beverages compared with

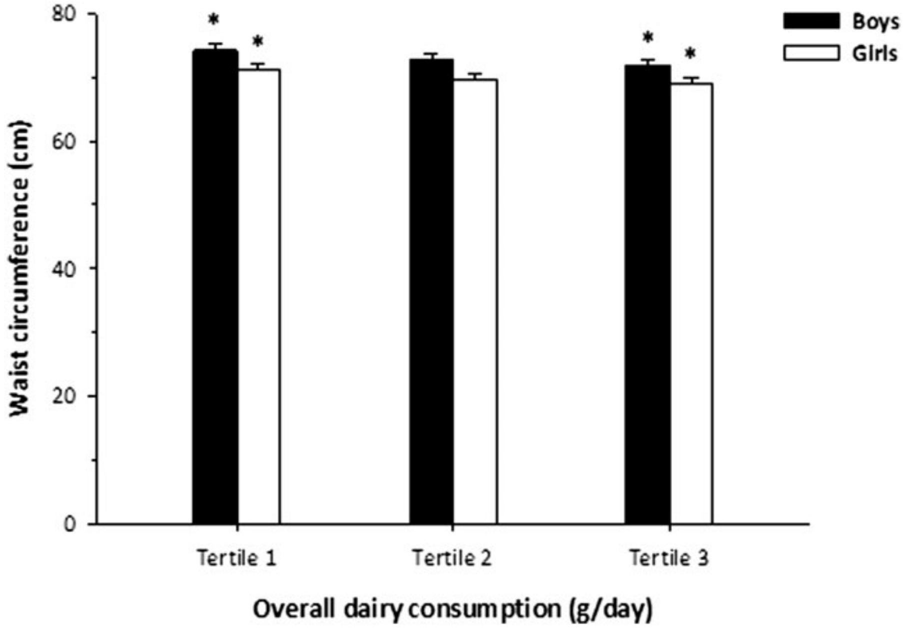

Figure 3 **Relationship between waist circumference (cm) and dairy consumption (g/d) in adolescent (12.5–17.5 years) boys and girls from 8 European cities participating in the Healthy Lifestyle in Europe by Nutrition in Adolescence Study**. Dairy consumption was divided into tertiles of consumption. Data are expressed as mean ± standard error. Asterisk indicates differences between tertiles of consumption at $P < 0.05$.

milk; 2) decreased satiety with consumption of high-sugar beverages, resulting in a higher intake of other foods and energy; or 3) lower energy expenditure linked to the consumption of high-sugar beverages. In support of hypothesis 2, Huang and McCrory[30] referred to a study in adolescents which found that compared with caffeinated or noncaffeinated sodas, low-fat milk intake yielded lower postprandial glucose, insulin, and free fatty acid responses, as well as lower scores of hunger and desire to eat.[31] Recently, it was observed that frequent yogurt consumption was associated with a high-quality diet, leading also to a healthier insulin profile in children.[32]

In addition, it has been suggested that several components naturally present in dairy foods, such as calcium, play a protective role in weight management. Numerous researchers have investigated the hypothesis of an inverse relationship between calcium intake and body weight, weight gain, and/or percent fat.[33] Several mechanisms have been proposed to explain the influence of calcium intake on body weight and/or body fat. While some mechanisms are related to whole-body energy balance, i.e., fecal fat excretion and appetite control, others seem to be linked to cellular processes such as fat mobilization and oxidation.[33] Dietary calcium may contribute to a negative energy balance through its ability to decrease intestinal fat absorption and elevate the amount of fatty acids eliminated in the feces, which consequently has a beneficial effect on circulating lipids.[33] That effect is attributable to the formation of insoluble calcium–fatty acids soaps, which then pass unabsorbed through the intestinal track.[33] Moreover, dietary calcium could also modulate body weight and/or body fat through an influence on appetite control. However, the satiating effect of calcium and/or dairy supplementation has not been confirmed in all of the studies conducted in this regard, and it is not clear whether that effect is due to calcium or to the food matrix present in dairy foods.[33] In terms of cellular mechanisms, Zemel[34] proposed that high-calcium diets attenuate body fat accumulation and weight gain by mediating circulating calcitriol, a regulator of adipocyte intracellular Ca^{2+}. Increased intracellular Ca^{2+} stimulates lipogenic gene expression and lipogenesis and suppresses lipolysis, which results in adipocyte lipid filling and increased adiposity. The increased calcitriol produced in response to low-calcium diets stimulates adipocyte Ca^{2+} influx-promoting adiposity, while higher calcium intakes inhibit lipogenesis; promote lipolysis, lipid oxidation, and thermogenesis; and inhibit diet-induced obesity.[34] An effect of dietary calcium on increased energy expenditure and thermogenesis has also been investigated; however, all studies have failed to confirm this hypothesis.[35] An inverse association between frequency of dairy consumption and serum inflammatory markers such as C-reactive protein, interleukin-6, and tumor necrosis factor-α was found in healthy individuals; however, not all studies support that hypothesis.[33]

Furthermore, it has been shown that dairy sources of calcium exert greater effects in accelerating fat loss compared with other food sources. This could be explained, in part, by several bioactive compounds present in the whey fraction of dairy, such as ACE inhibitors and branched chain amino acids (BCAAs), e.g., leucine, that act synergistically with calcium to attenuate weight and fat gain.[34] Whey proteins account for 20% of milk proteins, and lactoglobulin comprises about half of the total protein present in whey from cow's milk.[36] Whey proteins, specifically α-lactorphin and β-lactorphin, derived from α-lactoglobulin and β-lactoglobulin, respectively, together with albutensin, appear to have ACE inhibitory activity. These peptides are considered to be potent ACE inhibitory peptides because they are absorbed intact from the intestine to reach their target organ.[37] Casein-derived peptides, known as casokinins, have also been shown to have hypotensive effects.[36] Taking these findings into consideration, food-derived peptides would represent a safe option for decreasing high blood pressure.[37]

Dairy proteins seem to support better muscle protein synthesis than plant proteins.[37] Dairy foods, mainly whey proteins, contain the highest concentration of BCAAs, especially leucine, of all dietary proteins.[38] BCAAs have been found to be mostly available for protein synthesis, and, among them, leucine has been recognized as a potent stimulator of muscle protein synthesis.[38] This enhanced anabolism caused by milk proteins could potentially increase energy expenditure, but no conclusion can be drawn yet in this regard.[38] Additionally, leucine may also play a role in the repartitioning of dietary energy from adipose tissue to skeletal muscle, promoting fat loss.[39]

Conjugated linoleic acid (CLA) is present in dairy foods derived from ruminant sources. Many studies have shown a role of CLA in modulating body composition, especially by reducing the accumulation of adipose tissue.[39] Studies conducted in humans revealed that supplementation with CLA for short periods of time, i.e., no longer than 12 weeks, reduced body weight and body fat.[40] Available data suggest that CLA enhances sympathetic nervous activity, leading to increased energy metabolism and reduced adipose tissue mass.[40] Additionally, CLA's ability to reduce adipose tissue mass has been linked with induction of adipocyte apoptosis and/or differentiation and reduction of triglyceride accumulation in adipocytes.[40]

The consumption of yogurt may ensure changes in the balance and metabolic activities of the indigenous microbiota.[41] It has been observed that the intestinal microbiota in children who are overweight/obese is different from those with a BMI within normal ranges[42] or in lean children.[43] It has also been suggested that abnormal development of gut microbiota could contribute to the development of obesity during childhood.[44] Also in children and adolescents, consumption of a synbiotic that includes *Lactobacillus* spp. and *Bifidobacterium* sp. was shown to have a beneficial effect on weight control and cardiometabolic risk.[45] Mechanisms to explain the effect of probiotics in weight control are not yet clear; however, it seems they could be related to an interaction with the gut microbiota, thus affecting the metabolic pathways implicated in fat metabolism.[46] In humans, yogurt consumption may lead to changes in the equilibrium and metabolic activity of gut microbiota.[47,48]

CONCLUSION

In the HELENA study of adolescents in Europe, an inverse association was observed between consumption of yogurt and of milk- and yogurt-based beverages and some CVD risk factors, especially total and abdominal excess body fat. The association was stronger when milk intake was added to dairy product intake. To date, most of the data on dairy intake and health outcomes has been obtained from observational studies performed in the United States. More studies are needed in which yogurt is considered as an individual food category, which typically has not been the case. RCTs are also needed to provide evidence to support the HELENA findings and to further understand the mechanisms underlying the associations between dairy (especially yogurt) intake and obesity, diabetes, and other CVD risk factors.

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