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ORIGINAL ARTICLE

Associations of sugar-containing beverages with asthma prevalence in 11-year-old children: the PIAMA birth cohort

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BACKGROUND/OBJECTIVES: Recently, a few studies have linked soft drink consumption to increased asthma risk, but the contribution of different types of soft drinks is unknown. We investigated cross-sectional associations between six different types of soft drinks and asthma in 11-year-old children.

SUBJECTS/METHODS: We analyzed data of 2406 children participating in the Dutch Prevention and Incidence of Asthma and Mite Allergy birth cohort. At age 11, children self-reported consumption of sugar-added drinks, diet drinks, sweetened milk drinks, 100% fruit juice, energy drinks and sport drinks. The definition of asthma was based on parental reports of wheezing, prescription of inhaled corticosteroids and doctor's diagnosis of asthma.

RESULTS: The prevalence of asthma in this study was 5.8%. In adjusted logistic regression analyses, asthma risk was increased for high (⩾10 glasses/week (gl/wk) versus low (<4 gl/wk) consumption of 100% fruit juice (odds ratio (OR): 2.09, 95% confidence interval (CI): 1.21–3.60), sugar-added drinks (OR: 1.56, 95%CI: 0.95–2.56) and for very high (>21.5 gl/wk) versus low (<12.5 gl/wk) total sugar-containing beverage (SCB) consumption (OR: 1.91, 95%CI: 1.04–3.48). Consumption of other beverages and consumption of fruit were not associated with increased asthma risk. No evidence for mediation of the observed associations by body mass index was found.

CONCLUSIONS: This study indicates that high consumption of 100% fruit juice and total SCBs is associated with increased asthma risk in children. The positive association between consumption of 100% fruit juice and asthma is an unexpected finding that needs confirmation in future studies.

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INTRODUCTION

Worldwide, the prevalence of asthma tends to increase as communities adopt western lifestyles.[1] It has been suggested that a western diet may be one of the factors responsible for this increase.[2,3] Previous research on nutrition and asthma has mainly focused on the role of antioxidants and different fatty acids.[4] Recently, some studies showed evidence for a positive association between sugar-sweetened beverages and asthma in Swedish pre-school children,[5] US high-school students[6] and Australian adults.[7]

Two potential mechanisms for the association between soft drinks and asthma have been suggested in these studies.[6,7] Soft drinks contain high amounts of sugar that might promote inflammation.[8] Another possible mechanism involves sodium benzoate, a preservative present in soft drinks.[6] The consumption of beverages containing sodium benzoate has been associated with worsening asthma symptoms.[9]

A limitation of the previous studies is that they could not differentiate types of soft drinks, such as diet drinks, 100% fruit juice and energy drinks. The aim of our study in 11-year-old Dutch children was to provide further insight into the association between consumption of sugar-containing beverages (SCBs) and asthma. We studied six different types of beverages in relation to asthma. In addition, we investigated the role of body mass index (BMI) as a possible explanatory mechanism in the association between beverage consumption and asthma.

METHODS

Study population

This study used data of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort. For the PIAMA study, pregnant women were recruited from the general population, their children ($n = 3963$ at baseline) were born in the year 1996/1997. Parents were asked to complete questionnaires yearly up to the age of 8 years and again at the age of 11 years. At age 11 years, the children also completed a questionnaire themselves. In subgroups of children, medical examinations, including blood sampling, were conducted at ages 1, 4, 8 and 12 years. Details of the PIAMA study have previously been published.[10,11] The study protocol was approved by the medical ethical committees of the participating institutions, and all parents gave their written informed consent.

The present cross-sectional study used data from questionnaires completed by parents and children at age 11 years, and data from the clinical measurements at age 12 years. At age 11 years, 3541 families were still in the study and received questionnaires. In total, 2651 children (74.9%) completed their questionnaire, including detailed questions on beverage consumption. Data on asthma symptoms were obtained from the parental questionnaires. Children with information on their asthma status and on the consumption of at least one beverage were included in this study ($n = 2430$). Information on milk allergy was collected by parental

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report at the child's age 11 years. Parents reported whether the child ever tested positive for allergy, for which specific allergy, and whether the child was still allergic. In addition, parents reported whether the child was restricted to follow a diet for lactose intolerance prescribed by doctor or medical assistant. We excluded children with reported current cow's milk allergy or lactose intolerance ($n = 24$) from the study, because these conditions may affect beverage choices and cow's milk allergy may be associated with asthma. The final study population consisted of 2406 children.

Outcome assessment

Asthma was defined based on parental reports on wheezing in the past 12 months, prescription of inhaled corticosteroid in the past 12 months and a doctor's diagnosis of asthma ever. When the answer for two out of three questions was 'yes', the child was considered to have asthma. This definition of asthma was established by the European GA^{2}LEN (Global Allergy and Asthma European Network) consortium.[12] To gain more insight into the nature of the associations with asthma, we additionally investigated associations of all beverages with the separate asthma variables and with atopic asthma. Atopic asthma was defined as having asthma and having specific immunoglobulin E levels $\geqslant 0.35$ IU/ml for allergens of birch, cat, house dust mite (*Dermatophagoides pteronyssinus*) or grass (*Dactylis glomerata)*. Data on atopic asthma were available for the subgroup of children who participated in the clinical examination at age 12 years ($n = 1204$).

Exposure assessment

The 11-year child questionnaire included questions on consumption of six beverages: sugar-added drinks, 100% fruit juice, sweetened milk drinks, energy drinks, diet drinks and sport drinks. Questions were adopted from the Diet History Questionnaire that was validated against four 24-h dietary recalls.[13] Table 1 shows examples of the beverages (as they were also provided in the questionnaire), their average sugar content and types of sugar present in each of the beverages. The response options for most beverages were < 1, 1–3, 4–6, 7–9, 10–12, 13–15 and > 15 glasses/week (gl/wk). For sport- and energy drinks, cans or bottles instead of glasses were reported. For analyses, we converted cans/bottles into glasses assuming 330 ml cans or bottles and a normal glass of 150 ml.

The distributions of beverage consumption were skewed and differed between beverages. We therefore converted the variables into categorical variables with two or three categories, depending on the level of consumption. If $> 50\%$ of the children consumed $\geqslant 1$ gl/wk of a specific beverage, three categories were created: low (0–3 gl/wk), intermediate (4–9 gl/wk) and high ($\geqslant$10 gl/wk). This applied for sugar-added drinks, 100% fruit juice and sweetened milk drinks. Consumption of diet drinks, energy drinks and sport drinks was relatively low and was divided into two categories: low (< 2 gl/wk) or high ($\geqslant$ 2 gl/wk).

Consumption of total SCB was calculated by summing consumption frequencies of all beverages, excluding diet drinks. Total SCB consumption was analyzed in four categories: low (< 12.5 gl/wk), moderate (12.5–18.0 gl/wk), high (18.5–21.5 gl/wk) and very high (> 21.5 gl/wk).

Covariates

Gender, parental history of allergy, maternal education (low: primary school, lower vocational/secondary education; intermediate: vocational education or intermediate/higher secondary education; or high: vocational education and university) and breastfeeding ($\geqslant$16 wk) were reported when the child was 1 year old. Age, weight and height, and smoking in the child's home were reported by the parents at age 11 years. BMI (kg/m^2) *Z*-scores were calculated using the reference growth curves of the Dutch Fourth Nation-wide Growth Study.[14] Overweight (including obesity) was defined based on international cutoff points.[15] Fruit (portions/wk) and vegetable consumption (serving spoons/wk) were self-reported at age 11 years, and were included as indicators of healthy dietary habits.

Statistical analysis

Means and percentages were estimated of the main characteristics of the study population. Associations between beverages and asthma were analyzed using logistic regression. Based on previous literature,[16] multivariate analyses were adjusted for age, gender, breastfeeding, parental history of allergy, maternal education, (parental) smoking indoors, and fruit- and vegetable consumption. Physical activity was considered as a potential confounder in the association between beverages and asthma. However, correlations between the separate beverages and physical activity (as number of days/wk being active for at least 1h; and number of days/wk doing sports) were weak (Pearson's $r < 0.20$), and physical activity was not associated with asthma in our study population of 11-year-old children ($P > 0.05$). Therefore, we decided not to include physical activity as a covariate in the analyses. We anticipated that BMI could be a mediator or a confounder in the association between beverage consumption and asthma.[17,18] We therefore analyzed a second multivariate model including all covariates and also BMI *Z*-score. Effect modification by gender, maternal education, parental allergy and BMI was investigated by adding interaction terms to the statistical model using a significance level of $P < 0.10$. *P*-values for linear trend across beverage categories were estimated by including the categorical variable as a continuous variable in the model. In addition to overall asthma, we estimated associations for beverages with each individual component of the asthma variable (asthma diagnosis ever, wheeze in the last 12 months and prescription of inhaled corticosteroids in the last 12 months). Furthermore, we investigated associations of beverages with atopic and non-atopic asthma in a subgroup of children with specific immunoglobulin E measurements at the age of 12 years. All statistical analyses were performed in SAS version 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Characteristics of the study population and means of beverage consumption are shown in Table 2. Of the 2406 children included in the analyses, 5.8% had asthma ($N = 139$). Of all beverages, sugar-added drinks (7.2 gl/wk) were consumed most frequently. Table 3 shows crude and adjusted associations between beverage consumption and asthma. The multivariate analyses (without BMI as covariate) showed increased asthma risk for high fruit juice

Table 1. Examples of the separate beverages and their sugar content

Beverage	*Examples*	*Estimated[a] range of sugar content (g/100 ml)*	*Types of sugar[a]*
Sugar-added drinks	Cola, tonic, ice tea, cassis, Fanta, fruit drinks, fruit nectars and lemonade	1.4–11.1	Added: glucose, sucrose, fructose and high-fructose corn syrup
100% Fruit juice	Apple juice, orange juice, grape juice, multi-fruit juice and freshly pressed juices	2.9–15.7	Naturally present: fructose, glucose and sucrose
Sweetened milk drinks	Chocolate milk, Fristi and yogurt drinks	3.6–11	Naturally present: lactose. Added: fructose and sucralose (artificial sweetener)
Energy drinks	Red Bull, Bullit and Golden Power	10.7–10.8	Added: high-fructose corn syrup and maltodextrin
Sport drinks	Extran, Aquarius and AA Drink	5.7–16.5	Added: sucrose, fructose, glucose and maltodextrin
Diet drinks	Cola light, Cola zero, Fanta light, Crystal Clear and Rivella Light	0.0–0.2	Added: aspartame, saccharin, cyclamate and acesulfame-K (artificial sweeteners)

[a]Based on the Dutch Food Composition table (NEVO).

Table 2. Characteristics and beverage consumption among the study population ($N = 2406$)

Characteristic	n/N	Mean or %
Mean (s.d.)		
Age (years)	2398	11.0 (0.2)
Body mass index (*Z*-score)	2136	−0.0 (1.1)
Vegetable consumption (serving spoons/week)	2388	11.2 (4.9)
Fruit consumption (portions/week)	2343	7.1 (4.9)
Percentage (%)		
Gender (boy)	1214/2406	50.5
Overweight including obesity	227/2097	10.8
Asthma (yes)	139/2406	5.8
Inhalation of corticosteroids past 12 months (yes)	162/2400	6.8
Ever diagnosed with asthma (yes)	257/2389	10.7
At least 1 episode of wheezing past 12 months (yes)	99/2406	4.1
Allergic asthma	65/1219	5.3%
Non-allergic asthma	13/1219	1.1%
Maternal education	2400	
Low	471	19.6
Intermediate	1003	41.8
High	926	38.6
Allergic mother	676/2406	28.1
Allergic father	716/2405	29.8
Smoking indoors (at least once a week)	320/2404	13.3
Breastfeeding (⩾16 weeks)	874/2387	36.6
Sugar-added drinks (mean number of glasses/week (s.d.))	2400	7.2 (5.1)
Low (< 4 glasses/week; %)	709	29.5
Moderate (4–9 glasses/week; %)	944	39.3
High (⩾10 glasses/week; %)	747	31.1
100% Fruit juice (mean number of glasses/week (s.d.))	2401	4.5 (4.2)
Low (< 4 glasses/week; %)	1248	52.0
Moderate (4–9 glasses/week; %)	891	37.1
High (⩾10 glasses/week; %)	262	10.9
Sweetened milk drinks (mean number of glasses/week (s.d.))	2395	3.5 (3.8)
Low (< 4 glasses/week; %)	1525	63.7
Moderate (4–9 glasses/week; %)	688	28.7
High (⩾10 glasses/week; %)	182	7.6
Energy drinks (mean number of glasses/week (s.d.))	2374	0.6 (0.6)
Low (< 2 glasses/week; %)	2246	94.6
High (⩾2 glasses/week; %)	128	5.4
Sport drinks (mean number of glasses/week (s.d.))	2394	0.9 (1.0)
Low (< 2 glasses/week; %)	1934	58.8
High (⩾2 glasses/week; %)	460	41.3
Diet drinks (mean number of glasses/week (s.d.))	2400	2.1 (2.9)
Low (< 2 glasses/week; %)	1410	58.8
High (⩾2 glasses/week; %)	990	41.3

consumption (⩾ 10 gl/wk; odds ratio (OR): 1.92, 95% confidence interval (CI): 1.14–3.24). Sugar-added drinks and total SCB were borderline statistically significantly associated with asthma. After further adjustment for BMI, the observed associations became more pronounced, and the association between total SCB and asthma became statistically significant for the highest category of SCB consumption (> 21.5 gl/wk) compared with low consumption (< 12.5 gl/wk; OR:1.91, 95% CI: 1.04–3.48). When we included fruit juice and sugar-added drinks together as exposures, in the multivariate model including BMI, both associations became more pronounced (100% fruit juice OR: 1.71, 95% CI: 1.04–2.82; sugar-added drinks OR: 2.26, 95% CI: 1.30–3.93; data not shown). There was a significant trend over categories of consumption of fruit juice ($P = 0.01$) and total SCB ($P = 0.03$). As a *post hoc* analysis, we analyzed the association of fruit consumption with asthma and found no association (OR: 1.01, 95%CI: 0.98–1.05).

Associations with separate asthma variables were all in the same direction with some indication of associations being stronger for wheeze than for the other two components of the asthma definition for fruit juice, sugar-added drinks and total SCB (Table 4). Due to a low number of cases of non-atopic asthma ($n = 13$; Table 2), estimates for this outcome were unstable and we therefore only show results for allergic asthma. For allergic asthma, strong and statistically significant associations were observed for high consumption of 100% fruit juice (⩾10 gl/wk; OR: 3.53, 95% CI: 1.61–7.72); total SCB (> 21/5 gl/wk; OR: 3.29, 95%CI: 1.23–8.85) and sugar-added drinks (⩾10 gl/wk; OR: 2.34, 95% CI: 1.10–5.00; Table 4).

Fruit juice, sugar-added drinks and total SCB were not associated with higher BMI in our study population, indicating that BMI was not an explanatory factor in the association between SSB and asthma (results not shown).

Assessment of effect modification indicated no interaction by gender, maternal education or parental allergy. There was a significant interaction with BMI for fruit juice and total SCB consumption (*P*-values for interaction were 0.04 and 0.02, respectively), indicating that associations between consumption of these beverages and asthma weakened with increasing BMI. Because of the significant interaction with BMI, we repeated the main analysis in children with and without overweight separately. Due to the relatively low number of overweight children, estimates in this subgroup were unstable. We therefore only present results for the subgroup of normal weight children (those without overweight). In normal weight children (89% of the total study population), associations for sugar-added drinks, fruit juice and total SCB tended to be stronger than in the total study population (Table 5).

DISCUSSION

This study shows that high consumption of 100% fruit juice, sugar-added drinks and total SCB are associated with increased asthma risk in children. We extended observations from previous studies by showing strong associations specifically with atopic asthma. Our results do not indicate a mediating role of BMI in the observed associations.

Previous studies

Four previous studies have explored the association between the consumption of sugar-sweetened beverages and asthma prevalence. A cross-sectional study on Australian adults (⩾16 years) showed that high soft drink consumption (⩾ 0.5 l/day, including sport drinks) was associated with asthma and chronic obstructive pulmonary disease (OR: 1.26, 95%CI: 1.01–1.58).[7] No distinction was made in this study between light- and regular soft drinks. A similar association was found in US high-school children of ~16 years of age.[6] A high consumption of soda (> 3 times/day, excluding diet soda) was associated with asthma (OR: 1.64, 95%CI: 1.25–2.16). Another cross-sectional study conducted in New Zealand, including children aged 10–12 years, found non-significant associations between the consumption of 'fizzy drinks' (> 1 time/wk) and wheeze in the last 12 months (OR: 1.27, 95% CI 0.83–1.96) and asthma diagnosis ever (OR: 1.32, 95% CI: 0.91–1.93).[19] However, in this study, the highest consumption category was > 1 time/wk, so that moderate consumption could not be distinguished from high consumption. Finally, a Norwegian-nested case–control study found that adolescents with and without asthma (total $n = 169$) did not differ significantly in consumption of soft drinks (including carbonated soft drinks and other sugar-added drinks such as lemonade and ice tea) after adjusting for age and gender.[20] Although there were differences in the definitions used for beverages, the direction of associations of previous studies were similar to the association we found for sugar-added drinks. Earlier studies did not assess 100% fruit juice separately in relation to asthma.

Table 3. Associations between beverage consumption and asthma

Beverage	N	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	Adjusted OR (95% CI)[b]	P for trend[c]
Sugar-added drinks	2400	N = 2400	N = 2290	N = 2036	0.07
Low (< 4 glasses/week)	709	Reference	Reference	Reference	
Moderate (4–9 glasses/week)	944	1.07 (0.69–1.66)	1.13 (0.71–1.80)	1.17 (0.71–1.92)	
High (⩾10 glasses/week)	747	1.40 (0.90–2.17)	1.46 (0.92–2.33)	1.56 (0.95–2.56)	
100% Fruit juice	2401	N = 2401	N = 2290	N = 2034	0.01[d]
Low (< 4 glasses/week)	1248	Reference	Reference	Reference	
Moderate (4–9 glasses/week)	891	1.26 (0.87–1.83)	1.31 (0.88–1.95)	1.39 (0.91–2.12)	
High (⩾10 glasses/week)	262	1.75 (1.06–2.91)[d]	1.92 (1.14–3.24)[d]	2.09 (1.21–3.60)[d]	
Sweetened milk drinks	2395	N = 2395	N = 2284	N = 2028	0.76
Low (< 4 glasses/week)	1525	Reference	Reference	Reference	
Moderate (4–9 glasses/week)	688	0.83 (0.56–1.23)	0.83 (0.55–1.26)	0.97 (0.63–1.48)	
High (⩾10 glasses/week)	182	0.69 (0.33–1.45)	0.76 (0.36–1.62)	0.89 (0.42–1.90)	
Energy drinks	2374	N = 2374	N = 2263	N = 2015	–
Low (< 2 glasses/week)	2246	Reference	Reference	Reference	
High (⩾2 glasses/week)	128	1.09 (0.52–1.37)	0.99 (0.44–2.22)	1.18 (0.52–2.67)	
Sport drinks	2394	N = 2394	N = 2283	N = 2027	–
Low (< 2 glasses/week)	1934	Reference	Reference	Reference	
High (⩾2 glasses/week)	460	0.87 (0.55–1.37)	0.81 (0.50–1.31)	0.92 (0.56–1.52)	
Diet drinks	2400	N = 2400	N = 2289	N = 2033	–
Low (< 2 glasses/week)	1410	Reference	Reference	Reference	
High (⩾2 glasses/week)	990	1.12 (0.79–1.58)	1.04 (0.72–1.50)	1.08 (0.74–1.59)	
Total SCB[e]	2366	N = 2366	N = 2256	N = 2009	0.03[d]
Low (< 12.5 glasses/week)	546	Reference	Reference	Reference	
Moderate (12.5–18.0 glasses/week)	649	1.13 (0.68–1.88)	1.14 (0.66–1.97)	1.49 (0.82–2.72)	
High (18.5–21.5 glasses/week)	616	1.26 (0.76–2.10)	1.32 (0.77–2.25)	1.71 (0.95–3.10)	
Very high (> 21.5 glasses/week)	555	1.37 (0.82–2.29)	1.39 (0.80–2.40)	1.91 (1.04–3.48)[d]	

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; SCB, sugar-containing beverage. [a]Adjusted for age, gender, breastfeeding, maternal education, parental allergy, smoking indoors, fruit- and vegetable consumption. [b]Adjusted for age, gender, breastfeeding, maternal education, parental allergy, smoking indoors, fruit- and vegetable consumption, and BMI *Z*-score. [c]Based on the second adjusted model including all confounders and BMI. [d]Statistically significant based on the 95% CI (that is, the CI does not include 1). [e]SCB included sugar-added drinks, 100% fruit juice, sweetened milk drinks, and energy drinks and sport drinks.

Strengths and limitations

A major strength of this study was that we had data on six different beverages, and that we were able to investigate the potential mediating role of BMI. We found significant dose–response trends for asthma over categories of fruit juice and total SCB consumption. This study was limited by self-report of beverage consumption and covariates, which might have led to random misclassification. This would have obscured the associations, but it is unlikely that these associations would not have been found in case of more precise measurements. We distinguished between diet drinks and regular beverages, but we could not distinguish between hypo- and hypertonic sport- and energy drinks, although these differ in sugar content. Two-thirds of the children of the original PIAMA study population completed the questionnaires at age 11 years. There was selective loss to follow-up of participants with lower maternal education, which may have affected the generalizability of our results. We do not expect this to have influenced results, as maternal education did not modify the association between beverage consumption and asthma. Although we were able to adjust for a range of important potential confounders, residual confounding may have occurred. Due to the cross-sectional design, causality, nor the direction of the association can be established based on our study, but it seems unlikely that the presence of asthma would result in a higher consumption of 100% fruit juice and sugar-added drinks.

Interpretation

Several mechanisms linking SCB consumption to asthma have been hypothesized. It has been suggested that additives present in sweetened drinks, such as colorants, stabilizers or preservatives might be potential explaining factors. As an example, Park *et al.*[6] stated that the preservative sodium benzoate (E211), present in several soft drinks, might be such an additive. If these factors would be explanatory, associations would be expected for all beverages containing additives, including energy-, sport drinks and diet drinks. However, for these beverages, we observed no associations with asthma. In addition, additives such as sodium benzoate are unlikely to explain the observed associations with fruit juice, as only a few fruit juices (not those most commonly consumed) contain benzoate acid naturally. For these reasons, our study does not support a role for additives as the main mechanism behind the observed associations.

Another proposed mechanism is an inflammatory pathway initiated by sugar that is present in SCB in various amounts and forms. In agreement with the 'sugar hypothesis', an ecological study of 53 countries found that higher sugar consumption per capita during the perinatal period increased risk of severe asthma symptoms in children 7 years later.[21] A dietary pattern high in sugary drinks was associated with increased inflammatory markers in women.[22] Dietary sugar, especially fructose, has been found to increase levels of high-sensitivity C-reactive protein in a prospective randomized controlled trial.[8] Fructose is a major component of

Table 4. Associations of beverage consumption with individual asthma variables and with atopic asthma in a subgroup of children with specific IgE measurements[a]

Beverage	Ever asthma[b] OR (95% CI)	Wheeze[c] OR (95% CI)	Inhaled corticosteroids[d] OR (95% CI)	In a subgroup[e] (N = 1058) of children with specific IgE measurements: allergic asthma OR (95% CI)
Sugar-added drinks	N = 2036	N = 2036	N = 2031	N = 1051
Low (< 4 glasses/week)	Reference	Reference	Reference	Reference
Moderate (4–9 glasses/week)	1.16 (0.80–1.68)	1.35 (0.76–2.39)	1.07 (0.68–1.69)	1.72 (0.82–3.61)
High (⩾10 glasses/week)	1.41 (0.97–2.06)	1.55 (0.87–2.76)	1.29 (0.81–2.04)	2.34 (1.10–5.00)[f]
100% Fruit juice	N = 2034	N = 2034	N = 2029	N = 1050
Low (< 4 glasses/week)	Reference	Reference	Reference	Reference
Moderate (4–9 glasses/week)	1.15 (0.84–1.58)	1.28 (0.79–2.08)	1.38 (0.94–2.03)	2.24 (1.21–4.15)[f]
High (⩾10 glasses/week)	1.54 (0.99–2.40)	2.23 (1.22–4.07)[f]	1.76 (1.03–3.00)[f]	3.53 (1.61–7.72)[f]
Sweetened milk drinks	N = 2028	N = 2028	N = 2023	N = 1046
Low (< 4 glasses/week)	Reference	Reference	Reference	Reference
Moderate (4–9 glasses/week)	1.14 (0.83–1.57)	1.09 (0.68–1.74)	0.85 (0.56–1.28)	1.06 (0.58–1.94)
High (⩾10 glasses/week)	1.10 (0.63–1.90)	0.29 (0.07–1.20)	0.89 (0.45–1.78)	0.72 (0.21–2.48)
Energy drinks	N = 2015	N = 2015	N = 2010	N = 1042
Low (< 2 glasses/week)	Reference	Reference	Reference	Reference
High (⩾2 glasses/week)	1.36 (0.75–2.46)	1.07 (0.42–2.76)	1.18 (0.54–2.55)	1.89 (0.63–5.71)
Sport drinks	N = 2027	N = 2027	N = 2022	N = 1047
Low (< 2 glasses/week)	Reference	Reference	Reference	Reference
High (⩾2 glasses/week)	1.14 (0.79–1.64)	0.90 (0.51–1.59)	0.86 (0.53–1.39)	1.08 (0.53–2.17)
Diet drinks	N = 2033	N = 2033	N = 2028	N = 1050
Low (< 2 glasses/week)	Reference	Reference	Reference	Reference
High (⩾2 glasses/week)	1.12 (0.84–1.52)	0.84 (0.53–1.31)	1.09 (0.76–1.56)	0.92 (0.53–1.61)
Total SCB[g]	N = 2009	N = 2009	N = 2004	N = 1039
Low (< 12.5 glasses/week)	Reference	Reference	Reference	Reference
Moderate (12.5–18.0 glasses/week)	1.23 (0.79–1.92)	1.71 (0.84–3.47)	1.39 (0.80–2.39)	2.66 (1.02–6.95)[f]
High (18.5–21.5 glasses/week)	1.52 (0.98–2.35)	1.90 (0.94–3.84)	1.53 (0.89–2.62)	3.37 (1.31–8.70)[f]
Very high (> 21.5 glasses/week)	1.73 (1.11–2.69)[f]	2.07 (1.01–4.23)[f]	1.55 (0.89–2.71)	3.29 (1.23–8.85)[f]

Abbreviations: BMI, body mass index; CI, confidence interval; IgE, immunoglobulin E; OR, odds ratio; SCB, sugar-containing beverage. [a]Adjusted for age, gender, breastfeeding, maternal education, parental allergy, smoking indoors, fruit- and vegetable consumption, and BMI *Z*-score. [b]Doctors diagnosis of asthma ever. [c]Wheeze in the last 12 months. [d]Prescription of inhaled corticosteroids in the last 12 months. [e]Subgroup of children with allergen specific IgE measurements. [f]Statistically significant based on the 95% CI (that is, the CI does not include 1). [g]SCB included sugar-added drinks, 100% fruit juice, sweetened milk drinks, energy drinks and sport drinks.

added sugars and is present in fruit juice naturally and in sweetened drinks as added sucrose or isolated fructose. Fructose is distinct from other sugars in its ability to cause generation of uric acid,[23] which has a role in various inflammatory diseases such as gout, diabetes[23] and asthma.[24] There are indications that uric acid may be an essential initiator and amplifier of allergic inflammation.[25,26]

In our study, sugar-added drinks and 100% fruit juice were associated with asthma; sweetened milk drinks, energy- and sport drinks were not, although they all contain similar amounts of sugar/100 ml. The absence of associations with sport- and energy drinks might be explained by the low consumption of these drinks in our study sample. However, for sweetened milk drinks, low consumption cannot explain the absence of an association with asthma, as these drinks were consumed in substantial amounts. However, sweetened milk drinks vary greatly in sugar content and can contain artificial sweeteners. We could not differentiate sweetened milk drinks low or high in sugar, and this might explain the lack of association in our data.

Our finding that fruit juice consumption was associated with asthma may be in line with the 'sugar hypothesis', but was unexpected, as consumption of fruit was found to be protective against asthma in earlier studies.[4,27] We can only speculate about the differential associations of fruit and fruit juice with asthma. Various differences resulting from processing from whole fruit to juice might have a role. Differences in viscosity, carbohydrate bioavailability and sugar content might lead to differences in metabolism.[28] For example, one glass of orange juice contains the equivalent in sugar of about two oranges, implying that our category of high 100% fruit juice consumption contains the equivalent of ⩾20 oranges/wk.

Besides the mechanisms suggested previously, we hypothesized that BMI might explain associations observed between SCB and asthma, assuming an association between high SCB consumption and increased overweight, and an association between overweight and increased asthma. Our data showed no evidence, however, for this hypothesized mechanism.

CONCLUSION

High consumption of 100% fruit juice, sugar-added drinks and very high total SCB consumption were associated with increased asthma risk in this cross-sectional study. The positive association between 100% fruit juice consumption and asthma is an unexpected finding that needs to be confirmed and clarified. Beverage consumption is a modifiable factor, and if the current evidence on SCB and asthma is confirmed in further studies this might suggest a new direction for preventive strategies.

Table 5. Associations[a] between beverage consumption and asthma in normal weight children[b]

Beverage	N	OR (95% CI)
Sugar-added drinks	1868	N = 1784
Low (< 4 glasses/week)	532	Reference
Moderate (4–9 glasses/week)	735	1.40 (0.81–2.42)
High (⩾10 glasses/week)	601	1.58 (0.90–2.76)
100% Fruit juice	1866	N = 1782
Low (< 4 glasses/week)	967	Reference
Moderate (4–9 glasses/week)	691	1.55 (0.98–2.46)
High (⩾10 glasses/week)	208	2.56 (1.43–4.56)[c]
Sweetened milk drinks	1860	N = 1776
Low (< 4 glasses/week)	1183	Reference
Moderate (4–9 glasses/week)	533	1.08 (0.68–1.69)
High (⩾10 glasses/week)	144	0.50 (0.18–1.41)
Energy drinks	1852	N = 1768
Low (< 2 glasses/week)	1762	Reference
High (⩾2 glasses/week)	90	1.08 (0.42–2.79)
Sport drinks	1862	N = 1778
Low (< 2 glasses/week)	1511	Reference
High (⩾2 glasses/week)	351	1.04 (0.61–1.77)
Diet drinks	1865	N = 1781
Low (< 2 glasses/week)	1125	Reference
High (⩾2 glasses/week)	740	0.98 (0.64–1.50)
Total SCB[d]	1846	N = 1762
Low (< 12.5 glasses/week)	409	Reference
Moderate (12.5–18.0 glasses/week)	506	1.51 (0.76–3.03)
High (18.5–21.5 glasses/week)	487	2.15 (1.10–4.19)[c]
Very high (> 21.5 glasses/week)	444	2.16 (1.09–4.27)[c]

Abbreviations: CI, confidence interval; OR, odds ratio; SCB, sugar-containing beverage. [a]Adjusted for age, gender, breastfeeding, maternal education, parental allergy, smoking indoors, fruit and vegetable consumption. [b]Normal weight included children with underweight. [c]Statistically significant based on the 95% CI (that is, the CI does not include 1). [d]SCB included sugar-added drinks, 100% fruit juice, sweetened milk drinks, energy drinks and sport drinks.

CONFLICT OF INTEREST

GHK has received grants from the Dutch Lung Foundation, Biobanking and Biomolecular Resources Research Infrastructure and Stichting Astma Bestrijding. These organizations or study sponsors were not involved in the design or conduct of the current study. The remaining authors declare no conflict of interest.

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REFERENCES

1 Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; **59**: 469–478.
2 de Cassia Ribeiro Silva R, Assis AM, Cruz AA, Fiaccone RL, Dinnocenzo S, Barreto ML *et al.* Dietary patterns and wheezing in the midst of nutritional transition: a study in Brazil. *Pediatr Allergy Immunol Pulmonol* 2013; **26**: 18–24.
3 Wood LG, Gibson PG. Dietary factors lead to innate immune activation in asthma. *Pharmacol Ther* 2009; **123**: 37–53.
4 Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. *J Allergy Clin Immunol* 2011; **127**: 724–733 e721-730.
5 Stensson M, Wendt LK, Koch G, Nilsson M, Oldaeus G, Birkhed D. Oral health in pre-school children with asthma--followed from 3 to 6 years. *Int J Paediatr Dent* 2010; **20**: 165–172.
6 Park S, Blanck HM, Sherry B, Jones SE, Pan L. Regular-soda intake independent of weight status is associated with asthma among US high school students. *J Acad Nutr Diet* 2013; **113**: 106–111.
7 Shi Z, Dal Grande E, Taylor AW, Gill TK, Adams R, Wittert GA. Association between soft drink consumption and asthma and chronic obstructive pulmonary disease among adults in Australia. *Respirology* 2012; **17**: 363–369.
8 Aeberli I, Gerber PA, Hochuli M, Kohler S, Haile SR, Gouni-Berthold I *et al.* Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. *Am J Clin Nutr* 2011; **94**: 479–485.
9 Steinman HA, Weinberg EG. The effects of soft-drink preservatives on asthmatic children. *S Afr Med J* 1986; **70**: 404–406.
10 Brunekreef B, Smit J, de Jongste J, Neijens H, Gerritsen J, Postma D *et al.* The prevention and incidence of asthma and mite allergy (PIAMA) birth cohort study: design and first results. *Pediatr Allergy Immunol* 2002; **13** (Suppl 15): 55–60.
11 Wijga AH, Kerkhof M, Gehring U, de Jongste JC, Postma DS, Aalberse RC *et al.* Cohort profile: The Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort. *Int J Epidemiol* 2013; **43**: 527–535.
12 Keil T, Kulig M, Simpson A, Custovic A, Wickman M, Kull I *et al.* European birth cohort studies on asthma and atopic diseases: II. Comparison of outcomes and exposures--a GA2LEN initiative. *Allergy* 2006; **61**: 1104–1111.
13 Subar AF, Thompson FE, Kipnis V, Midthune D, Hurwitz P, McNutt S *et al.* Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires: the Eating at America's Table Study. *Am J Epidemiol* 2001; **154**: 1089–1099.
14 Fredriks AM, van Buuren S, Burgmeijer RJ, Meulmeester JF, Beuker RJ, Brugman E *et al.* Continuing positive secular growth change in The Netherlands 1955-1997. *Pediatr Res* 2000; **47**: 316–323.
15 Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; **320**: 1240–1243.
16 Nurmatov U, Nwaru BI, Devereux G, Sheikh A. Confounding and effect modification in studies of diet and childhood asthma and allergies. *Allergy* 2012; **67**: 1041–1059.
17 Papoutsakis C, Priftis KN, Drakouli M, Prifti S, Konstantaki E, Chondronikola M *et al.* Childhood overweight/obesity and asthma: is there a link? A systematic review of recent epidemiologic evidence. *J Acad Nutr Diet* 2013; **113**: 77–105.
18 Morgan RE. Does consumption of high-fructose corn syrup beverages cause obesity in children? *Pediatr Obes* 2013; **8**: 249–254.
19 Wickens K, Barry D, Friezema A, Rhodius R, Bone N, Purdie G *et al.* Fast foods—are they a risk factor for asthma? *Allergy* 2005; **60**: 1537–1541.
20 Bueso AK, Berntsen S, Mowinckel P, Andersen LF, Lodrup Carlsen KC, Carlsen KH. Dietary intake in adolescents with asthma--potential for improvement. *Pediatr Allergy Immunol* 2011; **22** (Pt 1), 19–24.
21 Thornley S, Stewart A, Marshall R, Jackson R. Per capita sugar consumption is associated with severe childhood asthma: an ecological study of 53 countries. *Prim Care Respir J* 2011; **20**: 75–78.
22 Schulze MB, Hoffmann K, Manson JE, Willett WC, Meigs JB, Weikert C *et al.* Dietary pattern, inflammation, and incidence of type 2 diabetes in women. *Am J Clin Nutr* 2005; **82**: 675–684. quiz 714-675.
23 Johnson RJ, Nakagawa T, Sanchez-Lozada LG, Shafiu M, Sundaram S, Le M *et al.* Sugar, uric acid, and the etiology of diabetes and obesity. *Diabetes* 2013; **62**: 3307–3315.
24 Li Lin, Wan Chun, Wen F. An unexpected role for serum uric acid as a biomarker for severity of asthma exacerbation. *Asian Pac J Allergy Immunol* 2014; **32**: 93–99.
25 Willart MA, Lambrecht BN. The danger within: endogenous danger signals, atopy and asthma. *Clin Exp Allergy* 2009; **39** , 12–19.
26 Kool M, Willart MA, van Nimwegen M, Bergen I, Pouliot P, Virchow JC *et al.* An unexpected role for uric acid as an inducer of T helper 2 cell immunity to inhaled antigens and inflammatory mediator of allergic asthma. *Immunity* 2011; **34**: 527–540.
27 Boeing H, Bechthold A, Bub A, Ellinger S, Haller D, Kroke A *et al.* Critical review: vegetables and fruit in the prevention of chronic diseases. *Eur J Nutr* 2012; **51**: 637–663.
28 Englyst KN, Englyst HN. Carbohydrate bioavailability. *Br J Nutr* 2005; **94**: 1–11.