



## The association of pure fruit juice, sugar-sweetened beverages and fruit consumption with asthma prevalence in adolescents growing up from 11 to 20 years: The PIAMA birth cohort study

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### ABSTRACT

Pure fruit juice is comparable to sugar-sweetened beverages (SSBs) with respect to its sugar and fructose content. However, it also contains favorable components like polyphenols. From this perspective, pure fruit juice is more comparable with whole fruit. SSBs have been associated with higher asthma risk, while whole fruit consumption has been associated with lower prevalence of asthma (symptoms). Associations with pure fruit juice have been rarely studied. Therefore, we studied the associations of consumption of pure fruit juice, SSBs and whole fruit with asthma prevalence in 3046 children of the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort growing up from 11 to 20 years. Consumption of pure fruit juice, SSBs and fruit was self-reported at the ages of 11, 14, 17 and 20 years. Presence of asthma was defined based on parental reports of asthma diagnosis ever, and wheezing and asthma medication in the last 12 months. Odds ratios (OR) were estimated using generalized linear mixed models accounting for correlation between repeated measurements within subjects. No associations were found between pure fruit juice, SSBs and fruit consumption and the overall prevalence of asthma from 11 to 20 years. An earlier reported association of low pure fruit juice consumption with higher asthma prevalence at the age of 11 years in the PIAMA population was confirmed, but no associations were found at the ages of 14, 17 and 20 years.

### 1. Introduction

Asthma is the most common chronic disease among children worldwide (Asher and Pearce, 2014). Sugar-sweetened beverages (SSBs) are popular among children and adolescents and have been associated with a higher risk of asthma (Al-Zalabani et al., 2019). Two potential underlying mechanisms have been proposed to explain why SSBs consumption may be linked to asthma. First, preservatives used in SSBs, especially sodium benzoate, may trigger asthma attacks (Freedman, 1980; Steinman and Weinberg, 1986). Second, it has been suggested that

unabsorbed excess fructose may contribute to the intestinal formation of pro-inflammatory advanced glycation end products, which may play a role in the development of asthma (DeChristopher et al., 2016). In the US, high-fructose corn syrup, a liquid sweetener alternative to sucrose, is used in many SSBs (White, 2008). Like SSBs, pure fruit juice also contains fructose and might therefore show similar associations with asthma. However, besides fructose, pure fruit juice also contains favorable components such as vitamin C and polyphenols. It has been suggested that these components may protect against asthma (Hatch, 1995; Tanaka and Takahashi, 2013). From this perspective, pure fruit

*Abbreviations:* BMI, body mass index; SSBs, sugar-sweetened beverages; PIAMA, Prevention and Incidence of Asthma and Mite Allergy birth cohort study; OR, odds ratio; CIs, confidence intervals.

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juice may be more comparable with whole fruit in its association with asthma. Available evidence is weak but supportive for the hypothesis that fruit consumption is associated with lower prevalence of asthma and asthma symptoms (Berthon et al., 2021; Hosseini et al., 2017; Garcia-Larsen et al., 2016; Nurmatov et al., 2011). Pure fruit juice can be both fresh juice and bottled juice from concentrate and never contains added sugars, artificial sweeteners or components as artificial colors and preservatives. Findings of previous research on the association between pure fruit juice consumption and asthma are inconsistent (Saadeh et al., 2015; DeChristopher and Tucker, 2020; DeChristopher et al., 2016; Berentzen et al., 2015; Wright et al., 2018). Negative (Saadeh et al., 2015), positive (DeChristopher and Tucker, 2020; DeChristopher et al., 2016; Berentzen et al., 2015) and no associations (Wright et al., 2018) have been observed. Most research has been performed in early and middle childhood. One previous study found an association between high apple juice consumption and asthma in 2–9-year-olds, but not in 10–16-year-olds (DeChristopher et al., 2016), suggesting that the association may be age-dependent. We previously reported that pure fruit juice consumption was associated with higher asthma prevalence at the age of 11 years in the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study (Berentzen et al., 2015). To get more insight into the association between pure fruit juice and asthma during adolescence, we extended this previous study in the PIAMA birth cohort with repeated measurements at the ages of 14, 17 and 20 years. We investigated the overall and age-specific associations of pure fruit juice, SSBs and fruit consumption with asthma prevalence from 11 to 20 years. By investigating consumption of pure fruit juice, SSBs and whole fruit in the same study population, we aimed to explore the question whether pure fruit juice is more similar to whole fruit or more similar to SSBs in relation to asthma.

## 2. Material and methods

### 2.1. Study design and study population

We used data from the Dutch PIAMA birth cohort study that started in 1996. A detailed description of the study has been provided elsewhere (Wijga et al., 2014). In brief, pregnant women were recruited from the general population. The baseline study population consisted of 3963 children born in 1996/1997. The first questionnaire was completed by the parents during pregnancy. Further questionnaires were completed by the parents when the child was 3 months old, and subsequently, every year until the child was 8 years old. At the ages of 11, 14 and 17 years both the parents and the adolescents completed questionnaires. At the age of 20, only the adolescents completed a questionnaire. The study protocol was approved by the Medical Ethics Committees of the participating institutes (Rotterdam, MEC 132.636/1994/39 and 137.326/1994/130; Groningen, MEC 94/08/92; Utrecht, MEC-TNO 95/50) and all parents gave written informed consent. For our analyses, we included participants with data on their asthma status for at least one of the ages of 11, 14, 17 or 20 years as well as data on the consumption of pure fruit juice, SSBs or whole fruit at that specific age ( $n = 3046$ ).

### 2.2. Exposure assessment

#### 2.2.1. Pure fruit juice consumption

Consumption of pure fruit juice was reported by the adolescents at the ages of 11, 14, 17 and 20 years. The definition of pure fruit juice was described in detail in the questionnaire and many (brand) examples were given. Consumption was reported in glasses/week. The response options in the questionnaire were not identical for all ages (Supplement 1). In the current study, we created 3 identical consumption categories for all ages:  $<1$ ,  $1-7$  and  $\geq 7$  glasses/week.

#### 2.2.2. SSBs consumption

At all ages, consumption of SSBs was reported by the adolescent and

included separate questions on soft drinks, energy drinks and sport drinks. Soft drinks were reported in glasses/week and sport drinks and energy drinks in bottles/cans per week. Response options in the questionnaire were not identical for all ages (Supplement 1). We first converted bottles/cans into glasses assuming 250 ml cans for sport drinks and 500 ml bottles for sport drink corresponding to one and two glasses, respectively. Subsequently, we determined midpoints for all categories to enable summing frequencies of all SSBs, and then created 3 identical consumption categories for all ages for our analyses:  $0-7$ ,  $7-14$  and  $\geq 14$  glasses/week.

#### 2.2.3. Fruit consumption

Fruit consumption (excluding apple sauce and canned fruit) was reported by the parents at the age of 11 and 14 years and by the adolescents at the age of 17 and 20 years. Response options in the questionnaire were identical at all ages: not,  $<1$ ,  $1-2$ ,  $3-5$ ,  $6-7$  days/week. We merged the lowest two categories into one because of the small number of children in these categories.

### 2.3. Outcome assessment

Presence of asthma was reported by the parents at the age of 11, 14 and 17 years and by the adolescents at the age of 20 years. Asthma was defined based on three questions: first, doctor's diagnosis of asthma ever, second, wheezing in the past 12 months, third, prescription of asthma medication in the last 12 months. When at least two out of these three questions were answered with a 'yes', the adolescent was defined as having asthma. This definition of asthma was established by the European MeDALL consortium (Pinart et al., 2014).

### 2.4. Covariates

Information on potential confounders was obtained from different questionnaires. The following potential confounders were obtained from the 1 year questionnaire: (1) parental education defined as the number of parents (0, 1 or 2) with a low level of education (i.e. primary school, lower vocational or lower secondary education); (2) Parental history of allergy (yes/no) defined as asthma ever and/or current house dust mite allergy and/or pet allergy and/or hay fever reported by at least one parent; (3) Breastfeeding (yes/no) defined as breast feeding (exclusive or not exclusive) for  $\geq 16$  weeks. Physical activity and active smoking were reported by the adolescents at the age of 11, 14, 17 and 20 years. Being physically active was defined as being active for at least 1 h on  $\geq 5$  days per week. Age-specific cut-off points were used to define active smoking; 11 years: active smoking was defined as 'ever smoked', at 14 years as 'smoking at least occasionally', at 17 and 20 years as smoking  $\geq$  once per week. Secondhand smoke exposure was reported by the parents at the age of 11, 14 and 17 years and by the adolescents at the age of 20 years and defined as  $\geq$  once per week (yes/no). Consumption of alcohol, crisps and vegetables were used as indicators of diet quality. Alcohol consumption was reported by the adolescents at the age of 11, 14, 17 and 20 years. Age-specific cut-off points were used to define alcohol consumers (yes/no); 11 years: alcohol consumption was defined as 'ever drank a whole glass', at 14 years as 'drank  $\geq 10$  glasses in his/her whole life', at 17 and 20 years as 'drinking  $\geq 7$  glasses per week'. Both consumption of crisps and vegetables were reported by the parents at the age of 11 and 14 years and by the adolescents at the age of 17 and 20 years. High consumption of crisps was defined as eating crisps  $\geq 3$  times per week. High consumption of vegetables was defined as eating vegetables  $6-7$  times per week. Selection of potential confounders was based on *a priori* theoretical considerations derived from the scientific literature (Nurmatov et al., 2012) and/or on a  $>10\%$  difference in effect estimate between crude and adjusted models.

## 2.5. Statistical analyses

Data were analyzed using SAS 9.4 software (SAS Institute Inc.). Spearman correlation coefficients were used to assess correlations between the exposures. We used generalized linear mixed models using a logit link to estimate odds ratios with 95% confidence intervals for the overall association of pure fruit juice, SSBs and fruit consumption with overall prevalence of asthma from 11 to 20 years. A random subject-specific intercept was included to account for within-subject correlation between the repeated measurements. Because the Dutch dietary guidelines (Health Council of the Netherlands. Dutch dietary guidelines, 2015) recommend a low consumption of SSBs and pure fruit juice and a high consumption of fruit, we used the lowest category as reference for pure fruit juice and SSBs consumption and the highest category for fruit consumption. The first model was adjusted for age and sex. The second model was adjusted for age, sex, and potential confounders, i.e. parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol consumption, crisps consumption, vegetable consumption and (1) SSBs and fruit consumption (for associations with pure fruit juice) OR (2) pure fruit juice and fruit consumption (for associations with SSBs) OR (3) pure fruit juice consumption and SSBs (for associations with fruit). Additionally, in the third model BMI was added as possible intermediate factor. Possible effect modification by parental history of allergy was investigated by including a product term in the model. We used logistic regression models to estimate odd ratios with 95% confidence interval for age-specific associations between pure fruit juice, fruit and SSBs consumption and asthma prevalence at the ages of 11, 14, 17 and 20 years.

**Table 1**

Characteristics of the study population at ages 11, 14, 17 and 20 years.

	11 years		14 years		17 years		20 years	
	%	n	%	n	%	n	%	n
N	2184		1948		1566		2137	
Sex								
Girl	49.5	1082	49.0	954	49.7	779	52.4	1120
Boy	50.3	1099	50.9	991	50.0	783	47.6	1017
Transgender	0.1	3	0.2	3	0.3	4	0	0
Asthma (yes)	7.0	153	6.3	122	5.4	85	7.6	162
Overweight (yes)	9.8	214	9.1	177	9.2	144	19.5	417
Breast feeding $\geq 16$ weeks	37.6	822	38.1	743	40.2	630	37.4	800
At least one parent with history of allergy	50.0	1092	51.6	1005	51.7	810	50.0	1069
At least one low educated parent <sup>1</sup>	30.8	673	28.6	557	27.5	430	30.8	659
Pure fruit juice consumption								
<1 gl/wk	25.1	546	21.6	420	23.5	368	42.1	899
1-<7 gl/wk	47.2	1028	48.5	944	52.6	824	45.3	968
$\geq 7$ gl/wk	27.8	606	30.0	584	23.9	374	12.6	270
Sugar sweetened beverages <sup>2</sup>								
0-<7 gl/wk	43.0	929	39.8	775	28.6	448	51.6	1102
7-<14 gl/wk	32.3	697	28.9	563	27.3	427	20.0	428
$\geq 14$ gl/wk	24.7	533	31.3	610	44.1	690	28.4	607
Fruit consumption								
<1 d/wk	5.0	109	10.3	201	16.4	257	16.9	362
1-<3 d/wk	9.8	214	17.3	336	21.5	336	21.5	459
3-<6 d/wk	32.6	712	34.1	663	31.6	494	32.1	685
$\geq 6$ d/wk	52.6	1149	38.4	747	30.6	479	29.5	631
Vegetable consumption ( $\geq 6$ times/week)	37.6	822	37.1	722	56.6	886	54.5	1164
Crisps consumption ( $\geq 3$ times/week)	7.9	172	11.0	215	11.2	176	9.1	194
Physical activity <sup>3</sup>	59.2	1293	48.5	945	37.1	581	41.5	886
Active smoking <sup>4</sup>	2.0	43	8.3	161	12.6	198	20.1	430
Secondhand smoke exposure <sup>5</sup>	12.5	273	10.4	202	8.5	133	8.7	185
Alcohol consumption <sup>6</sup>	6.7	146	7.9	154	13.4	210	29.9	639

<sup>1</sup> low-educated = primary school, lower vocational or lower secondary education.

<sup>2</sup> Included soft drinks, energy drinks and sport drinks.

<sup>3</sup> Physical activity was defined as being active for at least 1 h on  $\geq 5$  days per week.

<sup>4</sup> Active smoking was defined at age 11 as 'ever smoked', at age 14 as 'smoking at least occasionally' and at ages 17 and 20 as 'smoking  $\geq$  once a week'.

<sup>5</sup> Secondhand smoke exposure was defined as ' $\geq$  once a week'.

<sup>6</sup> Alcohol consumption was defined at age 11 as 'ever drank a whole glass', at age 14 as 'ever drank  $\geq 10$  glasses', at age 17 and 20 as 'drinking  $\geq 7$  glasses per week'.

## 2.6. Sensitivity analyses

We conducted a sensitivity analysis for SSBs including sweetened milk drinks as these are often consumed among Dutch children and popular types are sweetened with fructose. Data collection and preparation was done in the same way as it was done for soft drinks, as described earlier.

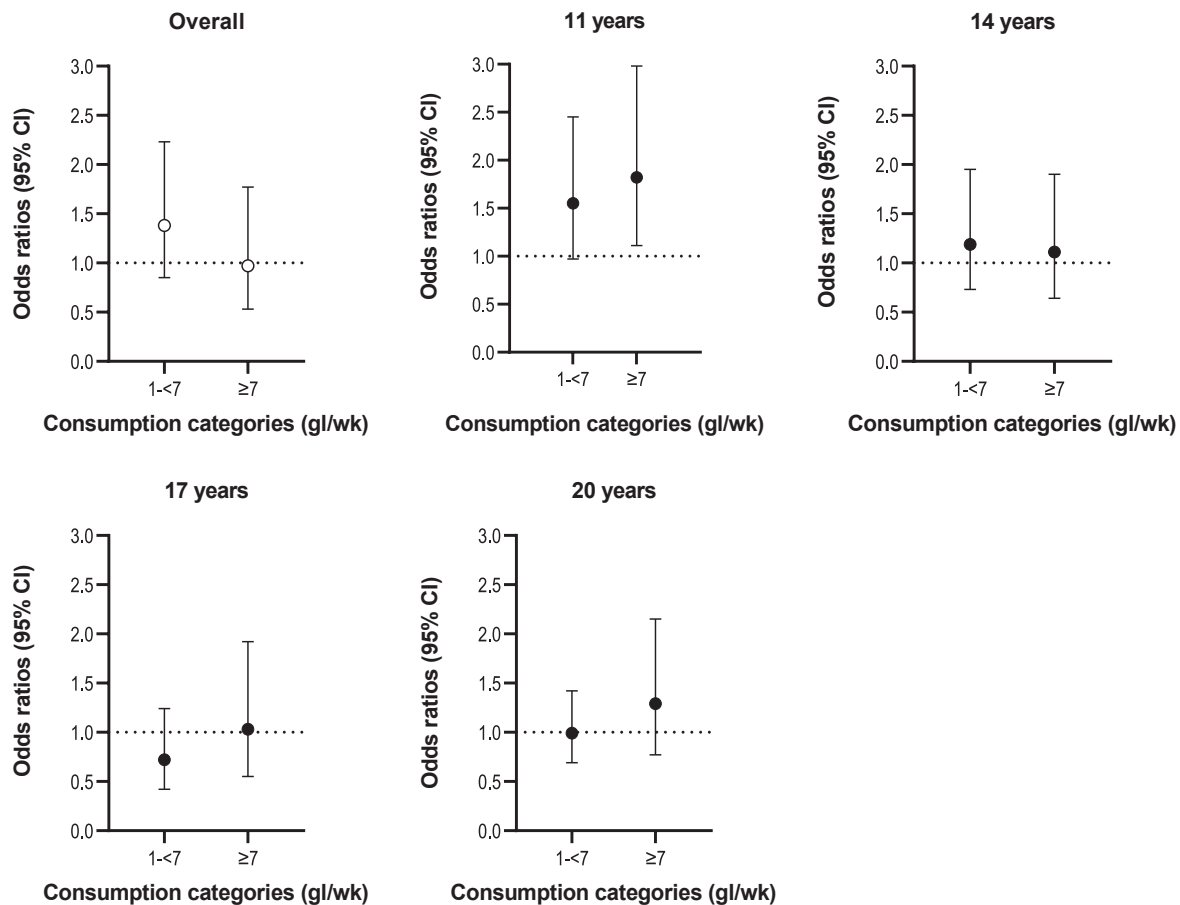
## 3. Results

### 3.1. Descriptive statistics

Table 1 shows the characteristics of the study population at each age. Pure fruit juice was consumed most frequently at the age of 14 whereas SSBs were consumed most frequently at the age of 17. Fruit was consumed most frequently at the age of 11. Correlations between the consumption of pure fruit juice, fruit and SSBs were, although statistically significant, low (Supplemental Table 1).

### 3.2. Association of pure fruit juice, SSBs and fruit consumption with overall asthma prevalence

With the lowest category as reference for pure fruit juice consumption (<1gl/wk) and SSBs (0-<7gl/wk) and the highest category as reference for fruit consumption (6 or 7d/wk), we found no overall association with prevalence of asthma from 11 to 20 years for any of the exposure variables (Figs. 1-3 and Table 2).



**Fig. 1.** Overall and age-specific association(s) of pure fruit juice consumption with asthma from age 11 to 20. Adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, SSBs and fruit. Consumption of <1gl/wk was used as reference category.

### 3.3. Age-specific associations of pure fruit juice, SSBs and fruit consumption with asthma prevalence

We confirmed the association between pure fruit juice consumption and asthma prevalence at the age of 11 years that we reported before. High consumption of pure fruit juice ( $\geq 7$ gl/wk) was associated with higher asthma prevalence compared to low consumption (<1gl/wk) after adjustment for possible confounders (OR: 1.782, 95% CI: 1.11–2.98; Fig. 1 and Supplemental Table 2). However, we found no associations with asthma prevalence at the ages of 14, 17 and 20 years. For both SSBs and fruit consumption no associations were found with asthma prevalence at either age after adjustment for possible confounders (Figs. 1-3 and Supplemental Tables 2-4).

### 3.4. Role of adjustment

Adjustment for possible confounders (models 2) yielded similar results for all overall associations (Table 2). Similar results were also found for consumption of pure fruit juice and fruit at all ages and for SSBs at ages 11, 14 and 17. At the age of 20 years, a statistically significant association with asthma prevalence for the highest SSBs consumption category attenuated and became non-significant after adjustment for possible confounders (Supplemental Tables 2-4). Additional inclusion of BMI (models 3) yielded very similar ORs and 95% CIs in all associations.

### 3.5. Test for interaction

Assessment of interaction indicated no effect modification by parental allergy for consumption of pure fruit juice ( $p = 0.56$ ), SSBs ( $p = 0.22$ ) and fruit ( $p = 0.43$ ).

### 3.6. Sensitivity analyses

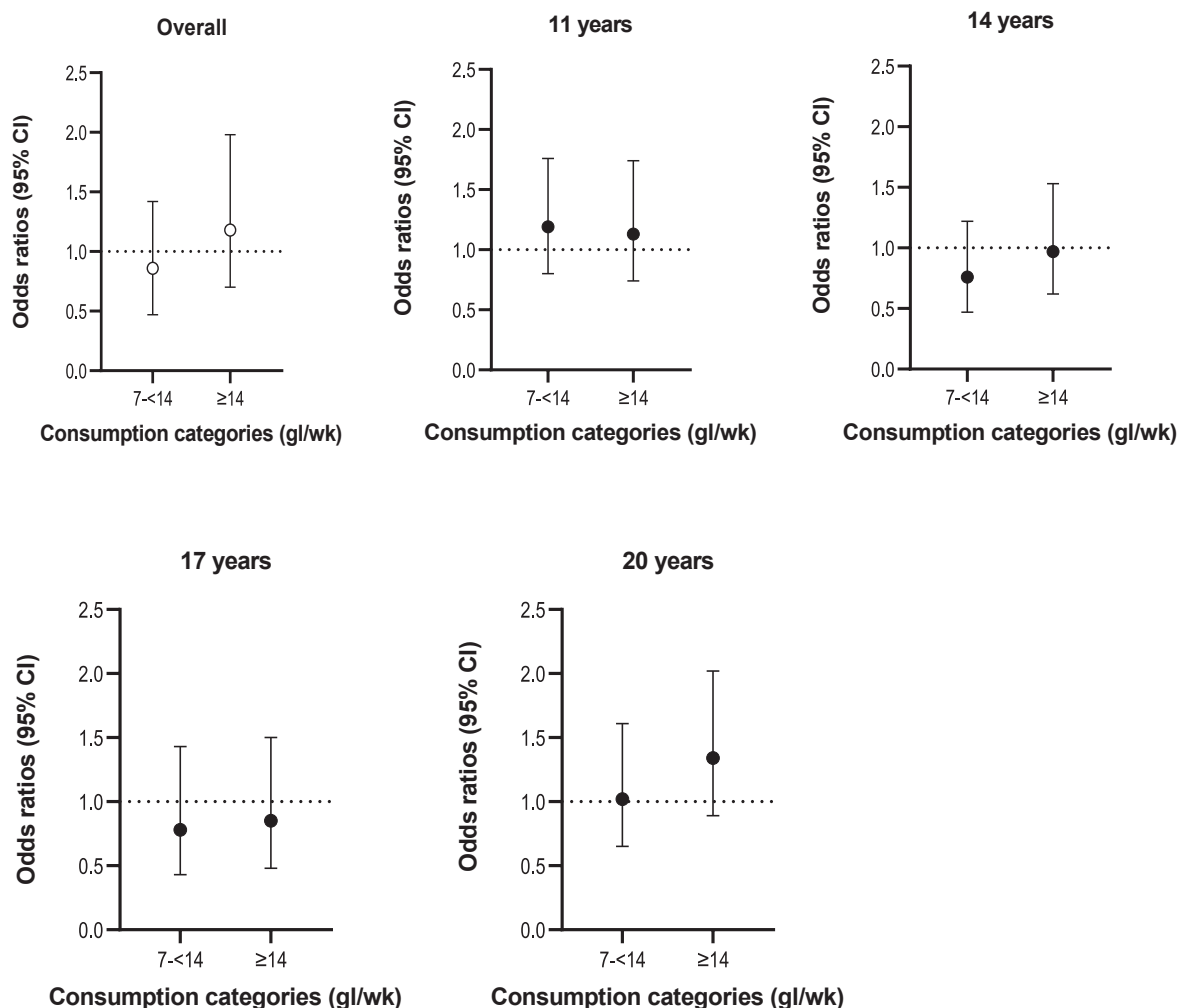
Including sweetened milk drinks in SSBs consumption yielded similar results as the analyses of SSBs without sweetened milk drinks (Supplemental Table 5).

## 4. Discussion

Except for the previously reported positive association for pure fruit juice consumption at the age of 11 years (Berentzen et al., 2015), our present extended analyses with repeated measurements at the age of 14, 17 and 20 years showed no association of pure fruit juice consumption with overall prevalence of asthma from 11 to 20 years and no age-specific associations at the age of 14, 17 and 20 years. We found no associations between consumption of SSBs or fruit and asthma prevalence.

### 4.1. Results of previous studies

A study in very young children in the US showed that moderate to daily consumption of pure fruit juice compared to low consumption was



**Fig. 2.** Age-specific and overall association(s) of SSBs consumption with asthma from age 11 to 20. Adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, pure fruit juice and fruit. Consumption of 0–<7gl/wk was used as reference category.

associated with a ~ 1.5 times higher asthma incidence in children aged 12–30 months (DeChristopher and Tucker, 2020). No association was found between pure fruit juice consumption and asthma prevalence in US schoolchildren with a median age of 7.7 years (Wright et al., 2018). DeChristopher found no association between orange juice consumption and asthma prevalence in children aged 2–9 years, but showed that those who frequently consumed apple juice had more than twice the prevalence of asthma than those with a low apple juice consumption ( $\leq 1$  time/month). No associations were found in 10–16-year-olds (DeChristopher et al., 2016). This finding is in line with our own observation of an association between pure fruit juice and asthma in 11-year-olds but not at later ages. In contrast, a study in French children aged 9–11 years showed that pure fruit juice consumption of  $\geq 3$  times per week, compared to none or occasional consumption, was associated with a 27% lower prevalence of lifetime asthma (Saadeh et al., 2015). In conclusion, evidence from previous studies on the association between pure fruit juice consumption and asthma in children and adolescents remains inconsistent.

Regarding SSBs consumption, a meta-analysis showed a positive association between soft drink consumption and asthma prevalence in children up to 18 years of age (Al-Zalabani et al., 2019). However, this meta-analysis has several limitations. The definition of ‘soft drinks’ varied widely between the 12 studies included. Most studies did not

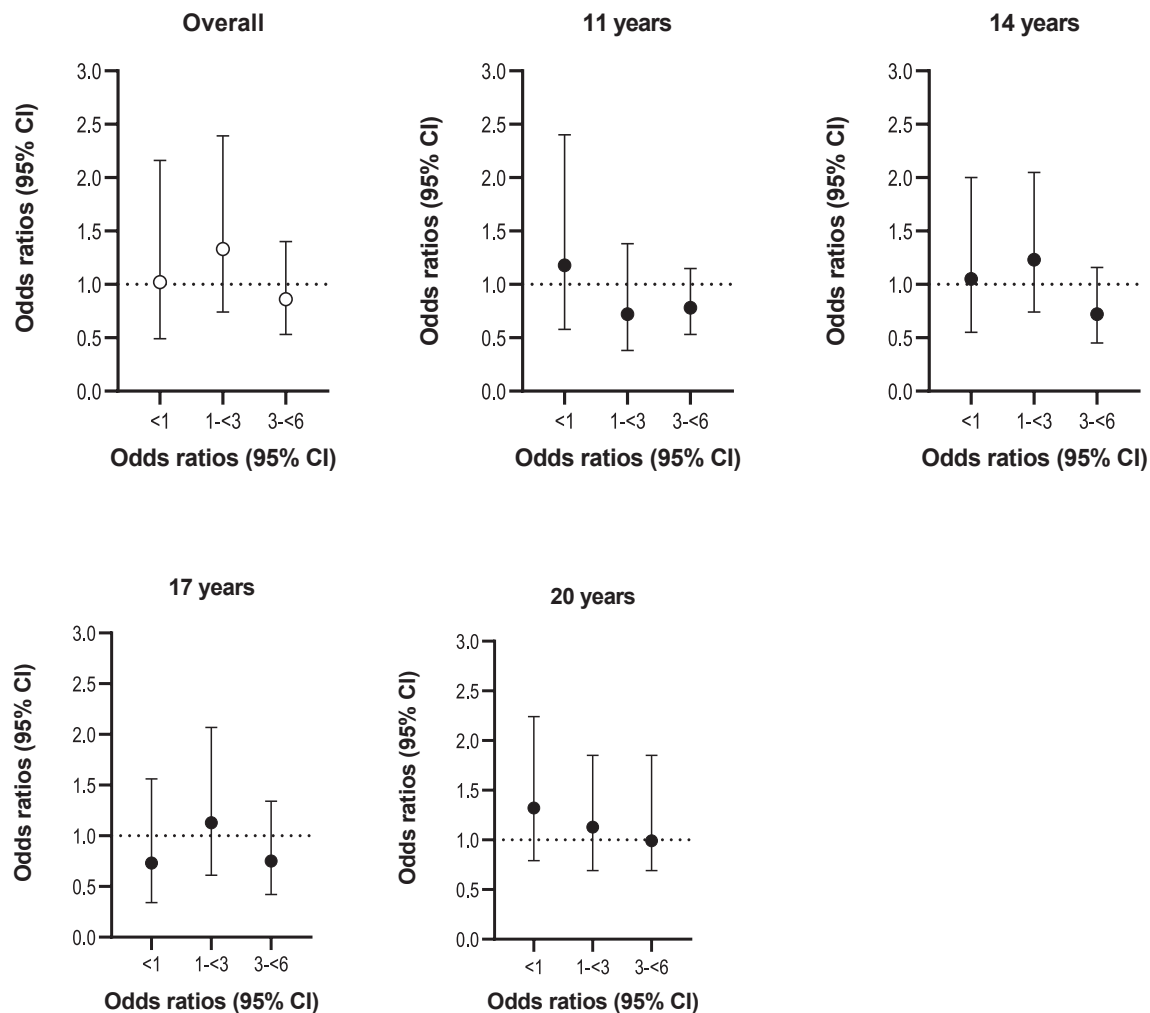
describe the exact question(s) from the questionnaire. Therefore, it is not clear whether pure fruit juice and artificially sweetened beverages have been excluded. Furthermore, separate analyses for consumption of sugar-sweetened soft drinks and carbonated drinks were done without defining these two categories. Therefore, it is not completely clear what kind of beverages have been studied, while these separate analyses showed different associations with asthma (no association for carbonated drinks, but an increased asthma prevalence for sugar-sweetened soft drinks). However, there was substantial heterogeneity among studies for sugar-sweetened soft drinks.

Concerning fruit, a meta-analysis on the association between fruit consumption and asthma in children, adolescents and adults found that whole fruit consumption was associated with a lower asthma severity and a lower prevalence of wheeze. However, similar to our findings, no association was found between fruit consumption and prevalence of asthma (Hosseini et al., 2017).

#### 4.2. Strengths and limitations

Availability of a large cohort with 4 measurement points in the period from childhood to young adulthood is an important strength of our study. This contributed not only to the power of the study, but also enabled us to assess age-specific associations in a phase of life





**Fig. 3.** Age-specific and overall association(s) of fruit consumption with asthma from age 11 to 20. Adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, pure fruit juice and SSBs. Consumption of 6 or 7d/wk was used as reference category.

characterized by major changes in lifestyle. We investigated pure fruit juice, SSBs and whole fruit in the same study population to gain more insight into the question whether pure fruit juice is more similar to whole fruit or more similar to SSBs in relation to asthma. Another strength in our data collection is that definitions of all beverages were described clearly in the questionnaires and were supported with examples of brands. This decreased the likelihood that participants reported non-pure fruit juice (with added sugars) as pure fruit juice. Furthermore, in the PIAMA study, the retention rate was relatively high with 3046 of the 3963 (77%) participants included at birth having completed one or more of the questionnaires administered at the ages of 11, 14, 17 and 20 years. Loss to follow-up in cohorts is often selective in the sense that participants with a low socioeconomic status (SES) tend to be over-represented among those lost to follow-up. However, in our study, the percentage of participants with at least one low educated parent was very similar at age 11 and 20 (see Table 1), indicating that during the study period, children from low SES families were not selectively lost to follow-up.

Some potential limitations should also be considered. Consumption frequency of pure fruit juice, SSBs and fruit were not asked in number of units (e.g. ‘glasses’) per week, but in categories like 1–3 per week up to > 15 per week. Moreover, we did not ask for an exact measure of portion sizes, but provided a semi-quantitative measure, such as a can, bottle, or

glass, and we did not ask about portion sizes of fruit consumption. This leads to an imprecise measure of consumption and therefore possible misclassification. We assume this misclassification has been random and may have led (if anything) to an attenuation of associations. Although, in the PIAMA study data were collected repeatedly from birth until the age of 20 years, the analyses in the present study are cross-sectional. We were not able to study consumption of pure fruit juice, SSBs and fruit with the development of new asthma in later age groups (asthma *incidence*), because at the ages of 11–20 years, the number of incident cases in children who never reported asthma before was very low.

#### 4.3. Possible mechanisms and interpretation of the present study

Two potential mechanisms underlying the possible association of SSBs and pure fruit juice consumption with asthma have been proposed. One of the hypotheses revolves around preservatives. There is no evidence that preservatives are responsible for the onset of asthma (Gul- tekin and Doguc, 2013), but they may cause reactions in a minority of asthmatic and sensitive person (Steinman and Weinberg, 1986; World Health Organization, 2000). Even if the effects of preservatives are limited to subgroups of sensitive persons, fear of harmful effects may lead to avoidance of SSBs by asthmatic children and adolescents and possibly to a preference for pure fruit juice. Reverse causation, i.e.

**Table 2**

Adjusted Odds Ratios and 95% confidence intervals for the overall association between pure fruit juice, SSBs and fruit consumption and asthma from age 11 to 20.

	Records <sup>1</sup> , n	Asthma prevalence, n	OR (95% CI)	OR (95% CI)	OR (95% CI)
Pure fruit juice consumption			Model 1 <sup>2</sup>	Model 2 <sup>3</sup>	Model 3 <sup>4</sup>
<1gl/wk	2233	145	1.00	1.00	1.00
1-<7gl/wk	3764	242	1.35 (0.84–2.16)	1.38 (0.85–2.23)	1.38 (0.85–2.23)
≥7gl/wk	1834	135	0.99 (0.55–1.80)	0.97 (0.53–1.77)	0.97 (0.53–1.78)
P-trend			0.94	0.99	0.99
SSBs consumption			Model 1 <sup>2</sup>	Model 2 <sup>5</sup>	Model 3 <sup>6</sup>
0-<7gl/wk	3254	215	1.00	1.00	1.00
7-<14gl/wk	2115	134	0.86 (0.52–1.42)	0.86 (0.47–1.42)	0.85 (0.51–1.40)
≥14gl/wk	2440	171	1.18 (0.71–1.96)	1.18 (0.70–1.98)	1.17 (0.69–1.97)
P-trend			0.57	0.58	0.6
Fruit consumption			Model 1 <sup>2</sup>	Model 2 <sup>7</sup>	Model 3 <sup>8</sup>
<1d/wk	929	70	1.06 (0.51–2.18)	1.02 (0.49–2.16)	1.03 (0.49–2.17)
1-<3d/wk	1345	98	1.39 (0.78–2.47)	1.33 (0.74–2.39)	1.32 (0.73–2.36)
3-<6d/wk	2554	145	0.90 (0.56–1.46)	0.86 (0.53–1.40)	0.86 (0.53–1.39)
6 or 7d/wk	3006	209	1.00	1.00	1.00
P-trend			0.51	0.47	0.45

<sup>1</sup> Each child could be 4 times in the analyses.<sup>2</sup> adjusted for age and sex.<sup>3</sup> adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, SSBs and fruit.<sup>4</sup> adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, SSBs, fruit and BMI.<sup>5</sup> adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, pure fruit juice and fruit.<sup>6</sup> adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, pure fruit juice, fruit and BMI.<sup>7</sup> adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, SSBs and pure fruit juice.<sup>8</sup> adjusted for age, sex, parental educational level, parental history of allergy, breastfeeding, physical activity, active smoking, secondhand smoke exposure, alcohol, crisps, vegetables, SSBs, pure fruit juice and BMI.

presence of asthma affecting SSBs and pure fruit juice consumption, may thus have influenced the associations between SSBs consumption and asthma that we observed.

The second potential mechanism linking both pure fruit juice and SSBs consumption to asthma is the 'fructose hypothesis'. DeChristopher et al. showed that apple juice (fructose-to-glucose ratio: 2:1) but not orange juice (fructose-to-glucose ratio: 1:1) was associated with higher asthma prevalence in 2–9 year olds (DeChristopher et al., 2016) and interpreted this finding as evidence for an effect of fructose intake on asthma prevalence. No association with apple juice was observed in 10–16 years olds in the same study and the authors suggested that fructose tolerance may occur with age (DeChristopher et al., 2016). We found no other evidence in the literature supporting this suggestion. Our questionnaires did not include separate questions on apple juice and orange juice, but data from the Dutch National Food Consumption Survey show that orange juice is the most consumed type of pure fruit juice in children/adolescents in the Netherlands (data not shown). According to the fructose hypothesis, the lower fructose content of orange juice (compared to apple juice) could be an explanation why we found no association between pure fruit juice and overall prevalence of asthma in our study. However, like pure fruit juice, whole fruits also contain fructose and no positive association has been found between fruit consumption and asthma prevalence in either the present study or previous research (Hosseini et al., 2017). These findings do not support the fructose hypothesis. Many studies on pure fruit juice and SSBs consumption in relation to asthma have referred to the fructose hypothesis to interpret their findings. However, the possible role of fructose is still an open question and no studies so far have actually measured fructose intakes. For future studies in this field, we therefore strongly recommend measurement of fructose intakes and of the fructose-to-glucose ratio of participants' diets.

## 5. Conclusions

While we confirmed the association between pure fruit juice consumption and asthma prevalence at age 11 we reported previously, we found no evidence that pure fruit juice, SSBs and fruit consumption were associated at later ages or with overall prevalence of asthma from 11 to 20 years. Based on our findings and the evidence from previous studies we cannot yet answer the question whether pure fruit juice is more similar to whole fruit or to SSBs in relation to asthma. However, our findings do not support the idea that pure fruit juice consumption should be limited to prevent asthma development.

## CRedit authorship contribution statement

**Floor R. Scheffers:** Investigation, Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Jolanda M.A. Boer:** Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Ulrike Gehring:** Conceptualization, Funding acquisition, Data curation, Writing – review & editing. **Gerard H. Koppelman:** Conceptualization, Funding acquisition, Data curation, Writing – review & editing. **Judith Vonk:** Writing – review & editing. **Henriëtte A. Smit:** Conceptualization, Funding acquisition, Data curation, Writing – review & editing. **W.M. Monique Verschuren:** Writing – review & editing. **Alet H. Wijga:** Conceptualization, Funding acquisition, Data curation, Methodology, Formal analysis, Writing – original draft, Writing – review & editing. All authors contributed to the interpretation of the results and review and editing of initial drafts. All authors were responsible for review and editing of the manuscript and they all read and approved the final manuscript.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

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### Trial Registration

<https://www.trialregister.nl/trial/9481>

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pmedr.2022.101877>.

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