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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Smoking habits among adolescents with asthma – data from a population-based birth cohort

To the Editor,

Personal smoking and secondhand smoke (SHS) are risk factors for asthma, and healthcare providers are encouraged to support a non-smoking environment for children and adolescents.^{1,2} However, several studies have shown that adolescents with asthma smoke to the same extent as other adolescents³, but most studies to date have investigated current asthma status and have been based on self-reported data.

The aim of this study was to investigate self-reported smoking habits at age 16 years among adolescents and parents in relation to phenotypes of asthma. In addition, to objectively assess adolescents smoking, we measured saliva cotinine concentrations as a biomarker of tobacco smoke exposure.

The study was conducted within the population-based birth cohort, BAMSE, consisting of 4089 participants followed with regular follow-ups and clinical investigations. Data were collected from questionnaires completed by participants and their parents from birth to 16 years. The final study population consisted of adolescents with questionnaire data regarding asthma symptoms, smoking habits, and parental smoking habits at 16 years ($n = 2994$). In a subset of participants ($n = 1605$), saliva samples were collected at the same age for cotinine analysis as previously described, and a cutoff of ≥ 12 ng/mL was used to discriminate smokers from nonsmokers.⁴

Adolescent-onset and persistent asthma phenotypes were defined based on reported timing of onset and persistence of asthma from ages 1 to 16 (see online repository). Smoking in adolescence was defined as daily or occasional smoking at age 16 years. Similarly, parents that reported daily or occasionally smoking were defined as smokers.

The study population was comparable with the original cohort in terms of baseline characteristics (Table S1).

At age 16 years, 14.1% ($n = 422$) of the participants had asthma with a comparable prevalence between males and females ($P = 0.36$). The prevalence of asthma phenotypes was 7.3% for adolescent-onset and 12.2% for persistent. In total, 11.8% ($n = 352$) adolescents reported smoking, 4.3% daily (mean 8 cig/day) and 7.4% occasionally

(mean 7 cig/week) (Table S2), and the mean age for start smoking was 14.7 years.

Adolescents with asthma smoked to the same extent as adolescents without asthma (11.4% vs 11.8%, $P = 0.79$). Among adolescents with asthma, females tended to smoke more than males but this was not statistically significant (13.5% vs 9.1% $P = 0.16$) (Figure 1).

The prevalence of smoking among adolescents did not differ great between those without asthma and adolescent-onset asthma (11.1% vs 13.0%, $P = 0.45$); however, adolescents with persistent asthma smoked less than subjects with adolescent-onset asthma (7.3% vs 13.0%, $P = 0.04$) (Figure 2). Persistent asthma was also associated with a reduced odds of smoking at age 16 years in a mutually adjusted model including parental smoking (OR 0.57; 95% CI 0.35-0.94).

When using saliva cotinine to discriminate smokers from non-smokers, in total 12.3% were classified as smokers (11.3% males and 13.2% females, $P = 0.26$). Among adolescents with asthma, cotinine levels ≥ 12 ng/ml were seen in 11.1% of males and 14.4% of females ($P = 0.46$) (Table S3). We observed no apparent differences in smoking prevalence using saliva cotinine levels, when excluding snus users, and phenotypes of asthma (Table S4).

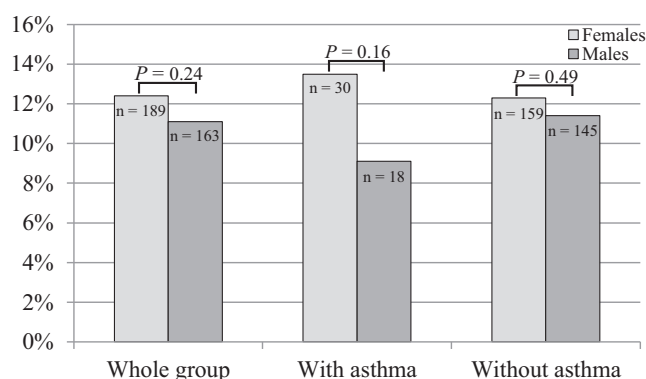


FIGURE 1 Prevalence of adolescent smoking in the whole group ($n = 2994$) and by asthma status

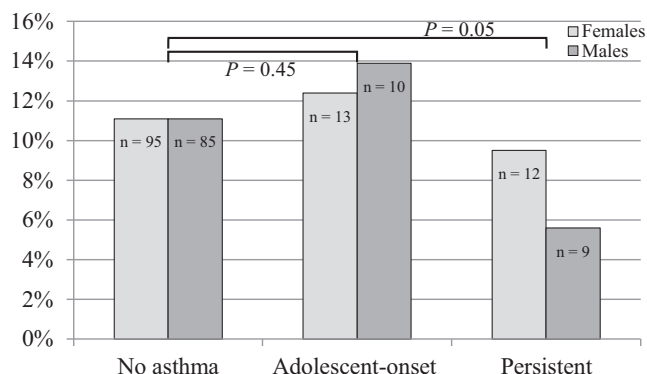


FIGURE 2 Prevalence of adolescent smoking by asthma phenotypes

Among parents, 18.4% ($n = 529$) were smokers, 13.2% daily and 5.2% occasionally. Parents of children with asthma smoked to the same extent as parents of children without asthma (17.6% vs 18.5%, $P = 0.65$) (Figure S1). Moreover, smoking was more common in adolescents whose parents smoked compared with those whose parents did not smoke (24.4% vs 8.7%, $P < 0.001$), and the same pattern was observed among adolescents with asthma (23.6% vs 8.6%, $P < 0.001$) (Figure S2). Following adjustment for sex and asthma at age 16 years, parental smoking was associated with more than a threefold increased odds of adolescent smoking at age 16 years (OR 3.39; 95% CI 2.65–4.33).

As reported by others, data from this birth cohort indicate that adolescents with asthma and their parents smoke to the same extent as families where adolescents do not have asthma.^{3,5} However, in the present study those with persistent asthma had reduced odds of smoking which may suggest that those with preexisting and current asthma symptoms are less inclined to smoke. In comparison to those with persistent asthma, subjects with adolescent-onset asthma tended to smoke more, highlighting the need for healthcare professionals to be more focused on this group. Another important group is young females with asthma, since this group tended to smoke more than young males.

Clinical guidelines state the importance of monitoring and documenting tobacco exposure in the care of children with asthma.⁶ However, in a paper from our group aiming to study adherence to Swedish national guidelines in the care of children with asthma, it was clear that there is a substantial gap between the care being provided for pediatric asthma and recommendations formulated in national guidelines.⁷ Information concerning exposure to parental secondhand tobacco smoke was present in only 14% of more than 450 medical records, and a recommendation to quit smoking was only documented in one case.

Asthma care providers need to be attentive to both secondhand and adolescents own smoking at an early stage and document this in medical records. A long-term relationship with a healthcare provider is linked with better adherence to treatment and advice.⁸ Moreover, adolescents need time to speak privately with a healthcare provider, as questions regarding smoking habits can be sensitive. Smoking

cessation must involve both parents and adolescents, and targeting adolescents before they become established smokers is vital.⁹

The prospective and population-based design, large sample size, and limited loss to follow-up are strengths of this study. Self-reported smoking habits among parents may be a limitation, since the information is collected through questionnaires and parents may under report. In contrast, a strength is that the self-reported smoking habits among the adolescents are confirmed with saliva cotinine tests.

In conclusion, data from the population-based BAMSE cohort suggest that smoking habits do not differ among adolescents with asthma or their parents, compared to those without asthma. This finding was also corroborated using saliva cotinine concentrations.

In comparison to those with persistent asthma, subjects with adolescent-onset asthma tended to smoke more. However, while some adolescents may stop smoking because of their asthma, other adolescent smokers may acquire asthmatic symptoms due to smoking. This highlights the need for healthcare professionals to be more focused on this group. Another important group is young females with asthma, since this group tended to smoke more than young males.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ETHICAL APPROVAL

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Keywords

adolescents, asthma, cotinine, smoking, tobacco

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SUPPORTING INFORMATION

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The relationship of habitual diet with esophageal inflammation and integrity in eosinophilic esophagitis

To the Editor,

The prevalence of eosinophilic esophagitis (EoE), affecting both adults and children, has strongly increased in recent years for reasons currently unknown. It is characterized by inflammation of the esophagus, dysphagia, and food impaction, and is a relatively new chronic immune-mediated manifestation within the spectrum of allergic diseases. We hypothesized that the habitual diet composition is a risk factor of the development and/or persistence of EoE, as nutrition can, either favorably or unfavorably, influence mucosal integrity and tolerance, local and systemic immune function, the oral and intestinal microbiome (and therefore probably also the esophageal microbiome),¹ and epigenetics. Immunomodulatory effects are known for certain fibers, fats, proteins, iron, zinc, copper, selenium, vitamins A, C, D, B6, and B12, omega 3 and 6 fatty acids and folate.²⁻⁵ Thus, nutrition may have an allergy-protective or allergy-provoking effect. However, no studies have been published yet on the habitual dietary intake in EoE patients. This study is the first reporting the relationship between habitual dietary intake in adult EoE patients, before starting any (elimination) diet other than self-imposed dietary measures, and esophageal inflammation and mucosal integrity. Our *aims* were to assess in adult EoE patients (a) the relationships of the habitual dietary intake with esophageal eosinophilic inflammation and mucosal integrity, and (b) the dietary intake in those patients with active disease compared to those in remission.

Our study had a cross-sectional design and was carried out in adult patients, previously diagnosed with EoE (≥ 15 eosinophils/high power field (HPF) and symptoms of esophageal dysfunction) after inclusion in two different studies in 2013-2015 (Trialregister.nl NTR4052 and NTR4892) in the Academic Medical Center, Amsterdam, the Netherlands. We used the data collected at baseline^{6,7} in 34 patients, including five patients who did not receive the intended treatment because of histologic remission assessed at baseline, after inclusion. Until this baseline assessment, the included EoE patients of these studies had no dietary intervention other than self-imposed dietary measures. All patients stopped the intake of steroids, leukotriene inhibitors, monoclonal antibodies anticoagulants, NSAIDs at least 8 weeks prior to the study. If necessary, continuation of proton pump inhibition in stable dosage was allowed. At baseline, habitual dietary intake, esophageal inflammation and mucosal integrity were assessed. No dietary analyses were performed during or after dietary intervention.

Esophageal inflammation was measured by peak eosinophil counts/HPF, and integrity by Electrical Tissue Impedance Spectroscopy (ETIS), transepithelial resistance (TER), and transepithelial flux of fluorescein and rhodamine. See Boxes S1 and S2, for more details on these measurements.

Patient characteristics are described in Table 1. Table 2 shows that in the multiple regression analyses the following nutrients or food groups had a statistically significant negative (favorable)

Online Repository Material. Smoking habits among adolescents with asthma in the BAMSE cohort

Methods

Asthma at age 16 years was defined as fulfilling at least two of the following three criteria: (1) doctor-diagnosed asthma ever (parental reported); (2) asthma medication in the past 12 months (adolescent reported); and (3) wheezing in the past 12 months (adolescent reported).

Phenotypes of asthma were defined as follows:

Adolescent-onset asthma was defined as being asthma free at ages 1, 2, 4, and 8 years and only having asthma at ages 12 or 16 years.

Persistent asthma was defined as having asthma at ages 1, 2, 4, or 8 years and also having asthma at ages 12 or 16 years.

Table E1. Distribution of selected exposure characteristics among all children in the BAMSE cohort (N = 4089) and children included in the current analyses (n = 2994)

	Original cohort (N=4089)		Study population (n=2994)		
	N	%	n	%	95%CI
Female sex	2024	49.5	1520	50.8	49.0-52.6
Parental allergic disease	1200	29.7	906	30.6	28.9-32.2
Breastfeeding $\geq$ 4 months	3116	79.5	2356	80.4	78.9-81.8
Maternal smoking during pregnancy*	527	12.9	357	11.9	10.8-13.1
Maternal smoking during pregnancy or infancy	563	13.8	383	12.8	11.6-14.0
Parental smoking during infancy	855	21.0	596	20.0	18.6-21.5
Maternal age < 26 years[†]	319	7.8	216	7.2	6.3-8.2
Manual workers[‡]	695	17.3	464	15.7	14.4-17.1

*Mother smoked at least one cigarette per day at any point in time during pregnancy.

[†]At birth of the child.

[‡]At baseline.

Table E2. Prevalence of smoking among adolescents and their parents at age 16 years (n = 2994)

	n (%)
Adolescent smoking*	352 (11.8)
Females	189 (12.4)
Males	163 (11.1)
Daily smokers	130 (4.3)
Occasional smokers	222 (7.4)
Any parental smoking*	529 (18.4)
Daily smokers	380 (13.2)
Paternal	206 (7.2)
Maternal	218 (7.3)
Occasional smokers	149 (5.2)
Paternal	96 (3.4)
Maternal	94 (3.2)
Smoking among adolescents without asthma	304 (11.8)
Smoking among adolescents with asthma	48 (11.4)

*Daily or occasional smoking

Table E3. Prevalence of adolescent smoking using saliva cotinine (12 ng/ml cutoff) by asthma status (excluding participants that used smokeless tobacco).

	Males	Females	Total
	n (%)	n (%)	n (%)
Adolescent smoking	82 (11.3)	116 (13.2)	198 (12.3)
Adolescents with asthma	11 (11.1)	19 (14.4)	30 (13.0)
Adolescents without asthma	71 (11.3)	97 (13.0)	168 (12.2)

Table E4. Prevalence of adolescent smoking using saliva cotinine (12 ng/ml cutoff) by asthma phenotype (excluding participants that used smokeless tobacco).

	Cotinine level <12 ng/ml	Cotinine level ≥12 ng/ml
Asthma phenotype	n (%)	n (%)
No asthma	810 (89.4)	96 (10.6)
Adolescent-onset asthma	82 (85.4)	14 (14.6)
Persistent asthma	144 (88.3)	19 (11.7)

Figure E1. Prevalence of parental smoking by adolescent's asthma status.

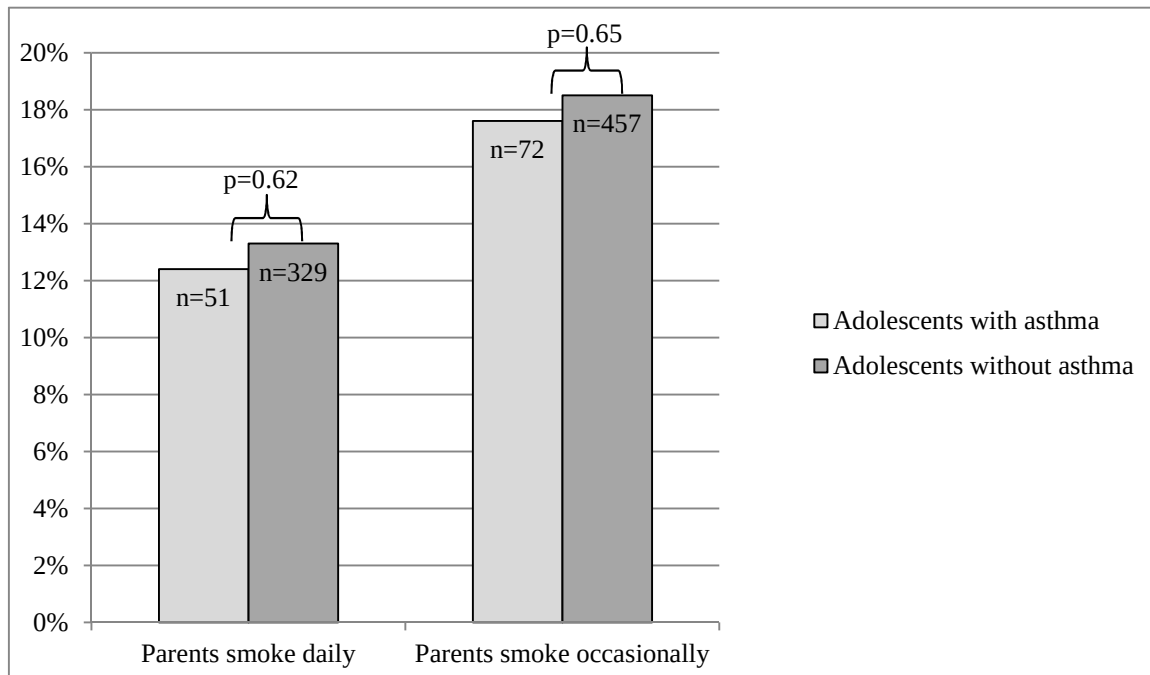


Figure E2. Adolescent smoking compared to parental smoking by adolescents asthma status.

