



Original article

Asthma in Childhood Reduces Smoking Initiation in Subsequent Teens Among Males

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A B S T R A C T

Background: The association between smoking habits and asthma is complex because subjects with asthma could avoid smoking, whereas smoking could increase asthma severity or incidence.

Purpose: The relation between asthma in childhood (0–10 years) and smoking initiation in the second decade (11–20 years) was investigated using the database of the Italian Study on Asthma in Young Adults, performed in 1998–2000 on people aged 20–45 years.

Methods: The cumulative incidence of smoking initiation was compared among (1) subjects not reporting asthma attacks in the first 20 years of life ($n = 17,384$), (2) subjects reporting asthma onset in the first decade and no disease remission by the age of 20 years ($n = 305$), (3) subjects reporting asthma onset in the first decade and remission in the first and second decades ($n = 573$).

Results: Among men, the cumulative incidence of smoking onset was higher among nonasthmatics (49%) than among asthmatics (35.6%), and intermediate among asthmatics with disease remission (44.2%) ($p = .001$). These differences were larger in males born between 1953 and 1965, and tended to decrease in males born between 1966 and 1979: cumulative incidence of smoking onset decreased from 54.3% to 43.8% in nonasthmatics, whereas it remained stable in asthmatics (from 36.8% to 35%). Women, instead, had similar cumulative incidence of smoking initiation, irrespective of asthma onset or remission ($p = .849$).

Conclusion: Asthma in childhood reduces smoking initiation during the subsequent teenage in men, but not in women. This protective effect tends to fade when asthma remission occurs. In the last decades, smoking initiation has decreased among nonasthmatic males, but not among asthmatic males.

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Smoking has been shown to increase asthma incidence [1] in adolescents [2–6] and young adults [7], worsen asthma severity [8], and impair asthma control [9]. Even environmental tobacco

smoke can increase asthma-like symptoms in children with allergic predisposition [10].

Hence, special efforts should be undertaken to prevent asthmatic adolescents from taking up smoking. Yet, most cross-sectional surveys [11–15] found a higher smoking prevalence among adolescents with asthma than among coevals without asthma. It should be reminded, however, that cross-sectional studies do not allow correct identification of the direction of a cause-effect relationship, hence it cannot be excluded that in

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those surveys smoking increased asthma prevalence, rather than the reverse.

Anyway, most longitudinal studies reported that smoking onset is similar in adolescents with asthma and their coevals without asthma [8,16–18]. “Smoking incidence” was even increased in Swedish male teenagers with asthma [2]. A gender-related difference was recently observed by a Dutch study [6]: asthma and asthma-like symptoms reduced the likelihood of smoking initiation among boys but increased the likelihood among girls. However, as the study focused on teenagers aged 13–15 years, this difference was partly attributed to earlier onset of adolescence in girls [6].

Moreover, to our knowledge, the effect of asthma remission has never been addressed. The aim of the present study was to investigate the influence of asthma on smoking initiation. Considering that asthma incidence is the highest in the first decade of life [19,20], whereas the critical age to start smoking is between 13 and 20 years [21,22], the present study focused on the relation between asthma in childhood (0–10 years) and smoking initiation in the second decade (11–20 years). Additional aims were to verify whether the influence of childhood asthma on smoking initiation was modified by asthma remission or varied as a function of gender and birth cohort. For these purposes, the database of the Italian Study on Asthma in Young Adults (ISAYA) was used, in which the information on age at first and last asthma attacks as well as age at smoking initiation and cessation was retrospectively collected.

Methods

Study design

This study was performed in the frame of ISAYA, whose protocol has been described elsewhere [19,21]. Briefly, between 1998 and 2000, a cross-sectional survey was performed on subjects born between 1953 and 1979 in nine Italian centers: six centers (Torino, Verona, Udine, Pavia, Sassuolo, Ferrara) were located in the Po Valley in Northern Italy, one center in Pisa in Tuscany, Central Italy, and two centers in the two major islands in Southern Italy (Sassari in Sardinia, Siracusa in Sicily).

In each center, 3,000 individuals (1,500 men and 1,500 women) were randomly selected from the general population aged 20–45 years, using the local health authority registry, and the selected individuals were sent a screening questionnaire by mail. Nonresponders to the first contact were contacted again, first by mail and then by phone.

Of 25,969 eligible subjects, 18,873 responded to the screening questionnaire, yielding a cumulative response percentage of 72.7%. Of these, 118 subjects who had not given information on lifetime asthma or on age at first asthma attack, as well as 143 subjects who had not provided information on smoking habits or age at smoking initiation, were excluded from the study. Among the remaining 18,612 subjects, 1,525 (8.2%) reported lifetime asthma, whereas 8,913 (47.9%) were ever smokers. As shown in Figure 1, 57.8% (882/1,525) of lifetime asthmatics had the first attack in the first decade (0–10 years), whereas 91.4% (8,145 of 8,913) of ever smokers started smoking in the second decade (11–20 years).

Because the main outcome of the study was smoking initiation, 40 subjects who had reported to have started smoking between 7 and 10 years were excluded from subsequent analyses, leaving 18,572 subjects for the final analysis. Mean age of

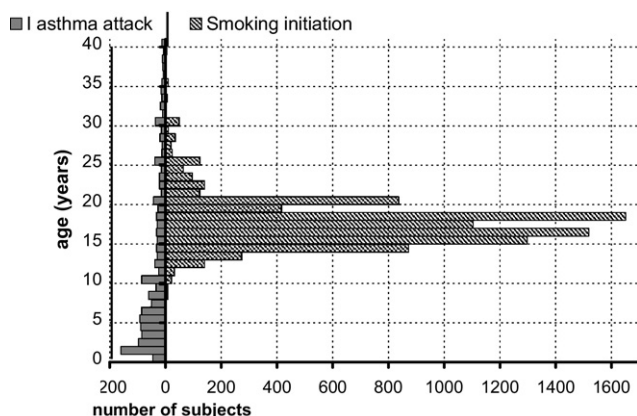


Figure 1. Distribution of age at first asthma attack and at smoking initiation in 18,612 subjects participating in the ISAYA.

selected subjects was 33.1 ± 6.8 years (mean $\pm$ SD) and male to female ratio was approximately 1 (9,135:9,426).

Screening questionnaire

The mailed questionnaire used in the present survey was the same screening questionnaire used in the European Community Respiratory Health Survey, with the addition of questions on smoking habits, asthma, and subjective perception of outdoor pollution [23].

The presence of lifetime asthma was defined by an affirmative answer to the question “Have you ever had asthma?”. Subjects were considered to have started smoking if they reported to have smoked at least one cigarette per day or one cigar a week for 1 year. Lifetime asthmatics and ever smokers were asked additional questions investigating, age at onset and remission of asthma, and age at starting and quitting smoking, respectively. Questions on smoking habits had been validated in a previous survey conducted in one participating center (Verona) [24].

Subjects were classified into five groups according to their asthma status: (1) nonasthmatics, that is, subjects not reporting asthma attacks in the first 20 years of life ($n = 17,384$), (2) subjects with childhood-onset asthma, that is, reporting asthma onset in the first decade and no disease remission by the age of 20 years ($n = 305$), (3) subjects with childhood-onset remitted asthma, that is, reporting asthma onset in the first decade and remission in the first and second decades ($n = 573$), (4) subjects with teenage-onset asthma, that is, reporting asthma onset in the second decade and no disease remission by the age of 20 years ($n = 236$) and (5) subjects with teenage-onset remitted asthma, that is, reporting asthma onset and remission both in the second decade ($n = 74$).

Statistical analysis

The relation between asthma (no asthma/asthma onset in the first decade/asthma onset in the first decade and remission in the first and second decades/asthma onset in the second decade/asthma onset and remission in the second decade) and smoking initiation in the second decade was evaluated by chi-squared test.

Significance of differences in categorical variables, as a function of asthma categories or smoking initiation, was evaluated by

Table 1

Main characteristics of the population under study, as a function of asthma history in youth

	No asthma (n = 17,384)	Childhood asthma (n = 305)	Remitted childhood asthma (n = 573)	Teenage asthma (n = 236)	Remitted teenage asthma (n = 74)	p value
Gender ^a						<.001
Males	8,470 (92.7)	174 (1.9)	353 (3.9)	102 (1.1)	36 (.4)	
Females	8,903 (94.5)	131 (1.4)	220 (2.3)	134 (1.4)	38 (.4)	
Birth cohort ^a						<.001
1953–1965	8,725 (95.3)	110 (1.2)	210 (2.3)	91 (1.0)	22 (.2)	
1966–1979	8,647 (92.0)	195 (2.1)	363 (3.9)	145 (1.5)	52 (.6)	
Geographic area						.001
Northern Italy	12,233 (94.0)	190 (1.5)	385 (3.0)	152 (1.2)	59 (.5)	
Central-Southern Italy	5,151 (92.8)	115 (2.1)	188 (3.4)	84 (1.5)	15 (.3)	
Percent rank in cumulative response (median, interquartile range)	34.6 (18.6–57.9)	20.0 (15.3–46.4)	20.0 (15.3–51.1)	20.0 (15.3–51.1)	25.9 (18.6–51.1)	<.001

Categorical variables are reported as absolute frequency with row percentage in parentheses, percent rank in cumulative response as median (interquartile range). Significance of differences was evaluated by chi-squared test for categorical variables, Kruskal–Wallis test for percent rank in cumulative response.

^a Information on gender and birth cohort was missing, respectively, in 11 and 12 subjects.

chi-squared test. Significance of differences in cumulative response percentage was evaluated by Kruskal–Wallis test, as the latter variable presented a highly skewed distribution according to Skewness–Kurtosis test.

Selection bias can affect both asthma and smoking habits [25]. Hence, each subject was attributed the median of the cumulative response percentage of the contact to which he or she had answered (first, second, and third postal contact, and telephone interview).

To rule out the possibility that smoking had caused asthma rather than the reverse (reverse causality), subsequent multi-variable analysis was performed after excluding 310 subjects with asthma onset in the second decade, irrespective of remission. The relation between smoking initiation and childhood asthma was further investigated by a two level [26] Poisson regression model [27], with subjects (level 1 units) nested into centers (level 2 units). The model had smoking initiation in the second decade as the dependent variable, a random intercept term at level 2 and asthma (no asthma/asthma onset in the first decade/asthma onset in the first decade and remission in the first and second decades), gender (men/women), birth cohort (1953–1965/1966–1979), and percent rank in cumulative response as fixed effects. The interaction between asthma status and each of the potential confounders was also tested. Significance was set at $p < .05$.

Results

The main characteristics of the population under study are described in Table 1, as a function of asthma history in youth. It can be appreciated that asthma onset was more common in males during the first decade and in females during the second decade. Asthma incidence nearly doubled from the 1953–1965 birth cohort to the 66–79 birth cohort and was higher in Central-Southern Italy. Subjects with asthma tended to respond earlier than nonasthmatics, that is, at a lower cumulative response percentage.

Cumulative smoking incidence in the second decade was higher in male adolescents (4,435/9,135 = 48.6%) than in female adolescents (3,706/9,426 = 39.3%), in the 1953–1965 birth cohort (4,526/9,158 = 49.4%) than in the 1966–1979 birth cohort (3,616/9,402 = 38.5%), and in people living in the Northern Italy

(5,919/13,019 = 45.5%) than in Central-Southern Italy (2,226/5,553 = 40.1%) ($p < .001$).

The pattern of smoking as a function of juvenile asthma history was different between genders (Table 2). Among men, the cumulative incidence of smoking was the highest among nonasthmatics (49%; 95% CI: 48%–50%) and subjects with teenage-onset asthma (51%, 41%–61%), and the lowest among subjects with childhood-onset asthma (36%, 29%–43%), being intermediate among asthmatics with disease remission (44%, 39%–50%, and 39%, 23%–57%, in childhood-onset and teenage-onset remitted asthma, respectively) ($p = .002$).

Women, instead, had similar cumulative incidence of smoking initiation, irrespective of asthma onset or remission: cumulative incidence was 39% (38%–40%) in nonasthmatics, 38% (32%–45%) in subjects with childhood-onset remitted asthma, and 41% (33%–50%) in childhood-onset asthmatics without disease remission ($p = .908$).

Table 2

Main characteristics of the population under study, as a function of gender and smoking initiation in the second decade of life

	Smoking initiation between 11–20 yrs	
	Males (n = 9,135)	Females (n = 9,426)
Birth cohort ^a		
1953–1965	53.8% (2,400/4,460)	45.3% (2,124/4,692)
1966–1979	43.5% (2,033/4,671)	33.5% (1,581/4,726)
	$p < .001$	$p < .001$
Geographic area		
Northern Italy	49.5% (3,148/6,315)	41.4% (2,769/6,697)
Central-Southern Italy	45.6% (1,287/2,820)	34.3% (937/2,729)
	$p < .001$	$p < .001$
Asthma history in youth		
No asthma	49.0% (4,151/8,470)	39.4% (3,505/8,903)
Childhood-onset asthma	35.6% (62/174)	41.2% (54/131)
Remitted childhood-onset asthma	44.2% (156/353)	38.2% (84/220)
Teenage-onset asthma	51.0% (52/102)	35.8% (48/134)
Remitted teenage-onset asthma	38.9% (14/36)	39.5% (15/38)
	$p = .002$	$p = .908$

Significance of differences was evaluated by chi-squared test.

Values are percentages while the corresponding ratios are shown between parentheses.

^a Information on gender and birth cohort was missing, respectively, in 11 and 12 subjects.

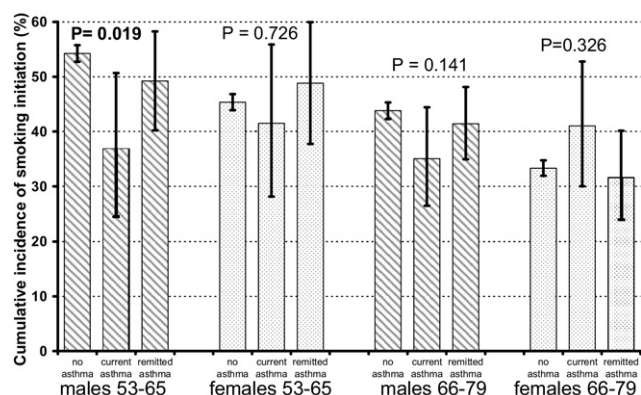


Figure 2. Cumulative incidence of smoking initiation as a function of asthma onset/remission, stratified by gender and birth cohort. Subjects with asthma onset in the second decade were excluded from the analysis, to avoid reverse causality. Columns are cumulative incidence values, bars are 95% confidence intervals. Significance was evaluated by chi-squared test.

Subsequent analyses were performed after excluding subjects with remitted or unremitted teenage-onset asthma, to remove the reverse causation effect.

Among men, the influence of juvenile asthma on smoking initiation was mainly confined to the 1953–1965 birth cohort ($p = .019$), and tended to fade in the 1966–1979 birth cohort ($p = .141$) (Figure 2), indeed, cumulative incidence of smoking onset decreased from 54.3% to 43.8% in nonasthmatics and from 49.2% to 41.4% in subjects with childhood-onset remitted asthma, while remaining stable in subjects without remission of childhood-onset asthma (from 36.8% to 35%). In females born between 1966 and 1979, cumulative smoking incidence even increased, although not significantly, in the presence of childhood-onset asthma, being 33.3% in nonasthmatics and 41.0% in subjects with childhood-onset current asthma ($p = .326$).

This pattern was substantially replicated by multivariate analysis. The Poisson regression model highlighted not only a significant first-order interaction between gender and childhood-onset asthma ($p = .005$), but also a second-order significant interaction among birth cohort, gender, and childhood-onset asthma ($p < .001$), confirming the different smoking behavior of male and female asthmatics born either between 1953 and 1965 or 1966 and 1979 (Table 3).

In males, childhood-onset asthma was associated with a lower hazard ratio (HR) of smoking initiation in both birth cohorts; however, the decrease in HR with respect to nonasthmatic coevals amounted to 29% in boys born between 1953 and 1965, being only 18% in boys born between 1966 and 1979. In females, the effect of childhood-onset asthma on smoking initiation changed completely as a function of birth cohort; however, with respect to nonasthmatic girls, the HR of smoking onset was 5% lower in girls with childhood-onset current asthma born between 1953 and 1965 and 27% higher in those born between 1966 and 1979. As expected, the HR of smoking initiation was higher in people answering to the mail survey at a later stage.

Discussion

The main findings of the present study are:

1. Asthma in childhood reduces smoking initiation during the subsequent teenage in men, but not in women.
2. Male teenagers with asthma remission present a propensity to start smoking intermediate between that of nonasthmatics coevals and current asthmatics.
3. The “protective effect” of childhood asthma on smoking initiation was particularly pronounced in males born between 1953 and 1965, and decreased in males born thereafter. In females born between 1966 and 1979, childhood asthma was even a “risk factor” for smoking initiation.

The current literature contains conflicting reports about smoking behavior of asthmatic teenagers. Most longitudinal studies reported that smoking initiation is not affected by asthma status [8,16,17]. Taking up smoking was even increased in Swedish male teenagers [2]. However, a cohort study, recently performed in The Netherlands between 2003 and 2004 [6], found results comparable to those observed in the present retrospective investigation; with respect to nonasthmatic coevals, smoking incidence was reduced in asthmatic males and increased in asthmatic females. Indeed, the same pattern was recorded in the Italian population born between 1966 and 1979. Of note, the present study considered smoking initiation over the entire second decade, so that the gender-related difference could not be attributed to the earlier development in girls.

According to ISAYA smoking prevalence has declined in Italy both in men as well as women [21]: the percentage of smokers at

Table 3

Relative risks (with 95% confidence interval in brackets) of smoking initiation in the second decade, after adjustment for the other variables

Variables	Risk ratios, adjusted for all other variables				p-value ^a
Percent rank in cumulative response: (per a 25% increase)	1.05 (1.01–1.09)				<.001
Interaction	1953–1965 birth cohort		1966–1979 birth cohort		
	Men	Women	Men	Women	
Cohort × gender × asthma status ^b					<.001
No asthma	1	.83 (.79–.88)	.82 (.79–.85)	.62 (.58–.67)	
Childhood-onset asthma	.71 (.49–1.02)	.79 (.61–1.01)	.67 (.52–.86)	.79 (.64–.99)	
Remitted childhood-onset asthma	.91 (.74–1.11)	.89 (.71–1.11)	.77 (.66–.89)	.59 (.50–.70)	

The risk ratios were obtained by a two level Poisson regression model with a robust error variance and no offset.

^a p-values of each variable were computed controlling for the other three variables. Significance of the interaction between two variables was computed controlling for the other two variables.

^b The joint effect of birth cohort, gender and childhood asthma status was presented, since a significant II-order interaction was detected among the three variables ($p < .001$).

the age of 20 years was 59.3% and 48.9%, respectively, in men and women born between 1953 and 1958 and declined to 41.2% and 32.1% in people born between 1974 and 1978. This favorable trend was attributed to effective anti-smoking campaign among teenagers and young adults. Apparently, these public health interventions were less effective among Italian asthmatics who could have been already aware of smoking noxious effects. Interestingly, a progressive deterioration of smoking behavior among subjects with asthma emerged also in the current literature; with respect to nonasthmatic coevals, smoking incidence in asthmatics was similar in studies performed in the 1970s and 1980s [16,17] and higher in studies performed during the 1990s [2] or afterward [6].

The reduced propensity to smoking initiation among asthmatic males is not surprising; healthy individuals are more likely to start smoking, and this self-selection phenomenon has been described as “healthy smoker” effect [28]. Accordingly, people surviving a childhood cancer are less likely to become smokers [29].

In contrast, adolescents with asthma are more prone to psychological problems. They more often feel lonely, report a greater number of negative social perceptions and feelings, and have more frequent psychosomatic symptoms [11]. These psychological attitudes have been related to the higher tobacco use among asthmatic compared with nonasthmatic adolescents, observed in many countries [11] and could explain the lack of smoking avoidance among female asthmatics recorded in the present study as well as in the Dutch study [6]. Alternatively, for girls with asthma, smoking could be a way to increase self-esteem, which has been shown to be lower in girls than in boys [30].

Recently, smoking onset among adolescents with asthma has been addressed by a longitudinal Dutch study [31] using the Theory of Planned Behaviour. This investigation found that smoking initiation was more often a planned behavior among asthmatic adolescents than among nonasthmatic coevals. Adolescents with asthma had a higher risk to start smoking when they presented a more positive attitude towards smoking at baseline, a lower perceived behavioral control and a higher pro-smoking subjective norm of parents. According to these findings, prevention programs based on the Theory of Planned Behaviour have been recommended for both adolescents with asthma and their parents. Perceived behavioral control should be improved by refusal skill training in adolescents themselves; parents should be advised to put pressure on their children to refrain from smoking, and, if smokers, they should be strongly recommended to quit smoking. It should be reminded that adolescents with asthma are even more likely to have smoking parents [32]. In addition, adolescents with asthma should be better informed about the harmful effects of smoking, which not only causes lung diseases, but also markedly reduces life expectancy. The present study suggests that educational interventions, tailored to adolescents with asthma, should also take into account gender and should be more intensive in females.

It has been reported that adult asthmatics with allergic rhinitis smoke less than asthmatics without this additional atopic disease [33]. In the present study retrospective information on allergic rhinitis was not collected: anyway, the protective effect of childhood asthma on smoking initiation in teenage was particularly pronounced among men reporting current allergic rhinitis during adulthood: cumulative incidence of smoking initiation decreased from 42.1% in nonasthmatics to 31.3% in the presence of childhood asthma ($p = .024$). Among men not report-

ing allergic rhinitis in adulthood, this decrease was not significant (from 50.5% to 44.8%; $p = .430$).

The present research has some limitations. First of all, reports of smoking status were not verified with biochemical methods. Indeed, other Italian Authors found that official tobacco sale rates exceeded self-reported cigarette consumption by 25%–35% [34]. However, it has been reported that smoking underreporting concerns more the number of cigarettes smoked daily than the actual status of smokers/nonsmokers [35]. Nevertheless, in one participating center (Verona), [24] a good agreement was found (Cohen's $k = .93$) between self-reported smoking consumption or abstinence and serum cotinine levels.

Second, the definition of asthma status was not the most rigorous available. However, results were substantially the same when excluding 107 subjects with self-reported asthma not confirmed by a doctor.

Third, the present estimates could have been affected by a recall bias: individuals tend to attribute the onset of a habit or a disease to an age closer to the time of interview than the true age at onset (telescoping bias) [36]. Hence, the age at asthma onset or smoking initiation could have been over-estimated by the interviewed. Nevertheless, no telescoping bias was detected in a similar epidemiological context, that is, the Italian branch of the European Community Respiratory Health Survey: age at start smoking, reported by 313 subjects interviewed twice 8.6 years apart, was $.01 \pm 2.01$ years lower (mean $\pm$ SD) in the second interview with respect to the first one, and no significant difference was observed among different birth cohorts.

Finally, information on exposure to environmental tobacco smoke in early life, which has been associated both to early-onset asthma [37] and to subsequent smoking initiation [38], was lacking in the present study. Hence, the “protective effect” of childhood asthma on starting smoking could be masked by a confounding effect of environmental tobacco smoke.

In conclusion, asthma in childhood reduces smoking initiation during the subsequent teenage in men, but not in women. This protective effect tends to fade when asthma remission occurs. Asthmatics seem to be less responsive to anti-smoking campaigns, maybe because they are already aware of smoking's noxious effects. Psychological attitudes favoring smoking initiation among female adolescents with asthma should be further investigated. Educational interventions, tailored to adolescents with asthma, should also take into account gender and should be more intensive in females.

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