

Environmental risk factors for asthma in 13-14 year old African children

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Abstract

Background Asthma prevalence in African children is high. Factors driving the prevalence or disease severity are poorly understood. This study aims to investigate environmental factors associated with asthma and severity in African children.

Methods Population based cross-sectional study of children aged 13–14 years from 10 African centers who participated in ISAAC III. Self-reported environmental exposures included engaging in physical exercise, television watching, various biomass and ETS exposure, consumption of paracetamol, large family sizes and having pets in the home. Univariable and multivariable analyses were done adjusting for center variations. Prevalences, odds ratio and 95% confidence intervals (CI) were calculated.

Results There were 258 267 children recruited among the 13-14-year-old participants. Of these, 28,391 respondents from 232 schools completed both the written questionnaire (WQ) and environmental questionnaire (EQ). The prevalence of asthma and severe asthma were 12.8% (CI 12.4-13.2), and 8.7% (CI 8.4-8.0) respectively. Factors strongly associated with asthma were maternal smoking (OR = 1.41; 95%CI: 1.23-1.64), open fire heating (OR = 1.28; 95%CI: 1.08-1.51) electric heating (OR = 1.13; 95%CI: 1.01-1.28), physical exercise (OR = 1.29; 95%CI: 1.11-1.50), monthly paracetamol use (OR 1.23; 95%CI 1.13-1.33), having an elder sibling (OR = 0.87; 95%CI 0.77-0.98). Factors associated with severe asthma were maternal smoking (OR = 1.61; 95%CI: 1.38-1.89), cat pet (OR = 1.14; 95%CI: 1.04-1.25), frequent physical exercise (OR = 1.42; 95%CI: 1.23-1.64) and monthly paracetamol use (OR = 1.20; 95%CI 1.07, 1.34).

Conclusion Several environmental exposures were associated with asthma and severe disease.

KEYWORDS

adolescents, Africa, asthma, environment, ISAAC, risk, severe

1 | INTRODUCTION

Asthma is the commonest chronic disease in children with marked geographic variation in prevalence.^{1,2} Asthma was considered to be less common in African children compared with those in high income

countries, however recent data from African studies suggests that the prevalence is as high as the global average and increasing.¹⁻⁵ Furthermore, a high proportion of African children with asthma have severe disease as defined by the International Study of Asthma and Allergies in Childhood (ISAAC) as more than three attacks of

wheezing in the preceding 12 months, sleep disturbed by wheezing, or at least one episode where in the preceding 12 months wheezing, limited speech to only one or two words at a time between breaths.⁶ Several environmental factors have been associated with the rise in asthma prevalence, but these have not been well studied in African children. Further, comparison of findings across African countries is complicated by lack of consistency in methods to define and assess asthma prevalence and severity and to measure environmental exposures.

The ISAAC study is a multi-country cross-sectional survey of the prevalence of asthma, allergic rhino-conjunctivitis, and atopic eczema in two age groups of school children: 6-7 years and 13-14 years.⁷ ISAAC used standardized written questionnaires of reported symptoms. The ISAAC study phases allow standardized comparisons of the prevalence of these disorders in different countries as previously published.^{8,9} An environmental questionnaire was included in the ISAAC phase III, enabling investigation of environmental factors associated with prevalence or severity of disease. The use of the written questionnaire (WQ) was compulsory for every center participating in ISAAC III, while the use of the environmental questionnaire (EQ) was optional.⁷ Although 10 sites in Africa participated in ISAAC III and completed the EQ, and despite studies having been completed several years ago, the environmental associations in African respondents have not yet been published. This information is still highly relevant as potentially harmful environmental exposures associated with asthma or severe disease are ubiquitous in Africa. Studies suggest that urbanizing populations may be especially susceptible to development of asthma, possibly through changes in diet and lifestyle and exposure to environmental pollutants. Key prevalent environmental factors in Africa include exposure to diverse types of biomass for cooking or heating the home, exposure to tobacco smoke, large family sizes, pets in the home, frequent lower respiratory tract infection, and life style changes that include transition to more sedentary living.³

The aim of this study was to investigate environmental factors associated with asthma prevalence or severity in 13-14 year old African adolescents participating in ISAAC III.

2 | MATERIALS AND METHODS

This was a cross-sectional study of African adolescents aged 13-14 years who participated in ISAAC III in African centers, between January 2001 and November 2002. Active or passive consenting processing were done to obtain consent from parents and school authorities, according to local ethical guidelines while assent was obtained from participants. Enrolled participants completed both a core written questionnaire and an environmental questionnaire (EQ), both of which were part of ISAAC III. The African data was obtained, with permission, from the ISAAC data center. The study was approved by the Faculty of Health Sciences University of Cape town research ethics committee. Each participating center also obtained ethics approval for the initial data collection at their sites.

2.1 | Data collection and quality control

All consenting participating centers in Africa who completed both the core WQ and EQ were chosen and included. The methodology for ISAAC has been well described; participation is self-initiated by an investigator for each centre.⁷ There were 12 centers in nine African countries who did not complete the EQ and were excluded from the analyses (Figure 1). As per the prescribed standardized ISAAC methodology, school children aged 13-14 years were invited to participate and were sampled in a prescribed geographic area for the specific centre, using schools as the sampling unit. A minimum of 10 schools were sampled in each center and through a multi-stage random process, 3000 children, which was the minimum target for the main ISAAC III study, were recruited using school class registers.⁷ This provided a study power of 90% to detect a comparable change in asthma prevalence of at least 1%, when compared to data from earlier ISAAC evaluations.⁷

The core and environmental questionnaires were completed according to standardized ISAAC III methodology.⁷ Centers that administered the questionnaires in languages other than English (Afrikaans, Xhosa, Arhmaic, French, Arabic) underwent a back-translation process as per ISAAC protocol.⁷ Double data entry was done at individual sites to minimize data entry errors and each center was responsible for initial data cleaning. Cleaned data that was transferred to the central ISAAC data center in New Zealand was utilized with careful quality control of data for analyses. These data have already been used in many publications of prevalence including those from Africa.^{10,11}

For this study, data from all African centers that completed both the written and environmental ISAAC questionnaire and satisfied the published methodology⁷ were included. Further sub-categorization for purposes of comparison by language (cultural) divide into Anglophone and Francophone countries was also done, as this may impact on their environmental influences. The self-administered written questionnaire (WQ) used for the study included questions on respiratory symptoms. Current asthma was defined according to the ISAAC definition, as wheezing or whistling in the chest in the past 12 months. Severe asthma was defined according to ISAAC as any of the following in the past 12 months: more than three attacks of wheezing, sleep disturbed by wheezing on average one or more nights per week, or at least one episode where wheezing limited speech to only one or two words at a time between breaths. These were the primary outcome variables for the study and were analyzed independently of each other.

The following variables were analyzed from the Environmental questionnaire(EQ): exposure to cooking and biomass fuels: electric cooking, gas cooking, open fire cooking, electric heating, gas heating, open fire heating (yes or no to each of electricity, gas, and open fires, with possibility of answering yes to more than one type); second-hand smoke exposure (Environmental Tobacco Smoke [ETS]), which we analyzed with separate analyses for mother, father, and any persons smoking at home,¹² (recoded as ETS in ≥ 3 smokers as we noted that any additional smoker in the house may include the adolescent participant). This was captured as ETS in ≥ 3 smokers at home, to enable

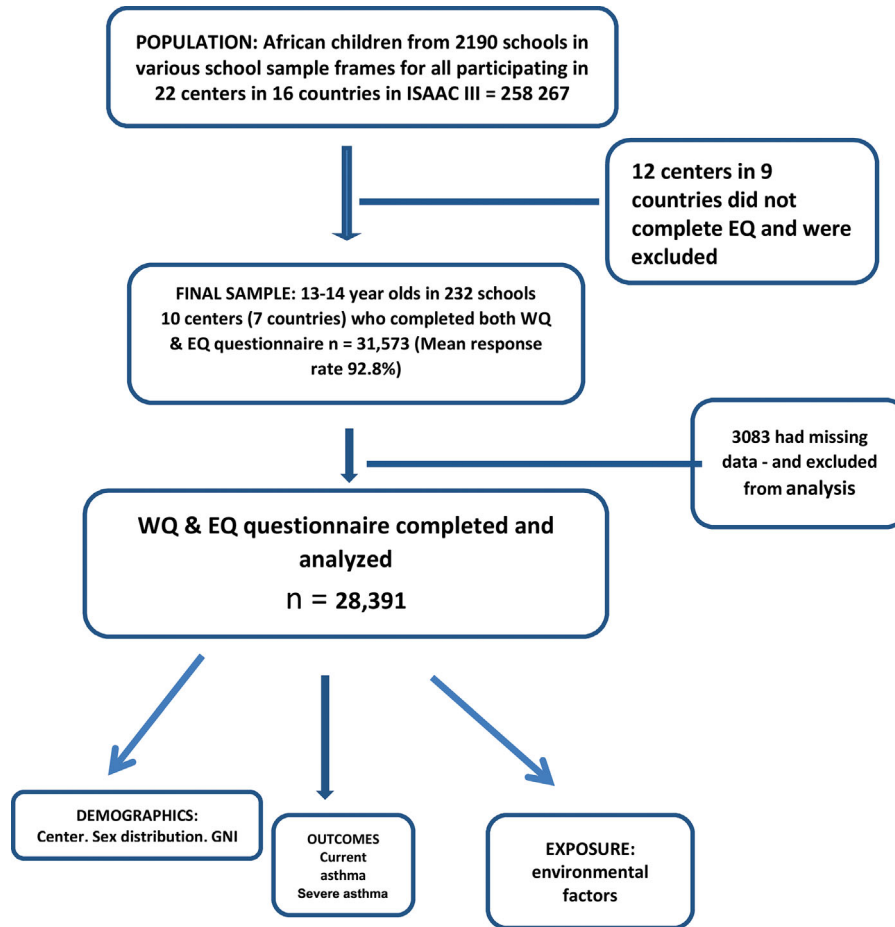


FIGURE 1 Flow chart for selection of adolescent participants in the environmental ISAAC III study for African centers

the analyses account additional smokers beyond the mother and father. Other variables were: having ≥ 2 older siblings, having ≥ 2 younger siblings, having pets at home (cat and dog), engaging in ≥ 3 weekly physical exercise, sedentary life style such as ≥ 5 h of daily television watching, and use of paracetamol at least once a month as compared to once or less in a year.¹²

2.2 | Data analyses

Data were analyzed using Stata version 13 (Stata Corporation). All environmental factors were analyzed as simple binary variables. Guided by the EQ ISAAC III guide manual for recording responses, a “yes” answer was written as “1” and “no” as “2”, (and recoded as “0”). All other responses (missing and indeterminate) were coded as “9.”¹² There were 3083 participants who had such missing data and were excluded from the analyses (Figure 1). As the frequency of invalid answers was less than 5% of total recorded answers in each of the environmental factors assessed, a further sensitivity analysis to determine what effect invalid answers could have on the data was not done.

Prevalences were calculated by the number of positive responses to each question in the asthma written questionnaire (WQ) and

environmental questionnaire (EQ); divided by the total number of completed questionnaires (positive and negative responses) in the various questionnaires. The participants who had positive asthma responses in the written questionnaire (WQ) options, were identified and their answers correlated with their answers to the EQ, as possible risk factors for their symptoms.

Univariable and multivariable logistic regression analyses were used to assess the relationship between the environmental and lifestyle variables adjusted for center with current and severe asthma. For children who indicated current asthma, a univariable logistic regression analysis was performed to assess the relationship between the environmental and lifestyle variables adjusted for center. Similar analyses were also done for children with severe asthma. All variables with a P -value < 0.2 were then built into a multivariable logistic regression model and a backward selection procedure was used to identify significant variables. Each model included 232 clusters for school attended to adjust for the correlation between children attending the same school in the standard errors of the estimated effects of the risk factors. The key findings were compared between the Anglophone and Francophone centers. All regression outputs were summarized as odds ratios (ORs) and corresponding 95% confidence intervals (CIs). A P -value < 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Participants

Amongst 258 267 13-14-year-old participants in ISAAC III from 10 centers in seven African countries, there were 28 391 respondents from 232 schools that completed both the written questionnaire (WQ) and environmental questionnaire (EQ), who had complete data and were analyzed, Figure 1. The 10 centers were geographically spread across Africa-three Anglophone centers in South, East, and West Africa (Cape Town, Addis Ababa, Ibadan); and seven Francophone centers in Central, West, North, and East Africa (Yaoundé, Urban Cote d'Ivoire, Port-gentil, Boulmene, Casablanca, Marrakech, Khartoum). Fifty percent of overall respondents were male with a variation of sex distribution across centers. There were four middle-income centers and six low-income centers. The average response rate was 92.8% (range 78.7-100%) across centers.⁸ This was in keeping with the acceptable rate of 90% for ISAAC III studies.⁷ The response rates for individual centers was high⁸: Cape Town (83.4%), Ibadan (99.7%), Addis Ababa (96.8%), Yaoundé (90.6%), Urban Cote d'Ivoire (82.5%), Port-Gentil (78.7%), Boulmene (100%), Casablanca (100%), Marrakech (99.9%), and Khartoum (96.5%), Table 1.

Three centers, Boulmene, Casablanca, and Marrakech had fewer than 2000 participants, but these centers were from the same country (Morocco), thus the total number recruited from that country (4720) was comparable to that obtained from the countries represented by only one centre.¹³

3.2 | Asthma prevalence

The overall prevalence of current asthma was 12.8% (95%CI 12.4-13.2), while the prevalence of severe asthma was 8.7% (95% CI 8.4-9.0); Table 2. There was a 4.5-fold difference in the prevalence of current asthma between centers with the highest and lowest prevalence rates, Table 2. The highest prevalence occurred in Cape Town, South Africa 20.4% (95%CI 19.3-21.5), and Urban Cote d'Ivoire, Ivory Coast 19.3% (95%CI 18.0-20.7) while the lowest prevalence was in Boulmene, Morocco 5.4% (95%CI 4.2-6.8), and Marrakech, Morocco 4.4% (95%CI 3.5-5.5).

3.3 | Prevalence of environmental risk factors

There was wide variability in prevalence of environmental factors across centers, Table 3. Across sites, the use of gas for cooking by 17 967 (63.1%), was twice as common compared to other cooking exposures: electricity, 7327 (25.7%) or use of open fires, 8051 (28.3%), $P < 0.001$. Exposure to gas as a means of home heating, was however the least common way of heating homes used by 3333 (11.7%), Table 3. Large family size was highly prevalent in all African sites, with 24 378 (85.6%) of respondents reporting two or more older siblings and 23 811 (83.6%) reporting two or more younger siblings. Exposure to environmental tobacco smoke (ETS) was common: 15 371 (54.0%) children reported homes with three or more smokers. There were 1959 (6.9%) who reported mothers who smoked, and 6156 (21.6%)

TABLE 1 Characteristics of participants in African centers in ISAAC III

Center	Cape Town (South Africa)	Ibadan (Nigeria)	Addis Ababa (Ethiopia)	Yaoundé (Cameroun)	Urban Cote d'Ivoire (Cote d'Ivoire)	Port-Gentil (Gabon)	Boulmene (Morocco)	Casablanca (Morocco)	Marrakech (Morocco)	Khartoum (Sudan)
Number of participants	5037	3142	3195	2983	3342	3166	1254	1777	1689	2896
Language divide	Anglophone	Anglophone	Anglophone	Francophone	Francophone	Francophone	Francophone	Francophone	Francophone	Francophone
Gender (Male %)	40	57	43	46	60	47	60	52	42	53
GNI gross national income	Middle	Low	Low	Low	Low	Low	Middle	Middle	Middle	Low
Response rate (%)	83.4	99.7	96.8	90.6	82.5	78.7	100	100	99.9	96.5

TABLE 2 Prevalence rates of asthma in adolescents in African centers in ISAAC III

Center	Cape Town (South Africa)	Ibadan (Nigeria)	Addis Ababa (Ethiopia)	Yaoundé (Cameroun)	Urban Cote d'Ivoire (Cote d'Ivoire)	Port-Gentil (Gabon)	Boulmene (Morocco)	Casablanca (Morocco)	Marrakech (Morocco)	Khartoum (Sudan)
Current asthma % (95%CI)	20.4 (19.3-21.5)	13.0 (11.8-14.2)	9.1 (8.1-10.1)	5.7 (4.9-6.6)	19.3 (18.0-20.7)	10.2 (9.2-11.3)	5.4 (4.2-6.8)	16.0 (14.4-17.8)	4.4 (3.5-5.5)	12.5 (11.3-13.7)
n/N ^a	1025/5037	408/3149	290/3195	169/2983	645/3342	324/3168	68/1254	285/1777	75/1689	361/2876
Severe asthma/Total (%) (95%CI)	12.4 (11.5-13.3)	9.5 (8.5-10.6)	8.2 (7.3-9.2)	4.3 (3.6-5.1)	12.0 (10.9-13.1)	5.9 (5.1-6.8)	2.7 (1.9-3.8)	8.7 (7.5-10.1)	2.2 (1.6-3.0)	9.5 (8.5-10.6)
Severe asthma/current asthma%(n/N) ^{a,b}	46.4 (47.6/1025)	39.2 (132/337)	63.8 (185/290)	47.3 (80/169)	61.9 (399/645)	44.1 (143/324)	48.5 (33/68)	54.0 (154/285)	48.0 (36/75)	58.2 (210/361)
Asthma ever	33.15	20.4	17.5	8.9	28.4	16.5	10.9	23.8	10.1	16.3
Severe/asthma ever proportion (%)	32.6	10.3	46.8	36.4	42.19/31	27.8	23.5	36.7	21.8	46.7

^aUnweighted prevalence.^bProportion of severe asthma of those with current asthma.

had a dad who smoked at home. Cat exposure occurred in 11 043 (38.8%) of homes, while dog exposure was less common in 9596 (33.7%) homes, $P < 0.001$. A sedentary lifestyle as assessed by watching television five or more hours per day occurred in 9603 (33.7%) participants, while engaging in regular physical exercise (three or more times in a week), was only reported by 5613 (19.7%); $P < 0.001$. Paracetamol was reported to be consumed at least once a month by 11 654 (40.9%), Table 3.

3.4 | Asthma and environmental risk factors

Environmental factors associated with current asthma on univariable analyses were maternal smoking (OR = 1.42; 95%CI: 1.23-1.64; $P < 0.001$), paternal smoking (OR = 1.14; 95%CI: 1.03-1.26, $P = 0.01$), use of open fires (OR = 1.28; 95%CI: 1.05-1.43; $P = 0.01$), or electricity (OR = 1.12; 95%CI: 1.00-1.26; $P = 0.05$) for home heating, having a cat at home (OR = 1.13; 95%CI 1.03-1.23; $P = 0.01$), engaging in regular physical exercise, three or more times every week (OR = 1.31; 95%CI: 1.14-1.51; $P < 0.001$), consumption of paracetamol at least once a month (OR = 1.24; 95%CI 1.15-1.35; $P < 0.001$). Respondents who had two or more older siblings had a reduced risk of current asthma (OR = 0.88; 95%CI 0.78-1.00; $P = 0.04$), Table 4.

Environmental risk factors associated with severe asthma on univariable analyses were exposure to ETS: maternal smoking (OR = 1.63; 95%CI 1.39-1.90; $P < 0.001$), paternal smoking (OR = 1.15; 95%CI 1.03-1.29; $P = 0.02$); and other smokers at home (OR = 1.17 95%CI 1.03-1.34; $P = 0.02$); having a cat at home (OR = 1.17; 95%CI 1.07-1.29; $P = 0.001$), engaging in physical exercise three or more times every week (OR = 1.42; 95%CI 1.23-1.63; $P < 0.001$) and ingestion of paracetamol at least once a month (OR = 1.21, 95%CI 1.09-1.36; $P = 0.001$).

On multivariable analysis, factors associated with current asthma were maternal smoking (OR = 1.41; 95%CI 1.23-1.64; $P < 0.001$), heating the home with electricity (OR = 1.13; 95%CI 1.01-1.28; $P = 0.04$), open fires (OR = 1.28; 95%CI 1.08-1.51; $P = 0.01$), engaging in regular physical exercise (three or more times in a week), (OR = 1.29; 95%CI 1.11, 1.50; $P = 0.001$), consumption of paracetamol at least once a month (OR = 1.23; 95%CI 1.13-1.33; $P < 0.001$), while having two or more older siblings was protective (OR 0.87; 95%CI 0.77-0.98; $P = 0.03$), Table 5.

On multivariable analysis, factors associated with severe asthma were maternal smoking (OR = 1.61; 95%CI: 1.38-1.89; $P < 0.001$), having a cat at home (OR = 1.14; 95%CI 1.04-1.25; $P = 0.03$), engaging in frequent and regular physical exercise (three or more times in a week), (OR = 1.42; 95%CI: 1.23-1.64; $P < 0.001$), or paracetamol at least once every month (OR 1.20; 95%CI 1.07-1.34; $P < 0.001$), Table 5.

3.5 | Asthma and environmental risk factors in Anglophone compared to Francophone countries

When analyzed by language divide, asthma prevalence in the Anglophone countries was 15.1% (1723/11381), 95%CI 14.5-15.8), compared to 11.3% (1927/17109), 95%CI 10.8-11.8), in Francophone

TABLE 3 Prevalence of environmental risk factors in Africa

Environmental factors (variables)	All African centers combined prevalence n(%)	Prevalence range of centers (%)
Mom smokes	1959 (6.9)	0.5- 27.9
Dad smokes	6156 (21.6)	2.8-42.3
≥3 Smokers at home	15 371 (54.0)	14.8-100
Electric cooking	7327 (25.7)	0.5-88.1
Gas cooking	17967 (63.1)	10.0-97.6
Fire cooking	8051(28.3)	0.1-85.8
Electric heating	7394 (26.0)	0.00-70.3
Gas heating	3333 (11.7)	0.00-27.7
Fire heating	6472 (22.7)	0.03-88.2
≥2 Older siblings	24 378 (85.6)	69.6-99.9
≥2 Younger siblings	23 811 (83.6)	67.5-99.9
Cat at home	11 043 (38.8)	20.0-75.3
Dog at home	9596 (33.7)	14.5-52.9
≥3 weekly exercise	5613 (19.7)	5.9-33.3
≥5 television hours	9603 (33.7)	17.1-58.9
Monthly paracetamol	11 654 (40.9)	16.4-64.3

sites, $P < 0.001$. Severe asthma prevalence was 11.0% (1257/11381), 95%CI 10.5-11.6), and 7.1% (1214/17109), 95%CI 6.7-7.5), respectively in Anglophone versus Francophone countries, $P < 0.001$.

In a multivariable analysis, the important environmental influences for asthma that were present in both areas included maternal smoking, three or more weekly physical exercise or monthly paracetamol use. In

addition in Anglophone countries associations were found for cat in the home (OR = 1.26; 95%CI 1.11-1.39; $P < 0.001$), and a protective role for use of gas for heating (OR = 0.80; 95%CI 0.67-0.96; $P = 0.02$) while in Francophone countries, gas heating (OR = 1.31; 95%CI 1.09-1.57; $P = 0.003$) or fire heating (OR = 1.25; 95%CI 1.01-1.56; $P = 0.04$) were significantly associated with asthma, Supplementary Tables S1 and S2.

TABLE 4 Environmental exposures and association with current asthma in African adolescents participating in ISAAC III

Variables ^a	Univariable			Multivariable ^b		
	OR	95%CI	P-value	OR	95%CI	P-value
Mom smokes	1.42	1.23-1.64	<0.001	1.41	1.23-1.64	<0.001
Dad smokes	1.14	1.03-1.26	0.01			
Smokers at home	1.07	0.96-1.19	0.21			
Electric cooking	1.00	0.89-1.13	0.99			
Gas cooking	1.01	1.00-1.14	0.85			
Fire cooking	1.01	0.86-1.20	0.84			
Electric heating	1.12	1.00-1.26	0.05	1.13	1.01-1.28	0.04
Gas heating	0.88	0.76-1.02	0.09			
Fire heating	1.28	1.05-1.43	0.01	1.28	1.08-1.51	0.01
Older siblings	0.88	0.78-1.00	0.04	0.87	0.77-0.98	0.03
Younger siblings	0.94	0.85-1.04	0.23			
Cat at home	1.13	1.03-1.23	0.01			
Dog at home	1.06	0.97-1.16	0.20			
≥3 exercise weekly	1.31	1.14-1.51	<0.001	1.29	1.11-1.50	0.001
≥5 hour daily television watching	1.06	0.97-1.16	0.21			
≥1 Monthly paracetamol	1.24	1.15-1.35	<0.001	1.23	1.13-1.33	<0.001

Significant P values are marked in bold.

^aAll variables individually adjusted for inter-center and cluster variability.

^bBackward elimination.

TABLE 5 Environmental exposures and association with severe asthma in African adolescents participating in ISAAC III

Variables ^a	Univariable			Multivariable		
	OR	95%CI	P-value	OR	95%CI	P-value
Mom smokes	1.63	1.39-1.90	<0.001	1.61	1.38-1.89	<0.001
Dad smokes	1.15	1.03-1.29	0.02			
Smokers at home	1.17	1.03-1.34	0.02			
Electric cooking	1.03	0.82-1.28	0.81			
Gas cooking	1.07	0.93-1.23	0.33			
Fire cooking	1.07	0.91-1.26	0.43			
Electric heating	1.00	0.87-1.14	0.99			
Gas heating	1.02	0.89-1.17	0.77			
Fire heating	1.15	0.94-1.40	0.17			
Older siblings	0.95	0.83-1.09	0.46			
Younger siblings	1.07	0.94-1.20	0.31			
Cat at home	1.17	1.07-1.29	0.001	1.14	1.04-1.25	0.03
Dog at home	1.11	1.00-1.24	0.06			
≥3 weekly exercise	1.42	1.23-1.63	<0.001	1.42	1.23-1.64	<0.001
≥5 hour daily television watching	1.12	0.99-1.24	0.07			
≥1 Monthly paracetamol	1.21	1.09-1.36	0.001	1.20	1.07-1.34	<0.001

Significant *P* values are marked in bold.

^aAll variables adjusted for inter- center and cluster variability.

^bBackward elimination.

There were similar associations with severe asthma in Anglophone and Francophone countries including maternal smoking (OR = 1.38; 95%CI 1.05-1.83; *P* = 0.02), engaging in three or more time weekly physical exercise (OR = 1.58; 95%CI 1.25-2.02; *P* = 0.002), or monthly paracetamol exposure (OR = 1.23; 95%CI 1.08-1.41; *P* = 0.003); and monthly paracetamol exposure (OR = 1.23; 95%CI 1.108-1.41 *P* = 0.003), Supplementary Tables S3 and S4.

4 | DISCUSSION

This large study of asthma in African adolescents participating in ISAAC III has shown high prevalence rates of asthma with a high proportion having severe asthma. Different diagnostic criteria for asthma, lack or variable access to care, lack of access to asthma guidelines, and sub-optimal access to asthma controller medications may contribute to the variations in reported asthma prevalence and severity between centers in our study, and as previously reported.^{6,14} The high and varying prevalence of severe asthma especially among those with current asthma may be affected by similar factors and may equally reflect lack of diagnosis or lack of affordable controller therapy or spacer devices to enable effective delivery of medication.¹⁵

Several environmental factors were highly prevalent and were associated with asthma or severe disease. Asthma prevalence was associated with use of open fires and electricity for heating the home, maternal smoking, frequent physical exercise, monthly paracetamol consumption, or having an older sibling; while severe asthma was associated with exposure to maternal smoking, gas used in the home

for heating, frequent physical exercise, or paracetamol consumption. There were consistent exposures associations with severe asthma in both Anglophone and Francophone countries.

Our study showed that smoke exposure was an important risk factor for asthma and for severe disease, as has been previously reported within and outside of Africa.¹⁶⁻²² These findings add to the available evidence for the adverse impact of environmental tobacco smoke (ETS), on lung health in children and adolescents. This is especially important in Africa where the prevalence of smoking is increasing and where adolescents may be at an increased risk of becoming smokers.¹⁹⁻²¹ The association of asthma with ETS exposure occurred even in areas with a reported low prevalence of maternal smoking. Cigarette smoking and second-hand smoke exposure of any intensity, are well documented triggers of asthma.^{16-18,21,22} Several suggested mechanisms include direct toxin effects on the bronchial epithelium and cilia, causing oxidative damage, affecting lung development, and making the airway asthma-prone and the release of proinflammatory mediators with resultant increase in epithelial permeability which leads to mucosal edema, contributing to asthma symptoms.^{23,24} Furthermore, cumulative exposure to tobacco smoke culminates in a decline in lung function.²⁵

Many households in low and middle-income countries burn biomass fuels in open fireplaces or in non-airtight cooking or heating stoves.^{26,27} This results in substantial emissions, with high levels of indoor pollution. Biomass exposure to wood for cooking or heating the home thus poses a significant risk for current asthma, due to high level of respirable particulate matter, further confirming findings from other studies.^{22,26-30} Many wood smoke constituents cause both acute and

chronic biologic, physiologic, and structural effects in the lungs including obstructive symptoms.²⁶ Further use of gas for heating or cooking is increasingly occurring in these areas, as the population becomes less poor. However, concerning data suggests that exposure to volatile organic compounds (from paraffin or gas) may also be associated with substantial respiratory morbidity including wheezing.^{22,28,29} However, in an analysis of global data, no evidence of an association between the use of gas as a cooking fuel and either asthma symptoms or asthma diagnosis.²⁸ The association of current asthma with electricity as the source for heating or of severe asthma with heating the home with gas in our study may not be a direct causal effect but rather a reflection of affluence, used more by higher income homes; asthma prevalence is well described to be higher in more affluent populations.²⁸ The reason for relative protective role of gas heating noted in Anglophone centers and not in Francophone countries is unclear but may be related to geographical location or environmental humidity. Soneja et al³¹ reported that hot humid air especially during summer, triggered asthma symptoms with increase in reported hospitalization rates. Another plausible explanation may be related to the ventilation in the homes as variation in may be found in Anglophone compared to Francophone homes. This is consistent with a study in the United States of America, that found that children who lived in well ventilated homes in which gas stoves were used, had higher lung function and lower odds of asthma and wheeze, compared to children from homes with poor or absent ventilation.³² Housing unit types were however not specifically assessed as part of ISAAC.

In those with older siblings, a protective effect was noted for current asthma, as previously reported.³³ Large family size was however not associated with severe asthma in this present study. This may be because the protective effect of frequent exposures to infection that comes from having many siblings, which influences the TH 1 pathway in the "hygiene hypothesis" may not totally account for the other inflammation pathways involved in developing severe asthma.^{34–36}

There was an increased risk of current asthma in children who engaged in regular physical exercise (three or more times in a week), similar to that reported in some studies.^{37–45} Though the exact mechanism is unknown, two theories have been proposed: an airway humidity theory, which suggests that air movement through the airway results in relative drying of the airway that serves as a trigger to a cascade of events that then result in airway edema and bronchospasm in susceptible children. The other theory, based on airway cooling phenomenon, notes that the air moving in the bronchial tree results in a decreased temperature, which triggers a hyperemic response within the bronchi, in an effort to re-heat the airway. This culminates in release of inflammatory mediators with resultant bronchial wall spasm.⁴⁵ However, it is also possible that exercise unmasks asthma symptoms in children with underlying uncontrolled or undiagnosed asthma. This is probable, given the high rates of undiagnosed or uncontrolled asthma found. Studies have also documented ethnicity, obesity, and various dietary factors to be associated with poor exercise tolerance and asthma.⁴¹ Obesity is associated with low lung function, exercise intolerance, and asthma.⁴² The association between BMI and asthma was noted in the global ISAAC data where there was a

relationship between overweight/obesity and asthma. Vigorous physical activity was also associated with asthma in adolescents.³⁷ Furthermore, a meta-analysis of 11 studies on the association between asthma and quantified physical activity, also found positive associations between new onset asthma and low physical activity in adolescents.⁴³ Asthma and rhinitis are also reported to be independently associated with low physical activities in boys.⁴⁴ Any notable EIB in a child with established should however be investigated to ensure medication adherence.

There was a consistent significant association in our study between current and severe asthma with monthly paracetamol consumption as also reported in other studies.^{46–48} Paracetamol when consumed, causes the total glutathione levels rise and this has been associated with marked functional bronchoconstriction.⁴⁸ These levels are reported to be increased in induced sputum of patients with mild and moderate asthma,⁴⁶ further buttressing the contribution of oxidative stress to the pathogenesis of airway inflammation.

One limitation of the study is reliance on recall and on written response to wheezing or whistling in chest in past 12 months as the measure of current asthma, especially as there is no word for wheezing in many African languages. However, this method has been widely used in ISAAC for the diagnosis of asthma. As this was a cross-sectional study causality cannot be inferred, and indoor air pollution or biomass exposure was not objectively measured. The sample was not weighted for the true population sizes and the centers that did not complete the environmental questionnaire, and thus excluded from analysis, may affect generalizability of results. However, the sites studied were widely spread across geographical divisions of Africa, represent a large number of children and are thus a representative sample. Further, differences across sites and schools within sites were accounted for in the regression analysis.

In conclusion, this study highlights that asthma is common and often severe in African children and that there are specific environmental exposures associated with disease. Several exposures of public health importance were identified, highlighting the need for stronger health policies and programs to reduce exposures associated with disease. Strategies to promote cleaner fuels and reduce smoking are urgently needed in African countries to improve child health.

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CONFLICTS OF INTEREST

None.

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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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****Supplementary tables: Environmental exposures and association with language (cultural) divide**

Table 6: Environmental exposures and association with current asthma in Anglophone African adolescents participating in ISAAC III

Variables*	Univariable			Multivariable**		
	OR	95% CI	p value	OR	95% CI	p
				value		
Mom smokes	1.40	1.18 - 1.66	<0.001	1.32	1.13 - 1.55	<0.001
Dad smokes	1.20	1.04 - 1.39	0.01			
Smokers at home	1.10	0.92 – 1.31	0.30			
Electric cooking	1.05	0.91 - 1.21	0.52			
Gas cooking	0.98	0.86 - 1.13	0.82			
Fire cooking	1.09	0.83 -1.42	0.52			
Electric heating	1.23	1.04 - 1.48	0.02			
Gas heating	0.76	0.63 –0.92	0.004	0.80	0.67 –0.96	0.02
Fire heating	1.30	1.02 - 1.66	0.03			
Older siblings	0.91	0.76 – 1.12	0.36			
Younger siblings	0.94	0.80 -1.09	0.39			
Cat at home	1.28	1.14 - 1.44	<0.001	1.26	1.11 - 1.39	<0.001
Dog at home	1.03	0.92 – 1.15	0.59			
≥3 exercise weekly	1.18	1.01 - 1.39	0.04	1.29	1.11 - 1.50	0.001
≥5 hour daily television watching	1.03	0.90 – 1.19	0.64			
≥1 Monthly paracetamol	1.21	1.06 - 1.38	0.01	1.23	1.13 - 1.33	<0.001

*All variables individually adjusted for inter- center and cluster variability. **Backward elimination

Table 7: Environmental exposures and association with current asthma in Francophone African adolescents participating in ISAAC III

Variables*	Univariable			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Mom smokes	1.52	1.23 – 1.88	<0.001	1.47	1.19 – 1.83	<0.001
Dad smokes	1.09	0.95 - 1.24	0.22			
Smokers at home	1.06	0.92 - 1. 21	0.43			
Electric cooking	0.90	0.71 - 1.15	0.41			
Gas cooking	1.05	0.85 - 1.29	0.66			
Fire cooking	0.96	0.78 - 1.18	0.72			
Electric heating	1.02	0.87 - 1.14	0.99			
Gas heating	1.18	1.00 - 1.40	0.05	1.31	1.09 - 1.57	0.003
Fire heating	1.18	0.96 -1.44	0.12	1.25	1.01 - 1.56	0.04
Older siblings	0.95	0.83- 1.09	0.46			
Younger siblings	0.95	0.83 – 1.08	0.40			
Cat at home	1.01	0.90 – 1.14	0.83			
Dog at home	1.09	0.95 - 1.26	0.22			
≥3 weekly exercise	1.46	1.16 - 1.83	0.001	1.45	1.15 - 1.82	0.002
≥5 hour television watching daily	1.08	0.95 - 1.21	0.22			
≥1 Monthly paracetamol	1.27	1.15 - 1.41	<0.001	1.27	1.19 - 1.83	<0.001

*All variables adjusted for inter- center and cluster variability and **Backward elimination

Table 8: Environmental exposures and association with severe asthma in Anglophone African adolescents participating in ISAAC III

Variables*	Univariable			Multivariable**		
	OR	95% CI	p value	OR	95% CI	p value
Mom smokes	1.68	1.39 – 2.02	<0.001	1.38	1.05 – 1.83	0.02
Dad smokes	1.23	1.05 - 1.43	0.01			
Smokers at home	1.45	1.16 – 1.81	0.001			
Electric cooking	1.06	0.89 - 1.26	0.51			
Gas cooking	1.02	0.88 - 1.17	0.81			
Fire cooking	1.12	0.87 -1.44	0.36			
Electric heating	1.06	0.87 - 1.30	0.55			
Gas heating	0.97	0.82 – 1.16	0.77			
Fire heating	1.05	0.78 - 1.40	0.76			
Older siblings	1.02	0.85 – 1.22	0.87			
Younger siblings	1.15	0.97 -1.37	0.10			
Cat at home	1.27	1.13 - 1.43	<0.001			
Dog at home	1.08	0.96 – 1.23	0.22			
≥3 exercise weekly	1.27	1.08 - 1.50	0.003	1.58	1.25 – 2.02	<0.001
≥5 hour daily television watching	1.13	0.97 – 1.31	0.64			
≥1 Monthly paracetamol	1.17	1.00 - 1.41	0.07	1.23	1.08 - 1.41	0.003

*All variables individually adjusted for inter- center and cluster variability. **Backward elimination

Table 9: Environmental exposures and association with severe asthma in Francophone African adolescents participating in ISAAC III

Variables*	Univariable			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Mom smokes	1.46	1.10 – 1.92	0.01	1.38	1.05 – 1.83	0.02
Dad smokes	1.09	0.92 - 1.29	0.34			
Smokers at home	1.04	0.89 - 1.21	0.65			
Electric cooking	1.00	0.75 - 1.34	0.99			
Gas cooking	1.16	0.87 - 1.56	0.31			
Fire cooking	1.02	0.82 - 1.27	0.86			
Electric heating	0.93	0.78 - 1.11	0.43			
Gas heating	1.14	0.93 - 1.40	0.22			
Fire heating	1.24	0.94 -1.62	0.12			
Older siblings	0.90	0.74- 1.10	0.29			
Younger siblings	0.99	0.83 – 1.18	0.919			
Cat at home	1.01	0.95 – 1.24	0.24			
Dog at home	1.15	0.95 - 1.41	0.12			
≥3 weekly exercise	1.61	1.27 – 2.04	0.001	1.59	1.25 – 2.02	<0.001
≥5 hour television watching daily	1.09	0.93 - 1.27	0.29			
≥1 Monthly paracetamol	1.25	1.09 - 1.43	0.001	1.23	1.08 - 1.41	0.003

*All variables adjusted for inter- center and cluster variability and **Backward elimination

*All variables adjusted for inter- center and cluster variability and **Backward elimination