

Associations between pediatric asthma and adult non-communicable diseases

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Abstract

Background: To date, there is no comprehensive study examining how asthma diagnosed in childhood or adolescence is associated with diagnoses of subsequent non-communicable diseases (NCDs) during adulthood. Our study aimed to examine the associations between pediatric asthma and several adult NCDs, with temporality and long interval times between asthma and NCD diagnoses.

Methods: We used RAND Indonesian Family Life Survey Fifth Wave (IFLS5) fielded in 2014-2015, to study whether being diagnosed with pediatric asthma at 0-19 years of age was associated with increased risks of hypertension, diabetes, rheumatoid arthritis, stomach diseases, kidney diseases, and heart diseases or stroke diagnosed in adulthood. We used the weighted Poisson regression adjusting for age, sex, urbanicity, and insurance status to estimate risk ratios. Subgroup analyses were performed by sex and age of asthma and other NCD diagnoses.

Results: Pediatric asthma significantly increased risks of hypertension, diabetes, and stomach diseases diagnosed at 20 years of age or above. Males with pediatric asthma diagnosed at 0-10 years of age had significantly higher risk of hypertension, while females with pediatric asthma diagnosed at 0-10 years of age had significantly higher risks of diabetes and stomach diseases. Females with pediatric asthma diagnosed at 11-19 years of age had significantly higher risks of diabetes, arthritis, stomach diseases, and kidney diseases. We also found varying associations by age of NCD diagnosis.

Conclusion: Our results suggest pediatric asthma is associated with increased risks of several adult NCDs, and these associations may vary by sex and age of asthma and other NCD diagnoses.

KEYWORDS

adolescents, adult non-communicable diseases, asthma, children, pediatric asthma, susceptibility

1 | INTRODUCTION

Asthma is a multifactorial respiratory disease affecting people of all ages. The prevalence of asthma continues to increase in many parts of

the world, particularly in low- and middle- income countries.¹ Although there have been many studies on the etiology of asthma, there has been a lack of epidemiological studies on the associations between asthma and subsequent chronic non-communicable diseases (NCDs).²

Asthma is a common pediatric disease that often occurs in early childhood, with more than 80% of asthmatic children experiencing their first episode before six years of age.³ Pediatric asthma differs from adult-onset asthma in several aspects, including immunological and inflammatory pathophysiology,^{4,5} phenotypes,^{6,7} risk factors,^{3,6,8} and sex predominance.^{3,6,8} Recently in 2017, the Forum of International Respiratory Societies has included pediatric asthma as one of the essential areas of focus in global health.⁹

To our knowledge, no population-based study has examined the associations of asthma diagnosed in childhood or adolescence with diagnoses of several types of NCDs during adulthood. Our study aims to examine the associations between pediatric asthma and adult NCDs diagnosed at 20 years of age or above, 20-39 years of age, 40-59 years of age, and 60 years of age or above. We also assessed whether age of asthma diagnosis (0-10 vs 11-19 years of age) and sex modified the associations between pediatric asthma and NCDs in adulthood. Finally, we performed a sensitivity analysis to eliminate the potential mediating effect of tobacco use on the pediatric asthma and adult NCD associations, by examining these associations among non-tobacco users.

2 | METHODS

2.1 | Study design and participants

We used the Indonesian Family Life Survey Fifth Wave (IFLS-5) collected from 2014 to 2015. The study design and methodologies of IFLS have been described elsewhere.¹⁰ The IFLS sampled approximately 7200 households across 13 provinces, representing approximately 83% of the Indonesian population.¹⁰ All analyses were weighted to represent the age, sex, and urbanicity distributions of the Indonesian population in these 13 provinces in 2014-2015.

A total of 29 826 IFLS-5 respondents aged 20 years and above were included in this study. For each analysis involving NCDs diagnosed at 20 years of age or above, 20-39 years of age, 40-59 years of age, and 60 years of age or above, we included participants whose age at questionnaire response allowed them to be at risk for developing NCDs at these particular age ranges. For example, when examining the association between pediatric asthma and NCDs diagnosed at 40-59 years of age, those younger than 40 years of age at questionnaire response were excluded from this analysis, because they could not possibly have been diagnosed with the NCD at 40-59 years of age.

2.2 | Ethical approval

The IFLS data are publicly available. The survey and its procedures have been reviewed and approved by institutional review boards (IRBs) at the RAND Corporation in the United States and the University of Gadjah Mada (UGM) in Indonesia. Written informed consent was obtained from all participants before data collection started.

Key Message

To our knowledge, this is the first population-based study to examine the associations of asthma diagnosed in childhood or adolescence with diagnoses of several types of non-communicable diseases (NCDs) during adulthood. We found pediatric asthma is associated with increased risks of several adult NCDs, and these associations may vary by sex and age of asthma and other NCD diagnoses. Understanding the susceptibility of those diagnosed with asthma in childhood and adolescence to develop NCDs in adulthood may improve the surveillance of NCDs and promote beneficial lifestyle changes among pediatric asthmatics, which may result in better NCD prevention.

2.3 | Measures

We analyzed only self-reported physician diagnoses for asthma and other NCDs, and excluded diagnoses by paramedics, nurses, or midwives. Diagnoses with asthma and other NCDs were determined from the questionnaire response to "Has a doctor ever told you that you had [disease name]?", while the year of diagnosis was obtained from the questionnaire response to "When was the condition first diagnosed?". Pediatric asthmatics were defined as those first diagnosed with asthma at 19 years of age or younger. Non-asthmatics were defined as those never reported to be diagnosed with asthma at questionnaire response. Participants with adult hypertension, diabetes, arthritis, stomach diseases, kidney diseases, heart diseases, or stroke were those first diagnosed with these NCDs at 20 years of age or above.

Age was determined based on the questionnaire response to "How old are you?" and was checked by the interviewer with Computer-Assisted Personal Interviewing (CAPI). Sex was measured using questionnaire response and checked with CAPI. Urbanicity (ie, urban or rural household location) was determined by the interviewer based on the IFLS classification of urbanicity for each province. Health insurance status was assessed with the questionnaire question: "Who in the household has a Health Card (Kartu Sehat), Social Health Insurance for the Poor (ASKESKIN), Public Health Insurance (JAMKESMAS), and National Health Insurance (BPJS or JKN) card?" (all household members, only head of household, number of persons). Based on the responses, the health insurance status was categorized as follows: all household members not insured, some household members insured, and all household members insured.

2.4 | Statistical analysis

For Table 1, we used weighted t test for continuous variables and weighted chi-squared test for categorical variables. For Tables 2-5, the weighted Poisson regression was used to estimate the risk ratio

TABLE 1 Characteristics of the pediatric asthmatics and non-asthmatics study population

Variables	Unweighted N (weighted %)		Weighted $p^{\dagger}$
	Pediatric asthmatics (N = 246)	Non-asthmatics (N = 29 580)	P
Age at questionnaire response (weighted mean $\pm$ standard error)	31.95 $\pm$ 0.71	40.99 $\pm$ 0.09	<.001***
Sex, n (%)			
Male	95 (39.96)	14 116 (49.12)	.008**
Female	151 (60.05)	15 464 (50.88)	
Urbanicity, n (%)			
Rural	50 (24.15)	12 187 (47.21)	<.001***
Urban	196 (75.85)	17 393 (52.79)	
Insurance status, n (%)			
Household not insured	122 (50.04)	14 846 (50.59)	.846
Some household members insured	51 (19.65)	6323 (20.75)	
All household members insured	73 (30.31)	8411 (28.66)	
Tobacco use, n (%)			
No	176 (70.77)	18 045 (59.98)	.002**
Yes	70 (29.23)	11 535 (40.02)	
Asthma diagnosis age, n (%)			
0-10 y	147 (60.33)	0 (0)	
11-19 y	99 (39.67)	0 (0)	
Non-communicable disease diagnosis, n (%)			
Hypertension	23 (10.17)	2341 (8.22)	.315
Diabetes	9 (3.87)	594 (2.00)	.058
Arthritis	7 (3.28)	983 (3.24)	.978
Stomach diseases	25 (12.43)	2215 (7.98)	.024
Kidney diseases	4 (1.33)	333 (1.16)	.793
Heart diseases or stroke	5(1.14)	632(1.90)	.572

† Weighted t test for continuous variables and weighted chi-squared test for categorical variables were performed.

*Significant at $P < .05$, ** significant at $P < .01$, and *** significant at $P < .001$.

(RR), risk difference, and 95% confidence interval (CI). We used IFLS5 household cross-sectional weights without attrition correction for all weighted analyses. The complete case method was used to handle missing data for the regression analyses. To control for confounding, the multivariable weighted Poisson regression model adjusted for age (continuous),¹¹⁻¹⁴ sex (male/female),^{11,13,14} urbanicity (rural/urban),^{13,14} and insurance status (all household members not insured/some household members insured/all household members insured).¹⁴ Analyses were carried out using STATA 15.1 (StataCorp). P -values < 0.05 were considered statistically significant.

3 | RESULTS

Table 1 shows the characteristics of the 29 826 participants aged 20 years and above. Asthma was more often diagnosed in females

and those who resided in urban areas. Diagnosis percentages of hypertension, diabetes, arthritis, stomach diseases, and kidney diseases at 20 years of age or above were greater among participants with diagnosed pediatric asthma than non-asthmatics.

Table 2 presents the RRs for the associations between pediatric asthma and various NCDs diagnosed at 20 years of age or above, among all participants and stratified by sex. Pediatric asthma was significantly associated with hypertension, diabetes, and stomach diseases after adjusting for confounding (see also Figure S1). We also found statistically significant associations in males or females after adjusting for confounding. Males with pediatric asthma had significantly increased risk of hypertension (RR = 3.03; 95% CI: 1.74-5.27). Females with pediatric asthma had significantly increased risks of stomach diseases and diabetes (RR = 1.86; 95% CI: 1.25-2.78 for stomach diseases; RR = 3.15; 95% CI: 1.51-6.61 for diabetes). We also calculated the confounding-adjusted absolute risk differences

		Sex	
	Overall	Male	Female
Hypertension			
Crude	1.24 [0.82-1.87]	2.11 [1.19-3.75]*	1.24 [0.82-1.87]
Adjusted [†]	1.72 [1.16-2.56] **	3.03 [1.74-5.27]***	1.16 [0.67-2.02]
Diabetes			
Crude	1.94 [0.98-3.83]	1.57 [0.40-6.19]	2.16 [1.001-4.66]*
Adjusted [†]	2.76 [1.42-5.38]**	1.32 [0.33-5.33]	3.15 [1.51-6.61]**
Arthritis			
Crude	1.01 [0.47-2.18]	0.77 [0.17-3.49]	1.06 [0.44-2.58]
Adjusted [†]	1.63 [0.77-3.44]	1.44 [0.33-6.33]	1.69 [0.71-4.02]
Stomach diseases			
Crude	1.56 [1.06-2.29]*	0.79 [0.30-2.11]	1.90 [1.27-2.86]**
Adjusted [†]	1.46 [1.003-2.13]*	0.75 [0.28-1.98]	1.86 [1.25-2.78]**
Kidney diseases			
Crude	1.15 [0.40-3.29]	0.66 [0.09-4.67]	1.87 [0.54-6.53]
Adjusted [†]	1.49 [0.52-4.25]	0.79 [0.11-5.57]	2.32 [0.67-8.04]
Heart diseases or stroke			
Crude	0.76 [0.29-1.97]	0.60 [0.13-2.74]	0.83 [0.26-2.72]
Adjusted [†]	1.26 [0.50-3.19]	1.11 [0.26-4.75]	1.30 [0.41-4.16]

[†]The adjusted weighted Poisson regression model controlled for age (continuous), sex (male/female, only included when not already controlled for by stratification), urbanicity (rural/urban), and insurance status (not insured/some household members insured/all household members insured).

*Significant at $P < .05$, ** significant at $P < .01$, and *** significant at $P < .001$.

of being diagnosed with adult NCDs between pediatric asthmatics and non-asthmatics. For every 100 diagnoses of pediatric asthma, there were 5.9 excess hypertension cases, followed by 3.69 excess stomach disease cases, 3.52 excess diabetes cases, and 2.04 excess arthritis cases (data not shown).

Table 3 presents the RRs for the associations between pediatric asthma and various adult NCDs diagnosed at 20-39, 40-59, or 60 years of age or above. Those with pediatric asthma had increased risks of all adult NCDs diagnosed at all age spectrum except for heart diseases or stroke (see also Figure S2). For NCDs diagnosed at 20-39 years of age, pediatric asthma was significantly associated with hypertension and diabetes (RR = 1.83; 95% CI: 1.01-3.32 for hypertension; RR = 5.49; 95% CI: 2.35-12.81 for diabetes) after adjusting for confounding. For NCDs diagnosed at 60 years of age or above, pediatric asthma was significantly associated with hypertension (RR = 2.13; 95% CI: 1.02-4.46) after adjusting for confounding. For stomach diseases diagnosed at 20-39 and 40-59 years of age, their crude associations with pediatric asthma were statistically significant, but these associations were no longer statistically significant after adjusting for confounding.

Table 4 presents the RRs for the associations between pediatric asthma diagnosed at 0-10 or 11-19 years of age and various adult NCDs diagnosed at 20 years of age or above, among all participants and stratified by sex. After adjusting for confounding, those diagnosed with asthma at 0-10 years of age had significantly

TABLE 2 Associations between pediatric asthma and various adult non-communicable diseases diagnosed at 20 y of age or above, among all participants and stratified by sex

increased risks of hypertension and diabetes (RR = 1.79; 95% CI: 1.09-2.93 for hypertension; RR = 2.82; 95% CI: 1.23-6.47 for diabetes). Those diagnosed with asthma at 11-19 years of age had significantly increased risk of arthritis after adjusting for confounding (RR = 2.59; 95% CI: 1.09-6.14). We also found statistically significant sex-specific associations after adjusting for confounding. Among males, those diagnosed with asthma at 0-10 years of age had significantly increased risk of hypertension (RR = 3.42; 95% CI: 1.87-6.26). Among females, those diagnosed with asthma at 0-10 years of age had significantly increased risks of diabetes and stomach diseases (RR = 2.67; 95% CI: 1.01-7.19 for diabetes; RR = 1.76; 95% CI: 1.07-2.90 for stomach diseases), while those diagnosed with asthma at 11-19 years of age had significantly increased risks of diabetes, arthritis, stomach diseases, and kidney diseases (RR = 3.83; 95% CI: 1.28-11.4 for diabetes; RR = 2.86; 95% CI: 1.12-7.26 for arthritis; RR = 2.02; 95% CI: 1.07-3.81 for stomach diseases; RR = 5.31; 95% CI: 1.54-18.33 for kidney diseases).

Table 5 presents the RRs for the associations between pediatric asthma and various adult NCDs diagnosed at 20 years of age or above among non-tobacco users. After adjusting for confounding, males diagnosed with pediatric asthma had significantly increased risk of hypertension (RR = 5.24; 95% CI: 2.57-10.7), while females diagnosed with pediatric asthma had significantly increased risks of diabetes and stomach diseases (RR = 2.83; 95%

TABLE 3 Associations between pediatric asthma and various adult non-communicable diseases diagnosed at 20-39, 40-59, or 60 y of age or above

	Age of NCD diagnosis, years		
	20-39	40-59	60+
Hypertension			
Crude	2.32 [1.28-4.23]**	1.95 [0.97-3.90]	2.42 [1.12-5.23]*
Adjusted [†]	1.83 [1.01-3.32]*	1.58 [0.80-3.15]	2.13 [1.02-4.46]*
Diabetes			
Crude	6.13 [2.70-13.93]***	1.93 [0.50-7.50]	2.10 [0.30-14.63]
Adjusted [†]	5.49 [2.35-12.81]***	1.65 [0.43-6.33]	1.35 [0.20-9.24]
Arthritis			
Crude	1.39 [0.35-5.55]	2.39 [0.89-6.46]	1.54 [0.24-9.97]
Adjusted [†]	1.19 [0.30-4.72]	2.19 [0.80-5.95]	1.72 [0.27-11.17]
Stomach diseases			
Crude	1.85 [1.18-2.89]**	2.90 [1.24-6.77]*	1.86 [0.29-11.84]
Adjusted [†]	1.27 [0.82-1.97]	2.25 [0.97-5.21]	1.50 [0.24-9.45]
Kidney diseases			
Crude	2.22 [0.70-7.04]	N/A	4.45 [0.60-33.19]
Adjusted [†]	2.00 [0.63-6.34]	N/A	3.82 [0.51-28.32]
Heart diseases or stroke			
Crude	0.98 [0.14-7.00]	2.15 [0.66-6.93]	0.96 [0.12-7.05]
Adjusted [†]	0.88 [0.12-6.21]	1.91 [0.60-6.06]	0.93 [0.14-6.27]

[†]The adjusted weighted Poisson regression model controlled for age (continuous), sex (male/female), urbanicity (rural/urban), and insurance status (not insured/some household members insured/all household members insured). N/A reflects insufficient sample size.

*Significant at $P < .05$, ** significant at $P < .01$, and *** significant at $P < .001$.

CI: 1.27-2.88 for diabetes; RR = 1.92; 95% CI: 1.27-2.88 for stomach diseases).

4 | DISCUSSION

To our knowledge, this is the first study to investigate the associations between diagnoses of pediatric asthma and several types of subsequent adult NCDs. We were able to assess these associations with temporality and long interval times between diagnoses of pediatric asthma and adult NCDs. We found pediatric asthmatics had significantly higher risks of adult hypertension, diabetes, and stomach diseases than non-asthmatics. To better understand the associations between pediatric asthma and adult NCDs, we stratified our analyses by sex and age of asthma diagnosis. Female pediatric asthmatics had higher risks of being diagnosed with adult diabetes and stomach disease, while male pediatric asthmatics had higher risk of being diagnosed with adult hypertension. These sex-stratified associations still existed when the analysis was restricted to non-tobacco users, showing that tobacco use was not a mediator of these associations. In addition, being diagnosed with asthma at 0-10 years of age was associated with higher risks of being diagnosed with adult hypertension and diabetes, while being diagnosed with asthma at 11-19 years of

age was associated with higher risk of being diagnosed with adult arthritis. These associations were unlikely explained by detection bias, as asthmatics and non-asthmatics were shown to have similar healthcare utilization in Indonesia.^{15,16}

Previous studies examined associations of pediatric asthma with childhood and adolescent NCDs, including diabetes and inflammatory bowel diseases,² but to our knowledge, only one study examined the association between pediatric asthma and adult NCDs, involving coronary heart diseases and stroke, which found the association was not statistically significant.¹²

There have been studies on the associations between predominantly adult asthma and NCDs diagnosed in adults, but some did not establish temporality due to their inability to ascertain the ages of asthma and NCD diagnoses,^{11,17,18} and few have examined effect of modification by sex.^{11,12,19} These studies found that asthmatics had increased risks of hypertension at 18-75 years of age,¹⁷ and in women aged 14+ years,¹¹ and 19-40 years of age¹⁹; rheumatoid arthritis at 20+ years of age,¹⁴ and in women aged 25+ years¹⁸; diabetes at 18+ years of age,² and in women aged 45+ years²⁰; chronic kidney diseases at 18+ years of age¹³; and heart diseases and stroke at 21+ years of age.¹²

We found the association between pediatric asthma and adult diabetes was especially strong for diabetes diagnosed at 20-39 years of age. A review paper indicated that the phenotype of diabetes

TABLE 4 Associations between pediatric asthma diagnosed at 0-10 or 11-19 y of age and various adult non-communicable diseases diagnosed at 20 y of age or above, among all participants and stratified by sex

	Overall		Male		Female	
	Age of asthma diagnosis		Age of asthma diagnosis		Age of asthma diagnosis	
	0-10 y old	11-19 y old	0-10 y old	11-19 y old	0-10 y old	11-19 y old
Hypertension						
Crude	1.33 [0.79-2.24]	1.10 [0.56-2.16]	2.57 [1.37-4.82]**	1.23 [0.33-4.67]	0.67 [0.27-1.62]	0.95 [0.43-2.09]
Adjusted [†]	1.79 [1.09-2.93]*	1.62 [0.85-3.11]	3.42 [1.87-6.26]***	2.08 [0.55-7.80]	0.93 [0.41-2.13]	1.49 [0.71-3.12]
Diabetes						
Crude	2.12 [0.91-4.95]	1.65 [0.53-5.11]	2.33 [0.60-9.09]	N/A	1.95 [0.69-5.50]	2.43 [0.79-7.49]
Adjusted [†]	2.82 [1.23-6.47]*	2.64 [0.87-8.01]	2.98 [0.76-11.68]	N/A	2.67 [1.01-7.19]*	3.83 [1.28-11.4]*
Arthritis						
Crude	0.66 [0.17-2.62]	1.54 [0.63-3.75]	0.84 [0.12-5.86]	0.62 [0.09-4.47]	0.54 [0.08-3.76]	1.72 [0.66-4.49]
Adjusted [†]	1.04 [0.27-3.97]	2.59 [1.09-6.14]*	1.46 [0.22-9.71]	1.38 [0.20-9.64]	0.84 [0.13-5.57]	2.86 [1.12-7.26]*
Stomach diseases						
Crude	1.50 [0.93-2.43]	1.65 [0.88-3.10]	0.90 [0.29-2.80]	0.55 [0.08-3.79]	1.85 [1.10-3.10]*	1.98 [1.04-3.77]*
Adjusted [†]	1.40 [0.88-2.24]	1.56 [0.84-2.91]	0.85 [0.28-2.61]	0.52 [0.08-3.57]	1.76 [1.07-2.90]*	2.02 [1.07-3.81]*
Kidney diseases						
Crude	0.56 [0.08-3.98]	2.05 [0.60-7.07]	0.98 [0.14-6.92]	N/A	N/A	4.25 [1.23-14.7]*
Adjusted [†]	0.67 [0.10-4.73]	2.59 [0.75-8.90]	1.14 [0.12-7.99]	N/A	N/A	5.31 [1.54-18.3]**
Heart diseases or stroke						
Crude	0.89 [0.31-2.59]	0.57 [0.08-3.97]	0.89 [0.20-4.07]	N/A	0.88 [0.20-3.82]	0.78 [0.11-5.43]
Adjusted [†]	1.39 [0.50-3.83]	1.04 [0.15-7.37]	1.52 [0.37-6.32]	N/A	1.30 [0.32-5.33]	1.30 [0.18-9.23]

[†]The adjusted weighted Poisson regression model controlled for age (continuous), urbanicity (rural/urban), and insurance status (not insured/some household members insured/all household members insured). N/A reflects insufficient sample size.

*Significant at $P < .05$, ** significant at $P < .01$, and *** significant at $P < .001$.

diagnosed in young adults of age below 40 years is more aggressive (ie, leads to more premature complications development) compared with diabetes diagnosed later in adulthood.²¹ Future studies will be needed to further understand the associations between asthma and different phenotypes of diabetes.

Our sex-stratified findings for the association between pediatric asthma and adult hypertension differed from those in two previous studies. A Korean study (which cross-sectionally analyzed those diagnosed with asthma and other NCDs at 19-40 years of age) and an Italian study (which cross-sectionally analyzed those diagnosed with asthma and other NCDs at 14+ years of age) found that ever diagnosis with asthma was significantly associated with hypertension in women, but not in men.^{11,19} However, both of these studies had the limitation of having no temporality. Other explanations for the differences in the findings may include the substantial under-diagnosis and under-reporting of hypertension in Indonesian men compared with Indonesian women, as well as the different average age of asthma diagnosis in our study compared with that in the other studies.

Several mechanisms may explain our findings. Asthmatics may be more likely than non-asthmatics to be diagnosed with other NCDs because of genetic predisposition (eg, involving systemic

inflammation^{17,22-24} and immune system impairment²⁵), as well as environmental factors (eg, involving asthma medication use^{13,17,26,27} and poorer lifestyle²⁸). Inflammation in asthmatics has been shown to be systemic rather than simply confined to the airways.²⁹ Asthmatics may also have impaired immune cell development, which may lead to immune system incompetency.²⁵ Drugs used in the treatment of asthma have been shown to influence the development of some NCDs, such as hypertension,¹⁷ diabetes,²⁶ stomach diseases,²⁷ and kidney diseases.¹³ Previous studies found that asthmatics have less healthy lifestyles compared with non-asthmatics, such as having reduced physical activity and poor sleep.²⁸

4.1 | Strengths and limitations

Our large nationwide population-based survey dataset allowed us to obtain temporality between pediatric asthma and adult NCD diagnoses, and to examine adult NCDs that were diagnosed many years after asthma diagnosis. However, our study was subject to several limitations. Our major study limitation is that asthma and other NCD diagnoses were self-reported, raising the concern of disease ascertainment accuracy. However, our self-reported NCD

TABLE 5 Associations between pediatric asthma and various adult non-communicable diseases diagnosed at 20 y of age or above among non-tobacco users

	Non-tobacco users	
	Male	Female
Hypertension		
Crude	3.16 [1.55-6.43]**	0.85 [0.47-1.53]
Adjusted [†]	5.24 [2.57-10.7]***	1.27 [0.73-2.20]
Diabetes		
Crude	2.36 [0.35-15.9]	1.86 [0.81-4.30]
Adjusted [†]	4.15 [0.60-28.7]	2.83 [1.27-6.28]*
Arthritis		
Crude	N/A	1.15 [0.48-2.80]
Adjusted [†]	N/A	1.86 [0.79-4.41]
Stomach diseases		
Crude	1.61 [0.53-4.88]	1.93 [1.27-2.93]**
Adjusted [†]	1.51 [0.50-4.60]	1.92 [1.27-2.88]**
Kidney diseases		
Crude	2.08 [0.29-14.84]	2.06 [0.59-7.18]
Adjusted [†]	2.88 [0.40-20.60]	2.48 [0.71-8.62]
Heart diseases or stroke		
Crude	1.45 [0.15-7.44]	0.91 [0.28-2.97]
Adjusted [†]	2.71 [0.51-14.39]	1.43 [0.45-4.55]

[†]The adjusted weighted Poisson regression model controlled for age (continuous), urbanicity (rural/urban), and insurance status (not insured/some household members insured/all household members insured). N/A reflects insufficient sample size.

*Significant at $P < .05$, ** significant at $P < .01$, and *** significant at $P < .001$.

prevalence is comparable to that of the Indonesian Basic Health Research (Riskesdas) survey, a nationwide population-based survey used by the Indonesian government to generate health indicators for the Indonesian population.³⁰ In addition, although the temporality between asthma and other NCDs in our study was based on self-reported age of diagnosis, the reported year of NCD diagnosis such as the year of asthma onset has been shown to be accurate.³¹ Another limitation is that we did not have information on the severity of asthma and other NCDs to examine associations involving disease severity. Our study could also only obtain disease information in those who were alive to answer the questionnaire, so those born in similar calendar years as our study participants but died from severe cases of diseases were not captured. Although we did not have complete potential confounder information for environmental exposures during childhood, childhood microorganism exposure is unlikely a significant confounder of the association between pediatric asthma and adult NCDs. While according to the hygiene hypothesis, childhood exposures to microorganisms may protect against the development of allergic diseases such as pediatric asthma, early-life infectious disease exposure was found to not be significantly associated with mortality from various chronic diseases in adulthood.³²

Our study also had low sample size and statistical power for the associations with some NCDs, such as kidney diseases, heart diseases, or stroke. It has been shown that some diseases are under-reported and under-diagnosed in Indonesia; however, we believe asthmatics and non-asthmatics reported NCDs in a similar fashion, resulting in non-differential misclassification and the likely underestimation of the risk ratios and differences.

4.2 | Conclusion

Understanding the susceptibility of those diagnosed with asthma in childhood and adolescence to develop NCDs in adulthood may improve the surveillance of NCDs and promote beneficial lifestyle changes among pediatric asthmatics, which may result in better NCD prevention. Further studies are needed to better understand the mechanisms responsible for the associations between pediatric asthma and adult NCDs, as well as explore how these associations differ by asthma phenotypes and severity.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Nirmin Juber: Conceptualization (equal); Data curation (lead); Formal analysis (lead); Methodology (equal); Writing-original draft (lead); Writing-review & editing (lead). **Chien-Chang Lee:** Writing-review & editing (equal). **Wen-Chi Pan:** Writing-review & editing (equal). **Jason Liu:** Conceptualization (lead); Formal analysis (equal); Methodology (lead); Supervision (lead); Writing-original draft (lead); Writing-review & editing (lead).

PEER REVIEW

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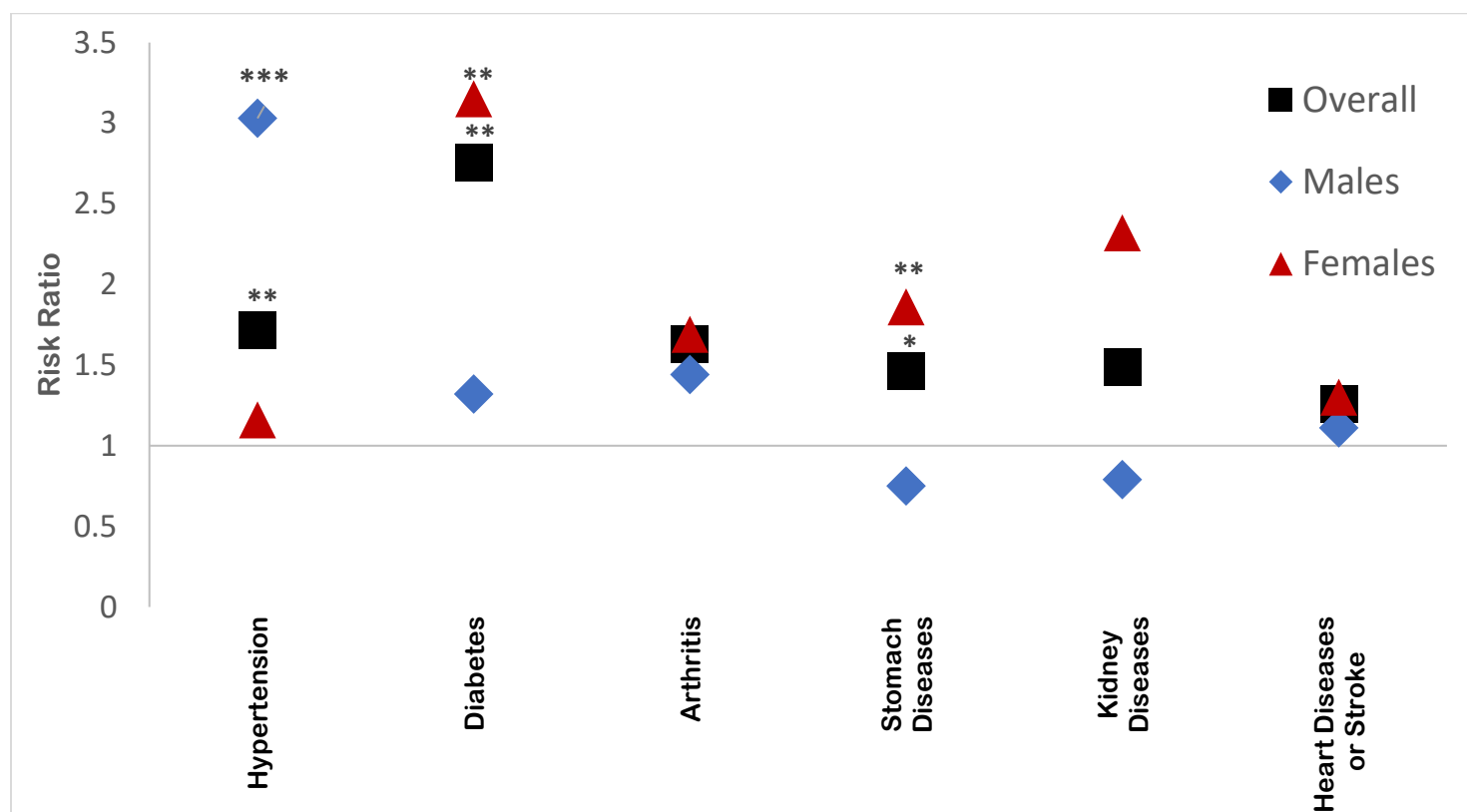
SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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SUPPORTING INFORMATION

Figure 1: Adjusted associations between pediatric asthma and various adult non-communicable diseases diagnosed at 20 years of age or above, among overall participants and stratified by sex (male and female).

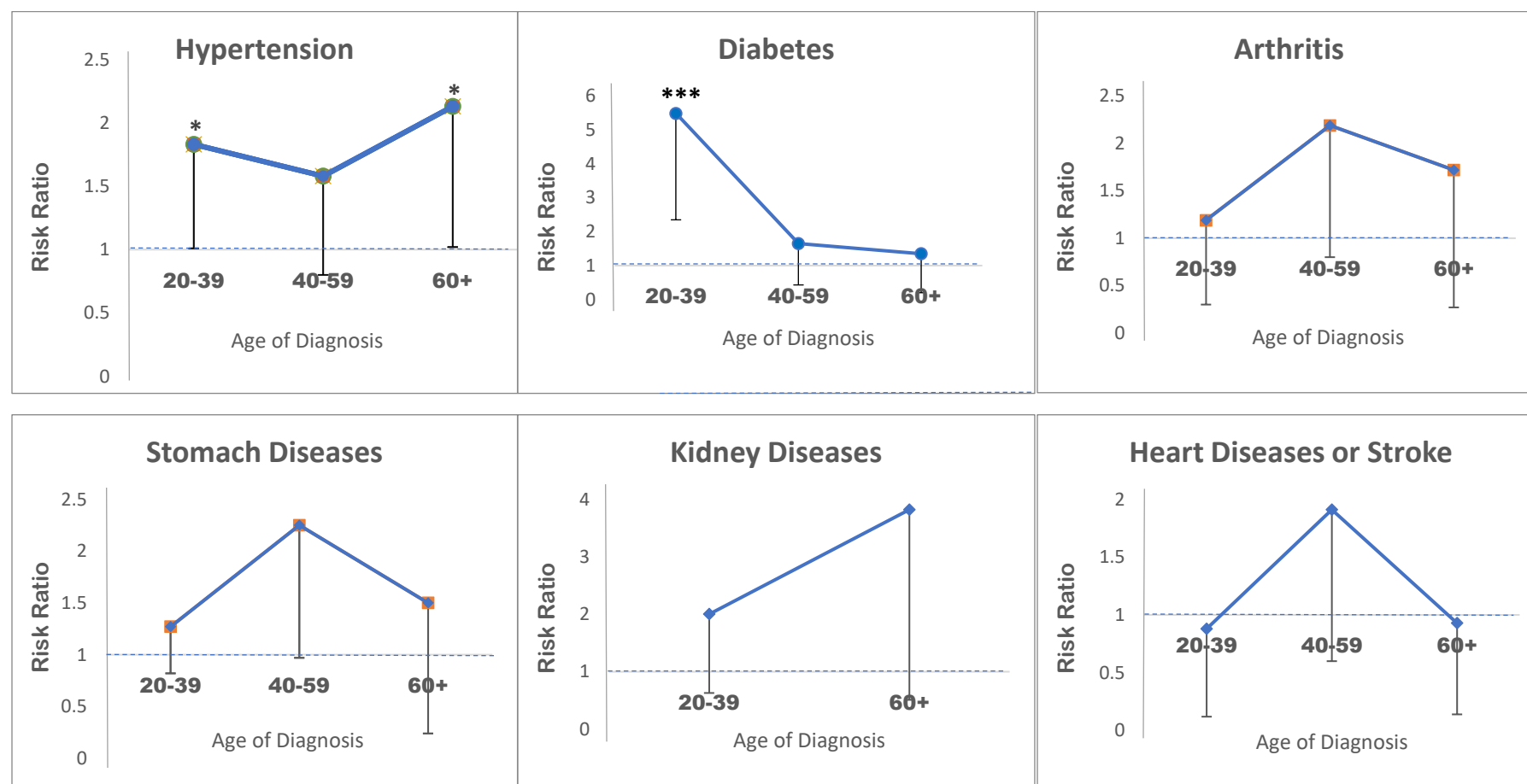


† Analyses were performed using weighted Poisson regression.

‡ The adjusted model controlled for age (continuous), sex (male/female, only included when not already controlled for by stratification), urbanicity (rural/ urban), and insurance status (not insured/some household members insured/all household members insured).

§ * significant at $P < 0.05$, ** significant at $P < 0.01$, *** significant at $P < 0.001$.

Figure 2: Adjusted associations between pediatric asthma and various adult NCDs diagnosed at 20-39, 40-59, or 60 years of age or above.



† Analyses were performed using weighted Poisson regression.

‡ The adjusted model controlled for age (continuous), sex (male/female), urbanicity (rural/ urban), and insurance status (not insured/some household members insured/all household members insured). For kidney diseases age of diagnosis of 40-59 are not available due to low sample size.

§ * significant at $P < 0.05$, ** significant at $P < 0.01$, *** significant at $P < 0.001$.