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Changing trends and challenges in the management of asthma in Asia

Woo-Jung Song, MD, PhD, Gary WK. Wong, MD

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Title: Changing trends and challenges in the management of asthma in Asia

Authors:

Woo-Jung Song MD, PhD¹ and Gary WK Wong MD²

1. Department of Internal Medicine
Seoul National University College of Medicine
Seoul, Korea

2. Department of Paediatrics
Prince of Wales Hospital
Chinese University of Hong Kong
Shatin, NT
Hong Kong

Corresponding author:

Professor Gary WK Wong, MD, Department of Paediatrics, Prince of Wales Hospital, Chinese
University of Hong Kong, Shatin, NT, Hong Kong SAR, China

E-mail: wingkinwong@cuhk.edu.hk

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Asthma has been recognized for thousands of years in Asia, and is even described in the ancient Chinese medical literature, *Huangdi Neijing*. Asthma is now one of the most common chronic disorders in Asian adults and children. Epidemiological studies have documented the rapidly increasing prevalence of asthma and atopic conditions during the past two decades in Asia, in parallel with increased urbanization.¹ However, the epidemic of asthma in Asia may have not yet peaked. This review will discuss the changing trends in asthma with a focus on epidemiology, the environment risk factors, and asthma control status in Asia.

EPIDEMIOLOGY OF ASTHMA IN ASIA

The epidemiology of asthma in Asian children has been intensively studied using the International Study of Asthma and Allergies in Childhood (ISAAC) survey instrument.¹ As reported in the ISAAC Phase I results, the prevalence of asthma in the Asia-Pacific region was generally lower than that documented in America, Oceania, or Western Europe.² However, marked variation in asthma prevalence was evident among various Asian cities and countries. Not surprisingly, asthma was more common in developed cities and countries such as Hong Kong, Japan, and Singapore. Furthermore, striking differences in prevalence were evident among populations with similar genetic backgrounds living in different environments. For example, the prevalence of current wheezing among children aged 13-14 years old was remarkably higher in Hong Kong (12.4%) than in mainland Chinese cities such as Beijing (5.1%) or Shanghai (3.3%).² These observations were supported by subsequent surveys of Chinese children (Online Repository Table E1). Such lines of evidence indicate that the urban environment had a major

influence on the changing trend of asthma. Furthermore, the burden of asthma is expected to increase further, as urbanization is ongoing in many other less developed regions of Asia.

In adults, there is no reliable data collected by standardized methodology to document the asthma prevalence in Asia for international comparison. Single-country studies have found that the asthma prevalence is generally less than 5% in most Asian countries, which is considerably lower than in Europe, Oceania or America.³ Similar to what was found in children, adult asthma is generally more prevalent in developed Asian countries than in developing ones.³ Although an association between urbanization and asthma prevalence is likely, the data are less conclusive for adults than for children. Adult asthma is rather heterogeneous and it is difficult to determine the extent of lifetime cumulative exposure to an urban environment. Due to the lack of longitudinal surveys using standardized protocols, it remains difficult to determine if there is a true changing trend of asthma prevalence in Asian adults.

ENVIRONMENTAL RISK FACTORS

Other environmental factors may also be important in explaining the changing epidemiology of asthma in Asia. The first is the dramatic disappearance of the rural environment. According to recent data from World Urbanization Projects of the United Nations, the proportion of rural residents remains high but is rapidly decreasing in Asia (Fig. 1A). Exposure to a rural environment has been consistently shown to be protective against asthma development.⁴ A comparative study of urban and rural areas in Beijing revealed a 4-fold difference in the prevalence of asthma among schoolchildren.⁵ Although exposure to large farm animals, consumption of farm milk, and related microbial exposure are major factors associated with

asthma protection in central Europe, residence in an agricultural farming environment of northern China is also associated with protection against asthma.⁵

Second, air pollution remains an emerging problem in many Asian countries. The extent of air pollution may not be directly related to the development of asthma, as asthma prevalence was relatively low in cities such as Chongqing, China where outdoor air pollutant levels were very high. However, exposure to ambient air pollutants is a major risk factor for asthma exacerbation in both Asian and western countries.⁶ The use of open fire cooking is quite common in rural areas in Asia. The global ISAAC Phase III analysis revealed that the use of open fire cooking was associated with more severe symptoms of asthma in children.⁷ According to a recent report by the World Health Organization, the annual mean concentration of particulate matter of aerodynamic diameter less than 2.5 μm (PM_{2.5}), a major indicator of outdoor air pollution, remains exceptionally high in many Asian regions compared to other continents (<http://maps.who.int/airpollution>) and the levels of PM_{2.5} are still rising (Fig. 1B). The reduction of pollution related to household burning of biomass and motor traffic should be prioritized.⁶

Third, high levels of cigarette smoking, particularly by males, remain problematic in many Asian countries (<http://www.who.int/gho/tobacco/use/en/>). Cigarette smoke status correlates with the prevalence of current asthma and bronchial hyper-responsiveness in older adults.^{3,8} In older asthmatics, the extent of cigarette smoke exposure may influence the asthma phenotypes. They may develop fixed airway obstruction or an exacerbation-prone phenotype.⁸

ASTHMA HETEROGENEITY IN ASIANS

Asthma is a syndrome characterized by different phenotypes and endotypes. This heterogeneity needs to be taken into consideration when seeking a better understanding of the changing epidemiology. However, phenotypes of Asian asthmatics remain largely unexplored. Despite recent reports from cluster analyses, direct comparison is not possible between western and Asian patients, due to the lack of standardized protocols.

The majority of Asian children with asthma belong to the atopic asthma phenotype. Atopic status has been assessed in very few community-based studies of Asian adults, but non-atopic asthma has been found to be the predominant type among older adults.⁹

One notable finding in Asian adults is that asthma prevalence increases with age; this has been termed as the “second peak” in asthma prevalence.³ This age-related pattern has been documented in many areas, including Bangladesh, China, India, Japan, Korea, Mongolia, Taiwan and Vietnam (Online Repository Table E2). This phenomenon remains poorly understood, but their asthma was frequently associated with smoking. Other risk factors include the female sex, urban residence, low socio-economic status, exposure to occupational irritants, obesity, rhinitis, a family history of asthma, or IgE sensitization to non-conventional allergens such as staphylococcal enterotoxins (Online Repository). Longitudinal studies using standardized protocols are required to determine the exact causes for this “second peak” in Asian adults.

CONTROL OF ASTHMA IN ASIA

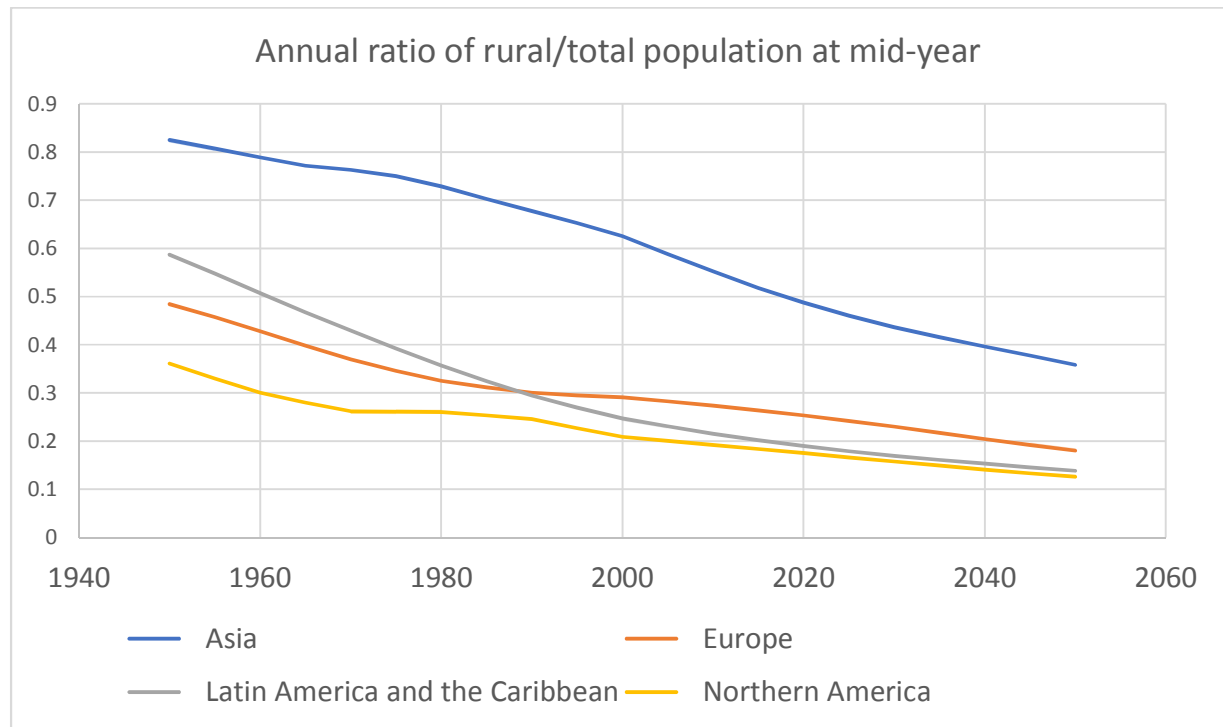
In terms of asthma control, Asia is rather poor when compared to other regions. In the Asthma Insight and Management survey conducted in 20 countries from 5 different global regions during 2009-2011,¹⁰ the proportion of patients who achieved complete asthma control as defined by

international criteria was only 2% in the Asia-Pacific region, thus much lower than the figures for the United States (29%) or Europe/Canada (16%). In addition, the rate of daily use of controller medications such as inhaled corticosteroid was much lower in Asia (32%) compared to the United States (80%). Thus, sub-optimal use of controller treatment, reliance on quick-relief medication and oral steroids are major problems in Asia (Online Repository). Different belief, poor knowledge, and/or the attitudes of patients physicians toward asthma, all contribute to the suboptimal care of asthma patients.¹¹ Thus, targeted intervention and education specific for different populations are needed to improve the control of asthmatics across Asia.

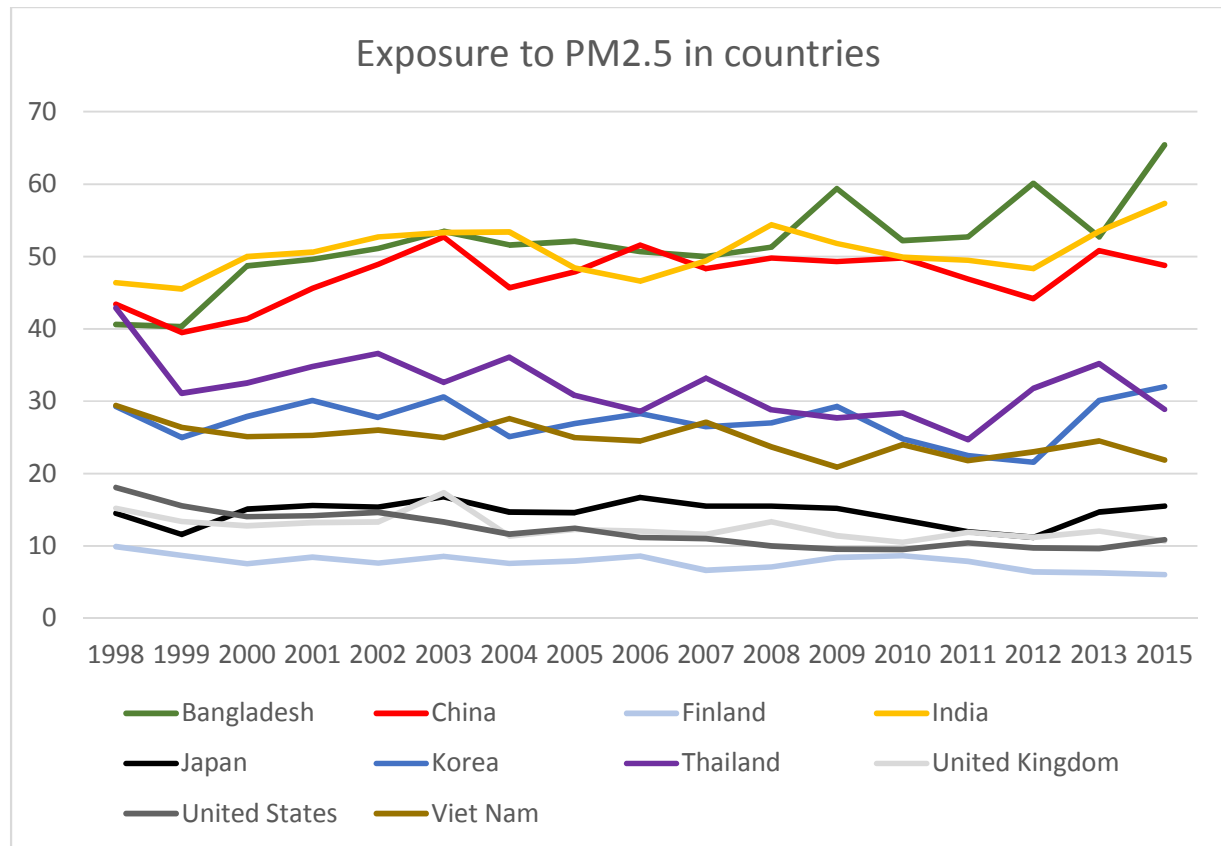
CONCLUSIONS

With rapid urbanization over the past decades, asthma has become one of the most common chronic disorders. However, despite recent progress in our understanding of the condition and improvement of management tools, we still face major challenges including the progressive loss of rural environments, uncontrolled air pollution, high prevalence of cigarette smoking, and poor asthma control (Fig. 2). These factors contribute to the increasing burden and morbidity related to asthma in Asia, and are triggering a second wave of asthma epidemics in Asian countries. In addition, factors underlying asthma heterogeneity and poor asthma control remain underexplored. Thus, further studies are urgently needed to determine the unique risk factors for asthma development and to develop appropriate interventions to control this emerging epidemic of asthma in Asia.

129 **Figure Legend**

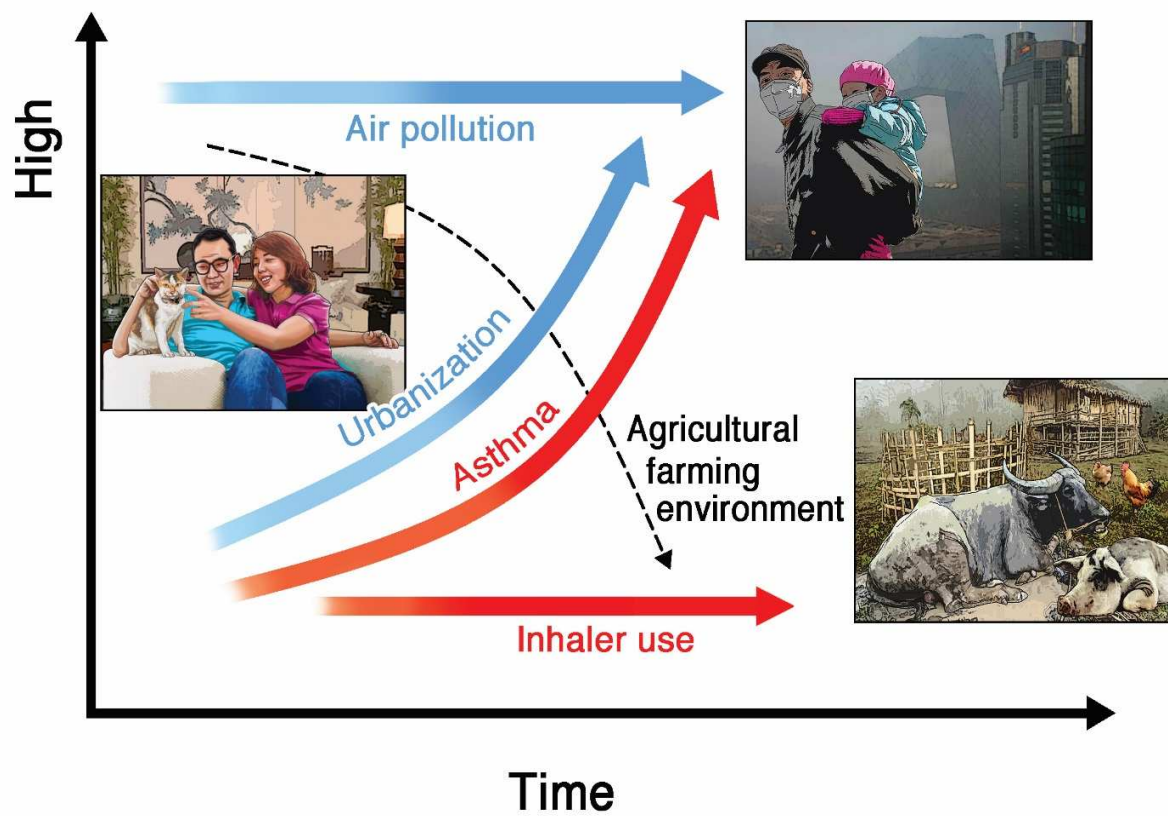


131 **Figure 1. (A) Historical trends in the ratio of rural per total population in different**
 132 **continents.** United Nations, Department of Economic and Social Affairs, Population Division
 133 (2014). World Urbanization Prospects: The 2014 Revision, custom data acquired via website
 134 (<https://esa.un.org/unpd/wup/DataQuery/>).



(B) Mean population exposure to particulate matter 2.5 (PM2.5) in Asian and western countries. Based on data from OECD (1998-2015), “Exposure to PM2.5 in countries and regions”, <http://stats.oecd.org> (accessed on 11 Sep 2017 01:57).

143 **Figure 2. Increasing burden of asthma and related environmental risk factors in Asia.**



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Online Repository

Title: Changing trends and ongoing epidemic of asthma in Asia

Authors:

Woo-Jung Song MD, PhD¹ and Gary WK Wong MD²

1. Department of Internal Medicine

Seoul National University College of Medicine

Seoul, Korea

2. Department of Paediatrics

Prince of Wales Hospital

Chinese University of Hong Kong

Shatin, NT

Hong Kong

Literature search

To review recent trends of asthma epidemiology in Asia, we searched Pubmed from January 1997 to August 2017 using the terms “asthma” (as text word and Mesh term) AND (“prevalence”, “incidence” OR “epidemiology”) AND either of country name or “Asia”. We also searched Google database to obtain recent data on air pollution, smoking, and degree of urbanization by region and country.

Urban-rural difference in asthma prevalence among Asian children

The associations between asthma prevalence and residence areas were examined in several surveys of Asian children populations (Table E1). Due to difference in study design and protocols, it is difficult to compare the prevalence directly. However, within each study, the prevalence of asthma or wheezing was mostly higher in children living in urban areas than those in rural areas. If genetic background is assumed to be similar within-study, the difference would strongly indicate the roles of environment. In the study comparing three South-East Asian populations, asthma prevalence was about six times higher in Hong Kong than in San Bu.¹ Two areas are 200 km apart and have similar climate, but had a considerable difference in urbanization in the survey year of 1992. In the study comparing three cities in China, environmental factors such as cooking with gas, foam pillows and damp housing were significantly associated with wheezing.² Early-life period is likely to be a critical window of period for urban effects on asthma. In a cross-sectional study in Shanxi, China, children who had grown up in urban environment had significantly more asthma than those grown up in rural environment.³ In the analysis of the ISAAC phase 3 survey, Chinese immigrants to Vancouver

had higher prevalence of wheezing than native residents in mainland China, but less prevalence than Canadian-born Chinese, suggesting the importance of timing and duration of environmental exposure.⁴ Data from the European Community Respiratory Health Survey II revealed that early life exposure to a farm environment might be associated with long-lasting effects in terms of reducing the risk of atopic asthma even into adulthood.⁵ Early exposure to rural environments may explain the lower prevalence of asthma (< 5%) in Asian adults.⁶

Protective factors against asthma and allergies from Asian rural environments may be postulated but the exact underlying mechanisms remain to be elucidated. Exposure to large farm animals, consumption of farm milk, and the related microbial exposure have been suggested to be the protective factors in Europe.⁷⁻⁹ In a comparative study of urban and rural Beijing, the prevalence of asthma in rural children was clearly lower than in urban children, but it was not significantly different between rural children who were exposed to livestock farms and those exposed to agricultural farms, suggesting protective factors in agricultural environments.¹⁰ In another study in southeast China, early life exposure to crop farming and high environmental endotoxin levels were inversely related to asthma.¹¹ These findings warrant further investigation for possible protective factors against asthma from Asian agricultural farms.

Meanwhile, the urban-rural difference was not consistently observed in Korean children.¹²⁻¹⁵ In the study by Kim, the prevalence of asthma, as measured by symptom questionnaires and airway hyper-responsiveness to methacholine, was higher in metropolitan Seoul than in a rural part of Chungju, but the difference was not statistically significant (5.2% vs. 4.1%).¹² In the ISAAC phase I survey, the prevalence of recent wheeze in Korea was higher than mainland China but lower than in Hong Kong.¹⁶ Factors underlying such regional discrepancy in urban-rural

relationships warrant further investigation. Some unique local allergens like citrus red mite, which was identified from citrus farms in Cheju island, may underlie high prevalence of allergic asthma in such particular areas.¹³

Age-related increase in asthma prevalence among Asian adults

We summarized recent reports on age-specific asthma prevalence among Asian adults in Table E2. Despite the narrative nature of this review and methodological heterogeneity between studies, the age-related increase in current asthma was a recurrent finding.¹⁷⁻²³ However, all were cross-sectional analyses, thus they cannot confirm whether the age-related pattern reflects cohort effects or indicates the increasing prevalence of late-onset adult asthma. Longitudinal studies using standardized protocols are warranted to determine whether there is a true increase in asthma in older adults.

Among the possible putative risk factors revealed by studies in Asian adults, smoking history was most frequently reported.^{17-19, 21-28} Thus, the validity of asthma definition may be questioned, and a confounding effect from smoking-related chronic obstructive pulmonary disease may be present. However, such age-related increase in asthma prevalence was consistently observed in some studies where the diagnosis of asthma was made using objective measurements.^{24, 29, 30} Occupational or environmental exposure to irritant dust or fumes was also reported in a few studies^{22, 28}. Obesity is a well-known risk factor for adult-onset asthma in western populations³¹, but obesity is rather uncommon in most Asian communities. In East Asians, obesity is less prevalent (less than 5%) and mean body mass index (BMI) is less than 25 kg/m².^{32, 33} However,

the increase of asthma has been reported to start at a BMI threshold of 23 kg/m² in Japanese women, which is lower than those reported from western populations.^{34, 35}

Presence of atopy was objectively assessed in few general adult population studies in Asia, but the associations of atopy with asthma were inconsistent.^{24, 30, 33} As the prevalence of atopy decreases with aging, it is less likely to contribute to asthma in older adults.³⁰ Based on recent findings, we speculate that IgE sensitization to non-conventional allergens like *Staphylococcus aureus* proteins and enterotoxins could be a risk factor for adult-onset non-atopic asthma.^{30, 36, 37} Staphylococcal enterotoxin-specific IgE sensitization was as prevalent as 30~60% in adult patients with asthma, either in Europe or Asia, and had significant relationships with asthma severity and type 2 airway inflammation irrespective of atopic status.³⁸⁻⁴⁰

Status of asthma control in Asian countries

Poor control of asthma created major burdens on the healthcare systems in Asian, despite the lower prevalence of asthma than in western countries. In the Asthma Insights and Reality (AIR) surveys in 1998-2001, asthma control status and rate of anti-inflammatory preventive medication were similarly poor between different continents.⁴¹ However, in the Asthma Insight and Management (AIM) surveys in 2009-2011, the outcomes were particularly poor in Asia-Pacific countries.⁴² The proportion of well-controlled asthma was only 2%, which was considerably lower than those in the US (29%) or Europe/Canada (16%).⁴² These findings from the AIR and AIM surveys indicate no significant improvement in the level of control over the last 10 years. According to the AIM surveys, only 32% of patients in the Asia-Pacific region reported daily use of inhaler medication as controller in previous 4 weeks, which was much lower than 80% and 52%

103 in the US and Europe-Canada respectively.⁴² Meanwhile, about 80% of participants in the Asia-
104 Pacific region took oral drugs as controller.⁴² The reliance on pill over inhaler as controller
105 medication was particularly frequent in China, India and Korea.⁴³ The rate of using oral steroids
106 as rescue medicine was also more frequently reported in the Asia-Pacific region (50% vs. 35% in
107 the United States).⁴² The reasons underlying poor asthma control and preference over oral
108 therapies in Asia would be diverse, including healthcare access, physician's knowledge and
109 attitudes, or patient's cultural barrier to inhaler medicines. Further researches are needed to
110 develop targeted intervention and education specific to each population and healthcare setting.

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Table E1. Comparison of recent asthma prevalence in young Asian children populations with similar genetic background but different resident areas

Study (First author and publication year)	Age and survey year	Regions	Asthma prevalence
Leung 1997 ¹	Children aged 12-18 yr (n=2,208) in 1992	Hong Kong, Kota Kinabalu in Malaysia, and San Bu in southern China	Wheeze or asthma ever - 11.6% in Hong Kong - 8.2% in Kota Kinabalu, Malaysia - 1.9% in San Bu, China
Kim 1997 ¹²	Children aged 7-19 yr (n=3,219) in 1994-1995	Two cities in Korea - Seoul, urban - Chungju, rural	Asthma (defined by recent asthma symptoms plus bronchial hyper-responsiveness to methacholine) - Seoul, urban: 5.2% - Chungju, rural: 4.1%
Zhao 2000 ⁴⁴	Children aged 6-7 yr (n=7,754) in 1995-1996	Two cities in China - Beijing, urban - Urumqi, rural	Wheezing in the past 12 months - Beijing, urban: 6.0% - Urumqi, rural: 2.9%
Kim 2002 ¹³	Children aged 7-18 yr (n=16,624) in 1999	A metropolitan area, two non-metropolitan cities, and two rural	Wheezing in the last 12 months - Daegu, a metropolitan area: 10.3%

		areas in Korea - Daegu, a metropolitan area - Cheonan and Naju, non-metropolitan cities - Eusung, a rural area with apple farms - Cheju, a rural area with citrus farms	- Cheonan and Naju, non-metropolitan cities: 7.8% - Eusung, a rural area with apple farms: 7.9% - Cheju, a rural area with citrus farms: 10.4%* *IgE sensitization to citrus red mite or two-spotted spider mite was suggested to underlie high prevalence of wheezing in this area.
Wong 2004 ²	Children aged 10 yr (n=10,902) in 1997-1998	Three cities in China - Hong Kong - Beijing - Guangzhou	Wheeze in the past year - Hong Kong: 5.8% - Beijing: 3.8% - Guangzhou: 3.4%
Norbäck 2007 ³	Children and adolescents aged 9-20 yr (n=2,116) in 2000	Urban and rural areas in Shanxi, China	Ever asthma - Grown up in urban area: 3.4% - Grown up in rural area: 0.5%
Wang 2008 ⁴	Chinese adolescents aged 13-14 yr (n=7,794), who participated in the ISAAC phase 3 survey in 2001	Four cities in China and Canada - Guangzhou, China - Beijing, China	Current wheeze - Native Chinese, Guangzhou: 5.9% (boys), 4.3% (girls)

		- Hong Kong, China - Vancouver, Canada	- Native Chinese, Beijing: 7.4% (boys), 7.0% (girls) - Native Chinese, Hong Kong: 11.0% (boys), 7.2% (girls) - Chinese immigrants, Vancouver: 8.0% (boys), 6.7% (girls) - Canadian-born Chinese, Vancouver: 11.2% (boys), 9.8% (girls)
Ma 2009 ¹⁰	Children aged 13-14 yr (n=7,077) in 2003-2004	Two areas (one urban and one rural) in Beijing, China	Current wheeze - Urban Chaoyang area: 7.2% - Rural Tongzhou area: 1.0%
Li 2011 ⁴⁵	Children aged 6-13 yr (n=23,791) in 2005	Eight metropolitan cities in China - Harbin - Shanghai - Guangzhou - Xi'an - Wuhan - Chengdu - Hohhot - Urumqi	Asthma ("Has the child had asthma in the past 12 months?") - Harbin: 1.7% - Shanghai: 7.0% - Guangzhou: 3.0% - Xi'an: 1.1% - Wuhan: 3.5% - Chengdu: 4.6% - Hohhot: 0.9% - Urumqi: 1.6%

Suh 2011 ¹⁵	Children aged 5-11 yr (n=30,893) in 2006	Metropolitan, provincial, rural and industrial areas in Korea	Wheezing in the last 12 months - Metropolitan area: 5.9% - Provincial area: 5.9% - Rural area: 6.0% - Industrial area: 6.1%
Lee 2012 ¹⁴	Children aged 9-12 yr (n=1,749) in 2008	Rural village, rural town, and urban area in Korea - Urban area in Seoul - Rural town in Jeongeup - Rural village in Jeongeup	Wheezing in the last 12 months by written questionnaire - Urban area, Seoul: 3.7% - Rural town, Jeongeup: 5.3% - Rural village, Jeongeup: 4.2% Wheezing symptoms ever by video questionnaire - Urban area, Seoul: 9.2% - Rural town, Jeongeup: 7.5% - Rural village, Jeongeup: 6.0%
Li 2013 ⁴⁶	Children aged 0-14 yr (n=12,082) in 2010	Urban, suburban and rural areas in Chengdu, China	Prospective diagnosis of asthma by physicians - Urban: 4.0% - Suburban: 2.4% - Rural: 2.4%
Yang 2015 ⁴⁷	Children aged 7-12 yr (n=10,681) in	Two areas in China	Doctor-diagnosed asthma

	2009	- Guangzhou, urban - Shaoguan, rural	- Guangzhou, urban: 6.6% - Shaoguan, rural: 2.5%
Zhu 2015 ⁴⁸	Children aged 14 yr and younger (n=13,513) in 2010-2011	Urban and rural areas in Beijing, China	Asthma diagnosis by physician - Urban: 3.7% - Rural: 1.3%
Feng 2016 ¹¹	Children aged 13-14 yr (n=7,164) in 2012	Two areas in Guangdong, China - Guangzhou, urban - Conghua, rural	Physician-diagnosed asthma - Guangzhou, urban: 6.9% - Conghua, rural: 3.4% Current wheeze - Guangzhou, urban: 6.1% - Conghua, rural: 1.5%

ISAAC, International Study of Asthma and Allergies in Childhood

Table E2. Summary of reports on age-related increase in prevalence of asthma among Asian adults

Study (First author and publication year)	Survey area and period	Population and survey characteristics	Asthma definition	Age-specific prevalence	Putative risk factors for asthma (based on the reports)
Chan-Yeung 2002 ¹⁷	Rural Beijing areas in China, 1996-1997	n=22,561, ≥15 yrs Random selection of residents in the rural Beijing areas	Asthma attack: "Have you had an attack of asthma in the last 12 months?"	15-19 yr: 0.1% (0.0-0.3) 20-29 yr: 0.3% (0.2-0.5) 30-39 yr: 0.7% (0.5-0.8) 40-49 yr: 1.5% (1.3-1.7) 50-59 yr: 2.9% (2.6-3.4) >60 yr: 5.9% (5.5-6.3)	Female sex Smoking habit Older age
Hassan 2002 ¹⁸	Bangladesh, 1999	n=5,642, ≥5 yr (mainly 15-44 yr) Random selection	Asthma: wheeze in the last 12 months	5-14 yr: 7.3% 15-44 yr: 5.3% ≥45 yr: 11.0%	Older age Smoking history
Kim 2002 ²⁴	Four cities/areas (urban and rural) in Korea, 2000	n=2,467, ≥20 yrs Random sample from the health service	Current asthma: current wheezing (in the last 12 months) and bronchial hyper-responsiveness to methacholine	≤39 yr: 2.0% 40-54 yr: 3.8% 55-64 yr: 7.7% ≥65 yr: 12.7%	Older age Baseline FEV1 Female sex Cigarette smoking Atopy
Tanihara 2002 ⁴⁹	Japan, 1984-1996	Patient Survey and	Asthma: receiving	Data in 1996;	NR

		Vital Statistics of Japan, 1984-1996	medical treatment for asthma	0-9 yr: 3520/100,000 10-24 yr: 846/100,000 25-44 yr: 430/100,000 45-64 yr: 598/100,000 65-74 yr: 1389/100,000 ≥75 yr: 1595/100,000	
Mishra 2002 ²⁵	India, 1998-1999	n=38,595, ≥60 yrs Multistage cluster sample, National Family Health Survey 2	Asthma: “Does anyone listed (in the household) suffer from asthma?”	60-64 yr: 8.5% 65-69 yr: 10.2% 70-74 yr: 12.4% ≥75 yr: 12.4%	Cooking smoke Tobacco smoke Older age
Jan 2004 ²⁶	Taipei, Taiwan, 1999	n=2,076, ≥18 yr Single-stage cluster sampling	Definite or probable asthma: Either of (1) asthma diagnosed by physician or (2) “yes” to at least one of following questions “Does your chest sound wheezy or whistling when you	18-49 yr: 5.2% ≥50 yr: 10.7%	Maternal asthma Allergic rhinitis Older age Smoking

			have a cold?" or "Does your chest sound wheezy or whistling occasionally apart from when you have a cold?"		
Aggarwal 2006 ¹⁹	Chandigarh, Delhi, Kanpur and Bangalore in India, early 2000s?	n=73,605, ≥15 yr Random selection	Asthma: Both positive responses to (1) wheezing or whistling sound from chest, or chest tightness or breathlessness in morning, and (2) having suffered from asthma, or having an attack of asthma in past 12 months, or using inhaled or oral bronchodilators	Data reported in odds ratio 15-24 yr: 1.00 25-34 yr: 1.62 (1.29-2.03) 35-44 yr: 2.82 (2.27-3.50) 45-54 yr: 4.84 (3.92-5.97) 55-64 yr: 7.50 (6.04-9.33) 65-74 yr: 11.33 (9.04-14.20) ≥75 yr: 13.47 (10.25-17.71)	Female sex Older age Urban residence Low socio-economic status Atopic conditions Family history of asthma Smoking habit
Dejsomritrutai 2006 ²⁹	Thailand in 2000	N=3,454, 20-44 yr	Definite asthma: either	20-24 yr: 1.20 (0.37-2.02)	NR

		Multistage stratified random sample	of (1) reversible airway obstruction by spirometry or (2) any symptoms compatible with asthma within the last 12 months in addition to bronchial hyper-responsiveness	25-29 yr: 2.45 (1.22-3.69) 30-34 yr: 3.46 (2.07-4.85) 35-39 yr: 3.65 (2.21-5.09) 40-44 yr: 3.92 (2.32-3.49)	
Sy 2007 ⁵⁰	Dalat, Vietnam, 2004	n=9,984, mostly ≥15 yr Random selection	Asthma or asthma-like symptoms: “Have you been diagnosed as asthma by a physician?” or any of (1) “Have you heard wheezing in your chest at any time in the last 12 months?”, (2) “Have you felt as if you were suffocating while reclining during	5-14 yr: 3.4% 15-24 yr: 0.7% 25-34 yr: 0.9% 35-44 yr: 1.2% 45-54 yr: 2.1% 55-64 yr: 5.0% 65-74 yr: 7.7% ≥75 yr: 11.8%	NR

			the day at any time in the last 12 months?”, (3) “Have you been awakened by an attack of breathlessness at any time in the last 12 months?”		
Fukutomi 2010 ²⁰	Japan, 2006-2007	n=23,483, 20–79 yr	Current asthma: “Have you ever had asthma?” followed by “Was this confirmed by a doctor?” and “Having at least one asthma-related symptom in the last 12 months?”	20-29 yr: 5.1% 30-39 yr: 5.4% 40-49 yr: 2.7% 50-59 yr: 3.5% ≥60 yr: 4.8%	NR
Parasuramalu 2010 ²¹	Bangalore, India, 2008	n=3,194, ≥18 yr Random cluster sample	Asthma: both positive responses to (1) whistling sound from chest, or chest tightness,	18-29 yr: 0.7% 30-49 yr: 2.2% 50-64 yr: 8.6% ≥65 yr: 13.6%	Tobacco smoking

			or breathlessness in the morning, and (2) having suffered from asthma, or having an attack of asthma in the past 12 months, or using bronchodilators		
Jindal 2012 ²²	India, 2007-2009	n=169,575, ≥15 yr The Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis	Asthma: at least one of the two questions on wheezing and tightness of the chest, plus one of the three questions on history of previous diagnosis of asthma, an attack of asthma and use of medication for asthma, in the past 12 months	Data reported in odds ratio 35-44 yr: 1.00 45-54 yr: 1.86 (1.66-2.09) 55-64 yr: 2.85 (2.53-3.20) ≥65 yr: 5.29 (4.72-5.92)	Usual urban residence Older age Asthma in family Cigarette smoker Bidi smoker Environmental tobacco smoke exposure Cooking with coal/wood
Agrawal 2013 ²³	India, 2005-2006	n=157,186, 20-49 yr	Asthma: "Do you	20-29 yr: 1.1% (1.0-1.2)	Female sex

		National Family Health Survey 3	currently have asthma?"	30-39 yr: 2.0% (1.8-2.2) 40-49 yr: 3.1% (2.8-3.8)	Daily/weekly consumption of chicken/meat BMI<16 kg/m ² or >30 kg/m ² Current tobacco smoking Ever use of alcohol
Bartlett 2013 ²⁷	Bangladesh, 2009	n=32,665, ≥25 yr	Asthma: "Have you had ever been diagnosed with asthma?"	25-34 yr: 2.3% 35-44 yr: 2.9% 45-54 yr: 4.1% 55-64 yr: 6.3% ≥65 yr: 9.5%	Older age Smoking history Insufficient physical activity
Kim 2013 ⁵¹	Korea, 2006-2010	≥15 yr, total adult population included in the National Health Insurance claim database	Asthma: Both of (1) diagnosed with asthma according to the 10th Revision of the International Classification of	Data in 2010; 18-29 yr: 3,344/100,000 30-39 yr: 4,087/100,000 40-49 yr: 4,582/100,000 50-59 yr: 5,821/100,000 60-69 yr: 9,288/100,000	NR

			Diseases, and (2) prescribed at least one asthma-related medication or asthma- related test throughout the entire study period	70-79 yr: 12,446/100,000 ≥80 yr: 12,848/100,000	
Kim 2013 ⁵²	Korea, 1998 and 2008	n=7,146 in 1998, and n=4,980 in 2008, 20– 59 yr The Korean National Health and Nutrition Examination Surveys	Physician-diagnosed asthma: “Have you ever been diagnosed with asthma by a doctor?”	Data in 2008; 20-29 yr: 1.7% 30-39 yr: 1.6% 40-49 yr: 1.9% 50-59 yr: 3.7%	Allergic rhinitis Rural residence
Wang 2013 ⁵³	Jinan, China, 2009	n=13,419, all ages Random sample	Asthma: Both positive responses to (1) “Have you ever been diagnosed with asthma by a physician?” and/or “Have you ever had	0-14 yr: 0.7% 15-24 yr: 0.1% 25-45 yr: 0.3% 46-60 yr: 0.7% ≥60 yr: 1.3%	Atopy Household size (≤2 persons) Older age Asthma family history

			asthma?"; and (2) "In the past, at any time, have you experienced recurrent (more than three times) sudden attacks of at least one of the following symptoms: whistling in the chest or paroxysmal dyspnea, wheezing, chest tightness or cough?"		
Wu 2013 ⁵⁴	China, 2010	n=13,157, ≥50 yr The Study on Global AGEing and adult health, China Wave 1	Asthma: "Have you ever been diagnosed with asthma by a health care professional?"	50-59 yr: 1.1% (0.8-1.5) 60-69 yr: 2.2% (1.8-2.8) 70-79 yr: 3.5% (2.7-4.5) ≥80 yr: 3.0% (2.0-4.5)	Older age Urban residence Low income
Song 2014 ³⁰	Changwon and Sancheong in Korea, 2007	n=1,080, ≥30 yr, Recruitment of community residents	Current asthma: current wheeze (in the last 12 months) and	31-40 yr: 0.0% 41-50 yr: 1.3% 51-60 yr: 4.8%	Older age BMI ≥ 27.5 kg/m ² Alcohol status

			methacholine airway hyperresponsiveness	61-70 yr: 6.4% ≥70 yr: 9.6%	Less atopy Rhinitis IgE sensitization to staphylococcal enterotoxins
Sonomjamts 2014 ⁵⁵	Ulaanbaatar, Mongolia, 2009	n=1,201, ≥20 yr Recruitment from family clinics	Doctor diagnosed asthma: “Have you ever been diagnosed to have asthma?”	20-29 yr: 2.0% 30-39 yr: 4.8% 40-49 yr: 4.0% 50-59 yr: 8.3% 60-69 yr: 11.0% ≥70: 13.0%	NR
Fu 2016 ²⁸	Seven major cities in China, 2012	n=9,974, ≥15 yr Random sampling of households	Lifetime asthma: “Have you ever been told by a physician or other health professional that you have asthma?”	Data reported in odds ratio 15-34 yr: Reference ≥60 yr: 3.04 (2.13-4.34)	Smoking history Clearance-related job Using coal for cooking Occupational exposure to industrial or occupational poisonous gas

					Large amount of carpet in the workplace
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NR, not reported; FEV1, forced expiratory volume in 1 second; BMI, body mass index

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