Urban vs. Rural Factors That Affect Adult Asthma

Yu Jie, Zaleha Md Isa, Xu Jie, Zhang Long Ju, and Noor Hassim Ismail

Contents

Y. Jie
Faculty of Medicine, Department of Community Health, National University of Malaysia, Kuala Lumpur 56000, Malaysia

School of Public Health, Zunyi Medical College, Zunyi, Guizhou 563003, People's Republic of China

Z.M. Isa • N.H. Ismail (✉)
Faculty of Medicine, Department of Community Health, National University of Malaysia, Kuala Lumpur 56000, Malaysia
e-mail: hassim@ppukm.ukm.my

X. Jie
School of Public Health, Zunyi Medical College, Zunyi, Guizhou 563003, People's Republic of China

Z.L. Ju
The First Department of Respiratory Diseases, First Affiliated Hospital of Zunyi Medical College, Zunyi, Guizhou 563003, People's Republic of China

D.M. Whitacre (ed.), *Reviews of Environmental Contamination and Toxicology Volume 226*, Reviews of Environmental Contamination and Toxicology 226,
DOI 10.1007/978-1-4614-6898-1_2,

1 Introduction

People in modern societies spend the vast majority of their time in indoor environments, including homes, workplaces, schools, and public spaces. Hence, indoor environmental quality has a significant impact on public health and well-being. Exposure or sensitization to indoor pollutants, including cigarette smoke (Hersoug et al. 2010), air pollution (Trupin et al. 2010), and allergens (Dottorini et al. 2007), is an important risk factor for asthma morbidity. Asthma, a common chronic respiratory disease, has been a growing international issue because its prevalence has been expanding in adults and children. The burden of this disease on governmental healthcare systems, patients and their families is increasing worldwide. It is estimated that there are approximately 300 million asthma patients worldwide and that 15 million disability-adjusted life years are lost annually by those afflicted with asthma (Fukutomi et al. 2010). Asthma usually arises from an interaction between host and environmental factors. A rapid increase in asthma in recent years cannot be ascribed to changes in genetic factors, but rather, to changes in environmental factors. In addition to increased indoor air contaminant exposures, several social factors that may contribute to developing asthma morbidity have been studied; among factors that have been given widespread attention are geographical variations, socioeconomic status (SES), and ethnicity.

It has been suggested that, compared to urban dwellers, people living in rural areas generally have better health, along with fewer disabilities and long-term limiting illnesses (Iversen et al. 2005). Moreover, rural residents smoke less, consume less alcohol, and are not as drug-dependent. Those residing in rural areas also have less psychiatric morbidity (Romans et al. 2011). Although they suffer poorer survival rates from lung or colorectal cancer, as compared to those living in urban areas, rural people encounter greater barriers to receiving healthcare services (Lu et al. 2010). Their access to care may be hindered by various factors, including inadequate insurance coverage, an undersupply of healthcare providers and facilities, lack of transportation and a proper healthcare policy where they reside. Coherent evidence shows that differences in the prevalence of asthma morbidity between urban and rural areas exists (Yemaneberhan et al. 1997; Ellison-Loschmann et al. 2004; Smith et al. 2009). Such difference in the prevalence of asthma morbidity may result from increasing urbanization, or from socioeconomic and cultural factors, as well as individual societal factors.

In Fig. 1, we present a diagram of our understanding of the human exposure pathways and potential factors that affect human asthma susceptibility between urban and rural areas. In this model, different environmental urban-based exposures (e.g., particulate or gaseous air pollutants from vehicular traffic, and industry), and similar ones in rural areas (e.g., indoor pollution from biomass fuel combustion, and keeping or herding animals) are known to potentially affect susceptible adult hosts. Such exposures may produce airway inflammation and obstruction. However, there

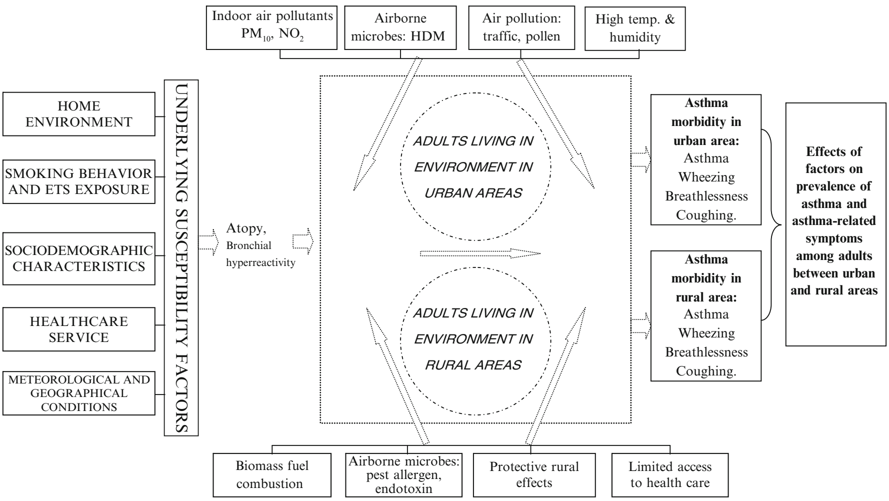

Fig. 1 A diagram of human exposure pathways and potential factors that affect adult asthma susceptibility between urban and rural areas (PM_{10}: particulate matter less than 10 microm in diameter; NO_2: nitrogen dioxide; ETS: environmental tobacco smoke; HDM: house dust mite; temp: temperature)

are disparities between urban and rural areas in the prevalence of asthma and asthma-related symptoms. Susceptibility factors are specific to urban and rural areas, and these differences potentially influence the incidence of asthma between the two areas. Factors that may be important in susceptibility to asthma include sociodemographic characteristics, type of home environment, availability of health-care services, meteorological or geographical differences, and degree of urbanization. Furthermore, factors like atopy and specific genetic background of exposed persons influence host susceptibility to environmental stimuli.

Because asthma and asthma-related symptoms constitutes a growing health problem around the world (Yu et al. 2011a, b), we undertook to investigate the disparities that exist between those living in urban vs. rural areas, in regard to the prevalence of asthma and asthma symptoms that they incur. In particular, we evaluated the importance of geographic variations and their effects on asthma prevalence and morbidity among adults. In addition, we evaluated the possible causes of asthma morbidity between urban vs. rural residents.

This article extends our earlier work (Yu et al. 2011a, b), in which we tried to determine the factors that affect the prevalence of asthma, allergy, and respiratory symptoms among adults, and whether rural/urban living has an effect on asthma prevalence. Investigating the differences that environmental risk factors pose to adults on prevalence of asthma and asthma-related symptoms in urban and rural locations may provide clues to the mechanisms by which asthma and asthma morbidity occur, and may also uncover needs that are currently unmet.

2 Differences Between Urban and Rural Environments

2.1 *Adult Asthma Prevalence and Morbidity in Rural vs. Urban Areas*

The prevalence of asthma throughout China has markedly increased in recent years, having previously been uncommon. Different indoor environmental quality and housing, human characteristics between urban and rural areas are likely to cause important differences in exposure to indoor environmental risk factors. Geographical variation in the prevalence of asthma and asthma-related symptoms may also be closely related to discrepancies in sociodemographic characteristics and other risk factors. For example, in North America, wood and natural gas are sources of heating fuel that are used in rural areas, coal is less frequently used, and depends on what is most readily available in a particular geographical region.

Differences in adult asthma prevalence and morbidity between rural and urban communities have been investigated by many researchers (Ellison-Loschmann et al. 2004; Jackson et al. 2007; Smith et al. 2009; Gao et al. 2011; Musafiri et al. 2011; Frazier et al. 2012). Jackson et al. (2007) reported results of a 2000–2003 survey of lifetime asthma prevalence and trends in metro and nonmetro counties of the USA; they indicated that the prevalence of lifetime asthma diagnoses was 12% for metropolitan counties and 11% for nonmetropolitan counties. The incidence of lifetime asthma diagnoses trended upwards across the rural–urban spectrum between 2000 and 2003, and states with the highest 2003 prevalence and the greatest increase in prevalence among non-metropolitan residents were concentrated in the West Census region (e.g., Arizona and California). Asthma prevalence in non-metropolitan counties was highest for those aged 18–34 (15.9%), the unemployed (13.5%), American Indians (12.7%) and women (12.4%). The recommended approach for diagnosing and treating asthma, Jackson et al. (2007) concluded, may be more difficult to implement in rural counties. Smith et al. (2009) conducted one cross-sectional study in the USA and explored the risk factors associated with healthcare utilization among 3,013 Arizona Medicaid patients with asthma. Urban areas had higher rates of asthma-related hospital visits compared to rural counties, and adults had higher rates than adolescents, but there were no differences in asthma-costs between urban and rural areas. This suggested rural exacerbations may be more costly or severe. In Rwanda, Africa, Musafiri et al. (2011) investigated the prevalence of atopy and asthma in an urban and a rural area. The prevalence of asthma was higher in the urban than in the rural area. Risk factors for asthma included allergy (OR: 4.01; CI: 2.86–5.13), female gender (OR: 1.99; CI: 1.18–3.69) and living in a metropolis (OR: 3.62; CI: 2.12–5.78).

Gao et al. (2011) investigated the prevalence of asthma in China's Qinghai Province in 24,341 adults between 2006 and 2007. The prevalence of asthma in rural, urban, half-farming and half-herding areas, and in pastoral areas was 0.64% (65/10,119), 0.27% (37/13,933), 0.15% (2/1,310) and 0.04% (1/2,489) respectively; the highest incidence was in rural areas and the lowest was in the pastoral areas.

In New Zealand, Ellison-Loschmann et al. (2004) observed regional patterns of asthma hospitalizations in Maori vs. non-Maori areas. The rate of asthma hospitalization was higher for Maori than for non-Maori peoples in two different age-groups: 15–34 years RR = 1.31; and 35–74 years RR = 2.97. Moreover, the differences were higher in rural areas (RR: 1.34 and 3.13) than in urban areas (RR: 1.22 and 2.79) (Ellison-Loschmann et al. 2004).

Frazier et al. (2012), in another study, found that the prevalence of self-reported current asthma among adults is similar in metropolitan and nonmetropolitan counties in Montana of the USA, although other sociodemographic differences existed.

2.2 Combustion Products

2.2.1 Environmental Tobacco Smoke

Environmental tobacco smoke (ETS) contains and delivers over 4,000 compounds to those who are exposed to it, and among the components are carcinogenic agents such as benzo(a)pyrenes, polycyclic aromatic compounds, and tobacco-specific nitrosamines (Haverkos 2004). In 1993, the Environmental Protection Agency (EPA) classified ETS as a known human carcinogen and estimated that ETS exposure is responsible for approximately 3,000 lung cancer deaths each year among adult nonsmokers (USEPA 1993). Exposure to ETS has been associated with many detrimental health consequences, ranging from increased risk of asthma and asthma-related symptoms to lung cancer.

Over the past decades, positive associations between development of asthma and asthma attacks have been reported in children that have existing disease and exposure to ETS in the indoor environment. In contrast, data on the effects of ETS exposure on adults with asthma are limited. Hersoug et al. (2010) found that indoor exposure to ETS is associated with respiratory symptoms and diminished lung function in adults (Hersoug et al. 2010). Furthermore, in one recent 10-year cohort study, Polosa et al. (2011) revealed that cigarette smoking is an important predictor of asthma severity and poor asthma control (Polosa et al. 2011).

Exposures to ETS and Smoking Behavior in Urban vs. Rural Areas

The relationship between adverse health impacts and ETS may be influenced by a disparity of geographic location (Ho et al. 2010). Collected evidence suggests that those residing in rural areas may be disproportionately affected by the health burden of tobacco use. For example, although China has made progress towards achieving a smoke-free environment, there remains a high degree of exposure to secondhand smoke. Xiao and colleagues (2010) have recently studied Chinese nonsmokers aged 15 years and older ($n = 13,354$) to determine the extent of their secondhand smoke exposure. Results showed that 72.4% (556 million) were exposed to secondhand smoke, with 52.5% (292 million) exposed to secondhand smoke daily. The prevalence of secondhand smoke (SHS) exposure was 70.5% for urban populations, and 74.2% for rural populations, respectively (Xiao et al. 2010). In addition, in another behavioral risk factor survey in the USA, Vander Weg et al. (2011) suggested that adults residing in rural areas were significantly more likely to smoke cigarettes, 22.2% vs. 17.3% (suburban) and 18.1% (urban); the exposure disparity resulted from both their own tobacco use and exposure to others' cigarette smoke (Vander Weg et al. 2011).

Differences in Prevalence of Asthma and Asthma Morbidity Among Adult Smokers in Urban vs. Rural Areas

There is conflicting evidence about the risk of asthma and asthma-related symptoms in adults living in rural areas, compared to those living in urban areas (Woods et al. 2000; Zhang et al. 2002; Ghosh et al. 2008, 2009; Lâm et al. 2011). Two cross-sectional studies were performed that indicated the prevalence of asthma morbidity was higher among rural smokers (Woods et al. 2000; Ghosh et al. 2009), and another two suggested the opposite (Ghosh et al. 2008; Lâm et al. 2011). A survey of 11,223 Canadian adults found that rural/urban locations modified the relationship of asthma prevalence and smoking, but only among women. Female smokers and ex-smokers in rural areas were 1.4 times (95% CI: rural smokers = 1.02–1.94, and rural ex-smokers = 1.02–2.02) more likely to be diagnosed with asthma, in contrast to non-smoking urban women. The reason that rural locations influence effects may result from females having more sensitive airways, may exacerbate respiratory symptoms from smoking and may have higher exposure to fumes and dusts in rural locations (Ghosh et al. 2009). A cross-sectional study of randomly selected young adult inhabitants (20–44 years old) in Australia produced similar results in south-eastern metropolitan Melbourne ($n = 4{,}455$) and rural south-western New South Wales ($n = 4{,}521$). Respondents from the Riverina in New South Wales reported a significantly higher prevalence of nocturnal dyspnea, chronic bronchitis, and asthma attacks in the previous 12 months, or ever having had asthma and doctor-diagnosed asthma, compared to those from Melbourne ($p < 0.05$). Riverina respondents reported a higher prevalence of smoking ($p < 0.05$) and smoked more cigarettes on average ($p < 0.001$) than Melbourne respondents (Woods et al. 2000).

By contrast, a cross-sectional study using the Canadian National Population Health data, collected from 1994 to 2000, showed that the prevalence of asthma among smokers and nonsmokers were more prominent in urban than in rural residents. Higher stress levels and lack of open spaces, compared with their rural counterparts, may be possible reasons for the higher asthma prevalence among smokers living in urban areas. Environmental factors and exposure to secondhand smoke may be possible reasons for the higher asthma prevalence among nonsmokers in urban areas (Ghosh et al. 2008). In Vietnam, 3,008 subjects living in an inner city area of Hanoi and 4,000 in a rural area of Bavi, in northern Vietnam, were studied. Results show that the prevalence of asthma in adults may have increased in both urban and rural Vietnam. Nearly One half (49.7%) of the men living in the inner city area of Hanoi were smokers, as were a majority (67.8%) living in a rural area of

Bavi; by contrast, only a few percent of women in both areas were smokers. The prevalence of ever having had asthma in Hanoi was 5.6% (Bavi 3.9%; $p=0.003$), with no major gender difference (Lâm et al. 2011).

The results of one study (Walraven et al. 2001) were inconsistent with others, because the study failed to link tobacco smoking to the onset of asthma in adults. These authors reported findings of a large study performed among 2,166 participants in the urban population vs. 3,223 participants in the rural population in Gambia. In the urban population, 4.1% reported asthma-related symptoms, 3.6% reported doctor-diagnosed asthma, whereas in the rural population, these figures were 3.3% and 0.7%, respectively. Both male and female participants who lived in rural locations (42%) smoked more than those who lived in urban areas (34%). Notwithstanding that, the risk of asthma was not elevated in active smokers compared with never-smokers.

2.2.2 Coal and Biomass Fuels

Almost half the world's population, and up to 90% of rural households in developing countries, still use solid fuels such as coal, firewood, wood chips, crop residue, and dung cakes for their domestic energy needs (Bruce et al. 2000). Indoor combustion of coal or biomass fuels produces both gases and particulate matter that can affect the development and exacerbation of asthma. The best understood of these substances are particulate matter, carbon monoxide, sulfur oxides, nitrous oxides, volatile organic compounds (e.g., formaldehyde), and polycyclic organic matter such as benzo[a]pyrene.

Particulate Matter

It has been documented in epidemiologic studies that there is a relationship between air pollution from indoor combustion sources and asthma and asthma-related symptoms (Qian et al. 2007; Mishra 2003). Although such collective evidence supports the role of particulate matter (PM) exposure in the development of asthma, and as a potential risk factor of asthma exacerbations, the mechanisms by which cooking fuel smoke (mainly particulate matter) influence asthma are not well understood. It has been postulated that particulate matter may induce pulmonary health effects through oxidative stress and pro-inflammatory effects, which have been documented to occur in both in vivo and in vitro studies (Lei et al. 2004; Riva et al. 2011).

Several studies have shown that pollutants from coal and biomass fuel combustion can be present in environment of rural and urban areas (Mestl et al. 2007a; Jiang and Bell 2008; Fullerton et al. 2009; Colbeck et al. 2010a, b). In a recent study from Pakistan, Colbeck et al. (2010a) found high indoor levels of PM during cooking, with concentrations in the range of 4,000–8,555 μg/m^3. The average indoor–outdoor ratios for PM_{10} (1.74), $PM_{2.5}$ (2.49), and PM_1 (3.01) in the living rooms of a rural home vs. an urban one corresponded to the ratios of PM_{10} (1.71), $PM_{2.5}$ (2.88), and PM_1 (3.47), respectively (Colbeck et al. 2010a).

Approximately, 3.1 million annual deaths in rural China are attributable to indoor air pollution (IAP) (Mestl et al. 2007b). Mestl et al. (2007a, b) reported the largest exposure burden to be in counties that rely heavily on biomass for energy, such as China does. The average exposure is estimated at 340 ± 55 μg/m^3 in southern Chinese cities, and 440 ± 40 μg/m^3 in northern ones, whereas the average rural population exposure was 750 ± 100 μg/m^3 and 680 ± 65 μg/m^3 in the south and north, respectively (Mestl et al. 2007a). Furthermore, in another study from China, in which the PM_{10} levels from biomass-burning in rural vs. non-biomass-burning urban households were compared, the monitoring results showed rural kitchen PM_{10} levels (202.1 ± 293.6 μg/m^3) to be three times higher than those in urban kitchens (67.00 ± 32.58 μg/m^3) during cooking. The highest $PM_{2.5}$ exposures occurred during cooking periods for urban and rural cooks. However, rural cooks (487.9 ± 874.9 μg/m^3) had 5.4 times higher $PM_{2.5}$ levels while cooking than did urban cooks (90.1 ± 120.9 μg/m^3) (Jiang and Bell 2008).

Few authors, to date, have evaluated the relationship between adult asthma and asthma-related symptoms and domestic fuel combustion exposures in houses between urban and rural areas. A survey of 3,709 Chinese adults in Beijing, Anqing City, and rural communities in Anqing Prefecture disclosed significant differences between study areas in the prevalence of chronic cough, chronic phlegm, wheezing and dyspnea ($p < 0.05$). The lowest prevalence of respiratory symptoms was observed in Anqing City, a higher prevalence occurred in rural Anqing, and the highest prevalence was observed in Beijing. In this study, median indoor concentrations of PM_{10} were similar in Anqing City (239 μg/m^3) and rural Anqing (248 μg/m^3), but were much higher in Beijing (557 μg/m^3), while median indoor concentrations of SO_2 were similar in all three areas (Venners et al. 2001). The measured indoor PM_{10} concentrations in this study were far higher than the American Society of Heating, Refrigerating & Air-Conditioning Engineer (ASHRAE)'s standards for indoor 24-h average PM_{10} of 150 μg/m^3 (ASHRAE 1989).

Although asthma is less common among rural populations where biomass fuels are in common use, compared with their urban counterparts, it should not be assumed that smoke exposure is not deleterious in these areas. The relationship between residential exposure to solid biomass fuels (animal dung, crop residue, and wood) and asthma morbidity was also examined in Nepal, in which a cross-sectional study ($n = 168$) of a representative sample of housewives was carried out (Shrestha and Shrestha 2005). The prevalence of asthma morbidity, including cough, phlegm, breathlessness, wheezing and asthma were higher among those living in mud and brick houses, compared to concrete houses, and the prevalence was also higher among residents living on hills and in rural areas, in contrast to those living on flatland and in urban areas.

Nitrogen Dioxide

Nitrogen dioxide (NO_2), a combustion by-product, is predominantly an indoor pollutant, and the major source of exposure to it is from household appliances fuelled by gas, particularly in households without flues for such gas appliances (Spengler et al. 1979). Inhaling high concentrations (>5 ppm) of NO_2 is associated with acute epithelial damage, whereas exposure to lower concentrations that exist in urban areas or in an indoor environment can aggravate preexisting lung disease, including asthma (Persinger et al. 2001). To date, the relationships between asthma and asthma-related outcomes and indoor nitrogen dioxide exposures in urban vs. rural areas have rarely been investigated. The results of a recent study, in which the levels of NO_2 were assessed at a Pakistani urban and two rural sites were interesting. In winter, NO_2 concentrations at all three sites were higher in kitchens than living rooms or outdoors. During the summer, NO_2 levels fell sharply at both rural sites (respectively from 256 μg/m^3 and 242 μg/m^3 to 51 μg/m^3 and 81 μg/m^3). However, at the urban site, the mean levels were slightly higher in summer (234 μg/m^3) than in winter (218 μg/m^3). Elevated NO_2 concentrations may pose a significant threat to health and especially to the vulnerable population (e.g., women and children) (Colbeck et al. 2010b).

The mechanisms by which inhaled NO_2 adversely affect human health are difficult to delineate. Sandstrom et al. (1992) reported that repeated exposure to 4 ppm of NO_2 may have adverse implication on local bronchial immunity by reducing total macrophages, B cells, NK lymphocytes, peripheral blood lymphocytes and by reducing the T-helper-inducer/T-cytotoxic-suppressor ratio in alveolar lavage (Sandstrom et al. 1992). In another study, it was demonstrated that NO_2 induced bronchial inflammation and a minimal change in bronchoalveolar lavage T-helper cells (Solomon et al. 2000). Prior studies suggest nitrous acid (HONO), a molecule that can be formed as a primary product of gas combustion or by the reaction of NO_2 with surface water, may contribute to adverse health outcomes previously attributed to NO_2 (Jarvis et al. 2005). The theoretical health risks of HONO include damage to the mucous membranes and lungs by direct contact with the acid, creation of carcinogenic nitrosamines secondary to the HONO combination with amines, and oxygen-free radical production through HONO photolysis in air (Peterson. 2012).

2.3 Biological Contaminants

Biological contaminants include a wide variety of biological agents commonly found in indoor environments. These contaminants include the following: (1) viruses; (2) bacteria (and any related endotoxins); (3) allergens, including house dust mite allergens [*Dermatophagoides farinae* 1 (Der f 1), *Dermatophagoides pteronyssinus* (Der p 1)], and allergens from animal dander [cat (*Felis domesticus* 1 (Fel d 1)), dog (*Canis familiaris* 1(Can f 1)), cockroach (*Blattella germanica* 1 (Bla g 1 & 2)), and mouse (*Mus musculus* 1 (Mus m 1)), mouse urinary protein (MUP) allergens], and fungi (including associated allergens, toxins, and irritants) (Yu et al. 2011a, b). Exposure to indoor allergens and molds, together with building dampness, is an important risk factor for the asthma morbidity of the occupants. However, the role of indoor allergen sensitization in contributing to asthma and asthma-related symptoms, among adults, remains a subject of controversy.

Geographic locations may have a predominant impact on the course of spore occurrence, biological contaminant levels, as well as on Seasonal Fungal Index (SFI) values. Biological contaminant levels and exposure characteristics in urban and rural areas have been compared in various studies (Taksey and Craig 2001; Armentia et al. 2002; Loureiro et al. 2005; El-Shazly et al. 2006; Kasprzyk and Worek 2006; Guinea et al. 2006; Oliveira et al. 2009).

2.3.1 Differences in Exposure to Fungal Allergens in Urban vs. Rural Areas

Several studies have suggested that exposure to fungal allergens could be different between urban and rural settings. The authors of one study in Poland's urban/rural areas found several spore types, including Alternaria, Botrytis, Cladosporium, Epiccocum, Ganoderma, Pithomyces, Polythrincium, Stemphylium, Torula, and Drechslera, that were significantly higher in rural than that in urban environments. Different habitat characteristics such as urbanization level, vegetation, and microclimate seem to play an important role in determining the composition and concentration of the fungal airborne spore population in urban and rural areas (Kasprzyk and Worek 2006). In Spain, Guinea et al. (2006) observed that, despite the different sampling techniques employed, Aspergillus/Penicillium spore concentrations were more frequent in urban than in rural environments in Madrid.

Oliveira et al. (2009) investigated allergenic airborne fungal spores in urban and rural areas of Portugal. The mean daily spore concentrations in the rural and urban areas were 934 and 531 spores/m^3, respectively. The most abundant fungal spore types in rural and urban locations were Cladosporium (59.5% vs. 62.7%), Agaricus (5.6% vs. 4.3%), Agrocybe (1.2% vs. 1.4%), Alternaria (1.1% vs. 1.0%), and Aspergillus/Penicillium (0.9% vs. 1.1%) (Oliveira et al. 2009). In the USA, Taksey and Craig (2001) found that different allergen levels do exist in different regions of the country. Allergies to dust mites, dogs, timothy grass, and ragweed are more often reported by residents in rural than in large metropolitan centers. In contrast, cockroach and Alternaria hypersensitivity were more common in large cities (Taksey and Craig 2001).

2.3.2 Differences in Exposure to Endotoxins in Urban vs. Rural Areas

Asthma and asthma-related symptoms are highly prevalent in both urban and rural areas, and the prevalence of such symptoms has been closely related to bacterial endotoxins. Endotoxin levels have been studied in residential environments in urban and rural communities. In the USA, Roy et al. (2003) quantitified the bacterial DNA and endotoxin content in dust in urban vs. rural areas of Mississippi. Dust endotoxin levels in farm homes (mean, 22.1 mg/g dust), rural homes (6.3 mg/g), and farm barns (2.2 mg/g) are much higher than those in urban and nonfarm homes (0.6 mg/g) respectively (Roy et al. 2003). In addition, asthma hospitalization rates were significantly higher among all demographic groups in the rural (Mississippi) Delta region compared with the urban Jackson Metropolitan Statistical Area ($p < 0.001$) (Roy et al. 2010).

2.3.3 Difference in the Prevalence of Allergic Diseases After Exposure to Biological Contaminants

Variability in urban–rural prevalence of asthma and asthma-related symptoms has been observed in many parts of the world (Nguyen et al. 2010). Several authors of international studies have reported that exposure of sensitized asthmatics to allergens affected asthma prevalence and morbidity in urban vs. rural areas.

Residents living in urban areas are more likely to experience asthma respiratory symptoms than those living in rural areas (Eduard et al. 2004; Douwes et al. 2007). The relationship between geographic locations and prevalence of allergic diseases was examined by monitoring trends and determinants of cardiovascular disease in a European project. This project was called Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA), and was a cross-sectional study ($n = 664$) of a representative sample of adult aged 25–75 years in Germany (Filipiak et al. 2001). Results were that, apart from asthma and sensitization against house dust mite, significant differences in risk of allergic rhinitis (OR. 1.5; 95% CI: 1.2–1.9), atopic sensitization (OR. 1.2; 95% CI: 1.0–1.4) and sensitization against pollen (OR. 1.5; 95% CI: 1.2–1.9) were found in urban vs. rural residents. Given that protective rural effects exist in allergic rhinitis, farmers may experience lower risks in allergic rhinitis, atopic sensitization, and sensitization against pollen and mites, in contrast to rural non-farming residents.

In a cross-sectional study performed with 55 patients in Poland, the differences in clinical test results were examined for patients suffering bronchial asthma. Some patients lived in rural, and some in urban areas. In this study, significant ($p < 0.05$) disturbances in respiratory parameters were found in 23% of patients living in the city, and in 50% of subjects from the rural area. The level of IgE against grass pollens was significantly ($p < 0.01$) higher in urban residents. The results showed important differences between clinical manifestation of asthma in rural and urban patients, and indicated that a difference in etiology may play an important role in asthma development (Krawczyk et al. 2003).

In contrast to other studies, one multicentre study from Turkey found a direct association between allergic diseases and visible mold at home. Living in a house with visible mold increased the risk of respiratory illnesses such as asthma and wheezing, especially in rural areas (Kurt et al. 2009).

Migration from rural to urban areas also may increase the risk of allergy. In Denmark, a prospective population-based study performed over an 8-year observation period showed that adults who had migrated from rural to an urban area (Copenhagen) were at increased risk of developing an allergy (OR: 3.4, 95% CI, 1.6–7.2). This finding showed that persons migrating from rural to urban areas may acquire some new risk factors in the urban environment, or may lose some protective factors resulting from life in the rural environment, thus decreasing immune tolerance and increasing allergy risk (Linneberg 2005).

2.3.4 Protective Effects of Rural Living on Development of Asthma and Asthma Morbidity

Previous studies have disclosed that people living in urban- or Western-lifestyle countries appear to be subject to higher asthma mortality. Exposure to livestock was increasingly associated with a decreased burden of asthma-related diseases (Ghosh et al. 2008). Protective factors were associated with farm milk operations that started very early in life (von Mutius and Vercelli 2010), rural ways of living (Viinanen et al. 2007; Anastassakis et al. 2010), and having had early childhood infections (e.g., parasitic infections) (Yemaneberhan et al. 1997; Nyan et al. 2001), as well as bacterial exposure from animals in rural settings (Senthilselvan et al. 2003). The mechanism for this is unclear. It was pointed out in early studies that the immune system, when exposed to high levels of allergens, or children when exposed early to infections, may induce forms of immune tolerance or immunological response; it is such events that reduce the risk of developing asthma (von Mutius et al. 2000; Busse and Lemanske 2001).

Numerous studies have shown that rural living is protective against asthma and asthma morbidity. To assess whether children who grow up in a farming environment have been protected against a general increase in atopic disorders in Sweden, Bråbäck et al. (2004) used the Swedish Military Service Conscription Register, the Register of the Total Population and the Population and Housing Censuses data to conclude and report the following: the adjusted risk ratios for asthma in conscripts from farming vs. non-farming families were 1.00 (95% CI, 0.93–1.07), 0.94 (95% CI, 0.88–1.01), and 0.85 (95% CI, 0.79–0.91) in conscripts born in 1952–1961, 1962–1971, and 1972–1981, respectively. An inverse association was observed between farm living and asthma. The protective effect of growing up on a farm on the risk of asthma appears to be a fairly recent phenomenon (Bråbäck et al. 2004).

It is possible that the farming environment and rural lifestyle may be associated with an unknown "protective farming" effect, in terms of the disparity of prevalence of asthma morbidity in urban vs. rural communities. In another cross-sectional questionnaire survey of 9,453 Mongolian residents (Viinanen et al. 2005), a subgroup of 869 underwent skin prick tests, spirometry and bronchodilation, or methacholine-challenge testing. In this subgroup, the prevalence of asthma, allergic rhinoconjunctivitis, and allergic sensitization (with 95% CI) were 1.1% (0.3–2.0%), 9.3% (4.0–14.6%), and 13.6% (7.4–19.9%) in Mongolian villages, 2.4% (1.4–3.5%), 12.9% (8.2–17.7%), and 25.3% (17.1–33.6%) in rural towns and 2.1% (1.3–3.0%), 18.4% (13.3–23.4%), and 31.0% (24.5–37.5%) in Ulaanbaatar city. The authors implied that the prevalence of atopic diseases was lower in rural than in suburban or urban areas. Moreover, rural living environments (e.g., presence of herd animals, fermented milk products exposure) protected against atopy (Viinanen et al. 2005).

Furthermore, in a large study in Scotland, Iversen et al. (2005) investigated rural/urban differences in the prevalence of self-reported asthma and asthma-related symptoms. In this study, a significantly lower prevalence of asthma (adjusted OR, 0.59; 95% CI, 0.46–0.76) and eczema (adjusted OR, 0.67; 95% CI, 0.52–0.87) were reported in rural than urban areas, as were the prevalence of persistent cough, phlegm, breathlessness, and wheezing, although no cause and effect relationship was found. The investigators inferred that rural residency may be associated with better health status because of the protective role afforded by the presence of livestock against allergy among subjects (Iversen et al. 2005).

Another cross-sectional study was performed on university students from Finland who spent their childhoods either on a farm or in a nonfarm environment (Kilpeläinen et al. 2001). In this study, a total of 10,667 subjects aged 18–25 years were recruited. Current asthma was found to exist in 3.1% of subjects having lived childhoods in a farm environment; the corresponding number for those living in a nonfarm environment was 12.4% (OR: 0.22; 95% CI, 0.07–0.70). A more moderate or severe bronchial hyperreactivity (methacholine PD_{20} $FEV_1 \leq 600$ μg) was found among subjects who resided as children in a nonfarm environment. Cat-specific IgE was significantly negatively associated with a childhood in a farm environment (1.5% vs. 13.1%; OR: 0.10, 95% CI, 0.02–0.47) (Kilpeläinen et al. 2001).

In addition, Raukas-Kivioja et al. (2007) reported a study of 1,346 Estonia adults aged 17–69 years, who lived in urban or suburban areas before the age of 5, and had a significantly increased risk for allergic sensitization compared to those who were rural residents. In this study, the most common sensitizer in urban areas was cockroach allergens; whereas, in rural areas, the primary sensitizer was storage mites. Positive skin prick test (SPT) results were found in 27% vs. 40% of the study subjects who had lived in a rural vs. urban environment during early childhood; the highest prevalence was found in the most heavily polluted urban areas (Raukas-Kivioja et al. 2007).

In previous studies that compared asthma prevalence between urban and rural settings, all findings indicated decreased prevalence of asthma in rural areas. These results may result from the higher beneficial exposure of rural populations to farming in general and to endotoxins (Valet et al. 2009). The role of endotoxins in asthma is somewhat paradoxic for how they affect children and adults in rural environments. Liu (2004) presumed that asthmatics are particularly sensitive to inhaled endotoxin, and inhalation induces both immediate and sustained airflow obstruction. The paradox of endotoxin exposure is that higher levels of exposure early in life may mitigate the later development of allergy and persistent asthma. With endotoxin exposure being significantly higher in homes with animals and in farming households, where allergy and asthma are less likely to develop, endotoxin and other microbial exposures in early life may keep allergen sensitization and asthma from developing by promoting Th1-type immune development (Liu 2004).

2.3.5 Atopy Associated with Asthma Among Adults Living in Rural and Urban Areas

The underlying factors that affect the course of asthma are not well understood in either rural or urban settings. Additionally, the interactions between atopy and environmental exposure in modulating asthma have not been investigated intensively. Three scientific articles were identified that associated atopy and asthma morbidity in urban vs. rural areas. Ige et al. (2011) recently reported that atopy is related to adult asthma in rural and urban communities in southwest Nigeria. Asthmatics in both urban and rural settings had significantly higher positive skin reactions to house dust mite, cockroach, mold, and mouse epithelium than did non-asthmatic controls ($p < 0.05$). Mean total serum IgE was also significantly higher in asthmatics than in nonasthmatic controls (Ige et al. 2011). Another study performed by Lourenço et al. (2009) in Portugal demonstrated that asthma was more frequently associated with nonallergic rhinitis (NAR) than with allergic rhinitis (AR) among adults. Although sensitization profiles were not different between the urban and rural patients, AR prevalence was higher in urban asthmatic patients than in rural asthmatics (77.3 vs. 68.2; $p = 0.009$). Grass pollen and mites were the major sensitizers for allergic rhinitis patients (Lourenço et al. 2009). Aggarwal et al. (2006) studied 73,605 respondents in urban and rural areas in Chandigarh, Delhi, Kanpur, and Bangalore, India, and found that the overall prevalence of asthma was 2.38%. Residing in an urban area and having a history suggestive of atopy combined with other factors (e.g., the female gender, advancing age, and lower SES) were associated with significantly higher odds of having asthma (Aggarwal et al. 2006).

2.4 Air Pollution and Geographical and Meteorological Conditions

2.4.1 Air Pollution

Outdoor air quality has a lesser or greater degree of influence on indoor air quality, depending on air exchange rates and the pollutant type involved. The major sources of air pollutants in the air of urban areas result from coal combustion, urban traffic emissions, suspended building construction dusts and the chemical industry. Moreover, there has recently been a rapid increase in the number of motor vehicles in some communities, especially in developing countries (e.g., the number of motor vehicles in Guangzhou increased 3.71-fold from 97,200 in 2002 to 555,200 in 2006; Guangzhou Statistics Yearbook 2007). This explosion of car ownership has produced traffic gridlock along with a proliferation of auto fumes, as the city's reliance on cars and trucks leaves its air with few reprieves.

People who live in urban areas tend to be more affected by asthma, allergy, and respiratory diseases than those who live in rural areas. Individuals exposed to higher levels of vehicular traffic have a higher frequency of asthma morbidity than those less exposed to traffic, which may explain some differences for those living in these two areas. Numerous authors have reported significant health impacts associated with exposure to air pollutants (Mugusi et al. 2004; Smith et al. 2009). Although the mechanism by which air pollution affects the development of asthma and asthma-related symptoms is unclear, increasing evidence has shown that the elevated indoor/outdoor levels of aeropollutants (e.g., particles from vehicular traffic) may enhance the severity of asthma morbidity in urban and rural areas.

Few measurements of aeropollutants in urban and rural areas have been reported in the scientific literature. Matson (2005) reported that the concentration of ultrafine particles from air pollution was higher in the metropolitan area of Copenhagen than in the medium-sized city of Gothenburg, and was lowest in more rural sites (Matson 2005).

The relationship between asthma prevalence and morbidity and ambient air pollution was studied in several previously published studies. In Australia, Woods et al. (2000) reported that among residents who had asthmatic attacks in the previous 12 those in Melbourne had a higher frequency of attacks than did residents of Riverina (a rural area). The impact from air pollution on the local population was greater in Melbourne than in Riverina (Woods et al. 2000). By contrast, one case–control study from Sweden explored 203 adult human cases, and 203 controls (aged 20–60 years), for differences in risk of asthma from traffic-related air pollution exposure at home. Differences were then compared between those living in urban and rural areas. Living in a rural area tended to increase the risk of developing asthma, when traffic pollution was adjusted for. Rural living may, therefore, be seen as an indicator of a certain lifestyle and of different exposure patterns (Modig et al. 2006).

Michnar et al. (2003) studied the incidence of allergic respiratory diseases between urban and rural areas against the environmental pollution level in Poland. They distributed a standard questionnaire to 1,223 adults living in randomly selected districts (Nałeczów, Puławy, Motycz-Lublin) of that country, wherein various levels of industrial pollution existed. No difference in bronchial asthma incidence was found in any of the districts, but the diagnosis rate of allergic rhinitis was higher in rural than in urban areas (Michnar et al. 2003).

To evaluate the extent to which climate and outdoor NO_2 pollution can explain the geographical variation in the prevalence of asthma and allergic rhinitis, a questionnaire-based survey of 18,873 adults (aged 20–44 years) was performed in Italy (de Marco et al. 2002). Those surveyed lived in 13 areas of northern Italy that enjoyed sub-continental and Mediterranean climates. Those living in the Mediterranean climate areas, characterized by higher annual mean temperature (16.2 °C vs. 12.9 °C) and lower NO_2 levels (31.46 $\mu g/m^3$ vs. 57.99 $\mu g/m^3$), had a significantly higher prevalence of asthma morbidity ($p < 0.001$) than subcontinental ones did. The investigators presumed that air pollution from traffic emissions may pose long-term adverse effects on adult pulmonary health such as asthma morbidity.

The World Health Organization cautiously concluded that traffic-related air pollution may enhance asthma development and exacerbate asthma-related symptoms, particularly among susceptible subgroups (Heinrich and Wichmann 2004). Nevertheless, air pollution may not be a major risk factor for developing asthma; rather, it is merely a minor trigger in some individuals. For example, in some regions (e.g., China and Eastern Europe) that have a high concentration of some air pollutants (e.g., PM_{10} and SO_2), there is generally a low rate of asthma prevalence. In contrast, some regions that have low levels of air pollution, such as some parts of New Zealand, still experienced a high prevalence of asthma. This suggests that even though it is plausible that outdoor air pollution plays a role in the increasing prevalence of asthma morbidity, other causes exist.

Study results from North America (Arif et al. 2004), Central America (Cooper et al. 2009), Europe (Filipiak et al. 2001), Asia (Viinanen et al. 2005), and Africa (Musafiri et al. 2011) have shown that the prevalence of asthma, and the morbidity associated therewith, is higher in urban than in rural environments. This is particularly true for pollinosis, whereas pollen counts are usually higher in urban than in rural areas (Armentia et al. 2002; Bousquet et al. 2008).

It has been demonstrated in several studies that plant pollen is present in both urban and rural environments. Armentia et al. (2002) reported that the protein content and allergenicity of *Lolium perenne* pollen was higher in urban than in rural areas. Such differences may explain why allergies to grass pollen more frequently occur in urban areas (Armentia et al. 2002). In comparing the distribution of pollen in urban and rural areas across an urbanization gradient, Bosch-Cano et al. (2011) found that the pollen burden from grass, ash, birch, alder, hornbeam, hazel and plantain exceeded the allergy threshold more often in rural than in urban settings, whereas, in urban areas, only plant-pollen quantities exceeded the allergy threshold more often than in rural areas (Bosch-Cano et al. 2011).

Asthma and asthma-related symptoms are common problems in both children and adults, but the causative pollen allergens vary by geographical area. Few academic studies have enumerated the correlation of asthma and/or allergen sensitivity with geography among adults. Loureiro et al. (2005) revealed, in a large study of 1,096 patients from Cova da Beira, Portugal, the frequency of aeroallergens sensitization. They compared the sensitization in urban vs. rural environments. Respectively, results of urban–rural sensitivity to various allergenic sources were as follows: *D. pteronyssinus* (32% vs. 34.7%), mold mixtures (15.3% vs.12%), cat dander (17.1% vs. 15.2%), grass mixtures (51.3% vs. 36.4%), and *Parietaria judaica* (29.4% vs. 14%). The sensitization to indoor aeroallergens was lower than that to pollens. The authors assumed that pollution-enhanced sensitization to pollens occurred in the urban environment (Loureiro et al. 2005). Moreover, in Germany, Filipiak et al. (2001) reported that allergic rhinitis from sensitization to pollen was 2.5 times (95% CI: 1.8–3.6) more prevalent in urban than in rural residents (Filipiak et al. 2001).

2.4.2 Climatic and Geographic Factors

A potential role of various seasonal and meteorological factors in the etiology of asthma and asthma-related symptoms has long been suspected. There is evidence that climate may affect asthma symptom prevalence and frequency, either directly (e.g., via an effect of air temperature on airway responsiveness) or indirectly (e.g., via altered exposure to infections, aeroallergens, or air pollutants) (Metintas and Kurt 2010; Franco et al. 2009; Hales et al. 1998; Verlato et al. 2002; Chen et al. 2006).

Different geographical and climatic properties (e.g., elevation, temperature, humidity) have a close relationship with asthma morbidity prevalence, such as allergic rhinitis among adults in urban and rural areas. Many geographic locations have climates that are favorable to indoor mold growth, for example, in tropical areas that routinely have high humidity.

In a national survey conducted in five geographic regions in Thailand, Dejsomritrutai et al. (2006) found the prevalence of current diagnosed asthma in northeastern rural regions (2.05%) to be more prevalent than in central urban regions (1.66%). The higher temperatures and rainfall, together with higher incomes of residents of central regions vs. those living in northeast regions, were thought to account for differences in the prevalence of asthma in Thailand (Dejsomritrutai et al. 2006). Moreover, Lewis et al. (1997) studied 31,470 adults in New Zealand and found that a high frequency of asthma symptoms were experienced by New Zealand adults (15.2%); Maoris (22.1%) and women (17.0%) experienced a higher rate of such symptoms. This study also shows significant urban–rural differences, as well as marked differences in prevalence among various rural areas (Lewis et al. 1997).

2.5 Socioeconomic Characteristics and Healthcare Services

Recent evidence suggests that prevalence of asthma and rates of exacerbation (e.g., asthma attacks and related emergency room visits and hospitalizations) may, in fact, be higher than previously thought (Yu et al. 2011a, b; Comhair et al. 2011; Nguyen et al. 2011). In addition, such outcomes, when they occur, are associated with geographic and socioeconomic circumstances. Identifying socioeconomic and regional factors that contribute to prevalence of asthma, allergy, and respiratory symptoms among adults is complicated. Such complications result from the influence of multiple demographic indicators, particularly race and income, and of system-level considerations such as hospital admission and prescription policies that may vary at the local level. In addition, poor SES may confound the relationship between indoor climate and respiratory disease, because SES is associated with both the exposure and the outcome variable (Skorge et al. 2005).

Many studies have shown that asthma continues to disproportionately affect minority and low-income groups. SES factors, such as cultural attitudes toward health (Ellison-Loschmann et al. 2004), low levels of education and income (Joshi et al. 2003), lack of healthcare coverage (Ansari et al. 2003), and poorly maintained housing, as well as poor hygiene conditions (e.g., cockroach, rodent, etc.) (von Mutius and Vercelli 2010), which are the typical characteristics of rural areas, may contribute to the differences in the prevalence of asthma morbidity between urban and rural areas. Using the 2005 Behavioral Risk Factor Surveillance System (BRFSS) data from the USA, Morrison and coworkers (2009) investigated adult sociodemographic and health behavior contributions to asthma prevalence. After adjusting for sociodemographic and behavior characteristics, results were that no significant difference existed for residents of urban vs. rural areas. However, asthma prevalence in metropolitan regions was less pronounced than those in remote areas (OR: 0.96; 95% CI, 0.90–1.02) (Morrison et al. 2009). In contrast, in a national study in Australia, Cunningham (2010) reported asthma prevalence was higher for indigenous Australians than for nonindigenous Australians. The age and sex-adjusted relative odds of contacting asthma was 1.2 (95% CI, 1.0–1.5) in the nonindigenous population vs. 1.0 (95% CI, 0.8–1.3) in the indigenous population.

The socioeconomic pattern of those contacting asthma among indigenous Australians is much less clear. This may be due, in part, to the episodic nature of asthma, and to the limited health literacy and/or limited access to health care of this group. It may also reflect the importance of exposures to socioeconomic effects among the indigenous Australians, such as racism or other forms of discrimination, social marginalization and dispossession, chronic stress and/or exposure to violence (Cunningham 2010).

In India, Gaur et al. (2006) found that the prevalence of asthma among the rural, urban city and urban-slum adult population of Delhi were 13.34%, 7.9% and 11.92%, respectively. The current prevalence of asthma was more pronounced if there was a history of family atopy, or where more vegetable debris, poor ventilation, air pollution and increased human density were present. There was also an association with increased smoking habits. However, no significant difference was noted in asthma prevalence between those living in urban and rural areas (Gaur et al. 2006).

More recently, an allergy report from Austria indicated that people with higher education levels, or those who are more highly qualified for jobs and who live in urban areas are more likely to be affected by allergies than are people from lower socioeconomic levels or rural areas (Dorner et al. 2007).

Access to healthcare services is a marker of primary care quality, because acute episodes of asthma are avoidable if they are managed and appropriately treated in the community. Gaps in access to medical services between urban and rural areas exist, and include such things as convenience of transportation, range of services provided locally, as well as the cost for medical treatment. The previous literature indicates that a lack of medical services and specialists are more common in rural than in urban areas (Rural Healthy People 2010), and there is a low utilization efficiency of hospice services in rural areas (Gessert et al. 2006); in addition, disparities exist in the threshold for admission to hospital or clinic care, between urban and rural physicians (Russo et al. 1999).

Several studies worldwide have demonstrated the differences that exist in access to healthcare services for those suffering asthma morbidity. In Hawaii, 4,318 adults, whose names were selected from insurance claims data, were studied and the results showed that the rate of office visits after emergency department (ED) treatment for asthma was significantly lower in rural compared to urban residents. Rural residents were less likely to receive follow-up care after ED visits (RR: 78, 95% CI, 0.63–0.96, $p=0.02$; adjusted for age, sex, and morbidity). Distance to care centers and number of available healthcare providers, rather than financial aspects accounted for the differences (Withy and Davis 2008). Ansari et al. (2003) reported trends and geographic variations in hospital admissions for asthma sufferers in Victoria. Asthma admission rates were consistently higher in rural than in metropolitan areas. Rural doctors were more likely to admit people to hospital care after light attacks, because of concern that their conditions might deteriorate before they could return to the hospital (i.e., considering that they lived further from the hospital than city dwellers do; Ansari et al. 2003).

A cross-sectional study in Wellington, New Zealand was performed in which the regional variations in asthma hospital admission among Maori and non-Maori (Ellison-Loschmann et al. 2004) peoples were investigated. Asthma hospital admissions were more prevalent for Maoris than for non-Maoris of different age groups: 15–34 years relative risk (RR) = 1.31; 35–74 years RR = 2.97. The differences were somewhat higher in rural (RR: 1.34, 3.13 respectively) than in urban areas (RR: 1.22, 2.79 respectively). The disparities among the urban and rural groups in asthma morbidity for those living in rural areas included inadequate access to appropriate health care (e.g., inadequate money for traveling to the doctor's surgery, for paying doctor's fees, for buying drugs, etc.), and poor asthma education and differential management of asthma. Mugusi et al. (2004) performed another study in Tanzania and in Cameroon on the prevalence of wheezing and on self-reported asthma and asthma care in urban vs. rural areas of the two countries. There were no consistent patterns of urban: rural prevalence. Although consistent patterns of urban–rural prevalence were not obvious, peak flow rates varied with age, peaking at 25–34 years, and were higher in urban areas (age adjusted difference 22–70 L/min), and in the Tanzania populations. Asthma awareness (83–86% vs. 52–58%) and treatment (43–71% vs. 30–44%) of asthma was higher among those with a current wheeze in rural areas, compared with those in urban areas. Diagnosis by traditional healers and use of traditional remedies prevailed among self-reported asthmatic patients in rural Cameroon, and a major gap in clinical care, particularly in urban areas, was revealed (Mugusi et al. 2004).

Moreover, Roy found that asthma hospitalization rates were significantly higher in rural Delta regions of Mississippi compared with the urban Jackson Metropolitan Statistical Area, especially among older adults (≥65 years) and blacks. Blacks with asthma are more likely to have multiple asthma hospitalizations in Mississippi. Higher odds of multiple asthma discharges for Delta residents were not explained by race, sex, age, or income, indicating that other contributing factors (e.g., environmental, social, and access to care factors) need to be further investigated (Roy et al. 2010).

3 Conclusions

Asthma is a complex inflammatory disease of multifactorial origin, and is influenced by both environmental and genetic factors. The disparities in asthma prevalence and morbidity among the world's geographic locations are more likely to be associated with environmental exposures than genetic differences. In writing this article, we did find some studies that addressed the question of disparities in the prevalence of asthma morbidity in various geographic locations (see Table 1). Some studies addressed differences in prevalence of asthma morbidity in relation to various environmental or social factors (see Table 2). Most authors, who published on the topic of this paper, used a cross-sectional design in their experiments.

Table 1 Urban–rural differences in the prevalence of asthma

Study year	Reference and study location	Prevalence (%)	
		Urban area	Rural area
1994–1995	Filipiak et al. (2001), Germany	2.3	1.4
1994–2000	Ellison-Loschmann et al. (2004), New Zealand	1.4	1.7
1996	Yemaneberhan et al. (1997), Ethiopia	3.6	1.3
1996–1997	Walraven et al. (2001), Gambia	3.6	0.7
1999	Woods et al. (2000), Australia	9.0	12.0
1999	Venners et al. (2001), China	1.5	1.7
1999–2000	Viinanen et al. (2005), Mongolia	2.1	1.1
2000	Dejsomritrutai et al. (2006), Thailand	1.7	2.1
2000–2001	Ghosh et al. (2008), Canada	7.7	6.7
2001–2002	Iversen et al. (2005), Scotland	23.8	14.0
2005	Gaur et al. (2006), Delhi, India	10.2	13.3
2005	Morrison et al. (2009), the USA	7.8	7.9
2006–2007	Gao et al. (2011), Qinghai, China	0.3	0.6
2007–2008	Lâm et al. (2011), Vietnam	5.6	3.9
2008	Frazier et al. (2012), Montana, the USA	9.9	9.3
2008–2009	Musafiri et al. (2011), Rwanda	9.3	8.3

We reviewed 145 papers that pertained to the topic of this chapter. The key question we addressed is whether there is a difference in the prevalence of asthma or asthma-related symptoms for people who live in rural vs. urban areas. The main conclusions we arrived at on reviewing this question are as follows:

1. Indoor environments influence asthma and asthma-related symptoms among adults in both urban and rural areas.
   In most studies, reported IAQ and asthma morbidity data strongly indicated positive associations between indoor air pollution and adverse health effects in both urban and rural areas. Indoor factors most consistently associated with asthma and asthma-related symptoms in adults included fuel combustion, mold growth, and environmental tobacco smoke, in both rural and urban areas. Environmental exposures may increase an adult's risk of developing asthma and also may increase the risk of asthma exacerbations.
2. People living in urban areas often suffer greater asthma morbidity.
   Asthma and asthma-related symptoms occurred more frequently in urban than in rural areas, and that difference correlated with environmental risk exposures, SES, and healthcare access. Environmental risk factors to which urban adults were more frequently exposed than rural adults were dust mites, high levels of vehicle emissions, and a westernized lifestyle.
   Exposure to indoor biological contaminants in urban environment is common. A broad review of the literature for indoor environment generally suggests a relationship between microbe exposure and asthma prevalence and morbidity. The main risk factors for developing asthma in urban areas are atopy and allergy to house dust mites, followed by allergens from animal dander. House dust mite exposure may be a main reason for a higher diagnosis rate of asthma among adults living in urban vs. rural areas.

Table 2 A summary review of studies that have addressed factors that potentially affect asthma among adults residing in urban vs. rural areas

Potential factors	Reference, study year, and location	Study design, subject characteristics, and sample size (rural/urban)	Health outcomes	Risk assessment	Summary of published findings
Exposure to smoking	Ghosh et al. (2009), Canada	Cross-sectional study Residents aged 18–64 years ($n = 1,362/4,240$)	Asthma	Rural female smokers 1.4 times (95% CI, 1.02–1.94) more likely to be diagnosed with asthma	Living in a rural area and smoking increased asthma prevalence.
	Ghosh et al. (2008), Canada	Cross-sectional study Residents aged ≥ 15 years, 19,600 households ($n = 20,095$)	Asthma	–	Asthma prevalence increased among rural and urban women.
	Woods et al. (2000), Australia	Cross-sectional study Young adults 20–44 years ($n = 3,106/3,194$)	Nocturnal dyspnoea, asthma attack	–	Asthma prevalence was higher in rural areas.
	Walraven et al. (2001), Gambia	Cross-sectional study Residents aged ≥ 15 years ($n = 3,223/2,166$)	Asthma and chronic cough	–	The risk of asthma was not elevated in active smokers.
	Lâm et al. (2011) Bavi/Hanoi, Vietnam	Cross-sectional study Residents aged 21–70 years ($n = 4,000/3,008$)	Asthma	–	Asthma prevalence increased in both urban and rural areas.
Exposure to coal and biomass fuels	Venners et al. (2001), China	Cross-sectional study Residents aged ≥ 18 years ($n = 1,245/1,184$)	Respiratory symptoms (e.g., chronic cough)	–	Differences were found between study areas in the prevalence of respiratory symptoms.
	Shrestha and Shrestha (2005), Nepal	Cross-sectional study Residents, aged ≥ 18 years, 98 households ($n = 168$)	Cough, phlegm, dyspnoea and asthma	–	Prevalence of respiratory illnesses was higher in hills and rural areas.

(continued)

Table 2 (continued)

Potential factors	Reference, study year, and location	Study design, subject characteristics, and sample size (rural/urban)	Health outcomes	Risk assessment	Summary of published findings
Exposure to biological contaminants	Filipiak et al. (2001), German	Cross-sectional study Residents aged 25–75 years (n = 1,470/3,110)	Allergic diseases	The urban population had an increased risk of allergic rhinitis (OR. 1.5; 95% CI, 1.2 ± 1.9).	A farming environment might be protective for preventing allergies.
	Kurt et al. (2009), Turkey.	Cross-sectional study Parents of school children (n = 10,289/15,554)	Asthma, wheezing, allergic rhinitis, and eczema	–	Living in a house with mold increased risk of respiratory illnesses.
	Linneberg (2005), Denmark	Cohort study Residents aged 15–69 years (n = 231 (emigrant)/ 171(city resident))	Allergy	Migration from rural to urban areas increases risk of allergy (OR: 3.4, 95% CI, 1.6–7.2)	Migration from rural to urban areas increases risk of allergy.
	Bråbäck et al. (2004), Sweden	Cohort study Conscripts aged 17–20 years (n = 197,547/1,119,437)	Asthma, allergic rhinitis, and eczema	Risk ratio for asthma in conscripts from farming vs. non-farming families was 1.00 (95% CI, 0.93–1.07)	Environmental changes increase in asthma in both farming and non-farming areas.
	Raukas-Kivioja et al. (2007), Estonia	Cross-sectional study Residents aged 17–69 years (n = 651/541)	Allergic sensitization	Living in capital was associated with cat (OR:1.96, 95% CI, 1.03–3.74)	Urban living was associated with higher prevalence of allergic sensitization.
	Viinanen et al. (2005), Mongolian	Cross-sectional study Residents aged 10–60 years (n = 304/896)	Asthma and allergic rhino conjunctivitis	–	Prevalence of atopic diseases was low in rural and increased with urbanization.
	Iversen et al. (2005), Scotland	Cross-sectional study Residents, aged ≥ 16 years (n = 1,099/1,497)	Self-reported asthma and asthma morbidity	Residents from rural areas have lower asthma prevalence (OR: 0.59; 95% CI, 0.46–0.76)	Living in rural area gave lower prevalence of asthma and wheeze.
	Kilpeläinen et al. (2001), Finland	Cross-sectional study First-year university students aged 18–25 years (n = 651/541)	Asthma and sensitization	Current asthma had a risk ratio of 0.22 (95% CI, 0.07–0.70) in subjects with childhood farm environment	Farm environment in childhood protects against adult asthma.
	Lourenço et al. (2009), Portugal	Cross-sectional study Patients aged ≥ 18 years (n = 268/226)	Asthma and allergic rhinitis	–	Allergic rhinitis prevalence was higher in urban asthmatic patients.

Air pollution, geographical and meteorological conditions	Cingi et al. (2010), Turkey	Cross-sectional study Caucasian inhabitants, aged ≥ 18 years (n = 499/4,125)	Allergic rhinitis	–	AR prevalence in coastal urban areas was higher than that in inner rural areas.
	Dejsomritrutai et al. (2006), Thailand	Cross-sectional study Residents, aged 20–44 years (n = 3,452)	Bronchial hyper responsiveness and asthma	–	Asthma prevalence was lower in southeast Asian countries.
	de Marco et al. (2002), Italy	Cross-sectional study Residents aged 20–44 years (n = 18,873)	Asthma and allergic rhinitis	Mediterranean climate increased asthma attack risk (OR: 1.19; 95% CI 1.07–1.31)	Traffic air pollution might pose long-term adverse effects on asthma morbidity.
Socioeconomic characteristics and healthcare services	Mugusi et al. (2004), Tanzania and Cameroon	Cross-sectional study Residents, aged ≥ 16 years (n = 4,560)	Wheeze and self-reported asthma	–	Asthma was an important clinical condition in sub-Saharan Africa.
	Withy and Davis, (2008), the USA	Cross-sectional study Residents, aged ≥ 18 years (n = 2,652/4,412)	Asthma	Rural residents were less likely to receive follow-up care (RR: 78, 95% CI, 0.63–0.96)	Rural residents were less likely to receive follow-up care for a diagnosis of asthma.
	Ansari et al. (2003), Australia	Cross-sectional study Residents (n = 10,079)	Asthma	–	Rural areas had higher asthma hospital admission rates.
	Ellison-Loschmann et al. (2004), New Zealand	Cross-sectional study Maori and non-Maori (n = 6,036/19,829)	Asthma	Asthma hospitalization rates were higher in rural (RR: 3.13) than in urban areas (RR: 2.79)	Asthma hospitalization rates were higher in rural than in urban areas.
	Morrison et al. (2009), the USA	Cross-sectional study Residents, aged ≥ 18 years (n = 341,932)	Asthma	Asthma prevalence (7.9%; 95% CI: 7.73–8.08) was not statistically different	Asthma prevalence was as high in rural as in urban areas.
	Cunningham (2010), Australia	Cross-sectional study Indigenous and nonindigenous adults, aged 18–64 years (n = 5,417/15,432)	Asthma	–	The socioeconomic patterning of asthma among indigenous Australians is lower.
	Gaur et al. (2006), India	Cross-sectional study Residents, aged 18–70 years (n = 1,552/1,876)	Asthma and allergic rhinitis	–	No difference in asthma prevalence between urban and rural population.

In addition, the prevalence of asthma morbidity increases with urbanization. High levels of vehicle emissions, Western lifestyles and degree of urbanization itself, may affect outdoor, and thereby indoor air quality. In urban areas, biomass fuels have been widely replaced by cleaner energy sources at home, such as gas and electricity, but in most developing countries, coal is still a major source of fuel for cooking and heating, particularly in winter. Noticeably, chemical emissions from new building materials and furniture, such as formaldehyde, are problematic in urban settings. Moreover, exposure to ETS is common at home or at work in urban areas.

3. The prevalence of asthma morbidity is less common in rural areas.
   There is evidence that asthma prevalence and morbidity is less common in rural than in urban areas. The possible reasons are that rural residents are exposed early in life to stables and to farm milk production, and such exposures are protective against developing asthma morbidity. Even so, asthma morbidity is disproportionately high among poor inner-city residents and in rural populations. A higher proportion of adult residents of nonmetropolitan areas were characterized as follows: aged 55 years or older, no previous college admission, low household income, no health insurance coverage, and could not see a doctor due to healthcare service availability, etc.

   In rural areas, biomass fuels meet more than 70% of the rural energy needs (China Statistical Yearbook 1998). Progress in adopting modern energy sources in rural areas has been slow. Household use of traditional biomass fuels including firewood, wood chips, crop residue, dung cakes and coal are still widespread in rural areas. The rural poor depend upon biomass fuels for their basic cooking, and water- and space-heating needs. The most direct health impact comes from household energy use among the poor, who depend almost entirely on burning biomass fuels in simple cooking devices that are placed in inadequately ventilated spaces. Future research is needed to assess the long-term effects of biomass smoke on lung health among adults in rural areas. Given the extensive use of biomass fuels in rural areas, public health efforts in the developing world that are concerned with respiratory health should address the risks IAP exposure. In Fig. 1, we summarize the underlying susceptibility factors that contribute to discrepancies in the prevalence of asthma morbidity among adults in urban vs. rural areas.

Geographic differences in asthma susceptibility exist around the world. The reason for the differences in asthma prevalence in rural and urban areas may be due to the fact that populations have different lifestyles and cultures, as well as different environmental exposures and different genetic backgrounds. Identifying geographic disparities in asthma hospitalizations is critical to implementing prevention strategies, reducing morbidity, and improving healthcare financing for clinical asthma treatment. Although evidence shows that differences in the prevalence of asthma do exist between urban and rural dwellers in many parts of the world, including in developed countries, data are inadequate to evaluate the extent to which different pollutant exposures contribute to asthma morbidity and severity of asthma between urban and rural areas.

Finally, we addressed potential biases of the studies reviewed to prepare this paper. Most reviewed studies utilized a cross-sectional design, which limits their use for inferring causality of effect. What constituted an urban or rural area and how these were defined in terms of population density or numbers varied considerable among reviewed studies. Therefore, it is difficult to compare studies conducted in widely different geographies. Furthermore, comparisons are different because populations have different lifestyles and cultures, as well as different environmental exposures and different genetic backgrounds. We suspect that the differences in how urban or rural areas were defined in different studies have affected some findings of the association between increased respiratory symptoms from indoor exposures or risk factors. In previous studies, synergism or additive effects from multiple indoor environmental exposures have been reported. In contrast, few study authors of papers in this review claimed to have observed interactive effects from multifactor exposures in either rural or urban surveys.

4 Summary

In this review, our aim was to examine the influence of geographic variations on asthma prevalence and morbidity among adults, which is important for improving our understanding, identifying the burden, and for developing and implementing interventions aimed at reducing asthma morbidity. Asthma is a complex inflammatory disease of multifactorial origin, and is influenced by both environmental and genetic factors. The disparities in asthma prevalence and morbidity among the world's geographic locations are more likely to be associated with environmental exposures than genetic differences. In writing this article, we found that the indoor factors most consistently associated with asthma and asthma-related symptoms in adults included fuel combustion, mold growth, and environmental tobacco smoke in both urban and rural areas. Asthma and asthma-related symptoms occurred more frequently in urban than in rural areas, and that difference correlated with environmental risk exposures, SES, and healthcare access. Environmental risk factors to which urban adults were more frequently exposed than rural adults were dust mites, high levels of vehicle emissions, and a westernized lifestyle.

Exposure to indoor biological contaminants in the urban environment is common. The main risk factors for developing asthma in urban areas are atopy and allergy to house dust mites, followed by allergens from animal dander. House dust mite exposure may potentially explain differences in diagnosis of asthma prevalence and morbidity among adults in urban vs. rural areas. In addition, the prevalence of asthma morbidity increases with urbanization. High levels of vehicle emissions, Western lifestyles and degree of urbanization itself, may affect outdoor and thereby indoor air quality. In urban areas, biomass fuels have been widely replaced by cleaner energy sources at home, such as gas and electricity, but in most developing countries, coal is still a major source of fuel for cooking and heating, particularly in winter. Moreover, exposure to ETS is common at home or at work in urban areas.

There is evidence that asthma prevalence and morbidity is less common in rural than in urban areas. The possible reasons are that rural residents are exposed early in life to stables and to farm milk production, and such exposures are protective against developing asthma morbidity. Even so, asthma morbidity is disproportionately high among poor inner-city residents and in rural populations. A higher proportion of adult residents of nonmetropolitan areas were characterized as follows: aged 55 years or older, no previous college admission, low household income, no health insurance coverage, and could not see a doctor due to healthcare service availability, etc. In rural areas, biomass fuels meet more than 70% of the rural energy needs. Progress in adopting modern energy sources in rural areas has been slow. The most direct health impact comes from household energy use among the poor, who depend almost entirely on burning biomass fuels in simple cooking devices that are placed in inadequately ventilated spaces. Prospective studies are needed to assess the long-term effects of biomass smoke on lung health among adults in rural areas.

Geographic differences in asthma susceptibility exist around the world. The reason for the differences in asthma prevalence in rural and urban areas may be due to the fact that populations have different lifestyles and cultures, as well as different environmental exposures and different genetic backgrounds. Identifying geographic disparities in asthma hospitalizations is critical to implementing prevention strategies, reducing morbidity, and improving healthcare financing for clinical asthma treatment. Although evidence shows that differences in the prevalence of asthma do exist between urban and rural dwellers in many parts of the world, including in developed countries, data are inadequate to evaluate the extent to which different pollutant exposures contribute to asthma morbidity and severity of asthma between urban and rural areas.

Acknowledgments This work was supported by the foundation of: National University of Malaysia, Kuala Lumpur, Malaysia (FF-013-2012); Key Technologies R&D Programme of Department of Science and Technology of Guizhou Province, China (SY[2012]3126) and (SY[2011]3029).

References

Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, Jindal SK, Katiyar SK, Kumar R, Shah B, Vijayan VK; Asthma Epidemiology Study Group (2006) Prevalence and risk factors for bronchial asthma in Indian adults: a multicentre study. Indian J Chest Dis Allied Sci 48(1):13–22

Anastassakis KK, Chatzimichail A, Androulakis I, Charisoulis S, Riga M, Eleftheriadou A (2010) Skin prick test reactivity to common aeroallergens and ARIA classification of allergic rhinitis in patients of Central Greece. Eur Arch Otorhinolaryngol 267:77–85

Ansari Z, Haby MM, Henderson T, Cicuttini F, Ackland MJ (2003) Trends and geographic variations in hospital admissions for asthma in Victoria. Opportunities for targeted interventions. Aust Fam Physician 32:286–288

Arif AA, Borders TF, Patterson PJ, Rohrer JE, Xu KT (2004) Prevalence and correlates of paediatric asthma and wheezing in a largely rural USA population. J Paediatr Child Health 40:189–194

Armentia A, Lombardero M, Callejo A, Barber D, Martín Gil FJ, Martín-Santos JM, Vega JM, Arranz ML (2002) Is Lolium pollen from an urban environment more allergenic than rural pollen? Allergol Immunopathol (Madr) 30:218–224

ASHRAE (1989) ASHRAE Standard 62-1989, ventilation for acceptable indoor air quality. ASHRAE, Atlanta, Ga

Bosch-Cano F, Bernard N, Sudre B, Gillet F, Thibaudon M, Richard H, Badot PM, Ruffaldi P (2011) Human exposure to allergenic pollens: a comparison between urban and rural areas. Environ Res 111:619–625

Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A (2008) Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 63:8–160

Bråbäck L, Hjern A, Rasmussen F (2004) Trends in asthma, allergic rhinitis and eczema among Swedish conscripts from farming and non-farming environments. A nationwide study over three decades. Clin Exp Allergy 34:38–43

Bruce N, Perez-Padilla R, Albalak R (2000) Indoor air pollution in developing countries: a major environmental and public health challenge. Bull World Health Organ 78:1078–1092

Busse WW, Lemanske RJ (2001) Asthma. N Engl J Med 344:350–362

Chen CH, Xirasagar S, Lin HC (2006) Seasonality in adult asthma admissions, air pollutant levels, and climate: a population-based study. J Asthma 43:287–292

China Statistical Yearbook 1997 (1998) State Statistical Bureau, People's Republic of China

Cingi C, Topuz B, Songu M, Kara CO, Ural A, Yaz A, Yildirim M, Miman MC, Bal C (2010) Prevalence of allergic rhinitis among the adult population in Turkey. Acta Otolaryngol 130(5):600–606.

Colbeck I, Nasir ZA, Ali Z, Ahmad S (2010a) Nitrogen dioxide and household fuel use in the Pakistan. Sci Total Environ 409:357–363

Colbeck I, Nasir ZA, Ali Z (2010b) Characteristics of indoor/outdoor particulate pollution in urban and rural residential environment of Pakistan. Indoor Air 20:40–51

Comhair SA, Gaston BM, Ricci KS, Hammel J, Dweik RA, Teague WG, Meyers D, Ampleford EJ, Bleecker ER, Busse WW, Calhoun WJ, Castro M, Chung KF, Curran-Everett D, Israel E, Jarjour WN, Moore W, Peters SP, Wenzel S, Hazen SL, Erzurum SC (2011) Detrimental effects of environmental tobacco smoke in relation to asthma severity. PLoS One 6:e18574

Cooper PJ, Rodrigues LC, Cruz AA, Barreto ML (2009) Asthma in Latin America: a public heath challenge and research opportunity. Allergy 64:5–17

Cunningham J (2010) Socioeconomic status and self-reported asthma in Indigenous and non-Indigenous Australian adults aged 18–64 years: analysis of national survey data. Int J Equity Health 9:18

de Marco R, Poli A, Ferrari M (2002) Italian study on asthma in young adults. The impact of climate and traffic-related NO_2 on the prevalence of asthma and allergic rhinitis in Italy. Clin Exp Allergy 32:1405–1412

Dejsomritrutai W, Nana A, Chierakul N, Tscheikuna J, Sompradeekul S, Ruttanaumpawan P, Charoenratanakul S (2006) Prevalence of bronchial hyperresponsiveness and asthma in the adult population in Thailand. Chest 129:602–609

Dorner T, Lawrence K, Rieder A, Kunze M (2007) Epidemiology of allergies in Austria. Results of the first Austrian allergy report. Wien Med Wochenschr 157:235–242

Dottorini ML, Bruni B, Peccini F, Bottini P, Pini L, Donato F, Casucci G, Tantucci C (2007) Skin prick-test reactivity to aeroallergens and allergic symptoms in an urban population of central Italy: a longitudinal study. Clin Exp Allergy 37:188–196

Douwes J, Travier N, Huang K, Cheng S, McKenzie J, Le Gros G, von Mutius E, Pearce N (2007) Lifelong farm exposure may strongly reduce the risk of asthma in adults. Allergy 62(10):1158–1165

Eduard W, Douwes J, Omenaas E, Heederik D (2004) Do farming exposures cause or prevent asthma? Results from a study of adult Norwegian farmers. Thorax 59:381–386

Ellison-Loschmann L, King R, Pearce N (2004) Regional variations in asthma hospitalisations among Maori and non-Maori. N Z Med J 117:U745

El-Shazly AM, El-Beshbishi SN, Azab MS, El-Nahas HA, Soliman ME, Fouad MA, Mel-S M (2006) Present situation of house dust mites in Dakahlia Governorate, Egypt. J Egypt Soc Parasitol 36:113–126

Filipiak B, Heinrich J, Schfer T, Ring J, Wichmann HE (2001) Farming, rural lifestyle and atopy in adults from southern Germany–results from the MONICA/KORA study Augsburg. Clin Exp Allergy Filipiak 31:1829–1838

Franco JM, Gurgel R, Sole D, Lúcia França V, Brabin B (2009) Socio-environmental conditions and geographical variability of asthma prevalence in Northeast Brazil. Allergol Immunopathol (Madr) 37:116–121

Frazier JC, Loveland KM, Zimmerman HJ, Helgerson SD, Harwell TS (2012) Prevalence of asthma among adults in metropolitan versus nonmetropolitan areas in Montana, 2008. Prev Chronic Dis 9:E09

Fukutomi Y, Nakamura H, Kobayashi F, Taniguchi M, Konno S, Nishimura M, Kawagishi Y, Watanabe J, Komase Y, Akamatsu Y, Okada C, Tanimoto Y, Takahashi K, Kimura T, Eboshida A, Hirota R, Ikei J, Odajima H, Nakagawa T, Akasawa A, Akiyama K (2010) Nationwide cross-sectional population-based study on the prevalences of asthma and asthma symptoms among Japanese adults. Int Arch Allergy Immunol 53:280–287

Fullerton DG, Semple S, Kalambo F, Suseno A, Malamba R, Henderson G, Ayres JG, Gordon SB (2009) Biomass fuel use and indoor air pollution in homes in Malawi. Occup Environ Med 66:777–783

Gao F, Yang QJ, Zhang HG (2011) An epidemiological study of bronchial asthma in Qinghai Province. Zhonghua Jie He He Hu Xi Za Zhi 34(3):165–168

Gaur K, Gupta S, Rajpal AB, Singh A, Rohatgi JN (2006) Prevalence of bronchial asthma and allergic rhinitis among urban and rural adult population of Delhi Indian Asthma. Indian J Allergy Asthma Immunol 20:90–97

Gessert CE, Haller IV, Kane RL, Degenholtz H (2006) Rural-urban differences in medical care for nursing home residents with severe dementia at the end of life. J Am Geriatr Soc 54:1199–1205

Ghosh S, Pahwa P, Rennie D, McDuffie HH (2008) Opposing trends in the prevalence of health professional-diagnosed asthma by sex: a Canadian National Population Health Survey study. Can Respir J 15:146–152

Ghosh S, Punam P, Donna CR, Bonnie J (2009) Gender-related interactive effect of smoking and rural/urban living on asthma prevalence: a longitudinal Canadian NPHS study. J Asthma 46:988–994

Guangzhou Statistics Yearbook 2002–2006 (2007) Guangzhou Municipal Statistics Bureau

Guinea J, Teresa P, Luis A, Emilio B (2006) Outdoor environmental levels of Aspergillus spp. conidia over a wide geographical area. Med Mycol 44:349–356

Hales S, Lewis S, Slater T, Crane J, Pearce N (1998) Prevalence of adult asthma symptoms in relation to climate in New Zealand. Environ Health Perspect 106:607–610

Haverkos HW (2004) Viruses, chemicals and co-carcinogenesis. Oncogene 23:6492–6499

Heinrich J, Wichmann HE (2004) Traffic related pollutants in Europe and their effect on allergic disease. Curr Opin Allergy Clin Immunol 4:341–348

Hersoug L, Lise LH, Torben S, Flemming M, Allan L (2010) Indoor exposure to environmental cigarette smoke, but not other inhaled particulates associates with respiratory symptoms and diminished lung function in adults. Respirology 15:993–1000

Ho MG, Ma S, Chai W, Xia W, Yang G, Novotny TE (2010) Smoking among rural and urban young women in China. Tob Control 19:13–18

Ige OM, Arinola OG, Oluwole O, Falade AG, Falusi AG, Aderemi T, Huo D, Olopade OI, Olopade CO (2011) Atopy is associated with asthma in adults living in rural and urban southwestern Nigeria. J Asthma 48(9):894–900

Iversen L, Hannaford PC, Price DB, Godden DJ (2005) Is living in a rural area good for your respiratory health? Results from a cross-sectional study in Scotland. Chest 128:2059–2067

Jackson JE, Doescher MP, Hart LG (2007) A national study of lifetime asthma prevalence and trends in metro and non-metro counties, 2000–2003. University of Washington, WWAMI Rural Health Research Center

Jarvis DL, Leaderer BP, Chinn S, Burney PG (2005) Indoor nitrous acid and respiratory symptoms and lung function in adults. Thorax 60(6):474–479
Jiang R, Bell ML (2008) A comparison of particulate matter from biomass-burning rural and non-biomass burning urban households in Northeastern China. Environ Health Perspect 116:907–914
Joshi K, Rajesh K, Ajit A (2003) Morbidity profile and its relationship with disability and psychological distress among elderly people in Northern India. Int J Epidemiol 32:978–987
Kasprzyk I, Worek M (2006) Airborne fungal spores in urban and rural environments in Poland. Aerobiologia 22:169–176
Kilpeläinen M, Terho EO, Helenius H, Koskenvuo M (2001) Home dampness, current allergic diseases, and respiratory infections among young adults. Thorax 56:462–467
Krawczyk P, Chocholska S, Mackiewicz B, Trembas-Pietraś E, Wegrzyn-Szkutnik I, Milanowski J (2003) Differences in clinical test results of patients with bronchial asthma and living environment. Research in rural and urban areas in the eastern part of Poland. Ann Univ Mariae Curie Sklodowska Med 58:452–458
Kurt E, Metintas S, Basyigit I, Bulut I, Coskun E, Dabak S (2009) Prevalence and risk factors of allergies in Turkey (PARFAIT): results of a multicentre cross-sectional study in adults. Eur Respir J 33:724–733
Lâm HT, Rönmark E, Tu'ò'ng NV, Ekerljung L, Chúc NT, Lundbäck B (2011) Increase in asthma and a high prevalence of bronchitis: results from a population study among adults in urban and rural Vietnam. Respir Med 105:177–185
Lei YC, Chan CC, Wang PY, Lee CT, Cheng TJ (2004) Effects of Asian dust event particles on inflammation markers in peripheral blood and bronchoalveolar lavage in pulmonary hypertensive rats. Environ Res 95:71–76
Lewis S, Hales S, Slater T, Pearce N, Crane J, Beasley R (1997) Geographical variation in the prevalence of asthma symptoms in New Zealand. N Z Med J J110(1049):286–289
Linneberg A (2005) Hypothesis: urbanization and the allergy epidemic–a reverse case of immunotherapy? Allergy 60:538–539
Liu AH (2004) Something old, something new: indoor endotoxin, allergens and asthma. Paediatr Respir Rev 5 Suppl A:S65–71
Loureiro G, Rabaça MA, Blanco B, Andrade S, Chieira C, Pereira C (2005) Urban versus rural environment–any differences in aeroallergens sensitization in an allergic population of Cova da Beira, Portugal? Eur Ann Allergy Clin Immunol 37(5):187–193
Lourenço O, Fonseca AM, Taborda-Barata L (2009) Asthma is more frequently associated with non-allergic than allergic rhinitis in Portuguese patients. Rhinology 47:207–213
Lu N, Samuels ME, Kletke PR, Whitler ET (2010) Rural-urban differences in health insurance coverage and patterns among working-age adults in Kentucky. J Rural Health 26(2):129–138
Matson U (2005) Indoor and outdoor concentrations of ultrafine particles in some Scandinavian rural and urban areas. Sci Total Environ 343:169–176
Mestl HE, Aunan K, Seip HM, Wang SX, Zhao Y, Zhang D (2007a) Urban and rural exposure to indoor air pollution from domestic biomass and coal burning across China. Sci Tot Environ 377:12–26
Mestl HE, Aunan K, Seip HM (2007b) Health benefits from reducing indoor air pollution from household solid fuel use in China—three abatement scenarios. Environ Int 33:831–840
Metintas S, Kurt E (2010) Geo-climate effects on asthma and allergic diseases in adults in Turkey: results of PARFAIT study. Int J Environ Health Res 20:189–199
Michnar M, Trembas-Pietraś E, Milanowski J (2003) Incidence of allergic respiratory diseases in the Lublin region in correlation with the level of environmental pollution. Ann Univ Mariae Curie Sklodowska Med 58(1):481–487
Mishra V (2003) Effect of indoor air pollution from biomass combustion on prevalence of asthma in the elderly. Environ Health Perspect 111:71–78
Modig L, Järvholm B, Rönnmark E, Nyström L, Lundbäck B, Andersson C, Forsberg B (2006) Vehicle exhaust exposure in an incident case-control study of adult asthma. Eur Respir J 28(1):75–81
Morrison T, Callahan D, Moorman J, Bailey C (2009) A national survey of adult asthma prevalence by urban-rural residence U.S. 2005. J Asthma 46:751–758

Mugusi F, Edwards R, Hayes L, Unwin N, Mbanya JC, Whiting D, Sobngwi E, Rashid S (2004) Prevalence of wheeze and self-reported asthma and asthma care in an urban and rural area of Tanzania and Cameroon. Trop Doct 34:209–214

Musafiri S, van Meerbeeck J, Musango L, Brusselle G, Joos G, Seminega B (2011) Prevalence of atopy, asthma and COPD in an urban and a rural area of an African country. Respir Med 105:1596–1605

Nguyen T, Lurie M, Gomez M, Reddy A, Pandya K, Medvesky M (2010) The National Asthma Survey–New York State: association of the home environment with current asthma status. Public Health Rep 125:877–887

Nguyen K, Zahran H, Iqbal S, Peng J, Boulay E (2011) Factors associated with asthma control among adults in five New England states, 2006–2007. J Asthma 48:581–588

Nyan OA, Walraven GE, Banya WA, Milligan P, Van Der Sande M, Ceesay SM (2001) Atopy, intestinal helminth infection and total serum IgE in rural and urban adult Gambian communities. Clin Exp Allergy 31:1672–1678

Oliveira AC, Martins AN, Pires AF, Arruda MB, Tanuri A, Pereira HS, Brindeiro RM (2009) Enfuvirtide (T-20) resistance-related mutations in HIV type 1 subtypes B, C, and F isolates from Brazilian patients failing HAART. AIDS Res Hum Retroviruses 25:193–198

Persinger RL, Blay WM, Heintz NH, Hemenway DR, Janssen-Heininger YM (2001) Nitrogen dioxide induces death in lung epithelial cells in a density-dependent manner. Am J Respir Cell Mol Biol 24(5):583–590

Peterson JS (2012) Nitrous dioxide toxicity—medscape. http://emedicine.medscape.com/article/820431-overview. Accessed 7 Aug 2012

Polosa R, Russo C, Caponnetto P, Bertino G, Sarvà M, Antic T, Mancuso S, Al-Delaimy WK (2011) Greater severity of new onset asthma in allergic subjects who smoke: a 10-year longitudinal study. Respir Res 12:16

Qian Z, He Q, Kong L, Xu F, Wei F, Chapman RS, Chen W, Edwards RD, Bascom R (2007) Respiratory responses to diverse indoor combustion air pollution sources. Indoor Air 17:135–142

Raukas-Kivioja A, Raukas ES, Meren M, Loit HM, Rönmark E, Lundbäck B (2007) Allergic sensitization to common airborne allergens among adults in Estonia. Int Arch Allergy Immunol 142:247–254

Riva DR, Magalhães CB, Lopes AA, Lanças T, Mauad T, Malm O, Valença SS, Saldiva PH, Faffe DS, Zin WA (2011) Low dose of fine particulate matter (PM2.5) can induce acute oxidative stress, inflammation and pulmonary impairment in healthy mice. Inhal Toxicol 23:257–267

Romans S, Cohen M, Forte T (2011) Rates of depression and anxiety in urban and rural Canada. Soc Psychiatry Psychiatr Epidemiol 46(7):567–575

Roy SR, Schiltz AM, Marotta A, Shen Y, Liu AH (2003) Bacterial DNA in house and farm barn dust. J Allergy Clin Immunol 112(3):571–578

Roy SR, McGinty EE, Hayes SC, Zhang L (2010) Regional and racial disparities in asthma hospitalizations in Mississippi. J Allergy Clin Immunol 125(3):636–642

Rural Healthy People (2010) Healthy people 2010: a companion document for rural areas. http://www.studenthere.com/redirect.php? Accessed 25 June 2011

Russo MJ, McConnochie KM, McBride JT, Szilagyi PG, Brooks AM, Roghmann KJ (1999) Increase in admission threshold explains stable asthma hospitalization rates. Pediatrics 104:454–462

Sandstrom T, Helleday R, Bjermer L, Stjernberg N (1992) Effects of repeated exposure to 4 ppm nitrogen dioxide on bronchoalveolar lymphocyte subsets and macrophages in healthy men. Eur Respir J 5:1092–1096

Senthilselvan A, Lawson J, Rennie DC, Dosman JA (2003) Stabilization of an increasing trend in physician-diagnosed asthma prevalence in Saskatchewan, 1991 to 1998. Chest 124:438–448

Shrestha IL, Shrestha SL (2005) Indoor air pollution from biomass fuels and respiratory health of the exposed population in Nepalese households. Int J Occup Environ Health 11:150–160

Skorge TD, Eagan TM, Eide GE, Gulsvik A, Bakke PS (2005) Indoor exposures and respiratory symptoms in a Norwegian community sample. Thorax 60:937–942

Smith K, Warholak T, Armstrong E, Leib M, Rehfeld R, Malone D (2009) Evaluation of risk factors and health outcomes among persons with asthma. J Asthma 46:234–237
Solomon C, Christian DL, Chen LL, Welch BS, Kleinman MT, Dunham E, Erle DJ, Balmes JR (2000) Effect of serial-day exposure to nitrogen dioxide on airway and blood leukocytes and lymphocyte subsets. Eur Respir J 15:922–928
Spengler JD, Ferris BG, Dockery DW, Speizer FE (1979) Sulfur dioxide and nitrogen dioxide levels inside and outside homes and the implications on health effects research. Environ Sci Technol 13:1276–1280
Taksey J, Craig TJ (2001) Allergy test results of a rural and small-city population compared with those of an urban population. J Am Osteopath Assoc 101:S4–S7
Trupin L, Balmes JR, Chen H, Eisner MD, Hammond SK, Katz PP, Lurmann F, Quinlan PJ, Thorne PS, Yelin EH, Blanc PD (2010) An integrated model of environmental factors in adult asthma lung function and disease severity: a cross-sectional study. Environ Health 9:24
United States Environmental Protection Agency (USEPA) (1993) Fact sheet: respiratory health effects of passive smoking. http://www.epa.gov/smokefree/pubs/etsfs.html. Accessed 22 June 2011
Valet RS, Perry TT, Hartert TV (2009) Rural health disparities in asthma care and outcomes. J Allergy Clin Immunol 123(6):1220–1225
Vander Weg MW, Cunningham CL, Howren MB, Cai X (2011) Tobacco use and exposure in rural areas: findings from the behavioral risk factor surveillance system. Addict Behav 36:231–236
Venners SA, Wang B, Ni J, Jin Y, Yang J, Fang Z, Xu X (2001) Indoor air pollution and respiratory health in urban and rural China. Int J Occup Environ Health 7:173–181
Verlato G, Calabrese R, De Marco R (2002) Correlation between asthma and climate in the European Community Respiratory Health Survey. Arch Environ Health 57:48–52
Viinanen A, Munhbayarlah S, Zevgee T, Narantsetseg L, Naidansuren T, Koskenvuo M, Helenius H, Terho EO (2005) Prevalence of asthma, allergic rhinoconjunctivitis and allergic sensitization in Mongolia. Allergy 60:1370–1377
Viinanen A, Munhbayarlah S, Zevgee T, Narantsetseg L, Naidansuren T, Koskenvuo M, Helenius H, Terho EO (2007) The protective effect of rural living against atopy in Mongolia. Allergy 62:272–280
von Mutius E, Vercelli D (2010) Farm living: effects on childhood asthma and allergy. Nat Rev Immunol 10:861–868
von Mutius E, Braun-Fahrländer C, Schierl R, Riedler J, Ehlermann S, Maisch S, Waser M, Nowak D (2000) Exposure to endotoxin or other bacterial components might protect against the development of atopy. Clin Exp Allergy 30:1230–1234
Walraven GE, Nyan OA, Van Der Sande MA, Banya WA, Ceesay SM, Milligan PJ, McAdam KP (2001) Asthma, smoking and chronic cough in rural and urban adult communities in The Gambia. Clin Exp Allergy 31:1679–1685
Withy K, Davis J (2008) Followup after an emergency department visit for asthma: urban/rural patterns. Ethn Dis 18:S2–S247
Woods RK, Burton DL, Wharton C, McKenzie GH, Walters EH, Comino EJ, Abramson MJ (2000) Asthma is more prevalent in rural New South Wales than metropolitan Victoria, Australia. Respirology 5:257–263
Xiao L, Yang Y, Li Q, Wang CX, Yang GH (2010) Population-based survey of secondhand smoke exposure in China. Biomed Environ Sci 23:430–436
Yemaneberhan H, Bekele Z, Venn A, Lewis S, Parry E, Britton J (1997) Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. Lancet 350:85–90
Yu J, Huang HJ, Jin F, Xu J (2011a) The role of airborne microbes in school and its impact on asthma, allergy and respiratory symptoms among school children. Rev Med Microbiol 22:84–89
Yu J, Noor HI, Xu J, Zaleha MI (2011b) Do indoor environments influence on asthma and asthma-related symptoms among adults in homes? A review of the literature. J Formos Med Assoc 110:555–563
Zhang LX, Enarson DA, He GX, Li B, Chan-Yeung M (2002) Occupational and environmental risk factors for respiratory symptoms in rural Beijing, China. Eur Respir J 20:1525–1531

Springer
http://www.springer.com/978-1-4614-6897-4

Reviews of Environmental Contamination and Toxicology
Volume 226
Whitacre, D.M. (Ed.)
2013, XI, 128 p. With online files/update., Hardcover
ISBN: 978-1-4614-6897-4