ERJ Express. Published on September 9, 2009 as doi: 10.1183/09031936.00027509

TITLE:

National income, self-reported wheezing and asthma diagnosis from the World Health Survey

AUTHORS:

Grace Sembajwe, Sc.D.[1, 2, 3]

Manuel Cifuentes, M.D., Sc.D.[1]

SangWoo Tak, Sc.D. [1]

David Kriebel, Sc.D.[1]

Rebecca Gore, Ph.D.[1]

Laura Punnett, Sc.D.[1]

Corresponding author:

Grace Sembajwe, Research Fellow, Department of Society, Human Development and Health, Harvard School of Public Health, Boston, MA 02115 USA USA, Telephone: 617-582-8365; Fax: 617-632-4858; E-mail: grace_sembajwe@dfci.harvard.edu

[1] Department of Work Environment, University of Massachusetts Lowell, Lowell MA 01854 USA

[2] Department of Society, Human Development and Health, Harvard School of Public Health, Boston, MA 02115 USA

[3] Center for Community-Based Research, Dana-Farber Cancer Institute, Boston, MA 02115 USA

Running head:

National income, respiratory symptoms in WHS

Funding:

This study was supported by WHO Agreement # GL GLO PHE 231 XD.04.Z.999.00 and Contract # 200-2005-M-11506 from the National Institute for Occupational Safety and Health.

Word Count: 197 (Abstract), 3520 (Main body of the manuscript

ABSTRACT

Question: The objectives of this study were to quantify and describe the variations in respiratory symptoms and diagnosis prevalence across world regions and by national income.

Methods: In 2002 and 2003, WHO implemented the World Health Survey (WHS), which used a standardized survey instrument to compile comprehensive baseline information on health and healthcare expenditure. We analyzed the WHS data to assess the global patterns of self-reported wheeze and doctor-diagnosed asthma, two commonly-reported measures of respiratory health.

Findings: There were 308,218 participants with complete records, from 64 countries. The weighted mean age of the survey population was 43 years. Global prevalence of current wheezing symptoms ranged from 2.4% in Vietnam to 24% in Brazil; the prevalence of diagnosed asthma ranged from 1.8% in Vietnam to 32.8% in Australia. Overall, the prevalence of symptoms and diagnosis showed a U-shaped pattern with the largest prevalence in low and high income countries and smallest prevalence found consistently in middle income countries.

Interpretation: These WHS analyses have provided global prevalence estimates of wheeze and doctor-diagnosed asthma using data that were gathered simultaneously and consistently across six continents. These findings support continued global respiratory illness surveillance for disease prevention, health policy and management.

Key words: Current wheezing symptoms, diagnosed asthma, per capita gross national income in purchasing power parity (GNI PPP), prevalence, urban/rural, income inequality (Gini), World Health Survey (WHS)

INTRODUCTION

Over the past several decades, worldwide increases in the prevalence of asthma have been reported in surveillance and epidemiological studies [1, 2]. Asthma is characterized by variable airflow limitation or airway hyperresponsiveness to various environmental stimuli [3-5]. Wheezing is the most common symptom associated with asthma, although wheezing, coughing, chest tightness, and shortness of breath are all symptoms often used to define asthma [6-11].

The Global Initiative for Asthma (GINA) reports adult asthma prevalence ranging from 5-18% with increases in associated morbidity and decreasing associated mortality in industrialized countries [1, 12, 13]. GINA was established in 1989 by the United States (US) National Heart, Lung, and Blood Institutes (NHLBI), National Institutes of Health (NIH), and the World Health Organization (WHO), to raise awareness among health professionals, governments, and the general public, about the dangers and increasing prevalence of asthma [13-16]. In 2003 and 2004, GINA published reports on the global burden of asthma, based on literature reviews primarily from peer-reviewed publications based on the International Study of Asthma and Allergies in Childhood (ISAAC) and European Community Respiratory Health Survey (ECRHS). GINA continues to update the reports as new information becomes available [13, 17].

In 2002 and 2003, WHO implemented the World Health Survey (WHS), which used a standardized survey instrument to compile comprehensive baseline information on a wide range of measures of health (including asthma) and healthcare expenditure. The broader aims of WHS were to develop low-cost, valid, reliable and comparable cross-national information and an evidence base for surveillance and policy adjustment [18]. All 192 WHO member states were invited to participate in this effort and just over one-third participated.

While WHS collected data from adults of 18 years and older, across six continents, ECRHS gathers information from Europe and Australia, and ISAAC is restricted to children under 15 years of age.

In the research described here, WHS data were utilized to assess the global patterns of respiratory disease. The objectives of this study were to quantify the prevalence of respiratory symptoms and diagnosis worldwide using data collected with identical survey questions and systematic population survey methods; and to describe the variations in respiratory symptom and diagnosis prevalence across world regions and by national income.

MATERIALS AND METHODS

Study subjects and data collection methods

WHS was administered in 70 countries, of which 68 responded to respiratory symptom questions and 64 reported on asthma diagnosis. Each country's national health ministry was responsible for the survey program. The countries that chose to participate in the survey, their economic standing (income status), sample size, and type of survey used (short or full) can be located on the WHO website for the WHS [18]. The full questionnaire included questions on several factors associated with living conditions in most economically developing nations (such as mud housing) and collected information on social habits in countries where such surveillance systems do not exist (such as smoking prevalence). The short version omitted several of these questions and was administered to mostly higher income countries. WHO provided each country with the relevant training to carry out the survey and conduct data analyses [18].

The WHS had a menu of choices and modules for the various survey components. The modules measured aspects of health in multiple domains; risk factors (e.g. tobacco, alcohol,

pollution); responsiveness of health systems and whether health systems met expectations; coverage, access and utilization of key health services (e.g. immunization, treatment of childhood illness, STD and HIV/AIDS); and health care expenditures. Each country chose which combination of modules to use.

A number of pre-tested survey administration tools were available and each country could choose the method that it judged most practical and cost-effective. The choices were the following: household face-to-face survey; computer-assisted telephone interview (CATI) survey, which were conducted using computerized systems when there was good telephone network coverage; and computer-assisted personal interview (CAPI) survey using a portable personal computer to replace paper-and-pen methods of data collection.

The eligible population for WHS consisted of adults of 18 years and older. The sample from each country was stratified by gender, age, and type of residence (rural/urban). Individuals were sampled from these strata and each respondent was given a separate sampling probability value (or weight). Only one person from a randomly selected household was interviewed for the individual questionnaire and was ultimately included in these analyses.

National income

Countries were grouped by their per capita gross national income in purchasing power parity (GNI PPP) [18, 19] that was taken from the World Bank's data and statistics tables available online [19, 20]. Countries were classified into tertiles based on GNI PPP: per capita income of US$3,000 or less (low income); between US$3,000 and US$8,000 (middle income); and more than US$8,000 (high income). All analyses were conducted on ungrouped countries as well as with the tertiles.

Sampling weights

WHS employed a probability sampling design. This meant that every individual in the sampling frame (18 years and over) had a known and non-zero chance of being selected into the survey sample. Some countries used a single-stage random sample strategy, however, most sites carried out multi-stage cluster sampling methods and probability weights were used for each stage. In either case, the WHS sampling frame aimed to cover 100% of the eligible population in the surveyed country. Therefore, the weighted estimates are corrected for the individual probabilities of being surveyed. Further details about the WHO sampling guidelines are available from WHO [18].

For a multi-stage cluster sample, the total probability of being sampled was calculated by multiplying all the probabilities within a sample stage. The inverse of this total probability was the probabilistic individual weight for a specific person within the country. A total weight was calculated for each country by adding all the individual weights and comparing the sum with the country population; for countries that used a single-stage random sample or when the sum of all the weights did not add up to the adult country population (of 18 years and older), a correction factor was used. Therefore, the weighted data represented pooled data corrected by the individual probability of being surveyed (based on age, gender, and urban/rural location) and country population.

Gender and Age

Gender was recorded as female or male on the basis of the interviewer's observation. The WHS questionnaire had two questions for age. The primary question for age was a continuous

variable. In cases where respondents declined to answer the question, interviewers were advised to estimate their age in categories. For the purpose of these analyses, the age ranges were re-grouped into three categories: 18 to 29 years old (reference group), 30 to 49 years old, and 50 years old or over. A subgroup analysis was conducted in 18 to 44 year-olds, to compare with analyses of the entire WHS population, since respiratory symptoms (for chronic obstructive pulmonary disease, for example) are far more common at older ages.

Smoking

The short version of the questionnaire omitted the questions relating to tobacco smoking. The question on the long version was, 'Do you currently smoke any tobacco products such as cigarettes, cigars or pipes?' with the following response choices: Daily; Yes, but not daily; and No, not at all. A respondent was considered a current smoker if he/she answered positively (Daily or Yes but not daily)."

Urban/Rural

The household survey for WHS included information on setting with the following categories used for classification: 1) Urban; 2) Peri-urban/Semi-urban; 3) Rural; and 4) Other. These along with external databases describing population distributions [21] for countries that had missing values in WHS (Australia, Nepal, Norway, Netherlands, and Slovenia) were used to distinguish urban and rural areas during analyses. Countries that had 50% or higher rural households were classified as mostly rural; those with lower than 50% rural were classified as mostly urban.

Income Inequality

An external database was used to import information on country level income inequality (Gini coefficient) to merge with the WHS data. [21] The Gini coefficient is a measure of household income inequality within a country [21, 22]. Gini values for the Comoros were not available and analyses were conducted by placing the country as a high inequality, then low inequality, then by leaving the country out entirely, to note any differences in disease prevalence for the categories. No difference was evident, so Gini for Comoros was left as missing. Countries with 45 or greater for a Gini coefficient were considered to have high income inequality, countries below 45 were considered to have low income inequality.

Further summaries for the country classifications are available in the appendix.

Respiratory outcomes

Five questions on respiratory symptom and diagnosis were used to describe current wheezing symptoms and diagnosed asthma.

Current wheezing symptoms were indicated if there was a positive response to any of the symptom questions: "During the last 12 months, have you experienced any of the following: (1) Attacks of wheezing or whistling breathing?" (Yes/No) or (2) Attacks of wheezing that came on after you stopped exercising or some other physical activity?" (Yes/No). These questions differ slightly from those used in ECHRS ("Have you had wheezing or whistling in your chest at any time in the last 12 months?") [11, 23] and ISAAC ("Have you had wheezing or whistling in the chest in the past 12 months?" and "How many attacks of wheezing have you had in the past 12 months?") [24-26].

Diagnosed asthma was indicated if there was a positive response to any of the diagnosis questions: (1) "Have you ever been diagnosed with asthma (an allergic respiratory disease)?" (Yes/No/Don't Know); (2) "Have you ever been treated for it?" (Yes/No/Don't Know); (3) "Have you been taking any medications or other treatment for it during the last 2 weeks?" (Yes/No/Don't Know). Responses of "Don't Know" were coded as "No" for the respiratory outcomes. These questions differ slightly from those used in ECHRS ("Have you ever had asthma?" and "Was this confirmed by a doctor?") [11, 23] and ISAAC (no direct questions on asthma diagnosis in the core questionnaire) [24-26].

Data analysis

The authors received the final country datasets from WHO in August of 2005. All analyses were conducted using SAS statistical software (SAS Institute, Inc. Cary, NC) [27, 28]. SAS survey procedures (proc surveyfreq and surveymeans) were used to account for sampling weights and the complex sampling design effect. Further details of the data analysis methods are explained elsewhere [29, 30]. Proc glimmix was used to obtain weighted multilevel prevalence ratios as a measure of risk in these cross-sectional data.

Except for a few nonparametric analyses (to obtain Spearman's rank correlation coefficients), all analyses used the individual weights described above and accounted for the complex sampling design effect. Results were stratified by gender, smoking status (where available), and national income.

Missing data

Respondents who did not provide data on respiratory outcomes were excluded from the analyses. Current wheezing symptoms were not asked in Hungary and Nepal, and diagnosed asthma was not obtained from Guatemala, Ethiopia, Nepal, Hungary, Israel, or Mexico. Consequently, these countries do not appear in any tables or figures for those outcomes.

Miscoded responses or out-of-range codes were changed to missing and excluded from the analysis. The question on tobacco smoking was not included in the short questionnaire, so the following countries were missing from the analyses with smoking: Austria, Australia, Belgium, Denmark, Finland, France, Germany, Great Britain, Greece, Ireland, Israel, Italy, Luxembourg, Netherlands, Norway, and Portugal.

The study materials and methods were approved by the institutional review board at the University of Massachusetts in Lowell.

RESULTS

The total sample in the WHS was 308,218 (Table 1). The weighted mean age of the survey population was 43 years. Finland had the highest weighted mean age overall (53 years) and Slovakia had the lowest at 34 years. Among the portion of respondents that answered the tobacco use questions, current smokers were less frequent than nonsmokers. Rural households accounted for 70% overall and there were slightly more countries with high income inequality (55%). The middle GNI PPP category accounted for 44% of the global study population, while 35% were in the low income group and 21% in the high income countries.

Respiratory outcomes and population characteristics

Current wheezing symptoms were more prevalent than diagnosed asthma (Table 1). Smokers and those over the age of 50 years showed the highest prevalence of both categories of asthma. Men more frequently reported current wheezing symptoms than women. Overall prevalence patterns of current wheezing symptoms and diagnosed asthma showed some expected patterns: an increase with age and more common in smokers than non-smokers.

Respiratory outcomes among countries

There was a ten-fold variation in current wheezing symptom prevalence across countries (from Vietnam at 2.4% to Brazil at 24.3%). With a few exceptions, most of the countries geographically in the global north had a higher prevalence of current wheezing symptoms than most of the countries in the global south (Figure 1).

Diagnosed asthma showed a narrower range in prevalence across countries; a majority of estimates fell within a four-fold range of prevalence, with Vietnam the lowest at 1.8% and Australia the highest at 32.8% (Figure 2).

Respiratory outcomes and national income

Regression analyses that included national income without grouping the countries into tertiles, showed almost no association with respiratory symptoms or diagnosis (adjusted PR=1.00001, 95% CI = 1.00001, 1.00002 for wheezing symptoms and PR=1.00003, 95% CI=1.00002, 1.00003). However, for countries grouped by national income, the high national income group had the highest overall weighted prevalence for all respiratory outcomes, with

current wheezing symptoms at 11.7% (Figure 1) and diagnosed asthma at 9.3% (Figure 2). Prevalence were lowest in the middle national income group, with current wheezing symptoms at 6.7% and diagnosed asthma at 4.5%. Nevertheless, the middle income countries had the largest inter-country range in prevalence of current wheezing symptoms (from China at 3.3% to Brazil at 24.3%). For diagnosed asthma, the widest range in prevalence was found in the high national income group (from Russia at 4.2% to Australia at 32.8%). Overall, the prevalence of current wheezing symptoms and diagnosed asthma showed a U-shaped pattern with higher prevalence of respiratory outcome reporting in low income countries and in high income countries. Exceptions to this pattern were found for mostly urban regions and low Gini countries, where the pattern showed a peak in current wheezing symptoms for middle income countries and an increasing upward trend in diagnosed asthma prevalence (moving from low income to high income countries) for urban regions only. This U-shaped prevalence pattern remained in individual categories of smoking and gender, as well as in mostly rural regions and among high Gini countries, even after adjusting for age (Table 2). The U-shaped pattern remained even in subgroup analyses of 18 to 44 year-olds.

It should also be noted that the highest prevalence of current wheezing symptoms was found in low income countries with high income inequality (Table 2).

The country-level correlation between diagnosed asthma and current wheezing symptoms was lowest in the middle national income group (Spearman's correlation coefficient, $r = 0.37$, $p<0.0001$) and somewhat higher in both the low national income group ($r = 0.46$, $p<0.0001$) and the high national income group of countries ($r = 0.45$, $p<0.0001$).

DISCUSSION

Among the 68 countries with responses to wheezing symptoms and 64 countries surveying diagnosed asthma outcomes in the World Health Survey, the prevalence varied greatly, ranging from 2.4% to 24.3% for current wheezing symptoms and 1.8%-32.8% for diagnosed asthma. In general, highly industrialized (higher income) countries, such as Australia and countries in Western Europe had the higher prevalence of current wheezing symptoms and diagnosed asthma, while lower prevalence was found in middle income countries, particularly in eastern and central Europe. Brazil, as a middle income country, was notable for its very high prevalence of both diagnosed asthma and current wheezing symptoms. Although Brazil was in the middle income countries, it had a high Gini coefficient [21] and thus high within country income inequality and also had almost 85% (appendix) of the survey population responding from urban households (high urbanization) indicating that both the income inequality and high urbanization might be factors in the high prevalence of respiratory disease reporting from Brazil [15].

At the community or national level, respiratory disease/asthma reporting could greatly affect the estimated prevalence, especially if mortality rates from these conditions are high. In most of the countries identified in the middle national income group, GINA reports have identified very high mortality rates due to asthma relative to the low prevalence reported for this group [13, 16, 17]. But, even with low country reporting rates, other influential factors may be at play, such as environmental (urban air) pollution, which has been identified as a risk factor for respiratory illness in both children [31-34] and adults [17, 35]; access to healthcare and disease information (which allow for disease identification, treatment, and management) [17, 36-38]; and the highly contested *hygiene hypothesis* [39-44], which postulates that a lack of exposure to

dirt in childhood may increase an individual's susceptibly to respiratory illnesses, asthma in particular, and may explain the high asthma prevalence observed for the high income countries [1, 2, 13, 17, 34, 40], although high urbanization is more likely to be the driving factor. Among low income countries, the influencing factors may be exacerbated by poorer access to healthcare.

The middle national income group was also distinguished by a high within-group range in prevalence of current wheezing symptoms, while for diagnosed asthma, the within group range was highest among the high national income group. This difference in within group range between diagnosed asthma and current wheezing symptoms may reflect the variation in reporting, as well as the disparity in access to health care and disease information between countries, particularly within the national income groups. For affirmative responses to diagnosed asthma, the participant had to have seen a physician and/or been taking asthma medications. Therefore, one would expect, as seen here, that asthma diagnosis questions would be more sensitive to country level of development (and hence access to medical care) than the current wheezing symptoms questions.

One might also expect that the correlation between current wheezing symptoms and asthma diagnosis would vary by socioeconomic and cultural differences, for which national income may be a partial proxy. Country-level features such as access to healthcare, health literacy, willingness to report symptoms, and cultural differences in how breathing problems are labeled and understood could all affect the ratio of current symptoms to diagnosis of asthma. Consistent with this idea, the country-level correlation between diagnosed asthma and current wheezing symptoms was lowest in the middle national income group (Spearman's correlation coefficient, $r = 0.37$, $p<0.0001$) and somewhat higher in both the low national income group ($r = 0.46$, $p<0.0001$) and the high national income group of countries ($r = 0.45$, $p<0.0001$).

The U-shape for the pattern of symptom prevalence across tertiles of GNI PPP seems counter to hypotheses that relate increases in respiratory symptom prevalence to increased industrialization (and thus, increased national income) [45-49]. However, country level factors other than national level income, such as pollution levels (as in urban settings), may be far more influential in the association with respiratory symptom prevalence [13, 15]. Clearly, the prevalence of both symptoms and diagnosis was quite high across urban regions regardless of national income. It is likely that this U-shape pattern represented a net effect of several different factors – some contributing to higher risk in low income countries (occupational hazards, pollution, poor access to healthcare) and others tending to increase asthma risk and reporting in high income countries (greater awareness of asthma, pollution). Factors like these may "balance out" in such a way that the middle income countries have the lowest risks.

A further challenge in data collection is that even in clinical settings, asthma is not very well-defined [9, 13-16]. Physician diagnosis varies greatly by country and many asthmatics are not diagnosed [13-16, 24]. These complexities in defining asthma also lead to difficulties in linking factors that may be associated with asthma etiology or exacerbation [1, 13-17]. Nevertheless, most surveys have found questions on wheezing to be a reliable indicator for asthma [9, 11, 13-17, 23, 24, 50, 51].

With these data, our analyses of WHS presents an effort to present information beyond that collected in other large respiratory disease studies, such as ECRHS and ISAAC.

Conclusions

These WHS analyses have provided global estimates of wheezing and doctor-diagnosed asthma prevalence using data that were gathered concurrently, in a consistent and reliable

fashion, across a wide sample of the world's nations. The patterns in these results suggest different causes for self-reported wheezing and asthma diagnoses in different socioeconomic contexts; there is a clear U-shaped pattern of disease prevalence across strata of national income. These analyses of validated questions in WHS identify relationships between country characteristics and respiratory disease prevalence that are consistent with global trends in socio-epidemiological approaches to structural determinants of health [13-17, 30].

Our analyses additionally strengthen the body of evidence supporting the use of questionnaires for studying respiratory symptoms. We encourage simpler, standardized sampling strategies to facilitate ongoing data collection in more countries worldwide. We further believe that these types of studies will be valuable in global respiratory illness surveillance for disease prevention, health policy and management.

CONTRIBUTORS

All authors contributed to editing of the manuscript. G Sembajwe conducted the analyses and developed the first draft of the report and worked with M Cifuentes and SW Tak on data management strategies and choice of analytical methods; R Gore offered statistical advice; D Kriebel advised on epidemiologic constructs along with L Punnett who defined the project goals and guided the overall analysis as the principal investigator on the contract with the World Health Organization.

ACKNOWLEDGEMENTS

Special thanks to Dr Annette Pruess-Ustun and the World Health Organization, Geneva, Switzerland, for access to the WHS database and for funding the primary analyses through WHO

Agreement # GL GLO PHE 231 XD.04.Z.999.00. Secondary analyses were supported by Contract # 200-2005-M-11506 from the National Institute for Occupational Safety and Health, Washington, DC., USA. The contents of this report are solely the responsibility of the authors and do not necessarily represent the official views of WHO or NIOSH. Additional thanks to Dr. Margaret Quinn and Dr. Anne Stoddard for their comments on this manuscript.

CONFLICT OF INTEREST

None of the authors have an affiliation with an organization that, to their knowledge, has a direct interest, particularly a financial interest, in the subject matter or materials described.

LITERATURE CITED

1. Bousquet J, Clark TJH, Hurd S, Khaltaev N, Lenfant C, O'Byrne P, Sheffer A. GINA guidelines on asthma and beyond. *Allergy* 2007: 62: 102-112.
2. Farrar JR. The global burden of asthma and current approaches to its management. Business Briefings: European Pharmacotherapy. Touch Briefings, Munich, Germany, 2005; pp. 1-6.
3. Eisen EA, Wegman DH, Kriebel D. Application of peak expiratory flow in epidemiologic studies of occupation. *Occup Med* 1993: 8(2): 265-277.
4. Kriebel D, Sama SR, Cocanour B. Reversible pulmonary responses to formaldehyde. A study of clinical anatomy students. *Am Rev Respir Dis* 1993: 148(6 Pt 1): 1509-1515.
5. Milton D K, Wypij D, Kriebel D, Walters M D, Hammond S K, Evans J S. Endotoxin exposure-response in a fiberglass manufacturing facility. *Am J Ind Med* 1996: 29(1): 3-13.
6. American Thoracic Society. Guidelines for the evaluation of impairment/disability in patients with asthma. *Am Rev Respir Dis* 1993: 147: 1056-1061.
7. Bernstein IL, Bernstein DI, Chan-Yeung M, Malo JL. Definition and classification of asthma. *In:* Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, eds. Asthma in the workplace. Marcel Dekker., New York, NY, 1999; pp. 1-3.
8. Driscoll T, Steenland K, D Imel Nelson, Leigh J. Occupational airborne particulates: assessing the environmental burden of disease at national and local levels. Geneva; 2004.
9. National Heart Lung and Blood Institute. Global Initiative for Asthma. National Institutes of Health pub no 95-3659.; 1995.
10. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. *Am Rev Respir Dis* 1987: 136: 225-244.

11. European Community Respiratory Health Survey (ECHRS). Main questionnaire. Department of Public Health Medicine UMDS St Thomas Campus., London, UK, 1993.
12. Abramson MJ, Bailey MJ, Couper FJ, Driver JS, Drummer OH, Forbes AB, McNeil JJ, E Haydn Walters, Victorian Asthma Mortality Study Group. Are asthma medications and management related to deaths from asthma? *Am J Respir Crit Care Med* 2001: 163(1): 12-18.
13. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee Report. *Allergy* 2004: 59(5): 469–478.
14. Britto MC, Freire EF, Bezerra PG, Brito Rde C, Rego Jda C. Low income as a protective factor against asthma in children and adolescents treated via the Brazilian Unified Health System.[Article in English, Portuguese]. *J Bras Pneumol* 2008: 34(5): 251-255.
15. Cooper PJ, Rodrigues LC, Cruz AA, Barreto ML. Asthma in Latin America: a public heath challenge and research opportunity. . *Allergy* 2009: 64(1): 5-17. Epub 2008 Nov 2028.
16. Kramer MS, Matush L, Bogdanovich N, Dahhou M, Platt RW, Mazer B. The low prevalence of allergic disease in Eastern Europe: are risk factors consistent with the hygiene hypothesis? *Clin Exp Allergy* 2009 39(5): 708-716.
17. Global Initiative for Asthma. Global strategy for asthma management and prevention: www.ginasthma.org., Hamilton, Ontario, 2006. Accessed: February 21, 2009.
18. World Health Organization. World Health Survey 2002. WHO Multi-country Survey Study on Health and Responsiveness 2000-2001. Accessed: August 25, 2009.
19. Population Reference Bureau. DataFinder Sources: http://www.prb.org/Content/NavigationMenu/PRB/DataFinder/DataFinder_Sources/DataSources.htm. Accessed: August 25, 2009.

20. Encylopaedia Tiscali. Encyclopaedia Search: http://www.tiscali.co.uk/reference/encyclopaedia/hutchinson/. Accessed: August 25, 2009.
21. Central Intelligence Agency. The World Factbook: https://www.cia.gov/library/publications/the-world-factbook/fields/2172.html. Accessed: August 25, 2009.
22. The World Bank. Quick reference tables: www.worldbank.org/data/quickreference/quickref.html. Accessed August 25, 2009.
23. European Community Respiratory Health Survey (ECHRS). Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1996: 9: 687–695.
24. Asher I. The International Study of Asthma and Allergies in Childhood (ISAAC). *N Z Med J* 2008 121(1279): 117-118.
25. International Study Asthma Allergy Childhood (ISAAC) Steer Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998: 351(9111): 1225–1232.
26. ISAAC Steering Committee. International Study of Asthma and Allergies in Childhood Manual. . Auckland, New Zealand/Münster, Germany: ISAAC, 1993.
27. SAS Institute Inc. SAS Language Reference, Version 8. SAS Institute, Inc, Cary, NC, 2001.
28. SAS Institute Inc. The Glimmix Procedure, Nov. 2005. SAS Language Reference, Version 9.1.3. SAS Institute, Inc, Cary, NC, 2005.
29. Sembajwe G. Common Variable Bias in Occupational Epidemiology [Doctoral Dissertation]. Lowell: University of Massachusetts Lowell; 2007.

30. Cifuentes M, Sembajwe G, Tak S, Gore R, Kriebel D, Punnett L. The association of major depressive episodes with income inequality and the human development index. *Soc Sci Med* 2008: 67(4): 529-539.
31. Beasley R, Keil U, Von Mutius E, Pearce N. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC *Lancet* 1998: 351 (9111): 1225-1232.
32. Gold DR, Wright R. Population disparities in asthma. *Annu Rev Public Health* 2005: 26: 89–113.
33. Weiland S, Husing A, Strachan D, Rzehak P, Pearce N, ISAAC Phase One Study Group. Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. *Occup Environ Med* 2004: 61(7): 609-615.
34. Nickmilder M, Carbonnelle S, Bernard A. House cleaning with chlorine bleach and the risks of allergic and respiratory diseases in children. *Pediatr Allergy Immunol* 2007: 18(1): 27-35.
35. Montnemery P, Bengtsson P, Elliot A, Lindholm LH, Nyberg P, Lofdahl CG. Prevalence of obstructive lung diseases and respiratory symptoms in relation to living environment and socio-economic group. *Respir Med* 2001: 95(9): 744-752.
36. American Thoracic Society. What constitutes an adverse health effect of air pollution? Official statement of the American Thoracic Society. *Am J Respir Crit Care Med* 2000: 161(2 Pt 1): 665-673.
37. Gauderman WJ, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, McConnell R, Kuenzli N, Lurmann F, Rappaport E, Margolis H, Bates D, Peters J. The effect of air pollution on lung development from 10 to 18 years of age. *N Engl J Med* 2004: 351(11): 1057-1067.

38. Gauderman WJ, Vora H, McConnell R, Berhane K, Gilliland F, Thomas D, Lurmann F, Avol E, Kunzli N, Jerrett M, Peters J. Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study. *Lancet* 2007: 369(9561): 571-577.
39. Erb K, Holloway J, Sobeck A, Moll H, Le Gros G. Infection of mice with Mycobacterium bovis-Bacillus Calmette-Guérin (BCG) suppresses allergen-induced airway eosinophilia. *J Exp Med* 1998 187(4): 561-569.
40. Goldberg S, Israeli E, Schwartz S, Shochat T, Izbicki G, Toker-Maimon O, Klement E, Picard E. Asthma prevalence, family size and birth order. *Chest* 2007: Apr 5. Online.
41. Hertzen LC. The hygiene hypothesis in the development of atopy and asthma--still a matter of controversy? *QJM* 1998 91(11): 767-771.
42. Douwes J, Pearce N. Commentary: The end of the hygiene hypothesis? *Int J Epidemiol* 2008: 37(3): 570-572. Epub 2008 May 2002.
43. Weiss ST. Eat dirt--the hygiene hypothesis and allergic diseases. *N Engl J Med* 2002: 347(12): 930-931.
44. Weiss ST. Asthma in early life: is the hygiene hypothesis correct?[Article in English, Portuguese]. *J Pediatr (Rio J)* 2008 84(6): 475-476.
45. Ebtekar M. Air pollution induced asthma and alterations in cytokine patterns. *Iran J Allergy Asthma Immunol* 2006: 5(2). 47-56.
46. Heinrich J, Wichmann HE. Traffic related pollutants in Europe and their effect on allergic disease. *Curr Opin Allergy Clin Immunol* 2004: 4(5): 341-348.
47. Ramos RG, Talbott EO, Youk A, Karol MH. Community urbanization and hospitalization of adults for asthma. *J Environ Health* 2006: 68(8): 26-32, 44.

48. Von Hertzen L, Haahtela T. Disconnection of man and the soil: reason for the asthma and atopy epidemic? *J Allergy Clin Immunol* 2006: 117(2): 334-344.
49. Von Hertzen LC, Haahtela T. Asthma and atopy - the price of affluence? *Allergy* 2004: 59(2): 121-123.
50. Ferris BG. Epidemiology Standardization Project (American Thoracic Society). *Am Rev Respir Dis* 1978: 118(6 Pt 2): 1-120.
51. Meyer JD, Holt DL, Chen Y, Cherry NM, McDonald JL. SWORD '99: surveillance of work-related and occupational respiratory disease in the UK. *Occup Med (Lond)* 2001: 51(3): 204-208.

TABLE 1: Characteristics of the WHS population and distribution of asthma

	All	
	n	%
Gender:		
Female	157,152	**52.2**
Male	125,005	**47.8**
Age:		
18-29	81,389	**25.8**
30-49	118,505	**39.9**
50+	82,480	**34.3**
Smoking status:		
Current	61,558	**29.9**
Non-smoker	194,185	**70.1**
Household setting:		
Mostly Urban	175,793	**29.7**
Mostly Rural	132,123	**70.3**
Income inequality (Gini coefficient):		
Low Gini	173,294	**55.4**
High Gini	132,762	**44.6**
GNI PPP stratum:		
Low	113,169	**34.7**
Middle	90,305	**44.4**
High	104,442	**20.8**
Respiratory outcome:		
Current wheezing symptoms	25,617	**9.2**
Diagnosed asthma	14,723	**6.0**

n = unweighted frequency, **%** = weighted percent
GNI PPP = per capita gross national income adjusted for purchasing power parity
Gini = Gini coefficient is a measure of household income inequality within a country [21, 22]

TABLE 2: Age-adjusted weighted prevalence of respiratory outcomes associated with country level income stratified by gender and smoking status.

	Current wheezing symptoms **%** (95% CI)			**Diagnosed asthma** **%** (95% CI)		
	Low GNI (n=8657)	Middle GNI (n=9551)	High GNI (n=7391)	Low GNI (n=4429)	Middle GNI (n=4705)	High GNI (n=5580)
Overall	**13.3** (12.3-14.4)	**7.6** (6.7-8.5)	**13.0** (12.3-13.7)	**8.2** (7.0-9.3)	**5.2** (4.3-6.0)	**9.4** (8.7-10.0)
Female	**12.5** (11.1-13.9)	**7.1** (6.7-8.7)	**13.0** (12.1-14.0)	**7.6** (6.5-8.8)	**5.1** (4.2-6.1)	**9.7** (8.8-10.7)
Male	**14.1** (12.8-15.4)	**7.4** (6.0-8.7)	**12.9** (12.0-13.7)	**8.6** (7.2-10.0)	**5.2** (3.9-6.5)	**8.8** (8.2-9.4)
Current smoker	**18.0** (16.1-19.8)	**7.3** (5.5-9.1)	**13.1** (11.5-14.6)	**10.4** (8.8-12.0)	**4.4** (3.0-5.7)	**5.9** (4.6-7.1)
Non-smoker	**10.7** (9.4-12.0)	**7.7** (6.7-8.6)	**12.1** (10.3-13.8)	**6.9** (5.8-8.0)	**5.5** (4.4-6.6)	**7.0** (5.4-8.6)
Mostly Urban	**9.9** (9.0-10.8)	**18.0** (17.2-18.8)	**13.2** (12.5-13.9)	**5.7** (5.1-6.3)	**8.9** (8.3-9.4)	**9.3** (8.8-9.9)
Mostly Rural	**13.3** (12.3-14.4)	**4.6** (3.5-5.7)	**10.8** (7.8-13.8)	**8.2** (7.1-9.3)	**4.1** (2.9-5.3)	**9.9** (7.2-12.7)
Low Gini	**13.1** (12.1-14.2)	**14.7** (13.8-15.8)	**13.5** (12.7-14.3)	**8.1** (7.0-9.3)	**4.8** (4.3-5.3)	**9.2** (8.5-9.8)
High Gini	**23.5** (22.3-24.7)	**6.8** (5.9-7.8)	**8.9** (8.1-9.7)	**10.8** (9.9-11.7)	**5.2** (4.3-6.1)	**12.6** (11.4-13.7)

n = unweighted frequency, % = weighted prevalence, 95% CI = 95% confidence interval
GNI PPP = per capita gross national income adjusted for purchasing power parity
Gini = Gini coefficient is a measure of household income inequality within a country [21, 22]

FIGURE 1: WHS weighted prevalence and 95% confidence intervals of current wheezing symptoms by country and per capita gross national income adjusted for purchasing power parity (GNI PPP)

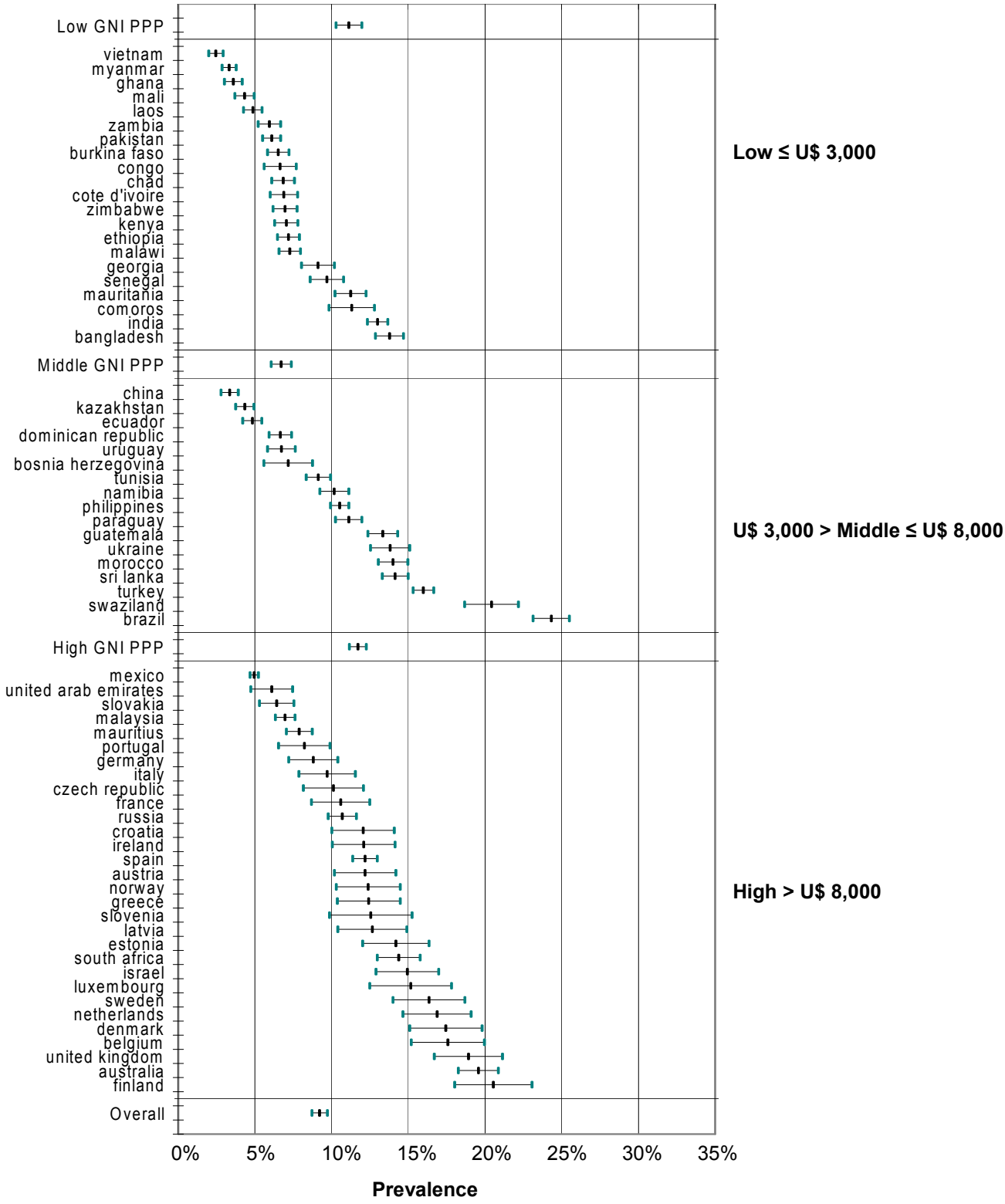
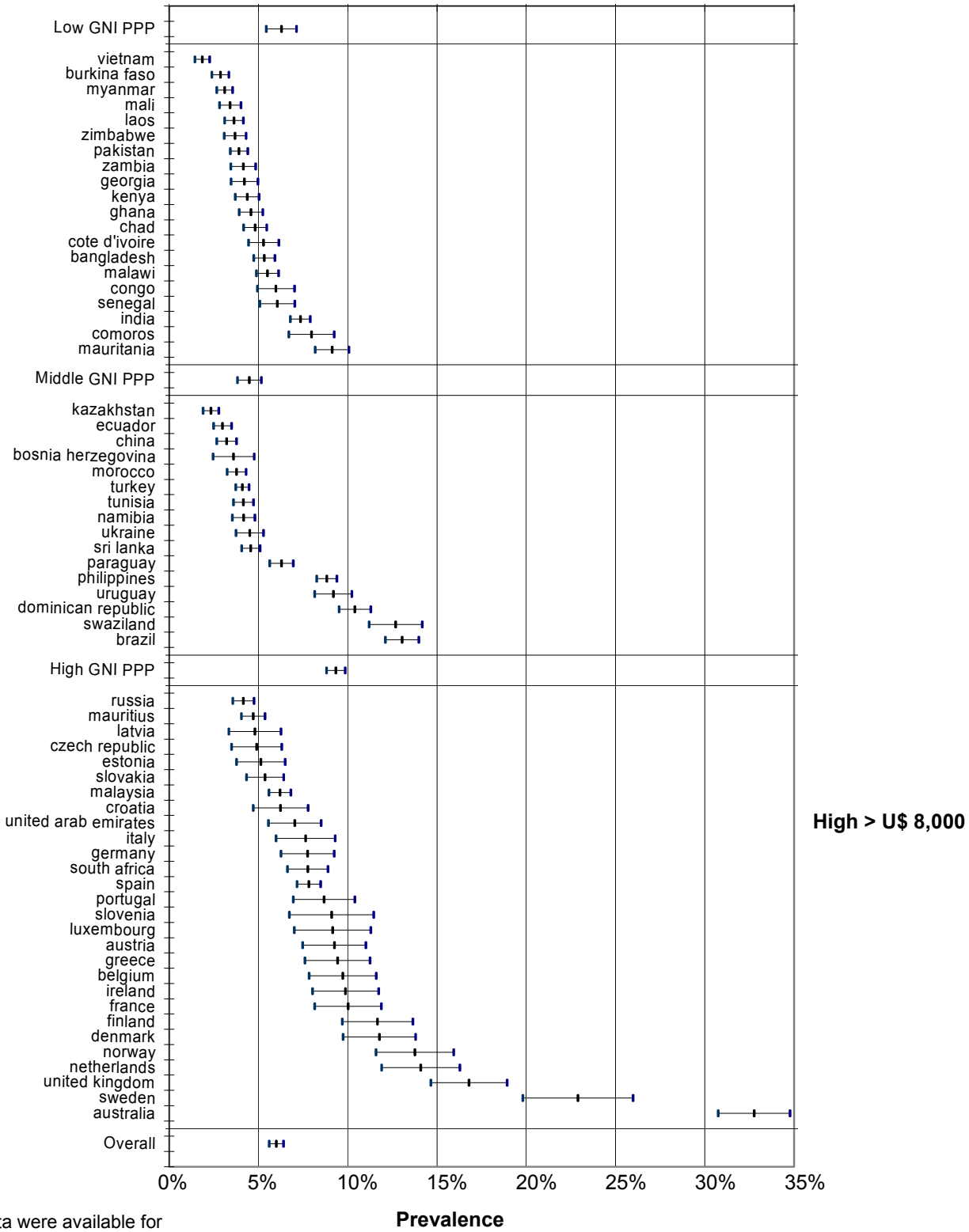


FIGURE 2: WHS weighted prevalence and 95% confidence intervals of diagnosed asthma by country and per capita gross national income adjusted for purchasing power parity (GNI PPP)



Note: No data were available for Guatemala, Ethiopia, Israel, and Mexico.