

## Study Protocol

# National and Sub-national Prevalence, Trend, and Burden of Asthma in Iran from 1990 to 2013; the Study Protocol

Mehdi Varmaghani MSc<sup>1,2</sup>, Arash Rashidian MD PhD<sup>3</sup>, Abbas Kebriaeezadeh PharmD PhD<sup>1</sup>, Maziar Moradi-Lakeh MD MPH PhD<sup>4</sup>, Mostafa Moin MD<sup>5</sup>, Anoosheh Ghasemian DDS<sup>2</sup>, Ehsan Rezaei-Darzi<sup>6,2</sup>, Sadaf Ghajarieh Sepanlou MD MPH PhD Candidate<sup>7,2</sup>, Niloofar Peykari MSc PhD Candidate<sup>2,8,9</sup>, Nazila Rezaei MD<sup>2</sup>, Mahboubeh Parsaeian MSc PhD Candidate<sup>6,2</sup>, Farshad Farzadfar MD MPH DSc<sup>2,8</sup>

## Abstract

**Background:** Asthma is a chronic inflammatory airway disease caused or worsened by environmental factors in genetically vulnerable people. The study of national and sub-national burden of asthma aims to provide a quantitative method and valid estimates for the prevalence, incidence, and economic burden of asthma disease in Iran from 1990 to 2013 and this papers explains measures, data sources, methods, and challenges that we will use in the study.

**Methods:** In order to conduct this study, we will use all available unpublished data sources, including claim databases and data collected by the food and drug organization (FDO). Moreover, we will devise and run a systematic review of all studies and literature published about asthma epidemiology in Iran, which includes all cross-sectional, cohort and case-control studies with asthma epidemiology focus that are population based. In this study, we will use two statistical models, including spatio-temporal and multilevel autoregressive models to estimate mean and uncertainty intervals for the parameters under study by gender, age, year, and province. All programs will be written in R statistical packages (version 3.0.1).

**Conclusion:** This study helps to obtain information concerning the variation among regions and provinces, and in general among sub-national divisions. Our study can be contribute to better allocation of resources, since it helps policymakers to recognize inequalities between regions and provinces and consequently help them to allocate resources more efficiently.

**Keywords:** Burden of disease, prevalence, asthma, Iran

**Cite this article as:** Varmaghani M, Rashidian A, Kebriaeezadeh A, Moradi-Lakeh M, Moin M, Ghasemian A, Rezaei-Darzi E, Sepanlou SG, Peykari N, Rezaei N, Parsaeian M, Farzadfar F. National and Sub-national Prevalence, Trend, and Burden of Asthma in Iran from 1990 to 2013; the Study Protocol. *Arch Iran Med.* 2014; **17**(12): 804 – 809.

## Introduction

Asthma is a chronic inflammatory airway disease<sup>1</sup> caused or worsened by environmental factors in genetically vulnerable people.<sup>2</sup> According to previous reports, 5% of the world's total population suffer from asthma.<sup>3,4</sup> Chronic respiratory diseases account for about 4.7% of global DALYs. Among the chronic respiratory diseases, chronic obstructive pulmonary dis-

ease (COPD) causes two thirds of the total burden of respiratory diseases and asthma ranks fifth among chronic respiratory diseases in terms of DALYs.<sup>5</sup> There are 300 million asthmatics worldwide.<sup>6</sup> About 1% to 18% of populations in different countries are asthmatics.<sup>7</sup> Asthma is the sixth major cause of hospitalization in the United States.<sup>8</sup> It is also the cause of more than 27% of referrals to physicians and 6 million days of absenteeism from work annually. About 18% of families' income is spent on asthma.<sup>9</sup> The World Health Organization (WHO) estimates that asthmatics experience 15 million DALYs annually, which encompasses 1% of the total burden of diseases. The mortality of asthma worldwide was estimated to be 250,000 people per year.<sup>1,10</sup>

In the report of global burden of asthma, published in 2003, the prevalence rate of asthma in Iran among all age groups was estimated at about 5.5%.<sup>11</sup> According to the latest report of the Global Initiative for Asthma (GINA) in 2004, the prevalence of asthma in Iran was between 5.1% and 7.5%.<sup>1</sup>

Costs of treating and controlling asthma-related diseases in the United States is estimated at about 6 to 10 billion dollars per year and more than 40% of these expenditures is due to the use of emergency rooms, hospitalization, and death of patients.<sup>12</sup> Additionally, asthma has a considerable economic burden and its annual direct and indirect costs reach almost 18 billion Euros in European countries<sup>13</sup> and 13 billion dollars in the United States.<sup>14</sup>

Estimating the burden of diseases and assessing their risk factors is crucial to recognizing important health priorities. The global and national patterns of diseases have been investigated by sever-

**Authors' affiliations:** <sup>1</sup>Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran. <sup>2</sup>Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. <sup>3</sup>Department of Health Management and Economics, School of Public Health, Tehran, Iran. <sup>4</sup>Community Medicine Department, Iran University of Medical Sciences, Tehran, Iran. <sup>5</sup>Immunology, Asthma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, I.R. Iran. <sup>6</sup>Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. <sup>7</sup>Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. <sup>8</sup>Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran. <sup>9</sup>Development of Research and Technology Center, Deputy of Research and Technology, Ministry of Health and Medical Education, Tehran, Iran.

**•Corresponding authors and reprints:** Farshad Farzadfar MD MPH DSc, Non-communicable Diseases Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, Iran; and Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Address: No. 4, 4th Floor, Ostad Nejatollahi St., Enqelab Ave., Tehran159966615, Iran. Telefax: 98-21-88913543, E-mail: f-farzadfar@tums.ac.ir. Accepted for publication: 12 November 2014

al studies in the world<sup>5,15-18</sup>; in addition, a study was conducted on the burden of diseases in six selected provinces at national level in Iran in 2003.<sup>19</sup> However, there is no study about the national and sub-national pattern of asthma in Iran. This study is part of the National and Sub-national Burden of Diseases (NASBOD) study in which the burden of diseases and risk factors in Iran will be estimated for the years 1990–2013.<sup>20</sup>

The study of national and sub-national burden of asthma aims to provide a quantitative method and valid estimates for the prevalence, incidence, burden and economic burden of asthma in Iran from 1990 to 2013.

## Materials and Methods

### Overview

This study will be conducted in three steps. In the first step, we will estimate the prevalence of asthma at national and sub-national levels using data from several sources, including: systematic review, pharmaceutical sales data, hospital inpatient data, insurance prescription data (outpatient data), and other sources. In the second step, we will measure the burden of asthma during 1990–2013 using DALYs methods. Finally, in the third step, we will conduct cost analysis of asthma using the data collected from utilization study, insurance prescriptions, and asthma-specific drug sales.

### Data source

In order to conduct this study, we will use all available unpublished data sources including 23 million pharmacy insurance claim records from three main Iranian health insurance organizations of the Social Security Insurance Organization, Medical Services Insurance Organization, and Armed Forces Medical Services Insurance Organization, from 2004 to 2011 which was collected by the Food and Drug Organization (FDO). We will also use information collected from hospital data project that covers 0.5% of the total inpatient admissions data in this study.<sup>21</sup> Moreover, we will use the pharmaceutical sales data from the FDO as well as the ministry of health and other authorities and reliable data sources including websites.

The first step: Estimation of the prevalence of asthma

#### A: Systematic review

**Search strategy:** A sensitive systematic search strategy will be utilized to cover all published data sources. The studies about the prevalence of asthma disease which have been published in English and/or Persian will be searched using several keywords presented in Table 1. We will search population based medical documents at national or sub-national levels published in PubMed/Medline, Scopus and ISI Web of Science, as well as those published papers that are available in Iranian databases including

**Table 1.** Search Strategy of Asthma.

Search strategy 1
<p><b>PubMed</b>            (((("Asthma"[Mesh]) OR "Bronchial Diseases"[Mesh]) OR "Asthma, Exercise-Induced"[Mesh]) OR "Asthma, Occupational"[Mesh]) OR "Status Asthmaticus"[Mesh]</p>
<p><b>ISI</b>            Asthma* OR "Bronchial Asthma" OR "Bronchial Diseases" OR "Asthma, Exercise-Induced" OR "Bronchospasm, Exercise-Induced" OR "Bronchospasm, Exercise Induced" OR "Asthma, Occupational" OR "Status Asthmaticus" OR "Asthmatic Crisis" OR "Asthmatic Shocks"</p>
<p><b>Scopus</b>            Asthma* OR "Bronchial Asthma" OR "Bronchial Diseases" OR "Asthma, Exercise-Induced" OR "Bronchospasm, Exercise-Induced" OR "Bronchospasm, Exercise Induced" OR "Asthma, Occupational" OR "Status Asthmaticus" OR "Asthmatic Crisis" OR "Asthmatic Shocks" OR "allergic asthma" OR bronchoconstriction</p>
Search strategy 2
<p><b>PubMed</b>            ((((((("Costs and Cost Analysis"[Mesh]) OR "Economics"[Mesh]) OR "Cost of Illness"[Mesh]) OR "Quality of Life"[Mesh]) OR "Health Care Costs"[Mesh]) OR "Health Expenditures"[Mesh]) OR "Economics, Medical"[Mesh]</p>
<p><b>ISI</b>            "Costs and Cost Analysis" OR "Cost Measures" OR "Cost Analysis" OR "Cost Analyses" OR "Economics" OR "Economic Factors" OR "Economic Conditions" OR "Home Economics" OR "Household Consumption" OR "Cost of Illness" OR "Illness Costs" OR "Sickness Cost" OR "Burden of Illness" OR "Illness Burdens" OR "Costs of Disease" OR "Disease Costs" OR "Quality of Life" OR "Life Quality" OR "Health Care Costs" OR "Health Costs" OR "Medical Care Costs" OR "Treatment Costs" OR "Health Expenditures" OR "Direct Expenditures" OR "Indirect Expenditures" OR "Expenditures" OR "Economics, Medical"</p>
<p><b>Scopus</b>            "Costs and Cost Analysis" OR "Cost Measures" OR "Cost Analysis" OR "Cost Analyses" OR "Economics" OR "Economic Factors" OR "Economic Conditions" OR "Home Economics" OR "Household Consumption" OR "Cost of Illness" OR "Illness Costs" OR "Sickness Cost" OR "Burden of Illness" OR "Illness Burdens" OR "Costs of Disease" OR "Disease Costs" OR "Quality of Life" OR "Life Quality" OR "Health Care Costs" OR "Health Costs" OR "Medical Care Costs" OR "Treatment Costs" OR "Health Expenditures" OR "Direct Expenditures" OR "Indirect Expenditures" OR "Expenditures" OR "Economics, Medical"</p>

IranDoc, Iranmedex, Scientific Information Database (SID), and Iranian journals not available online and unpublished documents, articles, and conference proceedings from 1985 to 2013. The Persian keywords will be equivalent to their English terms, and all probable combinations will be considered. We will choose the keywords based on MeSH terms and Entry Terms to search PubMed. For searching Scopus database, in addition to the MeSH keywords found in PubMed, we will use Emtree Terms. In order to extract the data, a predesigned form for data extraction will be used and the extracted data will be confirmed by two expert reviewers.

**Study selection criteria:** According to our predefined inclusion criteria, all English and Persian medical studies at national and sub-national levels, which are published between January 1985 and December 2013, will be included. All studies including population-based cross-sectional, cohort, and case-control studies, systematic reviews, disease registries, papers that report relevant data on disease parameters including incidence, prevalence, cost of illness, burden of disease, quality of life, and healthcare cost are potentially eligible to be included in the study. Our exclusion criteria will cover duplicated studies, biomedical, pharmacokinetic, non-clinical, animal studies, proceedings, and phase one and two clinical trials. The first review will include three steps. In the first step, titles of papers, in the second step the abstracts, and in the third step, full text papers will be investigated by two authors independently and in case of disagreement, the articles will be rechecked. In the second review, full-text articles will be reviewed and checked for inclusion based on predefined inclusion search terms. Moreover, the full-text articles will be selected and then checked by two independent reviewers who will use a quality assessment checklist. Disagreement between the two reviewers will be resolved by a third reviewer to decide about including them in the study. Disagreements between reviewers will be resolved via discussion and consensus. We will use critical appraisal tool for the quality evaluation of this study.

**Data extraction:** In this step, authors will extract data from eligible full-text papers and the two researchers independently enter the data into predefined forms. Then, another reviewer will assess the completeness and correctness of data mining. The required information, which is eligible to be extracted from full-text articles, will be entered in spread sheets. The collected data will include general information of the study, such as study name, citation, scope of study (rural/urban/both), level of study (national, provincial, district, community), publication year, study year, study design, sampling method, measurement, sample size, response rate, journal name, age and sex and study outcomes (proportion of cases to the total number of population included in the study (prevalence), incidence, mortality, relative risk, standard deviation, confidence interval).

*B: Estimation of the prevalence of asthma using insurance prescription data*

In this study, to estimate the prevalence of asthma, we will use 23 million prescriptions collected by FDO from 2004 to 2011. The collected data contains several types of information such as name of medicines, dosage, insurance type, province, and the number of each medicine. In this study, prescriptions which contain a minimum of one asthma-specific pharmaceutical are identi-

fied as a case of asthma. Finally, the prevalence of asthma will be estimated via calculating the ratio of patients with asthma in each age-sex group to the sum of patients which are identified in each province per year.

*C: Estimation of the prevalence of asthma using pharmaceutical sales data*

One of the methods to estimate the prevalence of asthma is to investigate information on the sales of drugs distributed by pharmaceutical companies in the country.<sup>22</sup> Given that  $P_{pm}$  is the estimated average number of people who used drugs in proportion to the total population in the same region;  $V_i$  is the total amount of  $i^{th}$  class of drug sold in a region per year;  $C_i$  is the estimated average consumption of  $i^{th}$  class of a drug per a person per year;  $N$  is the total number of population in that region in that year;  $J$  is the class of drug that is used to treat the disease;  $P_j$  is the proportion of people who take a combination of drugs. The prescription of one or more anti-asthma drugs for an individual indicates that the person is suffering from asthma. Since it is probable that multiple drugs are used for treating asthma, the prevalence of disease is calculated via the following equation:

$$P_{pm} = \sum_{i=1}^k \frac{V_i}{C_i} \cdot \frac{1}{1 + \left[ \sum_{j=2}^k (j-1) \cdot p_j \right]} \cdot \frac{1}{n}$$

In this method, the amount of anti-asthma drugs consumption can be used as a proxy to demonstrate the prevalence of disease in a district. In order to measure the average annual prevalence of asthma in every province, the proportion of prescriptions with more than one anti-asthma drug will be determined and 1000 prescriptions of anti-asthma drugs will be calculated. Using medical resources and viewpoints of asthma and allergy experts and specialists, the average annual consumption will be calculated. As a drawback, this method cannot estimate the prevalence of asthma among different age and sex groups.

**Statistical methods and analysis plans:** Although we will conduct a full investigation on all national data sources, it is impossible to find representative data for many provinces. Additionally, many studies do not include all age groups, both sexes, and both rural and urban areas of residency. To solve this problem, the spatio-temporal and multilevel autoregressive models are used to estimate mean and uncertainty interval for the parameters under study by gender, age, year, and province. These two models are utilized to assure that there is no model dependency in the results. The data on gender, age, year, and province will be used to build the models. However, the problem of misaligned areal units will arise for the provinces, which have been separated from other provinces in the given period of time. Both models can tackle the problem. Besides, the differences in the classification of summary statistics data will be settled using regression models and via cross walk between continuous and categorical values of given variables. The following paragraph briefly describes the specific features of the two models.

**Spatio-temporal model:** Spatio-temporal Bayesian hierarchical model with conditional autoregressive prior will be applied for spatial random effects.<sup>23</sup> In a spatial framework, it is assumed that observations closer in space are more correlated than observations

farther away. Consequently, the model can ‘borrow information’ from neighboring areal units to improve estimates for areas with missing values and/or small number of observations. Additionally, spatio-temporal misalignment modeling is used to combine incompatible areal units between data sources and/or over the years. The model takes account of covariates effects, non-linear age trends, and variations in quality of study and sources of data.

**Bayesian Autoregressive Multilevel model:** In this model, observations are hierarchically nested in districts, provinces, sub-regions, regions, and national levels.<sup>24</sup> The lower levels of a hierarchical model lend information to the higher levels and units of each level borrow information from each other depending on the degree of data availability. Several different factors are involved in the model, including linear time trends, nonlinear changes over time, covariate effects, nonlinearity associated with age, heterogeneity of data sources, and age-by-study variability. Time-varying district-level or provincial-level covariates inform the estimates, if practical.

Since Markov Chain Monte Carlo (MCMC) methods are generally applicable and are easy to implement, we will use these methods to accomplish Bayesian inference in both modeling frameworks. All programs will be written in R statistical package (version 3.0.1).

Overall, to extrapolate estimation of asthma prevalence in each province for the years 1990-2013 in Iran, we will use a collection of databases including outpatient data, inpatient data, pharmaceutical sales data, and also statistical models such as hierarchical multilevel model and spatio temporal and covariates of years of schooling, wealth index, urbanization index and food types.

#### The second step: Estimation of asthma burden

In this study, to calculate the burden of asthma, we will use the methods developed in the global burden of disease study; accordingly, first of all, we will design and complete life table for males and females and based on identified age groups, we will compute the disability-adjusted life years (DALYs).<sup>25</sup>

#### The third step: Calculation of the economic burden of asthma

Generally, chronic diseases such as asthma impose social and economic costs and have significant adverse mental effects on the health system, families and patients. In this study, costs of asthma will be estimated using data collected from utilization study, insurance prescriptions, and asthma-specific drug sales. Using those data, we will compute the rate of drug consumption through calculating Defined daily dose (DDD). DDD is a mechanism for the adjustment of drug dosage into different strengths in terms of milligrams; when we divide drug sales by DDD, we obtain the number of people who take a particular drug in a certain timeframe. We will use this information and also the results of health utilization study to estimate the money paid to general practitioners and specialists, then referral frequency will be calculated using insurance prescription data and other costs for asthma patients referred to a physician, such as CT-Scan, laboratory test, spirometry etc. will be computed through utilizing experts’ opinion.

## Discussion

The study of national and sub-national burden of asthma has sub-components including systematic review, estimation of prevalence, estimation of burden of disease, and economic burden of

asthma. In our comprehensive systematic review, we will include not only the literature of the burden of asthma disease, but also the studies about clinical and economic burden of asthma in Iran.

#### Burden of disease study in Iran and other countries

Burden studies of asthma have been conducted in several countries such as the USA,<sup>26-29</sup> New Zealand<sup>30</sup> and Australia.<sup>31</sup> Also, the economic burden of asthma has been studied to characterize the imposed financial burden of asthma at the national level.<sup>32</sup> The only burden of disease study was conducted in national level in Iran in 2003. In this study, the attributed burden of chronic respiratory diseases in both sexes was estimated to be about 872.1 DALYs per 100,000 population. The burden of asthma was estimated around 167.9 DALYs per 100,000 population. Also, out of the total national DALYs, 4.36% was accounted for by chronic respiratory diseases and 0.77% was attributed to asthma.<sup>19,33</sup>

Compared with the 2003 study, we use several sources and statistical models. Another difference is that in the previous study, Naghavi, et al., used data from six provinces of Iran to estimate the national level burden of disease<sup>19</sup> whereas we will use pharmaceutical sales data, insurance prescription data, and hospital inpatient data from all of provinces in Iran. Recently, this method has been used in other studies in Iran.<sup>34-36</sup>

The GBD 1990–2010 study yielded incomplete estimates of DALYs due to chronic respiratory diseases which were around 2248 (95%CI: 2036–2497) in 1990 and 1712 (95% CI: 1494–1968) in 2010. Asthma caused about 405 DALYs (95%CI: 304–531) in 1990 and 326 DALYs (95%CI: 249–424) in 2010.<sup>5</sup>

In a study performed in Wisconsin, trends in prevalence, mortality and morbidity were estimated. The results of this study showed that the prevalence of adult asthma was increasing and rates of asthma hospitalization and emergency admissions had decreased.<sup>26</sup>

#### Policy implications

Our study will present a comprehensive view on the importance of asthma among non-communicable diseases and can help policy makers to achieve a good mindset about the scale and distribution of asthma in different regions of Iran. This study will provide an appropriate baseline for evaluating and monitoring trends of asthma disease burden, economic burden, incidence, prevalence, and severity among Iranian population. Furthermore, the estimated prevalence and burden of disease at national and sub-national levels can help policy makers, insurance organizations and even local policy makers to make plans for providing required services and allocating resources, including financial and manpower resources, and making decisions for providing required beds in hospitals and health care centers. In addition, estimating the prevalence of disease at different sub-national regions can help local managers and policy makers to determine the priorities for intervention in their regions. Also, allocative efficiency will be one of the important outcomes of this study.

Estimation of asthma in sub-national regions (provinces) will help policy makers to achieve a clear mindset for controlling and executing interventions and it also helps them to measure inequality so that they can utilize plans to attain equity in distribution of health. The study provides detailed data on asthma that are essential inputs for evidence-based policy making. The result of this study can provide the evidence that will lead to improved population health. Overall, the results of this study will attract the atten-

tion of insurance system, planners, policy makers, and the ministry of health, as they can make decisions about resource allocation and geographic distribution of asthma disease.

#### Limitations

We face certain limitations in this study. There are limited data available on prevalence, incidence, age groups, sexes, and duration of asthma that may increase uncertainty in mortality and disability estimations. Also, we are facing data shortage at sub-national, regional, and provincial levels; hence, in study, we use hierarchical model to solve this problem. Furthermore, we will use methodological strategies for managing the likely specific heterogeneity between data sources.

The results of this study can lead to better allocation of resources, since it helps policymakers to recognize inequalities between regions and provinces. It also helps to plan, implement and evaluate interventions to improve the quality of asthma prevention, diagnosis, treatment programs and to evaluate and manage health care system. As a result, they can allocate resources such as manpower and financial resources more efficiently. Thus, modeling sub-national variations will help policy makers to identify and recognize epidemiological similarities and inequalities between sub-national regions and provinces.

#### Authors' contribution

**General designing of paper:** Arash Rashidian, Farshad Farzadfar, Mehdi Varmaghani

**Designing of method:** Farshad Farzadfar, Arash Rashidian, Abbas Kebriaeezadeh, Mostafa Moin, Maziar Moradi-Lakeh, Mehdi Varmaghani, Anoosheh Ghasemian

**Writing primary draft:** Mehdi Varmaghani, Farshad Farzadfar

**Manuscript revision:** Mehdi Varmaghani, Arash Rashidian, Abbas Kebriaeezadeh, Maziar Moradi-Lakeh, Mostafa Moin, Ehsan Rezaei-Darzi, Sadaf Ghajarieh Sepanlou, Farshad Farzadfar, Niloofar Peykari, Nazila Rezaei, Mahboubeh Parsaeian

#### Acknowledgments

The study is funded by the Ministry of Health and Medical Education of Islamic Republic of Iran and Setad-e Ejraie Farman Imam. This article is extracted from the PhD thesis of Mehdi Varmaghani. The authors would like to appreciate all those who helped them in this study with their valuable comments and kind consultations, especially Dr. Shirin Djalalinia, Dr. Masoud Moradi, and Iman Navidi.

#### Reference

- Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: Executive summary of the GINA Dissemination Committee report. *Allergy*. 2004; **59**: 469–478.
- Ministry of Health and Medical Education Undersecretary for Health Center for Non-communicable Disease Control National Committee on Asthma & Allergy Iran. National Asthma guideline; 2010.
- Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J, et al. *Harrison's Principles of Internal Medicine*. 17th ed. New York: MC GrawHill; 2008: 1596–41607.
- Lewis H. *Textbook of Medical Surgical Assessment and Management of Clinical Problem*. 5nd ed. St Louis: Mosby; 2000: 660.
- Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2013; **380(9859)**: 2197–2223.
- World Health Organization. Global surveillance, prevention and control of chronic respiratory disease: a comprehensive approach; 2007.
- Kasper DL, Longo DL, Braunwald E, Jameson JL, Fauci AS, Hauser SL. *Harrison's Principles of Internal Medicine*. 16nd ed. New York: MC GrawHill; 2005: 1205.
- Carroll P. How to intervene before asthma turns deadly. Available from: URL: <http://www.modernmedicine.com/modern-medicine/content/how-intervene-asthma-turns-deadly> (Accessed Date: 9/9/2014).
- Hodgkin J. *Pulmonary Rehabilitation Guidelines to Success*. 2nd ed. Philadelphia: Lippincott Press; 1993: 4–5.
- Beasley R. The Global Burden of Asthma report, Global initiative for asthma (GINA). Available from: URL: <http://www.ginasthma.org> (Accessed Date:9/9/2014).
- Masoli M, Fabian D, Holt S, Beasley R. *The Global Burden of Asthma*. United Kingdom: University of Southampton; 2003.
- Mason RJ, Broaddus VC, Murray JF, Nadel JA. *Murray and Nadel's Textbook of Respiratory Medicine*. 4nd ed. Philadelphia: Elsevier Saunders; 2004: 1168–1216.
- ENFUMOSA. The ENFUMOSA cross-sectional: European multi-centre study of the clinical phenotype of chronic severe asthma. *Eur Respir J*. 2003; **22**: 470–477.
- Redd SC. Asthma in the united states: burden and current theories. *Environ Health Perspect*. 2002; **110(suppl 4)**: 557–560.
- Wang H, Dwyer-Lindgren L, Lofgren KT, Rajaratnam JK, Marcus JR, Levin-Rector A, et al. Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of disease study. *Lancet*. 2010; **380(9859)**: 2071–2094.
- Salmon JA, Vos T, Hogan Dr, Gagnon M, Naghavi M, Mokdad A, et al. Common values in assessing health outcomes from disease and injury: disability weight measurement study for the Global Burden of Disease Study. *Lancet*. 2010; **380(9859)**: 2129–2143.
- Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age group in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study. *Lancet*. 2010; **380(9859)**: 2224–2260.
- Salomon JA, Wang H, Freeman MK, Vos T, Flaxman AD, Lopez AD, et al. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden Disease Study. *Lancet*. 2010; **380(9859)**: 2144–2162.
- Ministry of Health. Report of national burden of disease, injuries, Burden of health risk factors and life expectancy with health in Iran for 2003; 2005.
- Farzadfar F, Delavari A, Malakzadeh R, Mesdaghinia A, Jamshidi HR, Sayyari A, et al. NASBOD 2013: design, definitions, and metrics. *Arch Iran Med*. 2014; **17(1)**: 7–15.
- NiakanKalhori SR, Tayefi B, Noori A, Mearaji M, Rahimzadeh S, Zandian E, et al. Inpatient data, inevitable need for policy making at national and sub-national: a lesson learned from NASBOD. *Arch Iran Med*. 2014; **17(1)**: 16–21.
- Sartor F, Walckiers D. Estimate of disease prevalence using drug consumption data. *Am J Epidemiol*. 1995; **141**: 782–787.
- Parsaeian M, Farzadfar F, Zeraati H, Mahmoodi M, Rahimighazikalayeh G, Navidi I, et al. Application of Spatio-temporal Model to estimate burden of disease, injuries and risk factors in Iran 1990–2013. *Arch Iran Med*. 2014; **17(1)**: 28–32.
- Kasaecian A, Eshraghian MR, Rahimi Foroushani A, Niakan SR, Mohammad K, Farzadfar F. Bayesian autoregressive multilevel modeling of burden of diseases, injuries, and risk factors in Iran 1990–2013. *Arch Iran Med*. 2014; **17(1)**: 22–27.
- Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. GBD 2010: design, definitions, and metrics. *Lancet*. 2012; **380(9859)**: 2063–2066.
- Wisconsin Department of Health Services, Division of Public Health, Bureau of Environmental and Occupational Health. The Burden of Asthma in Wisconsin 2013. Available from: URL: <http://www.dhs.wisconsin.gov/publications/p4/p45055> (Accessed Date: 9/9/2014).
- Oregon Asthma Program. 2013. The Burden of Asthma in Oregon: 2013. Available from: URL: [http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Documents/burden/or\\_asthma\\_2013](http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Documents/burden/or_asthma_2013) (Accessed Date: 10/17/2014).
- Milet M, Tran S, Eatheron M, Flattery J, Kreutzer R. The Burden of Asthma in California: A Surveillance Report. Richmond CA. California Department of Health Services, Environmental Health Investigations Branch; 2007.
- Milet M, Lutzker L, Flattery J. Asthma in California: A Surveillance

- Report. Richmond CA. California Department of Public Health, Environmental Health Investigations Branch; 2013.
30. Holt SH, Beasley R. The burden of Asthma in New Zealand, Asthma and Respiratory Foundation of New Zealand 2001. Available from: URL: [www.asthmanz.co.nz](http://www.asthmanz.co.nz) (Accessed Date: 9/9/2014).
31. Australian Institute of Health and Welfare: Australian Centre for Asthma Monitoring 2009. Burden of disease due to asthma in Australia 2003. Available from: URL: [www.aihw.gov.au](http://www.aihw.gov.au) (Accessed Date: 9/10/2014).
32. Chang-yup Kim. The financial burden of asthma: a nationwide comprehensive survey conducted in the Republic of Korea. *Allergy Asthma Immunol Res.* 2011; **3(1)**: 34 – 38.
33. Naghavi M, Abolhassani F, Pourmalek F, Lakeh M, Jafari N, Vaseghi S, et al. The burden of disease and injury in Iran 2003. *Popul Health Metr.* 2009; **7**: 9.
34. Sharifi F, Najafi B, Fakhrzadeh H, Noroozian M, Naderi Magham Sh, Philp I, et al. National and Sub-national Trend of prevalence and Burden of Dementia in Iran, from 1990 to 2013; Study Protocol. *Arch Iran Med.* 2014; **17(12)**: 837 – 843.
35. Rezaei-Darzi E, Farzadfar F, Hashemi-Meshkini A, Navidi I, Mahmoudi M, Varmaghani M, et al. Comparison of two data mining techniques in labeling diagnosis to Iranian pharmacy claim dataset: Artificial Neural Network (ANN) versus Decision Tree Model. *Arch Iran Med.* 2014; **17(12)**: 816 – 820.
36. Teimouri M, Farzadfar F, Soudi Alamdari M, Hashemi-Meshkini A, Adibi Alamdari P, Rezaei-Darzi E, et al. Detecting Diseases in Medical Prescriptions Using Data Mining tools and Combining Techniques. *Iranian J of Pharm Res.* in press.