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

Farshad Sharifi MD MPH[1,2], Baharak Najafi MSc[1], Hossein Fakhrzadeh MD[1], Maryam Noroozian MD[3], Shohreh Naderimagham MPH, PhD[2], Ian Philp MD FRCP[4], Seyed Masood Arzaghi MD[1], Mahtab Alizadeh MPH PhD[1], Shervan Shoaee DDS[1], Tahereh Hassannia MD[5], Ali Sheidaei BS[6,2], Maziar Moradi-Lakeh MD MPH PhD[7], Farshad Farzadfar MD MPH DSc•[2,5], Bagher Larijani MD•[5]

## Abstract

**Background:** Dementia is a disabling syndrome, which generally affects aged population more than any other age groups. This syndrome has a growing prevalence and incidence worldwide. The prevalence and burden of this group of diseases in Iran have not been estimated in a community-based study yet. This paper aims to explain the systematic approach, data sources, research methodology, and statistical analysis that will be used to quantify the prevalence and burden of dementia at national and sub-national levels.

**Methods:** This is the protocol of a secondary data study that explains the design and method of conducting the study. We will use several sources of data that will include a systematic review of articles and gray literature which have reported the prevalence or incidence of dementia and its uncertainty at national and sub-national levels in Iran, in addition to data about dementia-specific drug sales per each year at provincial levels, as well as data extracted from 23 million health insurance prescriptions over 8 years and some data from medical documents of Iranian Alzheimer's Association members. The technical groups of National and Sub-national Burden of Disease will collect some covariate data, such as age and sex structure of population, urbanization status, mean years of schooling, plasma cholesterol, fasting plasma glucose, and systolic and diastolic blood pressure at provincial levels which will be used in our models. Two statistical models, namely spatio-temporal and hierarchical autoregressive models, will be used for interpolation and extrapolation of missing data.

**Conclusion:** It seems that the study of national and subnational burden of dementia could provide more accurate estimation of prevalence and burden of dementia in Iran with an acceptable level of uncertainty than the previous studies.

**Keyword:** Dementia, burden of disease, prevalence, Iran

## Introduction

Dementia is a chronic syndrome with a growing burden worldwide. Around the world, about 8.4% of people aged ≥60 years suffer from this syndrome. The frequency of dementia rises with aging, so that its prevalence increases globally from 1.3% in the age group 60–64 years to 63.9% in the age group ≥90 years.[1] The number of patients with dementia in 2013 was estimated at 44.35 million and it will reach 75.62 million in 2030.

**Authors' Affiliations:** [1]Elderly Health Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. [2]Non-Communicable Disease Research Center, Endocrinology and Metabolism Population Sciences Institute. Tehran University of Medical Sciences, Tehran, Iran. [3]Geriatric Education Group, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. [4]Hull and East Yorkshire NHS Hospitals Trust, East Riding of Yorkshire, UK. [5]Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran Iran. [6]Department of Biostatistics, Faculty of Paramedical sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [7]Community Medicine Department, Iran University of Medical Sciences, Tehran, Iran.
•**Corresponding author and reprints:** Farshad Farzadfar MD MPH DSc, Non-Communicable Disease Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran, and Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran. Address: No 4, 4th Floor, Ostad Nejatollahi St., Enqelab Ave., Tehran, Iran. Telefax: +9821-8880808, E-mail: farzadfar3@yahoo.com. Bagher Larijani MD, Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran. Address: 5th Floor, Shariati Hospital, North Kargar Ave., Tehran, Iran. Telefax: +9821-8880808, E-mail: emrc@tums.ac.ir
Accepted for publication: 12 November 2014

At present, 38% of these patients live in high income countries and 62% live in low income countries.[2] The Global Burden of Diseases, Injuries, and Risk Factors (GBD) study estimated disability-adjusted like years (DALYs) of dementia to be 11.349 (9.147–13.741) million in 2010, which had a growth of 99.3% compared with 1990.[3] Although it was the cause of only about 0.46% of the total burden of diseases,[3] the economic costs of dementia were approximately 604 billion dollars in 2010 which were similar to the costs of cardiovascular diseases and cancers.[4,5]

Some studies have indicated huge variability in the prevalence and burden of dementia in different regions and countries.[1,6,7] At least some of this variability could be justified by differences in the prevalence of risk factors of dementia in various regions and countries.[8] Taking into consideration the variation in the prevalence of most diseases in various regions of the world and also the changes in the prevalence of diseases over the time, a periodic estimation of the burden of diseases at national and sub-national levels is not only reasonable but also necessary for every country. This information can help policymakers at the national and regional levels to make better decisions about resource allocation. In Iran, the first study for estimating the burden of diseases was conducted in 2003.[9] Because of scarcity of data, these estimations of the burden of diseases were with high levels of uncertainty. Over the recent 10 years, evidences about the prevalence and incidence of diseases have extended significantly. In addition, new quantitative methods have been developed recently, which enable researchers to perform more accurate estimations about epidemio-

logic characteristics of diseases and risk factors. Therefore, conducting a new study about the burden of diseases seems necessary. This study will particularly consider detecting inequality between regions and provinces in Iran. We expect that our study provides essential health intelligence to inform policymakers about the importance of dementia in Iran.

Because of scarcity of the epidemiologic data about dementia in Iran, this paper explains the materials and methods of the study that aims to provide a relatively precise estimation of the prevalence and burden of dementia at national and sub-national levels over 24 years from 1990 to 2013, using a combination of data collected from a systematic review of prevalence, and also through some proxies such as dementia-specific drug sales, hospital inpatient study data, death registry data, and data from Iranian Alzheimer's Association (IAA).

## Materials and Methods

This will be a secondary-data study to estimate the burden of dementia and its time-trends over 24 years from 1990 to 2013 at national and sub-national levels in Iran. This study will be conducted by a technical team, which is one of the national and sub-national burden of diseases (NASBOD) technical teams[10] in collaboration with the core team. The teams will estimate the prevalence and burden of 290 diseases and 67 risk factors in Iran. More details about the NASBOD technical teams are presented elsewhere.[10] This study will have two phases. In the first phase, we will estimate the prevalence of dementia by sex and age group at national and provincial levels using the data from different sources such as a systematic review, dementia-specific drug sales data, insurances prescription data, data from the hospital inpatient study and other sources. In the second phase, we will calculate the burden of dementia using the DALYs method. DALY will be calculated as the sum of the years of life lost (YLL) due to early mortality in the population and the years lost due to disability (YLD).

### Data sources

The most important problem facing us is shortage of data on the prevalence and incidence of dementia in Iran. In most population-based health surveys in Iran, there are no data about the prevalence and incidence of dementia. Therefore, we need a comprehensive gray literature review for extracting related data, which have not been published or even reported.

### *Systematic review*

A systematic review of the prevalence of dementia and its related diseases will be carried out. This review will be conducted based on a protocol, which is compatible with the NASBOD protocols. The international source of search includes the Medline database of the National Library of Medicine (PubMed), Web of Science (ISI), Scopus, and Google scholar, as well as three Iranian databases includes IranMedex, Scientific Information Database (SID), and IRANDOC. In addition, gray literatures, including the reports of national and sub-national surveys, results of which have not been published as articles, and some studies which have not been reported or published will be considered. These studies will be found through consultation with the experts who work on the dementia domains.

### *a. Search strategies*

Search strategy will be designed through following guidelines provided by experts and also using MeSH-terms and Emtree-terms. After approving the search strategy by the technical team, it will be used for searching international databases. Iranian databases are very sensitive to the spelling of the words used for search, so all possible spellings of the words which are equivalent to English search terms will be applied. The Search fields will include the titles, abstracts, and keywords of articles, as well as thesis, dissertations, conference proceedings and reports that were published in English and/or Persian databases over the mentioned period.

The gray literatures will include reports and booklets of the Ministry of Health and Medical Education (MOHME), and the Ministry of Cooperatives, Labor, and Social Welfare, which have not been published as an article in the databases. This data will be found through interviewing and consultations with experts and the subjects who are focal points in aging fields.

### *b. Study selection criteria*

Our study will include those studies, which have been conducted during 1990 to 2014 and have reported the epidemiologic characteristics of dementia in Iran such as prevalence or incidence, and have used population-based sampling methods. On the other hand, only papers or gray literatures will be considered which have reported the prevalence or incidence of dementia in a population-based study, such as community-based cross-sectional studies, baseline of population-based cohort studies, population-based field trial studies, and also national and sub-national health surveys. Two trained researchers will review the eligible studies independently. In case of inconsistency between the reviewers about the inclusion of an article, a third reviewer will review the paper to make the final decision about the article. The same two reviewers will review the full text of papers included in the first step, again. In case of disagreement between the reviewers, the process will be similar to the first step. For those articles which will be selected finally and their full-text, will not be accessible or their data will be inadequate, three times correspondence will be made with corresponding author with a three-week interval. If we will not receive a response after three weeks from the last letter, we will exclude the article. In order to assess the sensitivity of the searches, the reference list of selected papers will be reviewed for the probable titles of articles, which are eligible but not included in the list. If the number of papers found will exceed 10%, the search protocol will be revised and the search will be conducted again. The final full-text articles will be critically appraised and their quality will be assessed by two independent reviewers using a checklist, which is designed based on the NASBOD appraisal tool, and disagreement will be settled at a meeting with the presence of reviewers. This tool has a scoring model and some of its items include sampling method, how much the sample is representative of the general population, sample size, and how dementia was diagnosed in that study.

### *c. Data extraction*

Data extraction from eligible full-text papers and other gray literatures will be performed by two reviewers independently using an Excel datasheet and inconsistency between the extracted data will be resolved by rechecking the data.

### *d. Types of data*

***General information:*** the source of data, including the name of

the authors, type of studies, language, place of study, time of data collection, time of publication, type of resource (peer-review article, conference proceeding, thesis or dissertation, reports etc.), and citation of the resource.

***Methodological data***: type of studies (cross-sectional, cohort, case-control, field trial etc.), the exclusion and inclusion criteria, age groups, sample size, method of sampling, ascertainment/dementia definition, tools and methods used for diagnosis of dementia, and response rate.

***Data on the prevalence and incidence:*** the prevalence and incidence with confidence interval (or standard error) of 95% will be recorded for 18 five-year age groups (5–9 years to ≥90 years) and for each sex separately (this age range is selected because the GBD 2010 study did not report any case of dementia in children less than five years).[3] If part of data does not exist in the article, we will try to communicate with the corresponding author to obtain the required data.

If we face various tools used in different studies for diagnosis of dementia, we will try to crosswalk between them to decrease the heterogeneity of the data.

### Dementia-specific drugs

In a panel with the presence of expert neurologists and psychiatrists who are familiar with the treatment of dementia and dementia related diseases, the drugs which are prescribed especially for treating dementia will be determined.

#### a. Dementia-specific drug sales data

Drug sales data from all Iranian provinces has been collected since about 15 years ago by MOHME. The dementia-specific drug sales data could provide an estimate about the crude prevalence of dementia in a certain province and year.

#### b. Insurance prescription date

From about overall 460 million insurance prescriptions over 8 years (from 2004 to 2011), about 23 million prescriptions were selected randomly. The prescriptions that contain at least one dementia-specific drug will be selected. We will use these data to estimate the proportion of the number of patients with dementia in each age-sex group of the total number of patients in a given year and province. Furthermore, we can calculate mean doses of each prescribed dementia-specific drugs and percent of each dementia-specific drug has been prescribed together by the other dementia specific medications in a specific age group.

Moreover, we use the artificial neural network (ANN) and decision tree models for labeling of the diagnosis of dementia from the insurance prescriptions. Details of these models are described elsewhere.[11]

### Hospital inpatient data

Although, patients with dementia are not usually admitted to hospital for their disease, the end stage patients or those with complication may be admitted to hospital. The hospital inpatient data that has been already collected could be useful, particularly for estimation of the prevalence of severe and complicated dementia. The protocol of this study is reported elsewhere.[12]

### Data from death registry

Death registry system is a component of vital registration sys-tem. If death registration is valid, it is the best source of estimation of cause-specific death rate. However, death registration in Iran, similar to other developing countries, is incomplete and entails misclassification.[13,14] The cause-specific age-sex group mortality is necessary for estimating the premature mortality caused by dementia. This data could help us to estimate the YLD. A group of the NASBOD is dealing with the problems of incompleteness and misclassification in the death registry system. The study of child and adult mortalities in Iran is explained elsewhere.[15,16]

### Data of Iranian Alzheimer's Association (IAA)

The medical records of more than 4000 patients with dementia are available in IAA branches. Some of these medical documents contain drug adherence rate of patients with dementia. It may help us to estimate drug-adherence among Iranian patients with dementia. The data on drug-adherence is applicable for estimation of dementia prevalence.

#### Estimation of dementia burden

After completing the table of age-sex specific prevalence in 31 provinces, we will calculate the DALY of dementia by summing up the YLL and YLD.[13]

#### Statistical methods of analysis

We need a matrix of data with 26784 data-cells (36 age-sex groups in 31 provinces over 24 years). A likely expected problem with this matrix is the presence of several empty cells because of shortage of data. Despite our systematic multidimensional approach for data collection, it is highly probable that the matrix suffers a considerable degree of incompleteness. Some covariates at the level of the provinces could be applied to estimate the missing data. These covariates include age and sex structure, socioeconomic status, urbanization status, mean years of schooling, mean fasting plasma glucose, mean plasma cholesterol, and mean systolic and diastolic blood pressure. Other NASBOD groups will provide considerable parts of the mentioned data.[17] Another problem with the data is a spatial misalignment of data (i.e., the estimates of Khorasan province before its division into three provinces are not aligned with those estimates of Southern, Northern, and Razavi Khorasan after division). Two mathematical approaches, naemly multi-level autoregressive and spatio-temporal hierarchical Bayesian models, will be used to extrapolate and interpolate the dementia sex-age specific prevalence and its uncertainty in each year and province through using temporal, juxtaposition and covariate data.

#### Hierarchical autoregressive multi-level model

In this model, the observed data will be nested in hierarchical geographic frameworks, including counties, provinces, sub-regions, regions, and national level. The higher levels lend the information to lower levels. This approach will address several other components such as linear and nonlinear time trends, mentioned covariate effects, nonlinearity in age group prevalence and other factors related to heterogeneity of the data sources. More details about this model are discussed elsewhere.[18]

#### Spatio-temporal model

The spatio-temporal Bayesian hierarchical models with conditional autoregressive prior for spatial random effects will be utilized for estimation of missing values in our study. This modeling

strategy assumes that the prevalence of dementia in juxtaposition of given region and temporary near the certain time are the proxy for estimation of dementia prevalence and its uncertainty in that region.[19] In addition, an age, sex, time, province missing box could borrow information from the nearest temporary and positional data in our matrix. In order to improve the model fitness, we will also consider the covariate and non-linearity of spatio-temporal and age-specific trends and quality of data.

## Discussion

Dementia strains health, social systems, and budgets because of severity of disability and long term care that patients with dementia need.[4,5] According to the results of the GBD study, the global burden of dementia had an increasing trend from 1990 to 2010.[3] It was estimated that this increasing trend will continue and even the slope of the trend will rise up to 2050 because of the global growing of the aged population proportion.[2] It is important that the proportion of the population suffering from dementia will increase more quickly in lower income compared to high income countries. So, this proportion will increase from 63% in 2010 to 71% in 2050.[1] Because of many reasons, such as the variation of lifestyles and genetic resources, there is huge diversity in the prevalence of dementia between regions and countries.[1]

Iran has experienced a rapid reduction in population growth over the recent decade. This caused a quick increase in the aged population.[11] Despite the WHO recommendation to countries for conducting studies to detect the prevalence of dementia at national levels,[20] the prevalence of dementia has not been investigated in a national survey in Iran yet. Moreover, there are very sparse studies which have addressed the prevalence of dementia at the subnational levels. Naghavi's study estimated the burden of dementia at national level in Iran in 2003. The findings of this study demonstrated that dementia accounts for about 0.445% of total calculated DALYs in Iran.[21] However, in the GBD study, the number of people with dementia was estimated at about 309,000 individuals and its burden was equal to 0.42% of the DALYs in Iran.[3] This discrepancy in burden of dementia between two studies may be due to the differences of data sources used for estimation of dementia burden or is because of various models which were used in these studies.

We expect to have wide variation in the prevalence of dementia in different regions of Iran because of the wide variety of risk factors (e.g., difference in the educational levels of older population).[22]

We hope our study will provide more accurate estimation about the prevalence and burden of dementia than Naghavi and GBD studies because we use multiple sources of data and newer mathematical and statistical models. In the previous study on the burden of diseases in 2003, data were extracted from six provinces of Iran,[21] while we will use the data of drug selling and prescription from all 31 provinces of Iran.

Furthermore, over the recent 10 years from 2003, when the previous study on the burden of disease was conducted in Iran, the prevalence of dementia in Iran is expected to have increased because of the increasing of the older people percent.[11] Our study will provide new information about the prevalence and burden of dementia and their trends over 24 years from 1990 to 2013 at both national and sub-national levels. The data about the prevalence of dementia and its trend at provincial level could determine

an inequality about dementia prevalence between the regions and provinces of Iran. This information helps researchers and health providers to detect the risk factors of dementia in each region and consequently, design interventions to reduce the inequity between provinces. The prevalence that will be reported by our study is useful for estimating the financial and human resources that are needed to provide care for the patients with dementia at the provincial level, as well.

In addition, these data could be used as baseline data for future studies that may be conducted on the effectiveness of big financial intervention in health system, which will be initiated by the Minister of Health in 2014.[23]

We will use drug consumption as a proxy for estimation of the prevalence of dementia since we do not have enough population-based cross-sectional data in Iran. This method could have compatible accuracy with traditional cross-sectional studies for estimating the prevalence of diseases, particularly for chronic diseases such as dementia that has a limited number of specific drugs.[24–26]

There are several sources of uncertainty in our study. The most important one is the utilization of some proxies for estimation of the prevalence. Nevertheless, using the data about disease-specific drug sales could lead to some biases which neglecting them may cause a biased estimation of prevalence. One of these biases is that patients with various severity of disease may not consume similar doses of disease-specific drugs, i.e., the anti-dementia drugs may be discontinued in patients with severe dementia because of inefficiency. The other likely bias is inappropriately prescribed drugs because patients may not consume the recommended doses. As a result, a given drugs may not be used by the patients according to the prescribed doses. To reduce these biases, we have paid special attention to the likely problems during study design. The number of patients with severe dementia will be extracted from several sources such as hospital inpatient and cause-specific death data. These sources of data could give us a relatively good estimation of the prevalence of severe dementia. Misdiagnosis and drug adherence rate is our other big challenges that we cannot deal with properly. As mentioned before, we will try to extract the drug adherence rate from documents of Iranian Alzheimer's association. However, this data may not be generalizable to all patients. Another issue to consider is that in our study the proportion of patients in age-sex groups in the population under the coverage of insurances will be generalized to the general population. Although the population with health insurance coverage may show higher demand for health services such as referring to doctors and getting treatment, we do not have any reason that the proportions of patients in each age group with insurance are different from the other population. Moreover, these two health insurance organizations (whose prescription we will use) have an extended coverage and cover more than 60% of the Iranian population.[27] Some of uncertainty could be caused by low validation of data source; e.g., data on drug sales may not be precise enough, or data which will be extracted from studies may have a high level of confidence interval because of the method of sampling and small sample sizes or methods of diagnosis of dementia.

Another source of uncertainty will be due to the models which will be applied in our study. Each model has a level of inherent uncertainty. We will try to reduce this source of uncertainty by choosing suitable models and better fitness.

In conclusion, it seems reasonable to conduct a study for estima-

tion of prevalence and burden of dementia in Iran at national and subnational levels. Despite the fact that the data used in our study will face some drawbacks, applying multiple sources of data and some new statistical models can relatively solve them and therefore provide good information about the prevalence and burden of dementia with an acceptable level of uncertainty for policymakers and researchers.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

The initial draft was organized by Farshad Sharifi and then revised by the all co-authors. All authors have given approval to the final version of the manuscript and designed by NASBOD team.

## Acknowledgments

## References

1. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement*. 2013; **9(1):** 63 – 75.
2. Prince M, Guerchet M, Prina M. Policy brief for heads of government:The global impact of dementia 2013–2050. Alzheimer's disease international, London, UK; 2013.
3. 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*. 2012; **380:** 2197 – 223.
4. Wimo A, Prince M. World Alzheimer Report 2010: The global economic impact of dementia. Alzheimer's disease international, London,UK; 2010.
5. Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. *NEJM*. 2013; **368:** 1326 – 1334.
6. Murray CJ, Richards MA, Newton JN, Fenton KA, Anderson HR, Atkinson C, et al. UK health performance: findings of the Global Burden of Disease Study 2010. *Lancet*. 2013; **381:** 997 – 1020.
7. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012; **380:** 2163 – 2196.
8. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012; **380:** 2224 – 2260.
9. Jafari N, Abolhassani F, Naghavi M, Pourmalek F, Lakeh MM, Kazemeini H, et al. National burden of disease and study in Iran. *Iran J Public Health*. 2009; **38(suppl 1):** 71 – 73.
10. Farzadfar F, Delavari A, Malekzadeh R, Mesdaghinia A, Jamshidi HR, Sayyari A, et al. NASBOD 2013: design, definitions, and metrics. *Arch Iran Med*. 2014; **17(1):** 7 – 15.
11. 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):** 837 – 843.
12. Niakan Kalhori SR, Tayefi B, Noori A, Mearaji M, Rahimzade S, Zandian E, et al. Inpatient data, inevitable need for policy making at national and sub-national levels: a lesson learned from NASBOD. *Arch Iran Med*. 2014; **17(1):** 16 – 21.
13. Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. GBD 2010: design, definitions, and metrics. *Lancet*. 2012; **380:** 2063 – 2066.
14. Dortag E, Bahrampour A, Haghdost A, Zendedel K, Jaberipour M, Marzeban M. Completeness of fars province deaths registry on cancer death using capture recaptures method. *Journal North Khorasan University of Medical Sciences*. 2011; **3(Biostatistics and Epidemiology Supplement):** 33 – 43.
15. Mehdipour P, Navidi I, Parsaeian M, Mohammadi Y, Moradi Lakeh M, Rezaei Darzi E, et al. Application of Gaussian Process Regression (GPR) in estimating under-five mortality levels and trends in Iran 1990 - 2013, study protocol. *Arch Iran Med*. 2014; **17(3):** 189 – 192.
16. Mohammadi Y, Parsaeian M, Farzadfar F, Kasaeian A, Mehdipour P, Sheidaei A, et al. Levels and trends of child and adult mortality rates in the Islamic Republic of Iran, 1990–2013; protocol of the NASBOD study. *Arch Iran Med*. 2014; **17(3):** 176 – 181.
17. Peykari N, Sepanlou SG, Djalalinia Sh, Kasaeian A, Parsaeian M, Ahmadvand A, et al. National and sub-national prevalence, trend, and burden of metabolic risk factors (MRFs) in Iran: 1990 - 2013, study protocol. *Arch Iran Med*. 2014; **17(1):** 54 – 61.
18. Kasaeian A, Eshraghian MR, Rahimi Foroushani A, Niakan Kalhori 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.
19. Parsaeian M, Farzadfar F, Zeraati H, Mahmoudi M, Rahimighazikalayeh G, Navidi I, et al. Application of spatio-temporal model to estimate burden of diseases, injuries and risk factors in Iran 1990 - 2013. *Arch Iran Med*. 2014; **17(1):** 28 – 33.
20. World Health Organization, Dementia: a public health priority. 2012; Aviaable from: URL: http: //www.who.int/about/licensing/copyright_form/en/index.html (cited 2012).
21. Naghavi M. National study of burden of disease s and injuries and burden of risk factors and healthy life expectancy in Islamic Republic of Iran in 2003. The Ministry of Health and Medical Education; 2006.
22. Lindsay J, Laurin D, Verreault R, Hebert R, Helliwell B, Hill GB, et al. Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging. *Am J Epidemiol*. 2002; **156(5):** 445 – 453.
23. Vice-President for Strategic Planning and Supervision, National annual budget law of the Islamic Republic of Iran in 2014. Available from: URL: http://www.spac.ir/Portal/View/Page.aspx?PageId=bd3f5fbe-85f3-44d4-bf1e-c71abe568504 (Cited 2013).
24. Karlstad O, Nafstad P, Tverdal A, Skurtveit S, Furu K. Prevalence, incidence and persistence of anti-asthma medication use in 2- to 29-year-olds: a nationwide prescription study. *Eur J Clin Pharmacol*. 2010; **66(4):** 399 – 406.
25. Mirandola M, Andretta M, Corbari L, Sorio A, Nose M, Barbui C. Prevalence, incidence and persistence of antipsychotic drug prescribing in the Italian general population: retrospective database analysis, 1999-2002. *Pharmacoepidemiol Drug Saf*. 2006; **15(6):** 412 – 420.
26. Sartor F, Walckiers D. Estimate of disease prevalence using drug consumption data. *Am J Epidemiol*. 1995; **141(8):** 782 – 787.
27. World Health Organization, Regional Health Systems Observatory-EMRO. Health system profile- Islamic Republic of Iran. Avilable form: URL: http://apps.who.int/medicinedocs/documents/s17294e/s17294e.pdf (Cited 2006).