National and Sub-national Burden of Breast Cancer in Iran; 1990–2013

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Abstract

Background: Estimating the burden of diseases, injuries and major risk factors is necessary for adopting appropriate health policies in every country, and this paper aims to explain the study protocol of national and sub-national burden of breast cancer in Iran from 1990 to 2013.

Methods: We will perform a systematic review of the confirmed databases and literature to gather data on breast cancer epidemiology in Iran. The definitions, data sources, organizing the team, methods of data gathering and data generating will be explained in this paper. The methodology of estimating the trend of prevalence, years of life lost due to premature death (YLLs), years of life lost due to disability (YLDs) and disability-adjusted life years lost (DALYs) of breast cancer by age groups, provinces and probable inequalities will be explained. We will tackle possible data problems due to the lack of data points on provinces and years and also geographical misalignment by using two advanced statistical methods, namely Bayesian autoregressive multilevel and Spatio-temporal models. Trend estimation will be reported using these two models together with uncertainty intervals.

Conclusion: This study provides a comprehensive assessment of breast cancer and its specific pattern in Iran. The results will help policy makers to know the trend of prevalence, the distribution, and the inequalities of breast cancer in Iran to allocate resources in a better way.

Keywords: Burden of diseases, breast cancer, Bayesian autoregressive multilevel model, spatio-temporal model, Iran

Study Protocol

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Introduction

Cancers are important health concerns and the cause of eight million deaths from 1990 to 2010 in the world. Among all cancers, breast cancer is the most common cancer in women in both developed and developing countries. The number of women diagnosed with breast cancer was 1.7 million in 2012, and there were 6.3 million women with a breast cancer diagnosed in the previous five years. It is now the cause of one in four of all cancers in women and the most frequent cancer among women in 140 of 184 countries. The most frequently diagnosed cancer in females of the Eastern Mediterranean Regional’s countries (EMRO) is also breast cancer.

The significant burden of this disease is the reason for its importance, and it was shown that a number of major developing economies such as India, China and Brazil will be facing breast cancer epidemics by 2020. Furthermore, breast cancer is a high-cost disease and imposes a remarkable pressure on financial resources of every country because of its high incidence and prevalence.

At a glance, the trend of breast cancer in the world shows that rapid societal and economic changes in developing countries made a shift towards the lifestyles of industrialized countries. This kind of lifestyle leads to an increase in the burden of cancers such as breast cancer - which are associated with reproductive, hormonal, and dietary risk factors. Although the incidence of this cancer is increasing in the world, there is great inequality between the poor and rich regions. In this regard, the incidence rate is higher in more developed countries, but the mortality is higher in less developed areas. This difference is due to better access to detection and treatments facilities in developed regions.

In Iran, cancers are the third cause of death after coronary heart disease and accidents and breast cancer is the most frequent cancer in women. Additionally, it is the fifth most common cause of death in Iranian women, and the first among diagnosed cancers in women who live in Tehran. The age of breast cancer incidence in Iran is about 10 years lower than Western countries, and there is a serious need for calculating its burden and making appropriate policies to prevent this cancer. Global Burden of Diseases (GBD) 2010 indicated that the mean death of all ages due to the breast cancer in Iran was 1932 per 100,000 with a mean DALY of 66765, a mean YLL of 63975 and a mean YLD of 2789.
Materials and Methods

Overview
In this paper, we will explain NASBOD study effort to estimate the trend of prevalence, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) of breast cancer by age groups and provinces and probable inequalities from 1990 to 2013. In addition, the uncertainty intervals related to the estimates of interest will be calculated.

Organizing working groups
An expert group consisting of an epidemiologist, a cancer surgeon, a gynecologist, and a health education specialist was formed. Since the panel will conduct the entire project and provide necessary advices for selecting the definition, it is necessary for panel members to have enough knowledge about the concepts of burden of diseases and the related skills for estimating the measures. Therefore, a series of workshops and meetings will be held to make all members familiar with the related topics.

Practical definition of breast cancer
Microscopic analysis of breast tissue is the most important indicator for breast cancer; therefore, only the diagnoses of breast cancer will be included in our study that have a histologic exam on specimens obtained by either needle or surgical biopsy.6

Data sources

Systematic reviews
We will use a systematic approach to form a database. The trend of prevalence and distribution of breast cancer will be extracted from the systematic review of the confirmed databases and literature. In the following sections, we will provide all details on data sources that will be used in this study.

Systematic reviews of the literature will be conducted using online search of international electronic databases: Web of Science, Scopus, and PubMed. Iranian search engines including IranMedex, Scientific Information Database (SID), and IranDoc will be searched, as well. Finally, we will search gray literatures on breast cancer.

Search strategy
Following the guidelines set by the scientific panel of NASBOD, we will search the main international electronic data sources which include medical data. To achieve the most comprehensive and efficient data, search terms used for the above mentioned medical electronic databases will be extracted using the Medical Subject Headings (MeSH) of PubMed (and entry terms or synonyms), and Emtree.

In addition, we will search IranMedex, Scientific Information Database (SID), and Irandoc, which are among the most comprehensive national electronic databases, with the most coverage of Iranian public health and medical journals.24

All of these six databases will be searched to find population-based studies related to the objectives of our study from January 1985 to December 2013, with no limitation in language.

Then, we will review and collect data from unpublished data sources such as governmental reports, project reports, conferences, and reference lists, in addition to all published abstracts, proceedings of international and national conferences, PhD or DSc dissertations, MSC, MSPH, MPH, and MD theses, reports in Persian language, and non-indexed Iranian English journals. Table 1 shows our search strategy and search terms for breast cancer in detail.

Inclusion criteria
Published papers and gray literature in English, published from January 1985 to December 2013, will be included. All papers that include data on prevalence and incidence from population-based or cross-sectional studies and registry systems will be selected. After extracting eligible papers, duplicated ones will be removed. Then, two experts will review the titles, abstracts, and finally the full-text of the articles. Two reviewers will use a checklist to critically appraise the full-text of selected articles. If there is any disagreement, the reviewers will discuss the eligibility of the articles and will decide about it. Studies which are not population-based will be excluded from our study.

Study selection process
The reviewer will check all titles. If they are not very far from our objectives, the articles will be selected. The same person will perform an abstract review to find whether or not the articles have reported the prevalence, distribution, and/or equality.

Quality assessment
The quality of every article will be assessed based on a “study characteristics sheet”. This form has three sections: a) general information about the selected article: a unique code will be allocated to each study, and its general information including name and characteristics of the corresponding author will be written at the top of the form; b) the quality of sampling: it refers to the response rate, sampling design, sampling type and sample size; c) the quality of measurement: such as self-report or pathologic based.

Each of the above items will obtain a score, and the total score will be calculated. Two reviewers will independently evaluate all selected articles via this method. In case of disagreement between the reviewers, consensus adjudication will be performed. One of
the members of the expert panel will control and confirm the decisions made by the reviewers.

Data extraction

After reviewing all selected articles, the needed information will be extracted and entered in the study characteristics sheet. This sheet has information on aggregated data including mean, standard error of mean, and the number of observations by each age-group, year and province. Scope of the study (urban/rural or both), coverage of the study, and other related variables will also accompany each of these data points. Data will be extracted from finally selected full-text articles. Then, data will be entered into electronic extraction sheets. We will contact the authors to take necessary information, if there are some articles in the final step that do not contain all required data. Selected articles should have the following items to be included in the extraction sheet: a) General information: study name, citation, the place of study, study year, journal, publication year, contact address of corresponding author, b) Population characteristics: age groups, c) Methodological information: study design, data source, coverage of the study (community, sub-national, and national levels), study scope (urban, rural), measurement tools, sampling method, sample size, sampling weight, and response rate, d) Study outcomes: prevalence, mortality (all stratified by age groups) presented with 95% uncertainty interval.

Other data sources

1) Cancer registry: All cancer reports throughout Iran are collected and analyzed by the Ministry of Health and Medical Education (MOHME) using a procedure, namely the National Cancer Registry (NCR) which is a population-based registration system. As breast cancer is diagnosed by biopsy, and its definitive diagnosis is by histologic tissue specimens obtained by different procedures such as needle biopsy or surgery, reports from pathology laboratories will be included in our study.

2) Death registry: Since accurate and complete cause-specific mortality data is an informative source for estimating the incidence of every disease, we will also use this registry system in our study. Death registry - like cancer registry - is administered by the MOHME. Death and cancer registration entail a degree of misclassification and incompleteness in a number of countries, including Iran. Therefore, we decided to use an accurate coding system to avoid any mistake in presenting cause-specific mortality and to compensate for the incompleteness of death registry.

3) National and sub-national surveys: The Non-Communicable Diseases Surveillance Survey (NCDSS) is one of the important surveys that has a STEP-wise approach according to WHO guidelines. The STEP survey data are available for six years (from 2005 to 2009 and 2011) but only the 2011 data includes information concerning breast cancer.

4) Inpatient data (Hospital data): Hospital discharge data is an important source for both acute and chronic diseases. Data will be collected about 0.5% of inpatient cases per year in each hospital (with at least 32 beds) from 1996 to 2013. All details about hospital registry system are explained in another paper.

5) Outpatient data: We also use prescriptions. For this purpose, a database consisting of 23 million pharmacies insurance claim records from three main Iranian health insurance organizations will be used. It contains information code including the name of medicine, potency, dosage form, number of each medicine, total price, insurance type and date of prescription, but no code related to the physician diagnosis. All details about the mentioned database are explained in another paper.

Statistical methods and analysis plans

Since there is no complete data for all years of our study, we will use two advanced statistical models, namely Spatio-temporal, and Bayesian autoregressive multilevel models, to estimate the prevalence and its uncertainty interval for each age group, province, and year. These models will use all available aggregated data. As some provinces have been divided into two or three distinct parts during our required period of time and are separated provinces now, misalignment will be addressed by both models. By using these two models, and comparing the results, we will assure that the results are not model-dependent.

The Spatio-temporal model in particular considers the spatial and temporal correlations using a conditional autoregressive (CAR) prior for spatial random effects. In this model, closer observations are assumed to be more correlated than farther ones.

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<th>Table 1. Search strategy of breast cancer.</th>
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<td><strong>Search strategy in PubMed/Medline</strong></td>
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**Archives of Iranian Medicine, Volume 17, Number 12, December 2014**
and this structure enables model borrowing information from the neighbor areal units to make estimations for areas with small number of observations and/or with missing values. Moreover, Spatio-temporal misalignment modeling lets us combine incompatible areal units between data sources and/or beyond the years. In this model, covariate effects, the quality of study, non-linear age trend, and the source of data variations will be considered. The covariates of our study include urbanization, years of schooling, wealth index, and food types.38

Another advanced statistical model that addresses all the above-mentioned problems is the Bayesian autoregressive multilevel model.39 In this model, observations at provinces, sub-regions, regions, and national levels will be respectively nested hierarchically. Structure levels of each hierarchy borrow information from each other and also from the upper hierarchy to improve estimates for areas with small number of observations and/or missing values. Furthermore, linear time trends, covariate effects, non-linear changes over the time, non-linearity associated with age, age-by-study variability, and heterogeneity of data sources are the components that will be included in this model. If practical, the estimation will also be performed using time-varying provincial-level and district-level covariates.

We will use the Markov Chain Monte Carlo (MCMC) method to fit both Bayesian autoregressive multilevel and Spatio-temporal models. R statistical package will be used for programming the models.

Discussion

Literature shows that among all diseases, cancers now considered the third leading cause of death worldwide, with more than 12 million new cases and 7.6 million cancer deaths estimated per year.40 By 2030, there will be more than 26 million of new cancer cases and 17 million cancer deaths per year.2,42 It is noticeable that the global distribution and types of cancer continue to change, especially in economically developing countries and the disparities among countries should be considered as the most fundamental evidence for better health policy.53 In the present study, we described the study protocol of breast cancer in Iran,13,20,26 which has a high pressure on the quality of life of affected patients and their family with a high cost for the country.53 In this way, there is a need for some changes in health actions such as policy making, planning and managing health programs, prioritizing, implementing and evaluating cost-effective educational interventions, training and allocating human and financial resources and implementing strategic researches on breast cancer.

After the Global Burden of Diseases (GBD) was introduced,18 its valuable results1,18,49–52 were used by researchers in the field of burden of diseases. Although assessing the Global Burden of Diseases study provides an estimation of diseases and risk factors profile for every country, only calculating the national and sub-national burden of diseases and risk factors can reveal the health status of population and the health services.53,54 The national burden of diseases studies could help to identify the underlying causes of morbidity and mortality in the country55 and makes it possible to take evidence-based health policies at local levels.54 On the other hand, performing the study on the burden of diseases at sub-national level may reveal the inequalities between all regions of a country.55 Therefore, following the GBD study, a number of countries assessed their Burden of Diseases (BOD) at different levels.22–24,40,41,53,54,56–65 Some of the countries - especially developed countries - have assessed BOD at national level, including the United States, Australia and New Zealand.54,57,58,60 Mexico has determined the burden of diseases at both national and sub-national levels.56 Taiwan and Switzerland determined BOD at sub-national level.56,59,60 Korea and Sudan51,62 assessed the burden of specific diseases, and Bur- kina Faso only estimated the Years of Life Lost (YLLs).63 In this regard, a study on the national burden of diseases and injuries was performed39 for six provinces of Iran in 2003, and over the past 10 years, there has been a need for a more comprehensive study. This need led Iranian health authorities to design the NASBOD study part of which is the present study. We can mention some advantages for this study compared with the first study on BOD in Iran, including: a) there is more literature on both breast cancer and GBD in comparison with the year 2003; b) there was no Persian search engine in 2003 but now we have access to various web-based Iranian search engines; c) nowadays, statistical methods of analysis have progressed; d) we will determine the burden of breast cancer at both national and sub-national levels; e) we will estimate uncertainty interval in our study.

In comparison with GBD, our results are mostly data-driven while GBD results are mostly model-driven. In addition, our study will be performed at sub-national level, then, the results will be classified based on districts and provinces (sub-national level) which will be more informative than national level.

Since one of the characteristics of our study is estimating the prevalence trend of breast cancer by age-groups and provinces and probable inequalities, it may lead policy makers to make the future planning on allocating resources for diseases – such as breast cancer - in a more appropriate way. Additionally, we can obtain valuable epidemiologic information about breast cancer in Iran. By recognizing the deficiencies, gaps and missing points in breast cancer information, the results of the study can be used for improving the infrastructure of health information and disease recording system in a way that the extraction of data on the burden, and the trend of prevalence of breast cancer can be routinely accessible. Collecting scientific evidences for prevalence and attributable burden of breast cancer leads health authorities to adopt necessary interventions for designing appropriate policies for breast cancer preventive programs. When we find the prevalence of breast cancer for every district and province, we can calculate the efficiency rate of diagnostic systems on the survival rate of breast cancer cases. Moreover, considering the fact that the survival rate of breast cancer varies by provinces in Iran,67 exploring probable inequalities in breast cancer distribution may lead health authorities to: a) adopt more effective decisions for managing this cancer based on geographical and regional determinants which affects the survival rate, b) think about the programs for screening and earlier detection of breast cancer.

There are some limitations in our study: a) our limited access to some of full-text articles is the main limitation of our study, hence, we will contact the authors to convince them for collaboration. However, we are expecting to have low response rates from the corresponding authors; b) there is also limited access to data at provincial level in Iran; therefore, we will use hierarchical models; c) when we use death registry65 in the study, incompleteness is one of the inevitable problems for which Generalized Growth
Balance, Synthetic Extinct Generation and a hybrid of these two methods will be used to meet this problem, and by using GPR, we will combine the three methods to correct and adjust the number of deaths. d) we will try to meet the scarcity and misalignment of data by using Spatio-temporal and Bayesian autoregressive multilevel models. e) uncertainty of the results is another limitation and we will try to reduce its impact through analyzing the heterogeneity; f) there will be some problems with missing data, especially at sub-national level that will be tackled by imputing missing data using the two above-mentioned statistical methods, and proxy covariates and extrapolating to every province-year.

Ethical considerations

The Ethics Committee of EMRI has approved this study, and we will take permission from study funders to publish the results.

Summary and conclusion

By determining the burden of breast cancer both at national and sub-national levels in Iran, we will know more about the prevalence of this cancer in the country. Additionally, we determine possible inequalities in the distribution of breast cancer and its determinants throughout the country. The results of this study can contribute to enhancing the knowledge about cost-effective interventions for primary and secondary prevention services.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

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Manuscript revision: Dr. Shohreh Naderimaghram, Dr. Farshad Farzadfar, Shirin Djalalalnia, Amir Kasaean, Dr. Ardeshir Khosravi, Dr. Hamid Reza Jamshidi

Approval: All authors have read and approved the content and the authorship of the final version of the submitted manuscript.

Acknowledgments

The study is granted by the Ministry of Health and Medical Education of Islamic Republic of Iran and Setad-e-Ejraie Farmane Imam. We would also like to express thanks to Dr. Masoud Moradi for his precise editing of the text and Ms. Rosa Haghshenas for her efforts in managing coordinative and administrative processes.

References


