Study Protocol

National and Sub-national Prevalence, Trend, and Burden of Metabolic Risk Factors (MRFs) in Iran: 1990 – 2013, Study Protocol

Niloofar Peykari MSc PhD Candidate[1,2,3], Sadaf G. Sepanlou MD MPH PhD Candidate[4,2], Shirin Djalalinia PhD Candidate[1,2,3], Amir Kasaeian PhD Candidate[2,5], Mahboubeh Parsaeian PhD Candidate[2,5], Alireza Ahmadvand MD PhD Candidate[2,5], Jalil Koohpayehzadeh MD PhD[6], Behzad Damari MD PhD[7], Hamid Reza Jamshidi PhD[8], Bagher Larijani MD•[1], Farshad Farzadfar MD MPH DSc•[1,2]

Abstract

Background: Non-communicable diseases (NCDs) and their risk factors are the major public health problems. There are some documented trend and point estimations of metabolic risk factors for Iranian population but there are little information about their exposure distribution at sub-national level and no information about their trends and their effects on the population health.

Methods: The present study protocol is aimed to provide the standard structure definitions, organization, data sources, methods of data gathering or generating, and data on trend analysis of the metabolic risk factors in NASBOD study. We will estimate 1990 to 2013 trends of prevalence, years of life lost due to premature mortality (YLLs), and years lived with disability (YLDs) and disability-adjusted life years DALYs for MRFs by gender, age group, and province. We will also quantify the uncertainty interval for the estimates of interest.

Conclusion: The findings of study could provide practical information regarding metabolic risk factors and their burden for better health policy to reduce the burden of diseases, and to plan cost-effective preventive strategies. The results also could be used for future complementary global, regional, national, and sub national studies.

Keywords: Burden, metabolic risk factors, prevalence, trend

Cite this article as: 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.

Introduction

It is stated over and over that epidemiological transition from communicable to non-communicable diseases (NCDs) is an evident sign of socioeconomic advancement in developing countries.[1] However, there is not enough evidences regarding the drivers of the transition which are necessary for directing health policies and programs at national or sub-national scales.[2] The Global Burden of Disease (GBD) Studies in 1990, 2000, and 2013 have revealed that metabolic risk factors are by far the most important determinants of emerging non-communicable diseases all over the world.[3–9]

Authors' affiliations: [1]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran, [2]Non-communicable Diseases Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, Iran, [3]Development of Research & Technology Center, Deputy of Research and Technology, Ministry of Health and Medical Education, Tehran, Iran, [4]Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran, [5]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran, [6]Community Medicine Department, Iran University of Medical Sciences, Tehran, Iran, [7]Health Information Managment Research Center, Tehran University of Medical Sciences, Tehran, Iran, [8]School of Medicine, Department of Pharmacology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
•Co-equal senior corresponding authors: Farshad Farzadfar MD MPH DSc, Non-communicable Diseases Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Address: 4th floor, No. 4, Ostad Nejatollahi St, Enqelab Ave, Tehran, Iran. Postal code: 1599666615.Tel/Fax: 98-21-88913543, E-mail: f-farzadfar@tums.ac.ir.
Bagher Larijani MD, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran. E-mail: Larijanib@tums.ac.ir
Accepted for publication: 3 December 2013

Reliable information on the trends of metabolic risk factors are needed for assessing population health status, priority setting, and program evaluation.[10,11] The trend of metabolic risk factors and their attributed burden depicts their pandemic.[4,12–16] Based on GBD 2010 results, high blood pressure, high total cholesterol, high body mass index, and high fasting plasma glucose respectively account for the 53 %, 29 %, 23 %, and 16 % of global Disability-Adjusted Life-Year (DALY).[4]

Developing countries in the Middle East are experiencing a steep rise in metabolic risk factors[12,13,15,16] leading to situation in which this region will observe one of the world's greatest increases in the absolute burden of NCDs and their risk factors in the near future.[6]

Even though there are trend and point estimations of metabolic risk factors for Iranian population[8, 15,17–19] there are little information about their exposure distribution at sub-national level and no information about their trends and their effects on the population health.[14,15,18]

Trend analysis of the metabolic risk factors is a sub-component of National and Sub-nation Burden of Diseases, Injuries, and Risk Factors from 1990 to 2013 (NASBOD) study in Iran,[20] which aims to quantify metabolic risk factors exposures and related attributed burdens and their trends and inequalities at national and sub-national levels. To the best knowledge of authors of this paper, there are few studies in developed and developing countries which provide estimations of trends of the risk factors exposure at sub-national (small area estimation) level.

This paper aims to explain definitions, organization, data sources, methods of data gathering or generating, and data on trend analysis of the metabolic risk factors in NASBOD study.

Methods and Materials

Overview

NASBOD is a multidisciplinary study that was introduced in 2012 through participation of key stakeholders at national and sub-national levels and with the support of Ministry of Health and Medical Education of Iran.[20] One of the sub groups of NASBOD team is the metabolic risk factors group that has benefited from local and international members and consultants from Tehran University of Medical Sciences, Harvard School of Public Health, and Imperial College London.

The team focuses on obesity and overweight, truncal obesity, high blood pressure, high blood glucose, hyperlipidemia and metabolic syndrome. We chose these risk factors based on the magnitude of their exposures, their trends and effect size,[14] and related data available at national and sub-national levels.[17, 18, 21] We will use mean and standard deviation of metabolic risk factors exposure or reported prevalence of high-risk groups for each risk factor by sex, age, and year at national and sub-national levels to be able to estimate and report the prevalence of metabolic risk factors by sex, age, year at national and sub-national form 1990 to 2013 (Table 1).

In the next step, using age-standardized prevalence of high-risk groups, the socioeconomic or geographical inequalities at national and sub-national levels will be evaluated. In the last step of the study, using directions and magnitudes of risk factors' effects on population health,[14] and risk factor exposure distributions, the theoretical minimum for each risk factor[12,13,15,16] as well as distribution of related DALYs,[8,10] and the health effect of each metabolic risk factor will be estimated. For all point estimations the sampling and model uncertainties will be quantified. In order to realize the study's objectives, we have adopted a comprehensive strategy for identifying available data sources, quality assessment, data extraction, and analyses. Figure 1 shows an overview of the study process.

Data sources

Systematic Literature Review

Through the scientific panel, we choose PubMed/Medline, Institute of Scientific Information (ISI), and SCOPUS as the main international electronic data sources. We will search these data sources using Mesh terms, Emtree, and related key words to obtain the most comprehensive and efficient hits.

On the other hand, IranMedex, Irandoc, and Scientific Information Database (SID) are chosen from among Iranian databases as the comprehensive national electronic data sources covering 89 % of Iranian medical and public health journals and with an access to gray literature. We will search all databases in order to identify population-based studies related to our objectives, published between 1985 and 2013. We will limit the search terms to adults but there is no limitation on language.

Search strategies are presented in appendix A.

In addition to electronic searches, we will consider manual searches for reviewing unpublished data sources such as governmental reports, projects' reports, conferences, and reference lists. In some cases, we will contact experts in the relevant fields and will ask for more information on their research results.

Selection criteria

Our study will include all National, provincial, district and community based studies from Jan 1985 to Dec 2013, that have reported the mean risk factor exposures in a continuous scale or the prevalence / incidence of high risk groups for each risk factors in a categorical scale in population level. Our target population is adults ($\geq$ 25 years). The studies that focused on special populations such as patients, employees, volunteers, immigrants, and also hospital-based studies will be excluded.

Study selection Process

In the study selection process, a reviewer skims the titles. The articles that do not look completely remote from our search objectives will be evaluated more in the next level. The abstract review phase is designed to identify studies reporting the prevalence, incidence, Mean ± SD and Mean ± SE of metabolic risk factors and other related indexes. Abstracts will be excluded if they meet one or more exclusion criteria. Then, the articles included based on abstract review will undergo independent parallel review to determine if they should be included for data extraction. Disagreements between reviewers regarding article inclusion or exclusion will be resolved through consensus adjudication.

Quality assessment

Quality assessment form has three parts: general information about the study, sampling quality, and measurement quality. Each study has a unique code and its general information such as the name and characteristics of the corresponding author are inserted at the top of the form. The sampling quality refers to response rate, sample size, and sampling design and the measurement quality includes type of measurement tools, calibration, and accuracy of measurement methods for each risk factor. Accordingly, each item obtains a score. For example, table 2 presents the quality assessment form of articles related to blood glucose measurement and sampling. Based on total score, the quality of article might be ranked as excellent (13 –19), good (6 – 12) or poor ($\leq$ 5). The quality score will be calculated for all included papers and its fixed effect will contribute to the model.

Data extraction

All included studies will be reviewed and the required information will be extracted and inserted in data extraction sheet. As an example, the main part of data extraction sheet of blood glucose studies is shown in table 3. In brief, the data extraction sheet contains detailed information on mean, standard deviation, standard error of mean, and the number of observations for each risk factor by age, sex, province/district of the country, year, coverage of the study (representativeness), scope of study (rural/urban/both), and other related variables such as fasting for fasting plasma glucose.

National Data Sources

National surveys, which are considered as the "secondary data sources" in the context of epidemiology and public health, are the next important resources of information for this study. One of the important surveys is the Non-Communicable Disease Surveillance Survey (NCDSS) following a STEPwise approach based on WHO guidelines. The STEP surveys' data are available for 6 years until the end of study duration; they are the only complete existing national data sources however they have their own shortcomings for instance they have only included consistent and unique data files and they have cleaned all kind of contaminated data (non-plausible values and outliers).

Table 1. Practical definition of metabolic risk factors

Metabolic Risk Factor	Classic Definition	Practical Definition		
High Body Mass Index (BMI)	The body mass index (BMI) is a measure for human body shape based on an individual's weight and height.	***Category***	***BMI range kg/m²***	
		Very severely underweight	< 15	
		Severely underweight	15.0–16.0	
		Underweight	16.0–18.5	
		Normal (healthy weight)	18.5–25	
		Overweight	25–30	
		Obese Class I (Moderately obese)	30–35	
		Obese Class II (Severely obese)	35–40	
		Obese Class III (Very severely obese)	> 40	
High Blood Pressure(BP)	Blood pressure (BP) refers to the arterial pressure of the systemic circulation.	***Category***	***systolic, mmHg***	***diastolic, mmHg***
		Hypotension	< 90	< 60
		Desired	90–119	60–79
		Prehypertension	120–139	80–89
		Stage 1 Hypertension	140–159	90–99
		Stage 2 Hypertension	160–179	100–109
		Hypertensive Crisis	≥ 180	≥ 110
High Fasting Plasma Glucose (FPG)	Blood glucose level is the amount of glucose present in the blood.	***Category***	***Fasting glucose mg/dl***	***Fasting glucose mmol/l***
		Normal	< 110	< 6.1
		Impaired fasting glycaemia	110–126	6.1–7
		Diabetes mellitus	> 126	> 7
High Total cholesterol (TC)	Total cholesterol is the amount of LDL and HDL in the blood.	***Category***	***TC range mg/dl***	***TC range mmol/l***
		Normal blood TC	<200	< 5.2
		Borderline blood TC	200–239	5.2–6.2
		High blood TC	> 240	> 6.2

Table 2. Quality assessment form for blood glucose studies

Question	Response	Score
Quality of measurement		
Fasting time fasting more than 8= 2 fasting less than 8 = 0		
Method of measurement Enzyme-based- automated = 2 Enzyme-based- manual = 1 Chemical –based- manual/not reported=0		
Calibration One center - using one kind of equipments= 2 Multi center -using one kind of equipments= 1 Multi center -using different kinds of equipments/ not reported = 0		
Time difference between loading sample and analyzing it Less than 7 days= 2 More than seven days= 0		
Quality of sample		
Response rate for taking sample Over 90% = 6 76-90% = 4 60-75% = 2 Less than 60% / not reported = 0		
Sample size by gender over 1000 = 3 500-1000 = 2 250-500 = 1 Less than 250 = 0		
Sampling design Simple random sampling = +3 One-stage systematic, clustered, or stratified sampling =+2 Multi-stage clustered stratified= +1		
TOTAL SCORE		

Table 3. The main part of data extraction sheet of blood glucose studies

ID	Female	Age_Start	Age_End	Median Age Range	Sample Size	Measure	Blood drawn from Vein=1 Capillary=2	Glucose measured in Plasma=1 Serum=2 Whole blood=3	Measurement method lab=1 Portable meter=2	Unit	Mean	SD	Lower Level of 95% CI	Upper Level of 95% CI	SEM	Prevalence of Diabetes Mellitus (Percentage)
BG-10053	1	19	29	24	131	FPG	1	3	1	mg/dl	93.8	9.5	–	–	–	0
BG-10053	1	30	39	34.5	241	FPG	1	3	1	mg/dl	92.2	11.9	–	–	–	1.4
BG-10053	1	40	49	44.5	340	FPG	1	3	1	mg/dl	95.8	11.4	–	–	–	8.3
BG-10053	1	50	59	54.5	276	FPG	1	3	1	mg/dl	100.8	13.7	–	–	–	9.6
BG-10053	1	60	70	65	212	FPG	1	3	1	mg/dl	99.4	13	–	–	–	11.7
BG-10053	0	19	29	24	222	FPG	1	3	1	mg/dl	93.8	13.6	–	–	–	1.1
BG-10053	0	30	39	34.5	241	FPG	1	3	1	mg/dl	95.6	12.3	–	–	–	2.7
BG-10053	0	40	49	44.5	204	FPG	1	3	1	mg/dl	96.9	12.9	–	–	–	6.1
BG-10053	0	50	59	54.5	181	FPG	1	3	1	mg/dl	103.1	11.9	–	–	–	10.5
BG-10053	0	60	70	65	152	FPG	1	3	1	mg/dl	104.3	15.5	–	–	–	12.5

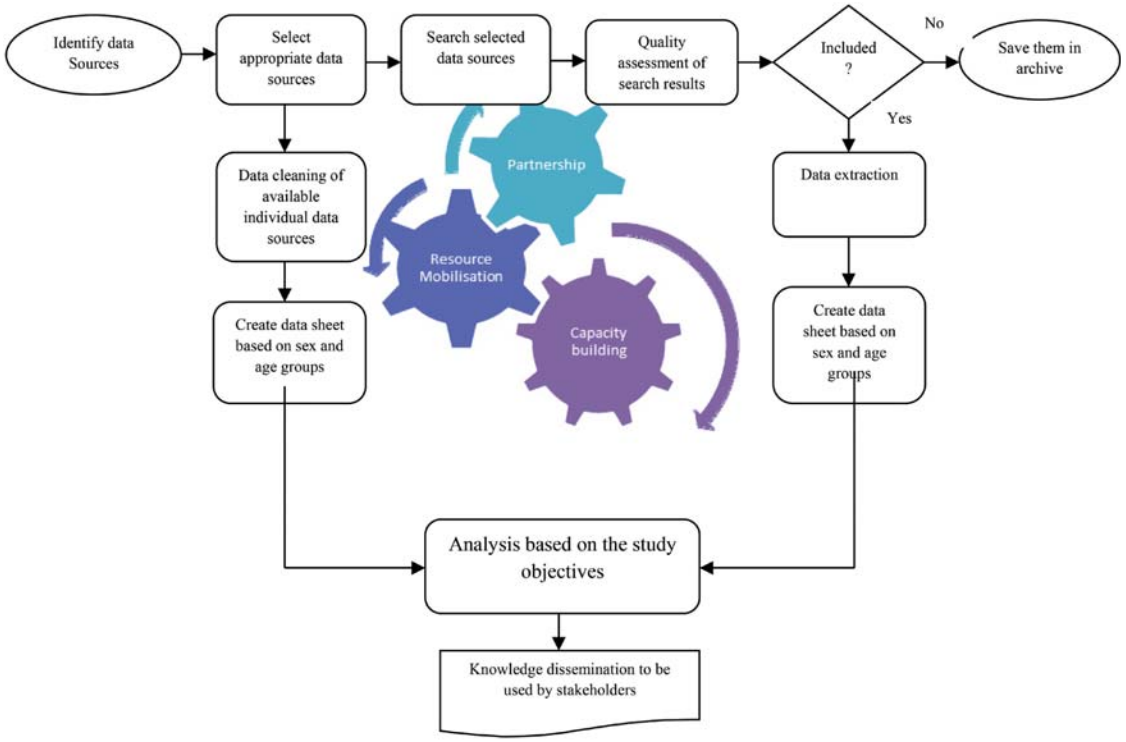

Figure 1. Study Process

The second and third national surveys are National Health Survey (NHS) in 1990 and 2000, and Demographic and Health Surveys (DHS) in 1992 and 1999, which mainly cover the first half of study duration for four distinct years. Nevertheless, one of the DHS data sources has not been accessible for the researchers of this study so far. We hope that we can attain the consent of its trustee before the beginning of analyses phase.

Further Data Sources

In addition to these national data sources and other published data, there are other community-based and provincial-based surveys such as Golestan Cohort Study, Tehran Lipid and Glucose Study, Isfahan Healthy Heart Program, and Persian Gulf Healthy Heart Study as other possible available data. It should be noted that sub-national and community studies might systematically differ from national representative ones because they might be undertaken in low-level or high-level zones and regions for each risk factor. They might also have more variation than national studies. This kind of variation will be dealt with using models in order to include an offset for sub-national and community data which will be empirically estimated and will allow weighting all data sources in order to give more weight to national data and low weight to sub-national and community data.

Dealing with data scarcity

Despite our extensive data searches, many age-sex-province-years and age-sex-district-years data points are missing, which lead to geographical and temporal scarcity of data. Moreover, because of measurement difficulties, a little number of health surveys has collected data about the measurements of risk factors such as serum total cholesterol and fasting blood glucose or they have just collect risk factors data in areas with specific diseases. Some data sources only cover certain age or sex groups, or are restricted to either rural or urban populations. The data scarcity patterns are vivid for older ages as well. Therefore, we have three types of scarcity; geographical, temporal, and old-age scarcity.

We will use a model that will combine information from available data sources to estimate mean of metabolic risk factors for each district × year × age or province × year × age. The model "borrows strength" across districts in the same province, across provinces in the same sub region, and across sub regions in the same regions, also time, age, and covariates to smooth over those places in the dataset where information is scarce. More important, it quantifies the uncertainty of the resulting estimates, which will be reflected in slightly conservative estimates and wider uncertainty intervals.

It is worth mentioning that we will do all analyses by sex, because levels of risk factors and trends can differ between men and women.

Statistical methods and analysis plans

It is expected that in contempt of our extensive search and access to all national surveys, there will be many provinces without data or without provincial representative data for many provinces. Moreover, many surveys do not include all age groups, both sexes, and/or both rural and urban areas of residency. We developed two distinct statistical models including spatio-temporal model and multilevel autoregressive model, to estimate mean (whatever the measure is) and its uncertainty interval by sex, age, year, and province. The models will be filled out by data of specific sex, age, year, and province and by other sex, ages, years, and provinces. For the provinces, which have become separated from other provinces in the desired period of time, the problem of misaligned areal units does exist. The problem is going to be addressed in both models. We are using two models to make sure that there is no model dependency in the results.

Bayesian Multilevel Autoregressive model

Another advanced method to handle previously mentioned challenges is Bayesian multilevel autoregressive model.[22] In this framework, observations are hierarchically nested in districts, provinces, sub-regions, regions, and national levels, respectively. In this hierarchical model, higher levels borrow information to the lower levels and units in each level borrow information to each other depending on the degree of data availability. The model considers several different components including linear time trends, nonlinear change over time, covariate effects, nonlinearity associated with age, heterogeneity of data sources, and age-by-study variability. Time-varying district-level or province-level covariates provide the estimates if practical.

Spatio-temporal model

One of the commonly used frameworks to overcome the above-mentioned issues is Spatio-temporal Bayesian hierarchical modeling with conditional autoregressive (CAR) prior for spatial random effects.[23] In spatial framework, observations, which are closer in space, are assumed to be more correlated than observations farther away. This structure enables model to "borrow information" from neighboring areal units to improve estimates for areas with missing values and/or with small number of observations. In addition, we will employ spatio-temporal misalignment modeling to combine incompatible areal units between data sources and/or over the years. The model includes covariates effects, non-linear age trend, and variations in study quality and source of data.

In both modeling frameworks, because of general applicability and ease of implementation the MCMC methods will be used to perform Bayesian inference. All programs will be written in R statistical packages (version 3.0.1).

In addition to these challenges, the other problem is about summary statistics that have been reported with different classifications. Using regression models, we cross walk between continuous and categorical measures of variables of interest.

Ethical considerations

All of the studies that will be included in our review will be cited in all reports and all publications of our study. Whenever we need more information about a certain study, we will contact the corresponding authors and will obtain the required information via reanalyzing data, which will make the author of that paper our collaborating coauthor. It is worth mentioning that our study has been approved by the ethical committee of Tehran University of Medical Science.

Discussion

The current study will have numerous achievements. To put it in a nutshell, this study will produce scientific evidences for the prevalence and attributable burden of metabolic risk factors- namely systolic blood pressure (SBP), body mass index (BMI), fasting plasma glucose (FPG), and total cholesterol (TC) - inequality in distribution and burden attributable to these risk factors, their

trend from 1990 to 2013, and prediction models with significant implications for policy making. This study will be conducted at sub-national scale so that inequalities between regions will be revealed and health policies and programs can be designed accordingly.[24] As mentioned in methodology, several sources of data and new quantitative methods will be used for our estimations, so that the probable low quality of data will be adjusted.

The Global Burden of Diseases Study was conducted at regional and national levels from 1990 to 2010.[4–7,25–31] Consequently, a number of studies at national levels were conducted, namely in United Kingdom and Australia[32,33] and in South Africa and Mexico.[34,35] The present study has certain advantages over the aforementioned estimations. First and most importantly, compared with previous studies, we have more data points at national and sub-national levels which make it possible to estimate the prevalence and attributable burden of risk factors with higher quality. Second, we have built the capacity for research centers and researchers across the country to participate in the project, which will provide an opportunity to collect high quality data at sub-national scale.

The national burden of disease study, which was conducted in Iran for the first time in 2003 did not include burden attributable to the risk factors in its estimations. The first study on burden attributable to risk factors was conducted in 2005 and was published in 2011; however, the results of this study were regional rather than provincial. Moreover, they were cross-sectional.[14] Thus, the need for reproducing a more comprehensive study after almost a decade is evident. Our present study has certain advantages over previous studies in Iran. Furthermore, in comparison with sub-national studies conducted in a number of other countries, our study is superior.[33,34] The population-based Non-Communicable Disease Surveillance Survey following a STEPwise approach provides data on measured BMI, FPG, SBP, and TC and their trends at national and provincial scale.[36] Additionally, as mentioned in methods, we have access to more comprehensive national studies relative to previous burden of disease study in Iran, and thanks to web-based Iranian search engines, we have also more access to a number of community-based epidemiological studies at smaller scales are also available that will be captured by systematic review of published and unpublished documents. Based on these data sources, YLD along with YLL (and consequently DALYs) can be estimated, which is an advantage over other subnational studies that were restricted to mortality.[32–34] Trends and inequalities can be estimated by province, sex, age, and area (rural and urban).

Our study has certain limitations as well. There is a misalignment between the sources of covariates and the source of outcomes of interest. The difference in nature of these two sources of data will impose evident noise on our estimations. To deal with this problem, we have developed a number of new statistical models.

The second limitation affecting our study is scarcity of data on FPG and TC since they need blood samples. In the main source of the current study, the non-communicable diseases surveillance survey, blood samples have been taken just in 2005, 2007, and 2011, which affects the accuracy of estimates on trends.

The third limitation threatening our estimations is the fact that estimating the joint effect of metabolic risk factors and their joint contribution to burden of disease is not possible. In previous studies, the joint effects have been calculated by assuming that these risk factors are independent from each other. The assumption affects the accuracy of estimations. Ultimately, there may be limited access to the full texts of certain published or unpublished epidemiological studies because of unwillingness of authors to participate in the study. The problem will partly be dealt with by contacting the authors of those studies.

The knowledge produced on distribution of metabolic risk factors across the country, regarding the costs of their control, can be an invaluable guide for relevant population-based interventions. The next step of upcoming plan of Non-Communicable Diseases Research Center will be estimating the allocative efficiency of health plans in the field of metabolic risk factors.

The results of the current study can be used for priority setting and policy making at both national and sub-national levels. The difference in estimated burden between regions has many distinct policy implications as both the exposure to the risk factors and their attributable burden may be quite different, which requires different and relevant health policies and programs at sub-national level. The inequalities between regions can also be a guide for just planning at sub-national level. Finally, the most important characteristic of this study is its trend analysis, which can make future projections and planning feasible.

This study can provide implications for improving information system in our country. By revealing the defects and missing points in health information system, the results of the study can be used for planning a health infrastructure capable of monitoring exposures to risk factors, their burden, their trend, and consequently can create a platform for planning cost-effective policies at sub-national level. The results of the study can be invaluable for future research at sub-national and national level, regional, and even global level. The knowledge acquired in this study will be disseminated at various scales through publications, workshops, symposiums, and training courses.

In conclusion, the present study is the first comprehensive systematic study on the prevalence, trend, and burden of Metabolic Risk Factors (MRFs) for the Iranian population at national and sub-national levels. The findings could provide practical information regarding metabolic risk factors and their burden for better health policy to reduce the burden of diseases, and to plan cost-effective preventive strategies. The results also could be used for future complementary global, regional, national, and sub-national studies.

Abbreviations

NCDs: Non-communicable diseases; GBD: Global Burden of Disease; NASBOD: National and Sub-national Burden of Disease; MRFs: Metabolic Risk Factors; DALY: Disability-Adjusted Life Years; YLL: Years of Life Lost due to premature mortality; YLD: Years of Life Lost due to Disability;

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

General designing of the paper was by the NASBOD core team. Niloofar Peykari, Sadaf G. Sepanlou, Shirin Djalalinia, Amir Kasaeian had equal contribution as the first authors. All co-authors had contribution in the general designing of paper, designing of systematic review, primary draft preparation, and revision. All authors have given approval to the final version of the manuscript.

Acknowledgments

The study is granted by Ministry of Health and Medical Education of Islamic Republic of Iran and Setad-e-EjraieFarmane Imam. This article is extracted from Ph.D. students' thesis. 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 on managing coordinative and administrative processes. we would also like to express thanks to Mr. Ali Rafei for his helpful cooperation.

References

1. Tunstall-Pedoe H. Preventing Chronic Diseases. A Vital Investment: WHO Global Report. Geneva: World Health Organization, 2005.
2. Chan M. From new estimates to better data. *Lancet*. 2012; **380(9859):** 2054.
3. Mathers CD, Fat DM, Boerma J. The global burden of disease: 2004 update: World Health Organization; 2008.
4. 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*. 2013; **380(9859):** 2224 – 2260.
5. Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. GBD 2010: a multi-investigator collaboration for global comparative descriptive epidemiology. *Lancet*. 2012; **380(9859):** 2055 – 2058.
6. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet*. 1997; **349(9064):**1498 – 1504.
7. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet*. 1997; **349(9063):** 1436 – 1442.
8. Alwan A. Global status report on noncommunicable diseases 2010: World Health Organization; 2011.
9. Lopez AD. The evolution of the Global Burden of Disease framework for disease, injury and risk factor quantification: developing the evidence base for national, regional and global public health action. *Global Health*. 2005; **1(5):** 1 – 8.
10. Mathers C, Stevens G, Mascarenhas M. Global health risks: mortality and burden of disease attributable to selected major risks: World Health Organization; 2009.
11. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ. Selected major risk factors and global and regional burden of disease. *Lancet*. 2002; **360(9343):** 1347 – 1360.
12. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, Cowan MJ, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5· 4 million participants. *Lancet*. 2011; **377(9765):** 568 – 577.
13. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2· 7 million participants. *Lancet*. 2011; **378(9785):** 31 – 40.
14. Farzadfar F, Danaei G, Namdaritabar H, Rajaratnam JK, Marcus JR, Khosravi A, et al. National and subnational mortality effects of metabolic risk factors and smoking in Iran: a comparative risk assessment. *Popul Health Metr*. 2011; **9(1):** 55.
15. Farzadfar F, Finucane MM, Danaei G, Pelizzari PM, Cowan MJ, Paciorek CJ, et al. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3· 0 million participants. *Lancet*. 2011; **377(9765):** 578 – 586.
16. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9· 1 million participants. *Lancet*. 2011; **377(9765):** 557 – 567.
17. Asgari F, Aghajani H, Haghazali M, Heidarian H. Non-communicable diseases risk factors surveillance in Iran. *Iran J Public Health*. 2009; **38**: 119 – 122.
18. Esteghamati A, Meysamie A, Khalilzadeh O, Rashidi A, Haghazali M, Asgari F, et al. Third national Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007) in Iran: methods and results on prevalence of diabetes, hypertension, obesity, central obesity, and dyslipidemia. *BMC Public Health*. 2009; **9(1):** 167.
19. Naghavi M, Abolhassani F, Pourmalek F, Lakeh MM, Jafari N, Vaseghi S, et al. The burden of disease and injury in Iran 2003. *Popul Health Metr*. 2009; **7(1):** 9.
20. 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.
21. Esteghamati A, Gouya MM, Abbasi M, Delavari A, Alikhani S, Alaedini F, et al. Prevalence of Diabetes and Impaired Fasting Glucose in the Adult Population of Iran National Survey of Risk Factors for Non-Communicable Diseases of Iran. *Diabetes care*. 2008; **31(1):** 96 – 98.
22. 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.
23. 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.
24. Di Cesare M, Khang Y-H, Asaria P, Blakely T, Cowan MJ, Farzadfar F, et al. Inequalities in non-communicable diseases and effective responses. *Lancet*. 2013; **381(9866):** 585 – 597.
25. 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.
26. 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 groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2013; **380(9859):** 2095 – 2128.
27. 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.
28. Salomon JA, Vos T, Hogan DR, Gagnon M, Naghavi M, Mokdad A, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. *Lancet*. 2013; **380(9859):** 2129 – 2143.
29. 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 2010. *Lancet*. 2013; **380(9859):** 2144 – 2162.
30. 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*. 2013; **380(9859):** 2163 – 2196.
31. 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 2010. *Lancet*. 2013; **380(9859):** 2071 – 2094.
32. Asaria P, Fortunato L, Fecht D, Tzoulaki I, Abellan JJ, Hambly P, et al. Trends and inequalities in cardiovascular disease mortality across 7932 English electoral wards, 1982–2006: Bayesian spatial analysis. *Int J Epidemiol*. 2012; **41(6):** 1737 – 1749.
33. Begg SJ, Vos T, Barker B, Stanley L, Lopez AD. Burden of disease and injury in Australia in the new millennium: measuring health loss from diseases, injuries and risk factors. *Med J Aust*. 2008; **188(1):** 36 – 40.
34. Bradshaw D, Nannan N, Groenewald P, Joubert J, Laubscher R, Nijilana B, et al. Provincial mortality in South Africa, 2000-priority-setting for now and benchmark for the future. *S Afr Med J*. 2008; **95(7):** 496 – 503.
35. Stevens G, Dias RH, Thomas KJ, Rivera JA, Carvalho N, Barquera S, et al. Characterizing the epidemiological transition in Mexico: national and subnational burden of diseases, injuries, and risk factors. *PLoS medicine*. 2008; **5(6):** e125.
36. Bonita R, Magnusson R, Bovet P, Zhao D, Malta DC, Geneau R, et al. Country actions to meet UN commitments on non-communicable diseases: a stepwise approach. *Lancet*. 2013. **381(9866):** 575 – 584.

Appendix A: Search Strategy of Metabolic Risk Factors

High Body Mass Index (BMI)
Search strategy in PubMed/Medline ("Body Mass Index"[Mesh] OR "Body Mass Index"[All Fields] OR "Overweight"[Mesh]) OR "Overweight"[All Fields] OR "Obesity"[Mesh] OR "Obesity"[All Fields] OR "Quetelet* Index"[All Fields] AND ("Iran"[Mesh] OR "iran"[All Fields]) OR Iranian[All Fields] OR I.R.Iran[All Fields] OR "I.R Iran"[All Fields] OR ("persia"[MeSH Terms] OR "persia"[All Fields])) AND (("1985/01/01"[PDAT]: "2013/12/31"[PDAT]) AND "humans"[MeSH Terms])
Search strategy in ISI Web of Science Time span=1990-2013. Databases=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH. Topic= ("Body Mass Index" OR "Overweight" OR "Obesity" OR "Quetelet* Index") AND (("Iran" OR Iranian OR I.R.Iran OR "persia") OR Address= (Iran))
Search strategy in Scopus (TITLE-ABS-KEY (Body Mass Index" OR "Overweight" OR "Obesity" OR "Quetelet* Index")) AND (TITLE-ABS-KEY (Iran OR Iranian OR I.R.Iran OR Persia) OR (AFFIL (Iran)) AND PUBYEAR > 1989 AND PUBYEAR < 2013
High Blood Pressure (BP)
Search strategy in PubMed/Medline ("Hypertension"[Mesh] OR ("hypertension"[MeSH Terms] OR "hypertension"[All Fields]) OR ("prehypertension"[MeSH Terms] OR "prehypertension"[All Fields]"pre-hypertension"[All Fields] OR "Blood Pressure"[All Fields] OR "systolic pressure"[All Fields] OR "diastolic pressure"[All Fields] OR "pulse pressure"[All Fields] OR "hypertensive*"[All Fields]) AND ("Iran"[Mesh] OR "iran"[All Fields]) OR Iranian*"[All Fields] OR I.R.Iran"[All Fields] OR "IR. Iran"[All Fields] OR ("persia"[MeSH Terms] OR "persia"[All Fields])) (("1985/01/01"[PDAT] : "2013/12/31"[PDAT]) AND ("humans"[MeSH Terms]))
Search strategy in ISI Web of Science Time span=1990-2013. Databases=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH. Topic= ("Hypertension" OR "prehypertension" OR "Blood Pressure*" OR "pre-hypertension" OR "systolic pressure" OR "diastolic pressure" OR "pulse pressure" OR "hypertensive" OR "hypertensives") AND (("Iran" OR Iranian OR I.R.Iran OR "persia") OR Address= (Iran))
Search strategy in Scopus (TITLE-ABS-KEY ("Hypertension" OR "prehypertension" OR "pre-hypertension" OR "Blood Pressure*" OR "systolic pressure" OR "diastolic pressure" OR "pulse pressure" OR "hypertensive" OR "hypertensives") AND (TITLE-ABS-KEY (Iran OR Iranian OR I.R.Iran OR Persia) OR (AFFIL (Iran)) AND PUBYEAR > 1989 AND PUBYEAR < 2013
High Fasting Plasma Glucose (FPG)
Search strategy in PubMed/Medline (("Diabetes Mellitus"[Mesh] OR "Diabetes Mellitus"[All Fields] OR "Hyperglycemia"[Mesh]) OR "Hyperglycemia"[All Fields] OR "Hyperglycemias"[All Fields] OR "Glucose Intolerance"[Mesh] OR "Blood Glucose"[Mesh]) AND "Blood Glucose"[All Fields] OR "Blood Sugar"[All Fields] OR "Fasting Plasma Glucose"[All Fields] AND ("Iran"[Mesh] OR "iran"[All Fields]) OR Iranian[All Fields] OR I.R.Iran[All Fields] OR "I.R Iran"[All Fields] OR ("persia"[MeSH Terms] OR "persia"[All Fields])) AND (("1985/01/01"[PDAT] : "2013/12/31"[PDAT]) AND "humans"[MeSH Terms])
Search strategy in ISI Web of Science Time span=1990-2013. Databases=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH. Topic= ("Diabetes Mellitus" OR "Hyperglycemia" OR "Hyperglycemias" OR "Glucose Intolerance" OR "Blood Glucose" OR "Blood Sugar" OR "Fasting Plasma Glucose" AND (("Iran" OR Iranian OR I.R.Iran OR "persia") OR Address= (Iran)) **Search strategy in Scopus** (TITLE-ABS-KEY ("Diabetes Mellitus" OR "Hyperglycemia" OR "Hyperglycemias" OR "Glucose Intolerance" OR "Blood Glucose" OR "Blood Sugar" OR "Fasting Plasma Glucose")) AND (TITLE-ABS-KEY (Iran OR Iranian OR I.R.Iran OR Persia) OR (AFFIL (Iran)) AND PUBYEAR > 1989 AND PUBYEAR < 2013
High Total cholesterol (TC)
Search strategy in PubMed/Medline Hypercholesterolemia"[Mesh] OR ("hypercholesterolaemia"[All Fields] OR "hypercholesterolemia"[MeSH Terms] OR "hypercholesterolemia"[All Fields]) OR ("hypercholesterolemia"[MeSH Terms] OR "hypercholesterolemia"[All Fields] OR "hypercholesterolemias"[All Fields]) OR " blood cholesterol"[All Fields]AND ("Iran"[Mesh] OR "iran"[All Fields]) OR Iranian[All Fields] OR I.R.Iran[All Fields] OR "I.R Iran"[All Fields] OR ("persia"[MeSH Terms] OR "persia"[All Fields])) AND (("1985/01/01"[PDAT] : "2013/12/31"[PDAT]) AND "humans"[MeSH Terms])
Search strategy in ISI Web of Science Time span=1990-2013. Databases=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH. Topic= (Hypercholesterolemia OR hypercholesterolemias OR " blood cholesterol") AND (("Iran" OR Iranian OR I.R.Iran OR "persia") OR Address= (Iran))
Search strategy in Scopus (TITLE-ABS-KEY ("Hypercholesterolemia OR hypercholesterolemias OR "blood cholesterol")) AND (TITLE-ABS-KEY (Iran OR Iranian OR I.R.Iran OR Persia) OR (AFFIL (Iran)) AND PUBYEAR > 1989 AND PUBYEAR < 2013