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Study Protocol

National and Subnational Cardiovascular Diseases Mortality Attributable to Salt Consumption in Iran by Sex and Age From 1990 to 2016

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Abstract

Background: Dietary salt consumption is an important factor for mortality from cardiovascular diseases (CVDs). Therefore, the aim of this study is to measure the levels of salt consumption and then estimate the effects of current levels of salt consumption on mortality from CVDs at national and subnational levels from 1990 to 2016 in Iran.

Methods: In this study, we will use national and subnational studies with data on salt consumption, including self-report or lab tests for sodium measurement and all available published data about salt and sodium (with conduct a systematic review) to estimate salt exposure levels. We will also use data from death registration system (DRS) to estimate CVDs mortality attributable to salt consumption. We will use mixed-effects model to explore the effects of some covariates on salt consumption and then spatial-temporal model will be used to take into account how the values of salt consumption in each point vary further across time, space, and age. We will compute the proportional reduction in CVD deaths that will occur if salt consumption reduces to an alternative level (5 g/d), using comparative risk assessment (CRA). The simulation analysis will be used to estimate the uncertainty of the number of deaths attributable to salt consumption. All analyses will be performed separately by sex in STATA and R software packages.

Conclusion: The findings of this study seem to be helpful for providing good information about the salt consumption and CVDs mortality attributable to it for policymakers in directing future policy decisions and planning cost-effective strategies in Iran.

Keywords: Cardiovascular diseases, Mortality, Salt, Sodium

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Introduction

Dietary salt consumption is an important determinant of individual and population levels of blood pressure.[1] Reducing dietary salt consumption reduces blood pressure and consequently lowers the risk of cardiovascular diseases (CVDs).[2,3] In this setting, in a global study, Mozaffarian et al reported that 1.65 million annual deaths due to cardiovascular events, including 7034 from Iranian population, were attributed to salt consumption above the 5 g/d (reference level).[4] Also, some studies observed that dietary salt intake is directly associated with risk of gastric cancer.[5–7] Other studies reported the association between sodium consumption and renal function and proteinuria[8–13] in patients with CVDs at baseline. High salt consumption can be a key factor which could increase morbidity and mortality of non-communicable diseases (NCDs) in developed and developing countries. Iran, as a developing country, is facing a rapid increase in the burden of NCDs[14] and a part of this increase might be due to high salt consumption in Iran. According to Nazeri and colleagues' study conducted in Tehran, the mean per capita daily salt consumption was 9.5 g.[15] Another study on adults aged 20–74 years from Yazd city indicated that the estimated mean per capita daily salt consumption were 10.04 g/d for males and 7.47 g/d for females.[16] There have also been dietary salt studies that used food frequency questionnaires to estimate salt consumption and these studies estimated that the average salt consumption for the population aged 2–79 was 10.3 g/d in Ilam, 7.7 g/d in Sari and 7.2 g/d in Rasht.[17,18] All above mentioned estimations depict that salt consumption of Iranians is high and varies from one province to another.

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Yet, the national effects of salt consumption and the heterogeneity of these effects according to age, sex, and geographic have not been clearly established. So we intend to measure the levels of salt consumption and then estimate the effects of current levels of salt consumption on mortality from CVDs at national and subnational levels from 1990 to 2016 in Iran. The study is a sub-component of the NASBOD study.[19–24] The current paper provides information on data sources and methods that we are using for estimating salt consumption exposure and its attributable death due to CVDs.

Materials and Methods

Overview

In this study, we will use all related and available data sources, including national and subnational studies with data on salt consumption, including self-report or lab tests for sodium measurement and all available published data about salt and sodium to estimate salt exposure levels. We will also use data from death registration system (DRS) to estimate CVDs mortality attributable to salt consumption. Analyses will be performed separately by sex and results will be provided by sex, age, province and year.

Process of Study

This study contains 11 steps:

1) Conducting a systematic review to collect published articles about salt or sodium whose studies were performed between January 1990 to December 2016 in Iran.
2) Gathering data from all national and subnational (provincial, district and community) epidemiologic studies from January 1990 to December 2016 that have data on salt or sodium consumption or urinary sodium in population level through communication to studies managers.
3) Data preparation.
4) Statistical analysis.
5) Effect size estimation of salt reduction on systolic blood pressure (SBP).
6) Effects size estimation of SBP on deaths from CVDs.
7) Setting reference levels of salt consumption.
8) Using SBP levels by national and subnational, age, sex from 1990 to 2016 that are prepared in another project in Iran.
9) Preparing cause-specific mortality data by national and subnational, age, sex from 1990 to 2016.
10) Estimating population attributable fraction (PAF) of salt consumption for CVDs, at national and subnational levels, by age and sex from 1990 to 2016.
11) Uncertainty calculation for all summary measures.

1. Conducting a Systematic Review to Collect Published Articles About Salt or Sodium

Data Sources

We will conduct a systematic review of the literature through searching online international electronic databases (PubMed, ISI Web of Science, and Scopus), and national electronic databases (scientific Information Database [SID], IranMedex and Irandoc).

Search Strategy

We will search the medical literature between January 1990 and September 2017, using international and national digital databases to find all published articles whose studies were performed between January 1990 to December 2016 in Iran. So, we will search the international databases for papers with any of the search terms of interest in the title or abstract that are extracted from the medical subject headings (MeSH) of PubMed and Emtree of Embase. Also, our searches will be limited to a given time period (between 1990 and 2017), to Iran, to human subjects with no language restriction. More details of the search strategy are available in online Supplementary file 1. For search in national databases (SID, IranMedex and Irandoc), we will use the Persian search terms that are equivalent to their English search terms. In addition, we will consider national registration systems, and national and subnational surveys (Table 1).

Study Selection Process

In this study, we will perform three steps for selection of papers. First, the titles of selected papers will be separately evaluated by two reviewers (The discrepancy between reviewers will be resolved through consensus). Second, the abstracts of selected papers will be reviewed by them, and if they agree that the article is not concordant with inclusion criteria (Table 2), the paper will be excluded. Third, the full text of selected papers will be extracted and reviewers will check papers using standard criteria (the discrepancy between reviewers will be resolved through consensus and use of a research specialist).

Quality Assessment Process

We will use the National Institute of Health (NIH) quality assessment forms to evaluate the quality of papers.[25] The NIH quality assessment forms are provided based on study design (cohort, case-control, cross-sectional and so on). These forms include items for assessing potential flaws in study methods or implementation, including sources of bias, confounding, study power, the strength of causality, and other factors. All selected papers will be independently rated for quality by two reviewers using the appropriate form. Quality reviewers may select "yes," "no," or "cannot determine/not reported/not

Table 1. National and Subnational Surveys From 1990 and 2016 Among Iranian Population

Survey (Abbreviation)	Year	Study Province
Household Income & Expenditure survey (HIEs)	2004–2016	All provinces of Iran
Comprehensive Project on Household Food Pattern and Nutritional Status	First survey:1991-1995 Second survey:2000-2002	All provinces of Iran
Non-Communicable Disease Surveillance Survey (NCDSS)	First survey: 2005 Second survey: 2006 Third survey: 2007 Fourth survey: 2008 Fifth survey: 2009 Sixth survey: 2011 Seventh survey: 2016	All provinces of Iran
The Tehran Lipid and Glucose Study (TLGS)	Phase I: 1999–2000 Phase II: 2001–2004 Phase III: 2005–2008 Phase VI: 2009–2011 Phase IV: 2012–2015	Tehran
Isfahan Healthy Heart Program (IHHP)	Phase I: 2000–2001 Phase II: 2001–2005 Phase III: 2006–2007	Isfahan
Isfahan salt study	Phase I: 1998 Phase II: 2001 Phase III: 2007 Phase VI: 2013	Isfahan
Persian Gulf Healthy Heart Study (PGHHS)	2003–2004	Boshehr
Mashad Study	2007–2008	Razavi Khorasan
Kerman Coronary Artery Disease Risk study (KERCARD)	2009–2011	Kerman
Yazd Healthy Heart Program (YHHP)	2003–2004	Yazd
Urban Health Equity assessment and Response Tool (Urban Heart-phase1)	2007	Tehran
Golestan Cohort Study (GCS)	2004–2012	Golestan
Kavar Cohort	2006	Fars
Shiraz Healthy Heart Cohort	2013	Fars
Zanjan Healthy Heart Cohort		Zanjan
Urban Health Equity assessment and Response Tool (Urban Heart-phase2)	2011	Tehran
Nutritional Knowledge, Attitude and Practice of Rural and Urban Iranian Household as well as Health Practitioners in three provinces (Pilot study) and NUTRIKAP Survey	2004, 2012	Bushehr, Sistan and Baloochestan And Golestan provinces
National Health Survey (NHS)	1999	All provinces of Iran

Table 2. Article Inclusion and Exclusion Criteria

Criteria	Additional Information
Including	
Date	1st Jan 1990 to 31th Dec 2016
Age group	Covering ≥ 35 years in groups 35–44, 45–54, 55–64, 65–74, 75–84 and ≥ 85 years of age
Gender	Both male and/or female
Measurement indicator	Salt or sodium consumption or urinary sodium
Type of data gathering source	Population sources
Excluding	
Date	Before 1st Jan 1990
Age group	Not covering ≥ 35 years of age
Type of data gathering source	Not mentioned as population sources
Study design	Any study such as cohort studies without population base data, hospital case-controls, case reports, case series, and also the studies that surveyed special populations (such as immigrants, specific employees, patients and volunteers), clinical trial studies, comparing studies like ethnic based, interventional studies.

applicable" in response to each item on the form. If the ratings differ, then reviewers discuss the paper to reach consensus. Otherwise, the paper will be forwarded to a methodologist for quality adjudication.

Data Extraction

In this stage, information from selected papers will be extracted and inserted in data extraction sheet independently by two researchers (The differences between them on the extracted data will be rechecked and resolved). Authors of studies that have not demonstrated the related data will be contacted (via e-mail or telephone for 3 times) to request the data. In case of non-cooperation, the paper will be deleted. Data extraction sheet includes general information and data information that are shown in Table 3. In brief, the necessary data

Table 3. Data Extraction Form

A: General Information
(I) Article code: The number of article in the folder. It begins from 1.
(II) Study code: The number of the survey in the article. It begins from 1.
(III) Article ID: For PubMed articles "PMID" and for ISI articles "DOI" will be recorded. If the study has a special name, it is written in the "Study name" column.
(IV) Publication date: It refers to the year that article has been published
(V) Corresponding author 's characteristics: Including the first name, family name and e-mail address
(VI) Study source 1. Iranian databases, 2. Foreign databases, 3. Non-indexed Iranian journals, 4. Health surveys, 5. Abstract of congress, 6. Theses, 7. Other un-published reports
(VII) Study setting 1. Rural, 2. Urban, 3. Both
(VIII) Level of study 1. National, 2. Provincial, 3. District, 4. Community, 5. Sub-region (2 or more provinces with similar ethnicity and race), 6. Two or more sub-regions
(VIIII) Sampling unit 1. Individualized data, 2.Household data
(X) Sampling method 1. Multi-level clustering random sampling, 2. One-level clustering random sampling, 3. Simple random sampling, 4. Others
(XI) Sample weight (The target group proportionates to Iran population's sex and age) 1. No, 2. Yes
B: Data information
(I) Age of participants: Min: Max: Mean: SD: Median:
(II) Sex: 1. Male, 2. Female, 3. Both
(III) Sample size: The sample size in each sex and age group of the study population.
(IV) Response rate: It refers to percentage of reported in Survey Info document or published manuscript
(V) Type of data 1. Intake (or consumption) data, 2. Expenditure data, 3. Other
(VI) Data collection year (start and end)
(VII) Diet Assessment Method 1. Multiple (≥ 2) short-term (up to 1 week) diet recalls/ records with correction for within-person variation 2. Multiple (≥ 2) short term (up to 1 week) diet recalls/ records without correction for within-person variation 3. FFQs, food surveys or household surveys 4. Single short-term diet recalls/records 5. other, please specify
(VIII) Data collection technique 1. Personal interview 2. Telephone interview 3. Self-administered questionnaire
(VIIII) Method of food record 1. Weighting 2. Non-weighting
(X) Questionnaire validation 1. Yes, 2. No
(XI) Dietary sodium 1. Total dietary sodium intake from all dietary sources (Optimal) 2. Total urinary sodium (First alternative) 3. Total salt intake (Second alternative)
Data extracted by, and data cross-checked by: The name of people who will extract and cross-check the data.

include mean, standard deviation (SD), standard error (SE) of mean and confidence interval (CI) for salt or sodium consumption or urinary sodium excretion by year, province, sex and age group.

2. Gathering Data From National and Subnational Based Studies

In this study, we will include all national and subnational based studies from January 1990 to December 2016 that have surveyed the salt/sodium consumption or urinary sodium in population level. Our target population is healthy Iranian adult population (≥35 years) living in Iran from 1990 to 2016. Hospital case-controls and studies that surveyed special populations (such as immigrants, specific employees, patients and volunteers) will be excluded. The epidemiologic studies at national and subnational levels include Tehran Lipid and Glucose Study (TLGS), Golestan Cohort Study (GCS), non-communicable disease surveillance survey (NCDSS) and other studies that are mentioned in Table 1.

3. Data Preparation

In this step, we will consider all prepared data points from selected articles and national and subnational

studies. In this context, data will be converted into a form suitable for further analysis and processing. Therefore, we will have data points based on year and province of data collection, sex and different age groups. We might encounter different methods for salt/sodium measurements. We will deal with this situation by using cross walking between obtained values of salt/sodium in different methods using regression models. Then, we will provide a frame that includes years of study (1990–2016), provinces of study (31 provinces in Iran), sex (male-female) and age groups (6 age groups: 35–44, 45–54, 55–64, 65–74, 75–84 and ≥85) and will merge prepared data to this frame. Sodium excreted from 24-hour urine captures ~90% of dietary sodium[26] and the remainder is excreted via sweat, intestinal fluids, and saliva; therefore, we will add 10% to sodium values that are converted from 24- hour urinary sodium. To convert dietary sodium consumption to salt consumption, we will multiply sodium consumption by 2.54.

4. Statistical Model

Despite our extensive search and attempt to access all national surveys, there might be some provinces without data or without provincial representative data in some years of the study. Furthermore, all age groups, both sex, and all study's years have not been included in some surveys (without data). To overcome this problem, we will use advanced statistical methods and proxy covariates to estimate data for without data points. To estimate mean (whatever the measure is) and its uncertainty interval by sex, age, year, and province, linear mixed-effect, spatio-temporal models and simulation analysis will be developed. Therefore, we will use mixed-effects model to explore the effects of some covariates on salt consumption and then we will predict it for all data points. Also, we will calculate the residuals of salt consumption (predicted - observed) for each data point in mixed-effects model. Then, spatial-temporal model will be used to take into account how the values of salt consumption in each points vary further across time, space, and age. The spatio-temporal model uses residuals (as valuable information) to predict new points data. Moreover, to combine incompatible areal units between data sources and/or over the years, spatio-temporal misalignment modeling will be used. The simulation analysis will be used to estimate the uncertainty interval for salt consumption. All statistical analyses will be conducted in STATA and R software packages.

5. Effect Size Estimation of Salt Reduction on Systolic Blood Pressure

Three recent meta-analyses assessed the effect of sodium reduction on BP,[2,4,27] among which Mozaffarian and colleagues' study is the newest and most detailed meta-analysis that assessed 103 trials that included 107 randomized group comparisons (6970 subjects).[4] This study observed a strong evidence for a linear effect of sodium reduction on blood pressure (BP) (*P*-linearity < 0.001).

The final meta-regression equation of Mozaffarian and colleagues' study was

$Y = \alpha + B_1X_1 + B_2X_2 + B_3X_3$

Where, Y = the BP change in each trial in mm Hg (standardized to a sodium reduction of 100 mmol/d (5.85 g/d salt consumption);

B_1 = the mean age of individuals in each trial in years (centered at age 50);

B_2 = whether the trial was conducted on normotensive or hypertensive individuals;

B_3 = whether the trial was conducted on non-Blacks or Blacks; and

α = the effect of a 100 mmol/d sodium (5.85 g/d salt consumption) reduction on SBP when mean subject age=50, individuals were normotensive, and individuals were not Black.

The final coefficients were: α = -3.735; B_1 =- 0.105; B_2 = -1.874; and B_3 = -2.489.

We will use this equation in the present study. But β_3 will be considered zero because this study will be conducted on non-Black people.

We will use STEPwise approach to surveillance of non-communicable diseases (STEPS) surveys to determine the percentage of hypertensive individuals. The STEPS surveys were conducted in 2005–2009, 2011 and 2016 in Iran. We will interpolate and extrapolate to estimate the percentage of hypertensive individuals in years without data. Then, we will use above regression formula in males and females with or without hypertension, separately. Then, weighted average will be used to combine the results.

6. Effects size estimation of SBP on deaths from CVDs

In two prior pooling projects (the Prospective Studies Collaborative [PSC] and the Asia Pacific Cohort Studies Collaborative [APCSC]),[28,29] the dose-response relationship between BP and CVD mortality has been established. These studies pooled data from 99 cohorts (1.38 million participants, and 65 000 cardiovascular events). The analyses of these studies demonstrate a proportional dose-response relationship between SBP and CVDs at any age. According to this evidence, we will assume a proportional dose-response between SBP and CVDs until a SBP level of 115 ± 6 mm Hg (lower from this level we will assume no further contribution to risk). In Singh' study to incorporate data from PSC and APCSC projects, the authors interpolated and

extrapolated age-specific relative risks of SBP on CVDs mortality in 10-year age groups across the studies.[30] We will use these age-stratified relative risks in our study.

7. Setting Reference Levels of Salt Consumption

The reference level of sodium (salt) consumption will be selected based on the observed consumption levels associated with lowest SBP in ecologic studies and in randomized trials and with lowest disease risk in meta-analyses of prospective cohort studies. According to the type of disease and study, the reference levels of sodium consumption are shown in Table 4. In ecologic studies, the lowest mean consumption level associated with both lower SBP and lower age-SBP was 614 mg/d.[31] The lowest surveyed consumption level associated with SBP reductions in randomized trials was 1500 mg/d.[32] Also, the lowest mean consumptions associated with lower risk of CVDs events in prospective observational studies ranged from 1787 to 2391 mg/d.[33] For this study which will focus on CVDs, we will use a conservative reference level of sodium 2.0 ± 0.2 g/d (salt = 5 ± 0.5 g/d) that is consistent with mean intakes in several countries, and with the World Health Organization (WHO) guidelines.[34]

8. Using SBP Levels by National and Subnational, Age, Sex From 1990 to 2016

In another study, we obtained data for SBP from published papers, unpublished health examination surveys and epidemiological studies from different regions of Iran. We used linear mixed-effect and spatio-temporal models to estimate mean of SBP and its uncertainty interval by sex, age, year and province accounting for whether each study was provincially representative.

9. Prepare Cause-Specific Mortality Data by National and Subnational, Age, Sex From 1990 to 2016

National and subnational death data reported by DRS will be included in this study to measure the CVD mortality based on age group and sex from 1990 to 2016. To overcome incompleteness of the DRS, we will use the mortality section of the NASBOD study.[20] For this study, we will use data on deaths due to ischemic heart disease, ischemic stroke and other CVD (hemorrhagic stroke, hypertensive heart disease, aortic aneurysm, rheumatic heart disease, inflammatory heart disease and other CVDs). In this study, we will consider only SBP effects on deaths due to the above diseases.

10. Estimating PAF of salt consumption for CVDs, at national and subnational levels, by age and sex from 1990 to 2016

In this study, we will estimate salt consumption attributed burden using comparative risk assessment (CRA).[35] This analysis (CRA) captures demographic and geographic variations in salt consumption, blood pressure, CVDs mortality, and their uncertainties. We will incorporate each province (subnational), age-specific, and sex-specific salt consumption, BP level, relative risk, and mortality data to estimate the fraction and numbers of deaths from CVDs attributable to salt consumption above the reference level.

In this study, we will compute the proportional reduction in CVD deaths that will occur if salt consumption is reduced to an alternative level (5 g/d). This is known as the population-attributable fraction (PAF) and measures the total effects of salt consumption. The PAF is calculated in 2 steps: (1) based on the age-, hypertensive-, and sex-specific BP effects of salt consumption to calculate the change in mean SBP that would be expected from reducing salt consumption to a reference level (5.0 ± 0.5 g/d); (2) based on the age-specific effects of SBP on CVDs to compute the resulting change in CVDs risk.

We will compute PAF using the following equation:

$$PAF = \frac{\int_{x=0}^{m} \boldsymbol{R}\ (x)P(x)d(x) - \int_{x=0}^{m} \boldsymbol{R}\ (x)P'(x)d(x)}{\int_{x=0}^{m} \boldsymbol{R}\ (x)P(x)d(x)}$$

Table 4. The Reference Levels of Sodium Consumption According to Type of Disease and Study

	Mean Intakes	Outcomes	Type of Study
1	614 mg/d	Lower systolic BP and lower age-BP slopes	Ecologic studies[31]
2	1245 mg/d	Lower incidence of gastric cancer	Meta-analysis of prospective cohorts[45]
3	1500 mg/d	Reduced BP	Randomized controlled trials[32]
4	2391 mg/d	Lower incidence of total stroke	Meta-analysis of prospective cohorts[33]
5	2245 mg/d	Lower incidence of stroke mortality	Meta-analysis of prospective cohorts[33]
6	1787 mg/d	Lower incidence of CHD mortality	Meta-analysis of prospective cohorts[33]
	Mean Intakes	**Major Dietary Guidelines**	
1	< 1500 mg/d	American Heart Association[46]	
2	< 1200 mg/d	UK National Institute for Health and Clinical Excellence, 2025 target[47]	
3	< 1500 mg/d	US Dietary Guidelines Advisory Committee[48]	
4	< 2300, <1500 mg/d	US Dietary Guidelines for Americans[49]	
5	< 2400 mg/d	UK Food Standards Agency[50]	
6	< 2000 mg/d	World Health Organization[51]	

Where x = current SBP level; P(x) = actual distribution of SBP at current salt consumption in the population; P'(x) = alternative distribution of SBP if salt consumption were at the alternative reference distribution in the population; RR(x) = the (age-specific) relative risk of each SBP-related disease for a unit change in SBP; and m = maximum SBP level.

We will calculate the number of deaths from CVDs that is attributable to salt consumption by multiplying its PAF by total deaths (from CVDs) in each province-age-sex stratum from 1990 to 2016.

11. Uncertainty Calculation for All Summary Measures

We will estimate the uncertainty of the number of deaths attributable to salt consumption (as will cause by sampling variability) using simulation analysis. To compute sampling uncertainty, we will use a simulation approach (1000 draws for each) to combine the uncertainties of salt consumption distributions, its effect on blood pressure, RRs, and CVDs mortality rates in each province-age-sex group (characterize by its mean and SD). We will incorporate sampling and non-sampling errors into final interval estimations.

Discussion

Although the importance of reducing salt consumption to less than 5 g/d is emphasized,[34] achieving this goal needs further efforts. These efforts could not lead to any result without accurate and coherent planning. Since a 30% relative reduction in mean population intake of salt/sodium is an important target of WHO global action plan,[36] the WHO advised ministers of health and national mandated agencies to develop population-wide policies and use all the available tools to ensure their effective actions.[34] In this regard, the Iranian action plan was prepared with a target of 4.30% relative reduction in the average salt intake in the population.[37] To achieve these targets, the dietary salt reduction program is the simplest and most cost effective pathway to decrease the burden of NCDs in developed and developing countries.[38] Such reductions have been achieved in China, Jamaica, and Nigeria.[39,40] Many countries, including the United Kingdom, Finland, Japan, and Portugal, have reduced population-wide salt consumption through public education, collaboration with the food industry and implementing regulations on the salt content in foods.[41] In this setting, Finland observed a significant reduction in salt intake of the Finnish population, from an average of approximately 12 g/d in 1979 to less than 9 g/d in 2002 as measured by 24 hours urinary sodium.[42]

Implementing health policies without planning and information can lead to waste of resources. We hope that the results of this study not only determine the necessity of health policy makers' actions in this field, but also direct them to more urgent population.

The primary outcome of this study is to determine mortality from CVDs attributable to salt consumption in Iran. As mentioned, achieving this outcome involves several steps that yield valuable information. One could be trend of salt consumption over time. In addition to health system plans, numerous interventions like informing people, changes in life styles and diet and aging population could affect the trend of salt consumption. Our results provide this opportunity for other researchers in this field to study the significance and magnitude of each factor by time, location, age and sex.

On the other hand, several studies have measured the mean of salt consumption among Iranian population. Moreover, some of them have extended their scope at national and subnational levels at the same time. Beside geographical expansion of our estimations, we believe that results can be representative of all Iranian population in all period of study. For instance, separate studies have been conducted in Tehran,[15] Yazd,[16] Ilam,[18] Sari and Rasht.[17] These studies just represent population of some cites of Iran and their information was collected in small cross-sectional studies. Although some cohort studies have collected food and salt data (such as TLGS, GCS, and so on), because of population of interest and basic outcome of these studies, they should be considered with more caution. Also, some nutritional studies have been conducted in Iran nationally,[43,44] but these studies have collected data in some specific years and are not representative for all years surveyed in our study.

Our approach focuses on collecting all available data sources including cohorts, cross-sectional, population based case-control studies and national representative surveys like Comprehensive Study on Household Food Consumption Patterns and STEPs studies, then using professional statistical modeling to extrapolate and interpolate the estimations. Gathering all available information could guarantee the reliability and precision of results. Our data gathering is not limited to salt consumption and we have a plan to use relevant proxy of consumption like household income expenditure survey (HIEs) and related covariates. The last advantage of this study is the support of NASBOD project team so that much information like death mortality rate is easily available.

In addition to all mentioned advantages, we face some issues. The main problem which could arise in this project is data scarcity in some years and provinces. Another problem could be the collaboration of other researchers in sharing data from their studies.

In conclusion, it seems that the results of this study might be helpful for better detection of CVDs mortality

attributable to salt consumption at national and subnational levels. Therefore, these findings provide good information about salt consumption and CVDs mortality attributable to it for policymakers in directing future policy decisions and planning cost-effective strategies in Iran.

Authors' Contributions

General designing of paper: AG, SK, FF; Designing of Models: AG, AS, MP, FF; Designing of systematic review: AG, HRB, SK, FF; Writing of primary draft: AG, AS; Manuscript revision: HRB, SK, FF;

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Supplementary Materials

The online version of this article contains supplementary file 1, which is available to authorized users.

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