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### A Scenario-based and Modeling Study on the Prevention of Heart Attack in Iran: A Mixed Methods Study Protocol

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#### Abstract

Background: Globally, cardiovascular disease (CVD) is the number one cause of mortality.

Objectives: This study aimed to provide policies for the management of CVD by focusing on the reduction of myocardial infarction (MI) mortality in Iran.

Methods: The sequential mixed methods design will be employed to predict the prevalence of MI in Iran in the next 10 years. This study consists of five phases. In the first phase, the risk factors of cardiovascular disease will be investigated using a systematic review. In the second phase, the uncertainty and impact of those factors will be evaluated by the experts. Moreover, the impact/uncertainty grid will be used to identify the most important drivers and critical uncertainties. In the third phase, the cross-impact matrix, the scenario logic and the scenarios will be developed. Once the scenario logic is established, details can be added to the scenarios. The next phase consists of statistical estimations of the rate of mortality due to heart attack using artificial neural networks. Finally, the policies will be developed based on the opinions of the panel of experts. The initial results will be published in mid-2021.

Results: This future study will develop policies to prevent from MI with scenario-based and modeling approaches. The findings can benefit healthcare professionals and policymakers by enhancing the management of MI patients.

Conclusion: Specific policy recommendations will help policymakers to make evidence-based decisions, re-design structures and processes of healthcare interventions, to decrease the MI mortality.

Keywords: Artificial neural networks, Cardiovascular disease, Future study, Health policy, Mixed methods, Prevention, Scenario

#### 1. Background

Non-communicable diseases (NCDs) are among the emerging causes of mortality worldwide. It is estimated that annually 17 million people die from cardiovascular disease (CVD), more specifically, from heart attacks and strokes (1, 2). The CVD is one of the leading causes of mortality in both genders. The mortality rate of CVD was 241.52 and 218.17 per 100,000 individuals for males and females, respectively, in 2017 (3). Like most Western Asian countries, CVD is the leading cause of death in Iran and is responsible for 46% of deaths. A high prevalence of risk factors for CVD has also been reported in this region (4). The financial burden of acute myocardial infarction (AMI) is very high mainly due to expensive healthcare services provided by hospitals (5). Nevertheless, such costs can be significantly reduced by the mitigation of CVD risk factors, resulting in saving millions of lives (6, 7). The largest portion of NCDs is due to the prevalence of CVD, especially MI (8). Many international agencies

have recognized CVD prevention as one of the important and challenging priorities of nations (9, **10**). Prediction of future CVD prevalence makes policymakers able to take proper measures to control and impact the prevalence and burden of these conditions (11, 12).

Future research is a type of research that uses a range of methods to analyze the past, present, probabilities, and expectations to predict the future in different fields of science and technology (13, 14). Future studies have been used for planning, decisionmaking, and policy-making processes (15). The scenario-based method appears to be the most popular approach in the economic, social, cultural, and political and security studies; in addition, it has been considered as the main tool in the field of information analysis (16). Moreover, it has been used to predict the future incidence and prevalence rate of wide range of communicable and nonа communicable diseases (17). For example, a scenario-based methodology was used to forecast the bio-economy of the countries in the Organization for

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Economic Co-operation and Development in 2030 and explore various policy options (17). In the project of foresight and modeling for European health policy and regulation, four scenarios and policy options were developed by involving stakeholders and policy-makers from healthcare, research, patient advocacy, and insurance, and proposed alternatives with promising results (18). However, to the best of our knowledge futures studies have not been used to develop strategies for effective prevention of NCDs, especially CVD, in Iran and other developing countries.

This research will use a future study design to develop prevention policies for the reduction of the mortality of MI in Iran. Scenario and modeling-based methods will be implemented to compare and provide proper policy options.

#### 2. Objectives

This study aimed to provide policies for the management of CVD by focusing on the reduction of myocardial infarction (MI) mortality rate in Iran.

#### 3. Methods

This study will make use of a multiphase mixed methods design, including different stages with quantitative and qualitative approaches (19) to be performed sequentially. Studies with a multiphase design combine sequential and concurrent collection and analysis of qualitative and quantitative data over a period of time (20). The study outlook will be for the next 10 years.

In this study, it will be attempted to develop scenarios for the prevalence and prevention of MI in Iran. The scenarios in this approach will be normative in terms of perspective, qualitative and quantitative mix method in terms of methodology, and deductive in terms of the construction of the process of scenarios. Afterward, the statistical modeling method will be used to estimate the mortality rate of MI. Finally, policy options will be developed with the help of the expert panels (Figure 1).

# 3.1. Phase 1: Identification of effective drivers of the incidence of cardiovascular diseases 3.1.1. Study Type

A comprehensive systematic review will be conducted based on the protocols developed by the Institute of Joanna Briggs (JBI) (21) and reported according to the the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

guideline. This study will aim to review and synthesize the qualitative and qualitative studies that have investigated the risk factors of cardiovascular diseases. It should be noted that conference abstracts, books, and opinions will be excluded from the study; however, thee sources will be used to identify further studies.

#### 3.1.2. Search method and strategy

MEDLINE, Scopus, ISI Web of Science, and Cochrane will be searched. Only the studies published since 2002 will be included since the World Health Organization (WHO) has focused on the prevention of NCDs in 2002.

The authors will develop and apply a search strategy based on the combination of relevant keywords. We will use the following terms and their variants including social, cultural, socio-cultural, technological, economic, political, ecological, driver, strategy, policy, cardiovascular disease, heart attack,





myocardial infarction, and prevention. Reference lists of other reviews were manually searched to find additional studies.

#### 3.1.3. Data Extraction and Synthesis

Both the qualitative and quantitative studies that are identified during this review will be evaluated using the JBI quality appraisal tools. Data extraction and methodological quality appraisal will be carried out by a researcher and will be double-checked by a second one. Differences in comments will be resolved through discussion by a third researcher. Textual data will be extracted by JBI data extraction tools for qualitative studies, quantitative studies, and expert opinions. The extracted data will include effective factors, background, study type, study objective, and outcome. The PRISMA flow diagram will be used to report the selection process of the included studies.

The findings will be extracted and reported in the social, technological, environmental, and economic, and political (STEEP) (17, 22) framework. This framework will be verified as needed during the review.

#### 3.2. Phase 2: Identification of the critical uncertainties and their impacts on the incidence of myocardial infarction

#### 3.2.1 Study type

This phase is qualitative and the identified drivers in the first phase will be rated by a panel of experts on the basis of their importance and uncertainty. A questionnaire will be developed during data collection. The importance and uncertainty will be scored based on a 10-point Likert scale.

#### 3.2.2. Sample size and sampling methods

At least 15 experts will participate in this phase. To facilitate the nationwide participation of experts from long distances we will establish communication through email and online meetings. Inclusion criteria for the selection of experts are occupation as a national health policymaker, scientific expertise in CVD prevention in Iran, and willingness to participate in the study.

#### 3.2.3. Analysis

The key drivers are classified based on the (envisioned) degree of their impact and the degree of uncertainty of their impact on the incidence of MI. Key drivers that are identified with high impact and high uncertainty are considered as the most important drivers for the definition of the scenarios that will represent structurally different but plausible descriptions of the future (Figure 2).

#### 3.2.4. Ethical considerations

Study participants will be informed that participants' withdrawal from the study will be voluntary. It will be ensured that their personal information will be analyzed and reported anonymously. Finally, they will be asked to read and sign the informed consent form of the study.

## Phase 3: Development of scenario logic and narrative expression for each scenario

#### 3.3.1. Study type

This phase of the study is qualitative. First, the mean impact score and uncertainty score will be determined; subsequently, the drivers whose impact and uncertainty scores are 20% higher than the total mean score will be selected. The Selected drivers will be merged and used as the horizontal and vertical axes of the cross-impact matrix.

#### 3.3.2. Sample size calculation and sampling methods

At least 15 experts will participate in this phase. To facilitate the nationwide participation of experts from long distances we will communicate with them via email and online meetings. Inclusion criteria for selecting experts are occupation as health





policymaker at the national level, scientific expertise in CVD prevention in Iran, and willingness to participate in the study.

#### 3.3.3. Analysis

In the third phase, the scenario logic consists of a matrix with four distinct scenarios. Two axes are defined by the key drivers and their plausible evolution. Key driving forces are used as the axes in scenario development diagrams to rise up four possible scenarios. Experts will grade the mutual impact of key driving forces based on the plausible evolution in the range of +3 to -3. Mean scores of each mutual plausible evolution will be calculated and the cross-impact matrix will be drawn by ScenarioWizard software (version?). The total impact score and inconsistency of the descriptor will be used to identify strong and weak scenarios. Consistent and believable scenarios are determined with an inconsistency coefficient of 0-2. The narrative expression for each scenario will be explained by the experts.

#### 3.3.4. Development of scenario logic

The scenario logic consists of a matrix with four distinct scenarios, two axes of which are defined by the key drivers and their plausible evolution. The narrative expression will be developed for selected scenarios. The scenario is a story description of the future that focuses on the causal processes of decision-making. Validity of the scenarios will be determined by experts with regard to several factors. Scenarios must have internal consistency which means that they must be potentially extracted from the data and facts and provide an acceptable view of the future. Moreover, the scenarios must be describing causal processes (23).

#### 3.3.5. Narrative expression of each scenario

Whether it seems probable or not, it is possible to take a logical path from the present to the future and draw an image. This means that it is possible to construct a scenario for the future which describes the logical path of the present towards the future. These scenarios should differ in one of the key factors. The future that is predicted by a scenario must not be completely different from the past. A scenario must address future challenges and reconcile events and facts in a way that challenges the logical models. Furthermore, a scenario must have a good title tailored to the type of predicted future. Eventually, three scenarios will be selected: the optimistic, baseline, and pessimistic scenarios. *3.3.6. Ethical consideration* 

#### Study participants will be informed that participation in and withdrawal from the study will be voluntary. It will be ensured that their personal

be voluntary. It will be ensured that their personal information will be analyzed and reported anonymously. Finally, they will be asked to read and sign the informed consent form of the study.

# 3.4. Phase 4: Estimate the mortality rate of myocardial infarction based on the existing scenarios 3.4.1. Study type

This phase of the study is quantitative. In this phase, the future mortality of MI will be estimated based on the projection of risk factors and the current data on the MI mortality using the artificial neural network (ANN). In addition, the mortality rate will be estimated for optimistic, baseline, and pessimistic scenarios that were selected by the experts in phase three using mixed linear regression.

#### 3.4.2. Sample size and sampling methods

At least 15 experts will participate in this phase. The experts will be selected using purposive sampling methods. Besides, consensus sampling will be used to include all the available risk factors and mortality rate data. To facilitate the nationwide participation of experts from long distances we will communicate with them via email and online meetings. The inclusion criteria for the selection of experts were occupation as a national health policymaker, scientific expertise in CVD prevention in Iran, scientific expertise in CVD prevention in Iran, and willingness to participate in the study.

#### 3.4.3. Data source

Two data sources will be used in this phase to predict the mortality rate of MI. A questionnaire will be designed to predict hypertension, smoking, body mass index (BMI), blood cholesterol levels, nutritional profile, physical activity, blood glucose levels, and mortality rate for 10 years (2018-2027) based on the opinions of experts using the mixed linear regression. These risk factors will be selected according to a model proposed by the American Heart Association (24).

The data comes from two sources: the WHO STEPwise Approach to non-communicable Disease Risk-Factor Surveillance (STEPs) project (2011-2013) and the national and subnational burden of diseases, injures, and risk factors (NASBOD) project. The collected data will be used to predict the mortality rate using ANN.

#### 3.4.4. Analysis

The mixed linear regression will be used to determine the relative and individual contribution for each risk factor based on the opinions of experts. Prerequisites for mixed regression include the normality. Independence, homogeneity of variances, and linearity of the relationship. The fitted values versus residuals and the distribution of the residuals (prediction errors) will be examined using the normal probability graphs.

Extracted data from STEPs and NASBOD will be used to predict the MI mortality rate using ANN (25-30). The modeling will be repeated 100 times to enhance the accuracy of the ANN model and

eventually, the mean value of repeated results will be used to predict the future. Moreover, the backpropagation algorithm and the logistic activation function will be applied to estimate the parameters. Independent variables (i.e., blood pressure, smoking, BMI, blood cholesterol, nutritional status, physical activity, and blood glucose) will be considered as input and the dependent variable (i.e. MI mortality) will be considered as the output. The modeling will continue until the relative error of testing is less than that of training. The 5% error will be considered statistically significant and automatic architecture selection will be utilized to determine hidden layers. Sensitivity analysis will be performed in case of the existence of any outlier data. The variable importance analysis will be used to select the final variables in the model. The collected data will be analyzed in SPSS software (version 17) (SPSS Inc., Chicago, IL, USA).

#### 3.4.5. Ethical considerations

Study participants will be informed that participation in and withdrawal from the study will be voluntary. It will be explained that their personal information will be analyzed and reported anonymously. Finally, they will be asked to read and sign the informed consent form of the study.

### Phase 5: Development of policy options for each scenario

#### 3.5.1. Study type

This phase of the study is qualitative and is comprised of two parts. In this phase, the document review and expert panel will be used to develop policy options. The first part consists of three trends based on the prediction of experts (optimistic, pessimistic, and baseline). Additionally, the result of the ANN model will be reported alongside the prediction according to the previous data in order to develop policy options for each trend.

#### 3.5.2 First part: Document review

#### 3.5.2.1. Sample size and sampling methods

National development plans and policies from 2002 onward will be extracted. Websites of the Ministry of Health of Iran and all Iranian medical universities will be reviewed. In addition, Google search engine will be used to search for any relevant content.

#### 3.5.2.2. Analysis

The results will be analyzed using the content analysis method. The documents will be organized according to their publication date and the duplicates will be discarded; afterward, the remaining documents will be analyzed using content analysis.

#### 3.5.3. Second part: Expert panel

*3.5.3.1.* Sample size and sampling methods

At least 15 experts will be included in the panel.

To facilitate the nationwide participation of experts from long distances we will communicate with them via email and online meetings. Inclusion criteria for the selection of experts are occupation as a national health policymaker, scientific expertise in CVD prevention in Iran, and willingness to participate in the study.

#### 3.5.3.2. Analysis

A list of policy options and interventions will be developed by the panel of experts for optimistic, baseline, and pessimistic trends and scenarios. The panel of experts will compare the policy options and determine their priority based on the indicators which are selected by panel members (by default; feasibility, political support, and impact on the general public). The Analytical Hierarchy Process (31) method will be used to prioritize policy options based on the selected indicators. Consistency of the views will be examined using the compatibility ratio (CR) index and the data will be analyzed in the Expert Choice software (version 11).

#### 3.5.3.3. Ethical considerations

Study participants will be informed that participation in and withdrawal from the study is voluntary. Moreover, it will be explained that their personal information will be analyzed and reported anonymously. Finally, they will be asked to read and sign the informed consent form of the study.

#### 4. Results

Scenario, as one of the most widely used foresight tools, provides a comprehensive framework for decision making and helps policymakers adapt to major changes more quickly (32). The intuitive logic approach in scenarios enables stakeholders to engage in the process and enables policymakers to become aware of the complexity and uncertainties they may encounter in the future. Essence of the intuitive logic approach is to identify the contextual environment, such as STEEP forces and internal factors (23). If the scenario method is restricted merely to the inner setting and does not scan the external environment, there may be a risk of ignoring critical uncertainties that could have a strong effect on future developments. Therefore, it is necessary to combine the perspective of beneficiaries with maximum diversity to escape unilateral views. This approach enables the integration and alignment of mental models and environmental factors in order to challenge current assumptions. The biggest potential of this approach lies in the reality that it offers various rather than onedimensional scenarios; consequently, with its holistic perspective, this approach allows policymakers to better address the uncertain environmental circumstances (22).

#### 5. Discussion

Effective prevention policies are the best interventions for the reduction of heart attacks. Future and scenario-based studies provide one of the best methods for the development of effective policies. However, enough attention has not been paid to the implementation of future studies in policy-making, especially in the development of disease prevention policies. A handful of studies have been conducted with a combination of qualitative and quantitative approaches to study the future of NCDs. It is expected that the results of this study will be beneficial for health policymakers by helping them develop more efficient policies with proper information about the future of CVD.

This study has some limitations. For example, experts are usually busy and it is difficult to access them. In the quantitative phase, the number of accessible experts might be low and this issue can limit the quantitative analysis. Furthermore, available quantitative data regarding the risk factor and drivers may be not be fully in line with the selected factors and drivers in the current study.

#### 5.1. Publication plan

Final reports of this study will be published in peer-reviewed academic journals. Additionally, early findings will be presented in scientific conferences, symposia, and other professional assemblies.

#### 6. Conclusion

Specific policy recommendations can help policymakers to make evidence-based decisions, redesign structures, and processes of healthcare interventions, and decrease the MI mortality.

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#### Footnotes

**Authors' Contribution:** All the authors contributed to the conception and design of the study. Gisoo Alizadeh and Rahim Khodayari-zaranq drafted the first version of the manuscript. Kamal Gholipour, Reza Dehnavieh, Mohamamd Asghari JafarAbadi, Mehrdad Azmin, and Ahmad Khanijahani revised the manuscript. All authors approved the final version.

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