

## Explaining the Decline in Coronary Heart Disease Mortality Rate Using IMPACT Model: Estimation of the Changes in Risk Factors and Treatment Uptake in Iran between 2007 and 2016

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### Original Article

#### Abstract

**INTRODUCTION:** Coronary heart disease (CHD) contributes significantly to mortality and morbidity in Iran. A model was fitted in this study to determine changes in risk factors and treatment uptake to CHD mortality rate reduction in Isfahan between 2007 and 2016.

**METHOD:** The IMPACT model was fitted to determine how much the decrease in CHD death can be explained by treatment uptake and significant risk factors included in the analyses for adults aged 35 to 84 years. Body mass index (BMI), diabetes, and smoking were considered as the CHD risk factors in the model. Medical and interventional treatments were studied in four different groups of patients. The primary data sources were obtained from the Persian registry of cardiovascular disease (PROVE), The Isfahan healthy heart program (IHHP), and the impact of self-care management and adopted Iranian guidelines for hypertension treatment on improving the control rate of hypertension (IMPROVE CARE) study, death registration system, and the Isfahan province Cemetery.

**RESULTS:** The CHD mortality rate decreased by 14% between 2007 and 2016 in Iran for adults aged 35 to 84 years and prevented or delayed 212 CHD deaths in 2016. Treatment uptakes caused 99% postponed or prevented death. Treatment for heart failure in hospitals explained approximately half of the death prevented by treatment. Risk factors caused about 15% of excess death. It appears that the prevalence of CHD is increasing while the death rate is decreasing because of these observed changes.

**CONCLUSION:** Risk factors worsened in 2016 and, without treatment, could lead to an increase in CHD mortality in Iran. Preventive policies should control the risk factor and contribute to the decrease in CHD death.

**Keywords:** Coronary Heart Disease, Mortality, Risk Factors, Treatment, IMPACT Model

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#### Introduction

Coronary heart disease (CHD) is the leading cause of mortality and morbidity worldwide.<sup>1</sup>

<sup>2</sup> According to earlier reports on the global burden of diseases, in 2015, Cardiovascular disease (CVD) accounted for 46% of all deaths and 20.23% of the disease burden in

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Iran.<sup>3</sup> In 2011, CVDs were responsible for 43.92% of all deaths in Isfahan province.<sup>4</sup> The CHD mortality rate has decreased in many countries since 1970. However, CHD remains a significant cause of mortality, morbidity, and premature mortality. In Iran, a decreasing trend began in 2006, suggesting that strategies to reduce CHD might differ from other countries.<sup>5</sup>

Medical and surgical treatments, including aspirin, beta-blocker, ACE-inhibitor, Percutaneous coronary intervention, and CABG, are readily and frequently used in Iran. Treatment uptake in other countries could account for 23% in Iceland to 41% in Turkey of CHD mortality decline.<sup>6, 7</sup> In most countries, risk factors, including total cholesterol, smoking, Body mass index (BMI), and diabetes, explained a large portion of CHD mortality changes, ranging from 25% of the reduction in the Netherlands to 73% in Iceland.<sup>6, 8</sup> However, in this study, treatment uptake played the most significant role in explaining the CHD mortality decline. Given the unique trend of CHD in Iran, the strategy for preventing and postponing CHD mortality could differ from other countries. Furthermore, CHD causes more than 4500 billion dollars annually in Iran.<sup>9</sup> Therefore, it is crucial to determine the contributions of risk factor changes and treatment uptake to the CHD mortality rate decrease to better understand and predict future trends, clarify policy options to prevent CHD, reduce the enormous costs of the disease and its social-psychological effects, prevent CHD mortality, and increase life expectancy.

The IMPACT model has been run in more than 20 countries to determine the contribution of risk factor changes and treatment uptakes on the CHD mortality rate.<sup>10-15</sup> To the best of our knowledge, no study has fitted the IMPACT model in Iran. The IMPACT model was provided for adults aged 35 to 84 years in Isfahan between 2007 and 2016.

## Materials and Methods

The cell-based IMPACT mortality model

was initially used in Scotland and further developed and refined in New Zealand, Finland, and England and Wales.<sup>(10, 12, 13, 16)</sup> The mortality IMPACT model was used to determine the contribution of treatment uptakes and significant risk factor changes to the decline of CHD mortality for men and women aged 35 to 84 in Isfahan between 2007 and 2016. The model collected and combined the number of CHD patients, treatment uptake, significant risk factor changes (BMI, smoking and diabetes), the effectiveness of treatment, and the mortality effect of changes in the population's significant risk factor.

### Data sources

Population information was obtained from the sum of the Isfahan district population.<sup>17</sup> The death registration system and Isfahan Central Cemetery data were used for mortality in 2007, and the death registration system data were used for 2016 mortality.<sup>18</sup>

Data on risk factors and medical and surgical treatment were obtained from research projects in the cardiovascular research institute. The number of patients with myocardial infarction and unstable angina came from the impact of self-care management. It adopted Iranian guidelines for hypertension treatment on improving the control rate of hypertension (IMPROVE CARE) study.<sup>19, 20</sup> IMPROVE CARE was a cross-sectional study performed among 2,107 locals of Isfahan. This study was completed from 2014 to 2016 in four stages.<sup>19, 20</sup> The number of patients admitted to the hospital with heart failure, and patients undergoing percutaneous coronary intervention came from the Persian registry of cardiovascular disease (PROVE).<sup>21-23</sup> The PROVE registry started in 2015. It collected patient data from hospitals and outpatient clinics.<sup>22</sup> Information about risk factors came from IMPROVE CARE and Isfahan healthy heart program (IHHP).<sup>17, 19, 20</sup> IHHP was a community-based program that started late in 2000. It was a prevention and control program for cardiovascular disease in the target population.<sup>24</sup>

Data on the efficacy of therapeutic interventions and the mortality reduction

from specific population cardiovascular risk factor changes were obtained from published randomized controlled trials, Meta-analyses, and cohort studies.<sup>25-38</sup>

#### *Death prevented or postponed*

The expected number of CHD deaths in 2016 was calculated by multiplying the age and sex-specific CHD death rate in 2007 by the population in 2016. It was assumed that the expected number of deaths in 2016 would have an unchanged age and sex-specific mortality rate since 2007. The total decline in CHD deaths is the difference between the numbers of observed and expected deaths in 2016. A combination of changes in risk factors and therapy uptake between 2007 and 2016 could explain the total number of CHD deaths prevented or postponed. There may be some unexplained decline in CHD death by the model, which could be assumed to be the result of unmeasured risk factors or imprecision in the model's parameters.

#### *Mortality changes attributable to treatment uptake*

Mortality reduction by treatment uptake was computed in four patient groups (acute myocardial infarction, unstable angina, percutaneous coronary intervention, heart failure in hospital). The death postponed or prevented by medical and surgical treatment is estimated by the product of the number of patients in each group, the proportion of those who receive specific treatment, compliance, relative reduction, and the one-year case fatality rate for that treatment.<sup>10, 13, 25-28, 30-32, 35, 38, 39</sup> Compliance is the proportion of treated patients taking therapeutically adequate levels of medication. It was assumed to be 100% in hospital patients, 70% in symptomatic community patients, and 50% in asymptomatic community patients.<sup>40</sup>

To avoid double-counting, potential overlap between different patient groups was identified, and appropriate adjustments were made.

In application, usually, more than one medication is used for treatment, and data on using multiple drugs are available. The additive effect of treatment could produce

an overestimation of treatment, but with the Mant and Hicks method, the number of reduced mortality by multiple medications could be estimated. This method calculated relative benefit as  $(1 - \text{relative reduction in case-fatality rate for treatment A}) \times (1 - \text{relative reduction in case-fatality rate for treatment B}) \times \dots \times (1 - \text{relative reduction in case-fatality rate for treatment N})$ <sup>41</sup>.

#### *Mortality changes attributable to risk factor changes*

Three major risk factors of coronary heart disease were considered: BMI (a continuous risk factor), and smoking and diabetes (binary risk factors).

For continuous risk factors, regression beta coefficients from extensive cohort studies and MONICA analyses were used.<sup>29, 34</sup> Increases in death were estimated by the expected end in 2016, beta coefficient, and changes in the mean of the risk factor between 2007 and 2016.

For discrete risk factors, the increase in the number of deaths was estimated by the product of the difference in population-attributable risk fraction in 2007 and 2016 and the expected number of deaths in 2016. The population-attributable risk fraction was calculated as  $[P \times (RR - 1)] \div [(1 + P) \times (RR - 1)]$ , where P is the prevalence of the risk factor and RR is the relative risk of death from coronary heart disease.<sup>33, 37</sup>

It was assumed that there was no synergy between the risk factor and treatment. Also, it was assumed that the lag time between the changes in risk factor levels and changes in CHD mortality rate is rapid, so these were not modeled.<sup>42</sup>

#### *Model validation: Comparison estimated and observed mortality changes*

The model's estimation of death changes due to major risk factors and medical and surgical treatment were summed and compared with the observed decline in mortality for both men and women in each specific age group. This criterion measured the model's ability to express observed changes in CHD deaths. Any shortfall in the model's overall estimation was

attributed to biases or unmeasured factors.<sup>13, 43</sup>

*Sensitivity analysis*

Sensitivity Analysis Sensitivity analysis was used due to uncertainties surrounding many values. In the sensitivity analysis, a 95% uncertainty interval around the model output was calculated, using the analysis of extreme values.<sup>13, 44</sup>

mortality rate (ICD10 I20-I25) decreased by 212 in men and women aged 35 to 84 years old. The number of observed CHD deaths in 2016 was 1310. If the age-specific death rate in 2007 had remained the same in 2016, the expected number of CHD deaths would have been 1522. Therefore, 212 CHD deaths were prevented or postponed. The expected deaths prevented were 13.82% in women and 14% in men. This means a total of 13.93% of expected deaths in 2016 could be prevented (Table1).

**Results**

Between 2007 and 2016 in Isfahan, the CHD

**Table 1.** Population aged 35 to 84, observed and expected death, and death changes in Isfahan between 2007 and 2016

Year	Men and Women		Men		Women	
	2007	2016	2007	2016	2007	2016
Population	657026	889181	337870	461895	319156	427286
Observed CHD death	1174	1310	715	811	459	499
Age standardizes rate (per 10 000)	17.87	14.73	21.16	17.56	14.38	11.68
Expected death	-	1522	-	943	-	579
DPP	-	212	-	132	-	80
% of expected deaths prevented	-	13.93	-	14	-	13.82

Medical and surgical treatment postponed or prevented 209 CHD deaths, and changes in

major risk factors increased CHD deaths by 32 (Tables 2 and 3).

**Table 2.** Death changes attributed to risk factors in Isfahan between 2007 and 2016

	Risk factors level		Changes in risk factors		Death changes			% of total death changes
	2007	2016	absolute	Relative (%)	Best estimate	Minimum estimate	Maximum estimate	
Total death postponed or prevented	-	-	-	-	212	-	-	-
Explained by changes in risk factor prevalence and risk factor levels	-	-	-	-	-32	-14	-60	-15%
Body mass index	27.16	28.16	1	3.68	-31	-14	-58	14.6%
Smoking(%)	10.6	13.3	2.7	25.47	-0.2	-0.05	-0.6	0.09%
Diabetes(%)	12.9	15.3	2.4	18.6	-0.8	-0.34	-1.6	0.38%
Unexplained by the present IMPACT model	-	-	-	-	35	-	-	16%

*Medical and surgical treatment*

Medical and surgical treatment postponed approximately 209 deaths (with a minimum estimate of 58 and a maximum estimate

of 494) in Isfahan between 2007 and 2016. A significant contribution came from the treatment for heart failure patients who required hospitalization, postponing about

114 deaths. A more negligible contribution of treatment was for unstable angina patients, which decreased CHD deaths by 49 (Table 3).

Aspirin and beta-blocker prevented or postponed 103 and 83 CHD deaths, respectively, accounting for all diseases (Table 3).

**Table 3.** Death prevented attributed to treatment uptakes in Isfahan between 2007 and 2016

Treatment by patient group	Number of patients eligible	Treatment uptake (%)	Death postponed or prevented (DPPs)			% of total DPPs
			Best estimate	Minimum estimate	Maximum estimate	
Total treatment	-	-	209	58	494	99%
Acute myocardial infarction	994	-	25	3	73	12%
Aspirin	-	99.08	20	8	42	10%
Beta-blocker	-	87.31	5	-5	31	2%
CABG	-	0.1	0.1	0.03	0.3	0.05%
Unstable angina	6510	-	49	6	132	23%
Aspirin	-	97.31	40	15	75	19%
Beta-blocker	-	82.16	9	-9	57	4%
CABG	-	0.12	0.1	0.03	0.3	0.05%
Percutaneous coronary intervention (PCI)	3105	-	21	7	44	10%
Statin	-	23.09	7	2	13	3.5%
Aspirin	-	38.42	7	3	16	3.5%
ACE-inhibitor	-	5.56	2	0.5	3	1%
Beta-blocker	-	17.47	5	2	12	2%
Heart failure in hospital	918	-	114	42	245	54%
Aspirin	-	81.79	36	13	78	17%
ACE-inhibitor	-	25.38	14	5	32	7%
Beta-blocker	-	63.31	64	24	135	30%

The Mant and Hicks method reduced the total DPP for treatments from 209 to 194 deaths. This includes 102 in heart failure patients, 48 in unstable angina patients, 24 in AMI patients, and 20 in PCI patients.

#### *Risk factor changes*

Changes in risk factors together resulted in 32 additional deaths (with a minimum estimate of 14 and a maximum estimate of 60) between 2007 and 2016. The most significant contribution was due to BMI (an increase from 27.16 to 28.16 kg/m<sup>2</sup>), which caused 31 additional deaths. Diabetes caused approximately one additional death due to an

increase in prevalence from 12.9% to 15.3% (Table 2).

#### *Model validation*

The CHD mortality decreased by 212 in men and women in Isfahan between 2007 and 2016. Risk factor changes resulted in 32 additional deaths, and medical and surgical treatment postponed or prevented 209 deaths. Therefore, it was explained that 177 CHD deaths were delayed or prevented, meaning the Iran IMPACT model could explain ≈ 84% of the decrease in CHD mortality. The remaining unexplained approximately 16% was attributed to biases or unmeasured factors.

## Discussion

Heart disease is the leading cause of death in Iran.<sup>45</sup> The age-adjusted CHD mortality decreased by 14% in Isfahan between 2007 and 2016, resulting in 212 postponed or prevented CHD deaths. Changes in risk factors resulted in a 15% increase in CHD deaths, while treatment uptakes accounted for a 99% decrease in CHD deaths.

Medical and surgical treatments postponed or prevented  $\approx 99\%$  of CHD deaths, which is significantly higher than in some Asian countries such as Turkey (47%), Japan (56%), and the West Bank (29%).<sup>7, 46, 47</sup> The most significant contribution came from the treatment of heart failure patients requiring hospitalization, which accounted for more than 50% of all deaths prevented or postponed. Unstable angina ( $\approx 23\%$ ), AMI ( $\approx 12\%$ ), and percutaneous coronary intervention ( $\approx 10\%$ ) followed in terms of contribution. Unfortunately, treatment for heart failure patients did not result in a significant gain in life-years due to the short life expectancy of these patients.<sup>48</sup> Percutaneous coronary intervention, while preventing a small number of CHD deaths, consumed substantial financial and political resources.<sup>49</sup>

In Iran's IMPACT model, heart failure ( $\approx 54\%$ ), Unstable angina ( $\approx 23\%$ ), Acute myocardial infarction ( $\approx 12\%$ ) and, percutaneous coronary intervention ( $\approx 10\%$ ) had greater contribution in explaining postponed or prevented CHD death than Japan (4.5%, 2.8%, 3.8%, and 1.1% respectively), Turkey (2.9%, 1.8%, 4.7%, and 4.9%) and West bank (1.5%, 1.1%, 1.9%, and 1.9%).<sup>7, 46, 47</sup>

Aspirin and beta-blocker explained about  $\approx 50\%$  and  $\approx 40\%$  of CHD death prevented by treatment, respectively accounted for all diseases which reflected high prescription in these medications. Aspirin and beta-blocker prevented twice death as in unstable angina as AMI patients.

Risk factor changes caused 15% excess CHD death. BMI increased from 27.16 to 28.16 kg/m<sup>2</sup> and generated  $\approx 14.6\%$  extra CHD death. BMI increased in men is approximately twice

as women and so causes twice CHD death in men. Diabetes and smoking prevalence increased from 13% to 15% and 11% to 13%, respectively between 2007 and 2016 and caused  $\approx 1$  and 0.2 extra CHD death.

Salt is a risk factor for diabetes and its consumption in Isfahan was more than twice that recommended by the World Health Organization.<sup>50, 51</sup> To control tobacco, Iran has adopted the Framework Convention on Tobacco Control (FCTC) Act and created a comprehensive and systematic program. Unfortunately, the total objectives of the program did not gain. Dietary and tobacco policies are required to improve and decrease the CHD death caused by the risk factor changes.<sup>52</sup>

Controlling major risk factors could be more effective in preventing CHD death and gaining life years.<sup>53</sup> The population-based policy should be taken more seriously. Salt intake was more than twice of WHO recommendation.<sup>51</sup> Studies showed that intervention programs aimed at behavioral change could reduce salt consumption.<sup>54-56</sup> Also, WHO recommended organizing social marketing campaigns, and interventions to increase the knowledge of the recipients and help them to choose healthier food.<sup>57</sup>

Changes in lifestyle in the modern world, dietary habits, increased consumption of fast foods and smoking, and reduction in physical activity due to technological development are risk factors for CHD. These factors necessitate policies and training programs to improve lifestyle. Furthermore, enhancing individuals' knowledge about relevant strategies and encouraging adherence to these strategies could improve public health.

The IMPACT model integrates data from various sources and analyzes a large amount of data.

The IMPACT model has some limitations. This model is dependent on the quality and extent of data available for CHD risk factors and treatment uptake.<sup>58</sup> The IMPACT model did not consider competing causes and focused on CHD death.<sup>59</sup> The model ignored years gained for life or disease incidence and only

considered death.<sup>48,60</sup>

Because of limitations in the data, the focus was on cases with ages between 35 to 84 years. The model did not consider lag time, although it seemed unimportant over nine years of analysis. In this model, due to limited data, three major risk factors - dyslipidemia, systolic blood pressure, physical inactivity, and other risk factors such as alcohol, psychosocial stress, saturated fat, consumption of fruits and vegetables - were not included.

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