Int Cardiovasc Res J.2018;**12**(1):1-6.icrj.55067

International Cardiovascular Research Journal

www.ircrj.com

# Economic Burden of Cardiovascular Disease in the Southwest of Iran

Sara Emamgholipour [1], Ali Akbari Sari [1], Mohsen Pakdaman [2], Sara Geravandi [1,*]

[1] Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, IR Iran
[2] Department of Health Care Management, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, IR Iran

ARTICLE INFO

*Article Type:*
Research Article

*Article History:*
Received: 16 Jun 2017
Revised: 15 Dec 2017
Accepted: 13 Jan 2018

*Keywords:*
Cardiovascular Diseases
Cost of Illness
Iran

ABSTRACT

**Background:** CVDs are the first cause of death globally. About 50% of annual deaths are related to this group of diseases in Iran; however, the economic cost of CVD on Iranian society has not been conducted.

**Objectives:** The aim of this study was to estimate the economic burden of CVDs in the southwest of Iran in 2016 from the social perspective.

**Materials and Methods:** This study is a cross-sectional descriptive-analytic study conducted using the cost of illness (COI) framework. The prevalence top-down method was used to quantify the annual cardiovascular costs. Productivity losses were estimated using the human capital approach and the friction cost method, with the discount rate of 3% to convert all future lifetime earnings into the present value.

**Results:** In 2016, the average total cost per patient was $1881.4 and the total costs resulted in 1159.62 $million. Direct costs accounted for 60% and indirect costs for 40% of the total costs. The results were robust to a 20% change in the average unit price of all medical and non- medical direct costs and to discount rate of 2% and 10%.

**Conclusions:** The total cardiovascular disease costs in 2016 represented approximately 6.7% of the Iran gross domestic product. The results of this study would be of special help for policymakers to evaluate the cost-effectiveness and outcomes of health care programs to allocate health care resources efficiently. Primordial Prevention of CVD including lifestyle modifications and dietary interventions resulted in substantial financial savings and is strongly recommended.

## 1. Background

Chronic diseases are closely related to the individuals' lifestyle. Chronic diseases which are also known as Non-communicable Diseases (NCDs) are the main important cause of mortality and burden of disease worldwide (1). Some primarily major risk factors, including tobacco use, physical inactivity, the harmful use of alcohol and unhealthy diets, lead to an increase in NCDs (2). Low-and middle-income countries account for about three quarters of all NCD deaths (3). Moreover, about 82% of the 16 million people who died prematurely before reaching 70 years of age occur in low-and middle-income countries (3). Cardiovascular diseases (CVDs) are the number 1 cause of death globally (4). CVDs are responsible for about 17.5 million deaths in 2012. Also, the number of people, who die from CVDs, mainly from heart disease and stroke, will increase to reach 23.3 million by 2030. CVDs are projected to remain the single leading cause of death (5).

About 80% of CVD deaths take place in low- and middle-income countries and occur almost equally in men and women (5). One reason is that people in low- and middle-income countries are more exposed to risk factors such as tobacco, which lead to CVDs and other non-communicable diseases. At the same time, they often do not have the benefit of prevention programs compared to people in high-income countries. Also, they have less access to effective and equitable health care services which meet their needs. As a result, many people in low-and middle-income countries die younger from CVDs and other non-communicable diseases, often in their most productive years (5). There is sufficient evidence to prove that CVDs and other non-communicable diseases can make the household experience poverty due to catastrophic health spending and out of pocket expenditure (6). Non-communicable

*Corresponding author: Sara Geravandi, Department of Public Health, Tehran University of Medical Science, Tehran, Iran. Cellphone: +98-9389381028
E-mail: houragerandi@gmail.com.

disease including cardiovascular disease and diabetes are estimated to reduce GDP by up to 6.77% in low-and middle-income countries experiencing rapid economic growth, as many people die prematurely (4). Also, these diseases cause a reduction in labor efficiency since the patients and their caregivers tend to absenteeism or poor performance during working time (7). In Iran, cardiovascular diseases are the number 1 cause of mortality in Iran (8). About 50% of annual deaths are related to this group of diseases, of which more than 19% are due to heart attacks (8). However, CVDs can be prevented by addressing the risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity, high blood pressure, diabetes, and raised lipids (6). Cost-of-illness studies measure the economic burden of a disease or diseases and estimate the maximum amount that could potentially be saved or gained if a disease were to be eradicated (9). Since cost-of-illness studies can show the financial impact of a disease on public programs, these studies are usually considered by the federal government and other specific stakeholders (3-5). For employers, those studies can show which diseases have an especially large effect on their costs (6, 7). Moreover, cost-of-illness studies provide the researchers with necessary information for cost-effectiveness analyses (10).

## 2. Objectives

Thus, in this study we aimed to estimate the costs of coronary heart disease (I25) in governmental and educational hospitals in the southwest of Iran, to estimate the economic burden of cardiovascular diseases in the southwest of Iran.

## 3. Materials and Methods

This study was conducted with the cross-sectional view of the costs. The basic approach in the cross-sectional view is that of prevalence. Thus, we used the method of prevalence to estimate the economic burden of coronary heart disease in 2016. By prevalence approach, we measured all medical care and morbidity costs for coronary heart disease within the study year. The mortality and permanent disability costs are calculated differently from the other costs. Discounted mortality and permanent disability costs are calculated for all patients who die or become permanently disabled in the study year for all years until the expected age of death (11, 12).

The economic burden of coronary heart disease (I25) was estimated based on the cost-of-illness (COI) method. A comprehensive cost-of-illness study includes both direct and indirect costs. Direct costs measure the opportunity cost of the resources used for treating a particular illness, whereas indirect costs measure the value of the resources lost due to a particular illness (8).

It should be mentioned that we ignored intangible costs of pain and suffering. This category of costs is often omitted because of the difficulty quantifying it in monetary terms accurately. The focus is often on direct financial costs because non-monetary costs can be difficult to capture (8, 12, 13).

Note that not only a disease can generate costs for patients and his or her family, but also it can produce costs for government, employers, insurance companies, and other members of the society. Therefore, to achieve a comprehensive analysis, this study was performed from the societal perspective including all direct medical and indirect costs for all members of the society. Key elements of the method for evaluating the economic burden of CVDs are as follows:

### *3.1. Calculating the Sample Size*

This study is a descriptive survey which does not test a hypothesis. In other words, this survey aims to describe the characteristics of a single group to reflect the real figure, such as a mean or a proportion, in the wider population. Therefore, we used simple random sampling. We worked through the following formula to determine an appropriate sample size, where d denotes the error and is considered as 0.1. The variance obtained from the previous studies is equal to 0.26. The value of z, given that $\alpha = 0.05$, was set to 1.96.

Thus, 100 patients were asked by a comprehensive self-administered questionnaire which was designed in accordance with the objectives of the study. The questionnaire consisted of several parts including demographic characteristics, direct medical costs, direct non-medical costs, and indirect costs. In addition to the questionnaire, hospital bills for outpatient and inpatient costs of the interviewed patients were reviewed. The information was collected from the governmental hospitals in Ahwaz, given that most of the patients in the surrounding cities are referred to this city for treatment. All analyses were performed, using SPSS, version (14).

### *3.2. Direct Costs*

To quantify the direct costs, we measured total direct costs containing the costs of the resources used. Direct costs of the disease consist of two parts: direct medical costs and direct non-medical costs. Direct medical costs include those of hospital inpatient, physician outpatient, emergency department outpatient, ambulance, nursing home care, rehabilitation care, specialists and other health professionals cares, diagnostic tests, prescription drugs, and medical supplies. To obtain more accurate estimates, we measured the payments made by the insurance and direct payments by the patients obtained from the hospitalization and outpatient bills (15, 16).

Non-medical direct costs contain the portion of direct payments by the patient and his family in order to receive the services. Non-medical direct costs include transportation costs to receive health care from the service providers, relocation expenses, complementary or alternative therapies, domestic help, and costs of making changes to one's diet, house, car, special equipment, travelling and accommodation, communication, mobile, telephone, housekeeping, and childcare or related items (15, 16). The patients were asked about these costs and their frequency; the responses were then recorded. Also, the weighted average of non-medical direct costs was calculated using formula I.

$$\bar{x} = \frac{\sum_{i=1}^{n} F_i X_i}{\sum_{i=1}^{n} F_i} = \frac{F_1X_1 + F_2X_2 + \ldots + F_kX_k}{F_1 + F_2 + \ldots + F_k} \quad \text{(I)}$$

*3.3. Indirect Costs*

Indirect costs include the loss of resources due to morbidity and mortality, which inherently places a monetary value on the value of life. Indirect costs represent the Productivity Lost due to the illness. They include mortality costs, morbidity costs due to absenteeism, and presenteeism. We used human capital approach to measure the indirect costs. The human capital method estimates production losses based on the remaining expected lifetime earnings for the individual. For mortality or permanent disability costs, the approach multiplies the earnings lost at each age by the probability of living to that age. The earnings in future years are discounted and often a one percent real annual growth rate in earnings is assumed (13, 17). The indirect costs due to mortality was estimated using formula II.

$$\text{Productivity Lost due to mortality} = \sum_{i=1}^{n} \frac{(y-c)\,(1+g)^i}{(1+r)^i} \quad \text{(II)}$$

Where y, c and g are Average Gross Domestic Production Per Capita (GDP Per Capita), Average Private Consumption Expenditure Per Capita, and the Average Rate of Iran Economic Growth, respectively, in the last 30 years. Also, n represents the number of years lost due to premature death. We used DALYs lost due to coronary heart disease as the average number of years lost due to premature death per patient, and r is the discount rate. In this study, according to the World Bank in 2014, Life Expectancy (LE) for both sexes in Iran is 74.07 years.

Since using the human capital approach (HCA) to estimate the production loss leads to overestimation of the indirect costs, the friction cost approach (FCA) was used to adjust these costs. The friction cost method measures only the production losses during the time it takes to replace a worker (18-20). This approach assumes that short-term work losses can be made up by an employee and the loss of an employee only results in costs imposed on the system during the time taken for a new employee to be hired and trained, which is known as the friction period, the time between the start of absence from work and replacement, that is estimated to be about 90 days (21). The friction period adjusted productivity loss was calculated by multiplying the unadjusted productivity loss, obtained as described above, by the friction period (90 days) and then dividing this product by the average duration of work incapacity that is calculated in this study for the CHD patients. The average days absent from work by the employed people with CHD was estimated about 119.35 days. By the friction cost approach, we adjusted the results of the human capital method using formula III.

$$\text{PL (FCA)} = \frac{PL\ (HCA) \times friction\ period}{work\ incapacity\ period} \quad \text{(III)}$$

FCA approach led to reduction of the values of productivity loss by 75.4% of the human capital approach in this study.

To estimate the indirect costs due to morbidity, we valued the days lost from work due to illness and also days of unpaid care and nursing by family or friends of the person receiving care. The indirect cost due to morbidity was estimated using formula IIII.

$$\text{Morbidity Costs} = (\overline{u_1} \times N \times W) + (\overline{u_2} \times N \times W_{min}) \quad \text{(IIII)}$$

Where $\overline{u}_1$, $\overline{u}_2$, W, $W_{min}$, represent the average number of days lost from work per patient, average number of days of unpaid care and nursing, average daily earnings and daily minimum wage rate, respectively. Also, N represents the number of patients with cardiovascular disease in Khuzestan Province.

*3.4. Discounting*

A discount rate is used to convert the future income or a cost stream into its present value. Choosing an appropriate discount rate depends on some factors specific to the country such as positive time preference, inflation, and productivity growth. A 3% discount rate is mostly common. We also used 5% discount rate to observe the effect of changing the discount rate on the total cost.

*3.5. Sensitivity Analysis*

Sensitivity analysis is recommended whenever there is uncertainty (22). Cost-of-illness studies rely on estimates with varying degrees of uncertainty and they should examine and vary the assumptions made to determine the range of possible values the costs of illness can take. We performed one-way sensitivity analyses to examine the strength of the results. For this purpose, we focused on variables considered to have a significant impact on the total cost in this study. We assessed the changes in the estimated total cost of CVD, resulting from a 20% change in the average unit price of all medical and non-medical direct costs. To examine the robustness of the indirect costs, we used the discount rates of 3% and 5%. All analyses were performed using the Microsoft Excel 2010.

**4. Results**

The mean age of the patients in this study was 53. Women were diagnosed more often with CVD than men (54% vs. 46%). 64% of the patients lived in urban areas and 36% resided in rural areas.

*4.1. Direct Costs*

The total direct costs of CVD in 2009 were $693.57 million, of which 61% ($ 424.23 million) were direct medical costs and 39% ($269.33 million) direct non-medical costs. Hospital costs and prescription drugs were the main cost categories of CVD direct medical costs. (35.4% and 31.9%). Diagnostic tests, outpatient care by the physician and nursing accounted for 23.03%, 9.1% and 0.48%, respectively. The majority of costs attributable to direct non-medical costs were allocated on complementary and alternative therapies (38.4%), travelling and accommodation (34.3%) (Figures 1 and 2).

*4.2. Indirect Costs*

In 2016, the indirect costs due to CVD morbidity were $693.57 million. The production losses due to mortality using human capital approach were $125.7 million, with the friction cost method reduced to $94.8 million. The total indirect cost due to CVD morbidity and mortality estimated by the human capital approach was $497 million. The average length of incapacity for all CVD patients was 119.35 days. Thus, by the friction cost approach, the costs were adjusted to 24%. However, after adjustment for friction period the estimate reduced to $466 million.

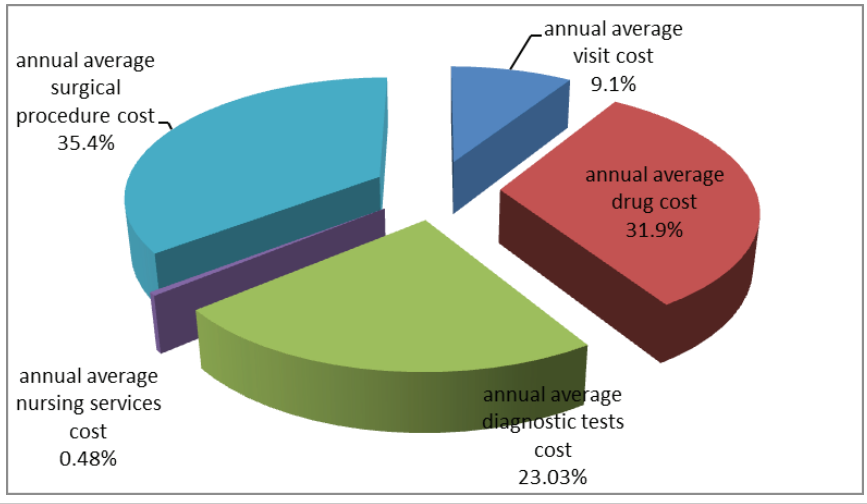


**Figure 1.** Medical Direct Cost

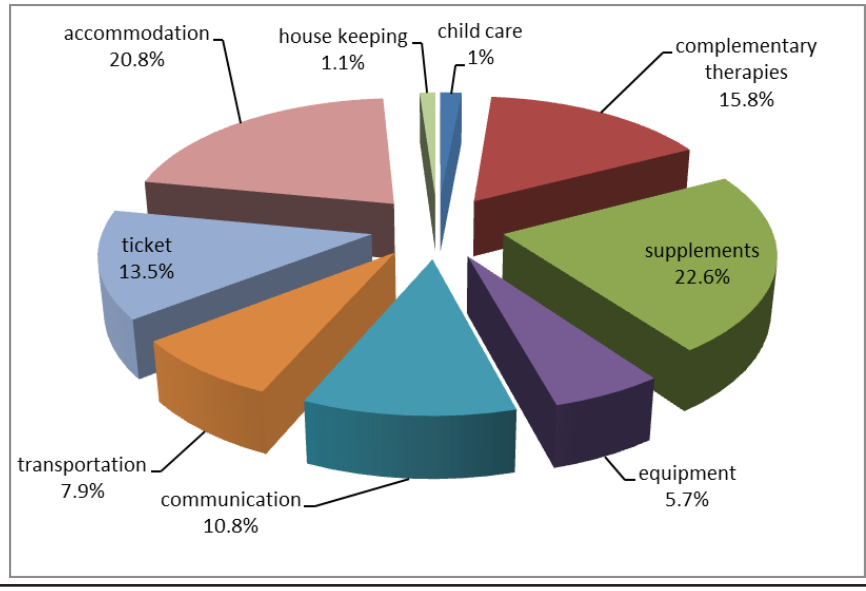


**Figure 2.** Non-medical Direct Cost

*4.3. Total Costs*

In 2016, the average total cost per patient was $1881.4 and the total costs resulted in $1159.62 million. Direct costs accounted for 59.82% and indirect costs for 40.18% of the total costs (Figure 3).

*4.3. Sensitivity Analysis*

A change of 20% in the average unit price of direct medical and non-medical cost produced a variation in the baseline estimate of the total cost of ± 4.6% and ± 2.9%, respectively. Assessing the robustness of the indirect, the discount rate of 5% was applied, resulting in the baseline estimate change into 7% (Table 1).

## 5. Discussion

CVDs impose a heavy burden on the health care system and economy of the countries. In 2016, the economic burden of CVD per patient was about $1881.4 in Iran. The average CVD direct medical costs per patient were over $4860. The results of the direct medical costs of CVD show that more than 66% of the costs are attributable to hospitalization including visits, and diagnostic, nursing and surgical procedures, while medication treatment represented over 32% of the direct costs. In the majority of studies on evaluation of economic burden of CVD, hospital costs were the most expensive direct category, with the values of 50 66% of the total direct cost, followed by pharmaceutical expenditures (18, 23, 24).

The estimated direct non-medical costs of CVD were $3085 per patient and more than 40% of the costs were attributable to transportation and travelling costs to health care providers. About 39% of the costs were attributable to complementary or alternative therapies and special equipment, while housekeeping and childcare accounted for only 1% and 1.1% of the direct non-medical costs, respectively.

The estimated total indirect costs of CVD were almost $4660 million, with more than 67% attributable to mortality. The cost of CVD in EU revealed that almost 70% of the indirect costs were attributable to mortality; in some EU countries, like Latvia, mortality represented 90.63% of the indirect costs (18).

In 2016, the average total cost per patient was $1881.4 and the total costs resulted in $1159.62 million. Direct costs

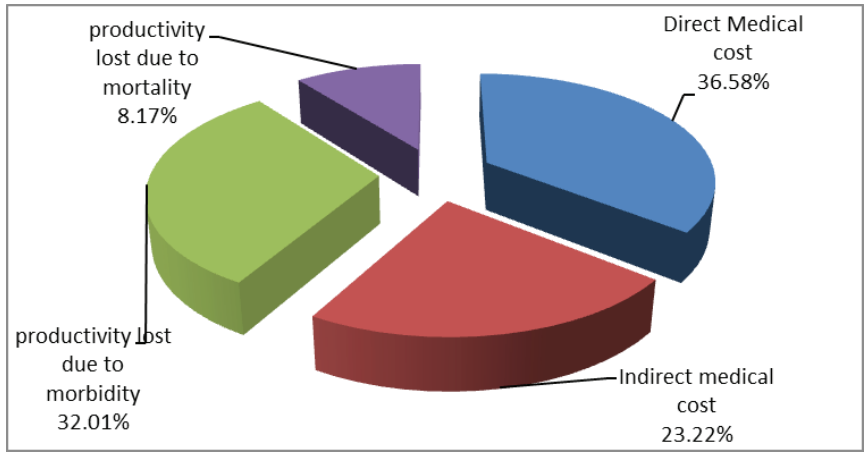


**Figure 3.** Indirect Cost

**Table 1.** The Total Costs of Cardiovascular Disease

| Direct Costs | | | | Indirect Costs | | | | Total Costs | |
|---|---|---|---|---|---|---|---|---|---|
| Medical | | Nonmedical | | Morbidity | | Mortality | | | |
| Value ($) | Percentage of total cost (%) | Value ($) | Percentage of total cost (%) | Value ($) | Percentage of total cost (%) | Value ($) | Percentage of total cost (%) | Value ($) | Percentage of total cost (%) |
| 424.24 | 36.58 | 269.33 | 23.22 | 371.26 | 32.01 | 94.8 | 8.17 | 1159.62 | 100 |

accounted for 60% and indirect costs for 40% of the total costs. In a study conducted to estimate the overall cost of heart failure across the globe in 2012, direct costs accounted for ~60% ($65 billion) and indirect costs for ~40% ($43 billion) of the overall expenditure (25). Also, in another study conducted in the enlarged European Union (EU), of the total cost of CVD, 62% were due to healthcare, 21% due to productivity losses, and 17% due to informal care (18). Bloom et al. (26) in the review article of published cost-of-illness studies on US populations, estimated that more than 48% of the total cost was attributable to indirect costs. On the contrary, a study conducted in Korea showed that the indirect cost in 2004 was USD 387.5 million, 58.8% of the total societal cost increased to US$481.5 million (52.4% of the total societal cost) in 2009 (27). In addition, studies conducted in UK, Canada, Finland and Mexico revealed that a much higher percentage (in some cases over 50%) of the total cost is attributable to indirect costs (23, 24, 28, 29). Such a difference could be explained by much lower average earning than in the above mentioned, Western market economics.

The magnitude of the total costs associated with CVD can be best represented as the percentage of gross domestic product (GDP). According to our results, the total cost of CVD in 2016 comprised approximately 6.7% of the total GDP; in 2009, the total CVD cost was 3.37% of the total American GDP. On the other hand, results of the study conducted in China in 2003 showed that 0.62% of the China GDP was attributable to direct costs only (30).

In Iran, women were diagnosed more often with CVD, mostly coronary heart disease. Similar results were shown in other studies (31, 32) where the prevalence of CVD was higher in women. However in South Korea among the ACS patients, approximately 60% were male with similar proportions of males in each year from 2004 to 2009 (27).

It is essential to make changes in the assumptions, in order to determine the ranges of possible values the costs can take (33, 34). The one-way sensitivity analysis indicated that a change of 20% in the average unit price of direct medical and non-medical cost produced a variation in the baseline estimate of the total cost of ± 4.6% and ± 2.9%, respectively. Assessing the robustness of the indirect, we applied the discount rate of 5%, resulting in the baseline estimate change into 7%. A similar study conducted in Serbia showed that after using sensitivity analysis, the volume or cost of hospitalizations and medicines are the components which were most likely to affect the estimated total cost, but the overall impact was small, less than 6% on the total cost estimate (35).

However, this study had several limitations related to measuring costs. First, we assumed that all CVD patients take measures to treat their disease; with this assumption, the estimation of the costs is likely to be exaggerated. On the other hand, we assumed all patients refer to public services for treatment. It was of particular concern in the present study. Because of the lower quality of health care services in public sector, patients with more income and wealth tend to refer to private sector with better quality services and higher expenditures compared to public sector. Thus, taking this assumption leads to underestimation of the costs in our study.

Second, we were unable to estimate some items such as intangible costs related to pain and emotional anxiety due to CVD because of data restrictions and objective quantification difficulties. By addressing such limitations in further research, more accurate and comparable estimation of CVD costs could be achieved.

In conclusion, CVD is a leading public health problem with considerable economic burden on the society. The total costs in 2016 represented approximately 6.7% of the Iran

GDP. As this study is the first cost of illness (COI) study to assess the economic burden of CVD in Iran, the authors believe that the results of this study would be of special attention for policy makers to evaluate the cost-effectiveness and outcomes of health care programs to allocate health care resources efficiently. Also in order to reduce medical costs and productivity losses on the society, Primordial Prevention of CVD including lifestyle modifications and dietary interventions resulting in substantial financial savings are strongly recommended. The findings of this study suggest that further research should be carried out to discover the ways to reduce the economic effects of CVD on the Iranian population.

**Acknowledgements**

This work was supported by Tehran University of Medical Sciences and the Ministry of Health and Medical Education of the Islamic Republic of Iran.

**Authors' Contribution**

Sara Emamgholipour is the Supervisor Professor and reviewed the draft of the manuscript. Ali Akbari Sari is Co-advisor Professor. Sara Geravandi: designed the study and wrote the draft of manuscript and Gathering data. Mohsen Pakdaman did the data analysis and verifed the analytical methods.

**Funding/Support**

There is no funding/support.

**Financial Disclosure**

There is no financial disclosure.

**References**

1. World Health Organization. Global status report on noncommunicable diseases 2014: attaining the nine global noncommunicable diseases targets; a shared responsability. *Global status report on noncommunicable diseases 2014: attaining the nine global noncommunicable diseases targets; a shared responsability*; 2014.
2. World Health Organization. Global action plan for the prevention and control of NCDs 2013-2020. 2013. 2016.
3. World Health Organization. Noncommunicable diseases. 2016 [updated 2016; cited]; Available from: http://www.who.int/mediacentre/factsheets/fs355/en/.
4. World Health Organization. Cardiovascular diseases (CVDs) Fact sheet. [cited [Updated May 2017]]; Available from: http:// www.who.int/mediacentre/factsheets/fs317/en/.
5. World Health Organization. NCD mortality and morbidity. 2016 [updated 2016; cited]; Available from: http://www.who.int/gho/ncd/mortality_morbidity/en/.
6. World Health Organization. Cardiovascular diseases (CVDs). 2016 [updated 2016; cited]; Available from: http://www.who.int/mediacentre/factsheets/fs317/en/.
7. DeVol R, Bedroussian A, Charuworn A, Chatterjee A, Kim I, Kim S, *et al*. An unhealthy America: the economic burden of chronic disease—charting a new course to save lives and increase productivity and economic growth. Milken Institute. October 2007. *URL: http://www milkeninstitute org/publications/publications taf*. 2008.
8. World Health Organization. The impact of chronic disease in the islamic republic of Iran. *Genouva: Organization*. 2002.
9. Emamgholipour S, Akbari Sari A, Geravandi S, Mazrae H. Estimation of Out-of-Pocket and Catastrophic Expenditures among Patients with Cardiovascular Diseases in Khuzestan. Journal of Payavard Salamat. 2017;11(3):297-307.
10. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS medicine*. 2006;**3**(11):e442.
11. Barlow WE. Overview of methods to estimate the medical costs of cancer. *Med Care*. 2009;**47**(7 Suppl 1):S33-6.
12. Max W, Rice DP, Sung HY, Michel M, Breuer W, Zhang X. The economic burden of prostate cancer, California, 1998. *Cancer*. 2002;**94**(11):2906-13.
13. Javadi M, Asgari H, Yaghoobbi M, Tavazohi H. Self-assessment of the non-communicable disease surveillance system in Medical University of Isfahan based on the model suggested by the World Health Organization. *Journal of School of Public Health and Institute of Public Health Research*. 2010;**8**(3):47-60.
14. Lim SS, Gaziano TA, Gakidou E, Reddy KS, Farzadfar F, Lozano R, *et al*. Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs. *Lancet*. 2007;**370**(9604):2054-62.
15. Economics Access. Cost of Cancer in NSW. *A report by Access Economics Pty Limited For The Cancer Council NSW*. 2007.
16. Segel JE. Cost-of-illness studies—a primer. *RTI-UNC Center of Excellence in Health Promotion Economics*. 2006:1-39.
17. Hutubessy RC, Baltussen RM, Torres-Edejer TT, Evans DB. Generalised cost-effectiveness analysis: an aid to decision making in health. *Appl Health Econ Health Policy*. 2002;**1**(2):89-95.
18. Leal J, Luengo-Fernandez R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. *Eur Heart J*. 2006;**27**(13):1610-9.
19. Lin J, Lingohr-Smith M, Kwong WJ. Incremental health care resource utilization and economic burden of venous thromboembolism recurrence from a U.S. payer perspective. *J Manag Care Pharm*. 2014;**20**(2):174-86.
20. Mathers C. *The global burden of disease: 2004 update*. World Health Organization; 2008.
21. Hodgson TA. Cigarette smoking and lifetime medical expenditures. *Milbank Q*. 1992;**70**(1):81-125.
22. Esmaeilzadeh F, Azarkeivan A, Emamgholipour S, Akbari Sari A, Yaseri M, Ahmadi B, et al. Economic burden of thalassemia major in Iran, 2015. *Journal of research in health sciences*. 2016;**16**(3):111-5.
23. Kiiskinen U, Vartiainen E, Pekurinen M, Puska P. Does prevention of cardiovascular diseases lead to decreased cost of illness? Twenty years of experience from Finland. *Prev Med*. 1997;**26**(2):220-6.
24. Liu JL, Maniadakis N, Gray A, Rayner M. The economic burden of coronary heart disease in the UK. *Heart*. 2002;**88**(6):597-603.
25. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. *Int J Cardiol*. 2014;**171**(3):368-76.
26. Bloom BS, Bruno DJ, Maman DY, Jayadevappa R. Usefulness of US cost-of-illness studies in healthcare decision making. *Pharmacoeconomics*. 2001;**19**(2):207-13.
27. Kim J, Lee E, Lee T, Sohn A. Economic burden of acute coronary syndrome in South Korea: a national survey. *BMC Cardiovasc Disord*. 2013;**13**:55.
28. Barcelo A. Epidemiological changes and economic burden of hypertension in Latin America: evidence from Mexico. *Am J Hypertens*. 2006;**19**(6):551-2.
29. Chan B, Coyte P, Heick C. Economic impact of cardiovascular disease in Canada. *Can J Cardiol*. 1996;**12**(10):1000-6.
30. Yang L, Wu M, Cui B, Xu J. Economic burden of cardiovascular diseases in China. *Expert Rev Pharmacoecon Outcomes Res*. 2008;**8**(4):349-56.
31. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, *et al*. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009;**119**(3):480-6.
32. Maetzel A, Li LC, Pencharz J, Tomlinson G, Bombardier C, Community H, *et al*. The economic burden associated with osteoarthritis, rheumatoid arthritis, and hypertension: a comparative study. *Ann Rheum Dis*. 2004;**63**(4):395-401.
33. Claxton K, Sculpher M, McCabe C, Briggs A, Akehurst R, Buxton M, *et al*. Probabilistic sensitivity analysis for NICE technology assessment: not an optional extra. *Health Econ*. 2005;**14**(4):339-47.
34. Geravandi S, Pakdaman M. Comment on: "Estimating Economic Burden of Cancer Deaths Attributable to Smoking in Iran in 2012". *J Res Health Sci*. 2016;**16**(2):96-7.
35. Lakic D, Tasic L, Kos M. Economic burden of cardiovascular diseases in Serbia. *Vojnosanit Pregl*. 2014;**71**(2):137-43.