



Economic burden of colorectal cancer in Iran in 2012

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Received: 7 Dec 2016

Published: 20 Dec 2017

Abstract

Background: Colorectal cancer is one of the most common cancers in Iran. However little is known about the economic burden associated with this cancer in Iran. The aim of this study was to estimate the economic burden of colorectal cancer in Iran in the year 2012.

Methods: We used the prevalence-based approach and estimated direct and indirect costs of all colorectal cancer cases in 2012. To estimate the total direct costs, we model the treatment process of colorectal cancer patients in initial and continuing phase in Iran. Then the average cost of each treatment in each phase was multiplied by the number of patients who received the treatment in the country in 2012. We used the human capital method to estimate the indirect costs. We extracted data from several sources, including national cancer registry reports, hospital records, literature review, occupational data, and interviews with experts.

Results: The incidence and 5-year prevalence of colorectal cancer in Iran in 2012 were 7,163 and 22,591 individuals respectively. The economic burden of colorectal cancer in Iran was US\$298,148,718 in 2012. Most of the cost (58%) was attributed to the mortality cost, and the direct medical cost accounted for 32.14 percent of the estimated total cost. The majority of the direct medical cost was associated with chemotherapy costs (50%).

Conclusion: The economic burden of colorectal cancer in Iran is substantial and will increase in the future years.

Keywords: Colorectal cancer, Economic burden, Cost, Iran

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Cite this article as: Vahdatimanesh Z, Zندهدل K, Akbari Sari A, Farhan F, Nahvijou A, Delavari A, Daroudi R. Economic burden of colorectal cancer in the of Iran in 2012. *Med J Islam Repub Iran.* 2017 (20 Dec);31:115. <https://doi.org/10.14196/mjiri.31.115>

Introduction

Colorectal cancer (CRC) is one of the most common types of gastrointestinal cancer. Worldwide around 1.4 million new cases of CRC are identified each year and about 0.7 million die because of this illness (1). Colorectal cancer is the third most common cancer in men and the second most common in women (2). The rates of incidence and mortality due to CRC are different across the world. Although about 55% of CRC cases occur in more developed regions, about 52% of CRC death occur in less developed regions (1).

In 2012, 3,811 men and 3,352 women were diagnosed

with CRC in Iran, making it the fourth and second most commonly diagnosed cancer among Iranian men and women respectively (1, 3). Due to the aging of the population, the incidence of CRC will increase in future years in Iran (4). According to the GLOBOCAN 2012 estimates, the incidence of CRC will double by 2030 in Iran (1).

Previous studies conducted in high-income countries showed that the CRC impose a high financial cost on societies (5, 6). According to Luengo-Fernandez et al. study, CRC cost EU €13.1 billion in 2009. This cancer was the third most costly cancer in the EU and accounts for 10%

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↑What is “already known” in this topic:

Colorectal cancer (CRC) is the fourth and second most commonly diagnosed cancer among Iranian men and women respectively. Previous studies conducted in high-income countries showed that the CRC impose a high financial cost on societies. No study has been conducted in order to estimate the economic burden of CRC in Iran.

→What this article adds:

The economic burden of colorectal cancer in Iran was US\$298,148,718 in 2012. Due to the increasing trend of CRC incidence and prevalence in Iran, the economic burden of this cancer will significantly increase in the future years.

of the overall economic burden of cancer (5). In another study conducted by Mariotto et al. the economic burden of CRC was estimated \$14.14 billion in 2010 in the US and this cancer was the second most costly cancer (7). Laudicella et al. in their study estimated that CRC cost £542 million to the England health system in 2010 due to hospital care (8). The economic burden of CRC was estimated \$810 million in Korea, where direct medical and non-medical costs of CRC were \$157 million and \$62 million respectively (9). Although there is limited knowledge about the economic burden of cancer in low and middle-income countries (LMCs) including Iran, given that the incidence and prevalence of cancer are increasing in LMCs, the economic burden of cancer expected to increase significantly in these countries in the near future (2).

In order to provide high-quality cancer care and control the rising cost of cancer, policymakers need to be aware of the cancer cost (10). Furthermore, studies on the economic burden of disease show the importance of a particular disease, provide a baseline for assessing new interventions and determine the medical research priorities (11).

CRC is one of the most common cancers in Iran, however, according to our knowledge the economic burden (direct and indirect cost) of CRC has not yet been estimated in Iran. This study provides an estimate of the economic burden of CRC in Iran in 2012.

Methods

There are two approaches to calculate the economic burden of disease: incidence-based and prevalence-based approaches (12, 13). In this study, we used the prevalence-based approach with a social perspective to estimate the economic burden of CRC in Iran in 2012. In the prevalence-based approach, the costs incurred in a period (most often 1 year) as a result of the prevalence of a disease during this same period are estimated, regardless of the onset of disease (13). Thus, in this study, the costs associated with all cases of CRC (including cases with the onset in or at any time before the year 2012) were estimated, however, only costs incurred during the year 2012 were counted.

Cost estimation

Usually, in the economic burden of disease studies, costs are divided into two main groups including direct costs and indirect costs. Direct costs are divided into medical costs and non-medical costs (costs of patients and their families). Direct medical costs include costs of diagnosis, hospitalization, outpatient treatment, and etc. Direct non-medical costs include costs of patients and their families' travel to healthcare centers, housekeeping services, alterations to property and costs for complementary and alternative medicine. Indirect costs are lost productivity of patients and their families. These are generally divided into two groups of morbidity costs and mortality costs. The former is the value of lost economic productivity of patients which are not capable of doing their jobs or daily activities. The latter is the current value of future lost productivity due to premature mortality (14, 15).

Direct medical costs

We estimated the direct medical costs for patients in initial (the first 12 months after diagnosis) and continuing phases of care (16). The initial care costs included the cost of diagnosis, surgery, chemotherapy and radiotherapy. The continuing care costs included the cost of outpatient visits and routine laboratory and radiology services, such as spiral chest CT scan and colonoscopy.

To estimate the total direct medical costs, we model the treatment process of colorectal cancer patients in initial and continuing phase in Iran. Then we estimated the average cost of each treatment in each phase and the number of patients who received the treatment in the country in 2012. The average cost for each treatment in each phase was then multiplied by the number of patients treated in the corresponding phase in 2012.

To estimate the average cost of inpatient care, including costs of surgery, chemotherapy and radiotherapy, we reviewed the medical records of about 250 patients who were treated at the Cancer Institute of Iran in 2012, the largest referral cancer hospital in the country, which admits patients from the entire country. Because the tariff of medical services is identical across Iran, the results from this center can be generalized to the country. Because the costs of main chemotherapy medications did not exist in patients' records, they were calculated according to the type of chemotherapy regimen. In this regard we identified the regimen employed for patients through interviews with specialists and from their medical records and the frequency of each regimen was determined based on the information obtained from medical records. Then, the average cost of each regimen was calculated according to the drugs' price and the prescription dose.

We used expert opinion, the medical tariff and clinical practice guidelines (CPGs) in Iran to estimate the average cost of outpatient care, including diagnostic tests, follow-up visits, and laboratory and radiology services. Since the tariff of medical services in the private sector differs from that in the public sector in the I.R. of Iran, we estimated the patients who are treated in the private sector and used the private tariff for them.

We calculated the number of patients received each of the treatments in 2012 according to the current clinical practice guidelines in Iran as well as epidemiologic and clinical attributes of patients, including stage of illness, age group, tumor size, and involvement of lymph nodes. We extracted these data from previous studies (17-23) and expert opinion. Because healthcare tariffs differ in public and private sectors, we calculated average costs on the basis of patient distribution in private and public sectors and related tariffs.

Direct non-medical costs

We estimated the patient time cost and transportation costs for the patients in the initial and continuing phases. We did not estimate other direct non-medical costs due to lack of data in this study. In order to calculate patients' travel costs, we supposed that the number of travels was equal to the number of visits to doctors' offices and healthcare centers. We used the clinical practice guide-

lines in Iran and interviewed experts to estimate the average number of travels. We calculated the cost of transportation by interviewing a number of CRC patients referred to the Cancer Institute of Imam Khomeini Hospital as well as using previous research and then multiplied by the total number of travels. To estimate the patient time cost, we used medical records and clinical practice guidelines in Iran and obtained an expert opinion to estimate the average number of days that each patient lost due to receiving care in the initial and continuing phases. Then, the average number of lost days was multiplied by the average daily wage and the time cost was calculated. We calculated patient time cost for both employed and unemployed patients. We assumed the daily income for unemployed patients to be the minimum daily wage approved by the Iranian Ministry of Cooperation, Labor and Social Welfare in 2012. We extracted the data related to wages from the website of the Ministry of Cooperatives, Labor and Social Welfare (24). Usually, a family member accompanies the patient during visits; thus, we estimated the time costs for the family member, assuming that the family members are unemployed.

Indirect costs

We used the human capital approach to estimate the indirect costs, assuming that the monetary value of productivity lost due to morbidity or premature death caused by an illness equals the current wage (25). Since most CRC patients are elderly and at disability age at the time of diagnosis (17), we ignored the costs of lost productivity due to morbidity, and we calculated only the costs of lost productivity due to premature mortality.

In the human capital approach to calculate the lost monetary value due to premature mortality, the death age of a person is subtracted from life expectancy at that age, and the total expected income is calculated for remaining years. The estimation of the mortality costs requires three parameters, including the number of deaths, the years of potential life lost and the value of the productivity lost (26). We extracted the number of deaths due to CRC classified in terms of different age and sex groups in 2012 from GLOBOCAN 2012 website (1). To estimate the potential years of life lost, defined as the remaining life expectancy at the age of death, we obtained life expectancy among Iranian males and females in 2012 in different ages from Iran life table (27).

We estimated the value of lost productivity based on the employment rate and the average annual wage. To calculate annual per capita income, we divided people into two groups of employed and un-employed. For unemployed and those who were older than 60 years, we used the min-

imum daily wage to estimate the annual average earnings and assumed that the current pattern of the employment rate remains constant over time and that there is a 10% increase in the annual wage according to the inflation rate in previous years (28). We extracted the data for employment rate from Statistical Center of Iran (29). We considered a 3% discount rate to convert the stream of lifetime earnings into a present value. We converted all the costs to US dollars (US \$) using the average annual 2012 exchange rate (US\$1=Rial 12,229) (30).

Results

The number of new CRC cases was 7,163 and the 5-year prevalence was 22,591 in Iran in 2012.

Direct medical costs

The direct medical costs of CRC are presented in Table 1. We estimated the total direct medical cost of CRC \$95,828,186 in 2012. The number of patients received surgery; radiotherapy and chemotherapy were estimated 6,722, 2,585 and 5,358, respectively. A major part of direct medical cost was related to chemotherapy cost and it accounted for 50.43 percent of all costs. The total cost of chemotherapy was \$48,326,017, that \$35,103,788 of it resulted from costs of chemotherapy drugs. The most commonly used chemotherapy regimens were 5FU/LV, FOLFOX and FOFIRI with 42%, 28% and 20% prevalence respectively. Following chemotherapy, the cost of surgery was the highest at 30.12% amounting to \$28,864,467.

Direct non-medical costs

We estimated that patients spend \$18,276,353 on transportation during their treatment. The average number of transportation for patients was about 20 trips. According to the treatment guidelines, patients with colon cancer would rarely receive radiotherapy, so the number of travels to get radiotherapy was only calculated for patients with rectum cancer. The number of travels in the initial care phase was 31 in colon cancer patients and 59 in rectum cancer patients; however, these numbers would be less for patients in the continuing care phase. The mean cost per journey was about \$41.

The average number of days lost due to receiving care in the initial phase was estimated 41 and 69 in colon and rectum cancer patient for each patient respectively. However, the average number of lost days in the continuing phase was 9 days. We estimated that the patient's time cost was about \$11,018,890 in 2012.

Table 1. The direct medical cost of colorectal cancer in the I.R. of Iran, 2012

Procedures	Number of patients	Mean cost, \$US	Total cost, \$US	Total cost (percent)
Diagnosis/staging	7,163	725	5,196,339	5.42
Surgery	6,722	4,294	28,864,467	30.12
Radiotherapy	2,585	3,181	8,221,675	8.58
Chemotherapy	5,358	9,019	48,326,017	50.43
Fallow-up	15,428	338	5,219,688	5.45
Total	-	-	95,828,186	100.00

Table 2. The mortality number and productivity cost for colorectal cancer in the I.R. of Iran, 2012

Age group (year)	Mortality number			Mortality cost \$US (Discounted at 3%)		
	Male	Female	Total	Male	Female	Total
15-39	132	131	263	25,079,023	12,370,450	37,449,473
40-44	110	107	217	15,975,144	7,707,318	23,682,462
45-49	156	168	324	18,565,931	10,236,241	28,802,172
50-54	195	224	419	17,724,595	11,057,669	28,782,264
55-59	227	258	485	14,336,600	9,733,708	24,070,308
60-64	223	247	470	8,592,571	6,360,020	14,952,591
65-69	229	218	447	5,331,978	3,143,083	8,475,060
70-74	290	219	509	3,102,849	1,237,795	4,340,644
75+	698	421	1,119	1,875,652	594,661	2,470,314
total	2,260	1,993	4,253	110,584,343	62,440,945	173,025,289

Table 3. The economic burden of colorectal cancer in the I.R. of Iran, 2012

Cost component	Cost \$US	Percent
Direct medical cost	95,828,186	32.14
Direct non-medical cost (transportation and time cost)	29,295,243	9.83
Indirect cost (mortality cost)	173,025,289	58.03
Total	298,148,718	100.00

Indirect costs

In Table 2, we provided the age-specific mortality number and the cost due to premature mortality of colorectal cancer. The number of CRC mortality in Iran in 2012 was 4,253 cases for both genders. We estimated the aggregate costs of lost productivity due to premature death with a 3% discount rate, \$110,584,343 for males and \$62,440,945 for females. Higher rates of employment and number of death due to CRC in males (2,260) than females (1,993), resulted in greater costs for males. In overall, the cost of lost productivity due to premature mortality in Iran in 2012 was at \$173,025,289.

The total economic burden of CRC in 2012 was \$298,148,718 in Iran. The main components of the cost were mortality cost (58.03%) and the direct medical cost (32.14%) (Table 3).

Discussion

According to our study results, the economic burden of CRC in Iran was \$298,148,718 in 2012. Most of this cost was attributed to productivity losses (58.03%). The direct medical cost of CRC was \$95,828,186 that 50% of it was related to chemotherapy cost. The major part of chemotherapy cost (73%) was attributed to drugs cost.

Due to the large variation in the method, type of estimated costs, and treatment models, comparing the result of cost of illness studies conducted in different countries is very difficult. However, a comparison of cancer costs in different countries and health systems could help to better understand the economic consequences of healthcare policies and plans (10).

Similar to previous studies conducted in other countries, we modeled the CRC treatment process to estimate the medical costs of CRC patients in Iran (31, 32). Tilson et al. developed a decision tree model to estimate medical costs of CRC in Ireland (33).

Our finding showed that the most part of direct medical cost was attributed to chemotherapy drugs and 5FU/LV was the most common chemotherapy regimen. These findings are consistent with the findings of the previous study conducted in Iran. Davari et al. estimated the direct medical cost of CRC in 320 patients referred to a hospital

in Iran. In their study, the highest share of medical costs was related to chemotherapy drugs and the 5FU/LV regimen was the most common chemotherapy regimen (34). Due to the high price of chemotherapy drugs, these drugs impose high financial costs on patients and societies. Although the most of new chemotherapy drugs have little impact on improving patients' outcome, their price is too high, so they may not be cost-effective. For example, the cost of FOLFOX regimen is about 6 times more than 5FU/LV regimen in Iran, while the two regimens are different in only one drug (i.e. Oxaliplatin). To control the cost of chemotherapy drugs, governments should control the drugs price and use cost-effectiveness data in funding decisions for cancer drugs (35). Furthermore, since generic drugs are usually less expensive than brand-name drugs, using generic drugs will decrease the cost of chemotherapy (36).

In our study, direct non-medical costs accounted for about 10 percent of the total economic burden of CRC and these costs were higher in rectum cancer than colon cancer. In a study conducted in France, 2.5 percent of CRC medical cost was attributed to transportation. Also, the transportation cost was three times higher for rectal cancer compared with colon cancer (37). In another study conducted in Korea, the direct non-medical costs account for about 8 percent of the total economic burden of CRC(9).

Our result showed that a large part (58%) of the economic burden of CRC was due to the value of productivity lost. this result is somewhat consistent with other studies conducted in other countries (9, 10). In the study conducted in Korea, the mortality cost consists the major part (54%) of the total economic burden of CRC followed by medical costs (19.4%).

The results of this study showed that the economic burden of CRC is substantial and this cancer imposes enormous costs on patients, their families and the society. Globally more than 90 percent of all CRC occurs after age 50 years (1). According to the last census in Iran, about 75 percent of Iran's population is young (below 40 years) (29), so if appropriate preventive and screening plans are not implemented in young ages, we will see a significant increase in CRC in Iran as this young population will be-

come middle-aged and more susceptible to colorectal cancer. Due to the increasing trend of CRC incidence and prevalence in Iran, the economic burden of this cancer will significantly increase in the future years. Many studies have shown that the medical costs of CRC in the early stages are lower than those in the advanced stages (18, 33, 37-39). For example, in Davari et al. study the average costs for the first 12 months of treatment course were \$10,715, \$15,920, \$16,452 and \$16,723 in the first to fourth stages respectively (18). In addition, the survival of patients in early stages is higher than those in the advanced stages (22). Thus early detection can reduce the medical cost as well as mortality cost of colorectal cancer. In recent years, due to introducing of population-based screening programs in most developed countries, the incidence, mortality, and burden of the CRC significantly reduced in these countries (40). Since LMCs countries including Iran are facing with a shortage of resources and cannot implement screening programs for several cancers, CRC can be a good option for screening in this countries and is likely to be cost-effective. Since the majority of CRC occurs after the age of 50 years, usually the screening program started in this age (40). However, there are several methods for screening CRC including fecal occult blood testing (FOBT), flexible sigmoidoscopy and colonoscopy. So in order to select the appropriate age and method for implementing screening program at the national level, conducting economic evaluation studies is necessary. The result of this study can provide data for such studies and appropriate estimation of the disease burden with and without screening in Iran.

To the best of our knowledge, this is the first economic burden study of CRC in Iran. We modeled the treatment process and used several databases to estimate the economic burden of CRC in Iran. However, this study had some limitations. First, because we used the human capital approach to calculate the mortality cost, the value of life for some groups, like children, women and retired people, are underestimated (25). Second, because of the inaccessibility of appropriate data, we could not estimate some kinds of expenditure, like intangible costs (the costs associated with pain, suffering and impairment in quality of life), the cost of terminal care and recurrence of CRC and the cost of informal and complementary therapies, so our estimation of medical costs may be low.

Conclusion

In conclusion, our study result showed that the economic burden of CRC in Iran is substantial and increasing, which indicate a need for implementing preventive and screening program at the national level. Furthermore, in order to select the cost-effective screening program, economic evaluation studies are needed to be conducted.

Acknowledgement

This work was supported by a grant from the cancer research center of the Cancer Institute of Iran (grant number 92-04-51-25063). The authors have no conflicts of interest that are directly relevant to the content of this manuscript.

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Ferlay J SI, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. 2013.
2. Stewart B, Wild CP. World cancer report 2014. 2014.
3. Iranian cancer registry national report: ministry of health; non-communicable disease management center. Cancer office; 2006-2009.
4. Abdifard E, Amini S, Bab S, Masroor N, Khachian A, Heidari M. Incidence trends of colorectal cancer in Iran during 2000-2009: A population-based study. *Med J Islam Repub Iran.* 2016;30:382.
5. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol.* 2013;14(12):1165-74.
6. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010-2020. *J Natl Cancer Inst.* 2011;103(2):117-28.
7. Warren JL, Yabroff KR, Meekins A, Topor M, Lamont EB, Brown ML. Evaluation of trends in the cost of initial cancer treatment. *J Natl Cancer Inst.* 2008 Jun 18;100(12):888-97.
8. Laudicella M, Walsh B, Burns E, Smith PC. Cost of care for cancer patients in England: evidence from population-based patient-level data. *Br J Cancer.* 2016 May;114(11):1286.
9. Kim SG, Hahm MI, Choi KS, Seung NY, Shin HR, Park EC. The economic burden of cancer in Korea in 2002. *Eur J Cancer Care (Engl).* 2008;17(2):136-44.
10. Yabroff KR, Borowski L, Lipscomb J. Economic studies in colorectal cancer: challenges in measuring and comparing costs. *J Nation Cancer Instit Monograph.* 2013;2013(46):62.
11. Daroudi R, Sari AA, Nahvijou A, Kalaghchi B, Najafi M, Zendeheel K. The Economic Burden of Breast Cancer in Iran. *Iranian J Pub Health.* 2015;44(9):1225.
12. Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, et al. Stage, age, comorbidity, and direct costs of colon, prostate, and breast cancer care. *J Natl Cancer Inst.* 1995;87(6):417-26.
13. Yabroff KR, Lund J, Kepka D, Mariotto A. Economic burden of cancer in the United States: estimates, projections, and future research. *Cancer Epidemiol Biomarkers Prev.* 2011;20(10):2006-14.
14. Brown ML, Yabroff KR. 12 Economic Impact of Cancer in the United States. *Cancer Epidemiol Prevent.* 2006:202.
15. Yabroff KR WJ, Knopf K, Davis WW, Brown ML. Estimating patient time costs associated with colorectal cancer care. *Med Care.* 2005;43(7):640-8.
16. Lang HC, Wu SL. Lifetime costs of the top five cancers in Taiwan. *Eur J Health Econ.* 2012;13(3):347-53.
17. Ansari R, Mahdavinia M, Sadjadi A, Nouraei M, Kamangar F, Bishehsari F, et al. Incidence and age distribution of colorectal cancer in Iran: results of a population-based cancer registry. *Cancer letters.* 2006;240(1):143-7.
18. Davari M, Maracy MR, Emami MH, Taheri D, Aslani A, Givi M, et al. The Direct Medical Costs of Colorectal Cancer in Iran; Analyzing the Patient's Level Data from a Cancer Specific Hospital in Isfahan. *Int J Prevent Med.* 2012;3(12):887.
19. Derakhshanfar A KHR, Niayesh A, Ezati A. Epidemiological Study of Colorectal Cancer at Ekbatan and Besat Hospitals of Hamadan during Ten Years (1998-2008). *J Surg Iran.* 2010;18(2).
20. Fateh Sh AM. An Epidemiologic Study of Colorectal Cancer in Arak during 1994-2004. *J Surg Iran.* 2008;16(2).
21. Jalali S.M KI, Jalali S.A. Epidemiological Characteristics of Colorectal Cancer in Patients Referred to Imam Khomeini Hospital During (1981-2001). *J Iran Uni Med Sci.* 2004;11(43).
22. Moghimi Dehkordi B, Safaie A, MR. Z. Survival Rates and Prognostic Factors in Colorectal Cancer Patients. *J Ilam Uni Med Sci.* 2008;16(1):33-42.
23. Safaei A MD, Fatemi SR, Ghiyasi S, Zali MR. Epidemiology of colorectal Cancer: Study the recorded cases in 1379- 86. *Zahedan J Res Med Sci (Tabib-E-Shargh).* 2007;9(3):209-16.
24. Ministry of Labour and Social affair, Labour Market Information

- System [Available from: <http://www.amarkar.ir/asp/statReport.aspx>.
25. Brown ML and Y. KR. Economic impact of cancer in the United States. *Cancer Epidemiology and Prevention*, Schottenfeld J, F, and Faumeni J Editors 2006, Oxford University Press New York, NY p 209-2022006.
 26. Max W, Sung HY, Stark B. The economic burden of breast cancer in California. *Breast Cancer Res Treat*. 2009;116(1):201-7.
 27. World Health Organization. 2014. Global Health Observatory Data Repository; available from: <http://apps.who.int/gho/data/?theme=mainandvid=60760>, accessed on:(01/10/2014).
 28. The Central Bank of Iran (CBI), The total price index of consumer goods and services in urban areas(inflation rate). Available at: <http://www.cbi.ir/simplelist/1589.aspx>, 2013.
 29. Iranian Statistical Center (2013). Iran Statistical Yearbook, available from: <http://www.amar.org.ir/Default.aspx?tabid=2153>, accessed on:(10.09.2015).
 30. Central Bank of The Islamic Republic of Iran, Exchange Rates [Available from: http://www.cbi.ir/ExRates/rates_fa.aspx.
 31. Will B, Le Petit C, Berthelot J, Tomiak E, Verma S, Evans W. Diagnostic and therapeutic approaches for nonmetastatic breast cancer in Canada, and their associated costs. *Br J Cancer*. 1999;79(9-10):1428.
 32. Will BP, Berthelot JM, Le Petit C, Tomiak EM, Verma S, Evans WK. Estimates of the lifetime costs of breast cancer treatment in Canada. *Eur J Cancer*. 2000;36(6):724-35.
 33. Tilson L, Sharp L, Usher C, Walsh C, Whyte S, O'Ceilleachair A, et al. Cost of care for colorectal cancer in Ireland: a health care payer perspective. *Eur J Health Econ*. 2012;13(4):511-24.
 34. Davari M MM, Emami MH, Taheri D, Aslani A, Givi M, et al. The Direct Medical Costs of Colorectal Cancer in Iran; Analyzing the Patient's Level Data from a Cancer Specific Hospital in Isfahan. *Int J Prevent Med*. 2012;3(12):887.
 35. Daroudi R, Mirzania M, Zendeheel K. Attitude of Iranian Medical Oncologists Toward Economic Aspects, and Policy-Making in Relation to New Cancer Drugs. *Int J Health Policy Manag*. 2016;5(2):99-105.
 36. Daroudi R, Mirzania M, Nikravanfard N, Sadighi S, Sedighi Z, Zendeheel K. Estimation of the prevalence and direct medical costs of chronic myeloid leukemia in the IR of Iran in the era of tyrosine kinase inhibitors. *Asia-Pacific J Clin Oncol*. 2016.
 37. Clerc L, Jooste V, Lejeune C, Schmitt B, Arveux P, Quantin C, et al. Cost of care of colorectal cancers according to health care patterns and stage at diagnosis in France. *Eur J Health Econ*. 2008;9(4):361-7.
 38. Lang K, Lines LM, Lee DW, Korn JR, Earle CC, Menzin J. Lifetime and treatment-phase costs associated with colorectal cancer: evidence from SEER-Medicare data. *Clinical Gastroenterol Hepatol*. 2009;7(2):198-204.
 39. Song X, Zhao Z, Barber B, Gregory C, Cao Z, Gao S. Cost of illness in patients with metastatic colorectal cancer. *J Med Econ*. 2011;14(1):1-9.
 40. Stock GT, Aguiar Jr PN, Tadokoro H, de Mello RA. *Cancer Epidemiology and Screening*. Int Manual Oncol Practice: Springer; 2015. p. 3-14.