



Catastrophic Health Expenditure After the Implementation of Health Sector Evolution Plan: A Case Study in the West of Iran



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Abstract

Background: One of the main objectives of health systems is the financial protection against out-of-pocket (OOP) health expenditures. OOP health expenditures can lead to catastrophic payments, impoverishment or poverty among households. In Iran, health sector evolution plan (HSEP) has been implemented since 2014 in order to achieve universal health coverage and reduce the OOP health expenditures as a percentage of total health expenditures. This study aimed to explore the percentage of households facing catastrophic health expenditures (CHE) after the implementation of HSEP and the factors that determine CHE.

Methods: A total of 663 households were selected through a cluster sampling based on the census framework of Sanandaj Health Center in July 2015. Data were gathered using face-to-face interviews based on the household section of the World Health Survey questionnaire. In this study, according to the World Health Organization (WHO) definition, if household health expenditures were equal to or more than 40% of the household capacity to pay, household was considered to be facing CHE. The determinants of CHE were analyzed using logistic regression model.

Results: The rates of households facing CHE were 4.8%. The key determinants of CHE were household economic status, presence of elderly or disabled members in the household and utilization of inpatient or rehabilitation services.

Conclusion: The comparison of our findings and those of other studies carried out using a methodology comparable with ours in different parts of Iran before the implementation of HSEP suggests that the implementation of recent reforms has reduced CHE at the household level. Utilization of inpatient and rehabilitation services, the presence of elderly or disabled members in the household and the low economic status of the household would increase the likelihood of facing CHE. These variables should be considered by health policy-makers in order to review and revise content of recent reform, thus financially protecting public against CHE.

Keywords: Catastrophic Health Expenditures (CHE), Health System Reforms, Health Expenditures, Iran

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Citation: Piroozi B, Moradi G, Nouri B, Mohamadi Bolbanabad A, Safari H. Catastrophic health expenditure after the implementation of health sector evolution plan: a case study in the west of Iran. *Int J Health Policy Manag.* 2016;5(7):417–423. doi:10.15171/ijhpm.2016.31

Article History:

Received: 25 October 2015

Accepted: 8 March 2016

ePublished: 14 March 2016

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Key Messages

Implications for policy makers

- Iran's health system has not yet achieved its goal in decreasing the ratio of households encountered with catastrophic health expenditures (CHE) to 1%, which was announced in fifth Economic, Social, and Cultural Development Plan.
- There has been a reduction in incidence of CHE since the introduction of the health sector evolution plan (HSEP).
- Some households/individuals characteristics are associated with increased incidence of CHE.

Implications for the public

Having supplemental insurance would result in more financial protection for the household. Since, using rehabilitation, dental, and inpatient services increases the possibility of facing catastrophic health expenditures (CHE), therefore, households should try to use preventive services more in order to need expensive services less in the future.

Background

As announced in the constitution of World Health Organization (WHO), the enjoyment of the highest attainable standard of health requires taking steps in order to achieve universal coverage. To achieve this goal, countries need a type of financial system which enables people to utilize health services without any financial barrier. One of the fundamental actions taken in order to reduce financial barriers of using

health services is replacement of pre-payment method with direct payment at the point of services delivery.¹

Direct payment is the most unfair and most inefficient way to financing health system and can lead to catastrophic payment.^{2,3} The WHO recognizes households facing catastrophic health expenditures (CHE) when the household out-of-pocket (OOP) expenditure on health is equal to or higher than 40% of the households' capacity to pay.⁴⁻⁶ The

households' capacity to pay is defined as the income left after all basic needs are satisfied.^{4,5}

According to the WHO, the case of CHE represents a failure of health systems to protect people against the financial consequences resulting from utilization of healthcare services.⁷ Serious concerns have been voiced over the distribution of financial load in many countries, and protecting the poor against CHE has been regarded as one of the priorities of governments.⁸

Various studies have pointed to three objectives for the measurement of CHE: (1) identification of changes in household well-being, (2) assessment of poverty level/low living status at the household level, and (3) evaluation of the performance of available medical insurance plans.^{9,10}

Overall, each year, about 150 million people are exposed to CHE when paying their health expenditures, of which about 100 million are impoverished people. CHE can occur not necessarily due to the costs of expensive treatment processes; many households with relatively low payments also face financial catastrophes.^{1,6}

Today, millions of people are deprived of healthcare services due to health expenditures at the time of service delivery, and most people who make use of such services also tend to face financial problems; or they are even pushed into financial poverty when paying the expenditures of healthcare services. One of the essential actions to alleviate the financial problems incurred due to the payments related to healthcare services involves replacing pre-payment method with direct payment method at the time of receiving services.^{5,7,11}

The sustainability of health financing systems, which is particularly taken into account when increasing health expenditures, is regarded as a serious concern in many countries. Worldwide, governments have engaged in health sector reforms. Discussions on health sector reforms focus more on equity-based financing systems.¹²

Four major forces stimulate reforms in the health sector of countries around the world: (1) increasing health expenditures, (2) rising public expectations of healthcare system, (3) limited capacity of governments to pay for healthcare, and (4) skepticism about traditional approaches.¹³

Overall, Iran's health system has not been in a favourable condition in recent years with respect to financing, payments, service packages, quality of services, medicine, and people's rights and satisfaction level in terms of delivering and receiving services; there have also been numerous forces operating in order to reform the health system.¹⁴ According to the report of the national health accounts (NHA) published by the Statistical Centre of Iran in the spring of 2011, the share of OOP payment in total health expenditure has increased over the years in a way that the rate was higher than 50% in 2008. According to the report, the share of healthcare, social security, and armed forces insurance (as the three primary insurance providers in the country) in the total health expenditure were only 6.6%, 10.9%, and 1.5%, respectively in 2008, which indicates the inefficiency of the insurance system.¹⁵ Moreover, according to the 2011 report of the Eastern Mediterranean Regional Office (EMRO) of the WHO in Iran, the share of OOP direct payments in the total health expenditure has been 58%. This high share of OOP payments suggests that a significant portion of expenditures

has been imposed on households instead of being provided by insurance organizations.¹⁶

As pointed out in the report of the demographic and health survey indices in 2010 published by the National Institute of Health Research, 17% of Iranian households were not covered by any health insurance.¹⁷

Furthermore, several regional studies conducted in Iran have a range of 8.3% to 22.2% for households facing CHE.^{7,18-20}

These pieces of evidence go against the objectives highlighted in the Fifth Economic, Social, and Cultural Development Plan; that is, decreasing the share of OOP payments in the total health expenditure by 30% and reducing the percentage of households facing CHE to less than 1%.²¹

The evidences mentioned above indicate that Iran's health system had not been in a favorable condition in many respects in recent years. Having the new government in power since early 2014, special attention has been paid to the health sector. The parliament and government have provided statutory and administrative facilities as well as adequate resources for the implementation of new reforms in Iran's health sector. In addition, the Ministry of Health and Medical Education (MoHME) has launched a series of reforms, called as the health sector evolution plan (HSEP), across the country since May 5, 2014. This plan focuses on three approaches of financial protection of people, provision of access to health services, and promotion of the quality of services, which each will be explained in more details.^{22,23}

Iran's Health Sector Evolution Plan

HSEP has been one of the most important events in the field of health sector in Iran during the past three decades; this plan can be compared with the primary healthcare network launched in the 1980's. The budget for the plan is provided from 10% of revenues coming from the targeted subsidy plan and a 1% increase in the rate of value-added tax.²² After more than one year since the start of this plan, three phases have been implemented. The first phase of HSEP was carried out in hospitals affiliated with MoHME and consisted of eight executive packages (started on May 5, 2014). One of these packages involved the reduction of the amount of money paid by patients qualified for basic health insurance by 6% and 3% of the total hospitalization expenditures for, respectively, urban and rural residents and residents of cities with less than 20 thousand population (having rural insurance) that go to public hospitals through a referral system. Under this plan, all people without basic health insurance can be covered free of charge. The second phase of the HSEP (started on May 22, 2014) focused on the primary healthcare.

Another issue in the HSEP involved informal payments in the medical community. The majority of doctors argued that the treatment tariffs were unrealistic and one of the main reasons for asking for informal payments; therefore, the government decided to render the tariffs realistic and make them closer to the actual final prices. To this end, the third phase of the HSEP was implemented, and a new book of relative value units of health services was published in September 29, 2014 whereby medical tariffs were increased with the aim of eliminating informal payments and establishing equity in the income of different specialties. The ultimate objectives of HSEP include increasing the responsiveness of the health system, reducing

OOP payments, reducing the percentage of households facing CHE and increasing the rate of child natural delivery.^{22,23} Along with the expansion of the health system reform plan in different domains, various aspects of the plan should also be monitored and evaluated. Timely monitoring and evaluation of reforms can provide evidence for (re)directing the implementation of the reforms. This study, thus, seeks to answer three main questions: (1) What is the percentage of households facing CHE after the implementation of the HSEP in the city of Sanandaj?, (2) What are the factors causing these catastrophic payments?, and (3) Have we achieved the objective highlighted in the Fifth Economic, Social, and Cultural Development Plan (ie, reducing the percentage of households facing CHE to less than 1%)?²¹ The findings of the study could provide implications for health policy-makers in order to evaluate the success of the HSEP and, if necessary, revise the health interventions and reforms to enhance the plan.

Methods

This is a cross-sectional, descriptive-analytical study conducted in July 2015 among the households in the city of Sanandaj. According to the formula in Equation 1, having $d = 0.025$ (minimal detectable difference), $\alpha = .05$ (type I error), and $p = 10\%$ (proportion of the households faced with CHE), sample size was obtained 553 households.²⁴ Since the sampling procedure was cluster sampling, the design coefficient of 1.2 was applied to enhance the accuracy of sampling. The final sample size was 663 (1.2×553) households, 646 of which completed the questionnaire.

$$n = \frac{Z^2 \cdot \frac{1-\alpha}{2} \times P(1-P)}{d^2} \quad (1)$$

The population under study consisted of all the households in Sanandaj (population: 435 904, the number of households: 126 987).²⁵ Cluster sampling, including 17 clusters of 39 households, was conducted based on the census framework of Sanandaj Health Center. The number of households in each cluster was calculated by dividing the total final sample size by the number of health centers in the city of Sanandaj. Each cluster represented the population covered by one of the 17 health centers in the city of Sanandaj. The file number of each household cluster head was randomly selected, and, after extracting the address and phone number of the household, an inquirer visited the household home in person, and, by standing behind the door of the first household home (the cluster head), he/she moved in the right direction until the cluster set was completed. If there was no access to a household within a cluster or if a household did not cooperate, an alternative household was inquired. At the household level, the first informant, who was 18 years old, willing, and able to answer the questions, was asked to complete the questionnaire.

Study Instruments

The data collection instrument included the “World Health Survey” questionnaire that was developed by the WHO in 2003 to evaluate the performance of health systems.³ This questionnaire has been translated in Iran in recent years, and

its validity and reliability have been confirmed in the study conducted by Kavosi et al.⁷ In this study we used two recall periods for expenditure questions: The last 30 days for the total household and healthcare expenditures, and the last 30 days and the last 12 months for outpatient and inpatient expenditures, respectively.⁷

Statistical Analyses

In this study, two methods of statistical analysis were employed to measure the households facing CHE and to analyze and predict the relationship and the likelihood of variables under study (viz, insurance status, gender of household head, household size, having members of over 65 years old, having members of under five years of age, having disabled members, household economic status, and receiving dental care, rehabilitation, inpatient, and outpatient services and the related expenditures).^{26,27}

Calculating the Catastrophic Healthcare Expenditures

CHE is important to measure equity in health financing. Households with healthcare expenditures higher than 40% of their capacity to pay were grouped under those households facing catastrophic healthcare expenditures.⁷ The capacity to pay refers to the household effective income minus its livelihood costs. The effective income is based on the household total expenditures within one specific time period; this income has been considered in many countries as a better measure than the income reported in the household surveys that represents purchasing power.^{7,19} In order to calculate the household livelihood costs, food poverty line (ie, a portion of the household total expenditures dedicating to costs related to food) was used; Xu et al have described this methodology in detail.⁴

Factors Affecting Catastrophic Healthcare Expenditures

In this study, Fisher exact tests were used to examine the relationship between the variables under study and CHE. Logistic regression model was also employed to predict the likelihood of facing CHE and to calculate the odds ratios (OR) using the model coefficients.

Results

The data related to 646 households (97.4%) were analyzed. Ninety-two percent of the household heads were men. The average age of household heads was 43 years (standard deviation [SD] = 1.2), and the average household dimension was 4.5 people (SD = 1.4). Most households (98.6%) had health insurance, most of which (48.8%) were of health services insurance type. Only 115 households (17.8%) had supplementary insurance (Table 1). Additionally, 115 households (17.8%) had members aged 65 and over, and 132 households (20.4%) had members younger than 5 years old. Moreover, 68 households (10.4%) had members with disabilities or in need of care.

According to the findings depicted in Table 2, the percentage (frequency) of households that were exposed to CHE were 31 households (4.8%). In addition, the average total monthly costs and the average total monthly expenditures associated with household healthcare are shown in the table.

The results of Fisher exact tests showed that there were not

Table 1. Demographic Characteristics of Households in Study, Sanandaj, Iran, 2015

Variable	Number	%
Gender of the head of household		
Male	594	92.0
Female	52	8.0
Household size		
Less than four members	282	43.7
More than four members	344	56.3
Status of the Basic health insurance		
Yes	637	98.6
No	9	1.4
Type of the basic health insurance		
Health services	315	48.8
Social security	185	28.6
Relief committee	50	7.7
Armed forces	87	13.4
Uninsured	9	1.4
Status of supplementary health insurance		
Yes	115	17.8
No	531	82.2

significant relationships between facing CHE and variables such as basic health insurance ($P=.359$), household size ($P=.843$), presence of members under 5 years of age ($P=.447$), and receiving outpatient services ($P=.225$). There were statistically significant relationships between the chances of facing CHE and such variables as status of supplementary health insurance ($P=.030$), presence of members over 65 years of age in the household ($P=.001$), presence of members with disabilities and in need of care in the household ($P=.001$), receiving hospital inpatient services ($P=.001$), gender of the household head ($P=.002$), household economic status ($P=.011$), and receiving dental care ($P=.001$) and rehabilitation services ($P=.001$; Table 3).

OR of exposure of different groups based on the variables under study were calculated using logistic regression. As seen in Table 4, the households without supplementary insurance ($OR=0.05$) as well as those with females as household heads ($OR=0.09$) experienced a greater likelihood of facing CHE. As for the variable related to receiving hospital inpatient services, those households receiving inpatient services had the chance of facing CHE 129.7 times more than other households. In addition, the chances of exposure to CHE in the households with members aged over 65 or members with disabilities and in need of care or in the households taking rehabilitation and dental care services were, respectively, 4.51, 5.21, 2.91, and 6.77 times more than other households. As for the economic status variable, the chance of facing CHE in households with low economic status (the poor) was 19.04 times more than the middle class and the rich. (It should be noted that the economic status variable initially consisted of three categories of *poor*, *middle*, and *rich*; but, the middle class and the rich

Table 3. Relationship Between the Status of Households Facing Catastrophic Expenditures and the Variables in the Study

Variables	Faced With CHE		P
	Yes (%)	No. (%)	
Status of the basic health insurance			
Yes	30.0 (5)	607.0 (95)	.395 ^a
No	1.0 (11)	8.0 (89)	
Status of supplementary health insurance			
Yes	1.0 (1)	114.0 (99)	.030
No	30.0 (6)	501.0 (94)	
Household size			
Less than four members	13.0 (5)	269.0 (95)	.843
More than four members	18.0 (5)	346.0 (95)	
Gender of the head of household			
Male	24.0 (4)	570.0 (96)	.002
Female	7.0 (13)	45.0 (87)	
Economic status			
Poor	30.0 (6)	476.0 (94)	.011
Moderate or rich	1.0 (0.7)	139.0 (99.3)	
Household having member over 65 years old			
Yes	13.0 (11)	102.0 (89)	.001
No	18.0 (3)	513.0 (97)	
Household having member(s) under 5 years old			
Yes	8.0 (6)	124.0 (94)	.447
No	23.0 (4.5)	491.0 (95.5)	
There are people with disabilities and in need of care			
Yes	9.0 (13)	59.0 (87)	.001
No	22.0 (4)	556.0 (96)	
Utilization of inpatient services			
Yes	30.0 (14)	184.0 (86)	.001
No	1.0 (0.3)	431.0 (99.7)	
Utilization of outpatient services			
Yes	30.0 (5)	555.0 (95)	.225
No	1.0 (2)	60.0 (98)	
Utilization of dental care services			
Yes	15.0 (12.5)	106.0 (87.5)	.001
No	16.0 (3)	508.0 (97)	
Utilization of rehabilitation services			
Yes	12.0 (17)	60.0 (83)	.001
No	19.0 (3.5)	555.0 (96.5)	

Abbreviation: CHE, catastrophic health expenditures.

^aResults of Fishers exact test.

were later merged into one category).

Discussion

The results of the study showed that the rate of households facing CHE was as high as 4.8%, which is a distance away from the Fifth Development Plan aiming to reduce the percentage of households facing CHE to less than 1%. In recent years, multiple interventions or steps have been taken to achieve this aim, the most important of which was the implementation

Table 2. Percentage of Households Facing to CHE and the Mean of Total Monthly Household Expenditure (in Iranian Rial) in 2015

Variable	Mean	SD	Number (%)
Percentage of households exposed to CHE	-	-	31 (4.8%)
Mean of total monthly household expenditure	9 230 650	3 125 810	-
Mean of total monthly household expenditure on health services	742 420	439 210	-

Abbreviation: CHE, catastrophic health expenditures.

Table 4. Relationship Between Determinants and Catastrophic Healthcare Expenditure

Variables		OR	CI (95%)	
			Lowest	Highest
Status of the basic health insurance ^a	Yes	0.02	0.00	7.91
	No			
Status of supplementary health insurance	Yes	0.05	0.00	0.63
	No			
Household size	Less than four members	0.79	0.29	2.19
	More than four members			
Gender of the head of household	Male	0.09	0.02	0.39
	Female			
Economic status	Poor	19.04	2.20	164.80
	Moderate or rich			
Household having member over 65 years old	Yes	4.51	1.55	13.12
	No			
Household having member(s) under 5 years old	Yes	1.89	0.60	5.50
	No			
There are people with disabilities and in need of care	Yes	5.21	1.49	18.21
	No			
Utilization of inpatient services	Yes	129.70	15.00	1096.00
	No			
Utilization of outpatient services	Yes	1.62	0.16	16.46
	No			
Utilization of dental care services	Yes	2.91	0.94	8.99
	No			
Utilization of rehabilitation services	Yes	6.77	1.91	23.97
	No			

^a All the variables were compared with the first group; 2 Log likelihood = 118.04; Nagelkerke R square = 0.57

of health system reform in May, 2014. Despite the steps taken, these expenditures are still high; however, compared with similar studies conducted using identical method in different parts of Iran prior to the implementation of health system reform plan, the results of our study showed the rate of households facing CHE to be lower, and this rate has decreased twofold or even more.^{7,19}

Piroozi et al study carried out in the province of Kurdistan in 2015 showed that OOP cost-sharing by inpatients for hospital bills in hospitals affiliated to MoHME reduced from 24% to 3% before and after the implementation of HSEP, respectively. Also during the same period, the proportion of inpatients in these hospitals making informal payment to physicians was reduced from 4.5% to 0%.²⁸

One reason why still the rate of CHE in the province of Kurdistan was high could be related to the lower degree of development and social welfare in this province compared with other provinces of the country. It is, thus, expected that the rate of exposure to CHE in Kurdistan would be higher than the national average. Another reason could lie in the increase in an tariffs for medical services as a result of the publication of a new book of relative value units of healthcare services in September 29, 2014 with the aim of making the tariffs closer to the actual final prices; accordingly, the tariffs for medical services increased, particularly in private sector.²² According to the results of the study, certain variables increase the chances of exposure to CHE. One of the most important determinants of facing CHE is the household economic status so that the higher the economic status of a household, the lower the chance of exposure to such expenditures. In 2012, Kavosi et al⁷ showed an inverse relationship between the rate of facing CHE among households and increasing economic

rank in economic quintiles; meaning that a lower percentage of households in upper quintiles has been exposed to CHE.⁷ The findings obtained by Somkotra and Lagrada in 2009 showed that, after the implementation of universal health coverage in Thailand, CHE changed direction from poor to rich households. As the researchers argued, the reason lied in the poor's higher use of the public services covered by the insurance system and the rich's greater use of the expensive services in the private sector.²⁹

According to the findings of the study, presence of the members with disabilities and in need of care or over 65 years old in a household had a significant relationship with CHE and also increased the chances of facing CHE. This finding has also been pointed out in some other studies.^{7,19,30} People with disabilities and in need of care are likely to be sicker than the ordinary people and, therefore, presence of such members makes households spend a greater part of their capacity to pay on health expenditures. These pieces of findings could help redirect the focus of health system policies toward the financial protection of such households through implementing supportive programs as well as insurance plans for special diseases.

As the results of the present study indicated, another key determinant of facing CHE includes the status of supplementary health insurance and the covered services. Thus, the households not covered by supplementary insurance or those taking services not included in the package of basic insurance companies (eg, dental care services) would allocate a higher percentage of their capacity to pay to health expenditures; studies in Iran and other countries have also confirmed this hypothesis.^{11,19,31} In this study, no relationship was found between household size and the chances of

facing CHE. Similarly, in 2012, Kavosi et al found no such a relationship.⁷ In their 2013 study, Amery et al concluded that the larger household dimension, the higher rate of households facing CHE.¹⁸ The results of Yardim et al study in Turkey in 2010 showed that for every one person increase in household size, the household spending would increase by 2%, and also the probability of facing CHE would increase by 0.4%.³⁰

In this study, there was no relationship between the presence of members under the age of five and the likelihood of facing CHE. In 2012, Kavosi et al also reported no such a relationship.⁷ However, Su et al demonstrated a significant relationship between the presence of members under five years old in the household and an increasing rate of taking the services provided by the private sector.³²

The results of the study indicated no significant relationship between receiving outpatient services and the chances of facing CHE, although the former tended to slightly increase the likelihood of exposure to CHE. The study conducted by Kavosi et al in 2014 revealed that for every instance of taking outpatient services, the probability of facing CHE would increase by 11%.¹⁹ Nevertheless, Amery et al, in their 2013 study, concluded that there was no significant relationship between receiving outpatient services and CHE.¹⁸

The results of our study also showed no significant relationship between having basic health insurance and the risk of exposure to CHE. However, Kavosi et al found that the status of basic health insurance is a key factor determining CHE and that households not covered by any insurance would dedicate a higher percentage of their payment capacity to healthcare services; a piece of finding that was not of statistical significance.¹⁹ Implementing insurance policies to protect households against CHE has been introduced in the studies conducted by Somkotra and Lagrada²⁹ in Thailand in 2009, and Sun et al³³ in China in 2009 as a solution to the problem of lacking the financial protection of health systems. Since the implementation of universal insurance in Turkey and Thailand, there has been a decline in the rate of direct payments for health as well as the number of households facing CHE and those that have been pushed into poverty.^{20,30,33}

The piece of finding in our study that there was no significant relationship between having basic health insurance and the chances of facing CHE could be related to the fact that the percentage of those people with basic insurance is almost 99%; although this coverage rate is high in number, the range of services covered is not wide enough so that almost all those who have been exposed to CHE possess basic insurance (97%).

Households that had used dental and rehabilitation services were more likely to face with CHE in comparison to those that had not used these services. Some other studies support these findings.^{7,19} In Iran, most of the dental and rehabilitation services are not covered by basic health insurance companies and patients should afford these costs.

Limitations

Our study was performed in Sanandaj city, located at west of Iran, so this might not be a representative picture of CHE status after implementation HSEP in Iran. Additionally, there was a probability of over- or under-reporting of the expenditures and respondent recall bias. We tried minimizing

recall bias by shortening recall period.

Conclusion

Considering the relevant studies conducted using similar method in different provinces of Iran^{7,19} prior to the implementation of the HSEP and comparing their results with those obtained in our study, it is concluded that despite the high rate of the CHE (4.8%) and not achieving the objective emphasized in the Fifth Economic, Social, and Cultural Development Plan (ie, reducing the proportion of households facing CHE to less than 1%),²¹ it appears that the occurrence of CHE has declined at the household level after the implementation of HSEP. Findings of this study could help policy-makers develop policies in line with the promotion of financial protection against CHE and also provide feedback to health policy-makers in order to review and revise the programs implemented in the framework of the health system reform plan. What is clearly evident is that policy-makers' attention directed toward the factors increasing the chances of facing CHE could greatly help decrease such expenditures as well as achieving the aim of financial protection of households against health expenditures. According to the findings of the current study, the healthcare packages provided by insurance organizations should be revised and such services as dental care and rehabilitation services that increased the likelihood of facing CHE should also be covered by the basic insurance package. In addition, in order to have more financial protection, the poor households and households having members over 65 years old or with disabilities should be exempted from paying some of the healthcare expenditures.

Acknowledgments

The research received financial support from the Kurdistan University of Medical Sciences (No. 93.145) in Sanandaj, Iran. We are also grateful to our colleagues working in the Social Determinants of Health Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran.

Ethical issues

The study was approved by the ethic committee of Kurdistan University of Medical Sciences, Sanandaj, Iran.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

BP and GM designed and coordinated the study; BP, GM, BN, AM, and HS contributed to literature searches, analysis of the data and prepared the drafted of manuscript. BP and GM were the main contributors and provided advice on all stages of the study. All authors verified the final version.

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