

ORIGINAL ARTICLE

Social Disparity in Breast and Ovarian Cancer Incidence in Iran, 2003-2009: A Time Trend Province-Level Study

Aliasghar A. Kiadaliri

Division of Health Economics, Department of Clinical Sciences-Malmö, Lund University, Malmö, Sweden; Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Purpose: This pioneering study aimed to investigate social disparities in breast cancer (BC) and ovarian cancer (OC) incidence rates among women across Iran's provinces from 2003 to 2009.

Methods: Provincial level population distribution data pertaining to women were obtained from the Statistical Centre of Iran. Age-standardized incidence rates of BC and OC were gathered from the National Cancer Registry. Human Development Index was used as the provinces' social rank (SR), and rate ratio and Kunst and Mackenbach relative index of inequality were used to assess social disparities. Annual percentage change (APC) was calculated using joinpoint regression, and Spearman rank correlation was used to examine the association between APC and SR. **Results:** It was found that over the study period, annual incidence rates rose

by 11.6% and 9.7% for BC and OC, respectively. Social disparities were substantial and stable in favor of provinces with lower SR in Iran, and were more profound for BC than OC. Correlations between APC and SR were small and nonsignificant for both BC and OC. **Conclusion:** The results showed that both BC and OC incidence increased in Iran during 2003 to 2009. There were positive associations between BC and OC incidence rates and the provinces' SR. This study's recommendations provide valuable information for health resource allocation pertaining to BC and OC control programs across provinces in Iran.

Key Words: Breast neoplasms, Health status disparities, Iran, Longitudinal studies, Ovarian neoplasms

INTRODUCTION

The universal goal of policy makers, to eliminate disparities in gender, social class, race/ethnicity, and place, with regard to health can be achieved by understanding its current state and causes. Disparities in the incidence and outcomes of cancer constitute a major component of social disparities in health [1].

Globally, breast cancer (BC) is the most common cancer afflicting women and is second overall, with an estimated 1,383,000 new cases diagnosed in 2008 [2]. An estimated 225,000 new cases of ovarian cancer (OC) were diagnosed worldwide, making it the seventh most common cancer among women in 2008. In the same year, these cancers were responsible for 598,000 deaths worldwide (17.9% of total deaths caused by cancer) [2]. Among Iranian women, BC is

the most common form of cancer and fifth leading cause of death. OC is the eighth most common form, and the 12th most frequent cause of death [3-5]. Furthermore, most Iranian women are in the advanced stages of BC and are at least a decade younger than their counterparts in developed countries [6,7].

Individual and regional social rank (SR), referring to socio-economic status, are well-known independent predictors of incidence, diagnosis, treatment, and outcomes of cancer [8]. While epidemiological studies have shown inverse associations between cancer incidence rates and regional SR, positive associations have been observed for BC and OC incidence rates [9-13]. A previous study conducted across the 22 districts of Tehran, Iran, reported positive associations between BC and OC incidence rates and the districts' SR [14]. In addition, case-control studies showed that higher education and employment were associated with a higher risk of BC in the country [15,16]. However, these studies are neither national level nor longitudinal studies and therefore, limited in their scope.

My study attempted to fill the gap and examined the distribution of BC and OC incidence rates in Iran using data from

Correspondence to: Aliasghar A. Kiadaliri

Department of Clinical Sciences-Malmö, Lund University, Malmö 20502, Sweden

Tel: +46-40-39-1425, Fax: +46-40-39-1370

E-mail: aliasghar.ahmad_kiadaliri@med.lu.se

Received: September 3, 2013 Accepted: December 7, 2013

the cancer registry at province level, across years 2003 to 2009. The focus of the research questions were on the following: were there any trends in BC and OC incidence rates across 2003 to 2009? Did social disparities exist in BC and OC incidence rates across provinces? How did these social disparities vary over time? Answers to these can guide decision making for health resource allocation for BC and OC control programs across the provinces in Iran.

METHODS

Data sources and variables

Iran, a lower-middle-income country, is located in the Eastern Mediterranean region with an area of 1,648,000 km² and a population of about 75 million (Statistical Centre of Iran Census, 2011).

The census and estimated data on population distribution of the provinces were obtained from the Statistical Centre of Iran. Data on age-standardized incidence rate (ASR) of BC and OC per 100,000 women were obtained from published reports by the Iran Cancer Registry. Up 2007, these reports included only cancer cases diagnosed in pathology departments across the country that were reported to the Office of Cancer and Genetic Diseases, a subdivision of the Center for Disease Control in the Ministry of Health [17]. Since 2008, these reports additionally include nonpathology cases (i.e., population-based registration) to avoid underestimation of cancer incidence rates (e.g., in 2009, 12.1% of all cancer cases were obtained from nonpathology resources) [18]. Human Development Index (HDI) was used as the provinces' SR, and related data was obtained from the President Deputy of Strategic Planning and Control. HDI is a composite index of three basic dimensions of human development: life expectancy at birth, educational attainment (based on a combination of adult literacy rate and primary to tertiary education enrolment rates), and income (based on GDP per head, adjusted for purchasing-power parity in US\$) (United Nations Development Program: Human Development Index [HDI]. <http://hdr.undp.org/en/statistics/hdi/>. Accessed October 18th, 2013).

Social disparity

Social disparity was evaluated using Cuzick's test for trend and disparity measures, rate ratio (RR) and Kunst and Mackenbach relative index of inequality (RII_{KM}) [19]. To calculate RR, the provinces were ranked and divided in five quintiles according to HDI using population weights. Negative binomial regression with a robust variance was used to calculate RR and its 95% confidence interval to compare the highest and lowest quintile. Its limitation is that it only considers the

population in two extreme socioeconomic groups. To therefore account for the whole population, RII_{KM} was calculated [19]. For RII_{KM}, the provinces were first ranked lowest to highest according to HDI and the population in each province was assigned a modified ridity-score (a fractional rank) based on the midpoint of range in the cumulative distribution of the population in a given province. For example, if a province with the lowest HDI comprised 10% of the population, a value of 0.05 (0.1/2) was assigned to this province, and if second province comprise 15% of population, a value of 0.175 [(0.1+(0.15/2))] was assigned to this province and so forth. Negative binomial regression was then applied to the expected number of cancer incidences in the provinces using these fractional ranks and population as an exposure variable. With the lowest SR as reference, an RII_{KM} value greater (lesser) than 1 indicates that age-standardized incidence rate (ASR) was higher among provinces with higher (lower) SR, where greater distance from 1 implies more disparity. In this particular case, RII_{KM} has an interpretation similar to risk ratio or relative risk. The expected numbers of BC and OC incidences were calculated by multiplying ASR and population size for each province. Microsoft Excel (Microsoft, Redmond, USA) and Stata version 11 (StataCorp LP, College Station, USA) software were used for these analyses.

To examine changes of ASR of BC and OC over time, annual percentage change (APC) with 95% confidence interval was calculated for the country and all provinces using the Joinpoint Regression Program 3.5.4.

APC was estimated using following regression:

$$\ln(I_t) = b_0 + b_1(t)$$

$$APC = (e^{b_1} - 1) \times 100$$

Where I_t shows ASR of BC (OC) for year t .

To examine if there was social disparity in APC across the provinces, Spearman rank correlation between HDI and APC was calculated. Moreover, I used *suest* command in Stata to compare the magnitude of disparity between BC and OC, and between the first and the last year of the study period.

RESULTS

Figure 1 present average ASR of BC and OC per 100,000 Iranian women over the 2003 to 2009, across the provinces. Substantial differences in the distribution of BC and OC incidence rates across the country were observed. Although the incidence of BC was higher than OC in the country, the distribution of these cancers across the provinces were similar (Spearman rank correlation (ρ) = 0.72, $p < 0.001$). The highest and the lowest BC incidence rates were observed in Tehran and Sistan & Baluchestan, respectively (7.4-fold difference).

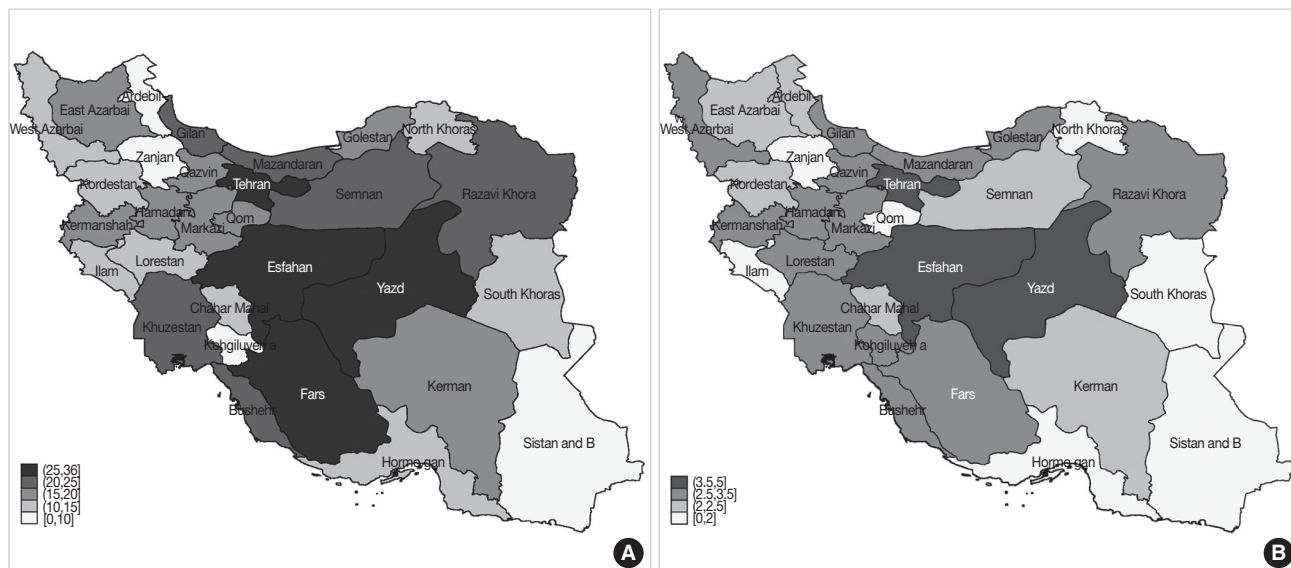


Figure 1. Average age-standardized incidence rates of breast cancer (A) and ovarian cancer (B) across Iran’s provinces over 2003 to 2009. As Northern Khorasan, Razavi Khorasan and Southern Khorasan formed a single province before 2005, the estimates for these provinces are based on data year 2005 to 2009.

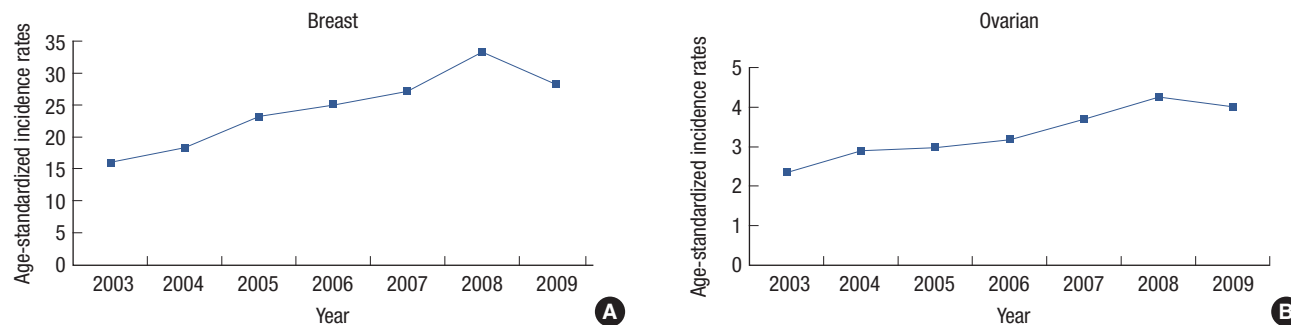


Figure 2. Age-standardized incidence rates of breast cancer (A) and ovarian cancer (B) through 2003 to 2009 in Iran. X and Y axes show data year and age-standardized incidence rates per 100,000 population, respectively.

On the other hand, the highest and the lowest OC incidence rates were observed in Tehran and South Khorasan, respectively (6.6-fold difference).

Figure 2 presents ASR of BC and OC for the country across the study period. ASR of BC per 100,000 people increased from 16 in 2003 to 28 in 2009. The corresponding figures for OC were 2 and 4 in 2003 and 2009, respectively. Table 1 presents the provinces’ mean HDI, ASR, and APC values across the study period. Overall APC indicates increasing trends for BC and OC in Iran through 2003 to 2009. Across the provinces, APC for BC and OC were positive and statistically significant in 22, and 13, out of 30 provinces, respectively. This implies that incidence rates of OC were stable in most provinces over the study period.

Figure 3 display ASR of BC and OC across five quintiles of HDI in Iran through 2003 to 2009. For both BC and OC, a

clear gradient was observed. The results of Cuzick’s test indicated positive significant associations between BC ($Z=4.47, p<0.001$) and OC ($Z=3.98, p<0.001$) incidence rates and the provinces’ SR. The social disparity measures are shown in Table 2. RR was significantly higher than 1, in every year of the study period, implying higher BC and OC incidence rates across the provinces in the highest quintile of HDI compared with the lowest one. The RII_{KM} values also showed that incidences of BC and OC were higher across the provinces with higher SR.

Comparison between RII_{KM} for BC and OC showed that in 4 out of 7 years, RII_{KM} values for BC were significantly higher than OC, implying that social disparity was more profound in the BC. In the other 3 years, no significant differences were found. Trend analysis of RII_{KM} showed that in both BC and OC, social disparities were stable over the study period. There was no significant difference between RII_{KM} in the first and

Table 1. Mean HDI, ASR, and APC (%) of breast and ovary cancers incidences in Iran's provinces, 2003 to 2009

Province	Mean HDI	Breast cancer		Ovary cancer	
		Mean ASR	APC (%)	Mean ASR	APC (%)*
Ardebil	0.723	9.26	8.06	2.15	14.39
Bushehr	0.762	20.79	14.34*	2.57	31.94*
Chaharmahal Bakhtiari	0.733	12.45	28.06*	2.39	21.01
East Azerbaijan	0.744	16.20	37.22*	2.33	49.68*
Fars	0.762	25.23	15.35*	3.21	14.52*
Gilan	0.762	24.51	14.91*	2.74	15.05*
Golestan	0.723	16.18	12.64*	2.98	8.72*
Hamedan	0.725	16.51	22.41*	2.51	21.44*
Hormozgan	0.747	11.86	17.36*	1.87	36.95*
Illam	0.714	10.89	20.39*	1.57	11.11
Isfahan	0.788	29.80	14.47*	3.70	13.30*
Kerman	0.734	15.90	9.84*	2.42	8.59
Kermanshah	0.727	19.87	14.73*	2.56	11.91*
Khuzestan	0.763	24.86	16.88*	2.90	20.75*
Kohgiluyeh & Boyerahmad	0.717	7.21	9.52	2.42	42.99
Kordestan	0.679	13.56	27.11*	2.35	17.69*
Lorestan	0.712	14.68	18.50*	2.58	19.31*
Markazi	0.767	18.16	25.36*	2.78	10.70
Mazandaran	0.756	24.37	16.17*	2.54	12.12*
North Khorasan†	0.718	10.33	14.09	0.74	18.62
Qazvin	0.770	18.13	11.91*	2.94	4.36
Qom	0.762	18.63	2.27	1.94	-0.97
Razavi Khorasan†	0.757	23.57	11.47	2.97	15.52
Semnan	0.784	21.80	19.93*	2.40	8.37
Sistan & Baluchestan	0.639	4.81	14.41	0.83	9.37
South Khorasan†	0.723	11.99	5.24	1.20	56.76
Tehran	0.813	35.69	10.19	4.88	6.57
West Azerbaijan	0.705	13.80	9.62*	2.76	-0.76
Yazd	0.784	29.42	6.05*	3.81	6.57
Zanjan	0.733	9.53	12.88*	1.32	14.93
Overall (Iran)	0.741	17.67	11.59*	2.48	9.73*

HDI=Human Development Index; ASR=age-standardized incidence per 100,000 population; APC=annual percentage change.

*Statistically significant result ($p < 0.05$); †Based on data year 2005 to 2009.

last years of the study. In addition, Spearman rank correlation between HDI and APC was found to be small and statistically insignificant ($\rho = -0.04$, $p = 0.84$ for BC; $\rho = -0.25$, $p = 0.19$ for OC) implying that there were no social disparities in changes of BC and OC incidence rates over the study period.

DISCUSSION

In this, first of its kind, national level study, I assessed social disparity in the distribution of BC and OC incidences across Iran's provinces over a period of 7 years (2003-2009). There were increasing trends in BC and OC incidence rates in the country across the study period. Moreover, I found substantial social disparities in BC and OC incidence rates across the country in favor of provinces with lower SR, which that re-

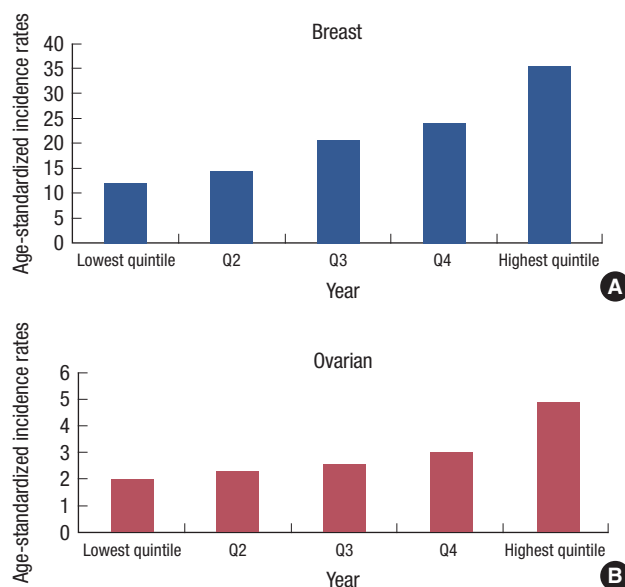


Figure 3. Age-standardized incidence rates of breast cancer (A) and ovarian cancer (B) across five quintiles of Human Development Index over 2003 to 2009 in Iran.

Table 2. Social disparity measures of breast cancer incidence in Iran, 2003 to 2009

Study year	Breast cancer		Ovary cancer	
	RR (95% CI)	RII (95% CI)	RR (95% CI)	RII (95% CI)
2003	4.63* (2.86-7.50)	4.87* (2.45-9.70)	3.72* (2.52-5.49)	3.30* (1.37-7.96)
2004	1.83* (1.33-2.52)	2.69* (1.50-4.83)	1.31 (0.98-1.75)	1.34 (0.83-2.16)
2005	2.38* (1.94-2.92)	2.94* (2.02-4.30)	2.01* (1.42-2.86)	1.99* (1.01-3.92)
2006	2.74* (2.16-3.48)	3.51* (2.39-5.14)	2.63* (1.99-3.48)	2.60* (1.52-4.43)
2007	2.70* (2.07-3.54)	3.30* (2.04-5.33)	1.94* (1.36-2.77)	2.12* (1.19-3.77)
2008	3.41* (2.73-4.26)	4.05* (2.63-6.24)	2.79* (2.09-3.74)	2.46* (1.44-4.19)
2009	2.86* (2.33-3.51)	3.53* (2.37-5.25)	2.04* (1.55-2.67)	2.07* (1.21-3.56)

RR=rate ratio (the highest vs. the lowest quintile of Human Development Index); CI=confidence interval; RII=relative index of inequality.

*Statistically significant result ($p < 0.05$).

mained stable over time. In addition, social disparities were more profound for BC than OC.

The annual increase in BC and OC was 11.6% and 9.7%, respectively through 2003 to 2009. These increasing trends are in line with previous studies conducted in Iran [3,6]. It is argued that lifestyle changes in favor of westernization, e.g., change in reproductive behavior, age of marriage, age at first birth, dietary habits, obesity, less physical activity, and smoking might partly explain these trends in the country [20]. Improving diagnostic and therapeutic services might be another reason for such upward trends. In addition, improving and expanding the cancer registry using confirmed histological cases to a population-based registry might explain the observed trends in Iran.

In line with previous studies, positive associations between BC and OC incidence rates and SR at the ecological level in Iran were found [11-14]. These positive associations might be partly explained by established reproductive risk factors for BC and OC [21,22]. Previous studies in Iran showed that women with better SR were generally older at time of their first marriage and first delivery, had fewer children, and had a later onset of menopause, than their counterparts with lower SR [23-25]. Although there is a lack of evidence for the association between SR, the use of hormone replacement therapy, and access to early diagnosis in Iran, previous studies suggest that these might partly explain positive associations between SR and incidence rates of BC and OC [26]. Furthermore, previous studies in Iran found a positive association between higher SR and conducting breast self-examination, which may have resulted in higher rates of observed BC incidence among women with higher SR [27,28].

Similar to studies in Italy and the United States, social disparity in BC and OC incidence rates were stable over time in Iran [29,30]. In addition, there were no significant differences in APC with respect to SR in the current study. These findings highlight the need for developing and conducting health interventions and programs to narrow social disparities in Iran, by especially focusing on the distribution of known risk factors of BC and OC.

The first limitation of this study is the error in recording and classification, specifically in pathology registries, which may be a source of bias. I expect this to be more common in provinces with lower SR. Therefore, it is suggested that there might be upward bias in estimates of social disparities. Second, data from the National Cancer Registry provide data at the province-level, which did not allow analysis for smaller geographic areas such as counties. This implies that the observed disparities in BC and OC incidence rates between-provinces are not necessarily applicable to smaller geographic units or individuals. Third, this study uses an ecological paradigm and no con-

trol for confounders (e.g., lifestyle factors) was applied. Thus, no causal inference can be drawn from the results.

In summary, the present study indicated that there have been increasing trends in BC and OC incidence rates in Iran through 2003 to 2009. I found substantial social disparities in the distribution of BC and OC incidence rates across the provinces in Iran in favor of provinces with lower SR. In addition, I found that these social disparities were stable over time. Further analyses are needed to explain observed social disparities in the current study. This study's recommendations provide valuable information for health resource allocation pertaining to BC and OC control programs across provinces in Iran.

CONFLICT OF INTEREST

The author declares that he has no competing interests.

REFERENCES

- Palmer RC, Schneider EC. Social disparities across the continuum of colorectal cancer: a systematic review. *Cancer Causes Control* 2005;16: 55-61.
- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893-917.
- Mousavi SM, Gouya MM, Ramazani R, Davanlou M, Hajsadeghi N, Seddighi Z. Cancer incidence and mortality in Iran. *Ann Oncol* 2009; 20:556-63.
- Arab M, Khayamzadeh M, Hashemi M, Hosseini M, Tabatabaeefar M, Anbiaee R, et al. Crude and age-specific incidence rate patterns for histopathologic subtypes of ovarian cancer in Iran. *Arch Iran Med* 2010; 13:203-8.
- Taghavi A, Fazeli Z, Vahedi M, Baghestani AR, Pourhoseingholi A, Barzegar F, et al. Increased trend of breast cancer mortality in Iran. *Asian Pac J Cancer Prev* 2012;13:367-70.
- Mousavi SM, Montazeri A, Mohagheghi MA, Jarrahi AM, Harirchi I, Najafi M, et al. Breast cancer in Iran: an epidemiological review. *Breast J* 2007;13:383-91.
- Harirchi I, Karbakhsh M, Kashefi A, Momtahan AJ. Breast cancer in Iran: results of a multi-center study. *Asian Pac J Cancer Prev* 2004;5:24-7.
- Weissman JS, Schneider EC. Social disparities in cancer: lessons from a multidisciplinary workshop. *Cancer Causes Control* 2005;16:71-4.
- Beiki O, Hall P, Ekblom A, Moradi T. Breast cancer incidence and case fatality among 4.7 million women in relation to social and ethnic background: a population-based cohort study. *Breast Cancer Res* 2012;14: R5.
- Jensen KE, Hannibal CG, Nielsen A, Jensen A, Nøhr B, Munk C, et al. Social inequality and incidence of and survival from cancer of the female genital organs in a population-based study in Denmark, 1994-2003. *Eur J Cancer* 2008;44:2003-17.
- Torres-Cintrón M, Ortiz AP, Ortiz-Ortiz KJ, Figueroa-Vallés NR, Pérez-Irizarry J, Díaz-Medina G, et al. Using a socioeconomic position index to assess disparities in cancer incidence and mortality, Puerto Rico,

- 1995-2004. *Prev Chronic Dis* 2012;9:E15.
12. Eberle A, Luttmann S, Foraita R, Pohlabein H. Socioeconomic inequalities in cancer incidence and mortality: a spatial analysis in Bremen, Germany. *J Public Health* 2010;18:227-35.
 13. Faggiano F, Partanen T, Kogevinas M, Boffetta P. Socioeconomic differences in cancer incidence and mortality. In: Kogevinas M, Pearce N, Susser M, Boffetta P, editors. *Social Inequalities and Cancer*. Lyon: International Agency for Research on Cancer; 1997. p.65-176.
 14. Rohani-Rasaf M, Moradi-Lakeh M, Ramezani R, Asadi-Lari M. Measuring socioeconomic disparities in cancer incidence in Tehran, 2008. *Asian Pac J Cancer Prev* 2012;13:2955-60.
 15. Naieni KH, Ardalan A, Mahmoodi M, Motevalian A, Yahyapoor Y, Yazdizadeh B. Risk factors of breast cancer in north of Iran: a case-control in Mazandaran Province. *Asian Pac J Cancer Prev* 2007;8:395-8.
 16. Ghiasvand R, Maram ES, Tahmasebi S, Tabatabaee SH. Risk factors for breast cancer among young women in southern Iran. *Int J Cancer* 2011; 129:1443-9.
 17. Ali Mohagheghi M, Mosavi-Jarrahi A. Review of cancer registration and cancer data in Iran, a historical prospect. *Asian Pac J Cancer Prev* 2010;11:1155-7.
 18. Center for Noncommunicable Disease Control. *National Cancer Registry in 2009*. Tehran: Iran Ministry of Health and Medical Education; 2012.
 19. Mackenbach JP, Kunst AE. Measuring the magnitude of socio-economic inequalities in health: an overview of available measures illustrated with two examples from Europe. *Soc Sci Med* 1997;44:757-71.
 20. Taheri NS, Bakhshandehnosrat S, Tabiei MN, Kashani E, Rajaei S, Behshar S, et al. Epidemiological pattern of breast cancer in Iranian women: is there an ethnic disparity? *Asian Pac J Cancer Prev* 2012;13:4517-20.
 21. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol Rev* 1993;15:36-47.
 22. Tsilidis KK, Allen NE, Key TJ, Dossus L, Lukanova A, Bakken K, et al. Oral contraceptive use and reproductive factors and risk of ovarian cancer in the European Prospective Investigation into Cancer and Nutrition. *Br J Cancer* 2011;105:1436-42.
 23. Kazerooni T, Talei AR, Sadeghi-Hassanabadi A, Arasteh MM, Saalabian J. Reproductive behaviour in women in Shiraz, Islamic Republic of Iran. *East Mediterr Health J* 2000;6:517-21.
 24. Ayatollahi SM, Ghaem H, Ayatollahi SA. Sociodemographic factors and age at natural menopause in Shiraz, Islamic Republic of Iran. *East Mediterr Health J* 2005;11:146-54.
 25. Torabi F, Baschieri A. Ethnic differences in transition to first marriage in Iran: the role of marriage market, women's socio-economic status, and process of development. *Demogr Res* 2010;22:29-62.
 26. Braaten T, Weiderpass E, Kumle M, Lund E. Explaining the socioeconomic variation in cancer risk in the Norwegian Women and Cancer Study. *Cancer Epidemiol Biomarkers Prev* 2005;14:2591-7.
 27. Noroozi A, Jomand T, Tahmasebi R. Determinants of breast self-examination performance among Iranian women: an application of the health belief model. *J Cancer Educ* 2011;26:365-74.
 28. Noroozi A, Tahmasebi R. Factors influencing breast cancer screening behavior among Iranian women. *Asian Pac J Cancer Prev* 2011;12: 1239-44.
 29. Spadea T, D'Errico A, Demaria M, Faggiano F, Pasian S, Zanetti R, et al. Educational inequalities in cancer incidence in Turin, Italy. *Eur J Cancer Prev* 2009;18:169-78.
 30. Schootman M, Lian M, Deshpande AD, Baker EA, Pruitt SL, Aft R, et al. Temporal trends in area socioeconomic disparities in breast-cancer incidence and mortality, 1988-2005. *Breast Cancer Res Treat* 2010;122: 533-43.