**Name of Journal: *World Journal of Gastrointestinal Oncology***

**ESPS Manuscript NO: 29510**

**Manuscript Type: Original Article**

***Observational Study***

**Bayesian adjustment for over-estimation and under-estimation of gastric cancer incidence across Iranian provinces**

Hajizadeh N *et al*. Regional misclassification in cancer incidence registry

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**Author contributions:** Pourhoseingholi MA was principal investigator and countributing in writing the manuscript; Hajizadeh N contributed to study conception and data analysis; Baghestani AR and Abadi A contributed to study conception and design; Zali MR contributed to interpretation the results; all authors contributed to editing, reviewing and final approval of the article.

**Institutional review board statement:** The study was reviewed and approved by research committee of research institute for gastroenterology and liver diseases (Tehran).

**Informed consent statement:** Hereby it is attested that this manuscript which is submitted for publication in World Journal of Gastrointestinal Oncology has been read and approved by all authors, has not been published, totally or partly, in any other journal.

**Conflict-of-interest statement:** There are no conflicts of interest to report.

**Data sharing statement:** No additional data are available.

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**Manuscript source:** Invited manuscript

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**Received:** August 17, 2016

**Peer-review started:** August 19, 2016

**First decision:** October 21, 2016

**Revised:** November 2, 2016

**Accepted:** November 27, 2016

**Article in press:**

**Published online:**

**Abstract**

***AIM***

To correct the misclassification in registered gastric cancer incidence across Iranian provinces in cancer registry data.

***METHODS***

Gastric cancer data is extracted from Iranian annual of national cancer registration report 2008. A Bayesian method with beta prior is implemented to estimate the rate of misclassification in registering patient’s permanent residence in neighboring province. Each time two neighboring provinces with lower and higher than 100% expected coverage of cancer cases are selected to be entered in the model. The expected coverage of cancerous patient is reported by medical university of each province. It is assumed that some cancer cases from a province with a lower than 100% expected coverage are registered in their neighboring province with more than 100% expected coverage.

***RESULTS***

The condition was true for 21 provinces from a total of 30 provinces of Iran. It was estimated that 43% of gastric cancer cases of North and South Khorasan provinces in north-east of Iran was registered in Razavi Khorasan as the neighboring facilitate province; also 72% misclassification was estimated between Sistan and balochestan province and Razavi Khorasan. The misclassification rate was estimated to be 36% between West Azerbaijan province and East Azerbaijan province, 21% between Ardebil province and East Azerbaijan, 63% between Hormozgan province and Fars province, 8% between Chaharmahal and bakhtyari province and Isfahan province, 8% between Kogiloye and boyerahmad province and Isfahan, 43% Golestan province and Mazandaran province, 54% between Bushehr province and Khozestan province, 26% between Ilam province and Khuzestan province, 32% between Qazvin province and Tehran province (capital of Iran), 43% between Markazi province and Tehran, and 37% between Qom province and Tehran.

***CONCLUSION***

Policy makers should consider the regional misclassification in the time of programming for cancer control, prevention and resource allocation.

**Key words:** Cancer incidence registry; Misclassification; Bayesian correction; Gastric cancer; Iran

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**Core tip:** Due to the lack of equipped health facilities in some provinces of the country, patients seek health care in neighboring full-featured provinces and they do not mention their own permanent residence. It makes misclassification error in cancer registry data. This error flaws planning for resource allocation to different regions of the country for cancer control and prevention. The aim of this study is to use a Bayesian method to estimate the rate of misclassification in cancer incidence registry among neighboring provinces of Iran and re-estimating the rate of gastric cancer in each province.

Hajizadeh N, Pourhoseingholi MA, Baghestani AR, Abadi A, Zali MR. Bayesian adjustment for over-estimation and under-estimation of gastric cancer incidence across Iranian provinces. *World J Gastrointest Oncol* 2016; In press

**INTRODUCTION**

Gastric cancer was 4th most common cancer among men and 5th among women diagnosed in 2012 in the world[1]. Generally, its incidence is about twice in males as in females. Eastern Asia, Eastern Europe and South America have the highest rates of gastric cancer incidence and the lowest incidence rates are belong to North America and most parts of Africa[2]. As a result of population aging and growth, and also adoption of cancer-related lifestyle like westernized diets and physical inactivity, the burden of cancer is increasing in developing countries[3]. Gastric cancer is the first common cancer among Iranian men and the 3th common cancer (after breast cancer and colorectal cancer) among Iranian women[4].

Nowadays, information about incidence and mortality is one of the most important needs for making effective medical decisions. Having information regarding chronic diseases, especially cancers as one of the major causes of human mortality, has a particular importance[5]. Considering different diseases with different etiologies, just incidence rate is not enough to be an index of burden in the population. The different incidence rates of cancer diseases in different regions, races and occupational groups emphasize the importance of comprehensive information about it. Identifying the distribution of disease between different populations is a good manner for finding causations and quantifying the potentials for disease prevention[6,7].

Incidence, the number of new cases occurring, is produced by population-based cancer registries. Cancer registries, which originated in the twentieth century, have expanded in the last 20 years[8,9] and is known as the main source of epidemiological data for all cancer fighting sectors at the local and international level. These registries collect information regarding burden of cancers by recording the incidence, mortality, prevalence and survival for different cancers in a systematic manner[10-12]. Their role has expanded into the planning and evaluation of cancer screening programs, detecting the impact of interventions and treatments to cancer control, improvement in patient care and specifying future needs for material and manpower resources. Accurate information of incidence and mortality rate is the most essential requirement to control cancer which is related to the correctness of information for individual cancer patients which is included the patient’s residence, date of diagnosis, primary site and histological type of tumor, and date of death[9].

Most cancer patients throughout the country seek diagnostic and medical treatment in Tehran (capital of Iran) or neighboring facilitate provinces either due to lack of proper facilities in their own residence or to obtain better-quality treatment and diagnostic services[13], and they don’t mention their permanent residence address. It makes misclassification error in cancer registry data. Misclassification error is the disagreement between the observed and the true value. As the evidence of existence of misclassification error, the expected coverage of cancer incidence in different provinces can be noted; that the observed rate of incidence is more than expected rate in some provinces, and on the other hand, it is much less than expected rate in neighboring provinces[14]. However it happens while it is expected that the rate of cancer incidence be about the same in neighboring provinces that are similar in lifestyle and environmental conditions.

There are two approaches to reduce the effects of misclassification error; the first is using a small validation sample[15] and the second is Bayesian method which provides subjective prior information for some of the parameters for estimating misclassification parameter and correcting the statistic[16-18]. Bayesian models also can accommodate unobserved variables like individual’s true information in the presence of Misclassification error. Bayesian method is a flexible method in which the prior information from previous studies can be incorporate with observed data in the analysis and even if vague priors are specified, Bayesian Monte Carlo Markov Chain (MCMC) method can be used to fit highly realistic models. The aim of this study is to use a Bayesian method to estimate misclassification rate in neighboring provinces in Iran using gastric cancer incidence registry data of 2008.

**MATERIALS AND METHODS**

Gastric cancer incidence data is extracted from Iranian annual of national cancer registration report in 2008[14].Firstly, the Age Standardized Rate (ASR) for gastric cancer [coded according to the 10th revision of the International Classification of Diseases (ICD-10; C16)] is calculated for all provinces of Iran using direct standardization method and the standard population in WHO 2000 for both genders and four age groups (0-14 years, 15-49 years, 50-69 years and over than 70 years old) in order to compare statistics on cancer in Iran with those for the rest of the world[19]. Then expected coverage of cancer cases is calculated for medical university of each province. In the process of cancer incidence registry, all new diagnosed cancer cases by pathology centers and other diagnostic centers in the country are entered in software which is made by ministry of health. Medical university of each province sends this information recorded in this temporary data bank to the ministry of health. Ministry of health after coding the recorded cancers based on 10th revision of international coding of disease and removing duplicates, makes a permanent data bank of cancer cases and sends it back to medical university of each province. So each medical university has an observed number of cancer cases and also has an expected coverage of cancer cases that is considered to be 113 per 100000. By dividing the observed number to the expected number of cancer cases, the percent of expected coverage for each province is calculated. For entering the data to the Bayesian model two vectors y1 and y2 were used. Vector $y\_{1}=[y\_{11},y\_{21},…,y\_{r1}]^{'}$ for the province that has an expected coverage less than 100% and vector $y\_{2}=[y\_{12},y\_{22},…,y\_{r2}]^{'}$ for a neighboring province with a more than 100% expected coverage. Subscript r shows the number of covariate patterns that is made by age group and sex group combinations. A Poisson distribution was considered for count data y1 and y2[20-22]. An informative beta prior distribution was assumed for $θ$ as the probability of registering a data in misclassified group; so $θ\~beta(a, b)$[23-25]. For selecting prior value for the parameters of beta distribution, the calculated expected coverage for the medical university which has a lower than 100% expected coverage was used as $b$ and $a$ was calculated with subtracting $b$ from 100. Thus a/(a + b) which is the expectation of beta distribution converges to the misclassified rate. Since $θ$ is unknown, a latent variable approach was employed to correct the misclassification effect[20,21]. The latent variable $U$ with binomial distribution, *i.e*., $U\_{i} | θ,y\_{1},y\_{2}\~Binomial(y\_{i2},P\_{i})$ that $P\_{i}=\frac{λ\_{i1}θ}{λ\_{i1}θ+λ\_{i2}}$, was considered as the number of events from the first group that are incorrectly registered in the misclassified group. Finally by using a Gibbs sampling algorithm, the posterior distribution appears in the following form; $θ | U\_{i},y\_{1},y\_{2}\~Beta(∑\_{i}U\_{i}+a,∑\_{i}y\_{i1}+b)$[20,26-28]. After estimating the misclassification rate between each two neighboring provinces, the rates of gastric cancer incidence for each province were re-estimated. Analyses were carried out using R software version 3.2.0.

**RESULTS**

All incidence records due to gastric cancer that have registered at Iranian annual of national cancer registration report in 2008 included in this study.

Twenty-one provinces from a total of 30 provinces of Iran are selected to be included in this study based on their expected coverage of cancer cases. In the other nine provinces, the number of cancer cases was about the same as their expectation from the number of cancerous patients that are registered in those provinces.

For example the reported percent of expected coverage of cancer incidence for Razavi Khorasan province in north-east of Iran was 155.5%. It means that Razavi Khorasan province have covered 55.5% more new cancer cases than its expectation, whereas the South and North Khorasan provinces that are in neighborhood of Razavi Khorasan have just covered respectively 41.4% and 34.8% of their expected coverage of cancer incidence; that is a clear indication of existence of misclassification error. The expected coverage for other provinces is mentioned in Table 1.

After implementation of the Bayesian method, it was found that there was 43% misclassification in gastric cancer incidence registry from North and South Khorasan provinces in Razavi Khorasan province, 72% misclassification from Sistan and balouchestan province located in south-west of Iran in Razavi Khorasan that is one of most facilitate provinces of Iran with equipment health care services, 8% misclassification from Kohgilouye and boyerahmad province in Isfahan province that is one of the biggest provinces in central region of Iran, 8% misclassification from Chaharmahal and bakhtyari province in Isfahan, 36% misclassification from West Azerbaijan province in East Azerbaijan province that is its neighboring facilitate province in north west of Iran, 21% misclassification from Ardebil province in East Azerbaijan, 43% misclassification from Golestan province in Mazandaran province in the margin of Caspian sea, 26% misclassification from Ilam province in Khozestan province in the south of the country that has more health facilities proportional to its neighboring provinces, 54% misclassification from Bushehr province in Khozestan, 63% misclassification from Hormozgan province in Fars province that is either one of the most facilitate provinces of Iran, 32% misclassification from Qazvin province in Tehran that is the capital of Iran in the central region of the country, 43% misclassification from Markazi province in Tehran and 37% misclassification from Qom province in Tehran. Number of gastric cancer incidence and age standardized rate (ASR) of gastric cancer before and after Bayesian correction in each province for total population and also separately for male and female appeared in Tables 2 and 3.

**DISCUSSION**

According to this study, incidence of gastric cancer in Iran’s provinces is registered with misclassification error and some patients are diagnosed and registered in their neighboring provinces; especially the provinces that don’t have equipment health centers with enough diagnostic devises and experts.

Knowledge about spatial pattern of diseases is useful for assessing the influencing factors on disease incidence and planning for disease prevention and control[29,30]. Geographic variations in the incidence of certain cancers (especially gastric cancer) have been investigated before[31]. High-risk areas for gastric cancer, with age-adjusted incidence rates over than 20 in 100000 person-years include Japan, China, South Korea, Brazil and Costa Rica. Areas with a moderate risk and standardized incidence of between 10 and 20 per 100000 persons include England, Germany, New Zealand and Turkey. Areas with low risk and adjusted incidence of less than 10 include America, Denmark and Sweden[32]. Iran is one of the countries with moderate risk of gastric cancer. Furthermore, different areas of the country has obvious geographical differences in gastric cancer incidence rate[33]. Clustering of gastrointestinal cancer incidence in counties of Iran at the margin of the Caspian Sea for 2008 has been reported a significant difference in the rate of gastrointestinal cancer incidence in different parts of this area[34]. A study in Ardebil province in north-west of Iran also showed that this province is a high risk area in terms of global statistics[35]. Another study investigated the clustering status of the gastric cancer incidence among provinces of Iran from 2004 to 2009 and showed that gastric cancer had a significant clustering status in northern, north-western and western provinces[36]. When a cluster of high incidence is not occurred by chance, we need to ask what could be the underlying causal mechanism. It is natural to look first at the known or hypothesized risk factors[34]. Several factors such as genetics, infection of Helicobacter pylori, excessive use of tobacco (especially cigarettes), high salt consumption, high intake of nitrates and inadequate intake of antioxidants, low social economic status (SES) and environmental factors were among the known risk factors for gastric cancer[37-39]. But major difference in gastric cancer incidence rate in neighboring provinces that are almost the same in environmental factors, dietary habits and lifestyle is only justifiable with existence of misclassification error in registering permanent residence of cancerous patients that are diagnosed and treated in neighboring facilitate provinces or Tehran as the capital of the country.

The study of Geographical spread of gastrointestinal tract cancer incidence in the Caspian Sea region also noted that a number of residents of Mazandaran and Golestan seek medical care outside the region, especially in Tehran, and occasionally in neighboring provinces[34]. In a study in Fars province (in the south of Iran) with aim of measuring the completeness of coverage of cancer registry information recorded between 2000 and 2009, actual registry data compared with the expected incidence rate. The maximum acceptable error rate was 5% for deficiencies in personal and demographic information (gender, age, father’s name and area of residence) and encoding the cancers. At the beginning of their program, the address of patients was not recorded with detail and in a systematic manner. Although the rate of deficiencies was decreased as a result of staff training, the error rate in address information (7.87%) remained above the 5% threshold by the end of the study period in 2009[8].

These findings confirm the existence of misclassification error and incompleteness of address-related information in Iran’s cancer registry that results underestimation of cancer incidence rate in some provinces and overestimation in some others.

In conclusion, despite international efforts to standardize cancer incidence data collection processes, the quality of data from many countries remains poor. Low quality of cancer incidence data leads to a misclassified registered data[40]. Iran as a developing country is not an exception. So, there are provinces with higher or lower incidence of gastric cancer than the registered rates, and policy makers employ these data to allocate the facilities and resources. Regionally misclassified cancer incidence data leads to misallocation of resources. So authorities should notice that low incidence rate of gastric cancer in some provinces, do not mean that they are in a good health condition and gastric cancer incidence is really low in these provinces, but quite the contrary, this may be the effect of misclassification error and it is needed to allocate them more health facilities, equipped health centers, and improve the quality of registration system.

Enhancing hardware and software resources, training and increasing the number of educated and motivated staff in all public and private sectors involved in the cancer registry program in order to complete the cancer case registry forms accurately and remit them to the appropriate center, expert researchers in medicine and cancer knowledge, computer science and biostatistics, and greater attention to epidemiological research are needed to qualify the cancer registry program and increasing its completeness; specially completeness of address-related information[41,42]. So, the better the quality of cancer registry data, better the possibility of effective use of these data in planning and prevention.

**COMMENTS**

***Background***

Most patients from low facility provinces, seek medical treatment in their neighboring facilitate provinces. Some of them do not mention their permanent residence. It makes misclassification error in cancer registry data and misleads health policy makers who use cancer registry data for resource allocation and cancer control programs. The aim of this study is to use Bayesian method for estimating the rate of misclassification between neighboring provinces and re-estimating the rate of gastric cancer incidence in each province of Iran.

***Research frontiers***

Information about geographic spread of cancers is so important for cancer control and prevention. Iran’s cancer registry data is subject to misclassification in patient’s permanent residence that leads to under-estimation of cancer risk in some provinces and consequently over-estimation in other provinces. Cancer registry data is usually used in spatial analysis to determine the high risk areas without considering the existence of misclassification error. The hotspot of this study is using the Bayesian method for accounting and correcting for misclassification in registering cancer incidence.

***Innovation and breakthroughs***

By using the Bayesian method, having prior information about the misclassification rate is enough and it is not needed to use valid data for estimating the misclassification rate. Bayesian method for correcting the misclassification is faster and more cost effective in comparison to data validation which is time consuming and in many cases is not achievable.

***Applications***

Since cancer registry data is used by health policy makers for allocating medical resources to different provinces, it is important to correct for misclassification in registering patient’s permanent residence, in order to have more accurate estimates from the rates of gastric cancer incidence and consequently better planning for cancer control and prevention.

***Terminology***

Misclassification is a measurement error which defines as disagreement between the observed value and the true value in categorical data. Bayesian method is a statistical approach that assigns a prior distribution to events or parameters, based on expert idea or previous knowledge and modifies those distributions after obtaining the data by using Bayes’ theorem.

***Peer-review***

In this manuscript, authors were aimed to correct the misclassification of gastric cancer incidence across Iranian provinces in registry data.

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**P-Reviewer: Li Y,** Zhang J **S-Editor:** Ji FF **L-Editor: E-Editor:**

**Table 1 Expected coverage of cancer cases for Iranian provinces in 2008**

|  |  |
| --- | --- |
| Medical University | Percent of expected coverage |
| Razavi Khorasan | 155.5 |
| North Khorasan | 34.8 |
| South Khorasan | 41.4 |
| Sistan and balochestan | 25 |
| East Azerbaijan | 123.6 |
| West Azerbaijan | 69 |
| Ardebil | 63 |
| Isfahan | 107.5 |
| Kohgiloye and boyerahmad | 25.1 |
| Chaharmahal and bakhtyari | 38 |
| Fars | 120.8 |
| Hormozgan | 19 |
| Khozestan | 101.19 |
| Bushehr | 25 |
| Ilam | 39.4 |
| Mazandaran | 338.4 |
| Golestan | 50.8 |
| Tehran | 155.62 |
| Qom | 53.9 |
| Qazvin | 66.3 |
| Markazi | 69.6 |

**Table 2 Number of gastric cancer incidence and the percent of change before and after Bayesian correction in Iranian provinces 2008**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Before bayesian correction | After bayesian correction |  |
| Province | Male | Female | Both | Male | Female | Both | Change% |
| Fars | 199 | 102 | 301 | 105 | 54 | 158 | -47.37 |
| Isfahan | 211 | 86 | 297 | 188 | 77 | 264 | -10.97 |
| Razavi Khorasan | 550 | 194 | 744 | 371 | 131 | 502 | -32.55 |
| East Azerbaijan | 399 | 148 | 547 | 237 | 88 | 325 | -40.53 |
| Mazandaran | 338 | 150 | 488 | 274 | 122 | 396 | -18.81 |
| Khozestan | 233 | 114 | 347 | 173 | 85 | 258 | -25.69 |
| Tehran | 1131 | 567 | 1698 | 1019 | 511 | 1530 | -9.88 |
| West Azerbaijan | 191 | 80 | 271 | 291 | 122 | 412 | 52.17 |
| Kohgiloye and boyerahmad | 38 | 18 | 56 | 50 | 24 | 74 | 31.88 |
| Hormozgan | 26 | 17 | 43 | 112 | 73 | 186 | 331.58 |
| Chaharmahal and bakhtyari | 46 | 24 | 70 | 56 | 29 | 85 | 21.06 |
| Sistan and balochestan | 38 | 9 | 47 | 147 | 35 | 182 | 288.00 |
| Ilam | 37 | 13 | 50 | 61 | 22 | 83 | 65.98 |
| North Khorasan | 42 | 15 | 57 | 94 | 34 | 127 | 123.56 |
| South Khorasan | 22 | 13 | 35 | 45 | 27 | 71 | 103.86 |
| Golestan | 104 | 35 | 139 | 173 | 58 | 231 | 66.04 |
| Qom | 58 | 26 | 84 | 98 | 44 | 142 | 68.64 |
| Ardebil | 172 | 69 | 241 | 229 | 92 | 321 | 33.33 |
| Bushehr | 17 | 9 | 26 | 54 | 28 | 82 | 216.00 |
| Qazvin | 80 | 33 | 113 | 119 | 49 | 168 | 48.27 |
| Markazi | 63 | 27 | 90 | 102 | 44 | 146 | 61.78 |

**Table 3 Age standardized rate of gastric cancer incidence before and after Bayesian correction in Iranian provinces 2008**

|  |  |  |
| --- | --- | --- |
| Province | Before Bayesian correction | After Bayesian correction |
| Male | Female | Both | Male | Female | Both |
| Fars | 12.21 | 7.01 | 9.61 | 6.43 | 3.69 | 5.06 |
| Isfahan | 0.94 | 5.56 | 3.25 | 0.84 | 4.95 | 2.89 |
| Razavi Khorasan | 10.24 | 24.18 | 17.21 | 6.91 | 16.31 | 11.61 |
| East Azerbaijan | 26.61 | 12.09 | 19.35 | 15.82 | 7.19 | 11.51 |
| Mazandaran | 28.53 | 15.57 | 22.05 | 23.16 | 12.64 | 17.9 |
| Khozestan | 13.82 | 7.78 | 10.8 | 10.27 | 5.78 | 8.02 |
| Tehran | 20.61 | 12.39 | 16.5 | 18.57 | 11.17 | 14.87 |
| West Azerbaijan | 17.26 | 8.68 | 12.97 | 26.27 | 13.21 | 19.74 |
| Kohgiloye and boyerahmad | 14.61 | 7.71 | 11.16 | 19.27 | 10.17 | 14.72 |
| Hormozgan | 4.71 | 4.02 | 4.37 | 20.33 | 17.35 | 18.85 |
| Chaharmahal and bakhtyari | 13.46 | 8.6 | 11.03 | 16.29 | 10.41 | 13.36 |
| Sistan and balochestan | 4.16 | 0.97 | 2.56 | 16.14 | 3.76 | 9.95 |
| Ilam | 17.16 | 6.33 | 11.75 | 28.48 | 10.51 | 19.5 |
| North Khorasan | 12.62 | 5.37 | 9 | 28.21 | 12.01 | 20.12 |
| South Khorasan | 9.7 | 7.62 | 8.66 | 19.77 | 15.53 | 17.66 |
| Golestan | 16.86 | 6.27 | 11.56 | 28 | 10.41 | 19.2 |
| Qom | 13.87 | 7.96 | 10.92 | 23.39 | 13.42 | 18.41 |
| Ardebil | 35.18 | 17.49 | 26.33 | 46.91 | 23.32 | 35.11 |
| Bushehr | 4.21 | 3.29 | 3.75 | 13.3 | 10.4 | 11.84 |
| Qazvin | 17.76 | 8.43 | 13.1 | 26.33 | 12.5 | 19.42 |
| Markazi | 11.67 | 5.75 | 8.71 | 18.88 | 9.3 | 14.09 |