Original Article

Relative Risk of Gastrointestinal Cancers in Isfahan County, Iran, 2005–2010

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Abstract

Background: Spatial disease mapping is a widespread tool in ecological analysis to obtain accurate estimates for incidence, relative risks (RRs), prevalence, or mortality rates regarding to increase the incidence of gastrointestinal (GI) cancer in Isfahan in recent years. This study aimed to inspect the RR of GI cancer in Isfahan counties using empirical and full Bayesian model. **Materials and Methods:** Data of this ecological study were GI cancer cases which registered in health-care system of Isfahan University of Sciences during 2005–2010. We applied shared component model to model the spatial variation incidence rates of the GI cancers. We compared three models such as Gamma–Poisson, lognormal, and Besag, York, and Mollie (BYM) Bayesian. WinBUGS and GIS 10.1 software were used. **Results:** According to the fitted model, BYM model had best fit to the data. However, in general, ranks of RRs in most counties are identical; counties with higher RR in one map have higher RR in other maps. Geographical maps for three cancers in women were smoother than men. Isfahan has high RR in women, whereas this point is slightly different in men. Daran, FreidoonShahr, and Isfahan are cities which have high RR in esophagus, stomach, and colon cancer, respectively. **Conclusions:** Lognormal and BYM maps had very similar results. Despite some differences in estimation values, in nearly all maps arias Isfahan had high RR in GI cancer. It is recommended to promote the use of screening programs and increase awareness of people in high RR areas to reduce the incidence of GI cancer.

Keywords: *Gastrointestinal neoplasms, Geographic Mapping, relative risk*

Introduction

Spatial disease mapping, as a comprehensive tool, uses a series of statistical techniques to obtain accurate estimates on diseases such as incidence, relative risks (RRs), prevalence, or mortality rates and then sets those estimates on the geographical maps to create more accurate spatial distribution maps of diseases. Disease mapping is useable in ecological analysis.[1,2] The most popular approach of spatial disease mapping, Besag, York, and Mollie (BYM) model, was suggested by Besag *et al*. and developed by numerous scholars.[3-5]

Bayesian models in disease mapping include various model and each of them has its own formulation, characteristics, advantages, and disadvantages. This reveals the necessity of evaluating and comparing these models. Although Fully Bayesian approach is a complex alternative to the empirical Bayes approach it has been suggested as a useful approach which require less data. it better estimates for uncertainty in data and it provides more detailed causal inferences and more flexibility in selecting crash count distributions.[6]

The first example of disease mapping was illustrated by John Snow in 1854 to address the cholera victims based on their distance from contaminated water resources.[7] Nowadays, public health planners consider mapping to assess disease RR; with awareness about geographical distribution of incidence rates, they are able to identify RR factors as well as valuate etiological hypotheses. Specifying high RR geographical areas plays an important role in allocating of funds, facilities, and human resources.[8]

Cancers are a set of diseases that have enticed policymakers because of high incidence, prevalence, and mortality rates. Cancer is one of the main causes of death and disabling causes all around the world. According to the World Health Organization, up to 2020, the incidence of cancer will be increased by 50%. In

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developing counties, gastrointestinal (GI) tract cancers including esophagus, stomach, and colon cancer are prevalent. According to the International Agency for Research on Cancer report, esophageal cancer is the eighth prevalent cancer and sixth cause of death due to cancer worldwide.[9]

Furthermore, stomach cancer was the 5th most common cancer and the 3th main death cause worldwide in 2012.[10] As stated by 2008–2009 report of Cancer Registry System in Iran, stomach cancer is the third most common cancer in Iran.[11] Around the world, colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of death after lung and stomach cancers.[12] Age-specific mortality rate (ASR) for esophageal cancer among men and women as per 100,000 cases was 7.7 and 2.7, respectively, in 2012 (GLOBOCAN2012). This amount in developed counties was 6.5 and 1.2, whereas in Iran, ASR was 6.15 and 5.88 in that order. However, in Isfahan esophageal cancer was in the tenth rank of cancers with the ASR of 2.53 for women and 2.83 for men in 2010. In addition, stomach cancer in Isfahan among women with the ASR of 7.35 was in the sixth rank and men with the ASR of 12.84 located in fifth place. Also colon and anal cancer among Isfahan women with the ASR of 12.09 have the third rating whereas it has the fourth rating for men with the ASR of 13.38.[13]

Regarding to increase the incidence of GI cancer in Isfahan in recent years, it is necessary to recognize the counties with high RR of GI cancer and then allocate more funding and facilities to them. Many studies have been done in the mapping of cancers in Iran. The other study reported that according BYM model, Tehran, Isfahan, and Yazd had high incidence risk of breast cancer.[5] However, there is no published study on the mapping of GI cancer in Isfahan province that includes adjacent areas, considers the effects of adjacency's county, and uses advanced models differentiated by gender. The aim of our study was inspecting the RR of GI cancer in urban area of Isfahan province using empirical and full Bayesian model. This is the first ecological study of GI cancer in the counties of Isfahan province with the use of advanced statistical models to explore the differences of incidence rates between males and females.

Materials and Methods

This ecological study is done on incident cases of GI cancers from 2005 to 2010 in urban area of Isfahan province. Data with just regarding to gender were gathered from health-care system of Isfahan University of Medical Sciences. Kashan and Aranobidgol counties were excluded from the analysis as there was no registry of incident reports due to GI cancers. We calculated RR for each cancer site, with the number of expected cases calculated using the average number of cases per region observed in Isfahan province and the Isfahan population in the 2005–2010 census.

We applied the shared component model to model the spatial variation incidence rates of the GI cancers. We compared three separated models: Gamma–Poisson, lognormal, and BYM Bayesian, which describe in following, using WinBUGS software. The results of the models were compared using the deviance information criterion (DIC).

Disease mapping models

In these models, (Oi, i = 1,…, n) and (Ei, i = 1,…, n) represent the number of observed and expected gastrointestinal cancer cases for province I, respectively. It is assumed that Oi has Poisson distribution with the rate of $\mu i = \Theta_i$ Ei, which $Ei = Pi(\sum_i O_i / \sum_i P_i)$ where pi related to population of ith counties. Where $\Theta_i = O_i/E_i$ represents RR for counties i.

Empirical Bayes

Empirical Bayes itself consist of two models:

Gamma–Poisson model

In this model, it is assumed that the number of incidences (Oi) in counties follows a Poisson distribution with mean Eiθi. Prior distribution of RRs is considered a Gamma (a, b), so posterior distribution become Gamma (a + O_i, b + Ei) with mean $\frac{a+Oi}{b+Ei}$ = wi SMRi+(1-wi) $\frac{a}{b}$ where wi=$\frac{Ei}{b+Ei}$

Hence, posterior means for area i is the weighted average of SMR for the area i and overall RR that weights are conversely related to SMR variance. If the expected and observed become high, the estimator tends to SMR, but if they become low, estimator tends to overall RR.

Advantages of this model are (1) it is full posterior, which allows hypothesis testing and calculates confidence intervals. (2) Even if the real distribution of RRs is Gamma, this model can estimate the mean and variance using maximum likelihood method, more valuable than moment method. However, not considering spatial correlation is the main disadvantage of this model.[14,15]

Lognormal model

Although Gamma prior distribution seems suitable for risk rate mathematically, Gamma–Poisson model has some restrictions. Due to difficulty of adjusting suitable independent variable and involving the spatial correlation between the rates of regions is impossible.

This model is more flexible than Gamma–Poisson. This model can contain covariates whereas Gamma–Poisson could not. In this model, v_i is included in order to consider similarity and spatial correlation of adjacent areas.[1,5]

$$y_i \sim \text{Poisson}(e_i \theta_i)$$

$$\log \theta_i = \alpha + v_i$$

$$v_i \sim N(0, \tau_v^2)$$

Full Bayesian model

BYM model: In this model, RR has three components:

$$\log \theta_i = \alpha + v_i + u_i$$

1. α: Overall level of RR (trend component)
2. 2) v_i: Nonspatial overdispersion (spatial uncorrelated heterogeneity) in these data, the variance is dependent on the number of neighbors, another component (v_i) is introduced, in order to justify this problem, that is an uncorrelated overdispersion parameter.

The prior distribution of this parameter is:. $v_i \sim N(0, \tau_v^2)$

3. u_i: Spatial overdispersion (spatial correlated heterogeneity): It is logical that the close areas have similar RRs. Random variable u_i added to model, in order to take these similarities into account.

This model considers two sources of changes for justifying the heterogeneity the rate of in risk in every region in addition to independent variables.

Spatial correlation structure is used where estimates for RR in each area are dependent on adjacent areas. The conditional autoregressive model proposed by Besag *et al*. is:

$$[u_i \mid u_j, i \neq j, \tau_v^2] \sim N(\overline{u_i}, \tau_i^2)$$

$$\overline{u_i} = \frac{1}{\sum_j \omega_{ij}} \sum u_i \omega_{ij}$$

$$\tau_i^2 = \frac{\tau_u^2}{\sum_j \omega_{ij}}$$

$\omega_{ij} = 1$ if i , j are adjacent

$\omega_{ij} = 0$ if i, j are not adjacent

Both τ_u^2 and τ_v^2 parameters control the variability of u and v. Bernardinelli has suggested Gamma prior distributions for these parameters.[3,4]

Expected values were calculated by multiplying total number of observed cancers to the ratio of population of each county within each gender.

According to the Brooks–Gelman–Rubin criteria, burning time was considered 1000000 iterations, and in order to solve autocorrelation in the iteration, from each 50 iteration, one considered in the model. Convergences were checked by using Brooks-Gelman-Robin plots.[16]

For the tau.u and tau.v parameters the prior Gamma distribution (0.5, 0.0005) was used, for the V parameter the prior distribution N (0, tau.v) was used and for the U parameter the mentioned conditional autoregressive distribution was used. Convergence was checked by using Brooks Gelman-Robin plots.

Results

The total number of registered cases for esophagus, stomach, and colon cancer in Isfahan province from 2005 to 2010 for men were 242, 897, and 1073, respectively, and for women were 117, 347, and 839 in that order. center of Isfahan province, with 161, 512, and 673 cases of esophagus, stomach, and colon cancer among men respectively and 63, 227, and 553 cases among women has the most incidences comparing with other counties.

Comparing DIC showed that among three models, BYM had the best fit on data except for esophagus cancer in female [Table 1]. In the all models, geographical maps for three cancers in women were smoother than men.

Esophagus cancer

Based on the Gamma–Poisson model for esophagus cancer among men, Daran and Isfahan with RR of 1.596 and 1.235 were in the first ranks, whereas Tiran and Ardestan with RR of 0.5074 and 0.5956 were in the last ranks. Among women, Semirom and Najafabad with RR of 1.386 and 1.27 were at highest RR, whereas Daran and Natanz with RR of 0.2992 and 0.5213 were at lowest RR. According to lognormal model for esophagus cancer among men, Daran and Isfahan had the most RR (2.34 and 1.685), whereas Tiran, Ardestan, and Khomeinishahr had the least RR (0.7196, 0.8226, and 0.8384). Among women, Isfahan, Khomeinishahr, and Semirom with RR of 1.087, 1.069, and 1.039 had the highest RR, whereas Najafabad, Mobarake, and Felavarjan with RR of 0.9587, 0.9746, and 0.9755 had the lowest RR. Regarding BYM model for esophagus cancer among men, Daran and Isfahan with the RR of 2.324 and 1.68 were at the highest order, whereas Tiran and Ardestan with the RR of 0.721 and 0.811 were at the lowest RR. Among women, Isfahan was at most RR (RR = 1.105) and Lenjan was at the least RR (RR = 0.9326) [Figure 1 and Table 2].

Stomach cancer

Based on the Gamma–Poisson model for stomach cancer among men, Freidoonshahr, Semirom, and Daran with RR of 1.894, 1.479, and 1.461 were in the first ranks, whereas Tiran and Natanz with RR of 0.2478 and 0.2705 were in the last ranks. For women, Isfahan and Semirom with RR of 1.176 and 1.125 were at the highest RR, whereas Ardestan and Natanz with RR of 0.6052 and 0.6072 were at the lowest RR. According to lognormal model for stomach cancer among men, Freidoonshahr, Semirom, and Daran with RR of 2.819, 2.089, and 2.059 had the highest RR and Tiran, Natanz, and Naiin with RR of 0.3884, 0.4278, and 0.5865 had the lowest RR. For women, Isfahan and Semirom had the most RR (1.394 and 1.271), whereas Ardestan and Natanz with had the least RR (0.8958 and 0.8959). Regarding BYM model for stomach cancer among men, Freidoonshahr and Semirom had the highest RR (2.97 and 2.147) and Tiran and Natanz had the lowest

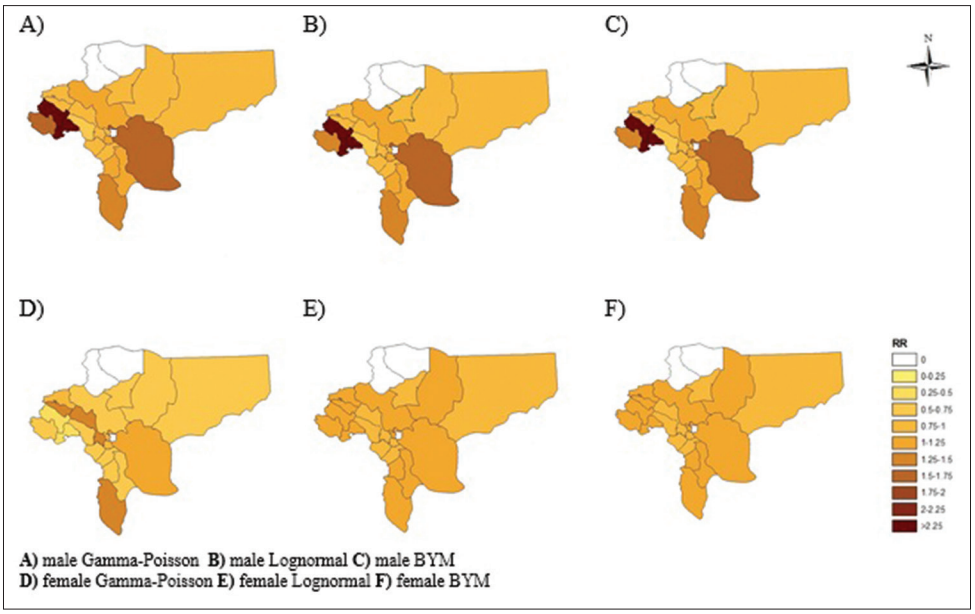

Figure 1: Maps of incidence risk of esophagus

Table 1: Deviance information criterion for models based on cancer sites

DIC	Male			Female		
	Gamma-Poisson	Lognormal	BYM	Gamma-Poisson	Lognormal	BYM
Esophagus	86.8	87.8	84.7	102.5	68.8	61.4
Stomach	113.1	115.3	87.3	91.6	96.0	89.6
Colon	113.2	117.2	111.2	99.6	101	92.8

DIC: Deviance information criterion, BYM: Besag, York, and Mollie

RR (0.42 and 0.3916). For women, Isfahan and Semirom with RR of 1.413 and 1.306 were in the first order and Natanz and Ardestan with RR of 0.8544 and 0.8777 were in the last order [Figure 2 and Table 2].

Colon cancer

Based on the Gamma–Poisson model for colon cancer in men, Isfahan had the highest RR (1.285) and Tiran and Natanz had the lowest RR (0.3563 and 0.366). For female, Isfahan was at the most RR (RR = 1.415), whereas Golpayegan and Tiran were at the least RR (RR = 0.2812 and 0.3291). According to lognormal model for colon cancer in men, Isfahan, Felavarjan, and Khansar with RR of 1.848, 1.223, and 1.218 were at the highest ranks, whereas Tiran, Natanz, and Golpayegan with RR of 0.6211, 0.653, and 0.799 were at the lowest rank. For female, Isfahan and Shahreza had the maximum RR (2.72 and 1.742); however, Golpayegan, Tiran, and Natanz had the minimum RR (0.5682, 0.6449, and 0.6999). Regarding BYM model for colon cancer in men, Isfahan, Felavarjan, and Khansar with RR of 1.853, 1.226, and 1.226 were at the first order, whereas Tiran and Natanz with RR of 0.6082 and 0.631 were at the last order. For female, the highest RRs were in Isfahan and Shahreza (2.726 and 1.76), whereas the lowest RRs were in Golpayegan and Tiran (0.5709 and 0.9354) [Figure 3 and Table 2].

Conclusions

According to the fitted model, BYM model had best fit to the data. the estimations showed that lognormal and BYM maps are very similar whereas there are some differences between Gamma–Poisson and lognormal and BYM maps. However, in general, ranks of RRs in most counties are identical; counties with higher RR in one map have higher RR in other maps. Our finding is in accordance with other studies. Mahaki *et al*. showed that comparing Bayesian model results in almost the same approximations.[17] In addition, the obtained results from Bayesian analysis were in line with studies such as Morris *et al*.,[18] Khoshkar *et al*.,[5] and Ahmadipanahmehrabadi *et al*.[19] Distinct cancer maps showed different geographical incidence pattern for each sex. It seems that adjacent areas in terms of geographical location have similar rates of disease incidence or death. It is appropriate that the spatial pattern is considered in the model. In overall, in the all models, geographical maps for three cancers in women were smoother than men.

The superiority of our study in comparison with others is that this is the first mapping of RR of GI cancer incidence in Isfahan at urban area based on genders, using advanced statistical models that consider the effects of adjacency's country. Therefore, the results of this study can be used as a guide for health planners to carry out preventive interventions

Table 2: The relative risk of gastrointestinal cancer in Isfahan counties for gender

Relative risk (counties)	Model (gender)	BYM			Lognormal			Gamma-Poisson		
		Stomach	Esophagus	Colon	Stomach	Esophagus	Colon	Stomach	Esophagus	Colon
Ardestan	Men	0.7645	0.8111	0.9734	0.8196	0.8226	0.9747	0.6134	0.5956	0.6741
	Woman	0.8777	1.018	0.9404	0.8958	1.01E+00	0.9207	0.6052	0.6019	0.4988
Isfahan	Men	1.636	1.68	1.853	1.65E+00	1.69E+00	1.848	1.19	1.235	1.3E+00
	Woman	1.413	1.105	2.726	1.394	1.087	2.72	1.176	1.208	1.42E+00
Barkhar and Meimeh	Men	0.8928	1.057	1.109	0.9047	1.06E+00	1.105	0.6605	0.7911	7.74E-01
	Woman	1.032	1.03	1.276	1.027	1.026	1.273	0.8256	0.5893	0.6725
Tiran and Karoon	Men	0.42	0.7213	0.6082	0.3884	7.20E-01	0.6211	0.2478	0.5074	0.3563
	Woman	0.9486	0.9849	0.6354	0.9488	0.9986	0.6449	0.7019	0.6638	0.3291
Khomeini Shahr	Men	0.8493	0.8337	1.027	0.8528	8.38E-01	1.024	0.6191	0.613	7.14E-01
	Woman	0.9995	1.09	1.036	0.9843	1.069	1.028	0.7738	0.7811	0.543
Khansar	Men	1.125	0.8667	1.226	1.088	0.8638	1.218	0.8157	0.6278	0.8673
	Woman	0.9516	1.016	0.7566	0.9639	1.016	0.7725	0.7133	1.038	0.4075
Semiromsofla	Men	2.147	1.391	1.101	2.089	1.36E+00	1.088	1.479	0.9964	0.765
	Woman	1.396	1.097	1.028	1.271	1.039	1.006	1.125	1.386	0.5441
Shahreza	Men	1.372	1.11	1.167	1.367	1.10E+00	1.16	0.9941	0.8235	0.8158
	Woman	0.9644	1.022	1.76	0.94	1.008	1.742	0.7052	0.6337	0.9123
Feriden	Men	2.027	2.324	1.018	2.052	2.34E+00	1.019	1.461	1.596	0.7132
	Woman	0.969	1.042	0.8889	0.9838	1.034	0.9033	0.7621	0.2992	0.4847
Feridoon Shahr	Men	2.97	1.572	1.148	2.819	1.481	1.136	1.894	1.074	0.8081
	Woman	0.8985	1.075	0.9297	0.942	1.035	0.9553	0.6911	0.7062	0.5177
Falavatjan	Men	0.9755	1.207	1.226	0.9808	1.22E+00	1.223	0.7159	0.9044	8.57E-01
	Woman	1.137	0.9697	1.108	1.114	0.9755	1.098	9.29E-01	0.9999	0.5834
Lanjan	Men	1.367	0.9702	1.056	1.383	9.77E-01	1.057	1.006	0.7242	0.7389
	Woman	1.157	0.9326	0.7325	1.135	0.9598	0.7292	0.9568	0.6847	0.3842
Mobarakeh	Men	0.7304	0.839	0.8585	0.7166	8.39E-01	0.8528	0.5257	0.617	5.82E-01
	Woman	0.9871	0.9644	1.518	0.9635	0.9746	1.504	0.7381	0.7387	0.7928
Naien	Men	0.5684	0.8597	1.011	0.5865	8.74E-01	0.9998	0.4241	0.6474	0.6983
	Woman	0.8871	0.9874	1.256	0.9019	0.986	1.226	0.6277	0.6673	0.6611
Najaf Abad	Men	1.338	0.9682	1.155	1.358	9.70E-01	1.154	0.9839	0.7154	8.08E-01
	Woman	1.176	0.949	1.478	1.17E+00	0.9587	1.488	0.9935	1.27	0.7824
Natanz	Men	0.3916	0.9217	0.631	0.4278	9.39E-01	0.653	0.2705	0.7012	0.366
	Woman	0.8544	0.9895	0.697	0.8959	0.9925	0.6999	0.6072	0.5213	0.3606
Golpaygan	Men	0.9894	0.8556	0.795	0.9736	8.55E-01	0.799	0.7204	0.6284	0.5293
	Woman	0.9743	1.013	0.5709	0.9827	1.011	0.5682	0.7503	0.797	0.2812
Chadgan	Men	2.027	2.324	1.018	2.052	2.34E+00	1.019	1.461	1.596	0.7132
	Woman	0.969	1.042	0.8889	0.9838	1.034	0.9033	0.7621	0.2992	0.4847
Semirom	Men	1.372	1.11	1.167	1.367	1.10E+00	1.16	0.9941	0.8235	0.8158
	Woman	0.9644	1.022	1.76	0.94	1.008	1.742	0.7052	0.6337	0.9123

BYM: Besag, York, and Mollie

as well as determined etiological cause of cancer. It is seen fit to perform screening tests in high RR regions and more epidemiological studies, so that prevention policies are grounded in such high RR areas such as Isfahan, Semirom, Daran, Feridonshahr, Khansar, Khomeinshahr, and Shahreza.

One of the limitations of the study was various division of County in different years. To solve this problem, we analyzed data just according to 1st year and cause-specific analysis was conducted. The other problem was that low number of data occurred in the earlier years as well as we could not access the data come after 2010 while many cancer cases in other counties and neighboring provinces such as Shahrekord were registered in the Isfahan and its caused to overestimate Isfahan county RR.

As age information was not available, we did not used age-standardized rates of incidence; this is a major limitation of the study. In addition to age, we did not have access to data about other risk factors of the cancers. Hence, the model does not contain any covariates. We used the prior distributions, which is used in the model based on suggestion from the published papers.

Based on the results and the mentioned limitation, there are some suggestions: It is suggested that this model be implemented for longer time period to better evaluate

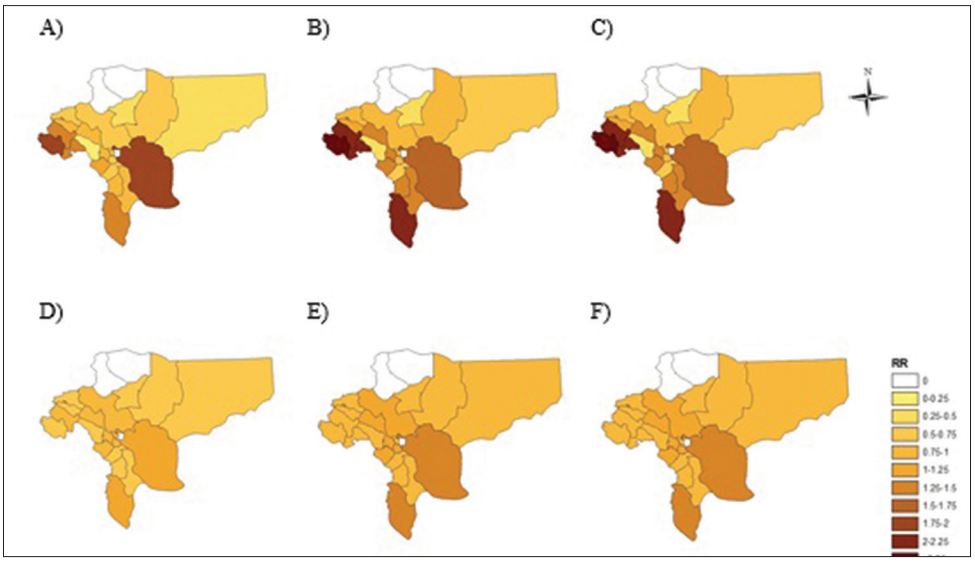

Figure 2: Maps of incidence risk of stomach

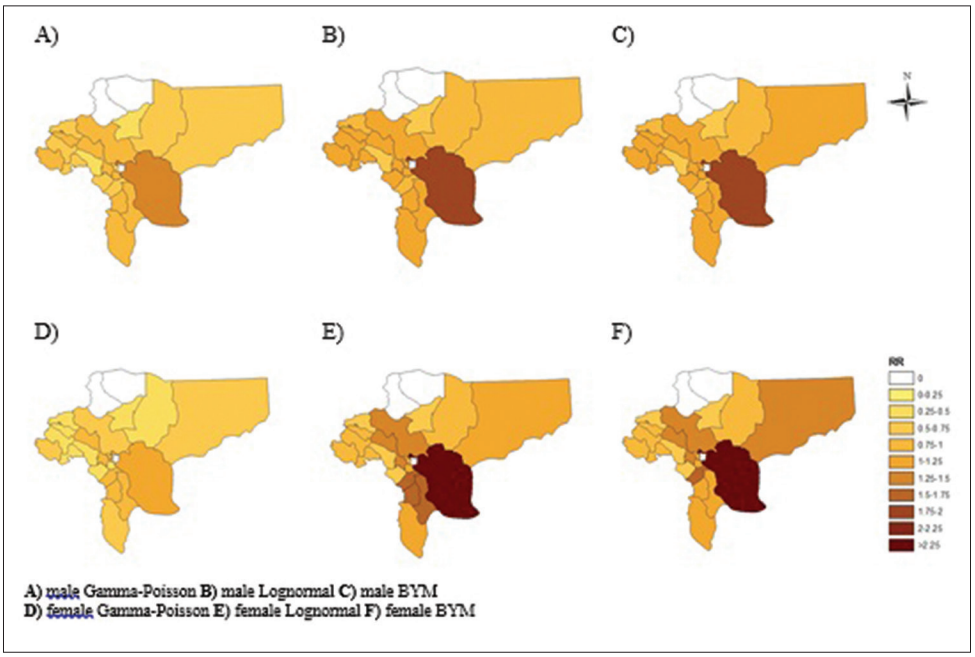

Figure 3: Maps of incidence risk of colon

the temporal trend. It is recommended to adjust for age and the most known factors affecting the incidence to make the results more interpretable. It is also suggested sensitivity analysis for different prior distributions be taken into consideration and the results of the distributions be compared. This will help estimate the sensitivity of the model to the prior distributions allocated to the parameters. Finally, this study provides useful information, on areas requiring more attention, for policy makers and medical experts. Since the urban lifestyle develops increasingly and direct association has been proved between Human Development Index and RR of GI cancer, it is necessary to conduct some measures to provide awareness for the people and improve their lifestyle for preventing from growing the incidence of GI cancer It is seen fit to perform more epidemiological studies in high RR regions, so that prevention policies are grounded in such high RR areas.

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Conflicts of interest

There are no conflicts of interest.

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