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Spatial-temporal Modelling of Oesophageal and Lung Cancers in Kenya's Counties

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Abstract: Oesophageal cancer is the cancer that forms in tissues lining the oesophagus (the muscular tube through which food passes from the throat to the stomach) while Lung cancer is the cancer that forms in tissues of the lung, usually in the cells lining air passages. In this study, Data collected by the Nairobi Cancer Registry (NCR) was used to produce spatial-temporal distribution of oesophageal cancer cases for counties in Kenya. The study revealed, counties where data was available Bomet had highest relative risk of oesophageal cancer, followed by Meru, Nyeri, Embu, Nakuru, Kakamega Nairobi, Mombasa, Kiambu and Machakos counties respectively. The study revealed that smoking and alcohol use were significant risk factors of oesophageal cancer in Kenya. Generation of spatio-temporal maps and identification of the risk factors from various counties with notified oesophageal cancer cases is a major milestone since previous studies focused on specific regions. The multiplicative effect of smoking was observed to be 1.012, indicating that oesophageal cancer is 1.2% higher to those who smoke compared to non-smokers. The multiplicative effect of alcohol use was observed to be 1.0346, indicating that oesophageal cancer was 3.5% higher to alcohol users as compared to non-alcohol users. The study findings revealed that, the multiplicative effect of smoking was 1.4021, indicating that lung cancer was 40.21% higher to smokers as compared to non-smokers from the available data. The multiplicative effect of alcohol use was 1.3689 indicating that the risk of lung cancer was 36.89% higher to alcohol users compared to non-alcohol users. Clearly, counties where the data was not available the relative risks were relatively low, therefore even though the data was not available in these counties application of spatial-temporal accounting for covariates revealed that there is risk of oesophageal and lung cancer in the counties. To enhance research on oesophageal, lung and other types of cancer in Kenya the National Cancer Registry in collaboration with Counties health departments should work very closely to enhance cancer data collection to facilitate research and to inform the appropriate measures to be implemented to mitigate the increase of cancer cases.

Keywords: Spatial-temporal, Integrated Nested Laplace Approximation, Generalized Linear Mixed Models

1. Introduction

Oesophageal cancer is the cancer that forms in tissues lining the esophagus (the muscular tube through which food passes from the throat to the stomach) [2]. According to study findings by Schaafsma et al. [18], Ferlay et al. [7] the rate of oesophageal cancer in Kenya is 17.6 per 100,000 which is one of the highest incidence in the Africa continent and is the most common male cancer in Eldoret. Hospital-

based studies conducted in Tenwek hospital in western Kenya by Tenge et al. [20] revealed that male: female ratio of 1.6:1.12 indicating higher incidence rates among males than females. Parts of East Africa and Southern Africa has high burden oesophageal cancers but the risks factors are not fully understood. In South Africa, Tobacco and alcohol have been shown to be clear risk factors [16] but they may not out-rightly explain the high rates in East Africa [10]. Kenya is one of a few countries that lie on Africa's oesophageal cancer corridor, which is a region situated in the geographic area of

the Eastern and Western rift-valley and is reported to have the highest incidences in Africa [18]. Therefore a study on the risk factors such as smoking and alcohol use on oesophageal cancer will be very appropriate.

In Kenya prostrate, oesophageal and colorectal cancers are the most prevalent among men while breast, cervical and oesophageal cancers are most common among women. Oesophageal cancer contributes 13.2% of cancer mortality which is the highest, cervical is the second contributing 10% of the cancer deaths while breast cancer comes third at 7.7% [6]. Kenya has a few hospitals which treat oesophageal cancer patients, some of which include Kenyatta National Teaching and Referral Hospital, Moi Teaching Referral Hospital, Tenwek Mission Hospital, Kijabe Mission Hospital, M. P. Shah Hospital/ Cancer Care Kenya.

People with oesophageal cancer may experience: difficulty and pain with swallowing, burning in the chest, frequent choking on food and indigestion or heartburn [1].

Identified alcohol drinking, genetic factors, dietary change/food preparation, and consumption of hot food as the main risk factors for oesophageal cancer in Kenya, they noted that there is a need to investigate the causal relationships between these major risk factors and the development of oesophageal cancer in Kenya [15].

Recent studies on oesophageal cancer has focused on specific regions, therefore mapping its rates, identifying the

risk factors as well as locating counties with high rates will help them prioritize control strategies and design ways to modify risk behaviors. Patel *et al.* [17] conducted a study in Moi Teaching and Referral Hospital (MTRH) in Uasin Gishu County where they identified oesophageal cancer as the leading cancer in men.

Lung cancer is the cancer that forms in tissues of the lung, usually in the cells lining air passages. The two main types are small cell lung cancer and non-small cell lung cancer [2]. According to American Cancer Society [3], the main risk factor for lung cancer is smoking resulting 80% of deaths, where the percentage might be higher for small cell lung cancer (SCLC). Other risk factors includes: Exposure to asbestos and radon a radioactive gas. Bandera *et al.* [4] and Korte *et al.* [11] suggested smoking-adjusted association for high alcohol consumption. Clinical manifestation of lung cancer include: coughing, shortness of breath, wheezing, fever and chest pain [8].

Therefore it is appropriate to conduct the study in Kenya to determine whether smoking and alcohol use are risk factors for oesophageal and lung cancers.

The main aim of the study was to create a spatial temporal model to determine whether smoking and alcohol use are contributing factors of oesophageal and lung cancer cases in Kenya's counties.



Figure 1. Kenya Administrative Units (Counties).

2. Materials and Methods

The study sought to create a spatial-temporal model for oesophageal and lung cancer from the counties data for the year 2015 and 2016. The data in this study was obtained from Kenya National Cancer Registry, which is a national Population-Based Cancer Registry (PBCR). Data includes the total number of oesophageal and lung cancer cases from ten counties namely Bomet, Embu, Kakamega, Kiambu, Machakos, Meru, Mombasa, Nairobi, Nakuru, and Nyeri County.

Kenya is divided into 47 administrative units (See Figure 1) and has a population of 47.5 million as per the Kenya Population and Housing Census that was conducted in 2019.

3. Methodology

The hierarchical Bayes statistical models are specified in hierarchical order since they involve multiple levels. The prior distributions and the covariates are combined then applied to estimate posterior distribution via Bayes method [9]. Data obtained from small areas (e.g county level) generally exhibits spatial autocorrelation. According to Lawson [12], introduction of spatially structured random effects and time varying covariates may account for the spatial autocorrelation in the model.

Integrated Nested Laplace Approximation (INLA) method can be used to estimate the posterior distributions of the parameters in the hierarchical Bayesian model by borrowing strength from the regions with available data to obtain smoothed county level estimates even when the data is sparse [9]. Depending on the available variables and data, various latent models among the convolution, besag and random-walk can be implemented using INLA package in R-software. A Generalized Linear Mixed Model (GLMM) which is a hierarchical Bayesian model was explored and applied to generate results in this study as illustrated in the sections below.

3.1. Generalized Linear Mixed Model

In Generalized Linear Mixed Models (GLMMs) the distribution of the response variable Y_i is assumed to belong to an exponential family as shown in equation (1)

$$p(y_i / \theta_i, \phi) = \exp\left(\frac{y_i \theta_i - b(\theta_i)}{a(\phi)} + c(y_i, \phi)\right) \quad (1)$$

for $i=1, \dots, n$ observations and θ_i is the scalar canonical parameter. Linking the mean $u_i = E(y_i / \beta f^i(\cdot), \phi)$ via monotonic function $g(\cdot)$ generates an additive predictor of the form:

$$g(\mu_i) = \eta_i = \beta_0 + \sum_{i=1}^n f_i(\mu_i) + \sum_{k=1}^m \beta_k x_{ki} + \varepsilon_i \quad (2)$$

Wide range of models may be applied such as spatial, spatial-temporal models and Time series when $f_i(\cdot)$ is varied.

3.2. The Model

Suppose that the index $s' \in (1, 2, \dots, S)$ represents the geographically connected regions. Two regions s and s' are neighbors if they share a common boundary.

According to Moraga [14], Standardized Incidence Ratios (SIRs) can be computed to evaluate disease risk.

For area $i, i = 1, \dots, n$, the SIR is obtained as follows:

$$SIR_i = \frac{Y_i}{E_i}$$

Y_i is the observed counts and E_i is the expected counts.

E_i is calculated using indirect standardization as

$$E_i = \sum_{j=1}^m r_j^{(s)} n_j,$$

$r_j^{(s)}$ is the disease rate in stratum j of the standard population, and n_j is the population in stratum j of the specific area.

Where $(SIR_i > 1)$ indicates the risk of cervical cancer is higher, equal $(SIR_i = 1)$ or $(SIR_i < 1)$ lower risk than that which is expected from the standard population.

SIR may give sense of spatial variability in some situation but it may result to very extreme values when very small or empty samples are involved, due to this shortcoming disease models are preferred to obtain relative risk estimates.

In this study the response variable assumed to be generated by a Poisson process, to model the data. A Generalized Linear Mixed Models assuming a Poisson process with spatial structure, unstructured and temporal random effects was considered.

$$y_i \sim \text{Poisson}(\mu_i)$$

$$\mu_i = \exp(X_i \beta + \text{offset}_i) \quad (3)$$

y_i 's are observed cancer cases (counts per county), X_i 's are the covariates and offset term represents population per county while μ_i is the mean of the observations. The Generalized Linear Mixed Models (GLMM) used to describe the cancer cases y_i is of the form:

$$g(\mu_i) = \beta_0 + \sum_j \beta_j X_{ij} + f_{\text{trend}}(\text{time}) + f_{\text{str}}(S_i) + f_{\text{unstr}}(S_i) \quad (4)$$

- i. $g(\cdot)$ is a monotonic link function in our case the \log .
- ii. β_0 is the overall intercept term.
- iii. $\beta_j X_{ij}$, where X_{ij} 's are the covariates β_j 's are the coefficients. The β_j 's for fixed effects $(\beta_j X'_{ij})$ were

assigned normal priors $\beta \sim N(0,100)$. In our model β_j 's are the coefficients of the proportion of smokers and alcohol users of covariates.

- iv. Correlated random time effects, f_{trend} , to account for time dependence, was modelled via first order random walk with precision $\tau_{\phi 1}$; assigned $\tau_{\phi 1} \sim \text{Gamma}(1, 0.001)$ prior.
- v. The spatial effects, $f_{str}(S_i)$ estimated at county level. Spatial effects were modelled via normal conditionally autoregressive priors (CAR)[5] to account for spatial auto correlation, the neighbouring counties were assigned weight of 1 and 0 otherwise..
- vi. Non-spatial random effects $f_{unstr}(S_i)$ by county, to model un correlated spatial random effects which was assigned a Normal prior, $f_{unstr} \sim N(0, \frac{1}{\tau_v})$, with precision $\tau_v \sim \text{Gamma}(1, 0.001)$.

The relative risk was presented as μ_i : ($\mu_i > 1$) indicated higher disease risk, ($\mu_i < 1$) lower risk while ($\mu_i = 1$) no risk.

3.3. Model Selection Criteria

Deviance Information Criteria

The Deviance Information Criterion (DIC) [19] is designed for hierarchical models and (in most cases) is well defined for improper priors, it also provides effective number of parameters. The deviance is

$$D(x, \theta) = -2 \sum_{i \in I} \log \pi(y_i/x_i, \theta) + \text{constant} \quad (5)$$

Models fitted was explored to determine contribution of different components namely spatial correlated, uncorrelated random effects, temporal or interactions and the covariates to examine spatial variation in county level oesophageal cancer and lung cancer rates. DIC is based on the deviance of the model penalised for model complexity and its interpretation is similar to the Akaike Information Criterion (AIC), with models having smaller DIC being preferred [19].

4. Results

Data in this study was analyzed using spatial temporal model R-packages. The package contains functions for Generalized Linear Mixed Model (GLMM) and INLA methodology.

4.1. Descriptive Statistics for Oesophageal and Lung Cancers

Table 1. Distribution of oesophageal cancer in 2015.

Gender	Count of Gender	Percentage
Female	349	44.52
Male	435	55.48
Grand Total	784	100

According to data in Table 1, 435 (55.48%) of oesophageal cancer cases were male while 349 (44.52%) of the cases were female.

Table 2. Distribution of oesophageal cancer in 2016.

Gender	Count of Gender	Percentage
Female	289	35.46
Male	526	64.54
Grand Total	815	100

In 2016 as shown in Table 2, 526 (64.54%) of oesophageal cancer cases were male while 289 (35.46%) of the cases were female.

Table 3. Distribution of lung cancer by gender in 2015.

Gender	Count of Gender	Percentage
Female	48	43.24
Male	63	56.74
Grand Total	111	100

In 2015 as shown in Table 3, 63 (56.74%) of lung cancer cases were male while 48 (43.24%) of the cases were female.

Table 4. Distribution of lung cancer by gender in 2016.

Gender	Count of Gender	Percentage
Female	63	43.15
Male	83	56.85
Grand Total	146	100

According to the data in Table 4, in 2016 83 (56.85%) of lung cancer cases were male while 63 (43.15%) of the cases were female.

4.2. Standard Incidence Rates (SIR)

Standard Incidence Rates (SIR) were generated as shown in Figure 2 ($SIR_i > 1$) indicates that area i has higher,

($SIR_i = 1$) equal or lower ($SIR_i < 1$) risk than expected from the standard population. The darker the colour the higher the risk.

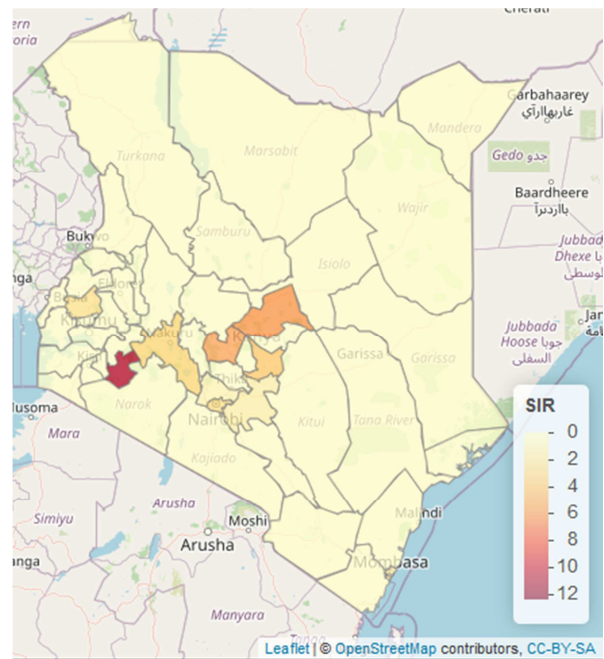


Figure 2. Standardized Incidence Rates (SIR) for oesophageal cancer.

From Figure 2 clearly in most counties there is greater risk of oesophageal cancer cases than expected from the standard population since all counties where data was available has a SIR value greater than 1 except in Kiambu.

Table 5. Standardized Incidence Ratios (SIR).

County	SIR
Bomet	10.09
Embu	4.25
Kakamega	1.91
Kiambu	0.87
Machakos	1.39
Meru	4.22
Mombasa	1.09
Nairobi	2.4
Nakuru	3.08
Nyeri	6.34

4.3. Spatio-temporal Models for Oesophageal Cancer

Four models were fitted, thereafter the most plausible model was selected based on the smallest value of Deviance information Criterion (DIC).

4.3.1. Models Where Smoking Is the Covariate

Model 1: With structured, unstructured spatial effect, trend effects and covariate

In R-INLA the model was specified through the formula as follows:

Model 1 $\langle -y \sim 1 + f(\text{Counties}, \text{model} = \text{"bym"}, \text{graph} = \text{Kenya.adj}) + f(\text{Counties.1}, \text{model} = \text{"iid"}) + f(\text{Time}, \text{model} = \text{"rw1"}) + \text{smoking}$

Model 2: With structured spatial effect, structured trend effect, global time effect and a covariate

This model was specified as follows:

Model 2 $\langle -y \sim 1 + f(\text{Counties}, \text{model} = \text{"bym"}, \text{graph} = \text{Kenya.adj}) + f(\text{Counties.1}, \text{model} = \text{"rw1"}) + \text{Time} + \text{smoking}$

Model 3: With structured, unstructured spatial effects, structured trend effects and a covariate

This third model was specified as follows:

Model 3 $\langle -y \sim 1 + f(\text{Counties}, \text{model} = \text{"bym"}, \text{graph} = \text{Kenya.adj}) + f(\text{Counties.1}, \text{model} = \text{"iid"}) + f(\text{Time}, \text{model} = \text{"rw1"}) + \text{smoking}$

Model 4: structured spatial effect, structured time effect, space-time interaction effects and a covariate

A fourth model allows for an interaction between space and time was specified as follows:

Model 4 $\langle -y \sim 1 + f(\text{Counties}, \text{model} = \text{"bym"}, \text{graph} = \text{Kenya.adj}) + f(\text{Time}, \text{model} = \text{"rw1"}) + f(\text{Counties. Time}, \text{model} = \text{"iid"}) + \text{smoking}$

Table 6. Results for various models fitted.

Variables	Model 1	Model 2	Model 3	Model 4
Intercept (e^{β_0})	0.001	0.9578	0.0005	0.0005
Smoking (e^{β_1})	1.0121	1.0523	1.0121	1.0121
Year (e^{β_2})	-	0.0004	-	-
DIC	200.91	46067344	200.89	200.63

Table 6 presents the covariate estimates and DIC

components for the four models: despite the added complexity due interaction between space and time, Model 4 was more plausible since it had the lowest DIC value. Model 4 was utilized in obtaining the relative risks per county as shown Table 7 below.

Table 7. The relative risks for counties with notified oesophageal cancer cases where smoking was the covariate.

County	Relative Risk
Bomet	11.71
Embu	2.91
Kakamega	2.28
Kiambu	0.68
Machakos	0.99
Meru	6.68
Mombasa	1.09
Nairobi	1.78
Nakuru	2.59
Nyeri	4.01

The multiplicative effect of smoking was observed to be $e^{\beta_1} = 1.012$, indicating that esophageal cancer is 1.2% higher to those who smoke compared to non-smokers.

4.3.2. Models Where Alcohol Use Is the Covariate

In this section, four models were fitted as in section 4.3.1 where alcohol use was the covariate.

Table 8. Results for various models fitted.

Variables	Model 1	Model 2	Model 3	Model 4
Intercept (e^{β_0})	0.0009	1.0725	0.0009	0.0009
Alcohol use (e^{β_1})	1.0346	1.0460	1.0346	1.0346
Year (e^{β_2})	-	0.0003	-	-
DIC	182.63	81715841	182.74	182.60

Table 8 presents the covariate estimates and DIC components for the four models: despite the added complexity due interaction between space and time, Model 4 was more plausible since it had the lowest DIC value.

The multiplicative effect of alcohol use was observed to be $e^{\beta_1} = 1.0346$, indicating that oesophageal cancer is 3.5% higher to alcohol users as compared to non-alcohol users. The relative risks were obtained for this model as shown in Table 7.

Table 9. The relative risks for counties with notified oesophageal cancer cases with alcohol as the covariate.

County	Relative Risk
Bomet	11.75
Embu	2.80
Kakamega	2.43
Kiambu	0.64
Machakos	0.99
Meru	7.78
Mombasa	1.05
Nairobi	1.78
Nakuru	2.39
Nyeri	3.23

4.3.3. Spatio-temporal Maps

Relative risks for the spatial-temporal distribution are displayed in Figures 3-6. Counties with relative risk greater than 1 had higher risk while those with value of less than 1 had lower risk than expected risk from a standard population. Darker regions indicated relative risk was greater than 1 and while purple colored areas indicated a posterior probability of above 0.8.

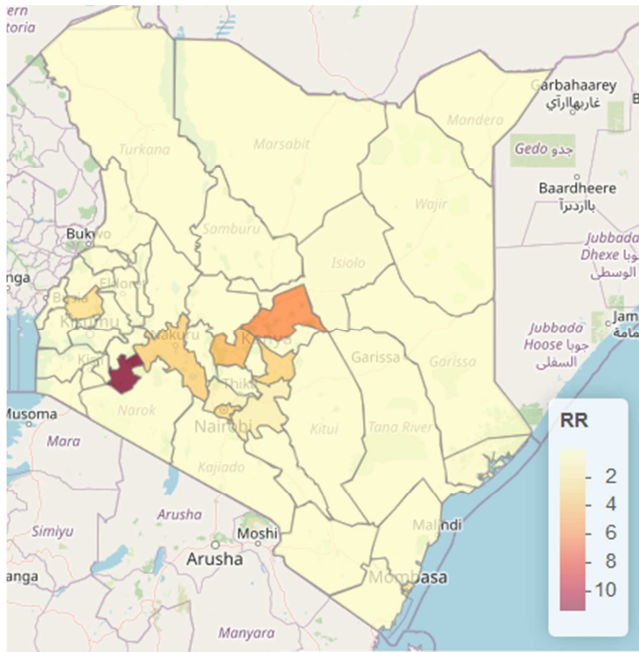


Figure 3. Spatio-temporal distribution of the relative risks for oesophageal cancer with smoking as the covariate.

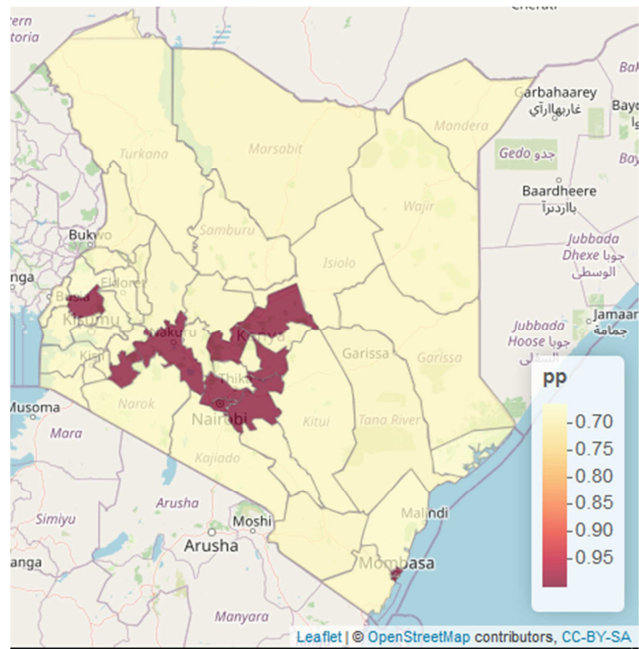


Figure 4. Map of the uncertainty for the spatial temporal effects accounting for smoking effect (oesophageal cancer) $\mu_i: p(\mu_i > 1|y)$.

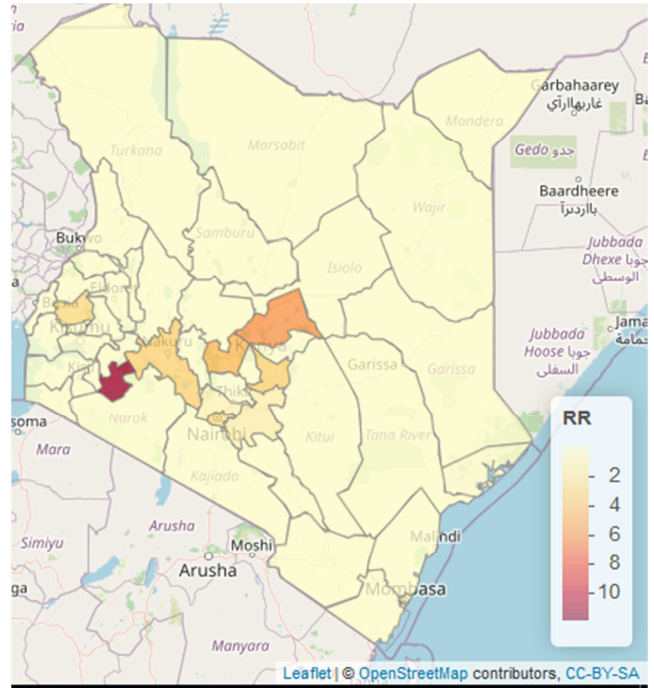


Figure 5. Spatio-temporal distribution of the relative risks for oesophageal cancer with alcohol use as the covariate.

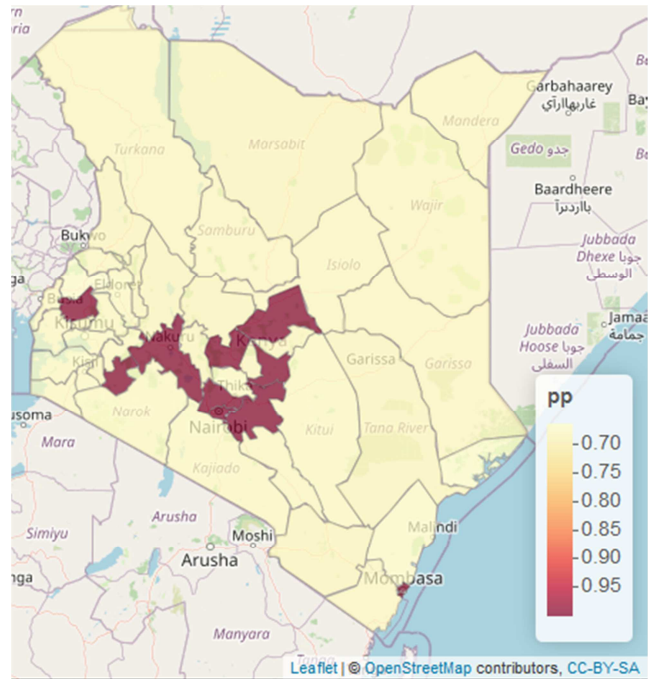


Figure 6. Map of the uncertainty for the spatial temporal effects accounting for alcohol use effect $\mu_i: p(\mu_i > 1|y)$ (oesophageal cancer).

4.4. Spatio-Temporal Models for Lung Cancer

4.4.1. Spatio-Temporal Model for Lung Cancer Where Smoking Was the Covariate

In this section, four models were fitted same as in section 4.3.1 where smoking was the covariate.

Table 10 presents the covariate estimates and DIC components for the four models, Model 4 was selected since it had the lowest DIC value compared to others:

The multiplicative effect of smoking was $e^{\beta_1}=1.4021$, indicating that lung cancer is 40.21% higher to smokers as compared to non-smokers from the available data.

Table 10. Results for various models fitted.

Variables	Model 1	Model 2	Model 3	Model 4
Intercept (e^{β_0})	0.0327	0.5886	0.0327	0.0343
Smoking (e^{β_1})	1.3324	1.1996	1.3338	1.4021
Year (e^{β_2})	-	0.0612	-	-
DIC	129.55	211.78	129.47	127.12

Table 11. The relative risks for counties with notified lung cancer cases with smoking as the covariate.

County	Relative Risk
Bomet	0.68
Embu	5.01
Kakamega	0.19
Kiambu	1.99
Machakos	3.26
Meru	2.42
Mombasa	1.30
Nairobi	3.69
Nakuru	2.02
Nyeri	4.98

Relative risk greater than 1 indicated that the risk of developing lung cancer was higher in the specific counties than in the standard population. The relative risks in Table 11 revealed that majority of the counties where data was available had higher risk of developing lung cancer with exception of Bomet and Kakamega. In Figure 7 the darker the colour the higher the relative risk.

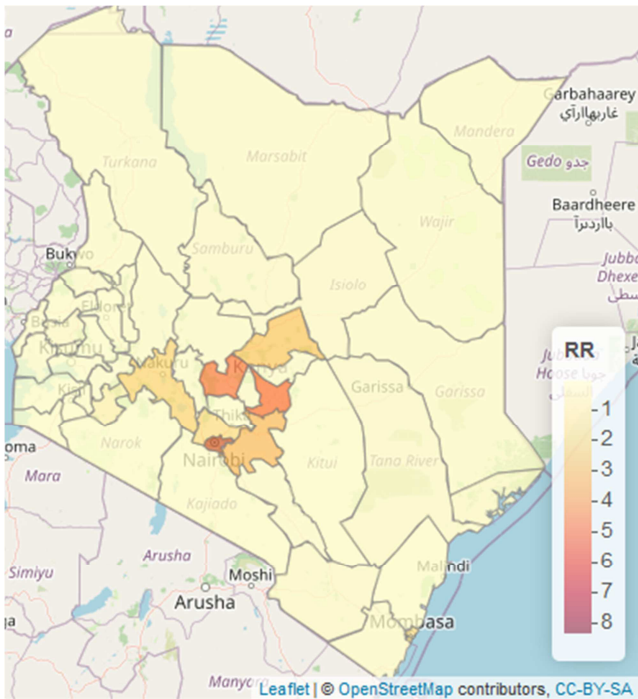


Figure 7. Spatio-temporal distribution of the relative risks for Lung cancer with smoking as the covariate.

4.4.2. Spatio-Temporal Model for Lung Cancer Where Alcohol Use Was the Covariate

Four models were fitted as described in section 4.3.1, where alcohol use was the covariate.

Table 12. Results for various models fitted.

Variables	Model 1	Model 2	Model 3	Model 4
Intercept (e^{β_0})	0.0302	0.6344	0.0347	0.0342
Alcohol use (e^{β_1})	1.3689	0.05948	1.3716	1.3716
Year (e^{β_2})	-	1.1817	-	-
DIC	128.61	209.67	128.77	128.78

Table 12 presents the covariate estimates and DIC components for the four models, Model 1 was selected since it had the lowest DIC value compared to others:

The study findings revealed, the multiplicative effect of alcohol use was $e^{\beta_1}=1.3689$, indicating that the risk of lung cancer is 36.89% higher to alcohol users compared to non-alcohol users.

Table 13. The relative risks for counties with notified lung cancer cases where alcohol use is the covariate.

County	Relative Risk
Bomet	0.69
Embu	5.00
Kakamega	0.19
Kiambu	1.78
Machakos	3.74
Meru	2.54
Mombasa	1.30
Nairobi	4.08
Nakuru	1.80
Nyeri	5.97

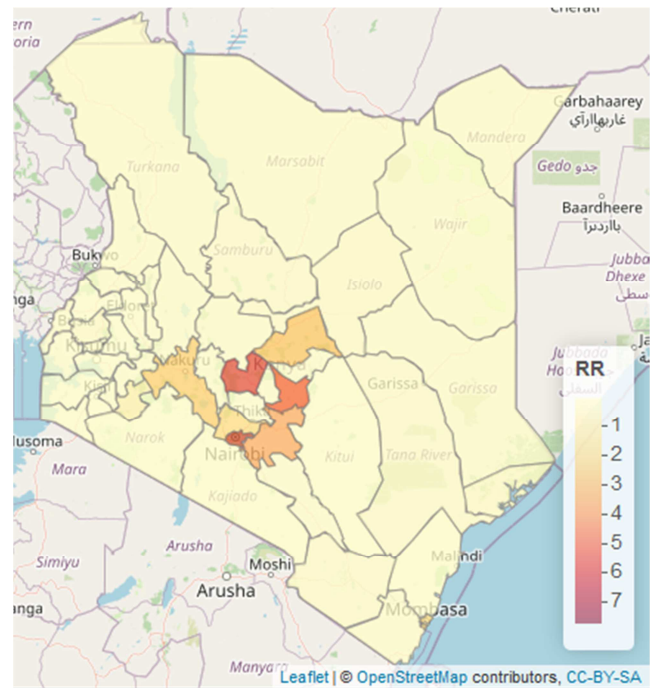


Figure 8. Spatio-temporal distribution of the relative risks for lung cancer with alcohol use as the covariate.

The relative risks in Table 13 indicated that in majority of

the counties where the data was available the risk of developing lung cancer was higher than expected in the standard population. In Figure 8 the darker the colour the higher the relative risk. Nyeri, Embu, Nairobi and Machakos Counties had the highest risks respectively. The relative risk of the areas where the data was not available ranged between 0.0539 and 0.7971.

5. Discussion and Conclusion

The study revealed, counties where data was available Bomet had highest relative risk of oesophageal cancer, followed by Meru, Nyeri, Embu, Nakuru, Kakamega Nairobi, Mombasa, Kiambu and Machakos counties respectively. Other counties had relatively low relative risks which ranged between 0.01-0.08, clearly even though the data was not available in these counties application of spatio-temporal accounting for covariates revealed that there was risk of oesophageal cancer in the counties.

The study revealed that smoking and alcohol use were significant determinants of oesophageal cancer in Kenya. The study findings are consistent with Odera *et al.* [15] who, identified alcohol drinking, genetic factors, dietary change/food preparation, and consumption of hot food as the main risk factors for esophageal cancer. Patel *et al.* [17] showed that there was positive and statistically significant relationship between tobacco smoking and development of oesophageal cancer in Kenya, where in one study smokers had 2.51 odds of developing oesophageal cancer than non-smokers.

Generation of spatio-temporal maps and identification of the risk factors from various counties with notified oesophageal cancer cases is a major milestone since previous studies on oesophageal cancer focused specific regions. Previous studies had indicated that oesophageal cancer is more prevalent in western region of Kenya, but the study revealed that it is also prevalent in other counties such as Meru, Embu and Nyeri.

It is evident that smoking and alcohol use were significant risk factors for lung cancer in Kenya. Meta-analyses conducted by Bandera *et al.* [4] revealed in alcoholics there is risk of lung cancer which is attributable to confounding of residuals since in non-smokers there was no consistent association. Therefore, even though alcohol use is not a direct risk factor for lung cancer it is a confounding risk factor. According to Malhotra *et al.* [13], control of occupational exposures, indoor and outdoor air pollution, understanding the carcinogenic and preventive effects of dietary and other lifestyle factors are some of preventive measures for lung cancer.

The national, county and private health institutions should work closely to create awareness by disseminating information on oesophageal cancer and lung cancer especially in high risk areas as revealed by the study. Screening and treatment facilities should be established based on hot spots of specific cancer cases which are generated from the spatial temporal models.

To enhance research on oesophageal, lung cancer and other types of cancer in Kenya the National Cancer Registry in collaboration with Counties health departments should enhance cancer data collection to facilitate research and to inform the appropriate measures to be implemented to mitigate the increase of cancer cases. We recommend further epidemiological studies to be conducted in areas with high relative risks to find out the other risk factors resulting to higher cases.

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