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Maastricht University

Faculty of Sciences
School for Information Technology
Master of Statistics

Master's thesis

The spatio-temporal modelling of colon cancer in Limburg

Fransis Mange
Thesis presented in fulfillment of the requirements for the degree of Master of Statistics, specialization Biostatistics

SUPERVISOR :
dr. Thomas NEYENS

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2019

Transnational University Limburg is a unique collaboration of two universities in two countries: the University of Hasselt and Maastricht University.

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Acknowledgements

First and foremost, great thanks goes to the Almighty God for the gift of life, knowledge and doors of education He opened for me from childhood. Having the opportunity to study in Hasselt University was a manifestation of his loving kindness and favor in my life. Without His blessings, this masters would have been far from reach.

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Fransis Mange

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Abstract

Cancer is a disease caused by abnormal growth of cells. In this paper we were interested in studying colon cancer, a cancer that forms in the tissues of the colon. It is important to study the simultaneous effects of space and time on a disease rather than studying those effects separately. Bayesian hierarchical modeling provides a good way to take these two into account (that is the spatial and temporal dependency). The objective of this study is to investigate the spatial and spatio-temporal distribution of colon cancer in Limburg from 1996 to 2005, and to make prediction of the true relative risk of colon cancer in each municipality. The data used has colon cancer incidence recorded from 1996 until 2005 in 44 Limburg municipalities. Since most diseases affect people of certain age dis-proportionally, indirect age standardization was performed to obtain standardized colon cancer incidence rates for comparison purpose. Bayesian hierarchical models were used in the analysis. To investigating the spatial distribution, two unstructured heterogeneity and two spatially structured heterogeneity models were fitted. Four spatio-temporal models were used in investigating the spatio-temporal distribution. We used WinBUGS software for analysis and MCMC approach with Gibbs sampling techniques for estimation of parameters in all models. Model selection was done using DIC criterion. Results show small variations between relative risks of colon cancer in the municipalities in Limburg. There is no municipality with significant elevated colon cancer risk in Limburg (1996-2005). Our results also show that, spatially structured heterogeneity dominates than unstructured heterogeneity in the data. In addition, we found that there is a decreasing time trend for colon cancer relative risk though this trend is not significant.

Key Words: Disease mapping, Heterogeneity, Hierarchical models, Prior distribution, Standardization.

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1 Introduction

1.1 Background

Cancer is a disease caused by a group of abnormal cells growing uncontrollably by disregarding the normal rule of cell division (Hejmadi, 2009). According to WHO (2018), cancer is the second leading cause of death globally. It is estimated that 9.6 million deaths in the year 2018 was caused by cancer. Globally, about 1 in 6 deaths is due to cancer. In 2018 the most common cancers were; lung cancer with 2.09 million cases, breast cancer with 2.09 million cases, colorectal cancer with 1.80 million cases, prostate cancer with 1.28 million cases, skin cancer with 1.04 million cases, and stomach cancer with 1.03 million cases (WHO, 2018).

Colon cancer is a cancer that forms in the tissues of the colon (NCI, 2016). The colon is an inverted,U-shaped part of the large intestine and is about 5 to 6 ft long. The large intestine consists of other parts, the cecum (and appendix) and ano-rectum, which are not included in the colon (Kapoor and Gandhi, 2018).

It is important to study the simultaneous effects of space and time on a disease rather than studying those effects separately. This study aimed to investigate the simultaneous effects of space and time on colon cancer. We are interested to identify areas with elevated risk levels and to estimate the temporal pattern in disease risk. Using classical analysis in this case, may not be appropriate because of spatial and temporal dependency in data. Bayesian hierarchical models can be used in disease mapping to estimates the spatial and spatio-temporal pattern in disease risk over an extended geographical region, to identify areas with elevated risk levels (Lee, 2011). Bayesian hierarchical models are models with multiple levels (hierarchical form) that estimates the parameters of the posterior distribution using the Bayesian method (Allenby and Rossi, 2006).

1.2 Objectives

This study aimed at investigating the spatial and spatio-temporal distribution of colon cancer in Limburg from 1996 to 2005, as well as making prediction of the true relative risk of colon cancer in each municipality.

2 Data

2.1 Data sources

Data used in this study were collected in the framework of the Limburg Cancer Registry (LIKAR). The LIKAR database contains the number of new histologically or cytologically confirmed primary cancers that were observed among male and female inhabitants of the Belgian province of Limburg within the period of 1996–2005 (Neyens et al., 2012). The area of the Limburg Cancer Registry consists of the province Limburg, situated in the north-east of Belgium. The territory covers 2,422 square kilometres which is 7.9 % of the Belgium territory (Lousberg et al., 2000). The province has 44 towns, with the largest populations centred in the middle of the province (Neyens et al., 2012). Data were obtained from all pathological laboratories located in the Limburg province and all pathological departments outside the province examines samples from Limburg inhabitants (Buntinx et al., 2003). All cancers are classified according to the International Classification of Diagnosis Oncology (ICDO) (WHO, 2019). In the Limburg Cancer Registry, data were checked on the completeness of the included information with respect to demographic and clinical aspects (Lousberg et al., 2000). More details about the Limburg Cancer Registry (LIKAR) can be found in (Lousberg et al., 2000) and (Buntinx et al., 2000).

2.2 Data description

This thesis focuses on colon cancer. The data-set used has colon cancer incidence counts for all 44 Limburg municipalities recorded for each year from 1996 until 2005 (inclusive). The colon cancer incidence counts were recorded separately for males and females of 18 categorized age groups (0 - 4 years, 5 - 9 years, 10 - 14 years, . . .,80 - 84 years and 85 + years). Also the data set contains a population of the 44 Limburg municipalities for each year separately for males and females. There were no missing values in the data set.

From 1996 to 2005, 3027 colon cancer incidence were recorded in the 44 municipalities of Limburg. Among those 3027 incidences, 1635 were recorded from males and 1392 were recorded from females. Figure 1 shows colon cancer incidence counts in each year in Limburg for both males and females. The maximum and minimum colon cancer incidence counts for males were 196 and 138 in the years 2005 and 1998 respectively while for females were 156 and 123 in the years

2000 and 1999 respectively.

From figure 1 we can see that colon cancer incidences were increasing with time, especially in males (red colour). In general, it has been observed that, colon cancer incidence increase with age. Figure 2 shows males colon cancer incidence counts at different age categories in Limburg.

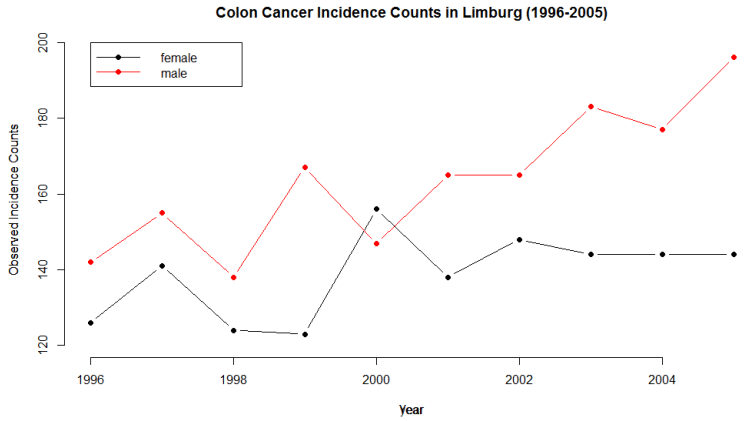


Figure 1: Colon Cancer Incidence Counts in Limburg from 1996-2005

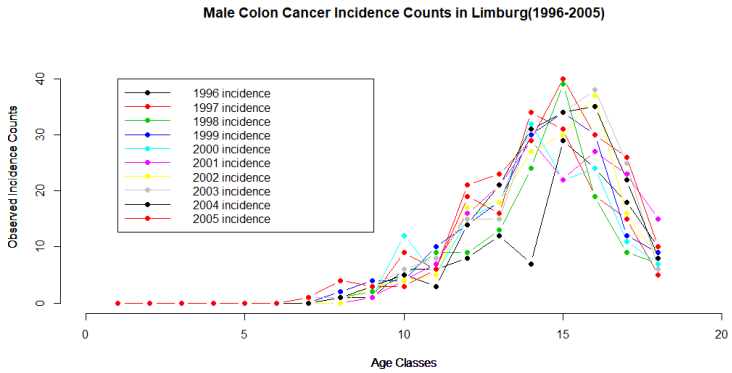


Figure 2: Males Colon Cancer Incidence Counts by Age in Limburg

In ten years (1996 to 2005), the highest colon cancer incidences was observed in Hasselt (186 in males and 180 in females) followed by Genk (131 in males, 111 in females), Sint-Truiden (84 in males, 88 in females) and Beringen (77 in males, 64 in females). There was no colon cancer incidence observed in Herstappe (0 in males, 0 in females) while, Voeren had only two incidences (1 in males, 1 in females).

2.3 Standardization

Comparing the colon cancer incidence rates among municipalities of Limburg is one of the objectives of this study. However, most diseases affect people of certain age dis-proportionally. In general, there is an increasing incidence of cancer with age, thus populations containing more people in higher age groups tend to have higher summary incidence rates than those of younger populations. As a result, the incidence rates for two areas may appear different, but this difference may be due to the difference in age distributions within the areas rather than to a difference in the underlying age-specific risk of a disease.

To make colon cancer incidence rates from different municipalities comparable, standardization is required. In addition, colon cancer is a rare disease hence the incidence rates from index populations (municipalities) may be statistically unstable. In such situation it is better to use the incidence rates from the standard population. In this study, an indirect standardization method was used because it uses incidence rates from the standard population rather than index populations.

The population of Limburg for each year, separately for males and females of 18 different age groups, was used as standard population. First we computed how many colon cancer incidences would be expected in each municipality i if it had the same age specific incidence rates as standard population (Limburg population).

$$E_{gi} = r_g^s n_{gi} = \frac{y_g^s}{n_g^s} n_{gi}$$

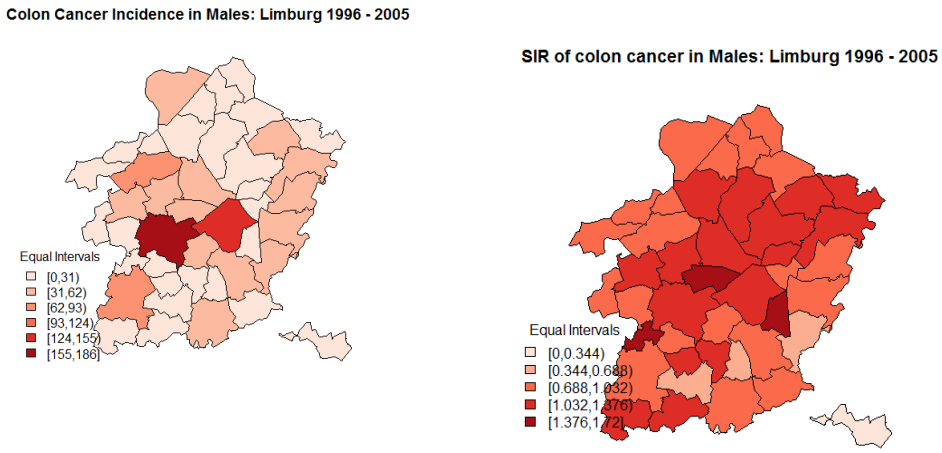
where r_g^s is the observed incidence proportion in age group g in the standard population, n_{gi} is the number of people at risk in age group g for municipality i. y_g^s is the number of cases in age group g for for the standard population. n_g^s is the number of people at risk in age group g for the standard population.

Then, a standardized incidence ratio (SIR) for municipality i was computed as the ratio of observed colon cancer incidence counts for municipality i ($y_i = \sum_{g=1}^{18} y_{gi}$) and the overall expected colon cancer incidence for municipality i ($E_i = \sum_{g=1}^{18} E_{gi}$).

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

where $i = 1, 2, 3, 4, ...44$.

Standardized incidence rates (SIRs) were mapped for each of the 44 municipalities and municipalities with SIR greater than one (SIR > 1) are an indication that there were more colon cancer cases than expected. Figure 3 a shows the observed colon cancer incidences in Limburg (1996-2005) for males while figure 3 b shows the map of the SIRs of colon cancer in Limburg(1996-2005) for males. The maps for SIRs suggest that there is spatial pattern in colon cancer risk.



(a) Observed incidences (b) SIRs

Figure 3: Males observed incidence and SIRs of colon cancer in Limburg, 1996-2005

3 Methods and Materials

3.1 Modeling Unstructured Heterogeneity

To estimate colon cancer relative risks one can use Binomial or Poisson models but the models have disadvantages for small areas where little information is available. Binomial and Poisson models use the information only from within the municipality to get the estimate; therefore for small areas where little information is available the estimates are unstable. In this study we considered the methods which allow borrowing information across municipalities. The small municipalities with little information also use information from other municipalities to get a better estimate. We assume that the relative risk θ_i comes from a certain distribution. The relative risk θ_i can have different distributions, we started by assuming that θ_i as exchangeable random effects in the sense that there is no spatial pattern among the θ_i. In exchangeable random effects models, Poisson-Gamma models and Poisson-Lognormal models were considered.

3.1.1 Poisson-Gamma Model

The Poisson-Gamma model is a common choice in disease mapping. In the Poisson-Gamma model we assume that the colon cancer incidence counts y_i in each municipality follows a Poisson distribution and the relative risks θ_i follows a gamma distribution (random effect, prior). The assumption of a prior distribution for θ_i allows over-dispersion or extra variation of the Poisson model. The Poisson model assumes the same mean and variance but with an assumption of a prior distribution for θ_i the variance is allowed to be larger than the mean.

$$y_i \sim Poisson(e_i\theta_i)$$

$$\theta_i \sim Gamma(a, b).$$

The mean of θ_i is $m_{\theta_i} = a/b$ and the variance of θ_i is $v_{\theta_i} = a/b^2$. Assuming a and b are fixed and known, the relative risk θ_i has the posterior gamma distribution with parameters $a + y_i$ and $b + e_i$. The posterior mean of the relative risk θ_i is a weighted average of the data-based SIR for the ith municipality, and the relative risk in the overall map (the prior mean m_{θ_i}). The

posterior mean of the relative risk θ_i is given by,

$$E[\theta/y_i] = \frac{a+yi}{b+e_i} = C_i SIR_i + (1-C_i)\frac{a}{b}$$

where,

$$C_i = \frac{e_i}{(m_{\theta_i}/v_{\theta_i}) + e_i}$$

For rare diseases and small areas, C_i is small and the posterior mean tends towards a global mean a/b, thereby producing a smoothed map. For areas with abundant of data, the posterior mean of the relative risk is close to $\frac{y_i}{e_i}$ (Lawson et al., 2003). Because of the mathematical convenience due to the conjugacy, the Poisson-gamma model has been one of the most commonly used models in disease mapping (Neyens et al., 2012).

3.1.2 Poisson-Lognormal Model

The Poisson-Lognormal model is an extension of the Poisson-Gamma model. Instead of using gamma as a prior distribution for a relative risk, this model incorporate normal random effect in the linear predictor of a log-relative risk. As in the Poisson-Gamma model, we assume that the colon cancer incidence counts y_i in each municipality follow a Poisson distribution while the prior distribution for a relative risk is given by;

$$log(\theta_i) = \alpha + x_i\beta + v_i$$

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

where α is the overall mean risk, x_i are explanatory spatial covariates (at municipality-level) having parameter coefficients β, and v_i is the heterogeneity random effect capturing extra-Poisson variability in the log-relative risks. It is an exchangeable random effect, it does not take into account any spatial structure. The parameter v_i represents the residual (log) relative risk in area i after adjusting for known covariates ($xi\beta$) and overall mean risk (α). The variance of the random effects, σ_v^2 reflects the amount of extra-Poisson variation in the data. Large variance of a random effect v_i means large variability among the relative risks and small variance means that the relative risks are very similar. Poisson-Lognormal model does not account for spatial

autocorrelation; it can be easily extended with a parameter representing correlated heterogeneity, resulting in a so-called convolution model (Besag et al., 1991).

3.2 Modeling Spatially Structured Heterogeneity

The models discussed in previous sub-section, the Poisson-Gamma and the Poisson-Lognormal models do not account for spatial correlation. These models are known as independent prior models, where the local estimates are a weighted average of area (municipality) data and a global weighted average of the data from all areas. Models considered in this sub-section (spatially structured heterogeneity models), can account for spatial correlation. The local estimates are a weighted average of area data and average of observations in neighbouring areas. In this study, the Improper Conditional Autoregressive (CAR) Model and the CAR-Convolution models were considered in modeling spatially structured heterogeneity.

3.2.1 Improper Conditional Autoregressive (CAR) Model

The CAR model starts with the same formulation as on the previous models, the counts y_i follow a Poisson distribution with mean given by the expected number times the relative risk parameter θ while the prior distribution for a relative risk is given by;

$$\theta_i = exp(\alpha + u_i),$$

where u_i is a random effect, it has a univariate normal distribution given the other random effect u_j

$$u_i/u_{j\neq i} \sim N(\bar{u}_i, \sigma_i^2).$$

The mean of u_i is given by a weighted average of of the random effect u_j and its variance is given by a parameter r divided by the weight c_{ij}.

$$\bar{u}_i = \frac{\sum_{j\neq i} c_{ij} u_j}{\sum_{j\neq i} c_{ij}}$$

, and

$$\sigma_i^2 = \frac{r}{\sum_{j\neq i} c_{ij}},$$

where c_{ij} are spatial dependence parameters defining which areas j are neighbours of area i. These parameters form the neighborhood/proximity matrix. The values of c_{ij} are larger when area i and j are close to each other and they are small (close to zero) when area i and j are far from each other. The c_{ij} values define the influence of area j on area i. We set c_{ii} equal to 0 meaning that no area is neighbor of its own. In this model we have used c_{ij} equal to 1 if municipality j is adjacent to municipality i and c_{ij} equal to 0 if municipality j is not adjacent to municipality i. Therefore ;

$$\bar{u}_i = \frac{\sum_{j\epsilon} \delta_i u_j}{n_{\delta_i}},$$

where δ_i is the set of neighbours of municipality i, and n_{δ_i} is the number of neighbors in the set. The conditional variance σ_i^2, depends on the number of neighbors and is defined as;

$$\sigma_i^2 = \frac{r}{n_{\delta_i}}.$$

The conditional variance σ_i^2 will be small when there are many neighbors and larger for few neighbors. In the CAR model, the relative risk of an area is smoothed towards the local average risk in a set of neighbouring areas, with variance inversely proportional to the number of neighbours (Buntinx et al., 2003).

3.2.2 The CAR-Convolution Model

The convolution model takes into account both spatially unstructured and spatially structured heterogeneity. The CAR-convolution model combines the Poisson-lognormal model with the Poisson improper condition autoregressive model. The model starts with the same formulation as in previous models, the counts Y_i follow a Poisson distribution with mean given by the expected number times the relative risk parameter θ_i. The prior distribution for a relative risk θ is given by;

$$log(\theta_i) = \alpha + x_i\beta + u_i + v_i,$$

where α is an overall level of the relative risk of colon cancer in Limburg and β is a covariate effect. In this study, no covariate effect was included in this model therefore there is no parameter β in the model. The parameter v_i is the uncorrelated heterogeneity for municipality i, it is

defined as;

$$v_i \sim N(0, \sigma_v^2).$$

The parameter u_i is the correlated heterogeneity for municipality i. It is specified by a condition auto-regressive random effect, and defined as;

$$u_i/u_{j\neq i,\tau_u^2} \sim N(\bar{u}_i, \sigma_u^2).$$

See sub-section 3.2.2 for more details on random effect u_i. The parameters σ_u^2 and σ_v^2 measure the amount spatially structured heterogeneity and unstructured heterogeneity respectively. Small values of σ_u^2/σ_v^2 indicates that unstructured heterogeneity dominates than spatially structured heterogeneity, and a model with unstructured heterogeneity term only may be sufficient. Large values of σ_u^2/σ_v^2 indicates that spatially structured heterogeneity dominates than unstructured heterogeneity, and a model with spatially structured heterogeity term only may be sufficient.

3.3 Spatio-Temporal Modeling

The CAR-Convolution model discussed in the previous sub-section can be modified to incorporate time effects. The modification allows studying both the space and time (spatio-temporal) simultaneous effects on a disease. The spatio-temporal models are hierarchically constructed following set of steps. The counts Y_{it} in municipality i at time (year) t follow a Poisson distribution with mean given by $e_{it}\theta_{it}$.

$$Y_{it} \sim Poisson(e_{it}\theta_{it})$$

$$log(e_{it}\theta_{it}) = log(e_{it}) + log(\theta_{it}),$$

$i = 1, 2, 3, ..., N$ and $t = 1, 2, 3, ..., T$,

where e_{it} is the expected number of colon cancer incidences in municipality i at time (year) t while θ_{it} is the unknown colon cancer relative risk in municipality i at time (year) t.

3.3.1 Model 1

The first spatio-temporal models considered in this study assumes the same linear effect of the covariate time on all municipalities. The second step of the model hierarchy is defined as;

$$log(\theta_{it}) = \alpha + u_i + v_i + \beta time_t,$$

where α is an overall level of the relative risk of colon cancer in Limburg, u_i and v_i are the random effects for the spatial structured and unstructured heterogeneity respectively. The parameter β is the mean linear time trend for all Limburg municipalities. As in the CAR-Convolution model, the same CAR prior distribution of the spatial random effects u_i is assumed in this model, $u_i/u_{j\neq i,\tau_u^2} \sim N(\bar{u}_i, \sigma_u^2)$. Also for the uncorrelated heterogeneity v_i, the same prior distribution as in the CAR-Convolution model was assumed in this model, $v_i \sim N(0, \sigma_v^2)$.

3.3.2 Model 2

Model 1 can be modified to accommodate different intercepts for each time period. Model 2 can be used as an alternative to model 1 for small number of time periods. This model has been discussed by Ugarte et al. (2009) and Knorr-Held and Besag (1998). The second step of the model hierarchy is defined as;

$$log(\theta_{it}) = \alpha_t + u_i + v_i,$$

where θ_{it} is the effect of year t, and u_i and v_i have the same definations and prior distributions as in model 1.

3.3.3 Model 3 (Bernardinelli Model)

Another option is to assume a linear time trend but additionally a space-time interaction. The model was proposed by Bernardinelli et al. (1995) and discussed by Ugarte et al. (2009). The second step of the model hierarchy is defined as;;

$$log(\theta_{it}) = \alpha + u_i + v_i + \beta time_t + \delta_i time_t,$$

where δ_i is the difference between the municipality-specific trend and the mean trend β. A prior distribution for the random effects δ_i is assumed to be $\delta_i \sim N(0, \sigma_\delta^2)$

3.3.4 Model 4

Model 3 can be modified to accommodate different intercepts for each time period to increase flexibility of the model. The second step of the model hierarchy is defined as;

$$log(\theta_{it}) = \alpha_t + u_i + v_i + \delta_i time_t,$$

where α_t is the effect of year t and δ_i is the difference between the municipality-specific effect and the time effect α_t.

3.4 Estimation

3.4.1 Bayesian Estimation

Unlike the frequentist hierarchical models in which the fixed and random effect can be distinguished, the Bayesian hierarchical models assumes prior distributions to all parameters and all parameters are random (Lesaffre and Lawson, 2012). The Bayesian approach takes automatically into account all uncertainty in the model parameters. In this study, all model parameters were estimated using the Markov Chain Monte Carlo (MCMC) approach in WinBUGS. The MCMC approach solves statistical modelling problems which are difficult or even impossible to solve with maximum likelihood procedures (Lesaffre and Lawson, 2012). The MCMC approach gives flexibility in relaxing the strong parametric assumptions prevalent in most frequentist hierarchical models (Lesaffre and Lawson, 2012). The Gibbs sampler introduced by Geman and Geman (1984) was used as a sampling algorithm. Gelfand and Smith (1990) showed the ability of the Gibbs sampler to solve complex estimation problems in a Bayesian frame work (Lesaffre and Lawson, 2012). For more details about MCMC see (Hitchcock, 2003).

MCMC approach need diagnostics measure to assess if the iterative simulations have reached the Markov chain equilibrium distribution (Lawson et al., 2003). In this study, the MCMC convergence was investigated visually using history and trace plots. After a burn-in of 20,000

iterations, 20,000 more iterations were used for each model and there were no problem with convergence.

3.4.2 Model Comparison

Spiegelhalter et al. (2002) proposed to use Deviance Information Criterion (DIC) as a model comparison tool in the Bayesian modeling framework. DIC compares a fitted model to a saturated model. DIC is defined as;

$$DIC = 2E_{\theta|y}(D) - D(E_{\theta|y}(\theta))$$

where $E_{\theta|y}(D)$ is posterior mean of the deviance and $D(E_{\theta|y}(\theta))$ is the deviance of the posterior mean of the parameters. Therefore, DIC comparares the average deviance and deviance of posterior expected parameter estimates. The DIC can be re-written as;

$$DIC = E_{\theta|y}(D) + pD$$

where $pD = E_{\theta|y}(D) - D(E_{\theta|y}(\theta))$ is the estimated effective number of parameters which represents the complexity of the model. In the Bayesian framework, most of the models are complex and it is less clear how many parameters are in the models. The advantage of DIC is that it can be directly calculated from an MCMC output and can be applied in a different kind of models, including hierarchical models, where the number of estimated parameters is unclear (Ntzoufras, 2009). Generally we prefer the model with smaller DIC.

In this study, two unstructured heterogeneity models, two spatially structured heterogeneity models and four spatio-temporal models were fitted. One model was selected from the group of spatially structured and unstructured heterogeneity models and another from the group of spatio-temporal models. The final models were chosen according to the DIC.

3.4.3 Sensitivity Analysis

Hierarchical models require hyperparameters, and the hyperparameters must have their own prior distribution (Gelman et al., 2006). In Bayesian approach, the choice of the prior distributions needs attention (Lesaffre and Lawson, 2012). Sensitivity analysis can be performed to see how

much does the choice of the prior distributions affect the results. In this study, different choices of prior distributions for precision parameters were considered as a sensitivity analysis.

3.4.4 Software

WinBUGS version 14, R version 3.5.1 and Microsoft Excel 2010 were used in the statistical analysis and data management. The Microsoft Excel 2010 was used for standardization of colon cancer incidences while the R software was used for exploratory data analysis and to convert the shape file into map file and visualization. WinBUGS software was used to fit all the models discussed in this study as well as visualization. When fitting the models in WinBUGS, two chains with different initial values were used. The advantage of using multiple chains is that they provide evidence for the robustness of convergence across different subspaces (Lawson, 2009).

4 Result

4.1 Model Comparison

4.1.1 Comparison of Spatially Structured and Unstructured Heterogeneity Models

Table 1 displays the DIC results for the two unstructured and two spatially structured heterogeneity models. Results show that the Poisson-Lognormal has the smallest DIC values followed by the convolution model. The two models are less than 2 units apart in DIC, therefore they are equally well fitting to the data. In this case the convolution model is more relevant than the Poisson-Lognormal model since it takes into account the spatially structured heterogeneity, therefore it was selected as the best model in the group.

Table 1: Comparison of Spatially Structured and Unstructured Heterogeneity Models

Model	Dbar	Dhat	pD	DIC	Gender
P-Gamma	282.278	266.602	15.676	297.953	Male
	268.679	255.364	13.315	281.994	Female
P-Lognormal	277.08	256.988	20.091	297.171	Male
	265.126	248.47	16.656	281.782	Female
CAR	290.954	276.961	13.993	304.947	Male
	277.683	268.092	9.59	287.273	Female
Convolution	282.617	265.299	17.317	299.934	Male
	270.593	257.498	13.095	283.688	Female

4.1.2 Comparison of Spatio-Temporal Models

Table 2 displays the DIC results for the four different spatio-temporal models. From the table we can see that, model 3 proposed by (Bernardinelli et al., 1995) yields the lowest DIC than the other spacio-temporal models. In this case, model 3 was selected as the final spacio-temporal model which fits well our data.

Table 2: Comparison of Spatio-Temporal Models

Model	Dbar	Dhat	pD	DIC	Gender
Model 1	1704.18	1686.09	18.093	1722.28	Male
	1548.03	1534.07	13.961	1561.99	Female
Model 2	1711.51	1685.35	26.159	1737.67	Male
	1555.08	1533.13	21.956	1577.04	Female
Model 3	1696.02	1673.48	22.533	1718.55	Male
	1544.73	1528.48	16.247	1560.98	Female
Model 4	1704.46	1674.48	29.977	1734.44	Male
	1551.68	1527.28	24.404	1576.09	Female

4.1.3 Sensitivity Analysis

Sensitivity analysis was performed for the selected models (the convolution model and spatio-temporal model 3). Three hyper-prior distributions for all the precision parameters, Gamma(0.01 , 0.005), Gamma(0.001 , 0.0001) and Uniform(0,10000), were compared to Gamma(0.5 , 0.0005). With those different choices of the hyper-prior distributions, the maps of the relative risks estimates which are presented on sub-section 4.2 did not change. This sensitivity analysis justifies the use of the priors used in the final models.

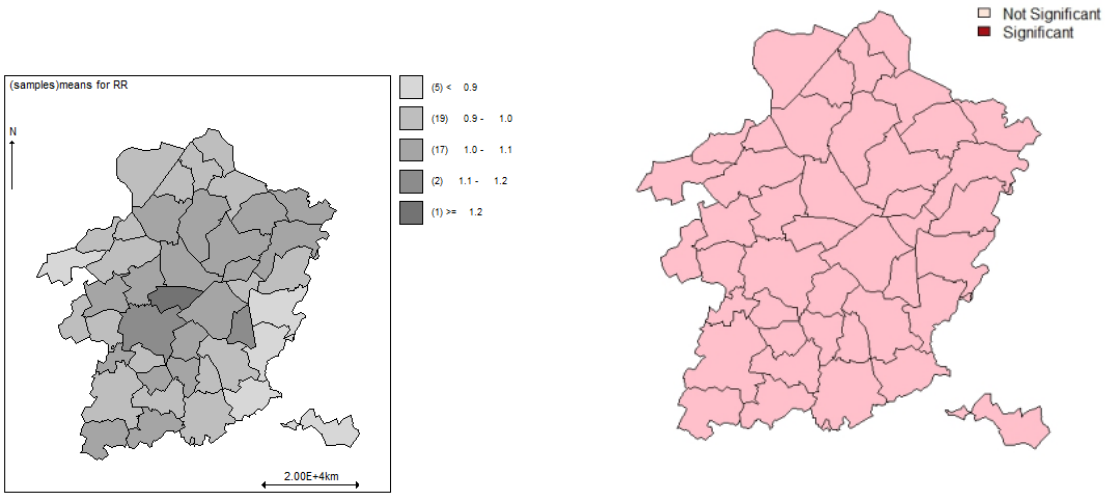
4.2 Model Results

Both selected models (the convolution and spatio-temporal model 3) show that there are small variations between relative risks in Limburg municipalities. In both populations (male and female population), all the relative risk estimates are close to one and all the 95% credibility intervals of the relative risks contain the value zero indicating that there is no difference in municipality risks from the overall risk in the province of Limburg (see figure 4 (b) and figure 5 (b)). For relative risk estimates of the convolution and spatio-temporal model 3, see table F3, F4, F5 and F6 in the appendix.

4.2.1 The CAR-Convolution Model

The male population results from the CAR-convolution model shows that, Zonhoven has the highest relative risk of 1.26 followed by Hasselt which has a relative risk of 1.137. In total there

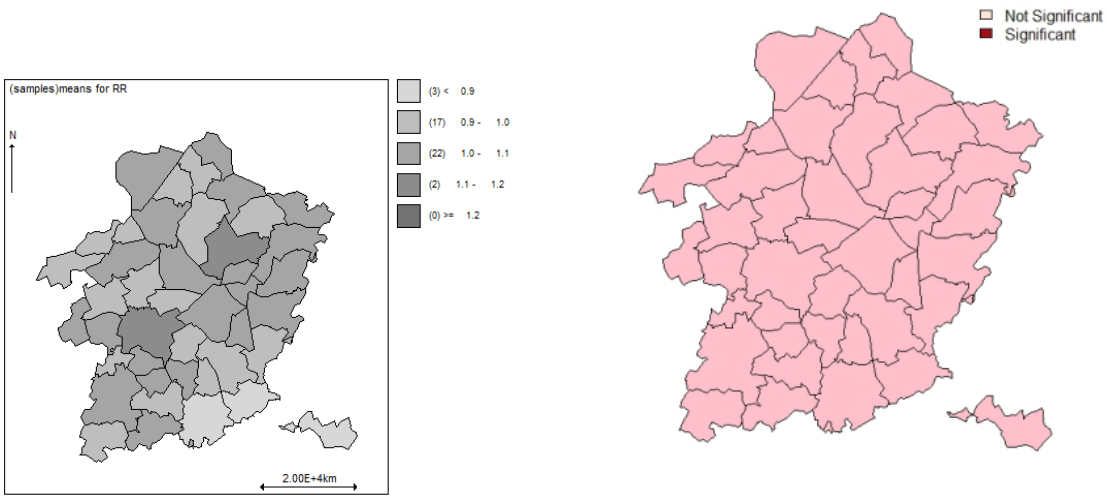
are 24 municipalities with the relative risks less than 1 and 20 municipalities with the relative risks greater than 1. For the female population, both Meeuwen-Gruitrode and Hasselt have the highest relative risk of 1.132. In total there are 20 municipalities with the relative risks less than 1 and 24 municipalities with the relative risks greater than 1. The spatially structured heterogeneity is 9.646 times the unstructured heterogeneity in male population while for female population is 11.98 times. This indicates that the spatially structured heterogeneity dominates than the unstructured heterogeneity. figure 4 and figure 5 shows the maps of relative risks in males and female population respectively based on the CAR-convolution model.



(a) Posterior Expected Relative Risk

(b) Significance of Elevated Relative Risk

Figure 4: Males Relative Risk for Colon Cancer in Limburg, 1996-2005 (CAR-Convolution Model)



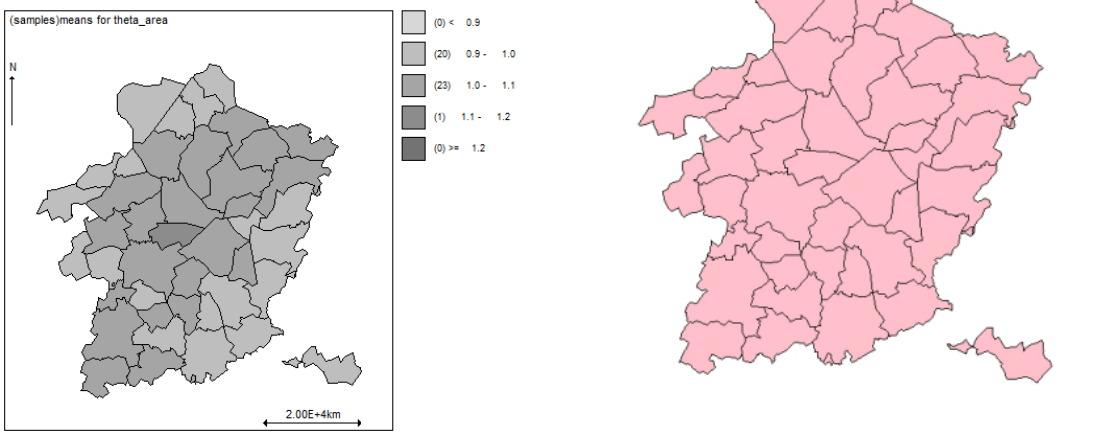
(a) Posterior Expected Relative Risk

(b) Significance of Elevated Relative Risk

Figure 5: Females Relative Risk for Colon Cancer in Limburg, 1996-2005 (CAR-Convolution Mode)

4.2.2 Spatio-Temporal Model (Bernardinelli Model)

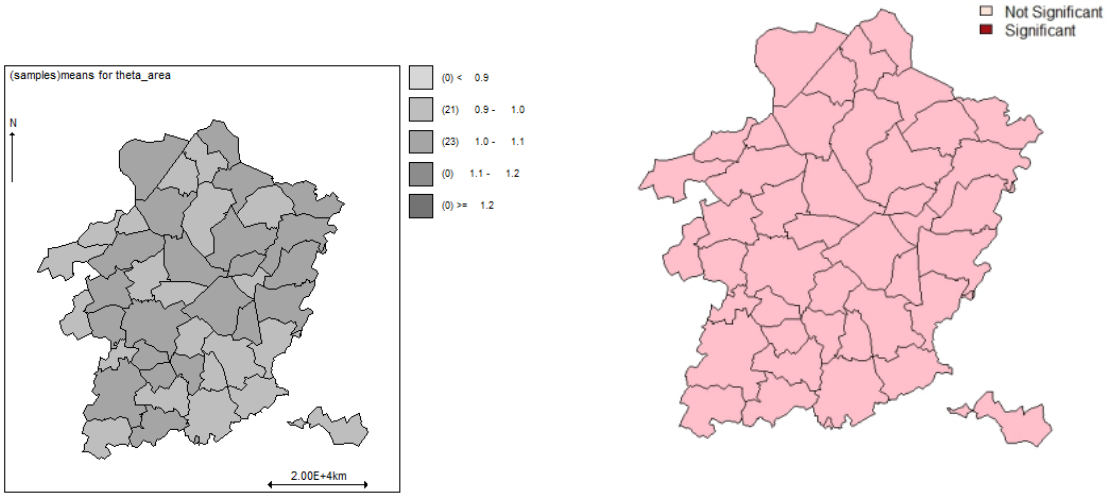
Figure 6 shows the maps of relative risks in male population based on the spatio-temporal model 3. Results of this model shows that, Zonhoven has the highest relative risk of 1.121 followed by Hasselt which has a relative risk of 1.079. As we have seen the results from the CAR-convolution model, also this spatio-temporal model identifies 24 municipalities with the relative risks less than 1, and 20 municipalities with the relative risks greater than 1.



(a) Posterior Expected Relative Risk (b) Significance of Elevated Relative Risk

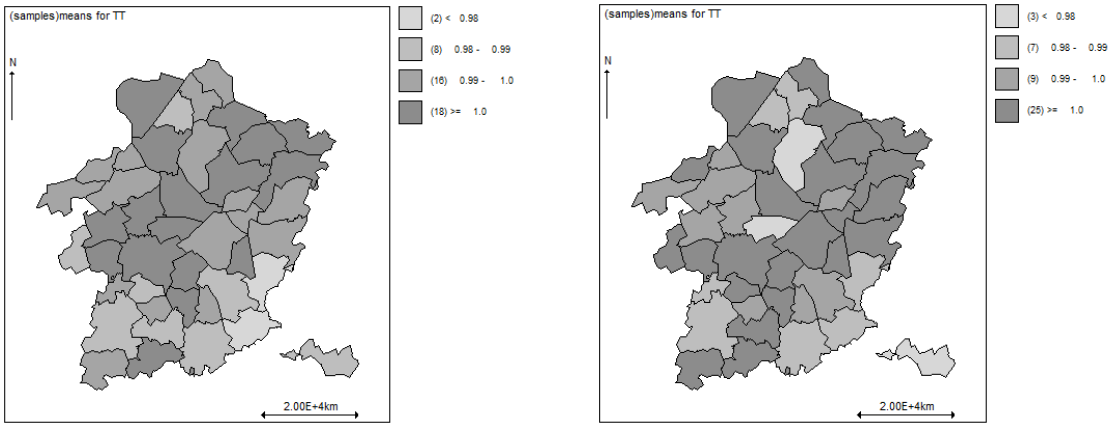
Figure 6: Males Relative Risk for Colon Cancer in Limburg, 1996-2005 (Spatio-temporal Model (Bernardinelli et al., 1995))

Figure 7 shows the maps of relative risks in female population based on the spatio-temporal model 3. Results of this model show that, Meeuwen-Gruitrode has the highest relative risk of 1.081 followed by Hasselt which has a relative risk of 1.072. There are 21 municipalities with the relative risks less than 1 and 20 municipalities have the relative risks greater than 1.



(a) Posterior Expected Relative Risk (b) Significance of Elevated Relative Risk

Figure 7: Females Relative Risk for Colon Cancer in Limburg, 1996-2005 (Spatio-temporal Model (Bernardinelli et al., 1995))



(a) Males (b) Females

Figure 8: Posterior Expected Temporal Trend for Colon Cancer in Limburg, 1996-2005 (Spatio-temporal Model (Bernardinelli et al., 1995))

Results from the spatio-temporal model 3 show that the mean time trend for colon cancer relative risk in male population is about 0.999 $(exp(-0.000929))$ indicating a 0.1% decrease in relative risk per year during a study period 1996 to 2005. For female population, the mean time trend for colon cancer relative risk is about 0.998 $(exp(-0.00202))$ indicating a 0.2% decrease in relative risk per year during a study period 1996 to 2005. The decrease in the relative risks is very small (almost zero) and 95% credibility intervals of mean time trend for both male and female populations show that there is no significant time trend (see table F5 in the appendix). Figure 8 shows the posterior expected temporal trend for colon cancer in Limburg during the study period 1996-2005.

5 Discussion

This study aimed at investigating the spatial and spatio-temporal distribution of colon cancer in Limburg from 1996 to 2005, and prediction of the true relative risk of colon cancer in each municipality. Several Bayesian hierarchical models were used to address the objectives of this study. In investigating the spatial distribution, two unstructured heterogeneity models (Poisson-Gamma model and Poisson-Lognormal model) as well as two spatially structured heterogeneity models (Improper CAR model and CAR-Convolution model) were fitted. Four spatio-temporal models were used to investigating the spatio-temporal distribution of colon cancer.

In WinBUGS software, MCMC approach with Gibbs sampling techniques was used for estimation of parameters in all models. One model was selected in the first group of four models (spatially structured and unstructured heterogeneity models) and another model in the second group of four spatio-temporal models using the DIC criterion was considered during model selection.

In the first group of models, convolution model which takes into account both spatially structured and unstructured heterogeneity was selected as the best model to describe the spatial pattern of colon cancer in Limburg. Further more, this model showed that spatially structured heterogeneity was more important than unstructured heterogeneity meaning that neighboring municipalities are likely to have similar colon cancer relative risks. In both populations (males and female population), there was no municipality with significant elevated colon cancer risk in the province of Limburg during the study period 1996 to 2005.

Meanwhile, for spatio-temporal models, our data suggested that colon cancer in Limburg can be modeled by assuming a linear time trend with additional space-time interaction (Bernardinelli et al. (1995) model). It was found that the mean time trend for colon cancer relative risk is about 0.999 in male's population and 0.998 in female population indicating a small decrease of 0.1% and 0.2% in relative risk per year in male and female population respectively. However, this decrease in mean time trend from both populations are not significant.

The two selected models were used for prediction of the true relative risk of colon cancer in each municipality. Both models showed that there are small variations between relative risks in Limburg municipalities.

In conclusion, our analysis showed that there are no municipalities in Limburg with elevated colon cancer relative risk. We also found out that there was no significant decrease in the risk of colon cancers in Limburg. Even if there is no municipality with an elevated colon cancer risk, people still needs to be encouraged to go for screening. According to (Flanderstoday.eu, 2017), In the year 2015, of the target population (Males and Females aged between 56 and 74 years) invited for a colon cancer screening, only 52% responded to the invitation for screening. This therefore implies alot of cases could have been missed hence posing questions on how our data approximates the real situation on ground. It was also noticed that there are no studies carried out on spatial temporal modeling of colon cancers which makes comparison of our results with other studies to become a challenge.

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6 Appendix

Table F1: Posterior Parameter Estimates for the CAR-Convolution Model

Gender	Parameter	Mean	Sd	MC error	2.50%	Median	97.50%
Male	alpha	-0.01313	0.03385	1.20E-04	-0.08235	-0.01236	0.05123
	mean	0.9875	0.03335	1.17E-04	0.9209	0.9877	1.053
	sigma.u	0.01147	0.02376	3.90E-04	2.01E-04	0.002228	0.08375
	sigma.v	0.0163	0.01309	1.57E-04	4.21E-04	0.01398	0.0479
	ratio	9.646	48.66	0.6	0.008603	0.1642	98.26
	tau.u	988.5	1401	18.69	11.94	448.9	4976
	tau.v	291.9	742.1	10.84	20.88	71.51	2373
Female	alpha	-0.01076	0.0338	1.21E-04	-0.07977	-0.00984	0.05305
	mean	0.9899	0.03337	1.18E-04	0.9233	0.9902	1.054
	sigma.u	0.01302	0.02254	3.36E-04	2.17E-04	0.003574	0.0785
	sigma.v	0.01027	0.01041	1.25E-04	2.86E-04	0.007118	0.03719
	ratio	11.98	46.1	0.5322	0.01289	0.5486	111.1
	tau.u	814.3	1306	18.48	12.74	279.8	4607
	tau.v	517.1	1004	13.21	26.89	140.5	3502

Table F2: Posterior Parameter Estimates for Spatio-temporal Model (Bernardinelli et al., 1995)

Gender	Parameter	Mean	Sd	MC error	2.50%	Median	97.50%
Males	α	-0.00775	0.05353	7.38E-04	-0.1135	-0.00764	0.09594
	β	-9.29E-04	0.009204	1.22E-04	-0.01902	-9.23E-04	0.01719
	mean	0.9937	0.05316	7.30E-04	0.8927	0.9924	1.101
	τ_δ	1028	1089	30.49	181.5	661	4186
	τ_u	1106	1475	49.3	19.98	550.8	5262
	τ_v	705.9	1132	40.86	28.64	234	4062
Females	α	-0.00279	0.05621	7.91E-04	-0.1148	-0.00229	0.1057
	β	-0.00202	0.01008	1.36E-04	-0.02184	-0.00207	0.01778
	mean	0.9988	0.05607	7.86E-04	0.8916	0.9977	1.111
	τ_δ	1621	1382	37.66	299.6	1193	5412
	τ_u	1164	1512	53.34	23.26	594.6	5418
	τ_v	851.1	1264	41.5	36.24	349.4	4464

Table F3: Relative Risk Estimates for Males in Limburg, 1996-2005: The CAR-Convolution Model

Municipality	mean	sd	MC_error	val2.5pc	median	val97.5pc
ALKEN	0.9665	0.1191	2.62E-04	0.7388	0.9642	1.214
AS	0.97	0.121	2.71E-04	0.7392	0.9677	1.226
BERINGEN	0.9932	0.08676	1.58E-04	0.8292	0.9905	1.173
BILZEN	0.9424	0.09084	2.46E-04	0.7649	0.9427	1.124
BOCHOLT	0.9934	0.1128	2.21E-04	0.7811	0.9893	1.234
BORGLOON	0.9024	0.1104	5.40E-04	0.6787	0.9067	1.111
BREE	1.094	0.127	4.24E-04	0.8797	1.08	1.38
DIEPENBEEK	1.012	0.1106	2.53E-04	0.8072	1.006	1.25
DILSEN-STOKKEM	0.9557	0.1012	2.85E-04	0.7563	0.9563	1.159
GENK	1.056	0.07934	1.96E-04	0.9103	1.051	1.222
GINGELOM	1.053	0.1253	3.03E-04	0.8352	1.041	1.336
HALEN	0.923	0.1166	4.44E-04	0.6917	0.9252	1.152
HAM	0.9364	0.1138	5.19E-04	0.7075	0.9392	1.16
HAMONT-ACHEL	0.9724	0.1033	2.85E-04	0.7718	0.9718	1.184
HASSELT	1.137	0.08096	4.46E-04	0.9912	1.133	1.305
HECHTEL-EKSEL	1.049	0.1292	2.87E-04	0.8219	1.038	1.337
HEERS	1.037	0.1291	2.64E-04	0.8089	1.025	1.326
HERK-DE-STAD	0.9917	0.111	2.33E-04	0.7814	0.9881	1.228
HERSTAPPE	0.9979	0.1423	3.34E-04	0.734	0.9911	1.311
HEUSDEN-ZOLDER	1.022	0.09579	2.73E-04	0.8476	1.016	1.228
HOESELT	0.924	0.1138	4.89E-04	0.6931	0.9278	1.144
HOUTHALEN-HELCHTEREN	1.016	0.09569	1.72E-04	0.8371	1.011	1.219
KINROOI	1.063	0.1255	4.05E-04	0.8495	1.049	1.348
KORTESSEM	1.037	0.1289	2.92E-04	0.808	1.025	1.326
LANAKEN	0.8273	0.102	5.89E-04	0.6281	0.8276	1.021
LEOPOLDSBURG	0.9123	0.103	5.04E-04	0.7019	0.9168	1.107
LOMMEL	0.9803	0.09013	1.52E-04	0.8085	0.9782	1.167
LUMMEN	1.051	0.1191	5.01E-04	0.8445	1.039	1.317
MAASEIK	1.062	0.1055	3.21E-04	0.8768	1.053	1.293
MAASMECHELEN	0.8934	0.08824	3.69E-04	0.7189	0.8947	1.062
MEEUWEN-GRUITRODE	1.079	0.13	5.92E-04	0.8662	1.063	1.38
NEERPELT	0.9335	0.1054	3.20E-04	0.7259	0.9346	1.143
NIEUWERKERKEN	1.071	0.1391	5.75E-04	0.8423	1.053	1.396
OPGLABBEEK	1.026	0.1266	3.05E-04	0.8018	1.014	1.31
OVERPELT	0.9653	0.1062	2.14E-04	0.7596	0.9643	1.185
PEER	1.017	0.1118	2.07E-04	0.8121	1.01	1.259
RIEMST	0.8869	0.1034	4.80E-04	0.6785	0.8899	1.081
SINT-TRUIDEN	0.9674	0.0805	1.70E-04	0.8123	0.9664	1.131
TESSENDERLO	0.8939	0.1044	4.25E-04	0.6845	0.8966	1.093
TONGEREN	0.922	0.08521	3.48E-04	0.7535	0.9232	1.087
VOEREN	0.872	0.1309	7.73E-04	0.6008	0.8795	1.111
WELLEN	1.032	0.1206	3.82E-04	0.8205	1.017	1.314
ZONHOVEN	1.26	0.1653	0.001031	0.9886	1.244	1.624
ZUTENDAAL	1.162	0.1887	0.001112	0.879	1.13	1.617

Table F4: Relative Risk Estimates for Females in Limburg, 1996-2005: The CAR-Convolution Model

Municipality	mean	sd	MC_error	val2.5pc	median	val97.5pc
ALKEN	1.026	0.1193	3.01E-04	0.8075	1.017	1.29
AS	1.001	0.1112	2.53E-04	0.7862	0.9979	1.239
BERINGEN	1.011	0.0871	1.64E-04	0.8463	1.008	1.195
BILZEN	0.9399	0.09072	4.29E-04	0.7546	0.9439	1.111
BOCHOLT	1.033	0.1085	2.65E-04	0.838	1.024	1.277
BORGLOON	0.9846	0.0997	3.37E-04	0.7837	0.9861	1.187
BREE	0.9604	0.1041	3.46E-04	0.7495	0.9633	1.166
DIEPENBEEK	0.9989	0.1019	1.97E-04	0.8023	0.9967	1.214
DILSEN-STOKKEM	1.044	0.1011	2.88E-04	0.861	1.035	1.269
GENK	1.031	0.07642	2.40E-04	0.8879	1.028	1.191
GINGELOM	0.9688	0.1038	4.34E-04	0.7533	0.9732	1.172
HALEN	1.005	0.1132	4.63E-04	0.7875	1.002	1.247
HAM	0.9753	0.1045	3.15E-04	0.762	0.9779	1.185
HAMONT-ACHEL	1.076	0.111	4.44E-04	0.8906	1.062	1.334
HASSELT	1.132	0.08191	5.25E-04	0.9904	1.127	1.306
HECHTEL-EKSEL	1.037	0.1241	4.93E-04	0.8148	1.027	1.317
HEERS	1.021	0.1161	2.59E-04	0.8074	1.014	1.279
HERK-DE-STAD	1.004	0.103	3.45E-04	0.8037	1.002	1.223
HERSTAPPE	1.006	0.1222	3.40E-04	0.7703	1.002	1.271
HEUSDEN-ZOLDER	0.9642	0.08812	2.70E-04	0.7865	0.966	1.138
HOESELT	0.955	0.107	5.85E-04	0.729	0.9616	1.158
HOUTHALEN-HELCHTEREN	1.034	0.09246	3.09E-04	0.8627	1.028	1.236
KINROOI	1.02	0.1083	3.69E-04	0.817	1.014	1.256
KORTESSEM	1.08	0.1276	5.46E-04	0.8738	1.061	1.383
LANAKEN	0.9515	0.09627	3.22E-04	0.7592	0.9534	1.142
LEOPOLDSBURG	0.979	0.09262	2.17E-04	0.7958	0.9788	1.172
LOMMEL	1.076	0.09957	4.28E-04	0.9073	1.065	1.301
LUMMEN	0.9865	0.1016	2.76E-04	0.7923	0.984	1.203
MAASEIK	1.051	0.09961	3.19E-04	0.8791	1.041	1.276
MAASMECHELEN	1.053	0.09272	3.08E-04	0.8892	1.045	1.258
MEEUWEN-GRUITRODE	1.132	0.1471	9.46E-04	0.9247	1.103	1.495
NEERPELT	0.9648	0.09994	4.11E-04	0.7683	0.9651	1.17
NIEUWERKERKEN	0.9207	0.1082	5.94E-04	0.6953	0.9268	1.124
OPGLABBEEK	1.013	0.1126	2.87E-04	0.8105	1.005	1.267
OVERPELT	0.9363	0.09777	4.21E-04	0.7339	0.9408	1.124
PEER	0.9278	0.1016	6.51E-04	0.7221	0.9312	1.125
RIEMST	0.892	0.1006	6.28E-04	0.6817	0.8984	1.072
SINT-TRUIDEN	1.018	0.08533	5.51E-04	0.8635	1.013	1.203
TESSENDERLO	0.9189	0.1026	5.32E-04	0.7034	0.9257	1.107
TONGEREN	0.8598	0.09433	7.43E-04	0.6677	0.8638	1.027
VOEREN	0.8867	0.1183	8.39E-04	0.6352	0.8957	1.098
WELLEN	1.019	0.1014	3.18E-04	0.8386	1.008	1.26
ZONHOVEN	0.8984	0.1085	8.47E-04	0.6734	0.9045	1.098
ZUTENDAAL	1.068	0.1569	5.62E-04	0.815	1.046	1.445

Table F'5: Relative Risk Estimates for Males in Limburg, 1996-2005: Spatio-temporal Model 3 (Bernardinelli et al., 1995)

Municipality	mean	sd	MC_error	val2.5pc	median	val97.5pc
ALKEN	0.9969	0.09859	7.65E-04	0.7993	0.995	1.215
AS	0.9971	0.09277	6.95E-04	0.8103	0.9959	1.199
BERINGEN	1.014	0.08404	8.07E-04	0.8573	1.008	1.201
BILZEN	0.9954	0.08277	7.91E-04	0.8304	0.9943	1.173
BOCHOLT	1.002	0.08851	6.62E-04	0.8288	0.9991	1.197
BORGLOON	0.9615	0.08899	0.001408	0.7594	0.9724	1.121
BREE	1.051	0.1045	0.001764	0.8841	1.032	1.307
DIEPENBEEK	1.005	0.08836	7.11E-04	0.8351	1	1.207
DILSEN-STOKKEM	0.9905	0.08256	7.00E-04	0.8185	0.9916	1.164
GENK	1.056	0.09009	0.001565	0.9107	1.04	1.272
GINGELOM	1.039	0.09778	0.001362	0.8796	1.023	1.282
HALEN	0.9719	0.09569	0.001187	0.7648	0.9779	1.161
HAM	0.9694	0.08775	0.001133	0.7723	0.9772	1.137
HAMONT-ACHEL	0.9946	0.08259	6.47E-04	0.825	0.9948	1.172
HASSELT	1.079	0.08842	0.002209	0.95	1.061	1.29
HECHTEL-EKSEL	1.023	0.1046	0.001123	0.8358	1.011	1.269
HEERS	1.022	0.09979	0.001013	0.8454	1.011	1.26
HERK-DE-STAD	0.9998	0.08578	5.15E-04	0.8286	0.9979	1.188
HERSTAPPE	1.004	0.1009	6.33E-04	0.8067	0.9993	1.234
HEUSDEN-ZOLDER	1.02	0.08307	9.24E-04	0.87	1.011	1.213
HOESELT	0.9613	0.08781	0.001254	0.7597	0.9719	1.123
HOUTHALEN-HELCHTEREN	1.012	0.07646	5.96E-04	0.8674	1.006	1.188
KINROOI	1.027	0.09524	0.001255	0.8636	1.014	1.262
KORTESSEM	1.025	0.09654	9.26E-04	0.8565	1.013	1.256
LANAKEN	0.9136	0.101	0.002409	0.6865	0.9292	1.079
LEOPOLDSBURG	0.9592	0.08224	0.001411	0.77	0.9709	1.104
LOMMEL	0.9834	0.07695	6.64E-04	0.8247	0.9851	1.144
LUMMEN	1.032	0.09668	0.001384	0.8668	1.018	1.264
MAASEIK	1.035	0.08773	0.001231	0.8896	1.022	1.249
MAASMECHELEN	0.9349	0.08367	0.001741	0.748	0.9462	1.076
MEEUWEN-GRUITRODE	1.047	0.102	0.001753	0.8925	1.027	1.305
NEERPELT	0.9696	0.08542	0.001061	0.7838	0.9769	1.135
NIEUWERKERKEN	1.049	0.1087	0.001767	0.8836	1.028	1.324
OPGLABBEEK	1.02	0.09658	9.18E-04	0.8456	1.009	1.249
OVERPELT	0.9966	0.0836	6.44E-04	0.8263	0.9963	1.175
PEER	1.021	0.09015	8.66E-04	0.8575	1.012	1.232
RIEMST	0.9577	0.08671	0.001508	0.7612	0.9685	1.113
SINT-TRUIDEN	1.012	0.07841	8.01E-04	0.8628	1.007	1.189
TESSENDERLO	0.9452	0.08953	0.001665	0.7403	0.9577	1.1
TONGEREN	0.9719	0.07713	0.001095	0.803	0.978	1.121
VOEREN	0.9409	0.1044	0.002236	0.6928	0.9583	1.117
WELLEN	1.024	0.08865	0.001011	0.8713	1.01	1.245
ZONHOVEN	1.121	0.1452	0.00378	0.9323	1.084	1.49
ZUTENDAAL	1.07	0.1425	0.002569	0.8633	1.04	1.436

Table F6: Relative Risk Estimates for Females in Limburg, 1996-2005: Spatio-temporal Model 3 (Bernardinelli et al., 1995)

Municipality	mean	sd	MC_error	val2.5pc	median	val97.5pc
ALKEN	1.008	0.09141	7.35E-04	0.8343	1.003	1.214
AS	0.9995	0.08323	6.57E-04	0.8341	0.9974	1.184
BERINGEN	1.011	0.07571	6.63E-04	0.8677	1.006	1.183
BILZEN	0.9644	0.07632	0.00117	0.792	0.9723	1.105
BOCHOLT	1.015	0.08267	8.89E-04	0.8647	1.008	1.21
BORGLOON	0.9896	0.07562	6.59E-04	0.8293	0.9919	1.146
BREE	0.9733	0.08149	9.15E-04	0.7949	0.9795	1.131
DIEPENBEEK	0.9968	0.07901	5.85E-04	0.8368	0.9958	1.168
DILSEN-STOKKEM	1.026	0.07992	9.75E-04	0.8864	1.016	1.216
GENK	1.016	0.07187	7.94E-04	0.8846	1.01	1.18
GINGELOM	0.9812	0.07791	7.66E-04	0.8089	0.9864	1.134
HALEN	0.9983	0.08714	8.05E-04	0.8223	0.9969	1.189
HAM	0.9851	0.07869	6.56E-04	0.8135	0.9885	1.145
HAMONT-ACHEL	1.044	0.08766	0.001399	0.9094	1.028	1.265
HASSELT	1.072	0.08031	0.002026	0.9575	1.055	1.269
HECHTEL-EKSEL	1.018	0.09436	9.59E-04	0.8464	1.01	1.238
HEERS	1.014	0.08686	6.76E-04	0.8551	1.007	1.218
HERK-DE-STAD	1.007	0.07848	6.22E-04	0.8542	1.003	1.183
HERSTAPPE	1.005	0.08832	6.04E-04	0.8338	1.002	1.202
HEUSDEN-ZOLDER	0.9901	0.07217	5.54E-04	0.8393	0.9917	1.14
HOESELT	0.9751	0.0804	0.001033	0.788	0.9833	1.125
HOUTHALEN-HELCHTEREN	1.02	0.07279	7.88E-04	0.8882	1.012	1.19
KINROOI	1.014	0.08213	7.24E-04	0.8609	1.007	1.204
KORTESSEM	1.05	0.09964	0.001743	0.9026	1.029	1.305
LANAKEN	0.9858	0.08179	7.46E-04	0.8143	0.9878	1.154
LEOPOLDSBURG	0.9994	0.07262	4.73E-04	0.8535	0.9978	1.16
LOMMEL	1.045	0.08355	0.001457	0.9148	1.029	1.251
LUMMEN	1.007	0.08048	6.21E-04	0.8537	1.002	1.191
MAASEIK	1.038	0.08249	0.001274	0.9067	1.024	1.243
MAASMECHELEN	1.031	0.07833	0.001113	0.898	1.02	1.22
MEEUWEN-GRUITRODE	1.081	0.117	0.00282	0.9379	1.048	1.393
NEERPELT	0.9978	0.07929	6.93E-04	0.8385	0.9959	1.173
NIEUWERKERKEN	0.969	0.08218	0.001162	0.7819	0.9778	1.123
OPGLABBEEK	1.018	0.0857	8.14E-04	0.8664	1.009	1.223
OVERPELT	0.9775	0.07598	8.80E-04	0.8059	0.9833	1.126
PEER	0.9799	0.07922	0.001064	0.8093	0.9836	1.139
RIEMST	0.9535	0.08061	0.001541	0.7653	0.9656	1.09
SINT-TRUIDEN	1.043	0.08178	0.001474	0.9127	1.029	1.241
TESSENDERLO	0.9617	0.08143	0.001323	0.771	0.9721	1.108
TONGEREN	0.9311	0.08117	0.002019	0.7408	0.9461	1.056
VOEREN	0.9521	0.09069	0.001724	0.7357	0.9659	1.107
WELLEN	1.018	0.07766	8.02E-04	0.8827	1.007	1.211
ZONHOVEN	0.9683	0.08848	0.001473	0.7701	0.9757	1.137
ZUTENDAAL	1.047	0.1226	0.001801	0.8589	1.026	1.355

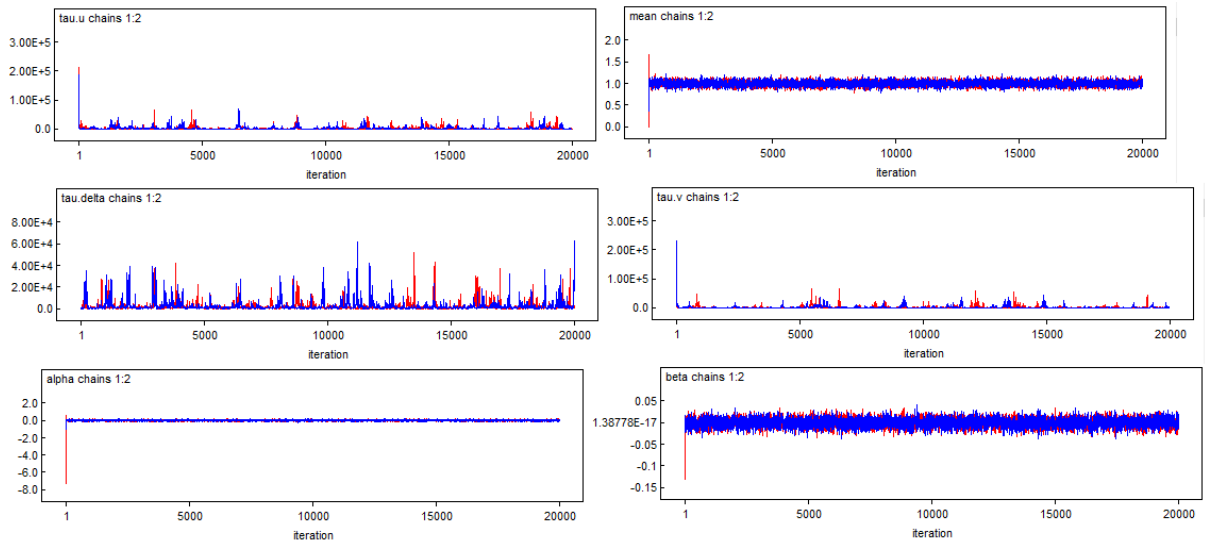

Figure F1: History plots for parameters in the Spatio-temporal Model 3 after 20,000 iterations.

6.1 WinBUGS codes

```
    #Poisson-Gamma Model
model
{
for (i in 1 : N)
{ # Poisson likelihood for observed counts
O[i] ~ dpois(mu[i])
mu[i] <- E[i]*theta[i]
# Relative Risks
theta[i] ~ dgamma(a, b)
}
# Vague prior distributions
a ~ dexp(0.01)
b ~ dexp(0.01)
# Additional estimates
m <- a/b
var <- a/pow(b,2)
}
# Initial values for Poisson Gamma Model
```

```
list(theta=c(
1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1,
1,1,1,1),a=1,b=1)

list(theta=c(
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8),a=1,b=1)

# Poisson-Lognormal Model
model {
for (i in 1 : N) {
# Poisson likelihood for observed counts
O[i] ~ dpois(mu[i])
log(mu[i]) <- log(E[i]) + alpha + v[i]
# Heterogeneity random effects
v[i] ~ dnorm(0, tau.v)
# relative risks
theta[i] <- exp(alpha + v[i])
}
# Vague prior distribution for intercept
alpha ~ dnorm(0.0, 1.0E-5)
# Hyperprior distibutions on inverse variance parameter
tau.v ~ dgamma(0.01, 0.01)
var.v <- 1 / tau.v
}
```

```
# Initial value for Poisson-Lognormal model
list(v=c(
1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1,
1,1,1,1),alpha=1,tau.v=1)

list(v=c(
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,0.8,
0.8,0.8,0.8,0.8),alpha=1,tau.v=1)

# Conditional-Autoregressive Model
model {
for (i in 1 :N) {
O[i] ~ dpois(mu[i])
log(mu[i]) <- log(E[i]) + alpha + u[i]
RR[i] <- exp(alpha + u[i])
}
# CAR prior distribution for random effects:
u[1:N] ~ car.normal(adj[], weights[], num[], tau.u)
for(k in 1:sumNumNeigh) {
weights[k] <- 1
}
# Other priors:
alpha ~dflat()
mean <- exp(alpha)
tau.u ~dgamma(0.5, 0.0005)
```

```
sigma.u<-1/tau.u
}

# Initial values for Improper CAR Models
list(alpha=0,  tau.u=0.5,
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)

list(alpha=0.01, tau.u=1,
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)

#Convolution model
model {
for (i in 1 :N) {
O[i] ~ dpois(mu[i])
log(mu[i]) <- log(E[i]) + alpha + u[i] + v[i]
RR[i] <- exp(alpha + u[i] + v[i])
v[i] ~ dnorm(0,tau.v)
}
# CAR prior distribution for random effects:
u[1:N] ~ car.normal(adj[], weights[], num[], tau.u)
for(k in 1:sumNumNeigh) {
weights[k] <- 1
}
# Other priors:
alpha ~dflat()
mean <- exp(alpha)
tau.u ~dgamma(0.5, 0.0005)
```

```
tau.v ~dgamma(0.5, 0.0005)
sigma.u<-1/tau.u
sigma.v<-1/tau.v
ratio<-sigma.u/sigma.v
}

# Initial values for Convolution model
list(alpha=0, tau.v=0.5, tau.u=0.5,
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)

list(alpha=0.01, tau.v=1, tau.u=1,
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)

# Spatio-temporal models
# Model1
model
  {
  for(i in 1:m)
  {
  for(k in 1:T)
 {
#Poisson likelihood for observed counts
 O[i,k]~dpois(mu[i,k])
```

```
 log(mu[i,k])<-log(E[i,k])+alpha+u[i]+v[i]+beta*t[k]
#Relative risk in each area and period of time
 theta[i,k]<-exp(alpha+u[i]+v[i]+beta*t[k])
 }
 theta_area[i]<-exp(u[i]+v[i])
 TT[i]<-exp(beta)
 }
 # CAR prior distribution for spatial structured heterogeneity
 u[1:m]~car.normal(adj[],weights[],num[],tau.u)
 #prior distribution for the uncorrelated heterogeneity
 for(i in 1:m)
 {
 v[i]~dnorm(0,tau.v)
 }
# weights
for(k in 1:sumNumNeigh)
{
 weights[k]<-1
}
#Improper distribution for the mean relative risk
alpha~dflat()
mean<-exp(alpha)
#Hyperprior distributions on inverse variance parameter of random effects
beta~dnorm(0,1.0E-5)
tau.u~dgamma(0.5,0.0005)
tau.v~dgamma(0.5,0.0005)
}
#Initial values for mdel1
list(alpha=0,beta=0,
tau.v=1,
tau.u=1,
```

```
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)
list(tau.u = 1.2, tau.v=1.2,  beta=0.01, alpha = 0.01,
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)

# Model2
model
  {
  for(i in 1:m)
  {
  for(k in 1:T)
 {
#Poisson likelihood for observed counts
 O[i,k]~dpois(mu[i,k])
 log(mu[i,k])<-log(E[i,k])+alpha[k]+u[i]+v[i]

#Relative risk in each area and period of time
 theta[i,k]<-exp(alpha[k]+u[i]+v[i])
 }
 theta_area[i]<-exp(u[i]+v[i])
 }

 # CAR prior distribution for spatial structured heterogeneity
 u[1:m]~car.normal(adj[],weights[],num[],tau.u)
```

```
  #prior distribution for the uncorrelated heterogeneity
 for(i in 1:m)
 {
 v[i]~dnorm(0,tau.v)
 }
# weights
for(k in 1:sumNumNeigh)
{
 weights[k]<-1
}

#Improper distribution for the mean relative risk in the study region
for(k in 1:T)
{
alpha[k]~dflat()
mean[k]<-exp(alpha[k])
}
#Hyperprior distributions on inverse variance parameter of random effects
tau.u~dgamma(0.5,0.0005)
tau.v~dgamma(0.5,0.0005)
}
# Initial values for Model1
list(tau.u =1 tau.v=1 , alpha = c(0, 0,0,0,0,0,0,0,0,0),
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0),v=c(0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)
list(tau.u = 1.2, tau.v=1.2, alpha = c(0.02, 0.02
, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02),
```

```
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)

# Mode3 (Bernardinelli  et al. 1995)
model
  {
  for(i in 1:m)
  {
  for(k in 1:T)
 {
#Poisson likelihood for observed counts
 O[i,k]~dpois(mu[i,k])
 log(mu[i,k])<-log(E[i,k])+alpha+u[i]+v[i]+beta*t[k]+delta[i]*t[k]
#Relative risk in each area and period of time
 theta[i,k]<-exp(alpha+u[i]+v[i]+beta*t[k]+delta[i]*t[k])
 }
 theta_area[i]<-exp(u[i]+v[i])
 TT[i]<-exp(beta+delta[i])
 }
 # CAR prior distribution for spatial structured heterogeneity
 u[1:m]~car.normal(adj[],weights[],num[],tau.u)
 delta[1:m]~car.normal(adj[],weights[],num[],tau.delta)
 #prior distribution for the uncorrelated heterogeneity
 for(i in 1:m)
 {
 v[i]~dnorm(0,tau.v)
 }
# weights
```

```
for(k in 1:sumNumNeigh)
{
 weights[k]<-1
}
#Improper distribution for the mean relative risk
alpha~dflat()
mean<-exp(alpha)
#Hyperprior distributions on inverse variance parameter of random effects
beta~dnorm(0,1.0E-5)
tau.u~dgamma(0.5,0.0005)
tau.v~dgamma(0.5,0.0005)
tau.delta~dgamma(0.5,0.0005)
}
#Initial values for # Mode3
list(alpha=0,beta=0, tau.v=1, tau.u=1, tau.delta=1,
delta=c(1, 1, 1, 1, 1, 1, 1, 1 ,1 , 1, 1,1, 1, 1, 1,
1, 1, 1 ,1 , 1, 1,1, 1, 1, 1, 1, 1, 1 ,1 , 1, 1, 1, 1, 1, 1,
1, 1, 1 ,1 , 1, 1, 1, 1, 1),
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0))
list(tau.u = 1.2, tau.v=1.2,  beta=0.01, alpha = 0.01,
tau.delta=0.01,delta=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)
```

```
# Mode4
model
  {
  for(i in 1:m)
  {
  for(k in 1:T)
 {
#Poisson likelihood for observed counts
 O[i,k]~dpois(mu[i,k])
 log(mu[i,k])<-log(E[i,k])+alpha[k]+u[i]+v[i] +delta[i]*t[k]

#Relative risk in each area and period of time
# theta[i,k]<-exp(alpha[k]+u[i]+v[i] +delta[i]*t[k])
 }
 theta_area[i]<-exp(u[i]+v[i])
# TT[i]<-exp(beta+delta[i])
 }

 # CAR prior distribution for spatial structured heterogeneity
 u[1:m]~car.normal(adj[],weights[],num[],tau.u)
 delta[1:m]~car.normal(adj[],weights[],num[],tau.delta)
 #prior distribution for the uncorrelated heterogeneity
 for(i in 1:m)
 {
 v[i]~dnorm(0,tau.v)
 }
# weights
for(k in 1:sumNumNeigh)
{
 weights[k]<-1
}
```

```
#Improper distribution for the mean relative risk
for(k in 1:T)
{
alpha[k]~dflat()
mean[k]<-exp(alpha[k])
}
#Hyperprior distributions on inverse variance parameter of random effects

tau.u~dgamma(0.5,0.0005)
tau.v~dgamma(0.5,0.0005)
tau.delta~dgamma(0.5,0.0005)
}
#Initial values for # Mode4
list( alpha = c(0, 0,0,0,0,0,0,0,0,0), tau.v=1, tau.u=1, tau.delta=1,
delta=c(1, 1, 1, 1, 1, 1, 1, 1 ,1 , 1, 1, 1, 1, 1, 1, 1,
1, 1 ,1 , 1, 1,1, 1, 1, 1, 1, 1, 1 ,1 , 1, 1, 1, 1, 1, 1, 1,
1, 1 ,1 , 1, 1, 1, 1, 1),u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0))
list(tau.u = 1.2, tau.v=1.2, alpha = c(0.02, 0.02, 0.02
, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02, 0.02), tau.delta=0.01,
delta=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0),
v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0
,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)
)
```