Final Exam

This analysis is concerned with assessing the risk of male lip cancer in Scotland from 1975 to 1980. Data were collected for each of the 56 counties in Scotland detailing the observed number of male lip cancer cases from 1975 to 1980, the expected number of cases, and the percentage of the population employed in agriculture, fishing, or forestry (referred to moving forward as "pcaff") during the same period. This analysis aims to determine whether male lip cancer incidence in Scotland demonstrates spatial dependence, and whether pcaff has any effect on male lip cancer incidence.

The data were originally published in the Atlas of Cancer in Scotland, 1975-1980: Incidence and Epidemiological Perspective¹, published by the International Agency for Research on Cancer. The expected counts were calculated using the method of Mantel and Stark², which assumes that different age groups experience different risks of lip cancer. This method involves splitting the population of each county into age brackets, and using an iterative approach to find the maximum likelihood estimate of the expected number of cases in each county from $E_i = \sum_j Y_{ij} \xi_j$, where E_i is the expected number of cases in each county i to be estimated, ξ_j is a rate parameter for each age bracket j to be estimated, and Y_{ij} is the total number of person-years in county i from age bracket j. It is not a great leap of faith to assume that data from The International Agency for Research on Cancer is accurate and of high quality. On the other hand, the greatest assumption made in this analysis is putting faith in the expected lip cancer counts, which will be treated as known constants for the purpose of analysis; this assumption will be discussed later.

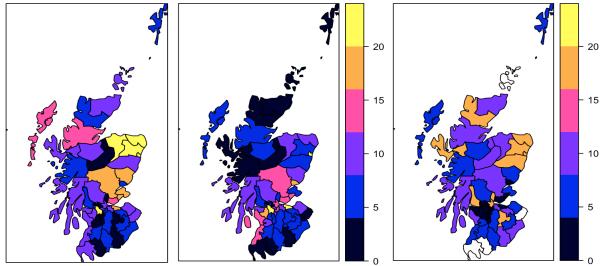


Figure 1: Spatial plots of observed male lip cancer counts (left), expected male lip cancer counts (center), and percentage employed in agriculture, fishing, or forestry (pcaff, right). Observed and expected counts are on the same scale, shown beside the center panel, with units of number of cases. For both plots of counts, values are capped at 20 for clarity of visualization, and all values greater than 20 are set to 21. The scale for pcaff is shown beside its plot with units of percent.

The data are visualized with spatial plots in Figure 1. From a simple visual examination, there does appear to be some spatial dependence in all three datasets. Observed lip cancer counts appear to be highest in several counties in the east, to also be high in several counties in central Scotland north of Edinburgh, and to decrease moving away from those areas to the north and south. Expected lip cancer counts tend to be highest in central Scotland near the cities of Edinburgh and Glasgow, and to decrease moving away from

those areas. It should be noted that count values are capped at 20 for the purpose of plotting, so some information is lost, especially in the plot of expected counts, where there are two counties with values of 50.7 and 88.7. Pcaff is high in a few coastal areas in northern Scotland, and is generally low in central Scotland near the larger cities.

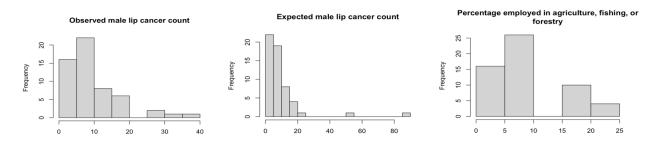


Figure 2: Histograms of the distribution of observed male lip cancer count (left), expected count (center), and pcaff (right) for the 56 counties in Scotland from 1975-1980. Variable units (counts or percentage) are on the x-axis, with frequency on the y-axis.

Histograms of the distribution of the same three variables are shown in Figure 2. Observed and expected lip cancer counts are extremely right-skewed. For the purpose of modeling the data, a normality assumption is not reasonable for these variables. A log transformation could be applied to make these distributions more nearly normal; however, analyzing observed lip cancer counts on their own is not particularly informative. The number of lip cancer cases in each county is only informative when analyzed in the context of the total population of the county. A more informative analysis therefore is based on the "region risk" of each county, the number of observed cases divided by the number of cases that would be expected given the size and age distribution of that county as discussed above. Modeling the number of observed cases in each county as Poisson distributed is more appropriate than as normally distributed because the Poisson distribution is designed to accommodate count data; it is a discrete distribution of nonnegative integers. Additionally, peaff is approximately normal enough to be used as an additional covariate in this model.

We assume that the number of observed lip cancer cases in each county follows a Poisson distribution with parameter $E_i\mu_i$, where E_i is the expected count of cases in county i and μ_i is the region risk for county i: $O_i \stackrel{ind}{\sim} P(E_i\mu_i)$. This assumes that each observation is independent; however, it has been shown that the data visually appear to exhibit some spatial dependence. Therefore, this is a good model with which to detrend the data before fitting an areal model, but is a poor choice for a final model. Additionally, assuming the observed case counts to follow a Poisson distribution assumes that they can be described with a single parameter equal to both the mean and variance of the observations. In fact, the observed counts have a mean of 9.57 and a variance of 62.54, so this model might tend to underestimate the variance in any predictions. However, in the absence of any simple more suitable model and since the goal of this areal analysis is more explanatory and less focused on prediction or forecasting, a Poisson distribution is assumed.

We further assume that each $\log(\mu_i) = \beta_0 + X_i\beta_1$, where β_0 and β_1 are country-wide parameters and X_i is peaff for county i. In other words, we assume that peaff is a covariate that linearly affects log region risk. Higher-order terms for peaff are not included as the effect of peaff on region risk is not noticeably nonlinear (see appendix) and adding higher-order terms does not significantly improve the fit. Fitting this model (see appendix for model summary), the effect of peaff is significant; each 1% increase in peaff is expected to increase the region risk by a factor of $e^{0.074} = 1.077$. From the residuals of the model, the value of Moran's I is 0.366, which is not especially large, but with a p-value of 0.001 is evidence of spatial dependence in the residuals. The value of Geary's C is 0.512, with a p-value of 0.001, which is

further evidence of spatial dependence in the residuals and evidence that this dependence is positive, as would be expected. Therefore, an areal model should be fit to capture the remaining spatial dependence.

$$\begin{aligned} & \text{O}_{\text{i}} \overset{ind}{\sim} \text{P}(E_{i}\mu_{i}) \\ & \log(\mu_{i}) = \beta_{0} + X_{i}\beta_{1} + \phi_{\text{i}} \\ & \phi_{\text{i}}|\phi_{\text{j}}, \text{j} \in \delta_{\text{i}} \sim \text{N}\left(\rho \frac{\sum_{\text{j} \in \delta_{\text{i}}} w_{\text{ij}}y_{\text{j}}}{w_{\text{i+}}}, \frac{\tau^{2}}{w_{\text{i+}}}\right) \end{aligned}$$

Equation 1: Description of the final model fit to the data. The observed counts are assumed to be Poisson distributed with parameter equal to the expected count times a region risk. Region risk follows a generalized linear model with log link and an intercept term, a linear term for pcaff (X_i) , and a CAR term. In the CAR model definition, δ_i refers to the set of counties neighboring county i, and W is the proximity matrix with entries w_{ij} .

	Prior	Posterior Mean	Posterior 95% Credibility Interval	
$oldsymbol{eta}_0$	$N(0, 10^6)$	-0.216	-0.459	0.035
β_1	$N(0, 10^6)$	0.037	0.009	0.062
ρ	U(0, 1)	0.862	0.514	0.987
$ au^2$	IG(1, 0.01)	0.510	0.273	0.930

Table 1: The prior distribution used for Bayesian areal modeling, the point estimate, and 95% credibility intervals for each of the four parameters associated with the final model as described in Equation 1. $N(\mu, \sigma^2)$ is a normal distribution with mean μ and variance σ^2 , U(a, b) is a continuous uniform distribution on the interval [a, b], and IG(a, b) is an inverse gamma distribution with shape parameter a and scale parameter b.

The final model is described in Equation 1. This model assumes that the log relative risk depends on an intercept, a term linear in peaff, and a spatial CAR term. This model assumes that the observed counts are Poisson distributed which, as discussed previously, is reasonable as long as the concern of the model is more with interpretation than forecasting and quantifying uncertainty. It assumes that the residuals of the nonspatial analysis ϕ_i follow a CAR structure, that each region risk follows a distribution whose mean is a proportion of a weighted average of region risk of neighboring counties. Finally, it assumes that there is no random error term ε_i as there is in a Gaussian model, which makes it impossible to assess the sub-area variability, which is useful for determining the relative magnitude of the variance of spatial dependence. In all, there are four parameters to estimate: β_0 , β_1 , ρ , and τ^2 . Parameters are estimated using Bayesian modeling for practicality due to the relative development of software for Bayesian methods and ease of use. The priors used for estimation are defined in Table 1 (they are specified as random distributions rather than fixed estimates for the purpose of Bayesian estimation), and parameters are estimated using the S.CARleroux function in R. Parameter estimates and 95% credibility intervals are shown in Table 1; full output from fitting the model is included in the appendix.

The estimate for β_1 of 0.037 supports the use of a spatial model, since the effect of pcaff is dampened when accounting for spatial dependence. With this model, each 1% increase in pcaff is expected to increase the region risk by a factor of $e^{0.037} = 1.037$. However, the 95% credibility interval does not include 0, so this effect is still significant. The estimate for ρ of 0.862 indicates some spatial dependence in the residuals, and the 95% credibility interval of [0.514, 0.987] suggests that this dependence is not especially strong, but is present. The estimate for the variance of the CAR spatial component τ^2 of 0.510 is difficult to put into context without having sub-area variability for comparison.

Trace plots and histograms for each of the four parameters for Bayesian Markov chain Monte Carlo simulation can be found in Figures S1-S4 (supplemental figures). The trace plots for β_0 and β_1 show good mixing, which is evidence that the algorithm converges to a stable solution. Further, in the density plot of β_1 , the value of 0 is quite far out in the tail, which is further evidence that β_1 is significantly greater than 0. The density plot of τ^2 is slightly right skewed (because the value of τ^2 cannot be less than 0) but is also

evidence of good mixing. Finally, the density plot of ρ peaks close to 1, which is further evidence of spatial dependence. However, there is some density in the tail extending all the way left to about 0.4 (the lower 95% credibility interval is 0.514), corroborating that the spatial dependence is not especially strong.

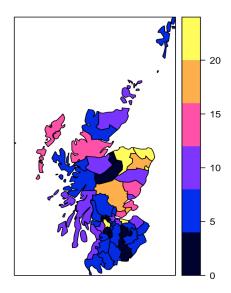


Figure 3: Fitted values for male lip cancer cases in Scotland from 1975-1980. Similar to before, any values greater than 20 are reset to 21 for clarity of visualization. Fitted values are calculated using the model described in Equation 1.

The fitted values for observed male lip cancer count using the Bayesian areal model described in Equation 1 and the parameter estimates in Table 1 are plotted in Figure 3. Visually, comparing the fit to the true observed lip cancer counts plotted in Figure 1, the fit appears to be very good; there are no counties in which the fitted value is more than one bin away from the true value. The full list of actual and fitted values for all 56 counties is included in the appendix and confirms that the fit is, overall, quite good. Because the fit is good, confidence in the reliability of the parameter estimates is increased: this is further evidence that there is spatial dependence in the data, and that peaff has a positive effect on male lip cancer incidence. This trend is seen in the data, as peaff is high in several coastal counties in northern Scotland (Figure 1, right), and the observed lip cancer count in those counties are higher than the expected count (Figure 1, left and center).

Although a trend is identified, this analysis does not investigate any potential reasons for the association between pcaff and male lip cancer incidence. It is possible that some aspect of occupation in agriculture, fishing, or forestry increases the incidence of cancer (such as by exposure to a particular carcinogen), but it is also possible that this association captures a relationship caused by other factors such as age or lifestyle habits of those employed in these industries. More analysis would be required to determine a reason for the existence of this association.

As mentioned previously, the accuracy of this analysis is very much dependent on the reliability of the expected lip cancer count in each county. The entire analysis is performed on the region risk, the ratio of observed counts to expected counts in each county, so even small changes in expected counts could have large effects on this ratio. The calculation of the expected counts assumes that different age brackets of men have different propensities for developing lip cancer, and that no other factors impact the chance of developing lip cancer. Factors that could impact this chance might include the socioeconomic status of each county, or the percentage of people employed in factories or other jobs that might expose workers to carcinogens. Accounting for the impact of variables such as these might give more accurate expected counts

of lip cancer, which would allow for a more accurate analysis of the effect of pcaff and spatial dependence in the data.

Further, this model assumes a static distribution of cancer cases; it has no time component, and no way of accounting for how cases might develop over time, only for the number of cases observed in Scottish counties during this 6-year time period. Because lip cancer is rare and non-communicable, the lack of a time component is likely a reasonable assumption. However, Scotland is a relatively small country with accessible internal movement. During the 1970's, the two largest cities of Edinburgh and Glasgow both experienced population declines^{3,4}, which is evidence of a relatively high level of migration during this time. This may introduce some uncertainty as to the appropriateness of a static model. For example, a patient might live much of their life in one county, and move to a different county or even a different country later in life, after which lip cancer develops; or a patient who lives in one county and develops lip cancer might choose to receive medical care in a different country.

This analysis was only done on data from the country of Scotland, so the conclusions might not necessarily be generalizable to other countries. For example, the only covariate under consideration was peaff, the percentage of the population employed in agriculture, fishing, or forestry during this time period. Agriculture is not an especially large industry in Scotland, which has relatively little arable land⁵; however, Scotland has extremely rich fishing waters, and fishing is a major industry in regions of northeastern and western Scotland⁶ (as reflected in the higher peaff values in these regions, Figure 1 right). This analysis might not be valid for a country with similar peaff values among its counties but with a different distribution of employment in those industries (for example, a landlocked country with little fishing but prosperous agriculture). Similarly, peaff values in Scottish counties range from 0% to 24%; the effect of peaff might be diminished or disappear at higher peaff values, so this analysis might not be valid for a country with overall higher peaff values (for example, one with counties whose peaff values range from 25% to 50%).

Perhaps most importantly, Scotland is an industrialized, developed, western nation, with an overall healthy population, so this analysis is likely only valid for countries with similar economies, healthcare systems, and standards of living. In Scotland, healthcare is provided by the public health service NHS Scotland, so one should be careful applying this analysis to countries without similarly accessible healthcare systems such that all lip cancer cases are able to be reported and treated. Finally, Scotland has large rural areas mostly inhabited by elderly people in which access to healthcare is more limited than in urban areas, compounding their already greater risk of developing health conditions⁷. Age distribution is accounted for in the analysis in the form of expected lip cancer counts, but one should be careful extending this analysis to countries with very dissimilar geographic population distributions.

Conclusion

Data were collected from 1975 to 1980 for each of the 56 counties in Scotland on the number of observed cases of male lip cancer, the number of cases that would be expected given the population age distribution, and the percentage of the population employed in agriculture, fishing, or forestry. The percentage of the population employed in agriculture, fishing, or forestry was found to have a positive effect on the risk of male lip cancer. Male lip cancer risk also exhibits positive spatial dependence: counties with high male lip cancer risk tend to be near other counties with high risk, and vice versa. The "risk" of male lip cancer is a proportion of the number of observed cases to the number of expected cases, and so depends on the number of expected cases, which is estimated, but is believed to be accurate enough that these conclusions are valid. However, one should be cautious in extending these conclusions to other countries. Fishing is prominent in Scotland, agriculture is of relatively little importance, and Scotland is an industrialized nation with a highly developed healthcare systems, so these conclusions might not extend to countries that differ greatly from these characteristics. Further, this report does not claim to identify a causal link between employment in agriculture, fishing, or forestry and male lip cancer, only the existence of an association, which may be due to other factors such as the age or lifestyle habits of those employed in agriculture, fishing, or forestry.

References

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Supplemental Figures

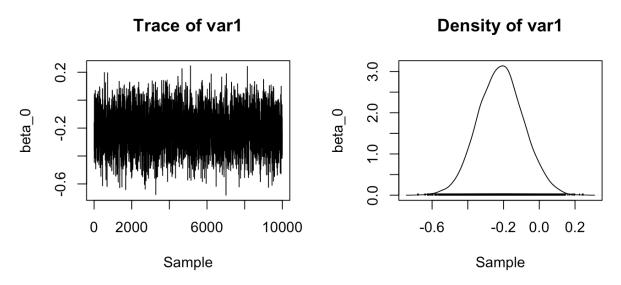


Figure S1: Trace plot and density plot of β_0 for Bayesian Markov chain Monte Carlo simulation.

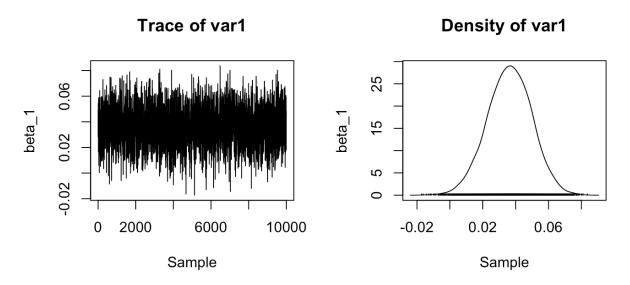


Figure S2: Trace plot and density plot of β_1 for Bayesian Markov chain Monte Carlo simulation.

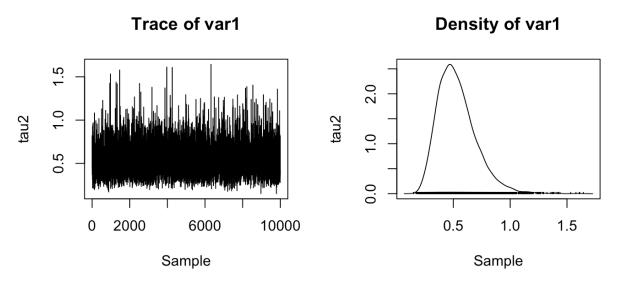


Figure S3: Trace plot and density plot of τ^2 for Bayesian Markov chain Monte Carlo simulation.

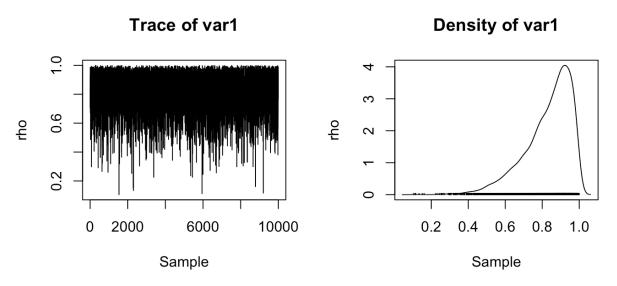
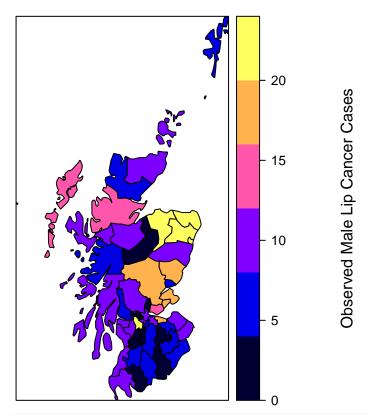


Figure S4: Trace plot and density plot of ρ for Bayesian Markov chain Monte Carlo simulation.

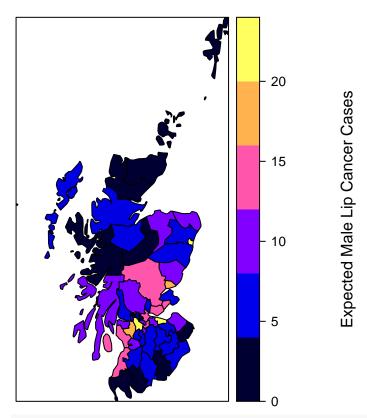
Appendix: All R Codes

```
library(CARBayes)
library(spdep)
library(grid)
set.seed(1)
load("lipscotland.RData")
# Exploratory Analysis
#######################
# Getting aspect ratio for plotting (converting degrees latitude/longitude to distance to
# correspond to how Scotland would look on a map)
# Distance of 1 degree latitude and average distance of 1 degree longitude in Scotland
long = cos(mean(lipscotland$latitude) * pi / 180)
aspect.ratio = 1 / long
# Observed counts
summary(lipscotland$observed)
     Min. 1st Qu. Median
                            Mean 3rd Qu.
    0.000
          4.750 8.000 9.571 11.000 39.000
##
lipscotland$observed.plot = ifelse(lipscotland$observed > 20, 21, lipscotland$observed)
# Cap observations at 20 for plotting; anything over 20 is treated as just > 20
breaks.obs = c(0, 4, 8, 12, 16, 20, 24)
spplot(lipscotland, "observed.plot", at = breaks.obs, aspect = aspect.ratio)
grid.text("Observed Male Lip Cancer Cases", x = unit(0.82, "npc"), y = unit(0.50, "npc"),
rot = 90)
```

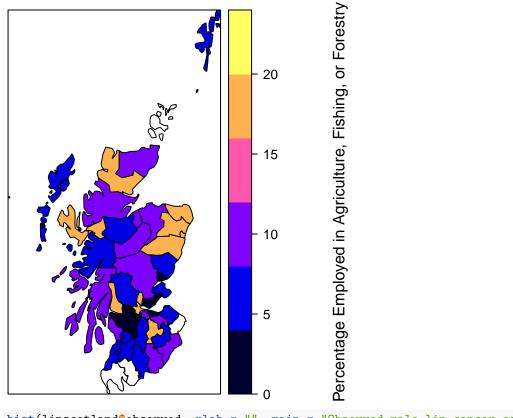


Expected counts summary(lipscotland\$expected)

```
##
      Min. 1st Qu. Median
                             Mean 3rd Qu.
                                              Max.
##
     1.100
            4.050
                    6.300
                            9.575 10.125 88.700
lipscotland$expected.plot = ifelse(lipscotland$expected > 20, 21, lipscotland$expected)
# Same as before; some information is lost as some of the expected counts are much higher
# than 20 (up to 89)
breaks.exp = c(0, 4, 8, 12, 16, 20, 24)
spplot(lipscotland, "expected.plot", at = breaks.exp, aspect = aspect.ratio)
grid.text("Expected Male Lip Cancer Cases", x = unit(0.82, "npc"), y = unit(0.50, "npc"),
 rot = 90)
```

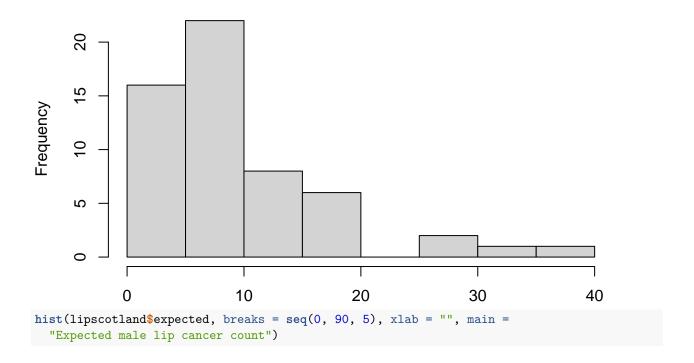


Percentage employed in agriculture, fishing, or forestry summary(lipscotland\$pcaff)

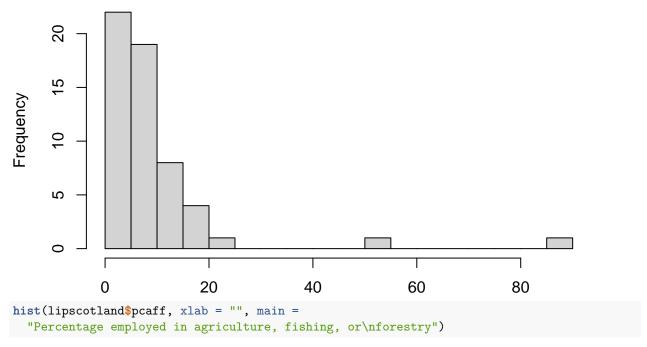


hist(lipscotland\$observed, xlab = "", main = "Observed male lip cancer count")

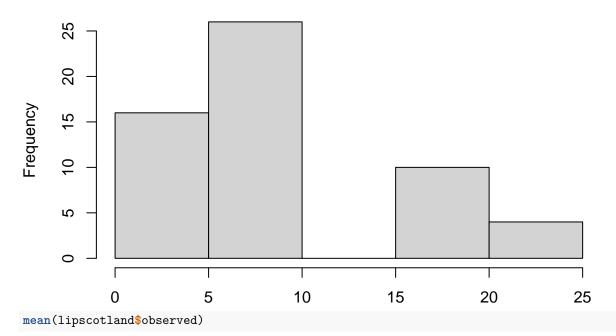
Observed male lip cancer count



Expected male lip cancer count



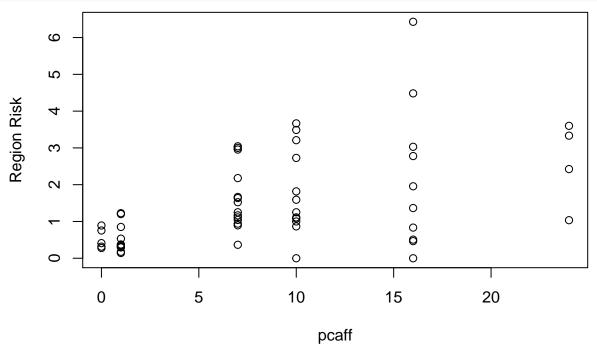
Percentage employed in agriculture, fishing, or forestry



[1] 9.571429

var(lipscotland\$observed)

[1] 62.54026



```
# Approximately; it's not obviously nonlinear

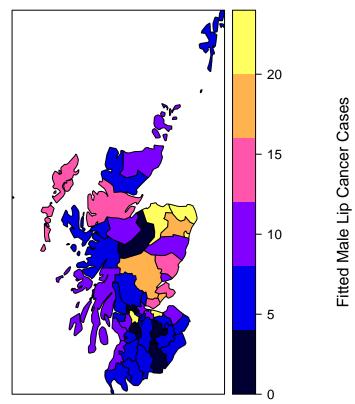
form = observed ~ offset(log(expected)) + pcaff
lip.nsa = glm(formula = form, family = poisson, data = lipscotland)
summary(lip.nsa)

## Coll:
```

```
## Call:
## glm(formula = form, family = poisson, data = lipscotland)
##
## Deviance Residuals:
##
       Min
                 10
                      Median
                                   3Q
                                           Max
## -4.7632 -1.2156
                      0.0967
                               1.3362
                                        4.7130
##
## Coefficients:
##
                Estimate Std. Error z value Pr(>|z|)
                                     -7.80 6.21e-15 ***
## (Intercept) -0.542268
                           0.069525
                                      12.38 < 2e-16 ***
## pcaff
                0.073732
                           0.005956
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
## (Dispersion parameter for poisson family taken to be 1)
##
##
      Null deviance: 380.73 on 55 degrees of freedom
## Residual deviance: 238.62 on 54 degrees of freedom
## AIC: 450.6
##
## Number of Fisher Scoring iterations: 5
mod.resid = lip.nsa$residuals
moran.mc(x = mod.resid, listw = W.list, nsim = 1000)
   Monte-Carlo simulation of Moran I
##
## data: mod.resid
## weights: W.list
## number of simulations + 1: 1001
## statistic = 0.36581, observed rank = 1001, p-value = 0.000999
## alternative hypothesis: greater
geary.mc(x = mod.resid, listw = W.list, nsim = 1000)
##
   Monte-Carlo simulation of Geary C
## data: mod.resid
## weights: W.list
## number of simulations + 1: 1001
## statistic = 0.51224, observed rank = 1, p-value = 0.000999
## alternative hypothesis: greater
##################
# Spatial analysis
##################
lip.spatial = S.CARleroux(formula = form, data = lipscotland@data, family = "poisson",
 W = W, burnin = 20000, n.sample = 120000, thin = 10)
print(lip.spatial)
## ################
## #### Model fitted
## ################
## Likelihood model - Poisson (log link function)
## Random effects model - Leroux CAR
## Regression equation - observed ~ offset(log(expected)) + pcaff
## Number of missing observations - 0
##
## ###########
## #### Results
## ###########
## Posterior quantities and DIC
##
##
                Median
                          2.5% 97.5% n.effective Geweke.diag
```

```
## (Intercept) -0.2200 -0.4683 0.0242
                                           2358.7
                                                         -0.9
## pcaff
                0.0368 0.0104 0.0627
                                           1999.9
                                                          0.7
## tau2
                0.5062 0.2722 0.9393
                                           5682.0
                                                         -1.0
## rho
                0.8571 0.5112 0.9865
                                           6522.7
                                                          0.7
## DIC = 299.2672
                         p.d = 30.53755
                                               LMPL =
                                                       -158.5
# Plot fitted values
lipscotland$fitted.car = fitted(lip.spatial)
lipscotland$fitted.car.plot = ifelse(lipscotland$fitted.car > 20, 21,
 lipscotland$fitted.car)
\# Same as before, capping fitted values at 20 and treat any greater values as just > 20
spplot(lipscotland, "fitted.car.plot", at = breaks.obs, aspect = aspect.ratio)
grid.text("Fitted Male Lip Cancer Cases", x = unit(0.82, "npc"), y = unit(0.50, "npc"),
  rot = 90)
```



Compare fitted values to true values
cbind(lipscotland\$observed, lipscotland\$fitted.car)

```
[,2]
##
         [,1]
##
   [1,]
           9 5.722570
##
   [2,]
           39 37.477423
   [3,]
           11 8.471580
##
##
   [4,]
           9 7.469910
##
   [5,]
           15 12.508956
   [6,]
           8 8.699272
##
   [7,]
           26 22.663224
   [8,]
           7 6.184539
##
##
  [9,]
            6 4.223221
## [10,]
           20 19.164116
```

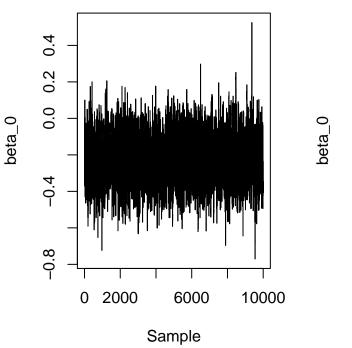
```
## [11,]
           13 12.666733
## [12,]
           5 5.361980
## [13,]
           3 2.652284
## [14,]
            8 6.987688
## [15,]
           17 15.373273
## [16,]
           9 9.505945
## [17,]
            2 2.158293
## [18,]
            7 5.071326
## [19,]
            9 10.276435
## [20,]
            7 6.351714
## [21,]
           16 14.283490
## [22,]
           31 35.399928
## [23,]
           11 11.829200
## [24,]
           7 4.721760
## [25,]
           19 18.615665
## [26,]
           15 13.571616
## [27,]
           7 5.873958
## [28,]
           10 10.140726
## [29,]
           16 17.800865
## [30,]
           11 8.979141
## [31,]
           5 4.056199
## [32,]
            3 4.301347
## [33,]
            7 6.647957
## [34,]
           8 6.630365
## [35,]
           11 10.525291
## [36,]
           9 7.638752
## [37,]
           11 11.339471
## [38,]
            8 5.539253
## [39,]
            6 7.215979
## [40,]
            4 3.015711
## [41,]
           10 10.037839
## [42,]
           8 11.153730
## [43,]
            2 4.021823
## [44,]
            6 6.722374
## [45,]
           19 20.825777
## [46,]
            3 4.817908
## [47,]
            2 2.656451
## [48,]
           3 4.061604
## [49,]
           28 31.824750
## [50,]
            6 8.873474
## [51,]
            1 1.640318
## [52,]
            1 1.684661
## [53,]
            1 2.301600
## [54,]
            1 2.883559
## [55,]
            0 3.483069
            0 1.606223
## [56,]
summarise.samples(lip.spatial$samples$beta, quantiles = c(0.5, 0.025, 0.975))
## $quantiles
                0.5
                          0.025
                                     0.975
## [1,] -0.21995367 -0.46826916 0.02418005
## [2,] 0.03681681 0.01035609 0.06266173
##
## $exceedences
```

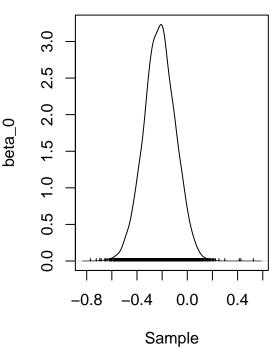
NULL

```
# Intercept
plot(lip.spatial$samples$beta[,1], ylab = "beta_0", xlab = "Sample")
```

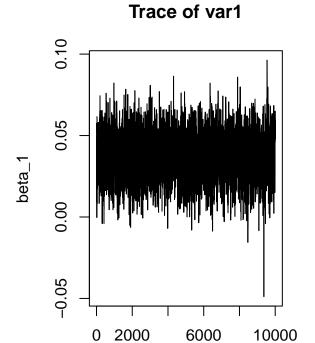
Trace of var1

Density of var1

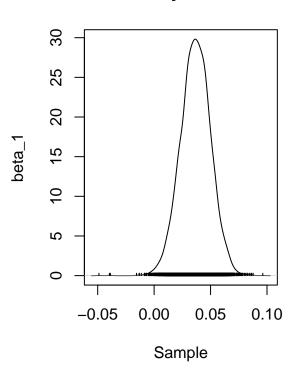




pcaff effect
plot(lip.spatial\$samples\$beta[,2], ylab = "beta_1", xlab = "Sample")



Density of var1



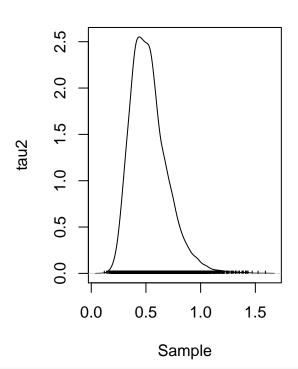
tau2
plot(lip.spatial\$samples\$tau, ylab = "tau2", xlab = "Sample")

Trace of var1

Sample

0.5 1.0 1.5 0.5 ample

Density of var1



rho
plot(lip.spatial\$samples\$rho, ylab = "rho", xlab = "Sample")

