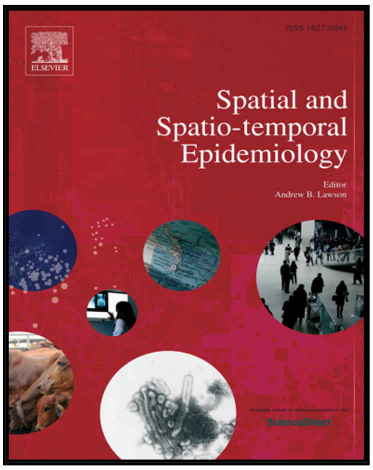

SpatialEpiApp: A Shiny Web Application for the Analysis of Spatial and Spatio-Temporal Disease Data

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SpatialEpiApp: A Shiny Web Application for the Analysis of Spatial and Spatio-Temporal Disease Data

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Abstract

During last years, public health surveillance has been facilitated by the existence of several packages implementing statistical methods for the analysis of spatial and spatio-temporal disease data. However, these methods are still inaccesible for many researchers lacking the adequate programming skills to effectively use the required software. In this paper we present SpatialEpiApp, a Shiny web application that integrate two of the most common approaches in health surveillance: disease mapping and detection of clusters. SpatialEpiApp is easy to use and does not require any programming knowledge. Given information about the cases, population and optionally covariates for each of the areas and dates of study, the application allows to fit Bayesian models to obtain disease risk estimates and their uncertainty by using R-INLA, and to detect disease clusters by using SaTScan. The application allows user interaction and the creation of interactive data visualizations and reports showing the analyses performed.

Keywords: Disease mapping, clusters, Shiny, INLA, SaTScan

1. Introduction

Public health surveillance provides information to identify public health problems and respond appropriately when they occur. This information is crucial to prevent and control a variety of health conditions such as chronic and infectious diseases, injuries, or health-related behaviors (Thacker and

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Berkelman, 1988; Lawson and Kleinman, 2005). There is a wide range of spatial and spatio-temporal methods and software that can be applied as a surveillance tool, and these are useful for highlighting areas at high risk (Moraga et al., 2015), detecting disease clusters (Moraga and Montes, 2011), assessing spatial variations in temporal trends (Moraga and Kulldorff, 2016), early detection of epidemics (Stelling et al., 2010), assessing disease risk in relation to a putative source (Wakefield and Morris, 2001), and identifying disease risk factors (Hagan et al., 2016).

For example, geographic information systems (GIS) provides a powerful tool for public health surveillance that can be used to store, analyze, and display spatial data. These capabilities allow to create maps showing the patterns of disease and potential risk factors and to perform basic spatial analysis. Another tool commonly used in spatial epidemiology is the GeoDa software (Anselin et al., 2006). This software facilitates exploratory spatial data analysis and visualization on lattice data, such as spatial autocorrelation statistics, and basic spatial regression analysis.

More complex spatial and spatio-temporal analysis such as estimation of disease relative risk can be performed using Bayesian disease models. The OpenBUGS software is part of the BUGS (Bayesian inference Using Gibbs Sampling) project (Lunn et al., 2009) and allows to perform Bayesian inference of complex disease models using Markov chain Monte Carlo (McMC) methods. Bayesian inference may also be performed using the Integrated Nested Laplace Approximation (INLA) approach (Rue et al., 2009) which is implemented in the R package `R-INLA` (Lindgren and Rue, 2015).

Detection of clusters in spatial, temporal, and space-time settings can be performed using the scan statistics methodology (Kulldorff and Nagarwalla, 1995; Kulldorff, 1997) which is implemented in the statistical package `SaTScan` (Kulldorff, 2006a) and R packages such as `DCluster` (Gómez-Rubio et al., 2005). Unfortunately, although all the aforementioned statistical packages are valuable for public health surveillance, many researchers with training in biomedical sciences lack the adequate programming and statistical skills to use them effectively.

In this paper we present `SpatialEpiApp`, a Shiny web application (Chang et al., 2016) for the analysis of spatial and spatio-temporal disease data. The application has been implemented in the R package `SpatialEpiApp` and its use does not require advanced programming or statistical knowledge. `SpatialEpiApp` is useful for interactive data visualization and integrates two of the most common approaches in public health surveillance: disease mapping and detection of clusters. SpatialEpiApp is mainly addressed to health researchers interested in understanding the spatial and spatio-temporal variations of disease but lacking the appropriate knowledge to carry out the statistical analysis and the processing of the results. The application is also useful for researchers with more advanced statistical skills since it allows to visualize the data using interactive maps and tables which can be useful prior to the statistical analysis.

In spatial epidemiology, availabe data can be point data containing the locations at which cases of disease occur, or areal data that arise when point data are aggregated over disjoint subregions of the region of study due to ethical concerns over data use and patient confidentiality. SpatialEpiApp is designed to work with areal data. Given information about the cases, population and optionally covariates for each of the areas in the study region and periods of time, the application allows to fit Bayesian disease models to obtain risk estimates and their uncertainty for each of the areas and dates by using R-INLA, and to detect spatial and spatio-temporal clusters by using the scan statistics implemented in SaTScan. To carry out these analyses users simply need to click the buttons that create the input files required, execute the software and process the output to generate tables of values and plots needed for the interpretation of the results. The application allows user interaction, creates interactive visualizations of the data and results, and generates reports showing the analyses performed.

The remainder of the paper is organized as follows. First, we briefly introduce the statistical methods and software used in spatial and spatio-temporal epidemiology. In Section 3 we illustrate the use of the application via a spatio-temporal analysis of lung cancer mortality in Ohio, United States, in years 1981 to 1984. Specifically, we discuss the input files required, show how to perform the statistical analyses and interpret the results, and explain how to generate reports. Instructions for the installation of the application are provided in Section 4. Finally, the conclusions are presented.

2. Spatial and spatio-temporal epidemiology

Spatial and spatio-temporal epidemiology is concerned with the description and analysis of spatial and spatio-temporal variations in disease risk with respect to risk factors such as sociodemographic and environmental covariates (Elliott et al., 2000). Over the past few decades, this field has been aided by the increased availability of geographically indexed health data, the development of geographic information systems (GIS), as well as the advances in statistical methodology such as disease mapping and cluster detection methods.

Disease mapping is widely used in public health surveillance since it allows to describe the spatial and spatio-temporal variation of the disease, identify areas which exhibit an unusual high risk and formulate etiological hypotheses (Lawson, 2009). Cluster analysis has also attracted a great interest, and various techniques have been developed for evaluating whether the incidence of a disease shows a particular tendency to group together (Kulldorff, 2006b). The information resulting from these analyses is crucial to appropriately implement prevention and surveillance programmes.

The available data in these type of studies can be point data containing the locations at which cases of disease occur, or areal data containing aggregated outcomes over a finite number of subregions forming a partition of the region of study. Whenever point data are available, it is recommended to perform the analyses at this level of resolution so detailed information do not get lost. However, the exact location of the individuals is not always available for various reasons, such as confidentiality. In the following subsections we introduce some of the most common statistical methods and software for disease mapping and the detection of clusters using areal data. These are the approaches that are implemented in `SpatialEpiApp`.

2.1. Disease mapping

Most disease mapping approaches estimate disease risks within areal units that form a partition of the study region such as zip codes or provinces, and this is mainly done for confidentiality reasons (Waller and Gotway, 2004). Often, the disease risk in area $i = 1, \dots, N$ is estimated by the standardized incidence ratio (SIR) which is obtained as the ratio of observed counts versus the expected counts: $\text{SIR}_i = Y_i/E_i$. The expected counts in each of the areas are calculated based on their population demographics and usually the internally standardized expected counts are used. Specifically,

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

where $r_j^{(s)}$ is the rate in stratum j in the standard population (usually the relevant national or regional population), and n_j is the population in stratum j of the area. The expected counts represent the total number of events one would expect if the observed population behaved the way the standard population behaved.

In areas with small populations SIRs can be very extreme and are insufficiently reliable for reporting. In contrast, Bayesian disease models are preferred to obtain risks estimates since they enable to borrow information from neighboring areas and may also incorporate covariate information to improve local estimates (Gelfand et al., 2010).

A common practice is to model the observed counts Y_i in area i, using a Poisson distribution with mean $E_i \times \theta_i$, where E_i is the expected counts and θ_i is the relative risk in area i. To model the relative risk θ_i, a log linear model is used which includes an intercept to model the overall disease level, and random effects that account for extra-Poisson variability in the observed data (Lawson, 2009; Moraga and Lawson, 2012). The standard model in disease mapping is expressed as

$$Y_i \sim Po(E_i \times \theta_i),\ i = 1, \ldots, N;$$

$$\log(\theta_i) = \alpha + u_i + v_i.$$

Here, α represents the overall risk in the region of study, u_i is a correlated heterogeneity (CH) component that models the spatial dependence between the relative risks, and v_i is an unstructured exchangeable component that models uncorrelated noise (UH). Sometimes other terms such as covariates and random effects that can deal with other sources of variability can also be included in the model.

The most popular model to spatial disease mapping is the Besag-York-Mollié (BYM) model (Besag et al., 1991). Here, the clustering component u_i is modelled with the conditional autoregressive (CAR) distribution. The CAR distribution smoothes the data according to a certain neighborhood structure given by a neighborhood matrix that is specified such as two areas are neighbours if they share a common boundary. The CAR distribution is expressed as

$$u_i|\mathbf{u_{-i}} \sim N\left(\bar{u}_{\delta_i}, \frac{\sigma_u^2}{n_{\delta_i}}\right),$$

where $\bar{u}_{\delta_i} = n_{\delta_i}^{-1} \sum_{j \in \delta_i} u_j$, δ_i represents the set of neighbours of area i, and n_{δ_i} is the number of neighbours of area i. The uncorrelated heterogeneity v_i is modeled as independent and identically distributed normal variables with mean zero and variance σ_v^2

Spatio-temporal disease mapping models are used when the interest is to understand the spatial and the temporal disease patterns (Knorr-Held, 2000). In the space-time setting, the disease count Y_{ij} observed in the area i and time period j, may be modeled as

$$Y_{ij} \sim Po(E_{ij} \times \theta_{ij}),$$

where θ_{ij} is the risk and E_{ij} is the expected number of cases in the given area and period of time. Then, three groups of components for $\log(\theta_{ij})$ can be considered:

$$log(\theta_{ij}) = \alpha_0 + A_i + B_j + C_{ij},$$

where A_i is the spatial group, B_j is the temporal group, and C_{ij} is the space-time interaction group (Lawson, 2009). For example, in Bernardinelli et al. (1995) these groups are defined as follows: $A_i = u_i + v_i$, $B_j = \beta t_j$ and $C_{ij} = \delta_i t_j$ where $u_i + v_i$ is an area random effect, βt_j is a linear trend term in time t_j, and $\delta_i t_j$ is an interaction random effect between area and time.

Bayesian inference may be performed using the Integrated Nested Laplace Approximation (INLA) (Rue et al., 2009). INLA uses a combination of analytical approximation and numerical integration to do approximate Bayesian inference in latent Gaussian models which includes a large class of models ranging from generalized linear mixed to spatial and spatio-temporal models. The INLA approach is implemented in the R package `R-INLA` (Lindgren and Rue, 2015; Blangiardo and Cameletti, 2015; Bivand et al., 2013). This package can be downloaded from the `http://www.r-inla.org` website which also includes documentation about the package, examples and a discussion forum.

2.2. Detection of clusters

Methods for the detection of clusters are designed for detecting and localizing specific clusters and evaluating their statistical significance. The scan statistics methodology (Kulldorff and Nagarwalla, 1995; Kulldorff, 1997) has been implemented as a major analytical tool for cluster detection in a spatial, temporal, and space-time setting. A statistical package, `SaTScan`, facilitates its use and can be downloaded from the `http://www.satscan.org` website (Kulldorff, 2006a).

Scan statistics gradually scan the study region with a huge number of overlapping windows and determine the windows which group together an unusual number of cases (Kulldorff, 1997). Typically, the spatial version uses circular windows with radius varying continuously from zero to some upper limit such as that it does not pass beyond 50% of the at risk population. In the space-time setting windows are defined as cylinders. The circular base defines a geographical area and the height the time period. For each choice of base all choices of the temporal height are considered and vice versa.

Conditioning on the observed total number of cases C, the scan test statistic S is defined as the maximum likelihood ratio over all possible windows Z. The likelihood ratio S is expressed as

$$S = max_Z \frac{L(Z)}{L_0},$$

where $L(Z)$ is the likelihood for window Z, and L_0 is the likelihood function under the null hypothesis which states that the probability of being a case inside Z is equal to the probability of being a case outside Z. When the number of cases in each window is Poisson distributed a Poisson model is used. Under this model, the ratio $L(Z)/L_0$ for a specific window is

$$\left(\frac{c}{E(Z)}\right)^c \left(\frac{C-c}{C-E(Z)}\right)^{C-c},$$

if $c > E(Z)$, and 1 otherwise. Here, c is the observed number of cases within Z, and $E(Z)$ denotes the covariate adjusted expected number of cases under the null hypothesis.

The window with the maximum likelihood constitutes the most likely cluster. The cluster statistical significance is obtained through Monte Carlo hypothesis testing (Dwass, 1957). Specifically, the previous procedure is repeated for a large number of replicas, say R, of data generated under the null hypothesis, and their respective test statistics are calculated. Next, the test statistic of the real data is combined with these, and the set of the $R+1$ values are ordered. The p-value is obtained as $M/(R+1)$, where M is the rank of the test statistic from the real data. Apart from the most likely cluster, secondary clusters can also be identified, ordered according to the value of S.

3. SpatialEpiApp

`SpatialEpiApp` is a Shiny web application that allows to visualize spatial and spatio-temporal disease data, estimate disease risk and detect clusters.

It has been implemented in the R package SpatialEpiApp, and is addressed to health researchers interested in analyzing disease data but lacking the appropriate programming skills to use the required statistical software. A brief summary of Shiny and a description of the main components used to implement the application are provided in the Appendix.

SpatialEpiApp allows to fit Bayesian disease models to obtain risk estimates and their uncertainty by using INLA, and to detect clusters by using the scan statistics implemented in SaTScan. To carry out these analyses users simply need to click the buttons that create the input files required, execute the software and process the output to generate tables of values and plots with the results. The application allows user interaction and creates interactive visualizations such as maps supporting padding and zooming and tables that allow for filtering. It also enables the generation of reports containing the analyses performed.

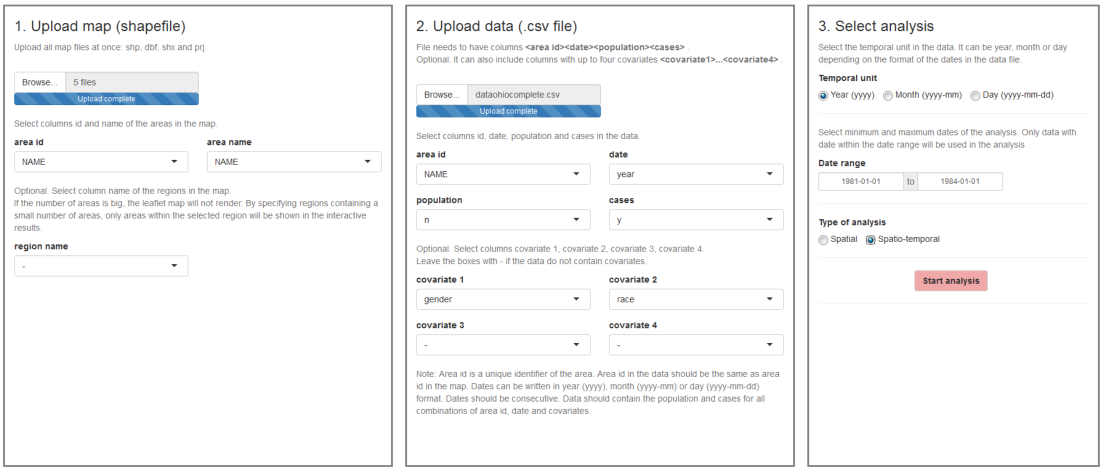
SpatialEpiApp consists of three pages: 1) an 'Inputs' page where the user can upload the input files and select the type of analysis; 2) an 'Analysis' page where statistical analyses are carried out, results can be visualized, and reports can be generated; and 3) a 'Help' page containing information about the application use and references. In the following subsections, we detail the content of each of the pages, and demonstrate the use of the application through a spatio-temporal analysis of lung cancer mortality in the Ohio counties in years 1981 to 1984. These data appear in Lawson et al. (2003) and are available at http://Paula-Moraga.github.io/software. The Ohio map has been obtained from the United States Census Bureau website, http://www.census.gov.

3.1. Inputs page

The 'Inputs' page is the first page we see when we launch SpatialEpiApp. In this page we can upload the required files and select the type of analysis to be performed. It is composed of four components: 1) Upload map; 2) Upload data; 3) Select analysis; and 4) Contents (see Figure 1).

3.1.1. Upload map

First, we need to upload the map file containing the areas of the region of study. The map file needs to be in shapefile format and it can be uploaded by clicking the 'Browse' button and selecting all the files corresponding to



1. Upload map (shapefile)

Upload all map files at once: shp, dbf, shx and prj.

5 files

Select columns id and name of the areas in the map.

area id: NAME

area name: NAME

Optional. Select column name of the regions in the map.
If the number of areas is big, the leaflet map will not render. By specifying regions containing a small number of areas, only areas within the selected region will be shown in the interactive results.

region name: -

2. Upload data (.csv file)

File needs to have columns **<area id><date><population><cases>** .
Optional. It can also include columns with up to four covariates **<covariate1>...<covariate4>** .

dataohiocomplete.csv

Select columns id, date, population and cases in the data.

area id: NAME

date: year

population: n

cases: y

Optional. Select columns covariate 1, covariate 2, covariate 3, covariate 4.
Leave the boxes with - if the data do not contain covariates.

covariate 1: gender

covariate 2: race

covariate 3: -

covariate 4: -

Note: Area id is a unique identifier of the area. Area id in the data should be the same as area id in the map. Dates can be written in year (yyyy), month (yyyy-mm) or day (yyyy-mm-dd) format. Dates should be consecutive. Data should contain the population and cases for all combinations of area id, date and covariates.

3. Select analysis

Select the temporal unit in the data. It can be year, month or day depending on the format of the dates in the data file.

Temporal unit

● Year (yyyy) ○ Month (yyyy-mm) ○ Day (yyyy-mm-dd)

Select minimum and maximum dates of the analysis. Only data with date within the date range will be used in the analysis

Date range

1981-01-01 to 1984-01-01

Type of analysis

○ Spatial ● Spatio-temporal

Figure 1: Inputs page. Selected options correspond to the Ohio example.

the map. Then we need to specify which are the names of the columns id and name of the areas, and optionally the name of the column name of the region. This is done by selecting the correct options from the dropdown menus which are populated with the names of the columns of the map.

The id area is the unique identifier of the area and should coincide with the id area we specify for the data. If we specify a region name, the areas shown in the maps and tables in the ’Analysis’ page can be filtered by region. This is particularly important when the number of areas in the map is large because in these situations the map may render very slowly. When we filter by region, the map shows fewer areas, only the ones corresponding to a given region, and this permits a faster rendering.

3.1.2. Upload data

In the second component of the ’Input tab’ we upload the data file. The file should be an .csv file with the following columns:

- area id: an unique identifier of the area. It should coincide with the id area we specify for the map;
- date: date that can be written in year (yyyy), month (yyyy-mm) or day (yyyy-mm-dd) format. Dates should be consecutive;
- population: population in each area and date; and

- cases: number of cases in each area and date.

Optionally, the data can also include columns corresponding up to four covariates such as gender and age group. Data should contain the population and the number cases for all combinations of area id, date and covariates. Here we also need to select the name of the data columns in the corresponding dropdown menus.

3.1.3. Select analysis

After uploading the map and the data files we need to specify several options that will be used in the analyses. First, we specify whether the temporal unit in the data is year, month or day.

Second, we select the date range that we want to consider. Data with dates outside this range are excluded in the analysis. The date range is specified by entering a minimum and maximum dates in a calendar. This calendar only permits the selection of dates expressed in day format (yyyy-mm-dd). If the temporal unit is year or month, the application only considers the year or the year and month of the selected date, respectively.

Finally, the type of analysis is selected. If the analysis selected is spatial, the data is aggregated for all dates and the analyses are performed as there is only one period of time. In the spatio-temporal case all the selected dates are considered.

3.1.4. Contents

When we upload the map and data files, their contents are shown at the end of the 'Inputs' page. This information is useful to know which are the variables of the data so we can correclty specify the inputs required such as the name of the columns, the temporal unit and the date range.

3.1.5. Start analysis button

Once we have uploaded all the files and selected the options required we click the 'Start analysis' button. When we do this, the application checks the files and options entered are correct and calculates the expected counts for each area and date. It also computes the ratio of the observed divided the expected. This ratio is called SIR irrespectively if data refers to mortality or incidence. Then the application redirects to the 'Analysis' page.

3.1.6. Example

In our example we first upload the Ohio map which consist of 88 counties. We need to upload all the files (.dbf, .prj, .shp, .xml and .shx) at the same time. Then we select NAME as area id and also as area name. We do not wish to filter by region so we select "-" as name region.

Then we upload the data. The data consist of the number of deaths and population for each race and gender for each of the counties in Ohio in years 1968 to 1988. The columns of the data file are the following:

- NAME: county name;
- gender: gender (1=male, 2=female);
- race: race (1=white, 2=nonwhite);
- year: year (1968 to 1988);
- y: lung cancer death counts;
- n: population counts.

We select area id as NAME, cases as y, population as n, covariate 1 as gender and covariate 2 as race. In covariates 3 and 4 we select "-".

After that, we specify the required options in the 'Select analysis' component. The temporal unit is year. Since we wish to analyze the data corresponding to years 1981 to 1984, the minimum date is entered as any day in 1981 and the maximum date as any day in 1984. Finally, we select type of analysis as spatio-temporal. The selected options are shown in Figure 1.

3.2. Analysis page

In the 'Analysis' page we can visualize the data, perform the statistical analyses, and generate reports. On the top of the page there are four buttons. The first one is 'Edit Inputs' and it is used when we wish to return to the 'Inputs' page to modify the analysis options or upload new data. The second button is 'Maps Pop O E SIR'. This button creates plots of the population, observed, expected and SIR variables. The third and fourth buttons are used for estimating the disease risk and their uncertainty, and for the detection of disease clusters, respectively. The 'Analysis' page also contains four tabs called 'Interactive', 'Maps', 'Clusters' and 'Report' that include tables and plots with the results. Details about the use of the buttons and the content of each of the tabs are provided in the following sections.

3.2.1. Interactive tab

The 'Interactive tab' includes three interactive visualizations that show the data and the results: a map, a temporal trend plot and a table. The map displays the values corresponding to the variable and date selected in the dropdown menus located on the left of the page. The variable can be the population, the observed cases, the expected cases or the SIR. If the estimation of risk and the detection of clusters analyses have been carried out, the choices also include the risk and the clusters. The map can be zoomed enabling a better examination of the areas, and when the mouse hovers on any area, that area is highlighted and its information is shown on the upper right corner.

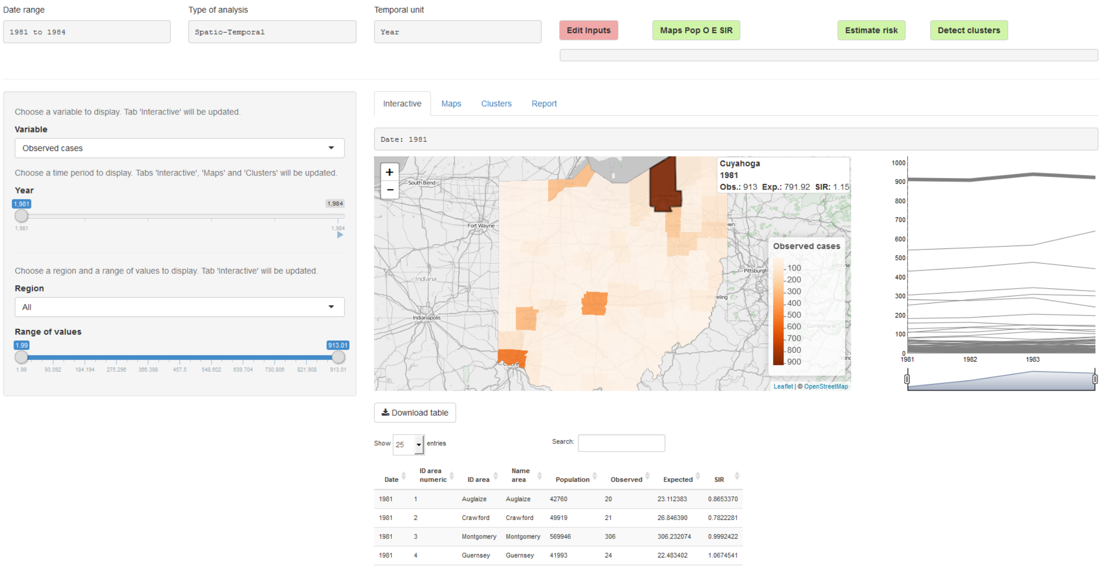
The temporal trend plot shows the values of the variable selected over time. The map and the temporal trend plot are linked and when the mouse hovers on any of the areas in the map, the trend corresponding to the same area is highlighted in the temporal trend plot.

The table displays the information of all areas in the map in the selected date. The user can filter the information by searching a word in any of the columns or in the entire table. It is also possible to sort the rows into ascending or descending order of the values of any of the columns.

In addition, the information shown in the map, the temporal trend plot and the table can be filtered by region and by range of values by selecting an option from the dropdown menu 'Region' and an interval of values from the slider 'Range of values', respectively. In this tab there is also a button called 'Download table' that permits to download the data contained in the table. This option is useful for users that wish to do further analysis or create their own tables and plots.

3.2.2. Maps tab

The button 'Maps Pop O E SIR' creates maps and temporal trend plots for the variables population, observed, expected and SIR for each of the dates in the study time period. When button 'Estimate risk' is clicked, the application estimates the risk and obtains lower and upper limits of 95% credible intervals showing the uncertainty of the estimates. To obtain these values the application fits a Bayesian model by using `R-INLA`. If the type of analysis selected is spatial or the data pertains to just one date, the BYM model presented by Besag et al. (1991) is used. If the type of analysis selected



Date range: 1981 to 1984

Type of analysis: Spatio-Temporal

Temporal unit: Year

Choose a variable to display. Tab 'Interactive' will be updated.

Variable: Observed cases

Choose a time period to display. Tabs 'Interactive', 'Maps' and 'Clusters' will be updated.

Year: 1,981 – 1,984

Choose a region and a range of values to display. Tab 'Interactive' will be updated.

Region: All

Range of values: 1.99 – 913.01

1.99 93.092 184.194 275.296 366.398 457.5 548.602 639.704 730.806 821.908 913.01

Date: 1981

Show 25 entries

Search:

Date	ID area numeric	ID area	Name area	Population	Observed	Expected	SIR
1981	1	Auglaize	Auglaize	42760	20	23.112383	0.8653370
1981	2	Crawford	Crawford	49919	21	26.846390	0.7822281
1981	3	Montgomery	Montgomery	569946	306	306.232074	0.9992422
1981	4	Guernsey	Guernsey	41993	24	22.483402	1.0674541

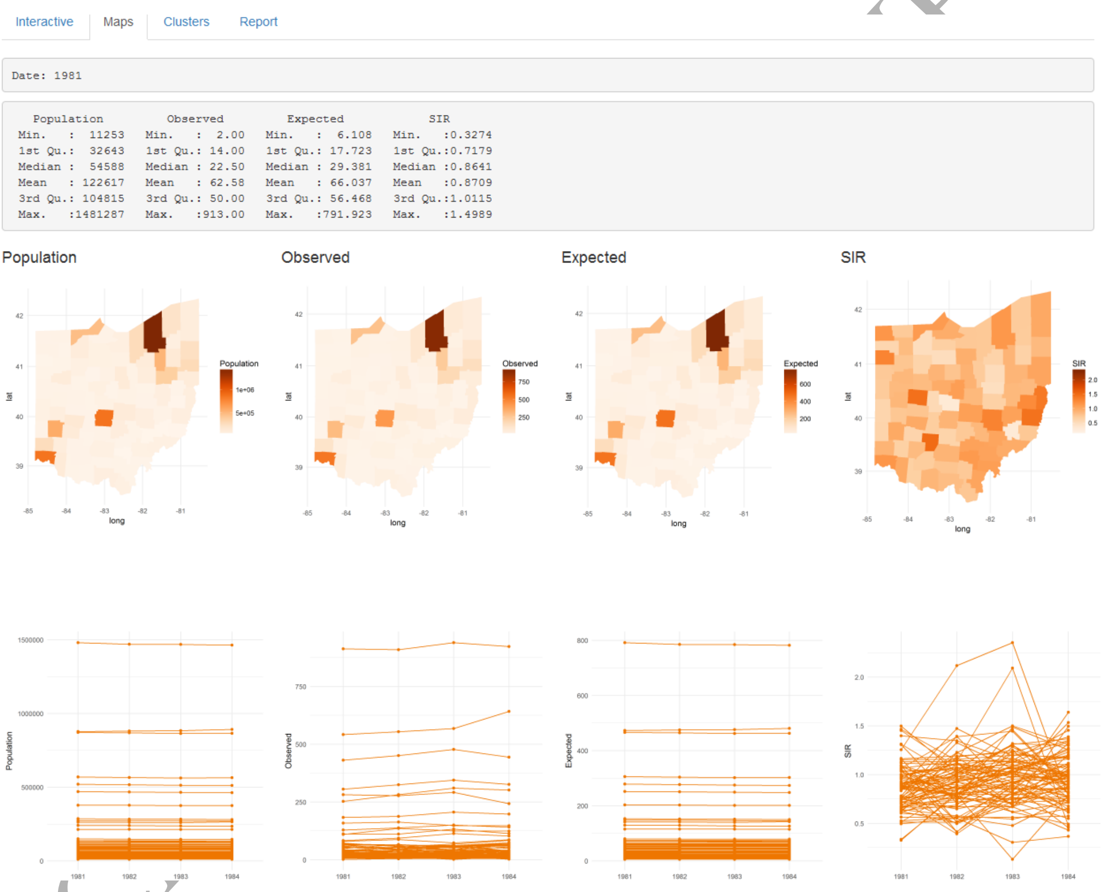
Figure 2: Interactive tab. Results correspond to the Ohio example.

is spatio-temporal and the data consist of more than one date, the model fitted is the one presented by Bernardinelli et al. (1995).

The 'Maps' tab shows a summary table, maps and temporal trend plots of the population, observed cases, expected cases, SIR, risk and lower and upper limits of 95% credible intervals that were obtained by clicking the 'Map Pop O E SIR' and the 'Estimate risk' buttons (see Figure 3).

3.2.3. Clusters tab

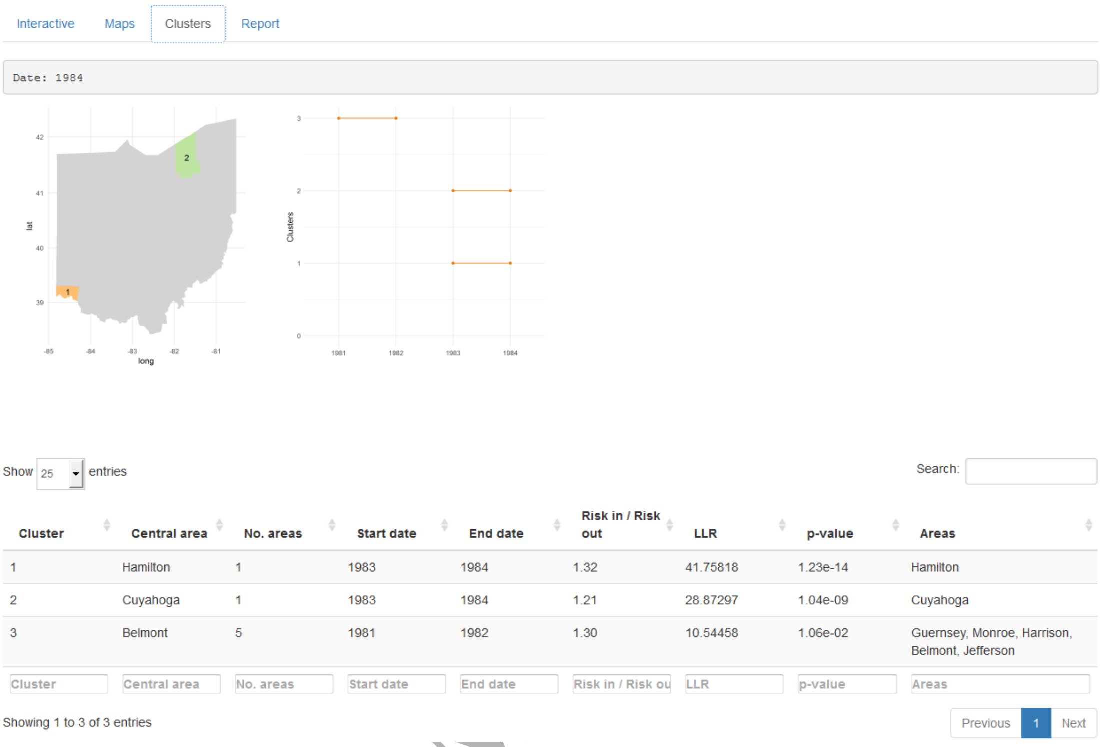
When clicking the button 'Detect clusters' the program executes the `SaTScan` software to detect spatial or spatio-temporal clusters. First the program creates the input files required by `SaTScan`, then `SaTScan` is executed, and finally the results are processed to generate the plots and tables with the detected clusters. This analysis is performed using 999 Monte Carlo simulations and a level of significance equal to 0.05. The 'Clusters tab' shows, for each of the dates of the period of study, a map with the clusters detected and a plot with all clusters over time. This tab also includes a table with the information relative to each of the clusters such as the central area, the areas



```
Date: 1981
```

```
  Population         Observed         Expected           SIR
 Min.   :  11253   Min.   :  2.00   Min.   :  6.108   Min.   :0.3274
 1st Qu.:  32643   1st Qu.: 14.00   1st Qu.: 17.723   1st Qu.:0.7179
 Median :  54588   Median : 22.50   Median : 29.381   Median :0.8641
 Mean   : 122617   Mean   : 62.58   Mean   : 66.037   Mean   :0.8709
 3rd Qu.: 104815   3rd Qu.: 50.00   3rd Qu.: 56.468   3rd Qu.:1.0115
 Max.   :1481287   Max.   :913.00   Max.   :791.923   Max.   :1.4989
```

Figure 3: Maps tab. Results correspond to the Ohio example.



Cluster	Central area	No. areas	Start date	End date	Risk in / Risk out	LLR	p-value	Areas
1	Hamilton	1	1983	1984	1.32	41.75818	1.23e-14	Hamilton
2	Cuyahoga	1	1983	1984	1.21	28.87297	1.04e-09	Cuyahoga
3	Belmont	5	1981	1982	1.30	10.54458	1.06e-02	Guernsey, Monroe, Harrison, Belmont, Jefferson

Showing 1 to 3 of 3 entries

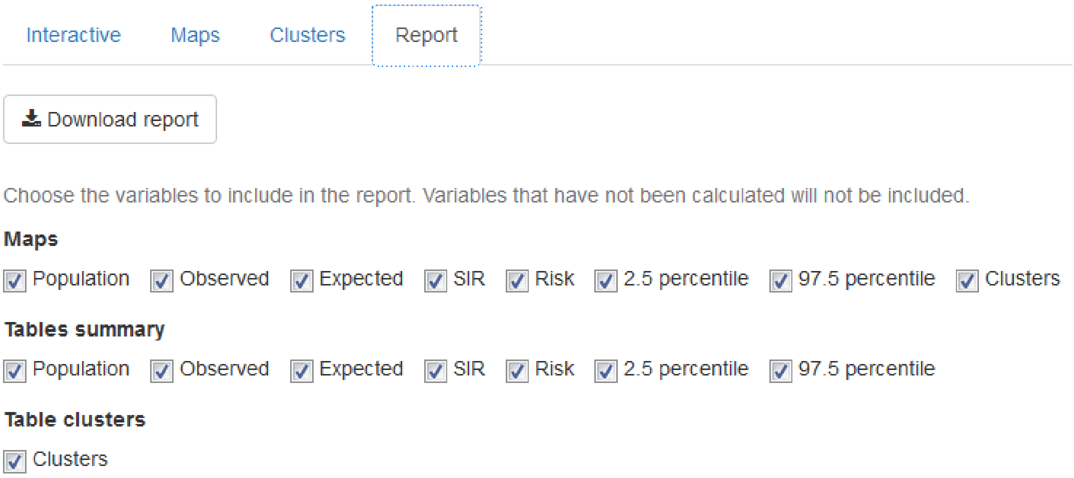
Figure 4: Clusters tab. Results correspond to the Ohio example.

included, the ratio of the risk inside over the risk outside, the log likelihood ratio and the significance.

Figure 4 shows the 'Clusters tab' corresponding to the Ohio data. There are 3 clusters detected. The most likely cluster consists of one area located in south west and encompasses years 1983 to 1984. The second cluster is one area located in the north in years 1983 to 1984. The last cluster is in the east and is composed of 5 areas in years 1981 to 1982.

3.2.4. Report tab

In the 'Report tab' we can download a PDF document showing the results of our analysis. The report includes maps and tables summarizing the variables population, observed, expected, SIR, risk, lower and upper limits of the 95% credible intervals and clusters for each of the periods of time. In this



Choose the variables to include in the report. Variables that have not been calculated will not be included.

Maps

☑ Population ☑ Observed ☑ Expected ☑ SIR ☑ Risk ☑ 2.5 percentile ☑ 97.5 percentile ☑ Clusters

Tables summary

☑ Population ☑ Observed ☑ Expected ☑ SIR ☑ Risk ☑ 2.5 percentile ☑ 97.5 percentile

Table clusters

☑ Clusters

Figure 5: Report tab.

tab there are several radio buttons that permit to choose the variables we want to include in the report. If the variables corresponding to risk or clusters are selected but the risk estimation or the detection of clusters analyses were not carried out, the report will be generated assuming these variables were not selected. Figure 5 shows the report tab where all the variables were selected. This generates a PDF document with all the analyses performed.

3.3. Help page

Both the 'Inputs' and the 'Analysis' pages include a 'Help' button that redirects to the 'Help' page. This page shows information about the use of the application, the statistiscal methodology and the developing tools employed.

4. Installation

SpatialEpiApp has been implemented in the R package SpatialEpiApp. Users can launch the application in R by installing the package and executing the following code:

```
library(SpatialEpiApp)
run_app()
```

To estimate risk the application uses the R-INLA package which can be downloaded from http://www.r-inla.org. Users wishing to perform clusters analyses need to download SaTScan from http://www.satscan.org and install it in their computer. They also need to place the SaTScanBatch64 executable in the SpatialEpiApp/SpatialEpiApp/ss folder which is located in the R library path.

Reports use the LaTeX typesetting system. Therefore, users need to have a TeX distribution such as MiKTex, http://miktex.org, or TeX Live, http://www.tug.org/texlive, and the pandoc document converter, http://pandoc.org, installed in their computer.

5. Conclusion

In this paper we presented SpatialEpiApp, a Shiny web application for the analysis of spatial and spatio-temporal disease data. The application is easy to use and allows health researchers to perform sophisticated surveillance analyses without the need of having advanced statistical or programming skills. Specifically, it allows to obtain disease risk estimates and their uncertainty by fitting Bayesian models with R-INLA, and to detect clusters by using SaTScan. It also serves as an exploratory tool for spatial and spatio-temporal disease data since it enables interactive visualization of maps and time series, and tables. SpatialEpiApp is an open-source tool which is implemented using R, Shiny and incorporating the functions from several R packages and statistical programs. Users wishing to publish the results obtained with the Bayesian disease mapping and detection of clusters analyses should provide the proper references to R-INLA and SaTScan, respectively.

Although the statistical methods SpatialEpiApp can perform are very common in surveillance, they are also restrictive. For example, the disease mapping models used are the model introduced by Besag et al. (1991) in the spatial case, and the model presented by Bernardinelli et al. (1995) in the spatio-temporal setting. In the detection of clusters analysis, SaTScan is used with determined options such as Poisson model and clusters with circular shape. Therefore, researchers that need to perform more complex analyses would need to resort to different statistical packages.

Despite these limitations, the methods implemented are very common in healh surveillance and we think SpatialEpiApp will be very useful for many researchers. Moreover, the application can be easily extended and in future versions we will increase its flexibility enabling more options for disease mapping and the detection of clusters, as well as custom data visualizations. Specifically, we will expand the type of analyses the application can perform so the user can choose among a wider range of models, incorporate covariates, include different types of spatial and temporal random effects, and choose among different shapes of clusters. Another extension will be the inclusion of statistical methods and visualizations for analysing point data. This will make the application useful for people wishing to analyze geostatistical or point process data.

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Appendix

Here, we give a brief summary of Shiny and explain the main components we used to implement `SpatialEpiApp` including control widgets, HTML widgets and R Markdown.

6.1. Shiny

Shiny is a web application framework for R that enables to build interactive web applications. Two R scripts are needed to create the application: an user-interface script called `ui.R` and a server script `server.R`. The user-interface script controls the layout and appearance of the application. The server script contains the R objects and the instructions about how they are displayed. Shiny applications use a functionality called reactivity to support interactivity. In this way, users can introduce texts, select dates or modify other inputs and automatically the R objects displayed will change.

Reactive objects can be created with the following steps. First, R objects are added to the user-interface. This is done by placing `*Output` functions that turn R objects into output in the `ui.R` script. Next, the R code that builds the objects is provided in `server.R`. This script contains an unnamed function with two list-like objects named output and input. Output contains all the instructions for building the R objects, and input stores the current values of the objects in the application. The objects are built by using a `render*` function and then saved in the output list. Reactivity is created by including an input value in a `render*` expression. For example, to create a reactive plot we need to add a `plotOutput` function in the `ui.R`. Then we use a `renderPlot` function to build the plot and add it to the output object in the `server.R` script.

To create Shiny applications there is not web development experience required, although it is possible to use HTML, CSS, or JavaScript to achieve greater flexibility and customization. Shiny applications can be run locally by users that have the application files and R installed in their computer. Applications can also be hosted as a web page at its own URL and can be navigated through the internet with a web browser. This facilitates its use to people without R knowledge. Examples of Shiny applications are provided in the gallery: `http://shiny.rstudio.com/gallery`.

6.2. Control widgets

`SpatialEpiApp` includes several control widgets users can interact with to send messages to the application. For example, in the 'Inputs' page we can upload the map and the data files by using a file upload control which is created by the `fileInput` function. In this page we can also specify the variables names by selecting the appropriate names from boxes containing the possible choices. These boxes are created with the `selectInput` function. The

'Inputs' page also includes a pair of calendars for selecting the analysis minimum and maximum dates that are created with the dateRangeInput function, and radio buttons that enable to specify the temporal unit in the data (year, month or day), and the type of analysis (spatial or spatio-temporal) that are created with the radioButtons function.

In the 'Analysis' page there is a slider bar created with the sliderInput function that allows to select a range of values by which we wish to filter the data. We also have the option to download tables with values and reports by clicking the corresponding download buttons that are created using the downloadButton function in ui.R and the downloadHandler function in server.R.

Finally, SpatialEpiApp includes some buttons that permit to switch between the 'Inputs', 'Analysis' and 'Help' pages, create plots, and carry out the statistical analyses. These buttons are created with the actionButton function.

6.3. HTML widgets

SpatialEpiApp includes three HTML widgets for interactive web data visualization, namely, leaflet for rendering maps (Cheng and Xie, 2016), dygraphs for plotting time series (Vanderkam et al., 2016), and DataTables for displaying data objects. HTML widgets are created with JavaScript libraries and embedded in Shiny by using the htmlwidgets package (Vaidyanathan et al., 2016).

leaflet is used to render maps depicting the values of the variables of interest in each of the areas. The created maps support interactive panning and zooming which is very convenient when the map contains small areas. dygraphs is used for showing the variables of interest over time. These plots include support for interactive features such as panning, zooming and series highlighting. DataTables is used to display interactive tables containing the information of the variables of interest. These tables support filtering, pagination, and sorting which is very helpful in situations where we wish to locate the information of one particular area or show the areas with the higher or lower values.

These three HTML widgets are included into the application by calling an output for the widget in the user-interface, and assigning a render call to the output on the server side in the same way as plotOutput and renderPlot functions work. leaflet uses leafletOutput and renderLeaflet, dygraphs dygraphOutput and renderDygraph, and DataTables dataTableOutput and renderDataTable.

6.4. R Markdown

The application allows the generation of reports in PDF format that include the results of the analyses performed. The reports are R Markdown documents (Allaire et al., 2016), that is, they are written in a plain text formatting syntax called markdown and include chunks of executable R code. They also include chunks of LaTeX code, http://www.latex-project.org. The reports are generated using the knitr package (Xie, 2015) which runs the R code and add the results of the code to the final document.

6.5. Dependencies

SpatialEpiApp is dependent on several statistical programs and R packages including SpatialEpi (Kim and Wakefield, 2016) for computing the internally indirect standardized expected disease cases; R-INLA (Lindgren and Rue, 2015) for performing Bayesian inference; SaTScan (Kulldorff, 2006a) for the detection of clusters; spdep (Bivand and Piras, 2015) for neighbourhood matrix manipulation; xts (Ryan and Ulrich, 2014) for creating time-series objects; and ggplot2 (Wickham, 2009) and maptools (Bivand and Lewin-Koh, 2016) for data visualisations. Information about all the dependencies is shown in Table 1.

Name		Description
Software		
R	(R Core Team, 2017)	Language and environment for statistical computing and graphics
`SaTScan`	(Kulldorff, 2006a)	Software that analyzes spatial, temporal and space-time data using scan statistics
R packages		
`dplyr`	(Wickham and Francois, 2016)	A fast, consistent tool for working with data frame like objects, both in memory and out of memory
`dygraphs`	(Vanderkam et al., 2016)	Interface to 'Dygraphs' Interactive Time Series Charting Library
`ggplot2`	(Wickham, 2009)	Creates elegant data visualisations using the grammar of graphics
`htmlwidgets`	(Vaidyanathan et al., 2016)	Provides a framework for easily creating R bindings to JavaScript libraries
`knitr`	(Xie, 2015)	Tool for dynamic report generation in R
`leaflet`	(Cheng and Xie, 2016)	Create Interactive Web Maps with the JavaScript 'Leaflet' Library
`mapproj`	(McIlroy et al., 2015)	Converts latitute/longitude into projected coordinates
`maptools`	(Bivand and Lewin-Koh, 2016)	Set of tools for manipulating and reading geographic data, in particular ESRI shapefiles
`RColorBrewer`	(Neuwirth, 2014)	Provides color schemes for maps and other graphics
`rgdal`	(Bivand et al., 2016)	Provides bindings for the Geospatial Data Abstraction Library (GDAL)
`rgeos`	(Bivand and Rundel, 2016)	Interface to Geometry Engine - Open Source (GEOS) using the C API for topology operations on geometries
`rmarkdown`	(Allaire et al., 2016)	Convert R Markdown documents into a variety of formats including HTML, MS Word, PDF, and Beamer
`R-INLA`	(Lindgren and Rue, 2015)	Performs full Bayesian analysis on generalised additive mixed models using Integrated Nested Laplace Approximations
`shiny`	(Chang et al., 2016)	Web Application Framework for R
`shinyjs`	(Attali, 2016)	Perform common useful JavaScript operations in Shiny apps that will greatly improve the apps without having to know any JavaScript
`sp`	(Pebesma et al., 2016)	Classes and Methods for Spatial Data
`SpatialEpi`	(Kim and Wakefield, 2016)	Contains methods for cluster detection, disease mapping and plotting methods
`spdep`	(Bivand and Piras, 2015)	Contains a collection of functions for spatial dependence: weighting schemes, statistics and models
`xts`	(Ryan and Ulrich, 2014)	Extensible time series class and methods

Table 1: Software and R packages used to develop `SpatialEpiApp`.