Supplementary Materials

Application of Epidemiological Geographic Information System: An Open-Source Spatial Analysis Tool Based on the OMOP Common Data Model

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Supplementary Methods S1: Statistical method in AEGIS

Expected count

In AEGIS, the expected count is used several statistical calculations. Specifically,

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

$r_j^{(s)}$ is the rate in stratum j in the incidence rate on indirect standardized population for age and sex of all patients included in the target cohort

n_j is the population in stratum j of the administrative district.

Standardized Incidence Ratio (SIR)

The disease risk is estimated by the SIR, which is calculated as the ratio of the observed number of outcomes to the expected counts:

$$SIR_i = \frac{Y_i}{E_i}, \tag{2}$$

Y_i is the case of the outcome in administrative district $\mathrm{i} = 1 \cdots \mathrm{N}$

E_i is expected counts of the outcome in administrative district.

Proportion

The proportion indicates the number of patient outcomes per n population in the administrative district. The fraction is used as a parameter to represent the value of the proportion.

$$Proportion_i = \left(\frac{Y_i}{\sum_{j=1}^{m} n_j} SIR_i\right) fraction \tag{3}$$

Scan Statistics

AEGIS supports to identify clusters by Kulldorff's scan statistics. This method scans an unusual number of cases, expanding a myriad of windows in the area of interest. Generally, a circle that does not contain more than 50% of the total number of patients in the target cohorts is detected using a window whose radius increases continuously from zero to the upper limit. Then, a likelihood ratio test is used to assess the occurrence of clusters statistically. The scan statistics method can assess disease occurrences and social inequalities in health quantitatively by detecting areas where adverse outcomes are concentrated. For the clustering results, *p*-value <0.05 was considered significant. Conditioning on the observed total number of outcomes C, the likelihood ratio of S is the expressed as

$$\mathrm{S} = max_Z \frac{L(Z)}{L_0}, \tag{4}$$

Z is the overall window

$\mathrm{L(Z)}$ is the likelihood for window Z

L_0 is a likelihood function under the null hypothesis that the probability inside Z is the same as the probability outside Z

$$\frac{L(Z)}{L_0} = (\frac{c}{E(Z)})^c (\frac{C-c}{C-E(Z)})^{C-c},$$

Bayesian mapping

To estimate disease risk in relatively poorly informed areas, the AEGIS uses the Besag-York-Molli é (BYM) model, which is a well-established method to estimate areas with a small sample size. Specifically,

$$Y_i \sim Poisson(E_i \lambda_i), i = 1, \cdots N;$$
$$\log(\lambda_i) = X_i \beta + U_i$$
$$U_i \sim BYM(\sigma_1^2, \sigma_2^2),$$

X_i are covariates

U_i is a spatial random effect. σ_1^2 is a spatially structured variance parameter and σ_2^2 is a spatially independent variance.

The R-INLA package was used for Bayesian calculations for small area estimation.

Global Moran's I

Global Moran's I representing the overall spatial autocorrelation of the area covered by the study. The values range from −1 (indicating dispersed distribution) to 1 (perfect clustering together). A value of 0 for indicates no autocorrelation. Global Moran's I is the expressed as

$$\mathrm{I} = \frac{n \sum_{i=1}^{n} \sum_{j=1}^{n} \omega_{ij} (x_i - \bar{x})(x_j - \bar{x})}{(\sum_{i=1}^{n} \sum_{j=1}^{n} \omega_{ij}) \sum_{i=1}^{n} (x_i - \bar{x})^2}$$

x_i is the attribute value of the I'th object

n is the number of objects

ω_{ij} is the weight of the commination i, j

Local Moran's **I**

AEGIS calculates regional autocorrelation between individual regions using the Local Indicators of Spatial Association (LISA) method to identify clusters Specifically,.

$$I_i = \frac{(x_i - \bar{x})}{S_x} \sum_{j \neq i}^{n} \omega_{ij} \frac{(x_j - \bar{x})}{S_x},$$

$$S_x = \sqrt{\frac{\sum_{i=1}^{n} (x_i - \bar{x})^2}{n-1}},$$

n is represents the number of unit areas

where, ω_{ij} is a spatial weight for judging whether 'spatial adjacency' is in the unit area i and j, and a space weight value is given based on whether the boundary between the two unit areas is shared. In other words, $\omega_{ij} = 1$ if unit i and j share a boundary, otherwise $\omega_{ij} = 0$.

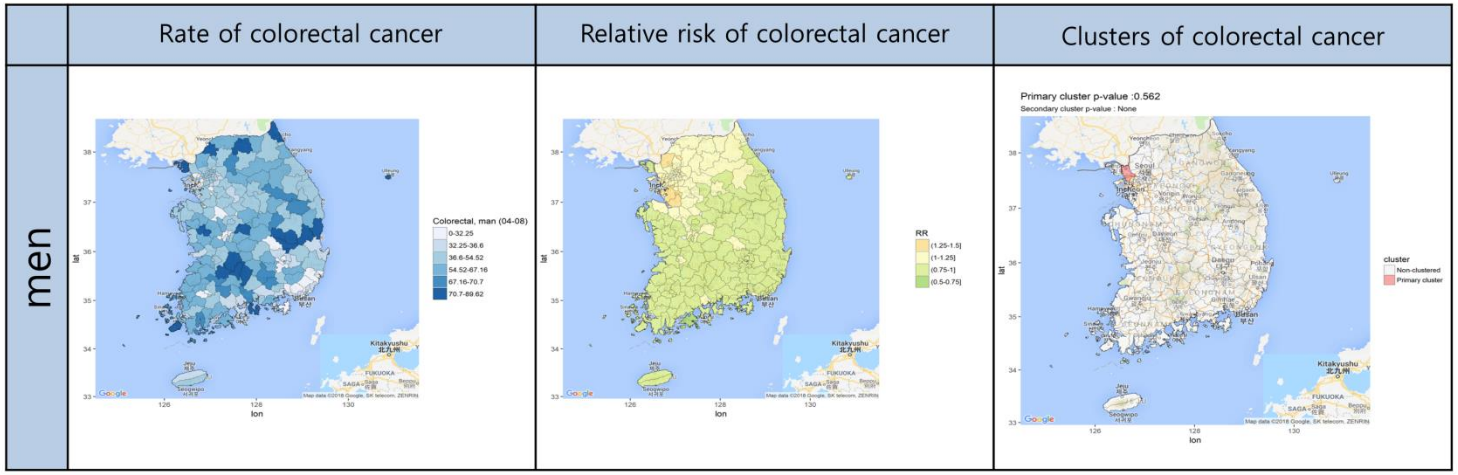
Supplementary Table S1. Comparison of the estimated major cancer incidences (age adjusted) from AEGIS with the findings of relevant published reports.

Cancer site	Classification	National incidences (cases per 100,000 persons)					
		2004–2008			2009–2013		
		AEGIS	Statistics Korea[a]	Won et al.	AEGIS	Statistics Korea[b]	Won et al.
Colorectal							
	Men	47.2 [31.8−66.6]	47.6	44.3	61.8 [41.7−86.9]	69.5	50.8
	Women	33.3 [22.2−47.2]	33.7	24.8	44.5 [29.1−64.4]	44.5	27.4
Liver							
	Men	48.9 [31.3−72.3]	45.9	42.3	46.4 [32.6−63.8]	49.3	36.8
	Women	17.4 [10.3−26.9]	15.4	11.4	18.5 [12.2−26.2]	17.4	10.2
Lung							
	Men	59.6 [42−81.8]	51.7	50.1	62.9 [47.5−80.6]	61.5	46.6
	Women	20.5 [13.5−28.9]	20.7	14.3	25.1 [13.6−41.4]	26.9	15.4
Stomach							
	Men	67.4 [47.8−91.8]	72.4	66.5	73.4 [52.5−99.2]	85.8	63.0
	Women	33.6 [23.9−45.4]	35.7	27.3	34.1 [26.9−42]	41.6	26.3
Thyroid							
	Men	8.6 [3.1−18.5]	9.5	9.8	24.8 [12.2−43.9]	28.3	24.3
	Women	52.1 [29.6−83.8]	56.6	55.2	104.9 [65.8−156.9)]	136.4	110.6
Breast							
	Men	-	-		-	-	
	Women	33.2 [23.3−45.0]	44.6	39.0	44.9 [26.1−70.9]	64.3	49.5
Prostate							
	Men	20.7 [11−34.6]	18.4	19.0	28.0 [15.3−45.9]	36.2	26.5
	Women	-	-		-	-	

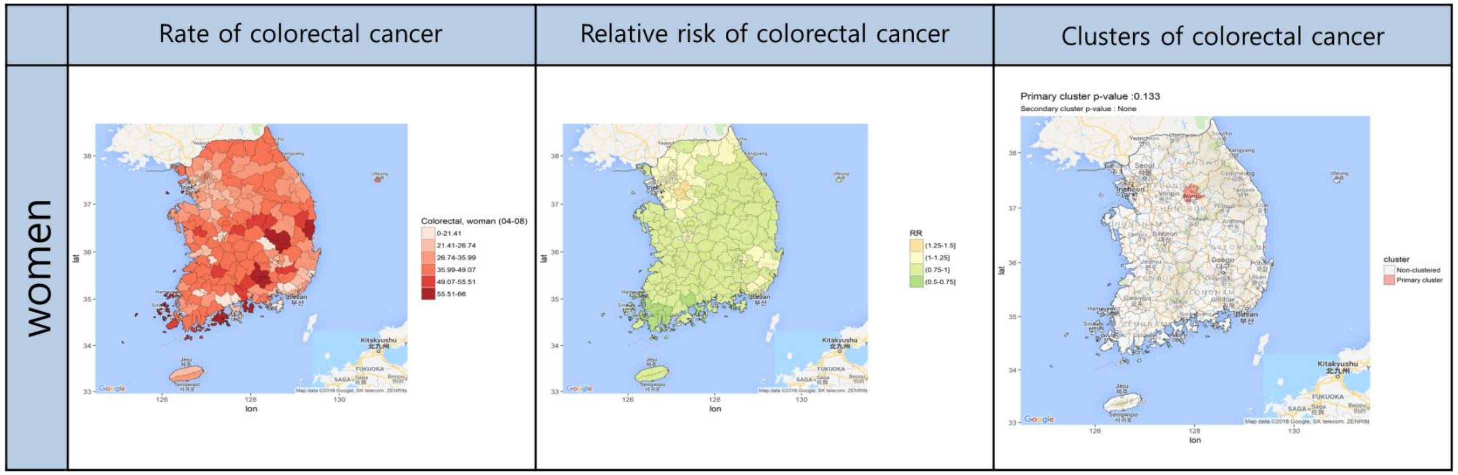
All cancer incidence reported by Statistics Korea is within the 95% CI range of all cancer incidence estimated by AEGIS. In addition, the trend of increasing or decreasing the incidence of cancer between the two periods (2004–2008 and 2009–2013) except male liver cancer incidence is the same as the one estimated by AEGIS and the one published by Statistics Korea. Geographical variations of major cancer incidence generated by AEGIS were similar to regional cancer incidence rates reported by the Statistics Korea and Won et al (*Won Y, Jung K, Oh C, Kong H, Lee DH, Lee KH. Geographical Variations and Trends in Major Cancer Incidences throughout Korea during 1999-2013. 2018;50(4):1281–1293.).* Even in case of studies that denote the same research objective and data, differences in incidence may occur; further, AEGIS has often been able to estimate intermediate results.

Supplementary Figure S1: County-level age-adjusted geographical variation in incidence and mortality of major cancers in Korea.

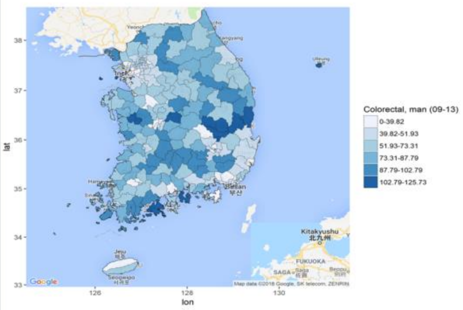
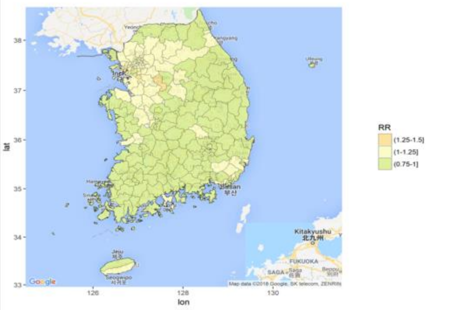
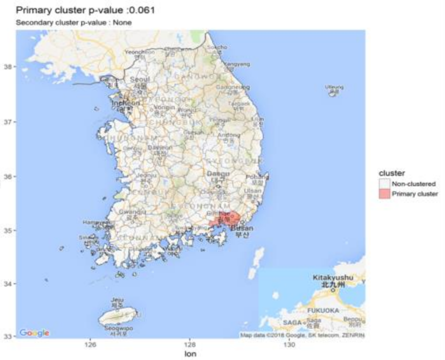
Age-standardized rate, relative risk and clustering of colorectal cancer incidence, men, 2004-2008



Age-standardized rate, relative risk and clustering of colorectal cancer incidence, women, 2004-2008

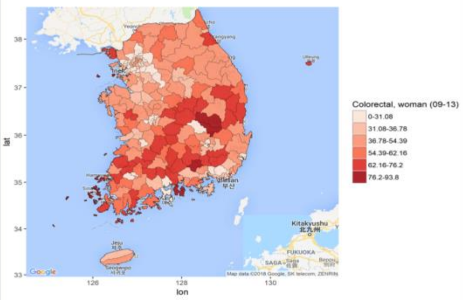
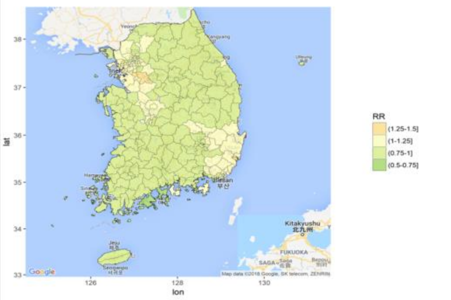
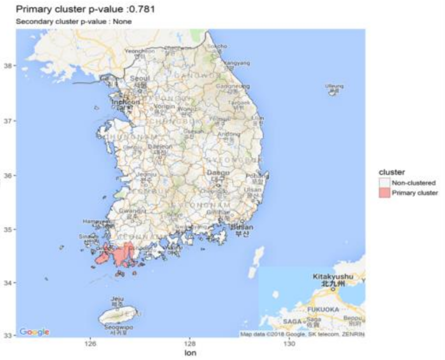

Rate of colorectal cancer
Relative risk of colorectal cancer
Clusters of colorectal cancer
women
Colorectal, woman (04-08)
0-21.41
21.41-26.74
26.74-35.99
35.99-49.07
49.07-55.51
55.51-66
RR
(1.25-1.5]
(1-1.25]
(0.75-1]
(0.5-0.75]
Primary cluster p-value :0.133
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon

Age-standardized rate, relative risk and clustering of colorectal cancer incidence, men, 2009-2013

	Rate of colorectal cancer	Relative risk of colorectal cancer	Clusters of colorectal cancer
men			

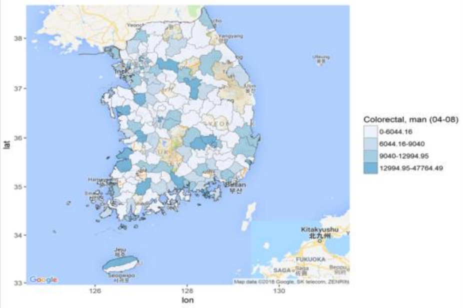
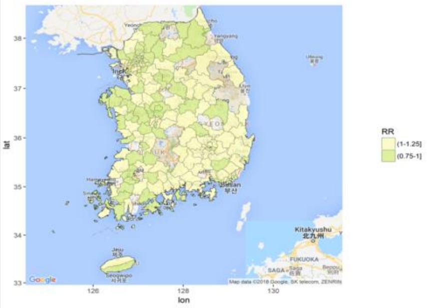
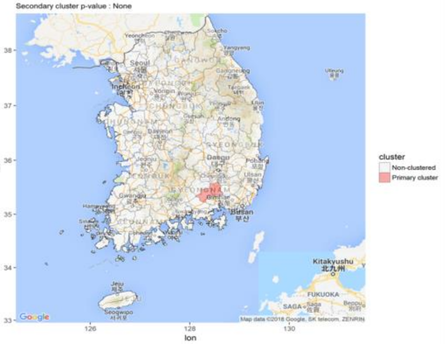
Primary cluster p-value :0.061
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon

Age-standardized rate, relative risk and clustering of colorectal cancer incidence, women, 2009-2013

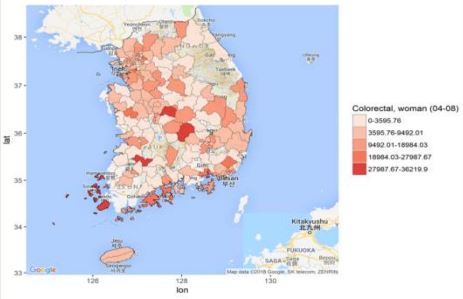
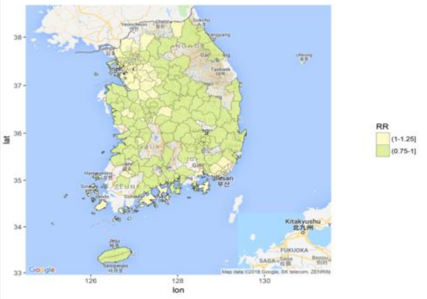
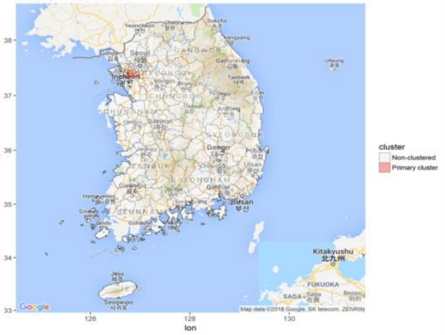
	Rate of colorectal cancer	Relative risk of colorectal cancer	Clusters of colorectal cancer
women			

Primary cluster p-value :0.781
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon

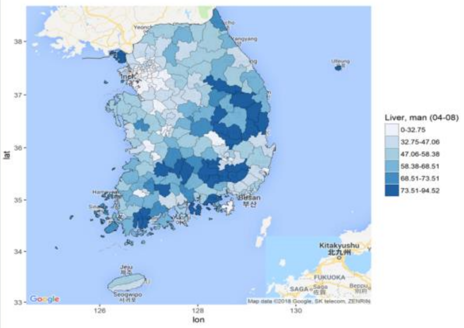
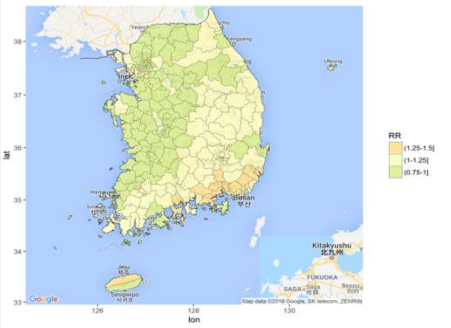
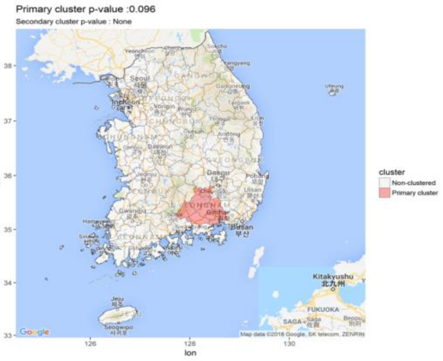
Age-standardized rate, relative risk and clustering of colorectal cancer mortality, men, 2004-2008

	Rate of colorectal cancer	Relative risk of colorectal cancer	Clusters of colorectal cancer
men	 Colorectal, man (04-08) 0-6044.16 6044.16-9040 9040-12994.95 12994.95-47764.49 lat lon		Primary cluster p-value :0.968 Secondary cluster p-value : None 

Age-standardized rate, relative risk and clustering of colorectal cancer mortality, women, 2004-2008

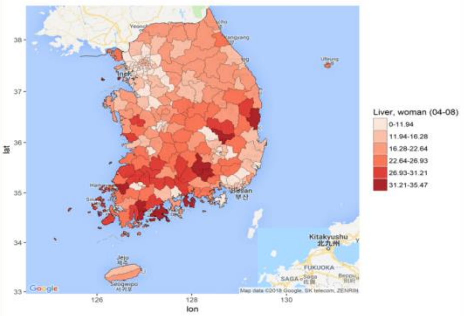
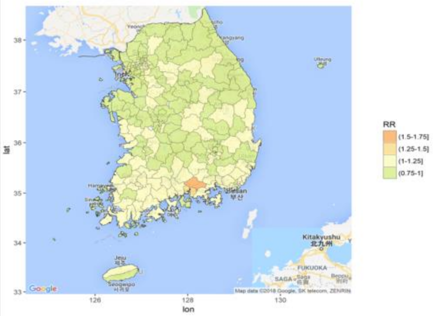
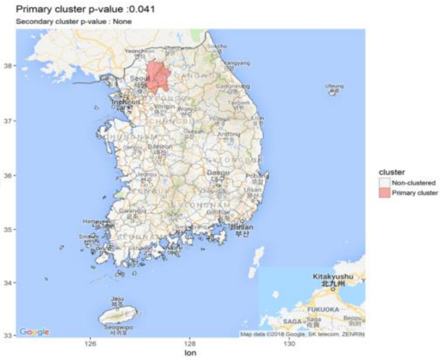
	Rate of colorectal cancer	Relative risk of colorectal cancer	Clusters of colorectal cancer
women	 Colorectal, woman (04-08) 0-3595.76 3595.76-9492.01 9492.01-18984.03 18984.03-27987.67 27987.67-36219.9 lat lon		Primary cluster p-value :0.992 Secondary cluster p-value : None 

Age-standardized rate, relative risk and clustering of liver cancer incidence, men, 2004-2008

	Rate of liver cancer	Relative risk of liver cancer	Clusters of liver cancer
men			

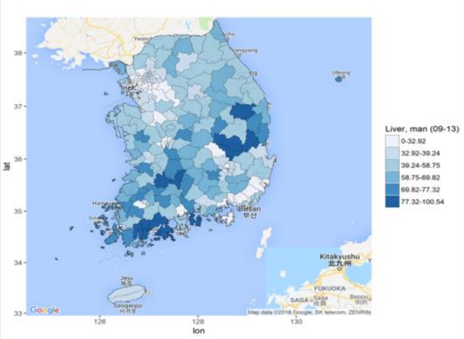
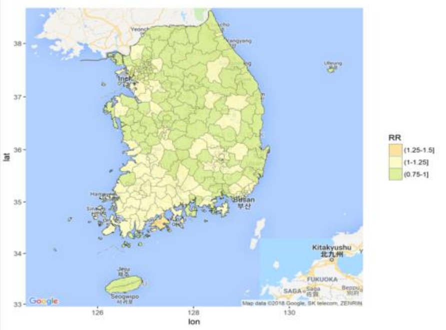
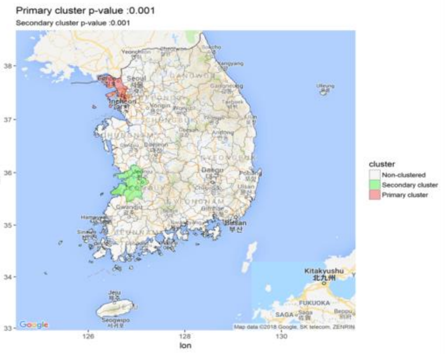
Primary cluster p-value :0.096
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon

Age-standardized rate, relative risk and clustering of liver cancer incidence, women, 2004-2008

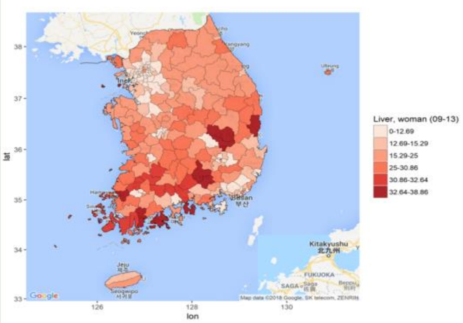
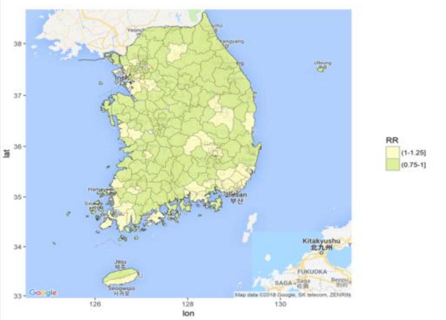
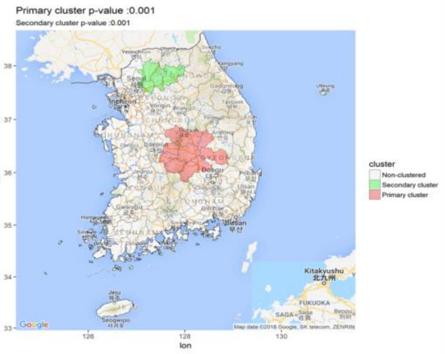
	Rate of liver cancer	Relative risk of liver cancer	Clusters of liver cancer
women			

Primary cluster p-value :0.041
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon

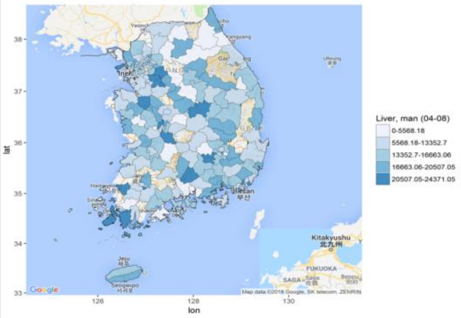
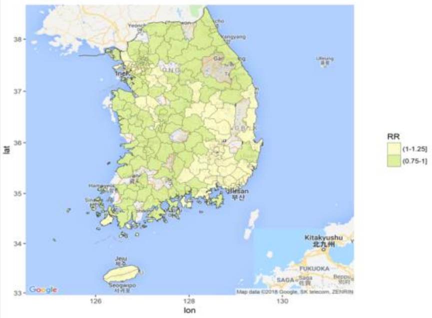
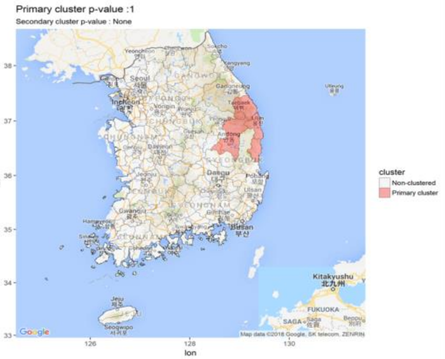
Age-standardized rate, relative risk and clustering of liver cancer incidence, men, 2009-2013

	Rate of liver cancer	Relative risk of liver cancer	Clusters of liver cancer
men			

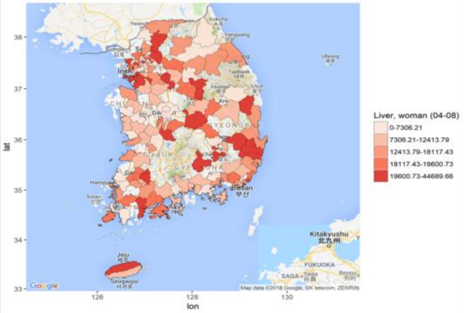
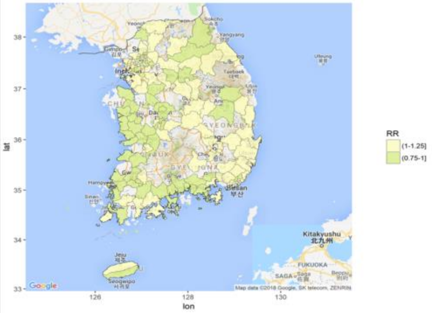
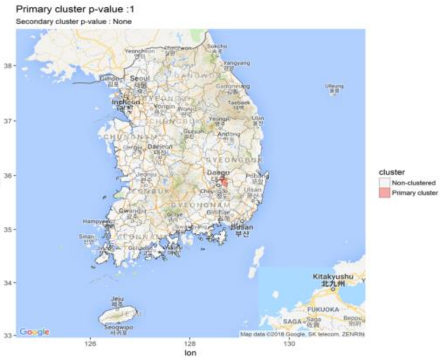
Age-standardized rate, relative risk and clustering of liver cancer incidence, women, 2009-2013

	Rate of liver cancer	Relative risk of liver cancer	Clusters of liver cancer
women			

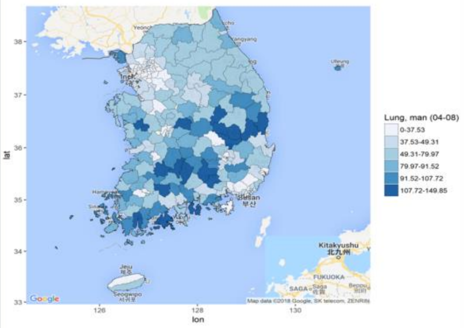
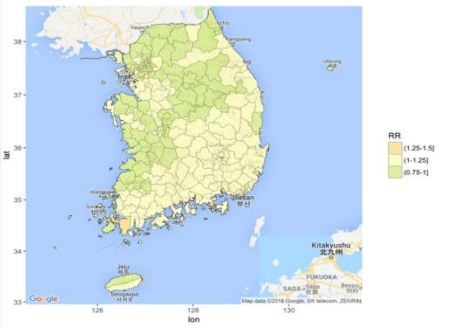
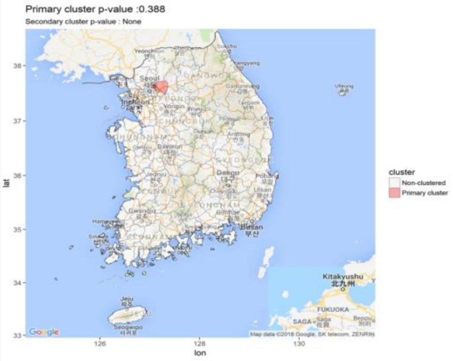
Age-standardized rate, relative risk and clustering of liver cancer mortality, men, 2004-2008

	Rate of liver cancer	Relative risk of liver cancer	Clusters of liver cancer
men	 Liver, man (04-08) 0-5568.18 5568.18-13352.7 13352.7-16663.06 16663.06-20507.05 20507.05-24371.05 lat lon		 Primary cluster p-value :1 Secondary cluster p-value : None cluster Non-clustered Primary cluster lat lon

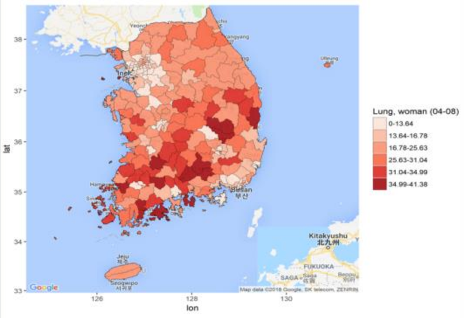
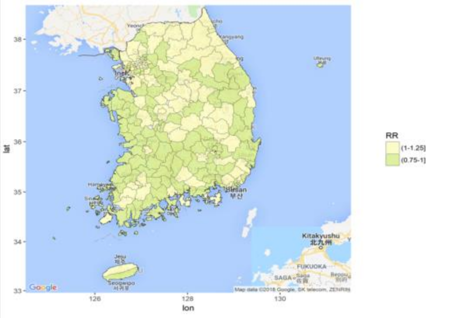
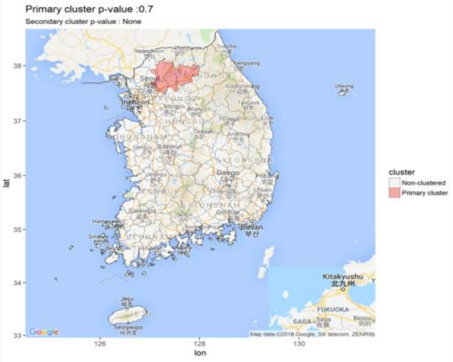
Age-standardized rate, relative risk and clustering of liver cancer mortality, women, 2004-2008

	Rate of liver cancer	Relative risk of liver cancer	Clusters of liver cancer
women	 Liver, woman (04-08) 0-7306.21 7306.21-12413.79 12413.79-18117.43 18117.43-19600.73 19600.73-44689.66 lat lon		 Primary cluster p-value :1 Secondary cluster p-value : None cluster Non-clustered Primary cluster lat lon

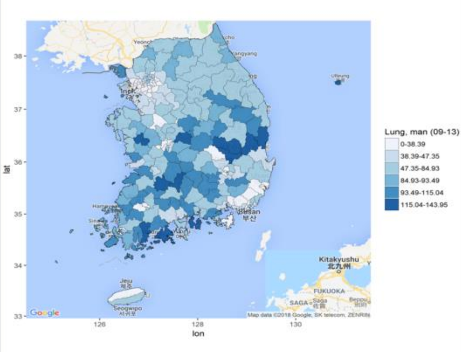
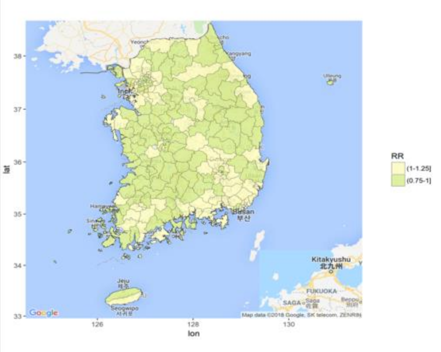
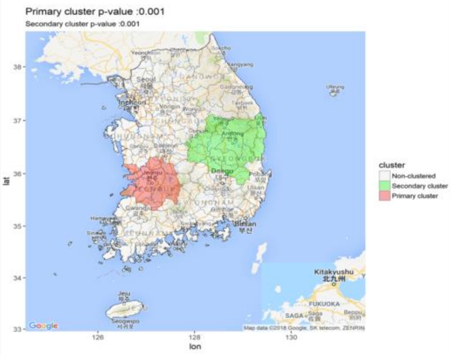
Age-standardized rate, relative risk and clustering of lung cancer incidence, men, 2004-2008

	Rate of lung cancer	Relative risk of lung cancer	Clusters of lung cancer
men			

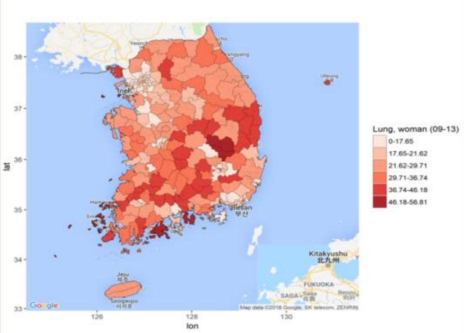
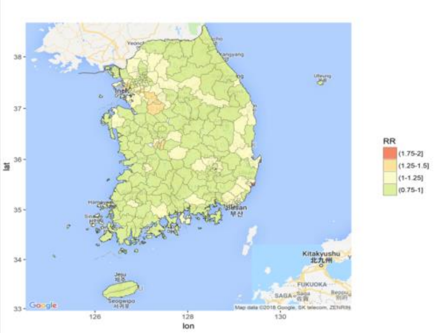
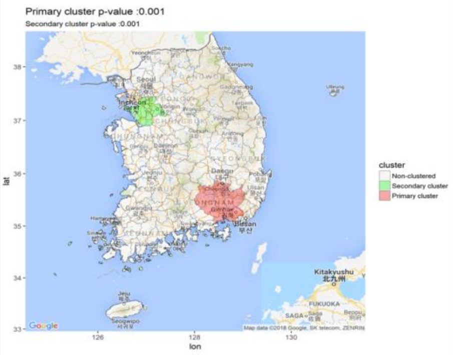
Age-standardized rate, relative risk and clustering of lung cancer incidence, women, 2004-2008

	Rate of lung cancer	Relative risk of lung cancer	Clusters of lung cancer
women			

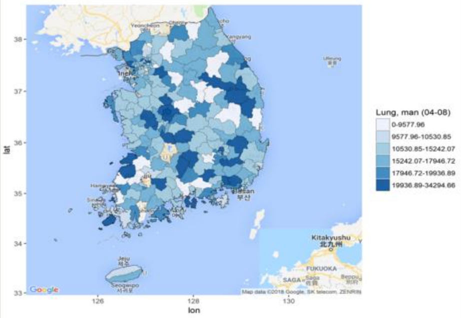
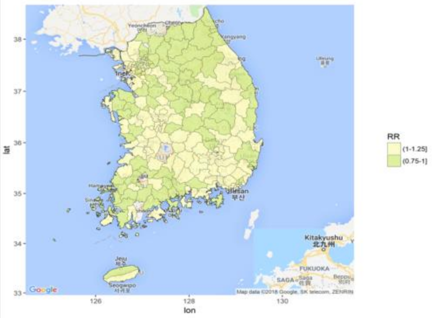
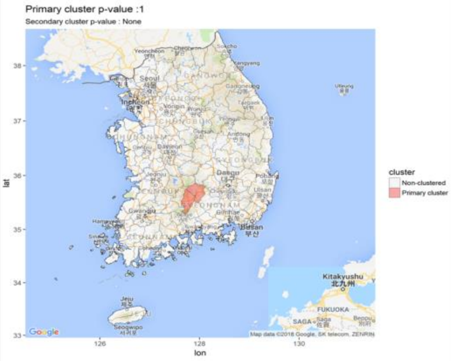
Age-standardized rate, relative risk and clustering of lung cancer incidence, men, 2009-2013

	Rate of lung cancer	Relative risk of lung cancer	Clusters of lung cancer
men	 Lung, man (09-13) 0-38.39 38.39-47.35 47.35-84.93 84.93-93.49 93.49-115.04 115.04-143.95 lat lon		 Primary cluster p-value :0.001 Secondary cluster p-value :0.001 cluster Non-clustered Secondary cluster Primary cluster lat lon

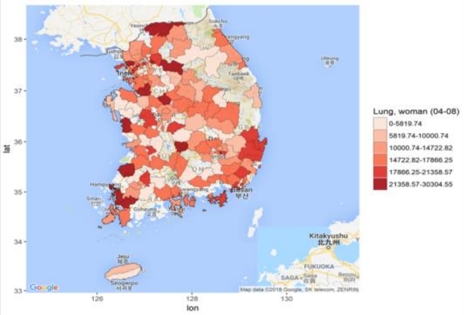
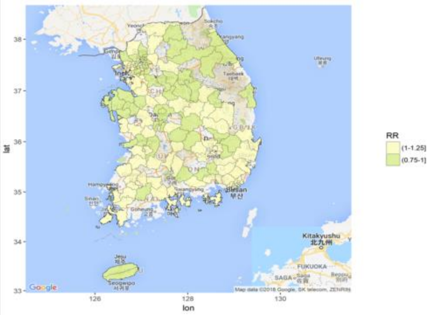
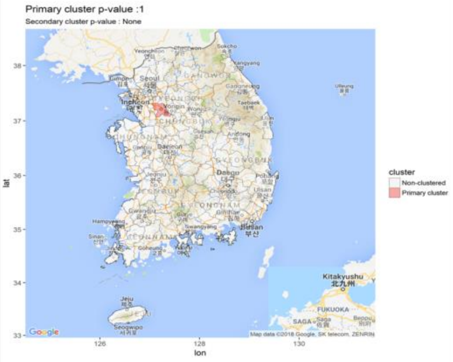
Age-standardized rate, relative risk and clustering of lung cancer incidence, women, 2009-2013

	Rate of lung cancer	Relative risk of lung cancer	Clusters of lung cancer
women	 Lung, woman (09-13) 0-17.65 17.65-21.62 21.62-29.71 29.71-36.74 36.74-46.18 46.18-56.81 lat lon	 RR (1.75-2] (1.25-1.5] (1-1.25] (0.75-1] lat lon	 Primary cluster p-value :0.001 Secondary cluster p-value :0.001 cluster Non-clustered Secondary cluster Primary cluster lat lon

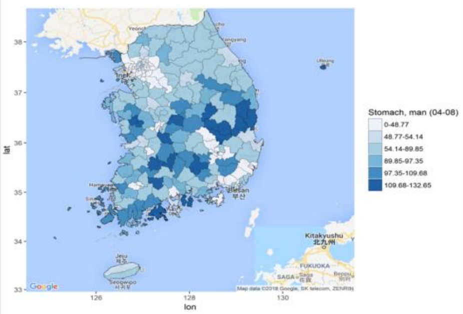
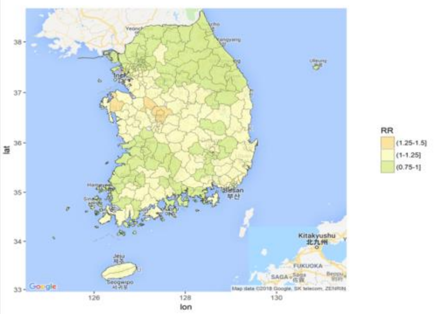
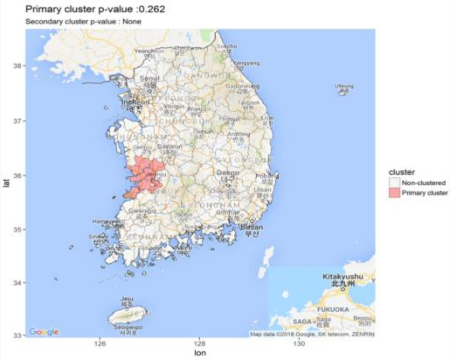
Age-standardized rate, relative risk and clustering of lung cancer mortality, men, 2004-2008

	Rate of lung cancer	Relative risk of lung cancer	Clusters of lung cancer
men			

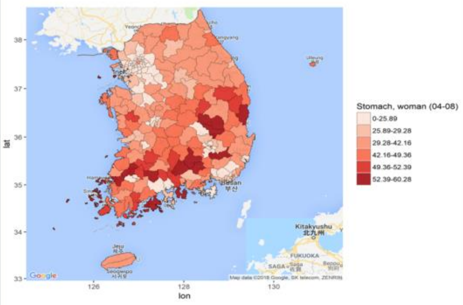
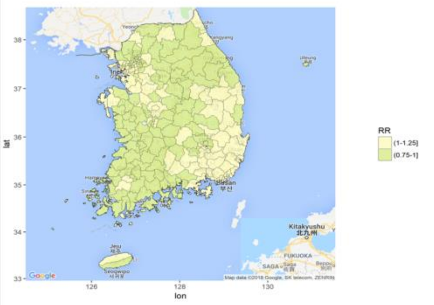
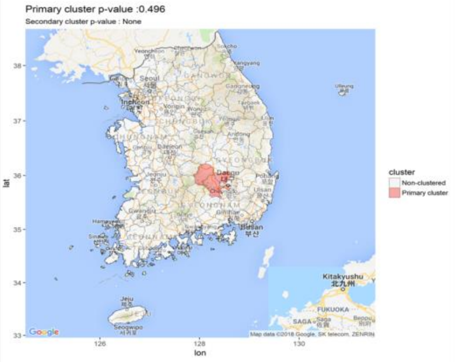
Age-standardized rate, relative risk and clustering of lung cancer mortality, women, 2004-2008

	Rate of lung cancer	Relative risk of lung cancer	Clusters of lung cancer
women			

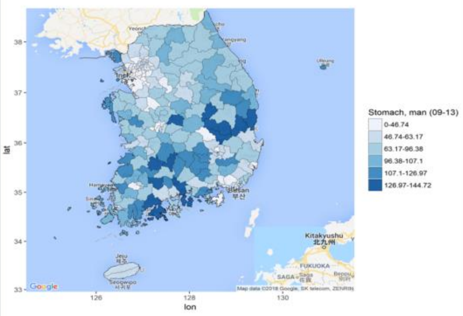
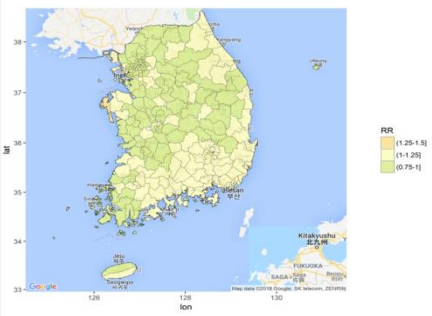
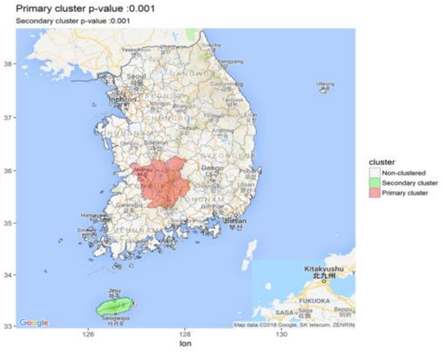
Age-standardized rate, relative risk and clustering of stomach cancer incidence, men, 2004-2008

	Rate of stomach cancer	Relative risk of stomach cancer	Clusters of stomach cancer
men			

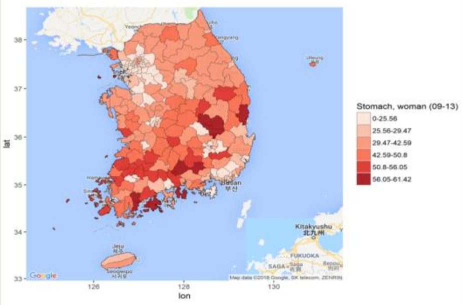
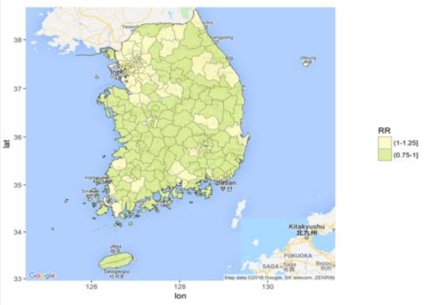
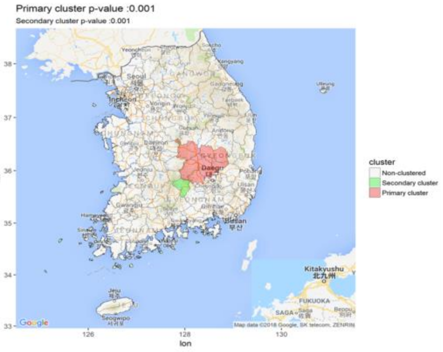
Age-standardized rate, relative risk and clustering of stomach cancer incidence, women, 2004-2008

	Rate of stomach cancer	Relative risk of stomach cancer	Clusters of stomach cancer
women			

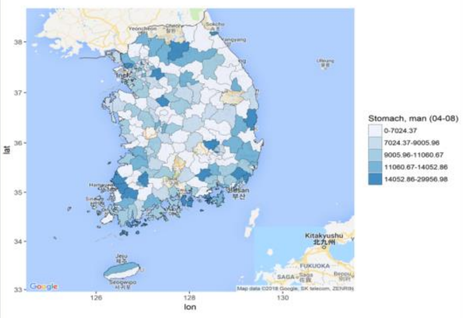
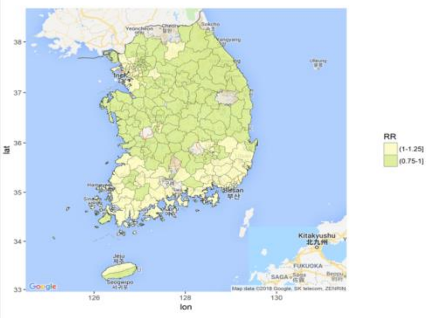
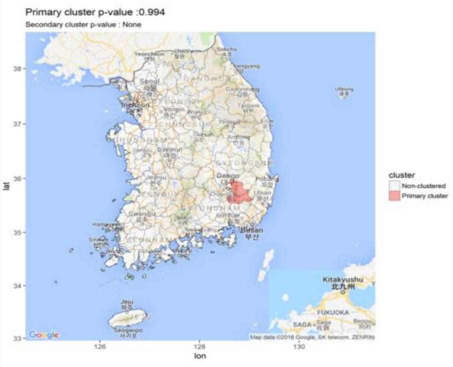
Age-standardized rate, relative risk and clustering of stomach cancer incidence, men, 2009-2013

	Rate of stomach cancer	Relative risk of stomach cancer	Clusters of stomach cancer
men			

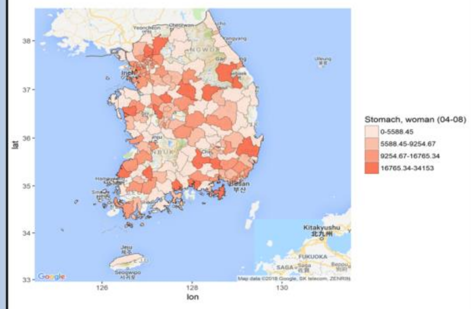
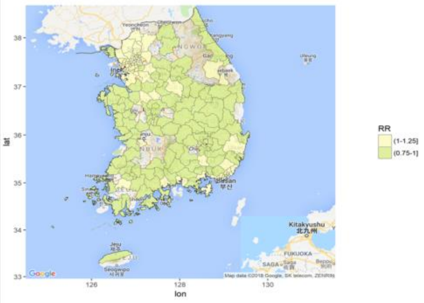
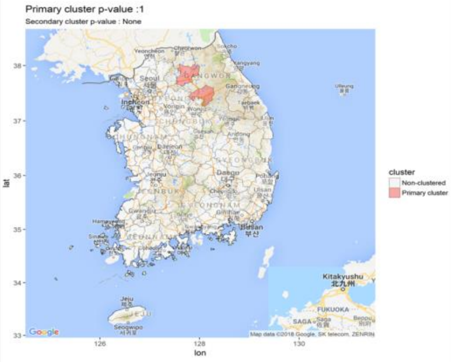
Age-standardized rate, relative risk and clustering of stomach cancer incidence, women, 2009-2013

	Rate of stomach cancer	Relative risk of stomach cancer	Clusters of stomach cancer
women			

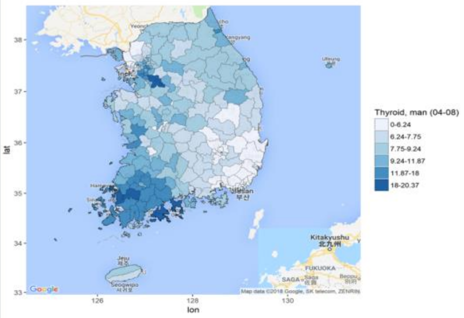
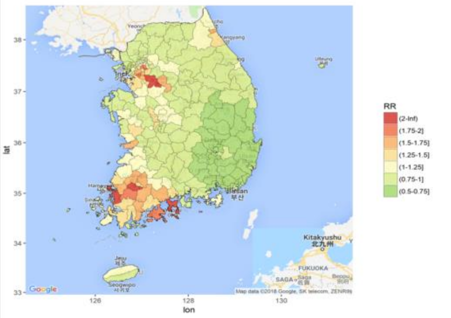
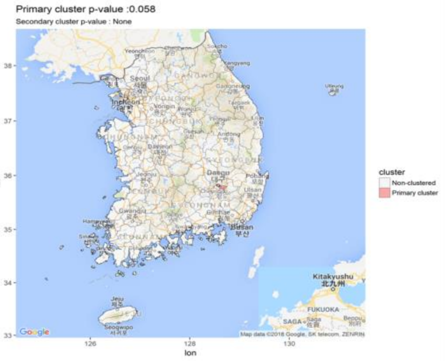
Age-standardized rate, relative risk and clustering of stomach cancer mortality, men, 2004-2008

	Rate of stomach cancer	Relative risk of stomach cancer	Clusters of stomach cancer
men			

Age-standardized rate, relative risk and clustering of stomach cancer mortality, women, 2004-2008

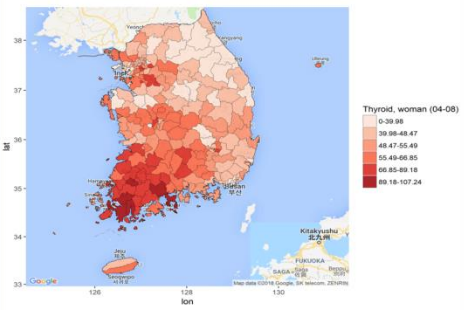
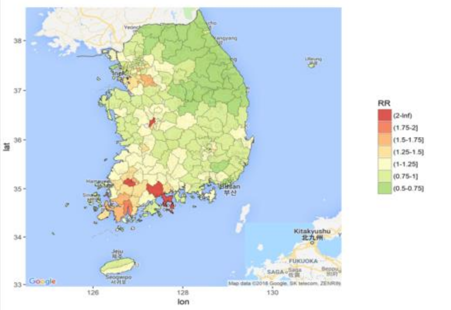
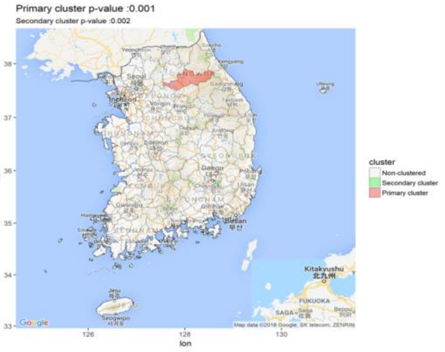
	Rate of stomach cancer	Relative risk of stomach cancer	Clusters of stomach cancer
women			

Age-standardized rate, relative risk and clustering of thyroid cancer incidence, men, 2004-2008

	Rate of thyroid cancer	Relative risk of thyroid cancer	Clusters of thyroid cancer
men			

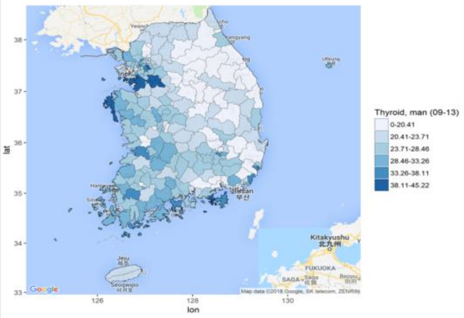
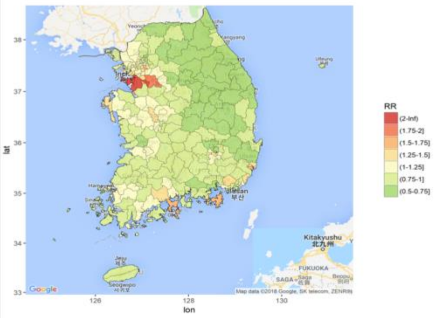
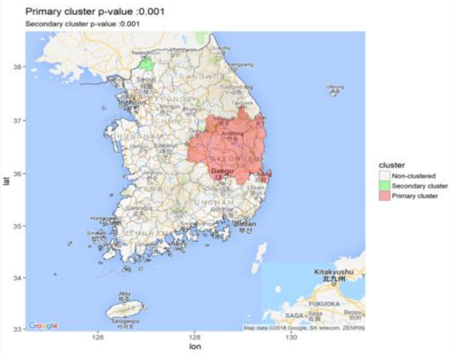
Primary cluster p-value :0.058
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon

Age-standardized rate, relative risk and clustering of thyroid cancer incidence, women, 2004-2008

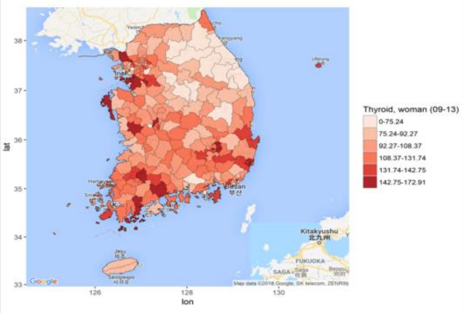
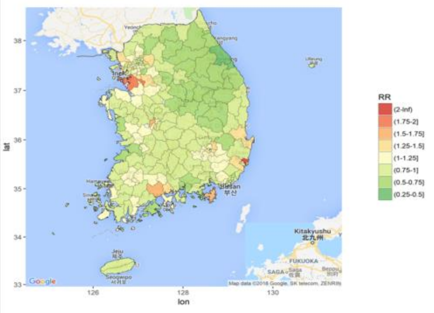
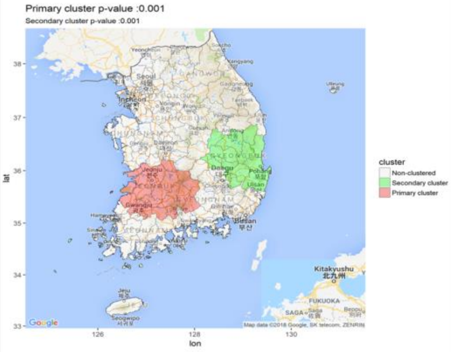
	Rate of thyroid cancer	Relative risk of thyroid cancer	Clusters of thyroid cancer
women			

Primary cluster p-value :0.001
Secondary cluster p-value :0.002
cluster
Non-clustered
Secondary cluster
Primary cluster
lat
lon

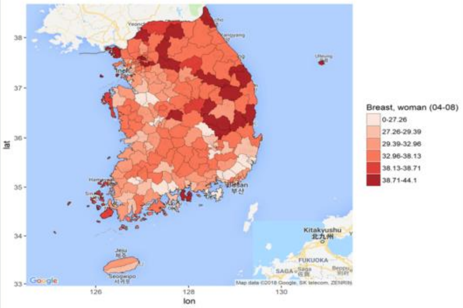
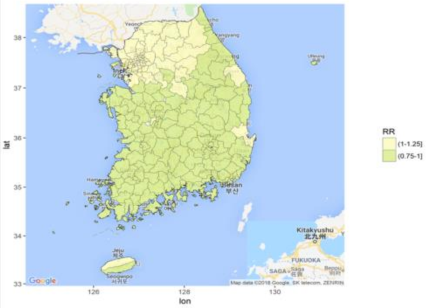
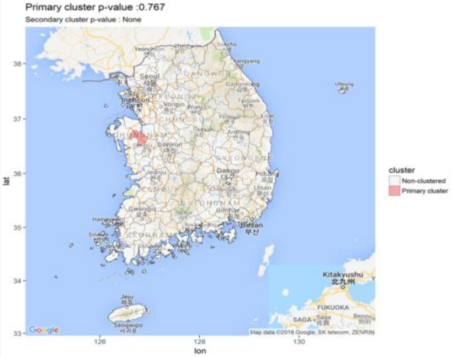
Age-standardized rate, relative risk and clustering of thyroid cancer incidence, men, 2009-2013

	Rate of thyroid cancer	Relative risk of thyroid cancer	Clusters of thyroid cancer
men			

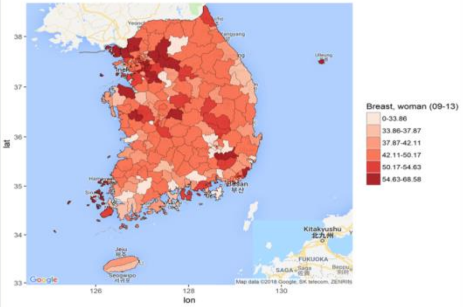
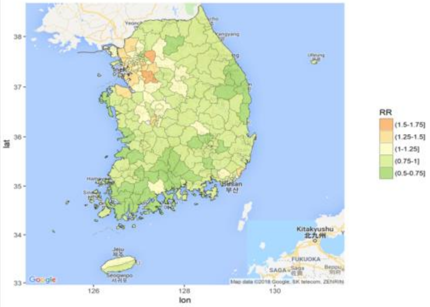
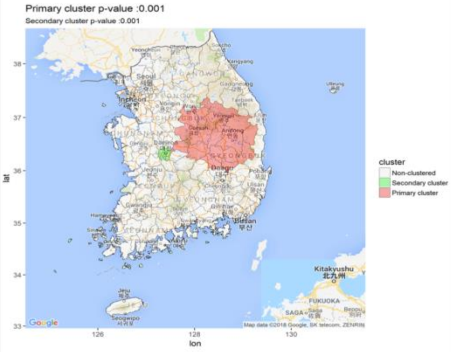
Age-standardized rate, relative risk and clustering of thyroid cancer incidence, women, 2009-2013

	Rate of thyroid cancer	Relative risk of thyroid cancer	Clusters of thyroid cancer
women			

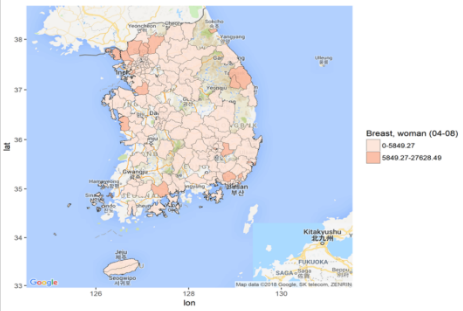
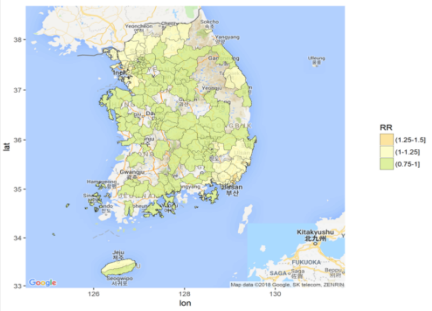
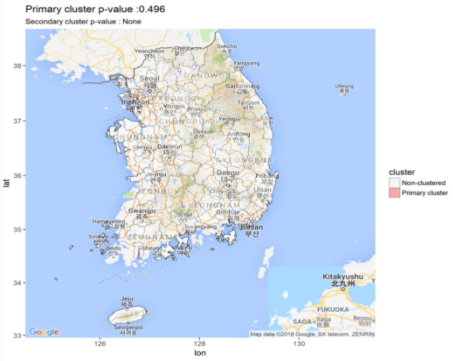
Age-standardized rate, relative risk and clustering of breast cancer incidence, women, 2004-2008

	Rate of breast cancer	Relative risk of breast cancer	Clusters of breast cancer
women	 Breast, woman (04-08) 0-27.26 27.26-29.39 29.39-32.96 32.96-38.13 38.13-38.71 38.71-44.1 lat lon 126 128 130 33 34 35 36 37 38	 RR (1-1.25] (0.75-1] lat lon 126 128 130 33 34 35 36 37 38	 Primary cluster p-value :0.767 Secondary cluster p-value : None cluster Non-clustered Primary cluster lat lon 126 128 130 33 34 35 36 37 38

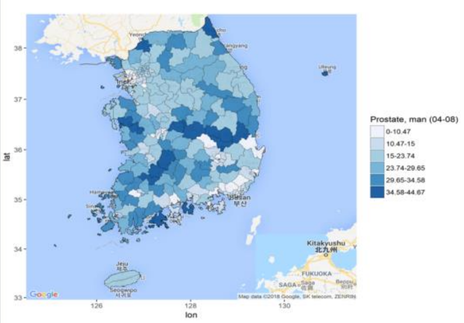
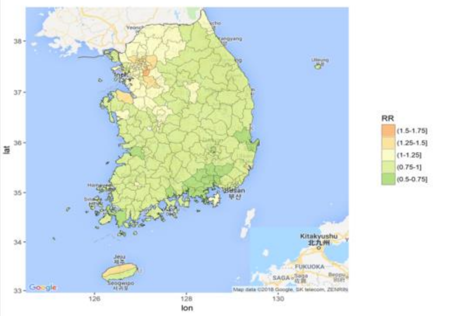
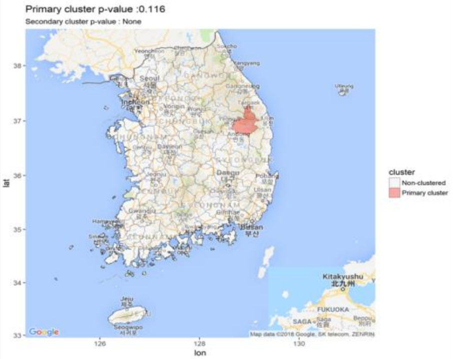
Age-standardized rate, relative risk and clustering of breast cancer incidence, women, 2009-2013

	Rate of breast cancer	Relative risk of breast cancer	Clusters of breast cancer
women	 Breast, woman (09-13) 0-33.86 33.86-37.87 37.87-42.11 42.11-50.17 50.17-54.63 54.63-68.58 lat lon 126 128 130 33 34 35 36 37 38	 RR (1.5-1.75] (1.25-1.5] (1-1.25] (0.75-1] (0.5-0.75] lat lon 126 128 130 33 34 35 36 37 38	 Primary cluster p-value :0.001 Secondary cluster p-value :0.001 cluster Non-clustered Secondary cluster Primary cluster lat lon 126 128 130 33 34 35 36 37 38

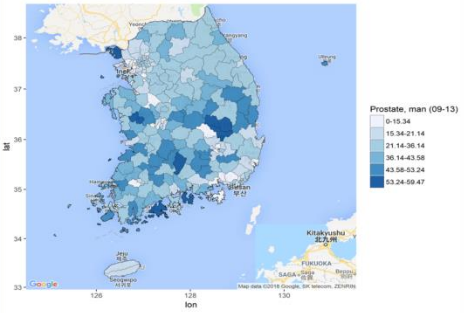
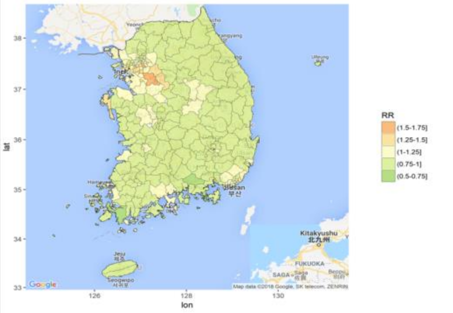
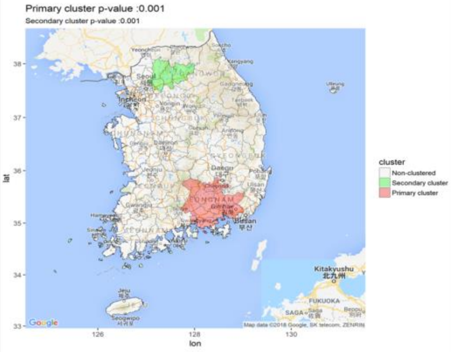
Age-standardized rate, relative risk and clustering of breast cancer mortality, women, 2004-2008

	Rate of breast cancer	Relative risk of breast cancer	Clusters of breast cancer
women			

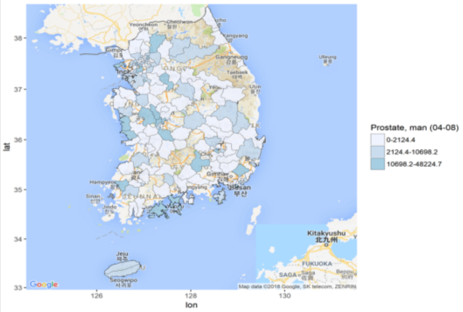
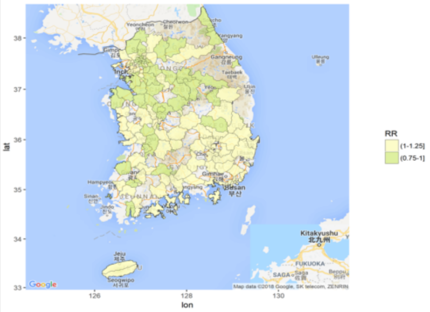
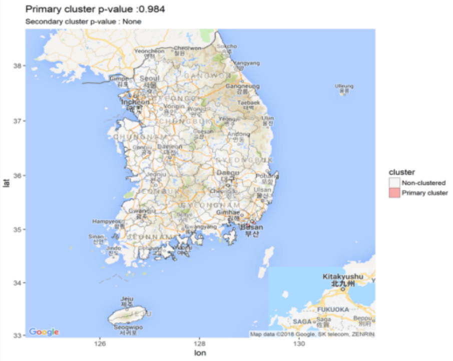
Age-standardized rate, relative risk and clustering of prostate cancer incidence, men, 2004-2008

	Rate of prostate cancer	Relative risk of prostate cancer	Clusters of prostate cancer
men			

Age-standardized rate, relative risk and clustering of prostate cancer incidence, men, 2009-2013

	Rate of prostate cancer	Relative risk of prostate cancer	Clusters of prostate cancer
men			

Age-standardized rate, relative risk and clustering of prostate cancer mortality, men, 2004-2008

	Rate of prostate cancer	Relative risk of prostate cancer	Clusters of prostate cancer
men			

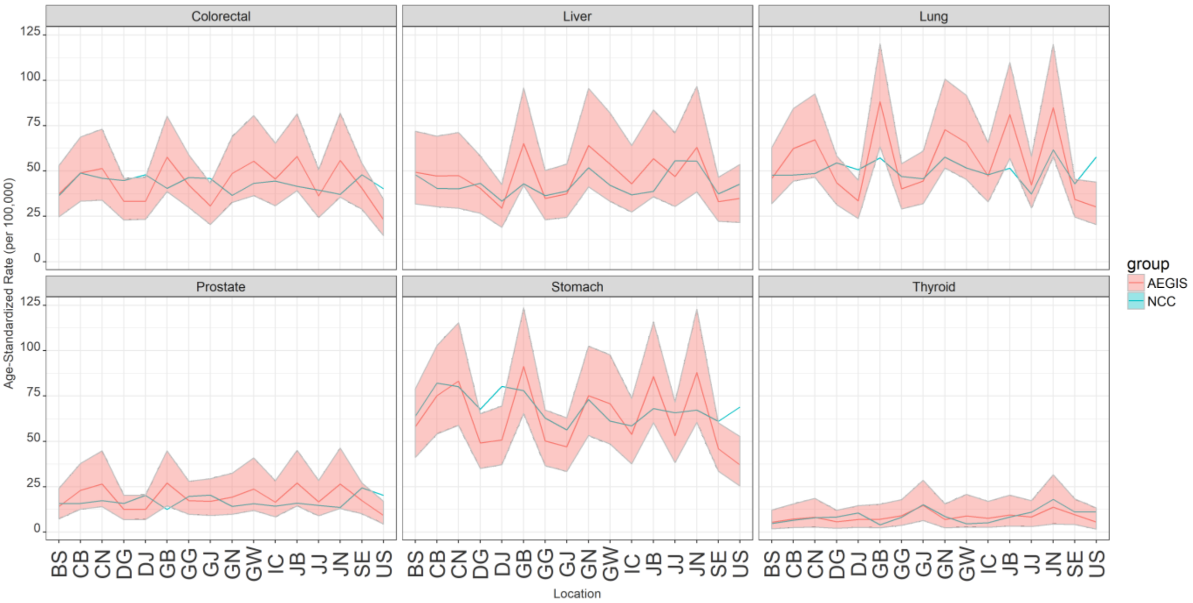
Prostate, man (04-08)
0-2124.4
2124.4-10698.2
10698.2-48224.7
lat
lon
Google
Map data ©2018 Google, SK telecom, ZENRIN

RR
(1-1.25]
(0.75-1]
lat
lon
Google
Map data ©2018 Google, SK telecom, ZENRIN

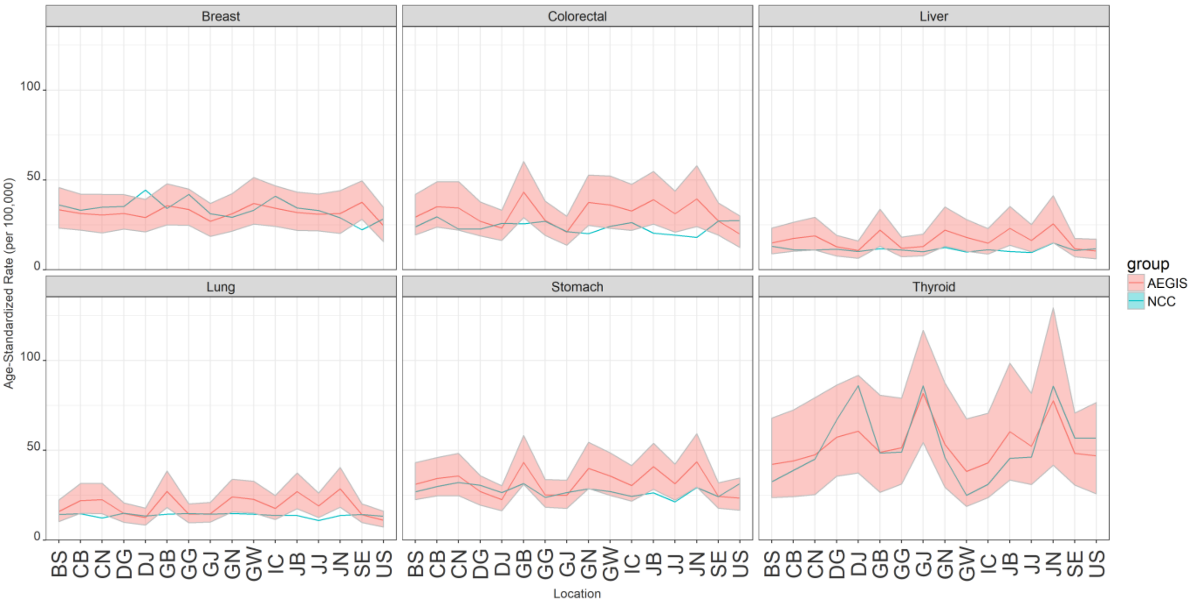
Primary cluster p-value :0.984
Secondary cluster p-value : None
cluster
Non-clustered
Primary cluster
lat
lon
Google
Map data ©2018 Google, SK telecom, ZENRIN

Supplementary Figure S2: Comparison of GADM-level 2 major cancer age-standardized incidence rate from AEGIS and major cancer age-standardized incidence rate from NCC in Korea.

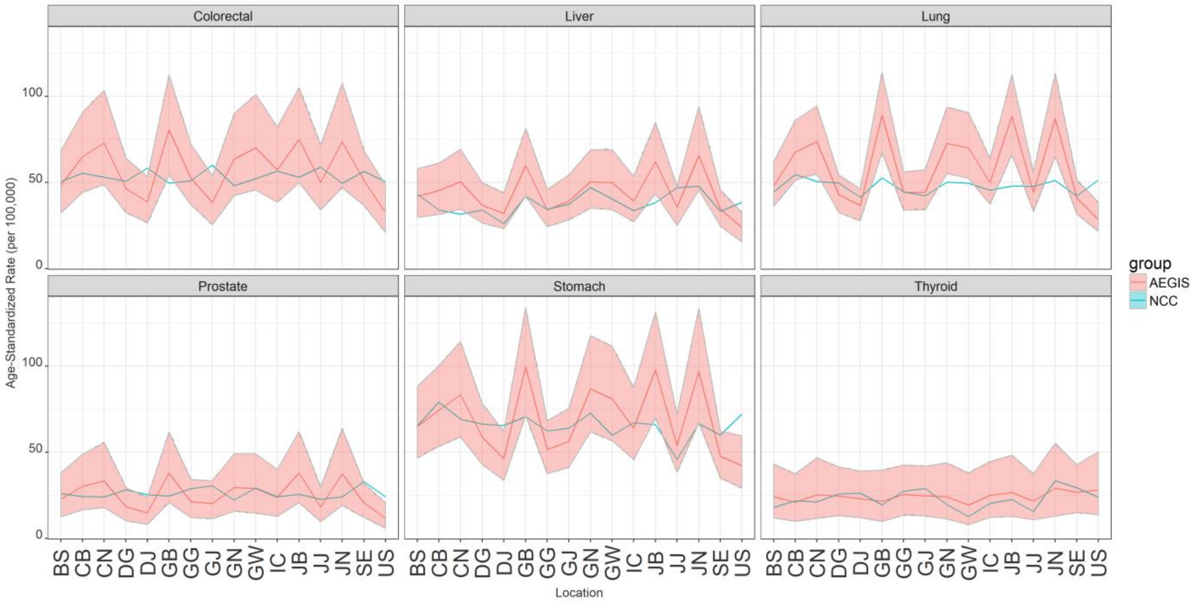
1. Comparison of age-standardized rate (red line) with 95% credible interval (red color) estimated from AEGIS and age-standardized rate reported from NCC (blue line) for major cancer between 2004 and 2008 in men.



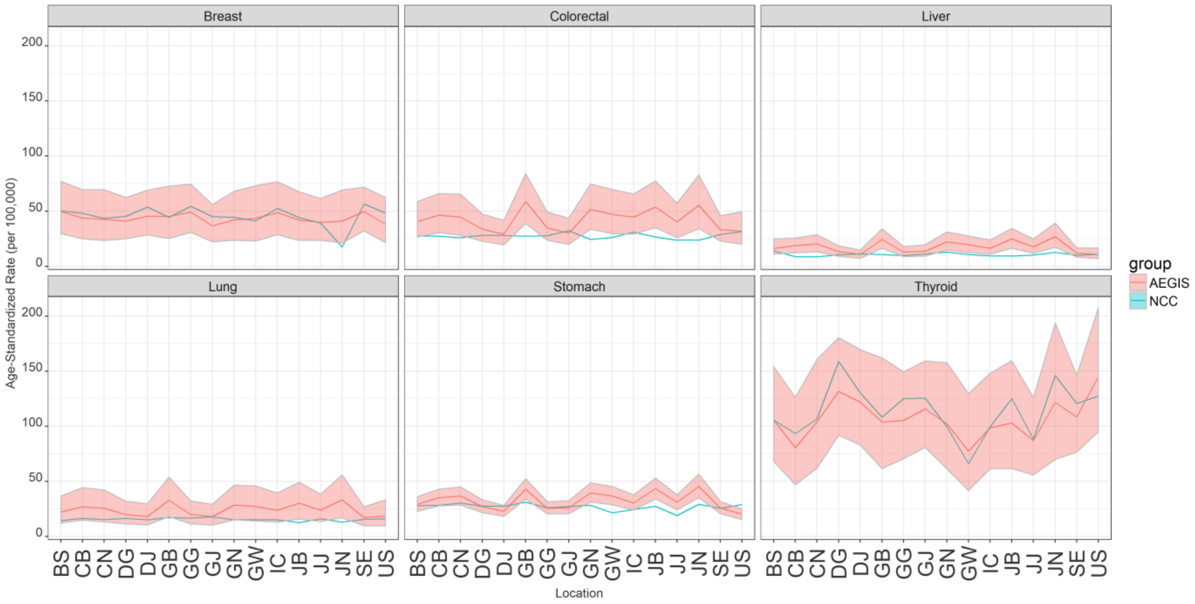
2. Comparison of age-standardized rate (red line) with 95% credible interval (red color) estimated from AEGIS and age-standardized rate reported from NCC (blue line) for major cancer between 2004 and 2008 in women.



3. Comparison of age-standardized rate (red line) with 95% credible interval (red color) estimated from AEGIS and age-standardized rate reported from NCC (blue line) for major cancer between 2009 and 2013 in men.



4. Comparison of age-standardized rate (red line) with 95% credible interval (red color) estimated from AEGIS and age-standardized rate reported from NCC (blue line) for major cancer between 2009 and 2013 in women.

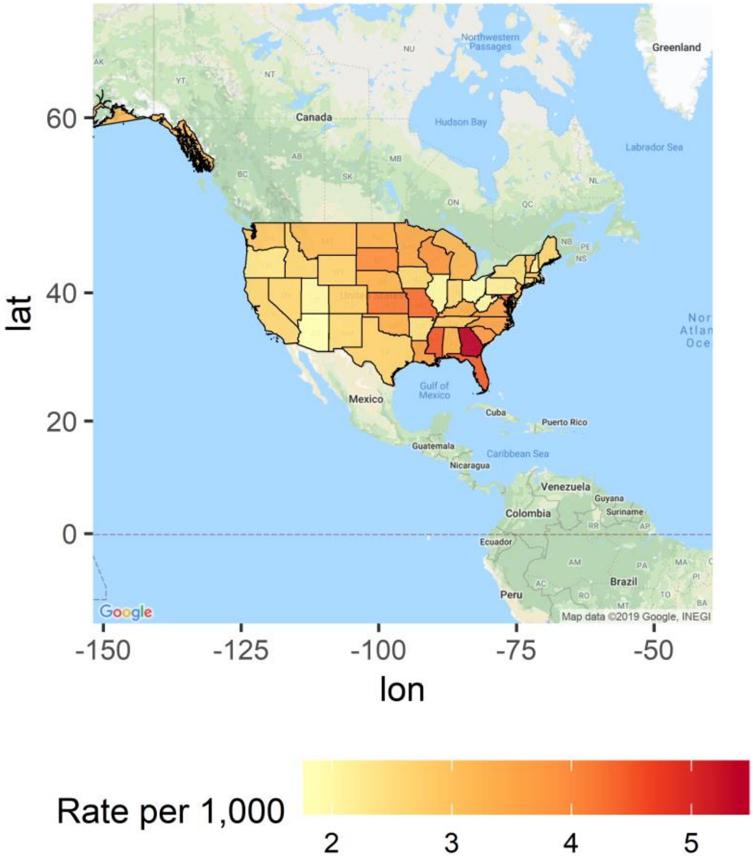


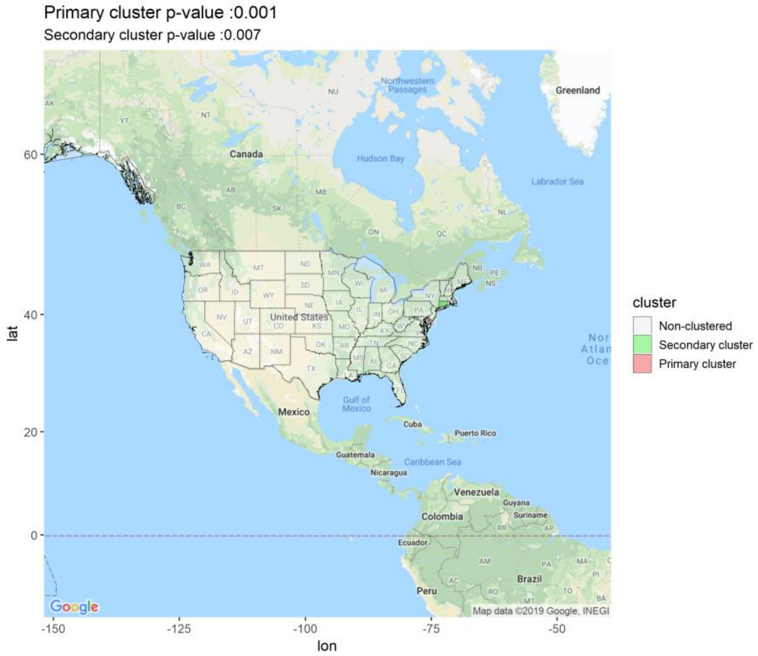
BS: Busan; CB: Chungcheongbuk-do; CN: Chungcheongnam-do; DG: Daegu; DJ: Daejeon; GB: Gyeongsangbuk-do; GG: Gyeonggi-do; GJ: Gwangju; GN: Gyeongsangnam-do; GW: Gangwon-do; IC: Incheon; JB: Jeollabuk-do; JJ: Jeju; JN:Jeollanam-do; SE: Seoul; US: Ulsan

Supplementary Figure S3: Disease mapping and clustering for regional differences in hospitalization rates due to heart-related diseases per 1,000 people in the United States from 2008 to 2010 (age and sex adjusted).

We also designed a spatial study involving a variety of heart diseases for further comparison with the previously published study 'Interactive Atlas of Heart Disease and Stroke' (https://www.cdc.gov/dhdsp/maps/atlas/index.htm) in US sources. The target cohorts were defined as the whole population in the database, and the outcome cohorts included patients hospitalized for stroke, acute myocardial infarction, cardiac dysfunction, coronary heart disease, heart failure, and heart disease, respectively, between 2008 and 2010.

1. Stroke


Northwestern Passages
NU
Greenland
AK
YT
NT
Canada
Hudson Bay
Labrador Sea
AB
MB
BC
SK
NL
ON
QC
NB
PE
NS
Nor Atlan Oce
Mexico
Gulf of Mexico
Cuba
Puerto Rico
Guatemala
Caribbean Sea
Nicaragua
Venezuela
Guyana
Suriname
Colombia
Ecuador
Brazil
Peru
Google
Map data ©2019 Google, INEGI
lat
60
40
20
0
-150
-125
-100
-75
-50
lon
Rate per 1,000
2
3
4
5


Primary cluster p-value :0.001
Secondary cluster p-value :0.007
Northwestern Passages
NU
Greenland
AK
YT
NT
Canada
Hudson Bay
Labrador Sea
AB
MB
BC
SK
NL
ON
QC
NB
PE
NS
WA
MT
ND
MN
OR
ID
SD
WI
MI
WY
NY
NE
IA
PA
NV
UT
United States
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TX
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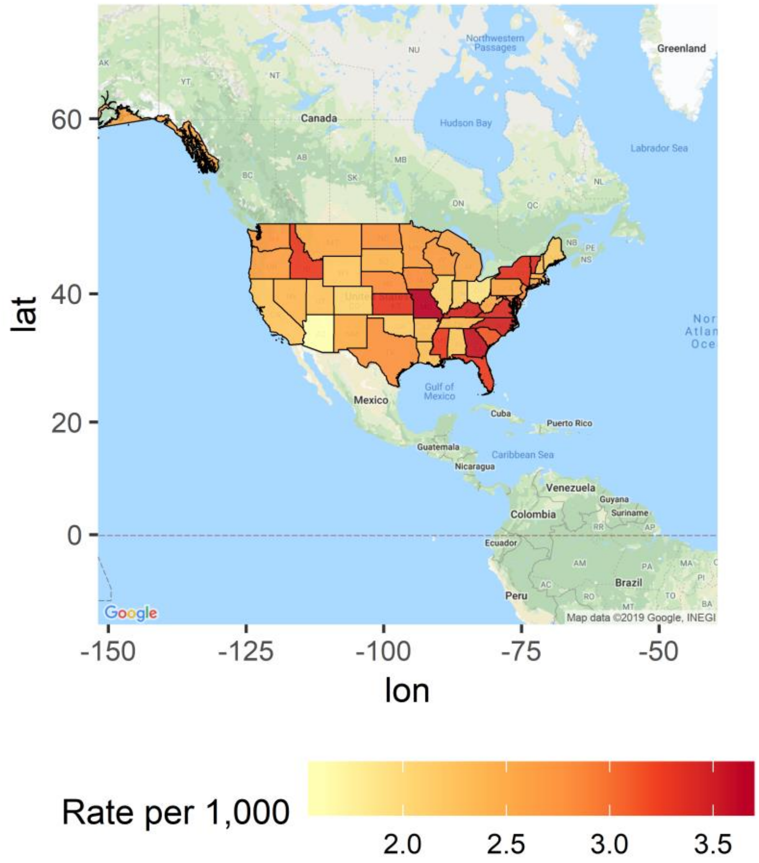
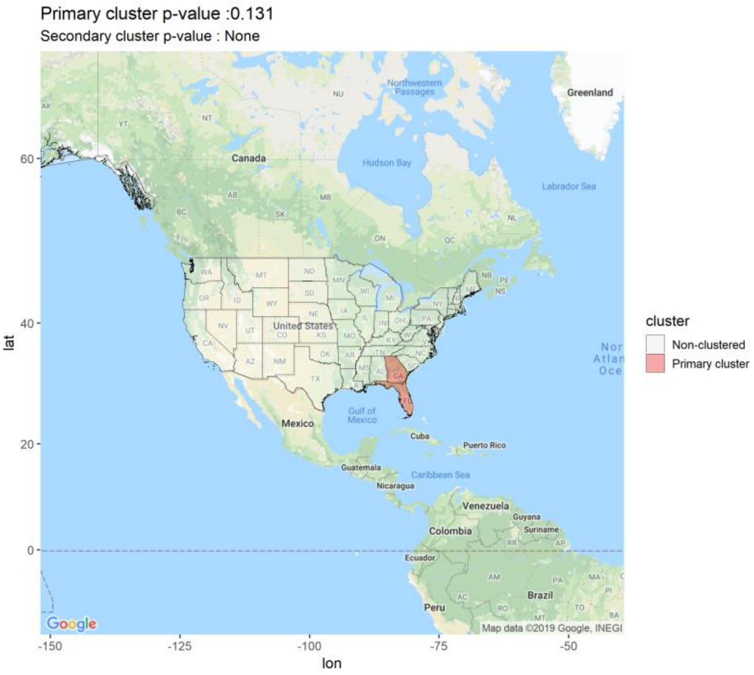
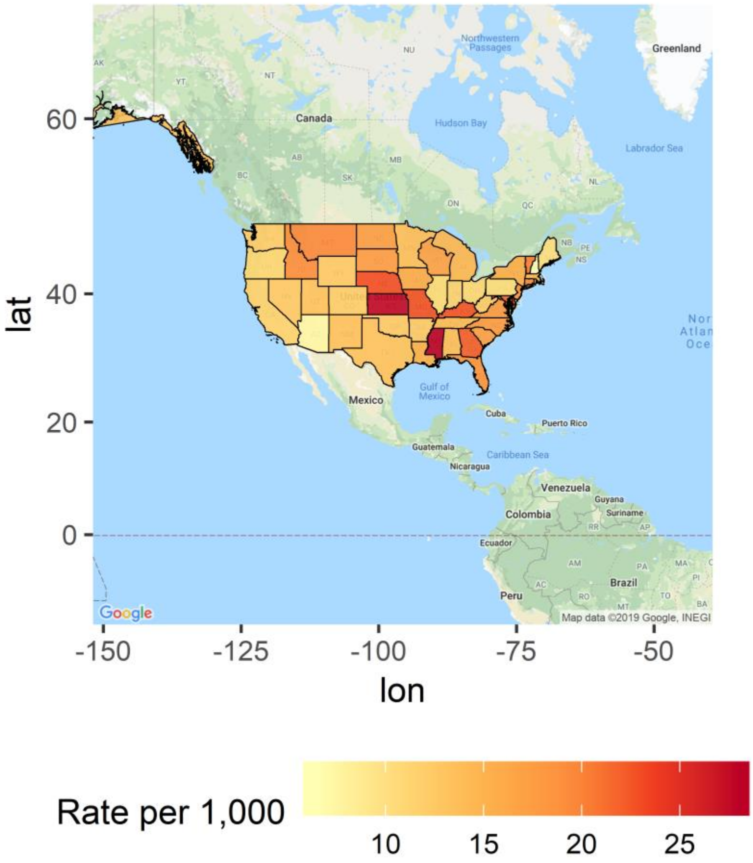
AL
GA
Nor Atlan Oce
Mexico
Gulf of Mexico
Cuba
Puerto Rico
Guatemala
Caribbean Sea
Nicaragua
Venezuela
Guyana
Suriname
Colombia
Ecuador
Brazil
Peru
Google
Map data ©2019 Google, INEGI
lat
60
40
20
0
-150
-125
-100
-75
-50
lon
cluster
Non-clustered
Secondary cluster
Primary cluster

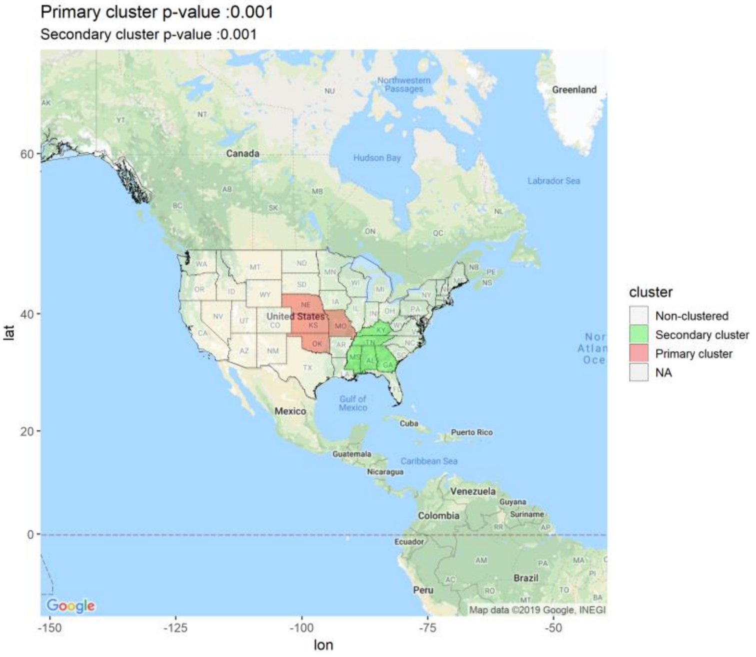
2. Acute Myocardial Infarction





3. Cardiac Dysrhythmia




Primary cluster p-value :0.001
Secondary cluster p-value :0.001
lat
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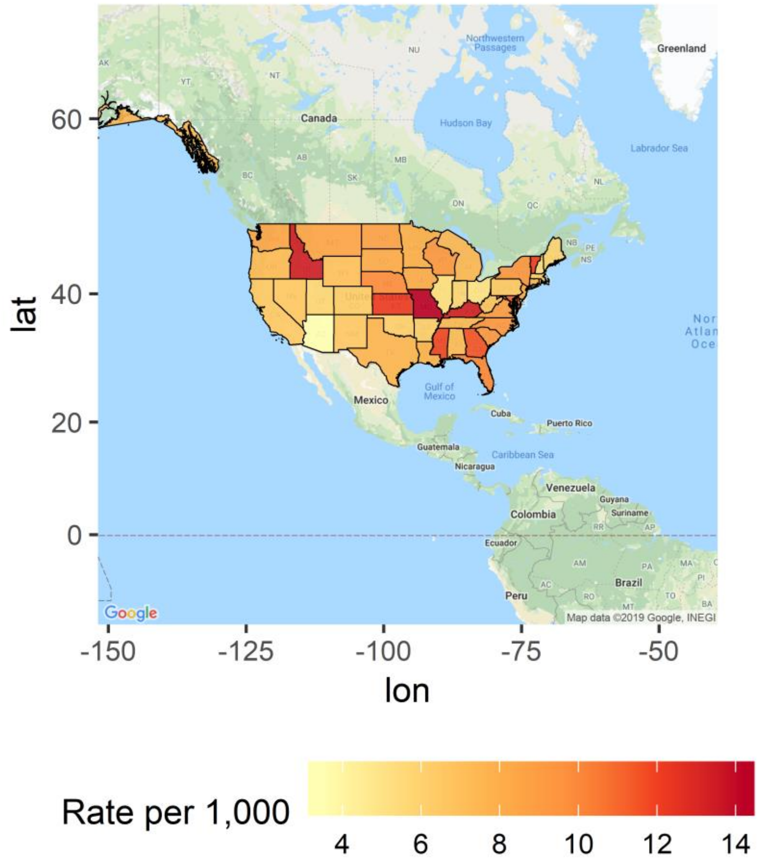
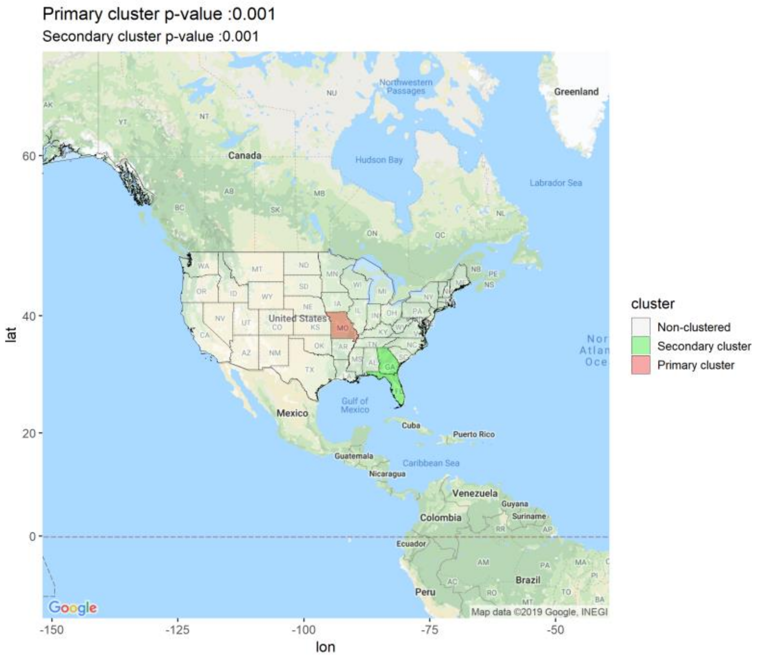
-125
-100
-75
-50
lon
cluster
Non-clustered
Secondary cluster
Primary cluster
NA
Map data ©2019 Google, INEGI

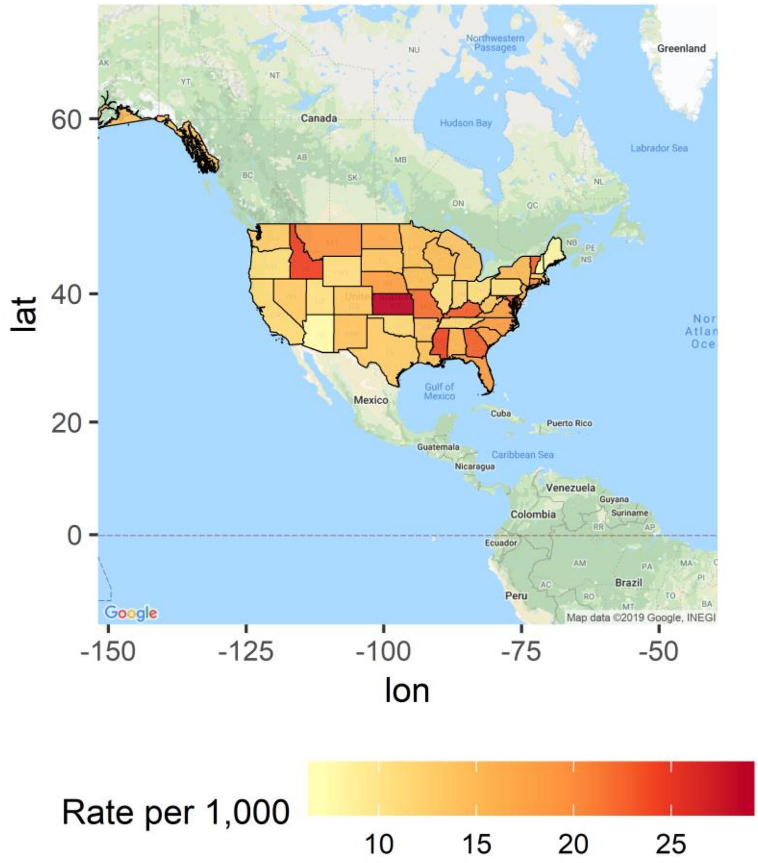
4. Coronary Heart Disease

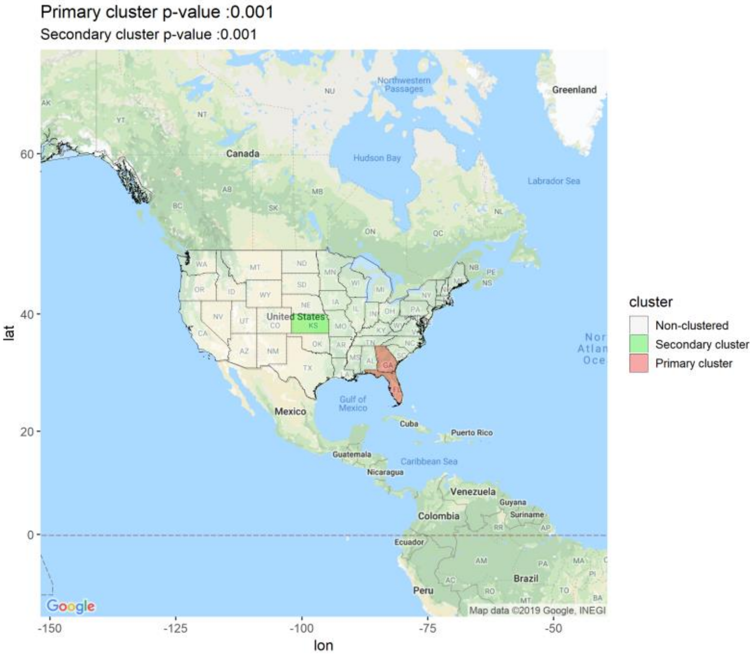



Primary cluster p-value :0.001

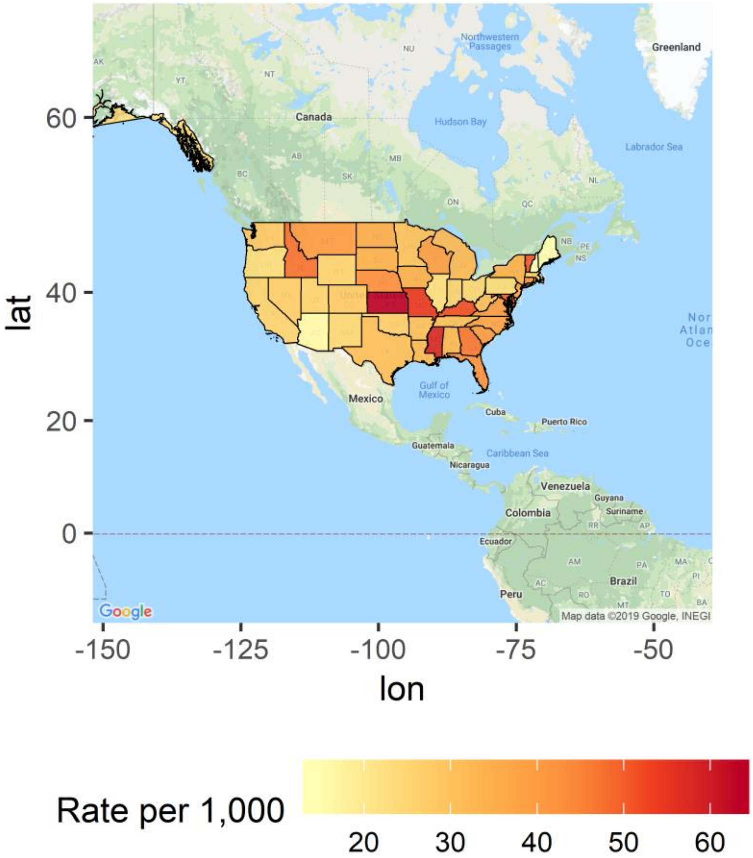
Secondary cluster p-value :0.001

5. Heart Failure




Primary cluster p-value :0.001
Secondary cluster p-value :0.001
lat
lon
cluster
Non-clustered
Secondary cluster
Primary cluster
Google
Map data ©2019 Google, INEGI

6. Heart disease


60
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lat
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-50
lon
Rate per 1,000
20
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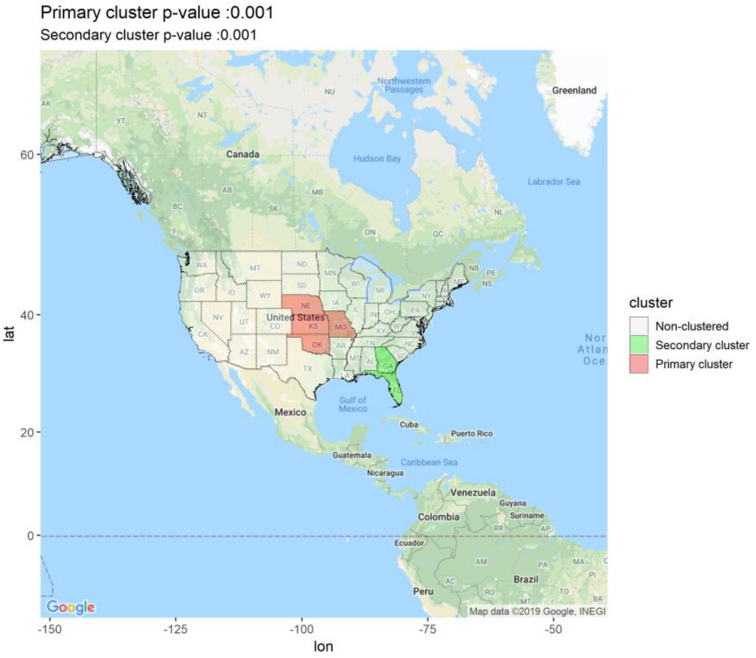
Canada
Hudson Bay
Greenland
Labrador Sea
Northwestern Passages
Mexico
Gulf of Mexico
Cuba
Puerto Rico
Caribbean Sea
Guatemala
Nicaragua
Venezuela
Colombia
Guyana
Suriname
Ecuador
Peru
Brazil
Google
Map data ©2019 Google, INEGI


Primary cluster p-value :0.001
Secondary cluster p-value :0.001
60
40
20
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lat
-150
-125
-100
-75
-50
lon
cluster
Non-clustered
Secondary cluster
Primary cluster
United States
NE
KS
MO
OK
GA
Canada
Hudson Bay
Greenland
Labrador Sea
Mexico
Gulf of Mexico
Cuba
Puerto Rico
Caribbean Sea
Venezuela
Colombia
Ecuador
Peru
Brazil
Google
Map data ©2019 Google, INEGI

Supplementary Information S1: Interactive web application

AEGIS interactive web application provides spatial analysis design by setting parameters in each function tabs on the left side (red box). Define the target cohort and outcome cohort to be analyzed from the population (green box). Combine two defined cohorts and GIS data, select options (including data handling options, method, and parameters; green box) for analysis and output the analysis results (blue box). The parameters provided through the interactive interface are shown in Figure A and are described below. It also provides a brief demonstration of the video format to help researchers who are new to AEGIS (https://youtu.be/tExqsZU7qYg).

WARNINGS: The results of AEGIS depend on the used healthcare database. AEGIS proportionate units of analysis and supports small area estimation techniques to prevent sampled location bias or false positive, but it does not guarantee nationwide results. Therefore, the results of AEGIS should be interpreted considering the geographical/medical rationale along with the characteristics of the data used.

A. *DB connection panel:* To configure the CDM server connection, set the server address, user name, password, database management systems, and CDM database schema.

B. *Cohorts:* Spatial analysis research design by setting user parameters. (1) select the target cohort and outcome cohort defined from the ATLAS; (2) set range of date to analyze with select windows parameter; (3) adjust age and gender differences between regions through age and gender adjustment parameters; (4) set the time-at-risk parameter for observing the outcome from the index date; and (5) select the country of study from the country list (total = 254 countries).

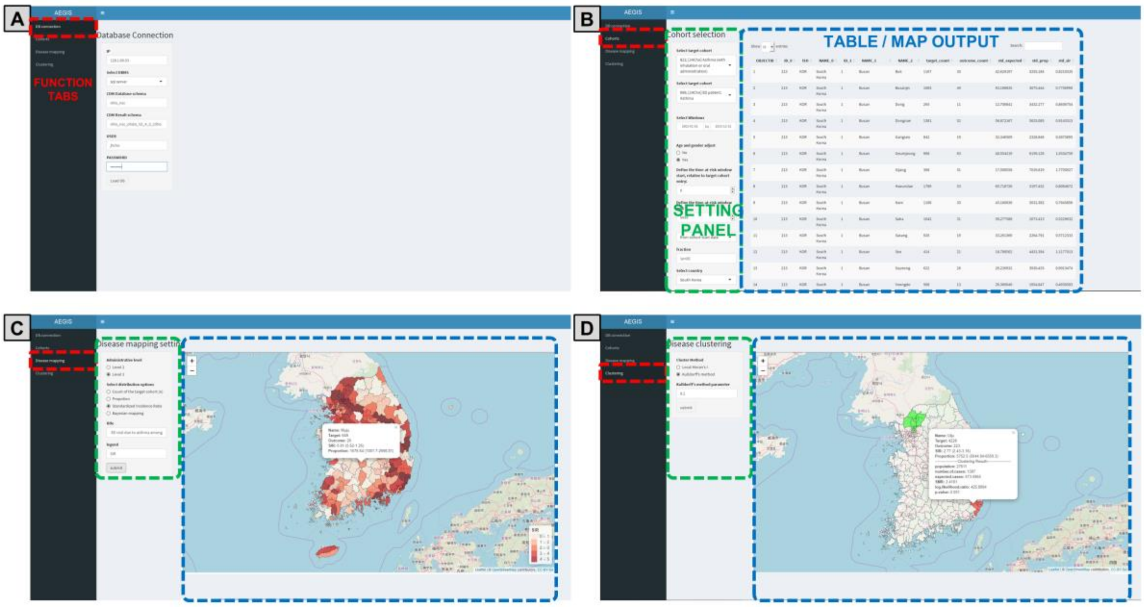
C. *Disease mapping:* From the settings designed in Cohorts tab, it is a panel for disease map visualization. Choose an administrative level with an administrative level parameter, and determine how to draw a disease map (Count of the target cohort (n), Proportion, Standardized Incidence Ratio, Bayesian mapping). Finally, set the entire title of the map and the title of the legend.

D. *Clustering:* In this tab, researchers can choose statistical methods (Local Indicators of Spatial Association, Kulldorff method) to detect disease clusters in which disease occurrences are concentrated. Visualize the results according to the selected method.

AEGIS can download and run packages from R with the following code:

```
install.packages("devtools")

devtools::install_github("cran/raster", ref="2.6-7")

devtools::install_github("ohdsi/DatabaseConnector")

devtools::install_github("ohdsi/SqlRender")

devtools::install_github("ohdsi/aegis")

AEGIS::AEGIS()
```

Figure A. Illustration of the AEGIS that performs spatial epidemiology analysis using observational health data based on OMOP-CDM.


A
AEGIS
FUNCTION TABS
Database Connection
IP
Select DBMS
CDM Database schema
CDM Result schema
USER
PASSWORD
Load DB
B
AEGIS
Cohort selection
TABLE / MAP OUTPUT
SETTING PANEL
C
AEGIS
Disease mapping setti
D
AEGIS
Disease clustering