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Chronic Kidney Disease Mortality in Costa Rica; Geographical Distribution, Spatial Analysis and Non-traditional Risk Factors

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Master thesis, 30 credits, in Geographical Information Sciences

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Abstract

Costa Rica has been facing with a public health issue, Chronic Kidney Disease (CKD). Experts have recently (2013) recommended spatial analysis of the relevant data for better understanding of the situation. The association between CKD in Central America and some environmental factors (e.g. temperature, agricultural activities) have been reported. The aim of this study is to evaluate geographical distribution of CKD in Costa Rica through spatial analysis of CKD mortality data. The study also looked at associations between CKD mortality and environmental factors. Moreover, this thesis aims to evaluate physician's knowledge about CKD affecting factors.

Using CKD mortality data from 1980 to 2012, mortality rates were calculated for each and every year of the study period. In order to evaluate geographical distribution of CKD mortality, standardised mortality ratios (SMRs) for 5-yearly intervals were calculated. SMRs were visualised and compared for six time-periods between counties, with national rates as reference. Local Moran's I was used for finding the hot spots. Ordinary Least Squares (OLS) regression was used to examine associations. Geographically Weighted Regression (GWR) was applied to show the regional variation. Multi Criteria Decision Analysis was used to weight factors affecting CKD from physician's perspective, create a risk map according to the weights and compare the risk map result with reality.

Over 5800 individuals died from CKD during the study period; of them 61% were males. A steady increase in the CKD mortality rates was observed over the study period; so that the risk of dying from CKD in 2012 was about three times more than 1980. The visualised SMR data on six 5-yearly maps well demonstrates the geographically progressive nature of the problem which has spread to the neighbouring areas over time; so that the spatial analysis of the most recent years (2008-2012) identified a significant part of the country in the North as

the hot spot. OLS regression showed significant associations between CKD mortality and temperature, permanent crops and precipitation ($p < 0.05$). Coefficients of GWR showed inconsistencies in the effect of temperature and precipitation in different parts of the country. Also the study showed an inadequate knowledge of the experts from the environmental risk factors of CKD.

The findings of this study are two folded. One relates to policy implications. Indeed, the findings of this study provided objective evidence on the progressive nature of the CKD problem in Costa Rica. The identified hot spots in the northern parts of the country warrants further investigations to see what practical measures could better control CKD in those areas. The second aspect relates to the newly emerging non-traditional risk factors for CKD (agricultural occupation, heat stress etc.). The study showed significant associations between CKD mortality and environmental factors. These associations provide further evidence in support of the link between the current CKD epidemic and farming activities (permanent crops) as well as heat stress (temperature & precipitation). The inconsistencies of the effects of temperature & precipitation in the GWR model is indicative that there should be another related causal factor (likely to be heat stress) in the exposure-outcome pathway. Further medical field studies are recommended.

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1 INTRODUCTION

1.1 Background

Costa Rica with an area of about 51,000 square kilometres is one of the smallest countries, but one of the progressive nations in Latin America. It has consistently been among the top-ranking Latin American countries in the Human Development Index, placing 68th in the world as of 2013 . Costa Rica consists of seven provinces, 81 counties and 472 districts. The map of counties of Costa Rica and neighbouring countries is shown in figure 1-1.

With a population of about 4.800,000, ethnically, Costa Rican people are mostly white followed by blacks and mulattos as the second largest ethnic group. Costa Rica managed to reduce poverty in recent years; so that about half of the urban and rural populations are middle class. Socioeconomically, it is one of the most homogeneous countries in Latin America.

Costa Rica has one of the best public health systems in the region. Despite this good public health system which provides free medical attention for all citizens, there has been report of a growing number of Chronic Kidney Disease in the country (public nephrology services have been available since 1968). As far as public nephrology is concerned, services have been available since 1968 and the first kidney transplant was performed several years ago in 1969 (Cerdas 2005).

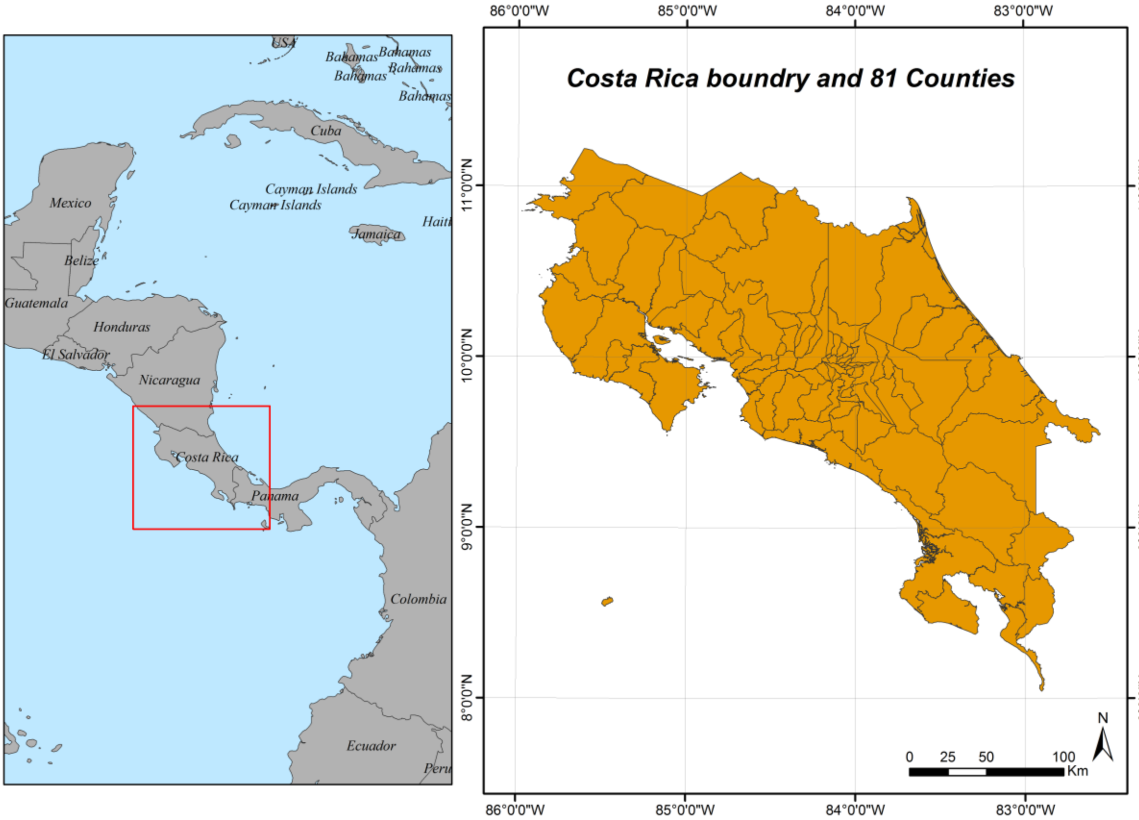


Figure 1-1: Costa Rica Map, neighbouring countries and 81 counties, Data: Atlas of Costa Rica

1.2 Chronic Kidney Disease (CKD), definition and risk factors

The two kidneys lie to the sides of the upper part of the tummy with the main function of filtering out waste products from the blood stream. Chronic kidney disease (CKD) happens when the function of the kidney is not as before which means the kidney is damaged. In medical terms, CKD is defined by the presence of kidney damage or decreased kidney function for three or more months, irrespective of the cause (Levin et al. 2013).

The prevalence of CKD in different countries varies widely, reportedly ranges from approximately 1 to 30 percent (Choi 2006; Chadban Steven 2003; Magnason Ragnar 2002; Jafar Tazeen 2005; Amato Dante 2005; Chen Jing 2005; Viktorsdottir Olof 2005; Garg Amit 2005; Hsu Chih-Cheng 2006). The prevalence of CKD increases with age and is highest at ages more than 60 years (Coresh et al. 2003; Otero et al. 2010). Globally, there has been an increase in CKD mortality rates from 9.6 per 100,000 populations in 1999 to 11.1 per 100,000 in 2010 (Lozano et al. 2012).

According to the national kidney foundation the two main reasons of chronic kidney disease are diabetes and high blood pressure. The most common causes in United States in 2012 were diabetes (44 percent), hypertension (28 percent), glomerulonephritis (6 percent), and cystic kidney disease (2 percent) (Lozano et al. 2012).

From the 1990s (Almaguer et al. 2014), chronic kidney disease with unknown cause have been emerging in several parts of the world including El Salvador (Peraza et al. 2012; Orantes et al. 2011), Nicaragua (Torres et al. 2010; O'Donnell et al. 2011b), Costa Rica (Cerdas 2005), Sri Lanka (Athuraliya et al. 2009; Athuraliya et al. 2011b; Nanayakkara et al. 2012), Egypt (El Minshawy 2011) and India (Rajapurkar et al. 2012b). As stated above, traditional CKD is typically associated with risk factors such as diabetes, hypertension, and aging whereas CKD of unknown origin has different characteristics. It occurs in young, otherwise healthy individuals (Chandrajith et al. 2011; Rajapurkar et al. 2012a; Cerdas 2005; Orantes et al. 2011; Wijkström et al. 2013).

CKD of unknown origin is threatening the public health of Mesoamerica (Wesseling et al. 2013). Due to the importance of this condition in the region, a new entity has emerged as Mesoamerican Nephropathy (MeN) (Wesseling et al. 2013) with the clinical definition of *"Persons with abnormal kidney functions by internationally-accepted standards, living in Mesoamerica and with no other known causes for CKD, i.e. diabetes, hypertension, polycystic kidney disease (PKD), and other known causes*" (Wesseling et al. 2014, p. 24).

Current research findings point to multifactorial causation for CKD of unknown origin (social determinants such as poverty appear to combine with harsh working conditions and exposure to environmental toxins) (Gorry 2014).

Heat stress is a factor which has been named to be able to induce renal damage(Crowe et al. 2013; O'Donnell et al. 2011a; Brooks et al. 2012; Wesseling et al. 2013) – although a recent publication (2014) from El Salvador did not identify ambient temperature, as a proxy for heat stress, to be a significant factor in the process of CKD of unknown origin (VanDervort et al. 2014). However, the general consensus of the experts (Wesseling et al. 2013) is that the strongest causal hypothesis for the CKD of unknown origin is repeated episodes of heat stress and dehydration during heavy work in hot climates. "Co-factors to consider interacting with heat stress or influencing the progression of CKD of unknown origin, include excess use of nonsteroidal anti-inflammatory drugs (NSAIDs) and fructose consumption in rehydration fluids. Contributing factors for the epidemic could include inorganic arsenic, leptospirosis, pesticides, or hard water"(Wesseling et al. 2013, p.7). There is a recent evidence from Costa Rica stating that "sugarcane harvesters are at risk for heat stress for the majority of the work shift"(Wesseling et al. 2013).

There are evidence suggesting that injury to kidney from exogenous toxins could be a possible mechanism for the CKD of unknown origin (Kumar et al. 2009) [in CKD of unknown origin cases the areas of the kidney which are indicators of damage by toxins (tubules and interstitial) are usually affected (Cerdas 2005; Athuraliya et al. 2011a; Wijkström et al. 2013; Peraza et al. 2012; O'Donnell et al. 2011a)]. In this context, toxic agrochemicals have been named as the main suspect (VanDervort et al. 2014; Orantes et al. 2011; Athuraliya et al. 2011a), but experts (Wesseling et al. 2013) have categorized pesticides as "*Unlikely but strongly believed"*. My literature search identified a recently published paper (2014) which has examined the spatial distribution of CKD of unknown origin in El Salvador(VanDervort et al. 2014). The authors concluded that "*CKD of unknown origin in El Salvador may arise from proximity to agriculture to which agrochemicals are applied, especially in sugarcane cultivation*" (VanDervort et al. 2014, p.1). It is worth mentioning that Central America is the largest consumer, per inhabitant, of insecticides in Latin America (Gorry 2014).

In summary, the main underlying causes of CKD are diabetes and hypertension, associated with aging and obesity. In addition to these, kidney damage due to infections, nephrotoxic drugs and herbal medications, environmental toxins and occupational exposure to heat stress and pesticides could lead to CKD (Almaguer et al. 2014).

1.3 Problem statement

In 2005, Cerdas reported that Costa Rica has doubled the number of patients on haemodialysis. He also reported Chronic Kidney Disease epidemic in Guanacaste in northern Costa Rica in which the disease looked different from other parts of the country. This appeared in men, long-term sugar-cane workers aged 20 to 40. The author suggested exploring their work environment to determine what in their daily activities puts them at increased risk for chronic renal failure (Cerdas 2005).

According to the 2013 Mesoamerican Nephropathy report (Wesseling et al. 2013), spatial analyses of CKD would be a potentially useful approach that has not yet been used in the region. That report proposed priorities for exploring hypotheses for causes of CKD of unknown origin in Central American countries (Wesseling et al. 2013) (the priorities have been mentioned in Appendix C of this proposal). My literature search identified a recently published paper (2014) which has examined the spatial distribution of CKD of unknown origin in El Salvador (VanDervort et al. 2014). However, the literature search did not identify spatial analyses of exposure in the context of CKD in Costa Rica. In order to address this, the current study was performed.

1.4 Research objectives

This study aims to:

1. Find a time trend of CKD mortality rate from 1980 to 2012 in Costa Rica.
2. Find a time trend of CKD mortality rate from 1980 to 2012 according to gender in Costa Rica.
3. Investigate if there is a shift in mortality rate in younger people.
4. Explore the mortality pattern of CKD in Costa Rica through spatial analysis of CKD mortality data.
5. Explore the associations between CKD mortality and environmental factors.
6. Take into account the expert's knowledge about CKD affecting factors in Costa Rica.

1.5 Methods

In order to satisfy the objectives of this study, geographical and medical data were gathered from two sources: Central American Population Centre and Atlas of Costa Rica. In order to find the time trends of CKD mortalities and achieve the first three objectives, mortality rates of CKD over the study period were calculated and time rends of CKD mortality rates from 1980 to 2012 were visualised on graphs and maps

In order to find the spatial pattern of CKD mortalities in Costa Rica (objective 4), 5-yearly Standardised Mortality Ratio (SMR), index for comparing mortalities of different geographical locations, for total population and population aged under 60 were calculated and mapped. Global and local Moran's I were used to find the hot spots of SMR.

Considering the objective 5 of this study, Ordinary Least Squares (OLS) and Geographically Weighted Regression Model (GWR) were created to find the associations between environmental risk factors of CKD and CKD mortalities. OLS regression as a global linear model enabled us to find the associations between CKD mortalities and environmental factors (e.g. precipitation, temperature, altitude and permanent crops) globally. GWR as local form of regression model helped us to investigate the regional variations between independent variables and CKD mortalities. Finally, these two models were compared to investigate which of these two models explained the associations better.

With regards to the last objective, Multi Criteria Decision Analysis (MCDA) was performed to investigate expert's knowledge about CKD affecting factors. Analytical Hierarchy Process as a structured technique in a group decision analysis was used to find the most and least important factors from physicians' prospective. The results were compared with reality to meseasure the level of agreement between the physicians 'opinions and reality.

2 LITERATURE REVIEW

From 2005 there has been some reports of high CKD mortality rate in Central America, especially in younger men and also in some areas of Pacific coast (Cerdas 2005; Orantes et al. 2011; Peraza et al. 2012; Torres et al. 2010).

Due to a high prevalence of CKD in Nicaragua Ramirez O. et al.(Ramirez-Rubio et al. 2013) performed a study to recognize the opinion or practice of physicians and pharmacists in the North Western of Nicaragua. In order to recognize their opinions, the semi-structured interviews were conducted in 2010. Nineteen physician and pharmacist participated in the interview. Acting on interviews' results, health experts perceived CKD as a serious problem in the region with the highest effect on young men working as manual labourers.

Another study was performed by Vela et al. in 2012 (Vela et al. 2014) who explored associated risk factors in two Salvadoran farming communities. 223 people of both genders (age > = 15) participated in this study. 50.2 % of the population under study had chronic kidney disease. In both farming communities more than 70 % of the participants were farm workers and more than 75% reported contact with agrochemicals. NSAID use recognized as another risk factor in both farming communities.

Another example of chronic kidney disease study in Central America was performed by VanDervort. et al. (VanDervort et al. 2014). They studied the spatial distribution of unspecified Chronic Kidney Disease in El Salvador by crop area cultivated and ambient temperature used geographically weighted regression analysis and Moran's indices to show data clustering. The results of the study showed that agricultural occupation can be a risk factor for CKD.

"*There has been an increasing interest in applying GIS into health and healthcare research in recent years*" (Sanati and Sanati 2013). Geographic Information System (GIS) has provided helpful methodologies such as mapping and spatial analysis for researchers and health professionals. The two main advantages of mapping and spatial analysis are exploring the health data visually and investigating the spatial relationship between health out-comes and potential risk factors.

The study conducted by Oviasu, O. (Oviasu 2012) can be a good example of use of GIS in CKD spatial analysis. He studied the spatial analysis of diagnosed Chronic Kidney Disease in Nigeria. The main spatial techniques carried out in the course of this study were using choropleth maps for visualizing the data, using Kernel density estimator to estimate the CKD density distribution and two models of network analysis. This study also employed statistical tests to explore the association between independent variables. Logistic regression was used to create a model for finding the factors which are likely to be related to the late diagnosis of CKD. He showed that density of CKD in urban areas is higher in comparison with rural areas. The results demonstrated that there were not a significant association between socio-demographical characteristics of the patient and the severity of CKD. This study also suggested other statistical techniques such as geographically weighted regression (GWR) to find the spatial relationship between the dependent variable and the independent variables locally.

One of the statistical methods that have been widely used in different researches for identifying the association between different variables is a regression model. The use of GWR as a local form of the regression has shown promise in public health research and other disciplines.

Sun W. et al. (Sun et al. 2015) used geographically weighted regression to explore the regional associations between Tuberculosis- a major risk public health problem in China- and its risk factors. Using GWR model helped him to show that each risk factors of Tuberculosis has different effect on different areas.

Hipp J. et al. (Hipp and Chalise 2015) used GWR in spatial analysis of diabetes prevalence in the United States at the county-level data. He detected variations in health behaviours across space.

Li et al. (Li et al. 2010) performed the combination of Ordinary Least Square (OLS) method and GWR to show the spatial non-stationary between urban surface temperature and environmental factors.

Local Moran's I as an indicator of spatial auto correlation (spatial auto correlation measures the degree to which spatial features are clustered or dispersed in space) have been widely used to identify the cluster of high values or "hot spots". Ruiz et al. (Ruiz et al. 2004) used local Moran's I method to find the hot spot area of human illness caused by the West Nile Virus (WNV) around Chicago. He showed statistically significant cluster areas of WNV in the north part of the study area.

Multicriteria Decision Analysis has been used in different disciplines including health. Rajabi et al. (Rajabi et al. 2012) used this method to create a susceptibility map of visceral leishmaniasis (VL) based on fuzzy modelling and group decision making. In his study he used AHP-OWA method using fuzzy quantifier to indicate the villages most at risk. For creating the weights, the opinion of experts was generalised into a group decision making. The result of this study showed that linguistic fuzzy quantifiers, by implementing an AHP-OWA model, are sufficient to find possible areas of VL occurrence with 80% precision. According to this study people living in 15 villages where the VL was highly dominant, were in high risk of contagion. The results would be beneficial to develop policies to control the disease in northwest of Iran.

Hanafi et al. (Hanafi-Bojd et al. 2012) used evidence-based weighting approach to investigate risk of transmission of malaria epidemic in Bashagard, Iran. In order to map malaria threat region, temperature, relative humidity, altitude, slope and distance to rivers were combined by weighted multi criteria evaluation. In the same way, risk map was produced by overlaying weighted hazard, land use/land cover, population density, malaria incidence, development factors and intervention methods. The result of this study is valuable for early warning system for controlling the disease and discontinuing spreading out of the disease, and also developing national policy to increase public health quality.

3 MATERIALS AND METHODS

At the first step, geographical and medical data were gathered according to the objectives of this study. Mortality rates of CKD were calculated and time rends of CKD mortality rates from 1980 to 2012 were studied. In addition, 5-yearly SMRs for total population and population aged under 60 were calculated and mapped. Global and local Moran's I were used to find the hot spots of SMR. Ordinary Least Squares (OLS) and Geographically Weighted Regression Model (GWR) were created to find associations between environmental risk factors of CKD. Finally, MCDA was performed to investigate expert's knowledge about CKD affecting factors.

3.1 Available data

Geographic and medical data were received and gathered in two periods. At the first period, the CKD mortality data was provided for 81 counties of Costa Rica (1980-2012) and in the second period, CKD mortality data was extracted for 472 districts of Costa Rica (2009-2013) from Central American Population Centre. Consequently, the questions with regard to the first 5 objectives were answered using the mortality data at the county level and the questions with regard to the last objective is answered using the mortality data of the district level. The administrative level of Costa Rica is categorized as: 1.Country, 2. Province, 3. County, 4. Districts.

International Classification of Disease (ICD) is the standard diagnostic tool which is used by physicians and other health professionals to classify diseases and other health problems (Organization 2015). During the study period, two versions of ICD were used (ICD 10 and ICD 9) to extract mortality data from Central American Population Centre database. Table 3-1 shows the cases of death according to two versions of ICD.

Table 3-1: ICD codes used for extracting CKD mortality data

ICD9 1980-1996
582 Chronic glomerulonephritis
583 Nephritis and nephrosis not specified as acute or chronic
585 Chronic renal failure
586 Renal failure, unspecified
587 Renal sclerosis
ICD10 1997 - 2012
N18 Chronic kidney disease
N19 Unspecified kidney failure

Geographical data was also received in two separate times. At the first step, Atlas of Costa Rica (version: 2008) was received, then in January 2015 we could access to Atlas of Costa Rica(version: 2014). However, the newly received Atlas didn’t contain updated features and most of the features which were essential for this study such as temperature and land use were identical to the old Atlas. One of the problems of the data was inadequate information about the features in a metadata, especially information regarding to the features' attributes.

In general, a major problem of this study was lack of updated geographical and environmental data. List of all data used in this study is provided in table 3-2.

Table 3-2: List of data used in the study

Name	Data Source	Date
CKD Mortality data	Central American Population Center UCR	1980 to 2013
Population	Central American Population Center UCR	1980 to 2013
Diabetes mortality Rate	Central American Population Center UCR	2007
Alcohol Cirrhosis mortality rate	Central American Population Center UCR	2007
number of schools per 10000 people	Central American Population Center UCR	2007
cardiovascular mortality rate	Central American Population Center UCR	2007
Temperature	meteorological station's record	1998-2002
Permanent crops	land cover of Costa Rica 1992 (Received from Costa Rica Atlas file)	1992
Annual crops	land cover of Costa Rica 1992 (Received from Costa Rica Atlas file)	1992
Precipitation	meteorological station's record	2008
Altitude	DEM	2008
Hospitals	The location of Hospitals (Received from Costa Rica Atlas file)	2008, 2014
Villages	The location of Hospitals (Received from Costa Rica Atlas file)	2008, 2014
SDI (Social Development Index)	Received from Costa Rica Atlas file in a district level	2013

The temperature map was created using interpolation method from 24 weather stations. Each weather station shows the average temperature from 1998 to 2002. Kriging as the spatial analytical method was used to predict unknown values from average adjacent known values. The precipitation map was created using 65 meteorological stations records as the average yearly rainfall in 2008, and the kriging as an interpolation method was used. Since our analysis is in county level,"zonal statistics" was used to assign a mean of temperature, precipitation and altitude to the related county. For each district, the area of cultivated land (annual and permanent crop) was calculated as an index for farming activities for each county. The number of hospitals that each village in a county can access in a 10- kilometre buffer zone is considered as a proxy for access to hospital.

Figure 3-1 shows the location of hospitals, elevation map of Costa Rica, distribution of permanent and annual crops, precipitation and temperature maps of Costa Rica.

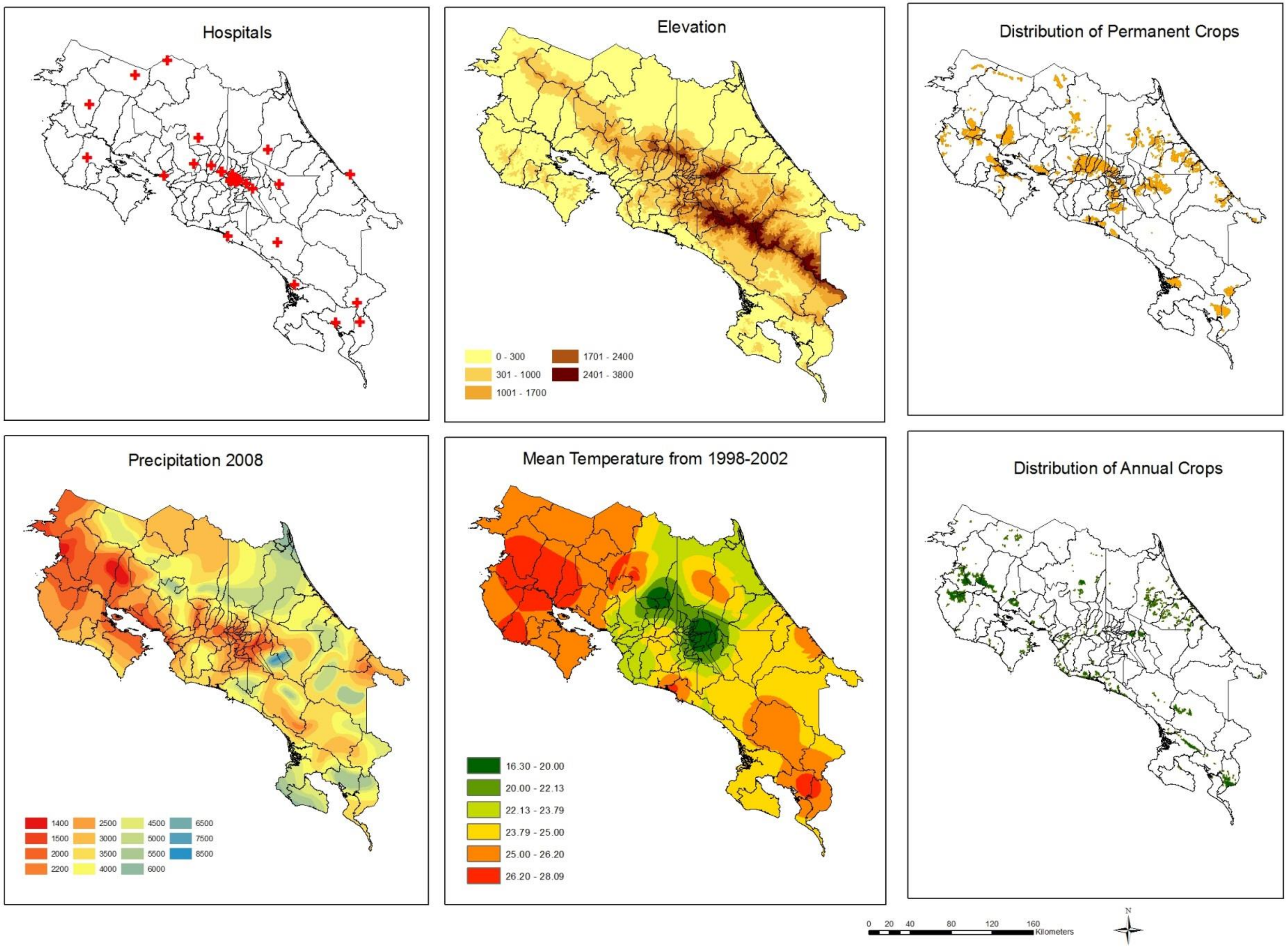


Figure 3-1: Maps of environmental factors and geographical location of hospitals in Cost Rica

3.2 Mortality rates, standardised mortality ratios and their trends over Time

Using 33 years of Costa Rican CKD mortality data (1980 to 2012) the following indexes were calculated and visualised on the map:

- Mortality rates for each and every year of study: mortality rates were used to look at the trend of mortality over time.
- Standardised Mortality Ratios (SMRs) for five-yearly intervals and 95% Confidence Intervals (95% CI) (Miettinen and Nurminen 1985; Graham et al. 2003; Curtin and Klein 1995): SMR equals to number of observed deaths divided by number of expected deaths (Equation 1) (Curtin and Klein 1995).

SMRs, as a mortality index adjusted for sex and 10-year age against national mortality enabled us to compare mortality in different geographic areas. Equation 1 shows how SMR is calculated.

$$SMR = \frac{\sum_i d_i}{\sum_i m_{si} * p_i} \qquad \textit{Eq 1}$$

Where:

d_i: the number of deaths in the i^{th} age interval,

m_{si}: the standard age specific death rates on a unit basis,

p_i: the population size in the i^{th} age interval

SMR maps of 5-yearly intervals were used to compare the pattern of CKD mortality in Costa Rica over the study period.

3.3 Spatial autocorrelation (global Moran's I)

Spatial autocorrelation has been well explained by "first law of geography" which states "everything is related to everything else, but near things are more related than distant things"(Tobler 1970). So the characteristics of locations close to each other are more similar than those faring away.

In geographical analysis, one of the most common ways of measuring spatial autocorrelation is Moran's I statistic. Equation 2 shows how Moran's I is calculated (Rogerson 2001):

$$I = \frac{n\sum_{i}^{n}\sum_{j}^{n} w_{ij}\left(y_i - \bar{y}\right)\left(y_j - \bar{y}\right)}{\left(\sum_{i}^{n}\sum_{j}^{n} w_{ij}\right)\sum_{i}^{n}\left(y_i - \bar{y}\right)^2} \qquad \textit{Eq 2}$$

where:

n: total number of features

y_i and y_j : individual observations

y: sample mean of the variable

w_{ij}: weights between the ith and the jth features

(if i and j are adjacent $w_{ij} = 1$, otherwise $w_{ij} = 0$)

Moran's I measures spatial autocorrelation based on both feature locations and feature values. Like classical correlation, Moran's I ranges from -1 to +1 and the value of zero means there is no spatial autocorrelation. When the Moran's Index is positive, it means that the dataset is clustered spatially (neighbouring spatial units have similar values) and when Moran's Index is near 0 it means that there is no clustering of high or low values in the dataset. Figure 3-2 illustrates how spatial data look when it is clustered or dispersed.

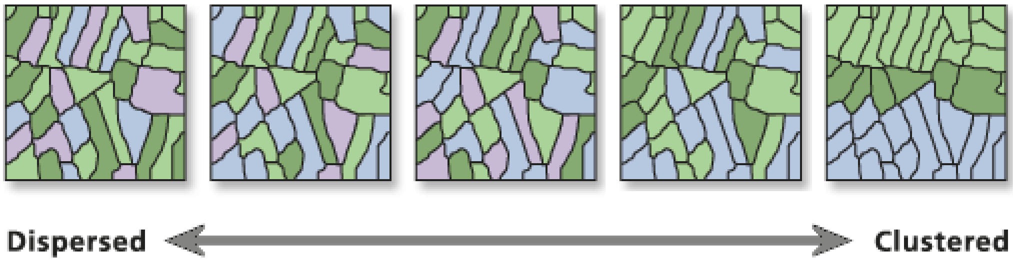


Figure 3-2: illustration of dispersed and clustered data (ESRI)

Since Global Moran's I is an inferential statistics, so the null hypothesis is defined to interpret the result of the analysis. The null hypothesis states that "*the attribute being analyzed is randomly distributed among the study area*". In other words, the statistical frame work is designed to allow one to decide whether there is a significant difference between any given pattern and a random pattern. So, z-statistic is created using the mean (E(I))and variance (V(I)) of I (equation 3, 4 and 5) (Rogerson 2001).

$$Z = \frac{I - E(I)}{\sqrt{V(I)}} \qquad \textit{Eq 3}$$

The expected and variance value of Moran's I under the null hypothesis of no spatial autocorrelation is:

$$\left.\begin{aligned} E(I) &= \frac{-1}{n-1} \\ V(I) &= \frac{n^2(n-1)S_1 - n(n-1)S_2 + 2(n-2)S_0}{(n+1)(n-1)^2 S_0} \end{aligned}\right\} \qquad \textit{Eq 4}$$

where:

$$
\left.
\begin{aligned}
S_0 &= \sum_{i}^{n}\sum_{j\neq i}^{n} w_{ij} \\
S_1 &= 0.5\sum_{i}^{n}\sum_{j\neq i}^{n} (w_{ij} + w_{ji})^2 \\
S_2 &= \sum_{k}^{n}(\sum_{j}^{n} w_{kj} + \sum_{i}^{n} w_{ik})^2
\end{aligned}
\right\} \qquad \textit{Eq 5}
$$

Like any other inferential statistics, the z-score value is then compared with the critical value found in the normal table. In this study, global Moran's I tool in ArcGIS was used which returns the z-score and *p*-value. Table 3-3 shows how to interpret the Moran'I *p*-value and z-score results:

Table 3-3: Interpreting the Moran's I result

$p > 0.05$	There is not a spatial clustering in the data set
$p < 0.05$ & $z > 0$	There is cluster of high values or low values in the dataset
$p < 0.05$ & $z < 0$	There is a dispersed spatial pattern in the dataset

3.4 Anselin local Moran's I

Hot spot areas can be identified visually by showing the variable on the map. However, objective analysis should be used to identify the hot spot areas statistically. There are few methods for this purpose such as Getis's G index (Getis and Ord 1996), spatial scan statistics (ISHIOKA et al. 2007) and local Moran's I index which was developed by Anselin in 1995 (Anselin 1995).

Local Moran's I identifies the hot spot areas by comparing each feature with respective neighbouring features (Zhang et al. 2008). In this study Local Moran's I tool in ArcGIS is used to find the cluster of high values in the study area since local Moran's I provide statistically significant spatial hot spots. By using the same notations as equation 2, for each attribute in the feature the local Moran's I statistics is expressed as equation 6. Positive and statistically significant I_i indicates the county is surrounded by similar high values.

$$\left.\begin{aligned} I_i &= \frac{x_i - \bar{X}}{S_i^2} \sum_{j=1, j \neq i}^{n} w_{i,j}(x_j - \bar{X}) \\ S_i^2 &= \frac{\sum_{j=1, j \neq i}^{n} (x_j - \bar{X})^2}{n-1} - \bar{X}^2 \end{aligned}\right\} \qquad \textit{Eq 6}$$

3.5 Ordinary least squares (OLS) regression

Ordinary Least Squares regression is a global linear regression which creates a single regression equation that best describes the overall data relationships in a study area (Mitchell 2005).

Associations between CKD mortality (SMR) and environmental factors were evaluated using Ordinary Least Squares (OLS) regression which is described in equation 7:

$$y_i = b_0 + b_1 x_{i1} + \ldots + b_p x_{ip} + \varepsilon_i \qquad \textit{Eq 7}$$

where:

y_i is the value of the i^{th} case of the dependent scale variable

p is the number of independent variables

b_j is the value of the j^{th} coefficient, j=0,...,p

x_{ij} is the value of the i^{th} case of the j^{th} independent variables

ε_i is the error in the observed value for the i^{th} case

OLS results are followed by some diagnostic reports which indicate the accuracy of the model. These diagnostic results are as follow:

- R^2 and adjusted R^2: both R^2 and adjusted $R^2$are indicators of the model goodness of fit; however, adjusted R^2 is a better measurement when comparing different models with different independent variables. This number provides the percentage of the total variation of the outcomes which are explained by the independent variables. High R^2 and adjusted R^2 show a better model fit(Gujarati and Porter 2009).
- Variance Inflation Factor (VIF) is a measure of redundancy (multicollinearity) among all variables.VIF above 7.5 shows the independent variable is highly correlated with one or two variables and should be excluded from the model(Allison 1999; ESRI).
- Joint Wald statistic test is used to assess the overall model statistical significance. The null hypothesis for this test states that “the independent variables in the model are not effective”(ESRI).
- Koenker (BP) Statistic: is a test to determine whether or not the independent variables in the model have a consistent relationship to the dependent variable. In other words, it determines if the independent variables have the same behaviour over the study area. The null hypothesis for this test is that the model is stationary (have the same behaviour over the study area)(ESRI).

- Jarque-Bera statistic: determines whether or not the distribution of residuals (observed values minus predicted value) is normal. If the residuals are not normally distributed or clustered, the model is biased. The null hypothesis for this test is that the residuals are normally distributed (Jarque and Bera 1980).
- Akaike Information Criteria (AICc) is a measure of model performance. AICc is a good measurement for comparing different competing statistical models with different independent variables. The model with the lower AICc provides a better model(Akaike 1985).

3.5.1 Dependent and independent variables

Heat stress and dehydration are proposed as highly likely risk factor of CKD of unknown origin in central America(Wesseling et al. 2013), so temperature and precipitation were selected to be considered in the modelling process. The literature review illustrated that there is a relationship between farming activities and chronic kidney disease function in Central America, so permanent crops and annual crops were also selected as other candidates in the modelling process. Peraze et al. (Peraza et al. 2012) also showed an association between decreased kidney function and altitude. So altitude as another factor was considered.

Moreover, the following covariates (table 3-4) which have been identified in the "Report from the First International Research Workshop on MeN" (Wesseling et al. 2013)were considered in the modelling process. According to the available data and suggested covariates in table 3-4, alcohol cirrhosis mortality rate (as a proxy for alcohol use), number of schools per 10000 people, access to hospital (as a proxy for socioeconomic condition) were entered into the model. In addition, diabetes mortality rate (diabetes has been widely mentioned in references including Taal review(Taal and Brenner 2006)), and cardiovascular mortality rate (as an indication for hypertension and also in Taal review of risk factors (Taal and Brenner 2006)) were included in modelling process.

Table 3-4: Suggested covariates by "MeN Report" (Wesseling et al. 2013)

Suggested covariates for consideration
Drug, tobacco, and alcohol use
Diet and nutrition
Genetics, using ethnic subpopulation categorization as a proxy
Poverty and socioeconomic status (necessary also because it can emerge as a confounding or obscuring variable)
Co-morbid conditions – diabetes, hypertension, kidney stones

Finally, Standardised Mortality Ratio (SMR) was considered as the dependent variable. Precipitation, temperature, permanent crops, annual Crops, cardiovascular mortality rate, alcohol cirrhosis mortality rate (as a proxy for alcohol use), diabetes mortality rate, number of schools per 10000 people and access to hospital (as a proxy for socioeconomic condition), and altitude were considered as candidates for independent variables.

3.5.2 Standardizing data

Variables were in different scales and therefore standardization was used in order to compare coefficients in the regression model.

There are different methods for standardizing the data. A common method used for standardizing in regression is subtracting its mean and dividing by its standard deviation. Subtracting the mean typically improves the interpretation of main effects in the presence of interactions, and dividing by the standard deviation puts all independent variables on a common scale (Gelman 2008).

3.6 Geographically weighted regression (GWR)

GWR – as a method which provides detailed information about local areas – is increasingly becoming more popular for regression analysis. GWR has a better description of the complex interplay between the variables in local areas by providing a local form of linear regression. The model constructs one equation for each feature by incorporating the independent variables falling within the bandwidth of each target feature.

The model is fully described by Fothering et al. (Fotheringham et al. 2002). GWR extends the concept of global regression model by adding regional parameters. Equation 8 descrobes the model:

$$y_i = \beta_0(u_i, v_i) + \sum_k \beta_k(u_i, v_i)x_{ik} + \varepsilon_i \qquad \textit{Eq 8}$$

where:

(u_i, v_i): the location of point i in the space

β_0 *and* β_k : the coefficients

ε_i : the random error term at point i

β_0 and β_k are the parameters that should be estimated. To estimate these parameters, each observation is weighted according to its distance to the target point i. In order to weight the observations, Gaussian weighting kernel function is used (equation 9). The Gaussian kernel curve is shown in figure 3-3. Closer observations get higher weights in the spatial context of Gaussian kernel.

$$w_{ij} = \exp(-\frac{d_{ij}^{\ 2}}{b^2}) \quad \textit{Eq 9}$$

where:

d_{ij} : distance between point i and j

b: bandwidth

Increasing the value of the bandwidth leads to the inclusion of more neighbouring data in the local regression model result. A bandwidth value can be directly employed to the model when we have some previous knowledge or experience about the likely effect of neighbouring data. Otherwise, the Akaike Information Criterion (AIC) can estimate the optimal bandwidth for the model. In this study, the latter was chosen.

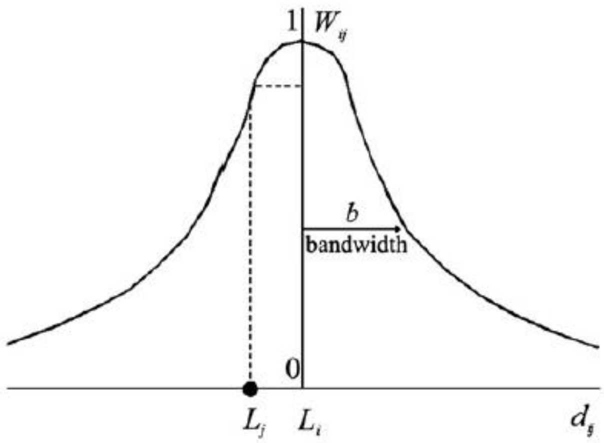


Figure 3-3: Gaussin Kernel function (Fotheringham et al. 2002)

3.7 Multi criteria decision analysis (MCDA)

At this part of the study, it was decided to include expert's knowledge about the risk factors of CKD in order to know their opinions about the factors affecting CKD and identifying the importance of each factor in comparison with other factors, and finally create a risk map according to the information received from the physicians to show which areas are more in danger from the physicians' perspective.

To this end, some approaches were needed to solve the problems related to decision support. One approach, which is a principle of Multi Criteria Decision Analysis, is based on dividing the decision problem into small, understandable parts and after analyzing each part combine them in a logical manner (Malczewski 1999). MCDA can reveal the decision maker's preferences and GIS can provide techniques for analyzing MCDA problems. Accordingly, these two distinct areas can complement each other (Malczewski 2006). Consequently, a group of experts cordially invited to participate in this study to define and rank the possible risk factors of CKD.

According to Eastman (Eastman) GIS based MCDA has five stages as below, which were followed in this study as well.

1. selecting the criteria.
2. standardizing the factors (from 0-1 or 0-255).
3. determining the weight of each factor.
4. aggregating the criteria.
5. evaluating the result.

3.7.1 Criteria selection

Since it was not easy to gather all physicians together to decide on the possible risk factors of CKD, the identification of the risk factors of CKD was performed by the two main physicians who had a good knowledge of CKD in Costa Rica: Dr.Kristina Jakobsson, a senior consultant and associate professor at Lund University, and Dr.Ineke Wesseling, a chairwoman of

Consortium for the Epidemic of Nephropathy in Central America and Mexico. So, the risk factors of CKD were categorized into seven groups:

1. factors related to the general environment.
2. factors related to land use, especially agriculture.
3. factors related to the work environment.
4. socio economic and demographic factors (individual level).
5. socio economic and demographic factors (collective level).
6. life-style factors.
7. medical and related conditions.

However, we didn't have access to all data related to each group. The available data only covered the factors related to "general environment", "socio economic and demographic factors (individual level)" and "socio economic and demographic (collective level)" factors. Consequently, according to the available data, the following criteria were used in this study:

Factors related to the general environment:

- temperature
- altitude
- rainfall
- housing proximity to crop land

Socio economic and demographic factors (individual level)

- sex
- age

Socioeconomic and demographic factors (collective level)

- access to health care
- social development index (SDI)

General environment include environmental factors that affect everyone living in the region. Socio economic and demographic factors (individual level) are characteristics which can be defined based on individual characteristics of all inhabitants in the area, however, only data regarding to demographic factors were available in this study (the complete sub-factors can be seen in appendix B). Socioeconomic and demographic factors (collective level) are neighbourhood/area socioeconomic characteristics that are not made up of individual´s data (like lack of access to different resources; a deprived neighbourhood).

The map for each criterion was created using the available data. In order to be able to overlay all layers in GIS, all criteria maps were in raster with the cell size of 100 m* 100 m. Table 3-5 shows the criteria maps created for each factor.

Table 3-5: Criteria maps used in MCDA

Criteria	Criteria maps
Temperature	Temperature raster map
Altitude	Digital Elevation Model
Rainfall	Precipitation raster map
Proximity to crop land	Distance map which shows the Euclidean distance from each point in the map to the closest crop land
Sex	Sex ratio map showing the No. Of man/No. Of Women in each district
Age	Age ratio map showing the No. Of people aged above 60/No. Of people aged below 60 in each district
Access to health care	Distance map which shows the Euclidean distance from each point in the map to the closest hospital
SDI	Social development Index for each district

The temperature map was created using interpolation method from 24 weather stations. Each weather station shows the average temperature from 1998 to 2002. Kriging as the spatial analytical method was used to predict unknown values from average adjacent known values. The precipitation map was created using 65 meteorological stations records as the average yearly rainfall in 2008, and the kriging as an interpolation method was used. For creating proximity to crop land and access to health care maps “Euclidean Distance” tool in ArcGIS is used. This tool creates a raster map which shows the Euclidean distance from each point in the map to the closest hospital. Age ratio and sex ratio and SDI were in district level.

3.7.2 Standardizing the factors

In order to be able to compare the values in the criteria map we need to transform them to a comparable unit. There are different ways for standardizing the data such as linear scale transformation, value/utility function approaches, probabilistic approaches and fuzzy membership approaches (Malczewski 1999). In this study, a linear transformation as a most commonly used technique in multi-criteria analysis is used for creating commensurate criteria maps.

The value of standard maps can range from 0 to 1; the higher the score the higher the risk of CKD incidence. According to the type of criteria, they should be maximised or minimised. When the value is maximised high values get the higher score and when it is minimised high values get the lower scores. For example, experts believe that there is positive correlation between high temperature and CKD mortality rate, thus temperature should be maximised. In other words, we should assign high scores (close to 1) to the high temperature and low scores to the low temperature (close to 0). Transformation of maximised and minimised criteria can be performed as equation 10 and 11 respectively (Malczewski 1999):

$$x_{ij}' = \frac{x_{ij} - x_j^{\min}}{x_j^{\max} - x_j^{\min}} \qquad \textit{Eq 10}$$

$$x_{ij}' = \frac{x_j^{\max} - x_{ij}}{x_j^{\max} - x_j^{\min}} \qquad \textit{Eq 11}$$

All the participants had the same opinion about the minimisation or maximisation of almost all factors except for precipitation. For precipitation the opinion of the majority is considered.

According to the questionnaire, proximity to crops, altitude, precipitation and Social Development Index were minimised and temperature, access to hospital, age ratio and sex ratio were maximised.

3.7.3 Determining the weight of each factor

In order to weight each criteria map, Analytical Hierarchy Process (AHP) was used. AHP was developed by Saaty (Malczewski 2006) and it involves pair wise comparisons. In this method, a hierarchy structure is needed to represent the problem and pair wise comparison should be built to show their relationships. Having selected the main criteria, sub criteria were selected according to the level of dependency to the main criteria. The hierarchy structure for this study is shown in figure 3-4.

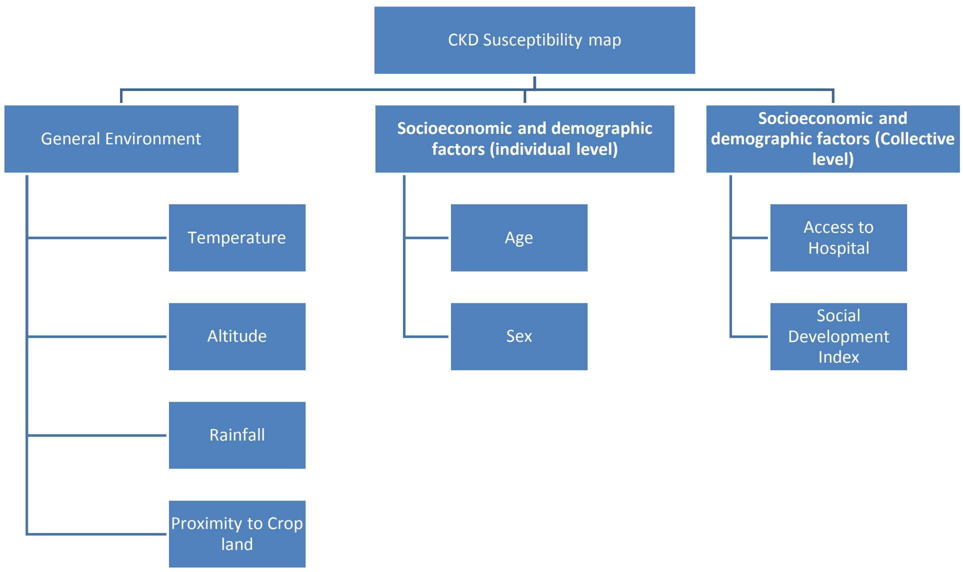


Figure 3-4: MCDA Criteria and Sub Criteria

In each level, each pair of criteria should be compared and weighted from 1 to 9 according to its influence on CKD. The scale to use when comparing each pair of criteria is shown in Table 3-6.

Table 3-6: Values for the experts for pair wise comparison of criteria

Choice	*Importance Value*
Equally preferred	1
Moderately preferred	**3**
Strongly preferred	**5**
Very Strongly preferred	**7**
Extremely preferred	**9**
Values in between preferences	**2, 4, 6, 8**

A questionnaire was designed and sent to the physicians (see appendix B), the questionnaire covered the whole seven criteria distinguished by the physicians. The questionnaire for exploration of expert's opinions was sent to 10 professionals. Among them, five experts answered the questionnaire. So, the opinions of the 5 physicians were included in the result of this study. For each factor tables was designed to perform a pair wise comparison. Figure 3-5 shows a sample table with regard to Socioeconomic and demographic (collective level) factor.

		Extreme								Equal								Extreme	
		9	**8**	**7**	**6**	**5**	**4**	**3**	**2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
1	**Access to health care**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Social development index**

Figure 3-5: pair wise comparison for Socioeconomic and demographic factors (collective level)

After receiving the whole results, a comparison matrix was constructed according to the experts' scores. Equation 12 shows the structure of comparison matrix for each criterion:

$$A = \begin{pmatrix} 1 & c_{12} \cdots & c_{1n} \\ c_{21} & \ddots & c_{2n} \\ \vdots & & \vdots \\ c_{n1} & c_{n2} & 1 \end{pmatrix}$$ where : $c_{ij} = 1/c_{ji}$ *Eq12*

3.7.4 Aggregating the criteria

To aggregate individual opinions the geometric mean (equation 13) was used as an efficient model(Wu et al. 2008).

$$A_{aggregate} = \begin{pmatrix} 1 & \sqrt[m]{\prod_{k=1}^{m} c^{k}_{12}} \cdots & \sqrt[m]{\prod_{k=1}^{m} c^{k}_{1n}} \\ \sqrt[m]{\prod_{k=1}^{m} c^{k}_{21}} & \ddots & \sqrt[m]{\prod_{k=1}^{m} c^{k}_{2n}} \\ \vdots & & \vdots \\ \sqrt[m]{\prod_{k=1}^{m} c^{k}_{n1}} & \sqrt[m]{\prod_{k=1}^{m} c^{k}_{n2}} & 1 \end{pmatrix}$$ *Eq 13*

The weight for each criteria and sub criteria was calculated using the AHP tool created by Thomas Pyzdek (Institute).

Saaty suggest calculating the Consistency Ratio (CR) to examine how the preferences of the participant have been consistent. He suggests a maximum ratio of 0.1 is acceptable and when the consistency ratio exceeds 0.1 re- examination is needed(Saaty 1987).

At the final stage a linear combination was used to combine all criteria and sub criteria weights (equation 14).

$$F = \sum w_{c_i} \sum w_{sc_i} Sc_i$$ *Eq 14*

where:

$$\sum w_{c_i} = 1 \qquad \sum w_{sc_i} = 1$$

W_{ci} : weight of each Criteria

W_{sci} : weigh of sub critera

Sci : sub criteria values (map layers)

Having calculated the weights of each criteria and sub criteria using AHP analysis, the corresponding weights were applied to the model using the formula in equation 14. The combination of all criteria maps was performed by "Raster calculator" tool in ArcGIS.

3.7.5 Evaluating the result

In this study, Kappa statistics is used to evaluate if there is an agreement between physician's decisions and reality. The calculation is based on the difference between how much agreement is actually observed compared to how much agreement would be expected to be present by chance alone (Viera and Garrett 2005). The value of Kappa ranges from -1 to 1, where 1 means 100% agreement and 0 is exactly what would be expected by chance and negative values indicate agreement less than chance. The Kappa statistics was checked using SPSS software.

4 RESULTS

Overall, 5821 individuals died from CKD over the study period from 1980 to 2012. Of them, 3585 (62%– 95% CI: 60% – 62%) were males and 2236 (38% – 95% CI: 37% – 39%) were females ($p < 0.05$). The result showed that Canas county has the highest SMR (703.19 – 95% CI: 701.33– 705.05), the highest mortality rate per 10000 people (22.2 – 95% CI: 17.07 – 28.9) in the period of 2008-2012 and also the highest mortality rate growth (Slope: 1.35 – 95% CI: 0.97 - 1.72) from 1980 to 2012.

The overall time trends of mortality rate, identification of hot spots and the procedures for creating regression models are explained in details in the following subsections.

4.1 Time trends and hot spots

Figure 4-1 shows that, over the study period there was a significant increase in overall mortality rate – from less than 3 in 1980 to more than 7 per 100000 populations in 2012. So the relative risk shows about 3 times more risk of death due to CKD in 2012 compared to 1980 (RR: 2.94 – 95% CI : 2.21 – 3. 89) .

Figure 4-1: CKD Mortality Rate per 100,000 people from 1980 to 2012

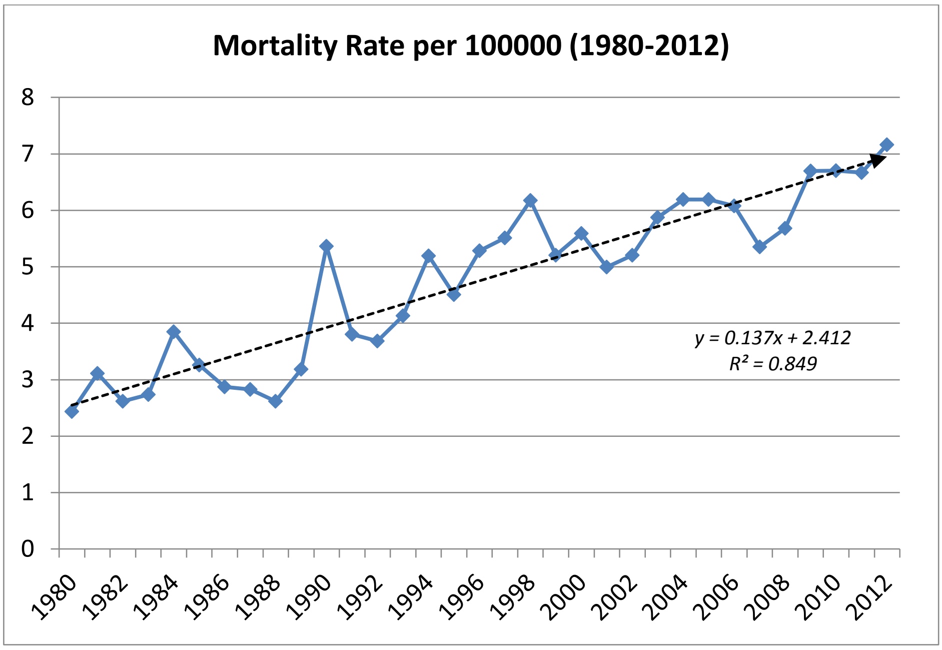


Figure 4-2 and 4-3 show higher slope of mortality rates over time in men compared to women. The discrepancy are more visible when limiting the data to under 60-years of age (females start with the mortality rate of around 1.5 and they have almost similar mortality rate at the end of study period). This increase of mortality in younger males is in line with the literature.

Figure 4-2: CKD Mortality Rate per 100,000 people according to gender from 1980 - 2012

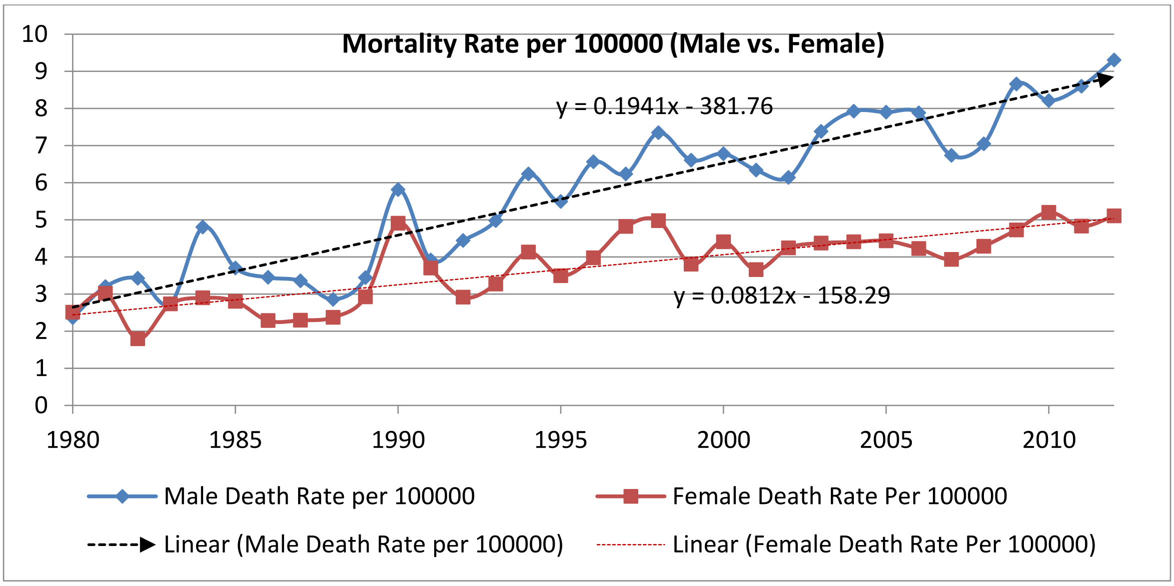
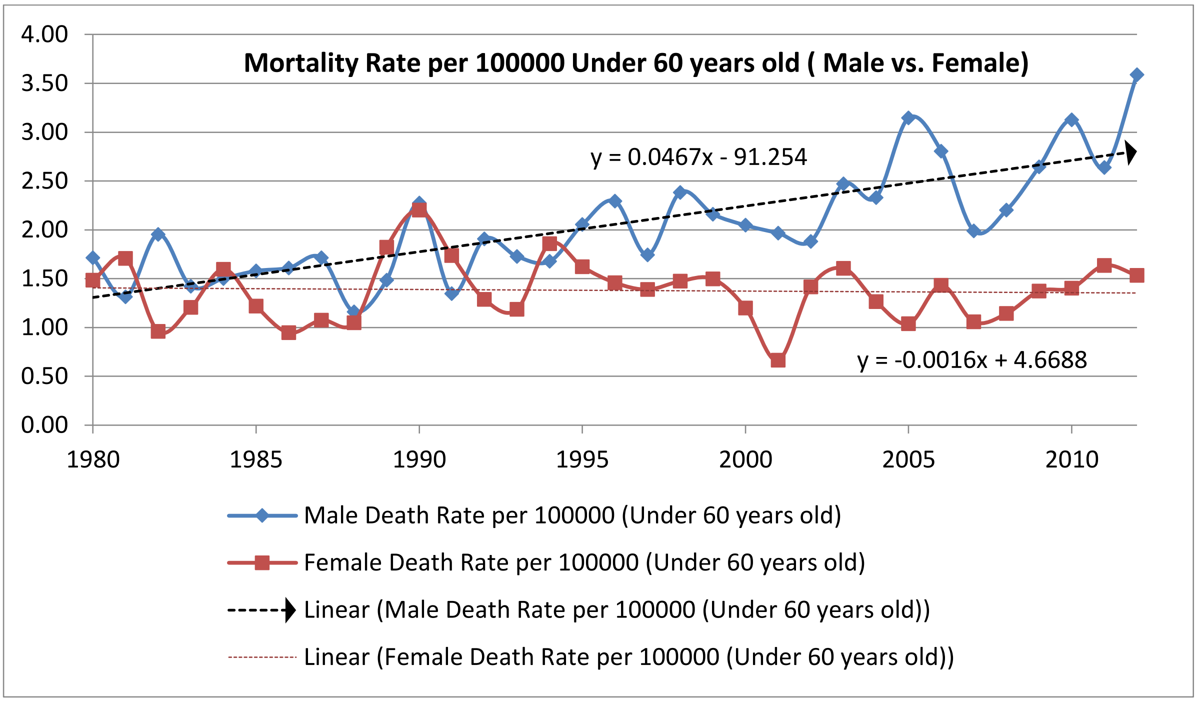
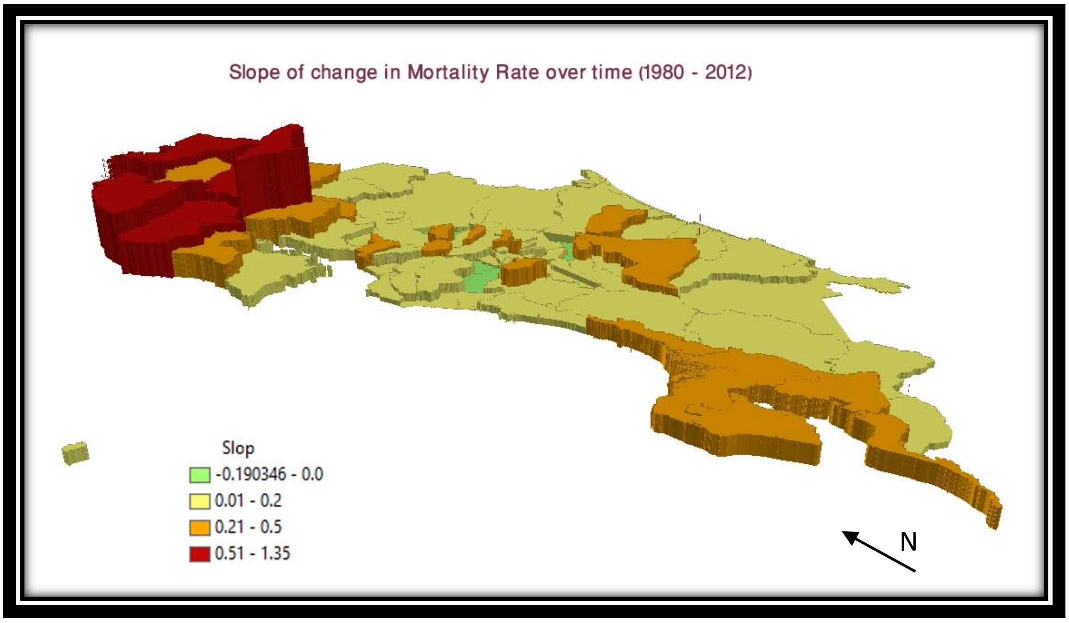


Figure 4-3: Mortality Rate per 100, 000 people (under 60 years old)



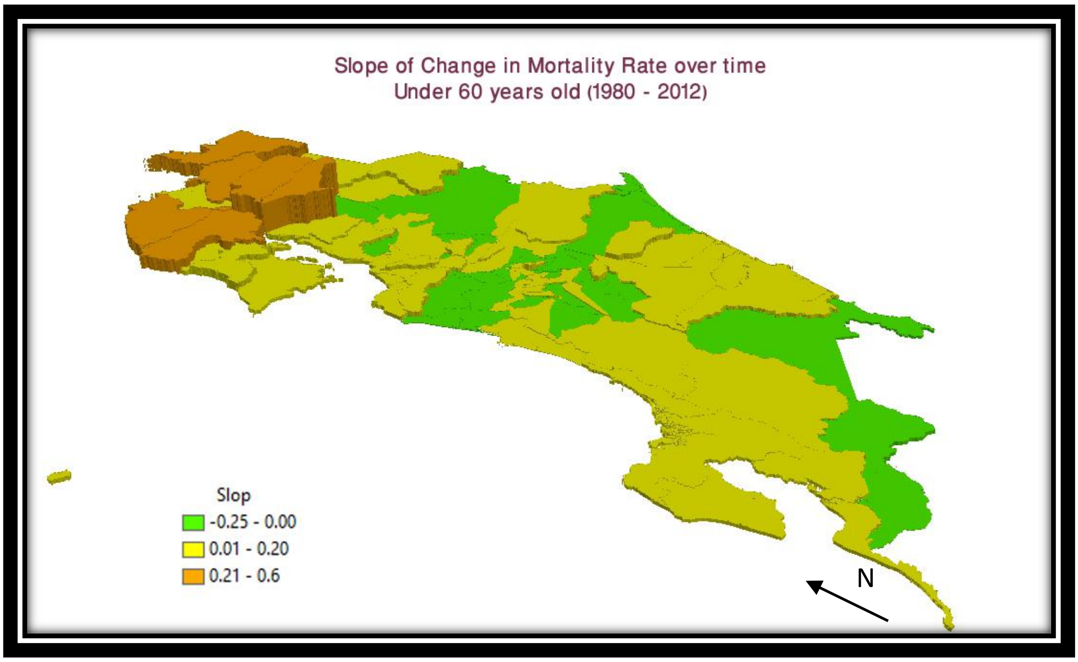
Considering the mortality rate growth from 1980 to 2012, the slope of change was calculated for each district. Figure 4-4 shows the slope of increase or decrease in mortality rate over the study period. As figure 4-4 shows, northern counties have the highest CKD mortality rate growth. The map also shows that there has been a decrease in CKD mortality rate over time for noticeable parts of the central counties over the study period.

Figure 4-4: Mortality Rate Growth from 1980 to 2012 (Slope of change of the Mortality Rate)



Limiting the data to under 60 years old, the slope of change in mortality rate shows that there is an increase in mortality rate in northern part of the country, compared to the central and southern (figure 4-5).

Figure 4-5: Mortality Rate Growth from 1980 to 2012 for under 60 years old (Slope of change of the Mortality Rate for under 60 years old)



SMR -a useful index for demonstrating the mortality rate adjusted by age and sex- is calculated for each county of Costa Rica. An SMR of 100 indicates that CKD mortality rate in the corresponding county is the same as the mortality rate of the whole country. The value of SMR greater than 100 indicates there is a higher mortality rate in the corresponding county than in Costa Rica, and the value less than 100 indicates there is a lower mortality rate in the county than in Costa Rica.

Consequently, 5-yearly SMRs were calculated and mapped in figure 4-6. It can be seen that the problem existed in a geographically limited area in northern part of the country in 1980s and gradually spread to neighbouring areas in time; so that most of northern part are among the highest SMR areas in the map of 2008-2012. In addition, for each 5-yearly period, the SMR maps for people aged under 60 (figures 4-7 to 4-12) were also mapped and compared with SMR of total population.

Visually, the maps of SMRs of total population and SMR of under 60 show almost the same pattern in 1980s and the early 1990s (figure 4-7 to figure 4-9) except for the recent set of maps in 2000 to 2012 (figure 4-10 to figure 4-12). In maps of 2008-2012, northern districts have higher SMRs for the calculation of under 60 compared to the SMRs for the whole population.

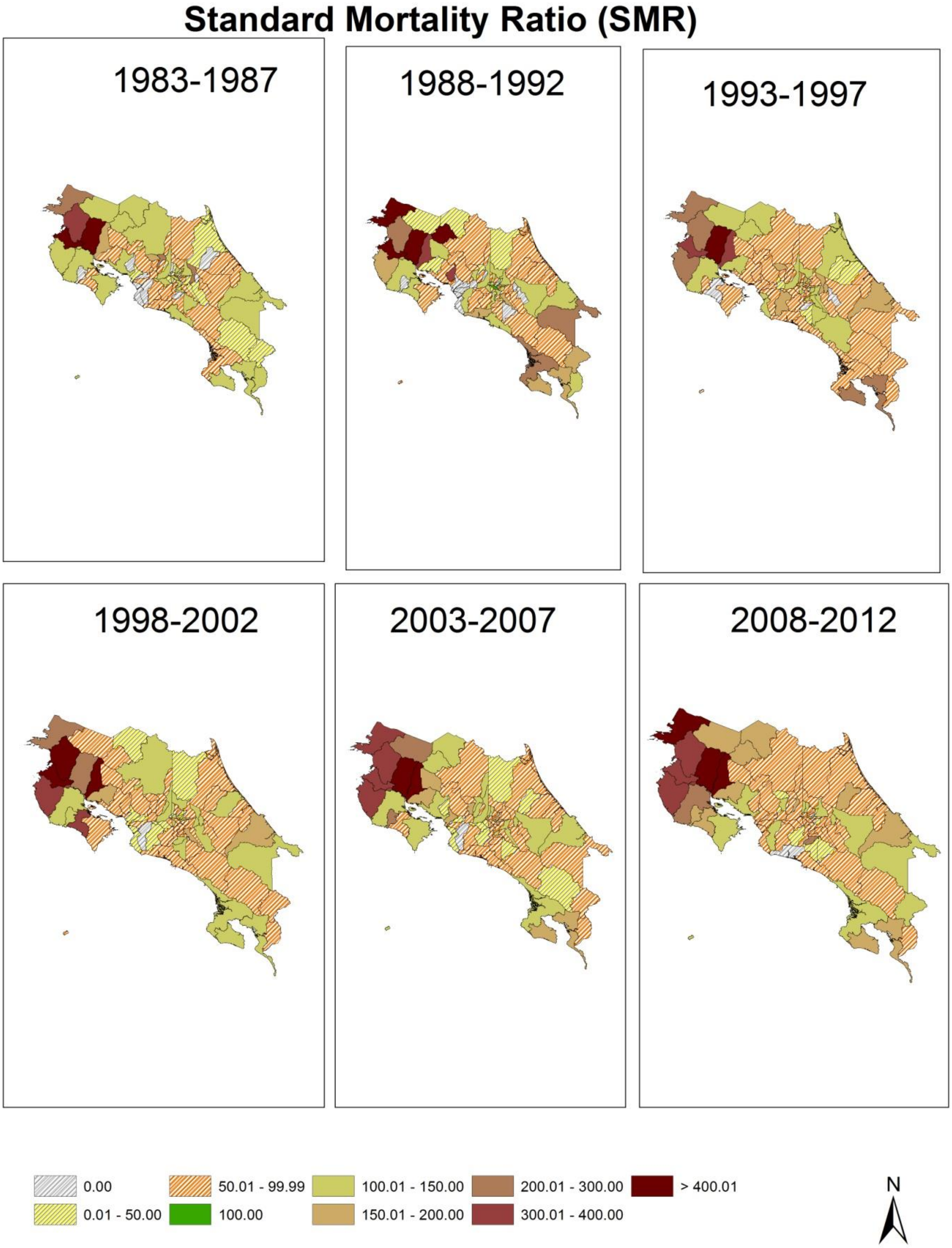


Figure 4-6: SMRs for 5-yearly intervals from 1983-2012

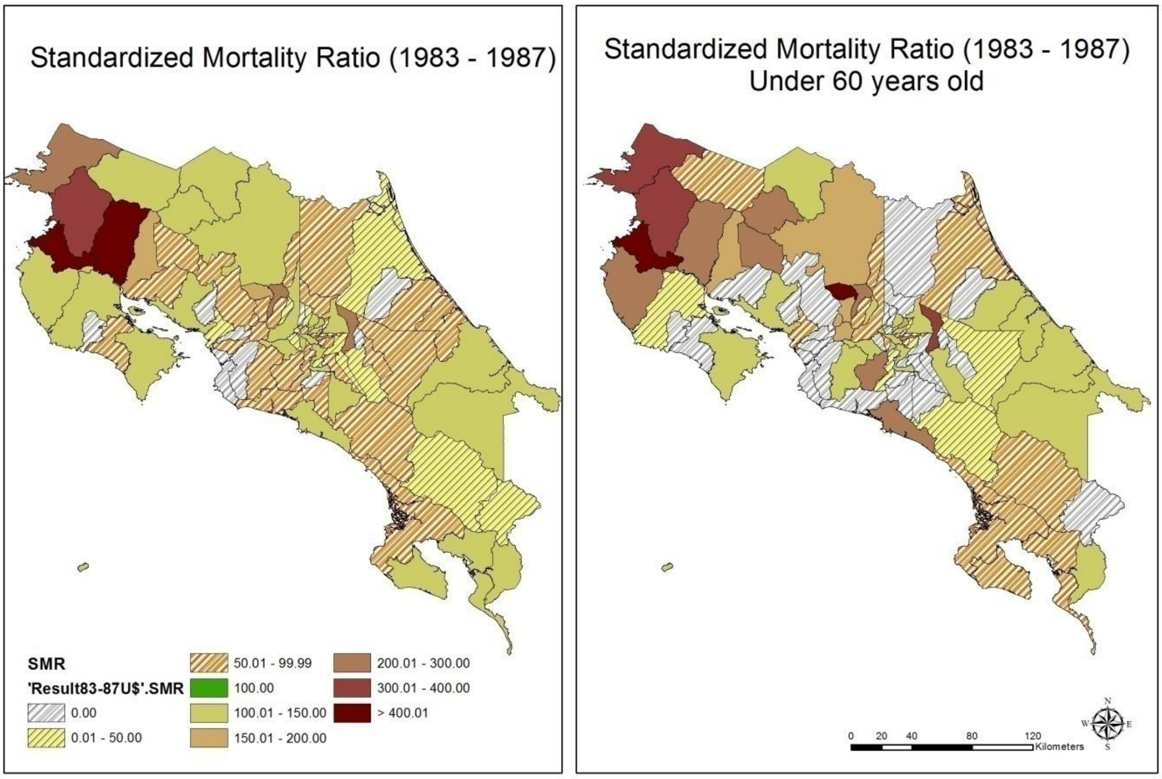


Figure 4-7: Standardized Mortality Ratio (1983 – 1987)

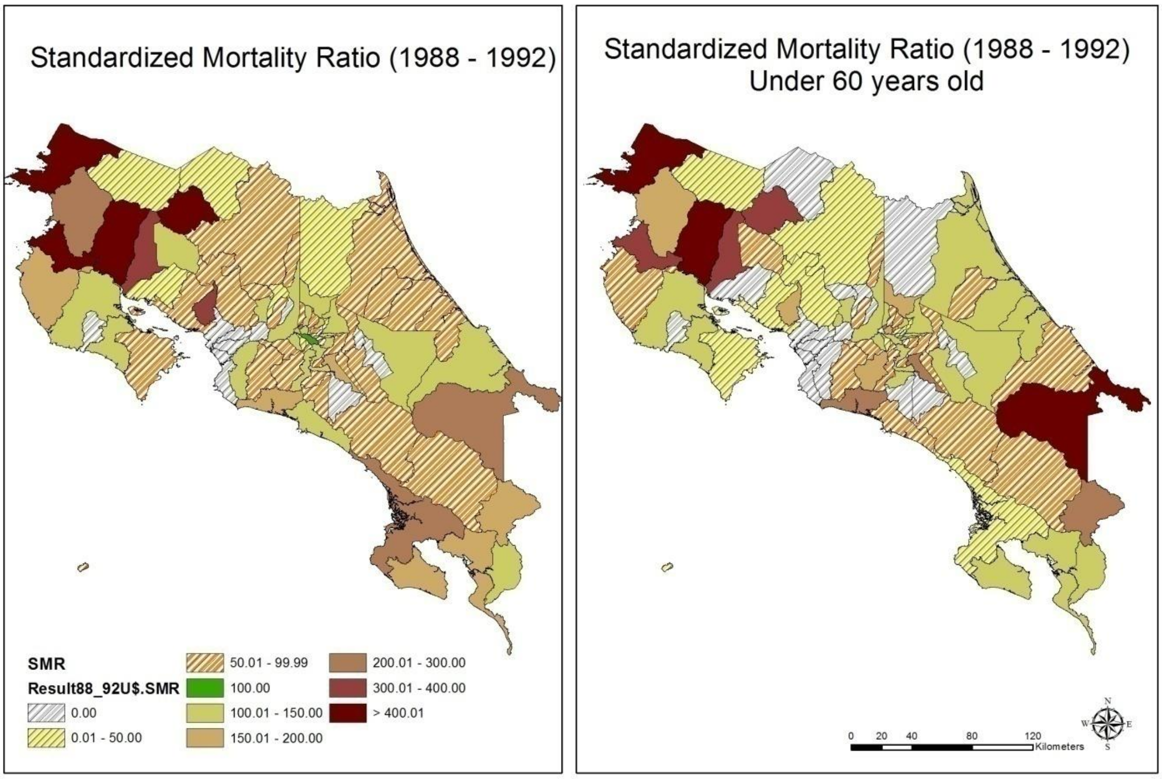


Figure 4-8: Standardized Mortality Ratio (1988 – 1992)

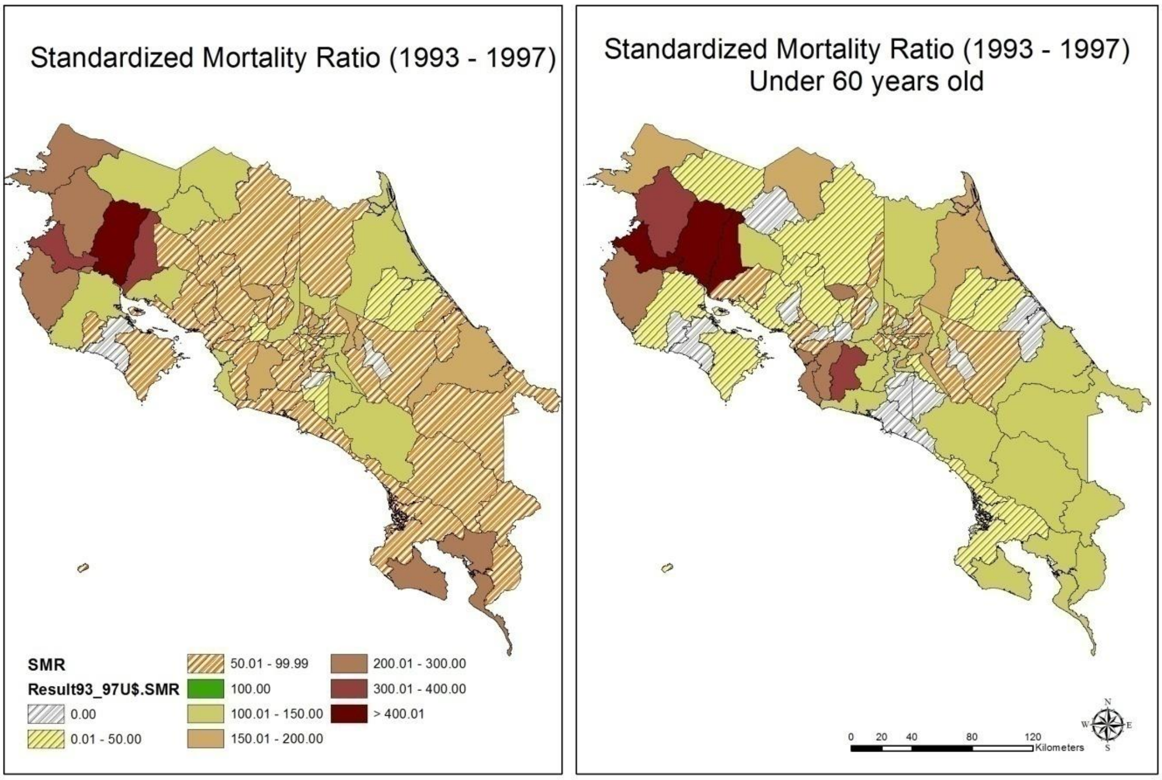


Figure 4-9: Standardized Mortality Ratio (1993 – 1997)

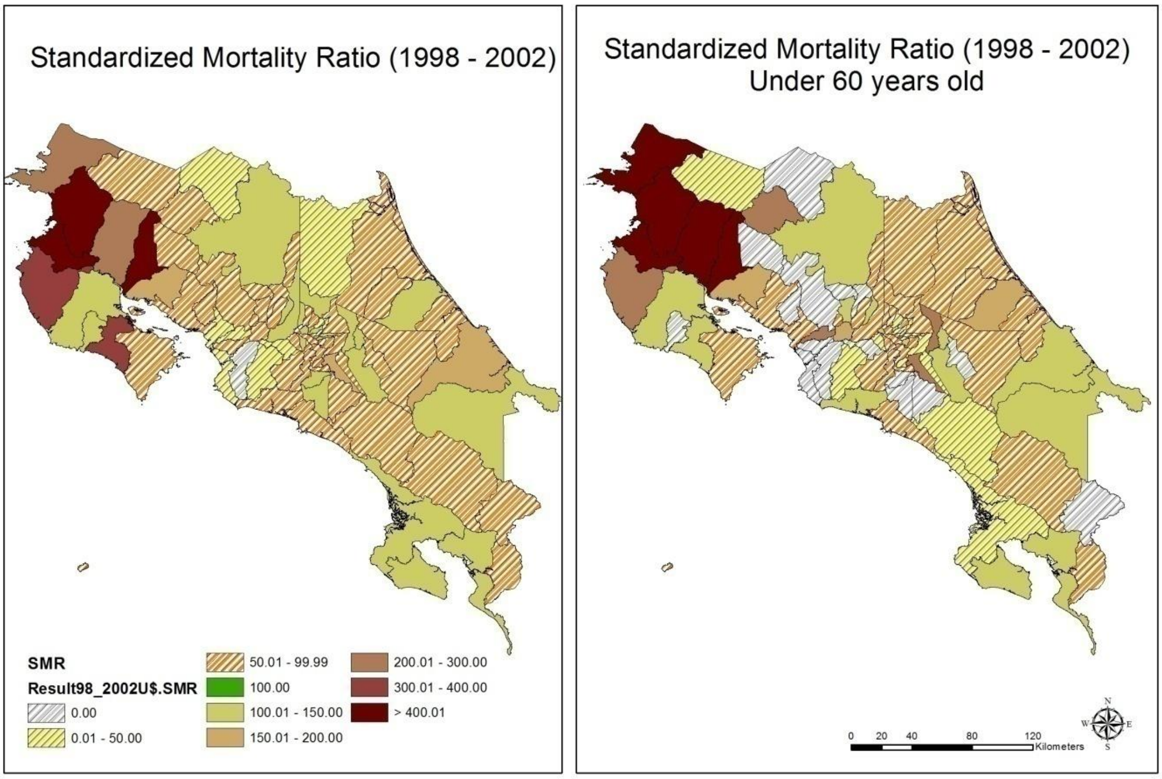


Figure 4-10: Standardized Mortality Ratio (1998 – 2002)

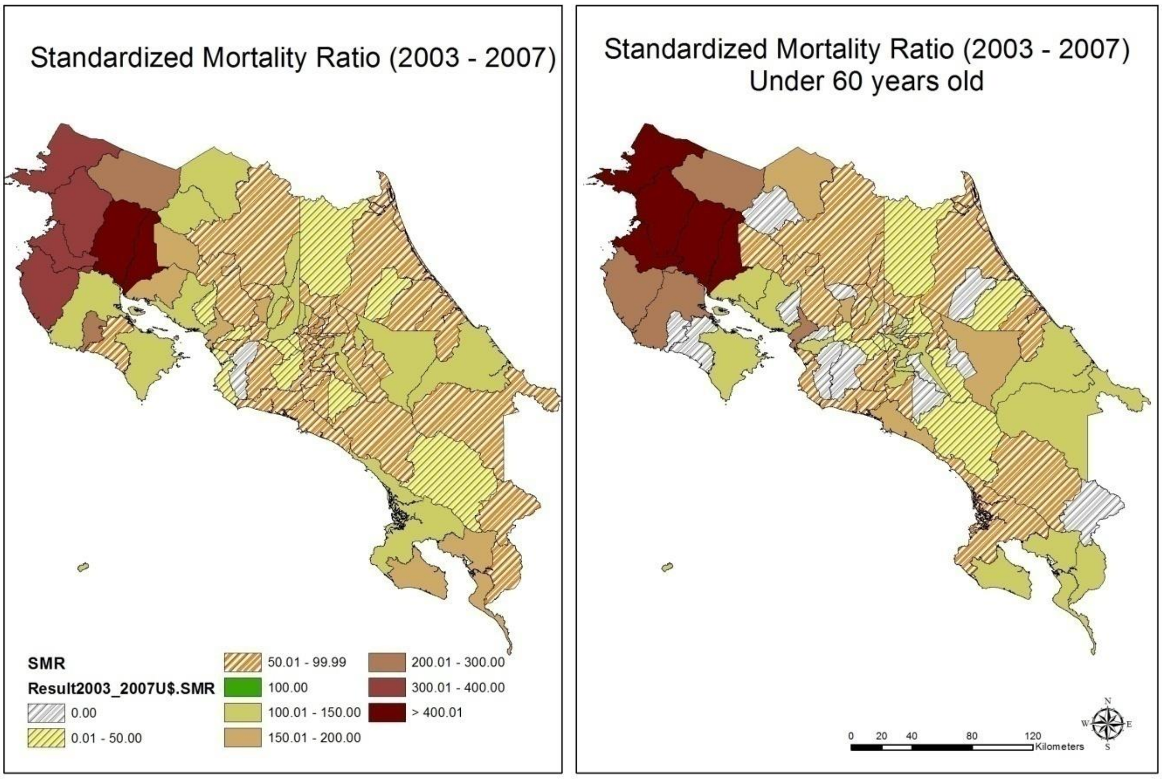


Figure 4-11: Standardized Mortality Ratio (2003 – 2007)

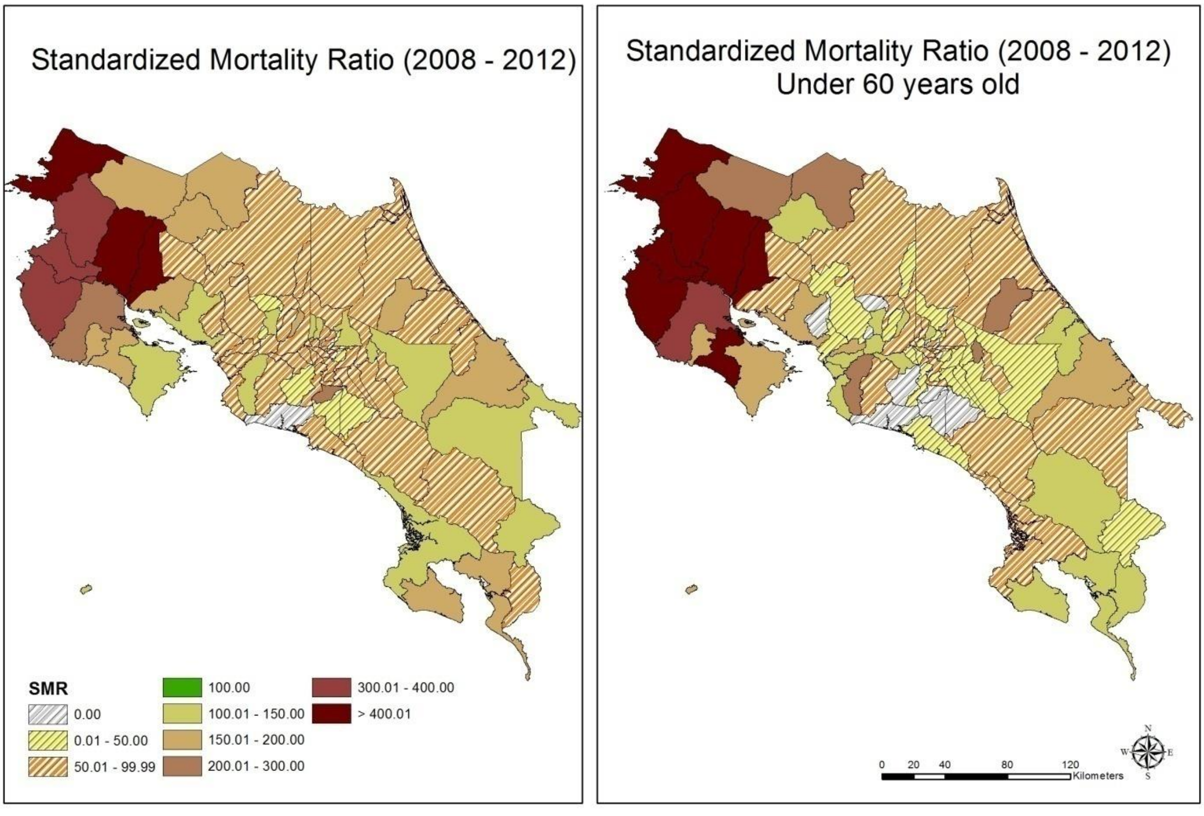


Figure 4-12: Standardized Mortality Ratio (2008 – 2012)

The cluster of high SMR values was demonstrated visually on figure 4-8 to figure 4-12. However, spatially clustered counties should to be identified statistically. Consequently, spatial auto correlation Global Moran's I was applied to identify if there was a statistically clustered pattern in the SMR values. In this study, the SMR of the whole population calculated for the latest period (2008-2012) was selected for statistical analysis.

The result of the global Moran'I is shown in table 4-1. As it was explained in table 3-4, the significant *p* value and positive z-score indicated that there was a cluster of high or low values of SMR (2008 – 2012) in the dataset. Although global Moran's I demonstrated there was a cluster of mortalities in the dataset, cluster areas should be identified. Hotspot detection was conducted using Anselin Local Moran's I.

Table 4-1: Result of spatial autocorrelation (Global Moran's I)

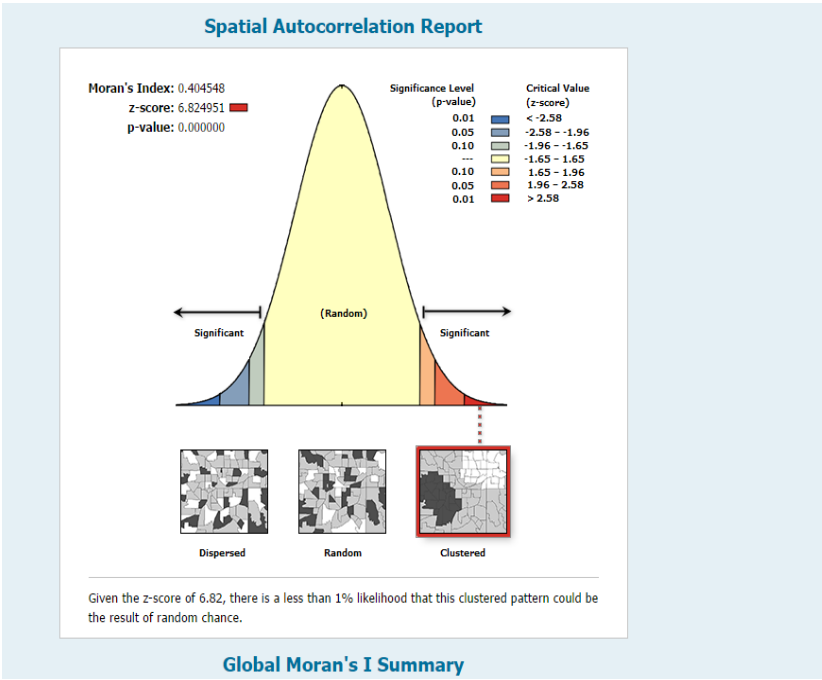
<table>
<tr><td>Moran's Index</td><td>0.40</td><td rowspan="3">
</td></tr>
<tr><td>Z-score</td><td>6.82</td></tr>
<tr><td>p-value</td><td>0.00</td></tr>
</table>

Figure 4-13 shows the results of Anselin Local Moran's I. According to the result, seven counties identified as statistically significant cluster of high SMR values. These counties included Bagaces, Canas, Carrillo, La Cruz, Liberia, Santa Cruz and Upala.

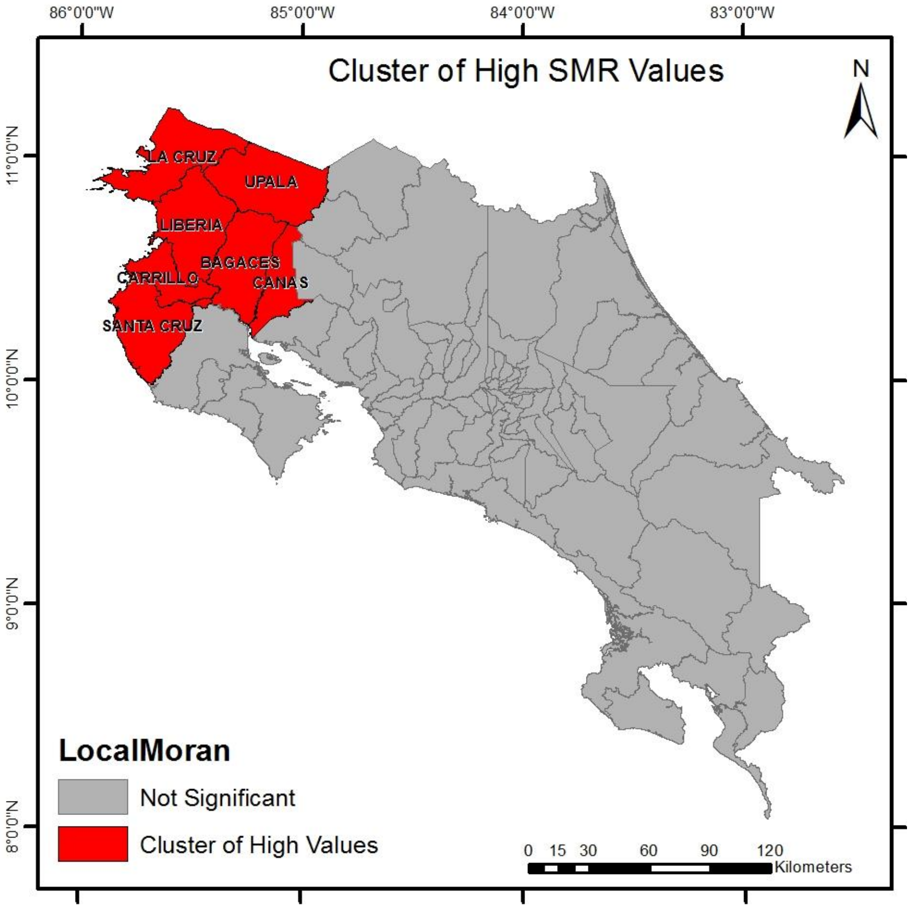


Figure 4-13: Anselin Local Moran's I map

4.2 Ordinary least squares and geographically weighted regression

The spatial relationship between CKD mortality cases and its risk factors can be determined by implementing two of the common methods in geography, Geographically Weighted Regression (GWR) and Ordinary Least Square (OLS). In global regression models such as OLS, the results are unreliable when the relationships between dependent and independent variables are inconsistent across the study area (i.e. regional variation or nonstationary). In this study, both OLS and GWR models were examined to determine which method would provide a better fit to the observation.

4.2.1 Model selection

SMR (2008 – 2012) was selected as a dependent variable. Cardiovascular mortality rate, diabetes mortality rate , alcohol cirrhosis mortality rate , access to hospital , schools rate per 10000 people, temperature, permanent crops, annual crops, precipitation, and altitude were selected as candidates for independent variables.

One of the assumptions in regression model is avoiding redundant variables, so we need to determine which candidate on independent variables are highly correlated. A bivariate correlation matrix was used to measure the strength and relationship between the variables by measuring the correlation between two variables X and Y. A variable with high correlation (more than 0.7) with others should be excluded from the analysis(Clark and Hosking 1986).

As can be seen in table 4-2, cardiovascular mortality rate, alcohol cirrhosis mortality rate and school rate didn't show a significant correlation with SMR ($P > 0.05$), so they should be excluded from the independent variables. A high relationship can be seen between altitude and temperature (r = - 0.73, $p<0.05$), so one of these variables should be excluded from the independent variables as well. Since temperature shows a higher correlation with SMR, altitude was excluded.

So, the final model incorporated 6 independent variables, of which four related to environmental factors (Permanent crops, Annual crops, Precipitation, Temperature), one related to traditional risk factor of CKD (Diabetes Mortality Rate), and one related to socio economic factor (Access to hospital).

Table 4-2: a bivariate correlation matrix between all variables

Correlations												
		SMR	**AnnaulCrop**	**PermanentC**	**Precipitat**	**Altitude**	**temp**	**AlchoholCir**	**Diabetes**	**SchoolRate**	**CardioVasc**	**AccessHosp**
SMR	*Pearson Correlation*	1	.368**	.410**	-.268*	-.367**	.487**	-.090	.415**	-.094	.181	-.254*
	Sig. (2-tailed)		.001	.000	.016	.001	.000	.425	.000	.406	.106	.022
	N	81	81	81	81	81	81	81	81	81	81	81
AnnaulCrop	*Pearson Correlation*	.368**	1	.460**	.122	-.549**	.481**	-.049	.284*	-.065	.095	-.364**
	Sig. (2-tailed)	.001		.000	.277	.000	.000	.661	.010	.565	.400	.001
	N	81	81	81	81	81	81	81	81	81	81	81
PermanentC	*Pearson Correlation*	.410**	.460**	1	.269*	-.408**	.429**	.035	.244*	.197	-.027	-.369**
	Sig. (2-tailed)	.000	.000		.015	.000	.000	.757	.028	.079	.809	.001
	N	81	81	81	81	81	81	81	81	81	81	81
Precipitat	*Pearson Correlation*	-.268*	.122	.269*	1	-.190	.203	-.138	-.306**	.014	-.316**	-.415**
	Sig. (2-tailed)	.016	.277	.015		.090	.069	.220	.005	.901	.004	.000
	N	81	81	81	81	81	81	81	81	81	81	81
Altitude	*Pearson Correlation*	-.367**	-.549**	-.408**	-.190	1	-.731**	.283*	-.340**	.269*	-.251*	.492**
	Sig. (2-tailed)	.001	.000	.000	.090		.000	.010	.002	.015	.024	.000
	N	81	81	81	81	81	81	81	81	81	81	81
temp	*Pearson Correlation*	.487**	.481**	.429**	.203	-.731**	1	-.255*	.322**	-.178	.168	-.652**
	Sig. (2-tailed)	.000	.000	.000	.069	.000		.021	.003	.111	.135	.000
	N	81	81	81	81	81	81	81	81	81	81	81
RateMortAl	*Pearson Correlation*	-.090	-.049	.035	-.138	.283*	-.255*	1	.127	.837**	-.360**	.009
	Sig. (2-tailed)	.425	.661	.757	.220	.010	.021		.259	.000	.001	.936
	N	81	81	81	81	81	81	81	81	81	81	81
RateMortDi	*Pearson Correlation*	.415**	.284*	.244*	-.306**	-.340**	.322**	.127	1	.060	.410**	-.137
	Sig. (2-tailed)	.000	.010	.028	.005	.002	.003	.259		.593	.000	.223

	N	81	81	81	81	81	81	81	81	81	81	81
SchoolRate	*Pearson Correlation*	-.094	-.065	.197	.014	.269*	-.178	.837**	.060	1	-.458**	-.072
	Sig. (2-tailed)	.406	.565	.079	.901	.015	.111	.000	.593		.000	.522
	N	81	81	81	81	81	81	81	81	81	81	81
CardioVasc	*Pearson Correlation*	.181	.095	-.027	-.316**	-.251*	.168	-.360**	.410**	-.458**	1	.119
	Sig. (2-tailed)	.106	.400	.809	.004	.024	.135	.001	.000	.000		.290
	N	81	81	81	81	81	81	81	81	81	81	81
AccessHosp	*Pearson Correlation*	-.254*	-.364**	-.369**	-.415**	.492**	-.652**	.009	-.137	-.072	.119	1
	Sig. (2-tailed)	.022	.001	.001	.000	.000	.000	.936	.223	.522	.290	
	N	81	81	81	81	81	81	81	81	81	81	81

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

4.2.2 OLS and GWR model results

The strength and direction of relationship between SMR and the independent variables are shown in the table 4-3. The sign of the coefficients showed a negative correlation between access to hospital and precipitation, implying inverse relationships between SMR and those independent variables. In contrast, a positive correlation was found between permanent crops, annual crops, temperature, and diabetes mortality rate.

Among the independent variables, the coefficients of access to hospital, diabetes mortality rate and annual crops were not statistically significant meaning that they did not contribute much to the model. However, the coefficient of precipitation, permanent crop and temperature were significant at 0.05 level.

The summary of OLS regression with regard to the model fit and other statistical reports is shown in table 4-4. The global model fit (OLS), gave R^2 and adjusted R^2 of 0.48 and 0.43 respectively. Thus, over 40% of variability in SMR could be explained by these variables (permanent crops, annual crops, precipitation, temperature, diabetes mortality rate, and access to hospital). All VIF values were less than 7.5, suggesting no variable was redundant. The Joint Wald statistic values and its associated *p*-value ($p<0.05$) showed the model was statistically significant. A significant *p*-value of BP statistic indicated independent variables were inconsistent to the dependent variables, meaning that there was a regional variation (nonstationay) between independent and dependent variable. The significance of Jarque-Bera Statistic showed the residuals deviated from a normal theoretical distribution. Likewise, the global Moran'I statistics was applied to examine the presence of spatial clustering in the residuals. The result showed the residuals were clustered (Figure 4-14).

Table 4-3: coefficients of variables in the regression model

Variable	Coefficient	Probability	VIF
Intercept	121.46	0.000000*	…..
Precipitation	-45.76	0.000084*	1.53
Permanent crop	32.31	0.003619*	1.47
Temperature	37.04	0.005405*	2.1
DiabetesMortalityRate	7.08	0.504230	1.42
Annual crops	7.59	0.481845	1.44
AccesstoHospital	-5.96	0.636212	2.05

Table 4-4: summary of OLS regression result

Dependent Variable	SMR2008_2012	
Number of Observations	81	
Multiple R-Squared	0.48	
Adjusted R-Squared	0.43	
Akaike's Information Criterion (AICc)	949.59	
		Probability
Joint Wald Statistic	34.93	0.000000*
Koenker (BP) Statistic	21.00	0.000005*
Jarque-Bera Statistic	111.64	0.000374*

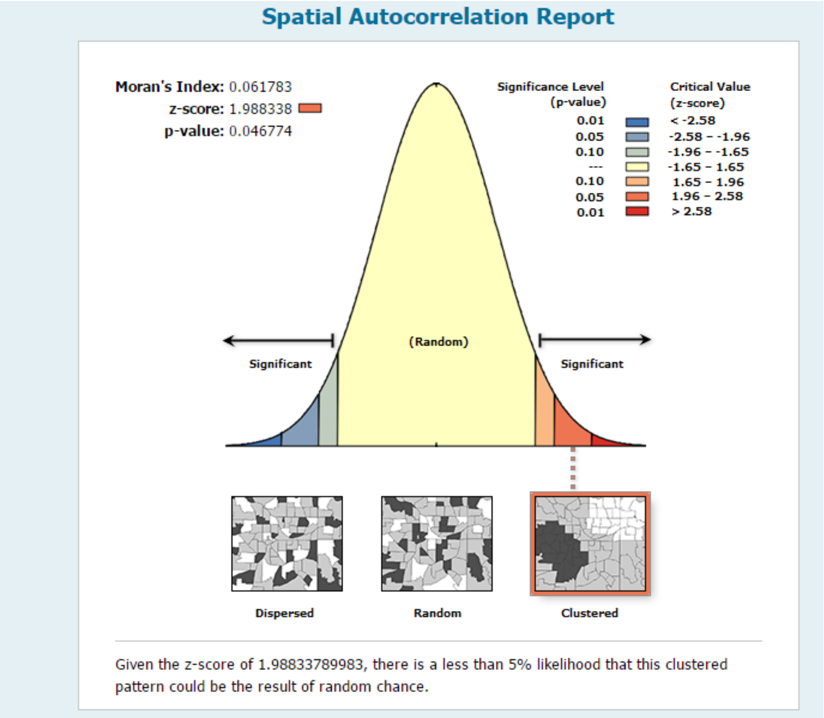


Figure 4-14: Result of global Moran'I on standard residuals for OLS model

The result of global Moran's I as well as Koenker BP statistics indicated the existence of nonstationary and clustered residuals respectively. Sufficient evidence therefore existed for resorting to GWR (Cardozo et al. 2012; Getis and Ord 1996).

Temperature, precipitation and permanent crops were the only statistically significant variables which contribute more to the model, so these variables were considered as inputs in the GWR model.

The adjusted R^2 (Adjusted R^2 = 0.65) obtained using GWR implied a considerable improvement in the model fitness with respect to OLS model (Adjusted R^2 = 0.43).

AICc ,an index for comparing two regression models, in GWR model is lower and it decreased from 949.59 in OLS model to 909.7 in GWR model. The lower the AICc the better the model.

Likewise, the analysis of the residuals of GWR model showed a random distribution of the residuals which implied GWR was a better model comparing to OLS. The result of the analysis of the residuals of GWR model using global Moran'I is shown in figure 4-15.

The comparison between GWR model and OLS model can be seen in table 4-5.

Table 4-5: Comparison between GWR and OLS model

GWR			OLS		
Adjusted R^2	***AICc***	***Residuals***	***Adjusted R^2***	***AICc***	***Residuals***
0.65	909.7	Random	0.43	949.59	Clustered

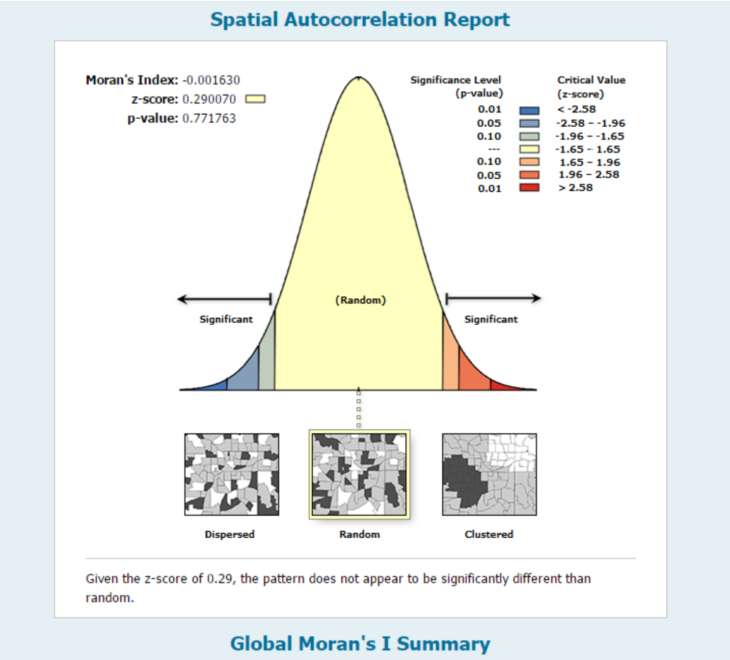


Figure 4-15: Result of global Moran's I for residuals of GWR model

As it was explained in the method part of this study, GWR constructs one equation for each feature by incorporating the independent variables falling within the bandwidth of each target feature. Thus, each county has a separate regression model with different coefficients for each independent variable. Figure 4-16 shows the variation of the coefficients for each independent variable across the study area.

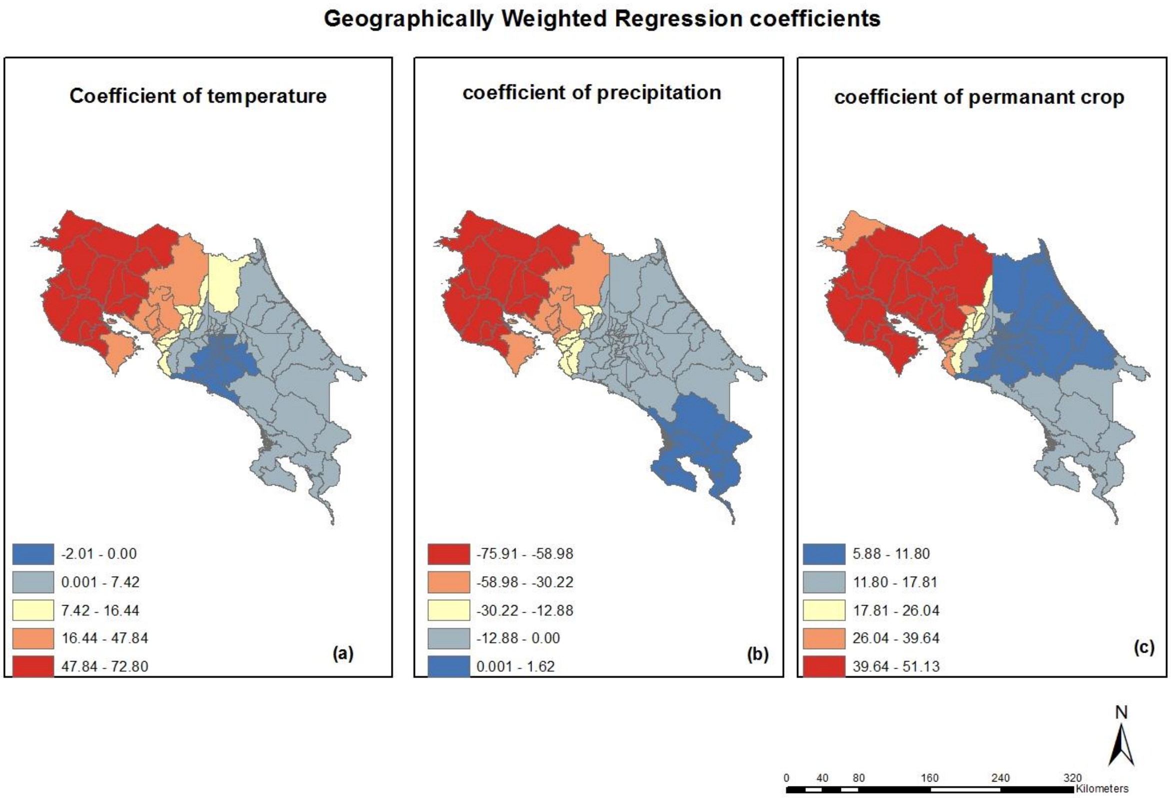


Figure 4-16: GWR coefficients for all independent variables, (a)Coefficients of GWR model for temperature, (b) Coefficients of GWR model for precipitation,(c) Coefficients of GWR model for precipitation

As can be seen in figure 4-16, the coefficients of GWR showed consistency in the effect of permanent crops (the coefficients are positive all over the study area), but inconsistencies in the effect of temperature and precipitation in different parts of the country since the coefficients of precipitation and temperature could be positive or negative for different locations. The effect of temperature is highly positive in the north unlike to precipitation which is highly negative in the north. What is interesting in comparing the coefficients of all three independent variables is that the effect of all three variables was dominant in the north.

4.3 Multi criteria decision analysis

The weight of each criteria and sub criteria derived from AHP analysis are shown in figure 4-17. The consistency ratio for comparing three main criteria and general environment factors were 0.03 and 0.01 respectively which was less than 0.1. The lowest weight was assigned to general environment and the highest weight was assigned to socioeconomic and demographic factors.

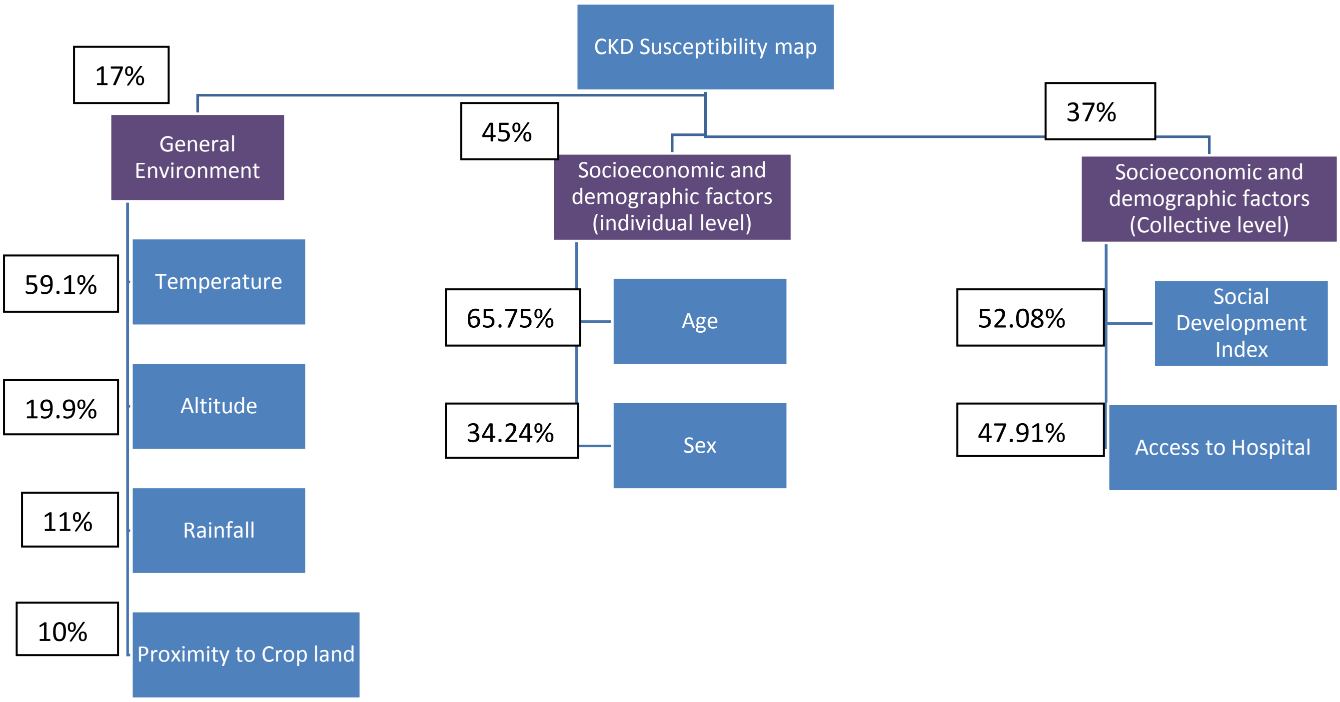


Figure 4-17: The weight for each criteria and sub criteria

The result of MCDA is shown in figure 4-18. The result assigned each unique value to each cell of the output raster, the higher the value the higher the risk of CKD. According to the weights that experts assigned to each criteria and sub criteria, central part of the country has the lowest values/risk.

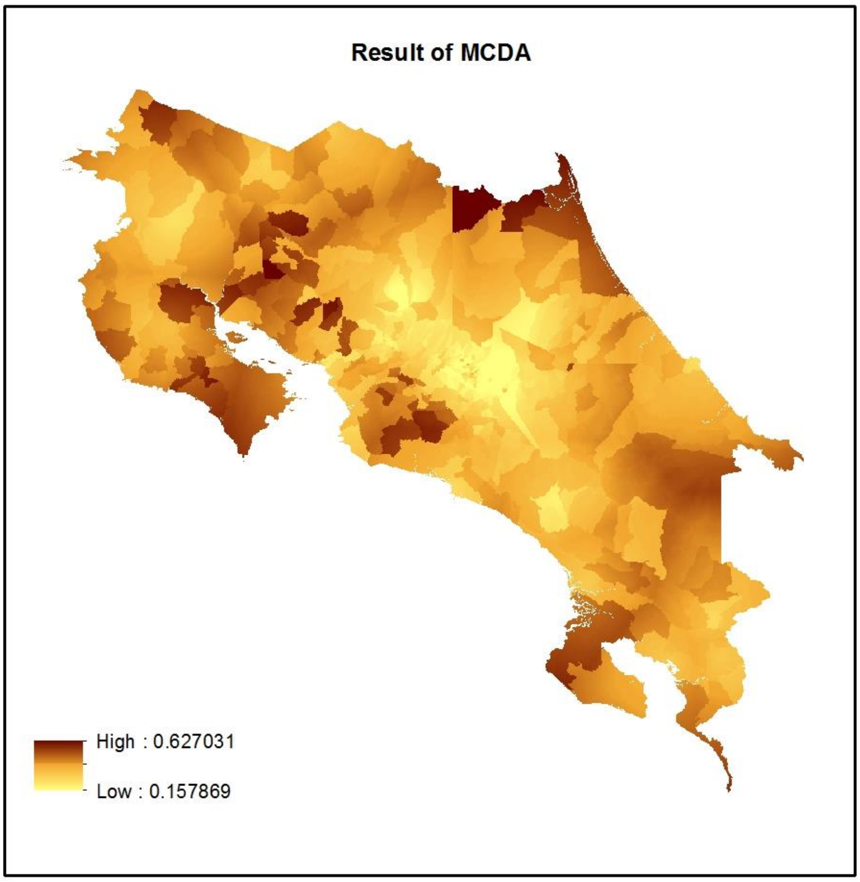


Figure 4-18: Result of MCDA

In order to be able to compare the results of the MCDA to SMR, the maximum score of each district was extracted and classified into three groups: high, medium and low risks.

Similarly, the reclassification was performed to the SMR values. Table 4-6 shows how the classification was performed according to the values of each map. For classification of MCDA score, a natural break technique was used to classify the result to low, medium and high risk. The advantage of using this method is that the break point is set where there is a relatively big difference in data values. With regard to SMR, the values more than 200 (the counties with the mortality rate twice more than the national) were classified as high risk, values below 100 were categorised as low risk and the values in between were classified as medium risk. Figure 4-19 shows the comparison between SMR and MCDA maps classified according to the risk level. In both maps central parts of the country was considered as the low risk regions. More districts in the northern parts of the country were identified as high risk in comparison with MCDA map.

Table 4-6: categorisation of SMR values and MCDA scores

MCDA		SMR	
Low risk	0.16-0.38	Low risk	0-100
Medium risk	0.38-0.47	Medium risk	100-200
High risk	0.47-0.62	High risk	>200

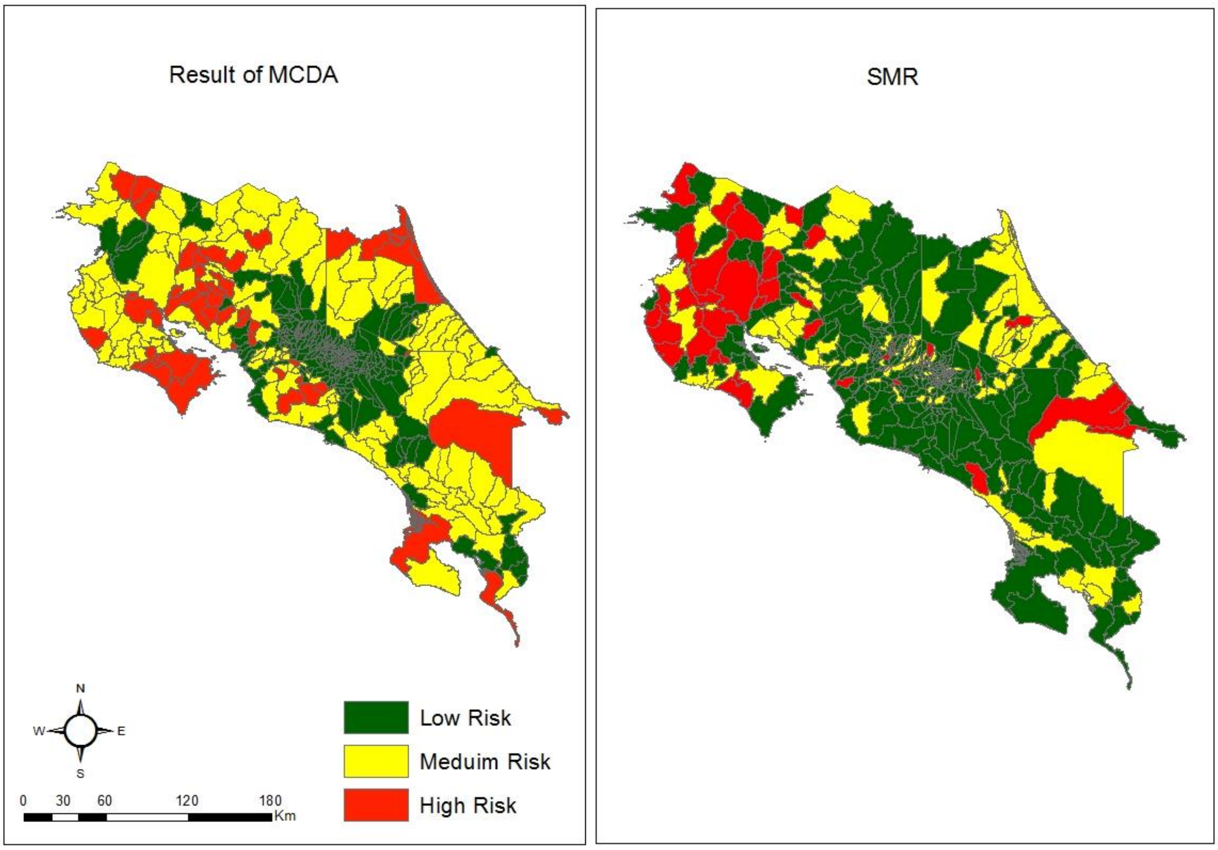


Figure 4-19: Comparison between MCDA and SMR

Table 4-7: Cross tabulation and Kappa result

MCDA* SMR Crosstabulation

			SMR			Total
			Low	Meduim	High	
MCDA	Low	Count	206	67	10	283
	Meduim	Count	85	35	22	142
	High	Count	27	11	9	47
Total		Count	318	113	41	472

	Value	Approx. Sig.
Kappa	**.087**	.016

Table 4-7 compares the number of districts classified in low, medium or high risk in the MCDA map with low, medium or high risk districts in the SMR map. The Kappa statistic with associated *p*-value was also estimated (Kappa: 0.087, $p<0.05$) and showed in table 4-7.

For interpreting a Kappa value Landis and Koch (1977) gave table 4-8 (Landis and Koch 1977), so in this study the Kappa value of 0.087 showed a slight agreement between MCDA result and reality.

Considering the high risk districts, according to table 4-7, nine districts were recognised as high risk in both maps.

Table 4-8: Interpreting Kappa value

kappa	***< 0.01***	***0.01 - 0.20***	***0.21 - 0.40***	***0.41 - 0.60***	***0.61 - 0.80***	***0.81 - 1.00***
Interpretatio n	Poor agreement	Slight agreement	Fair agreement	Moderate agreemen t	Substantial agreement	Almost perfect agreement

The decision makers assigned 17% of the weight to the general environment, which was the lowest weight among the three main criteria. According to my findings in the regression model, CKD showed a high association with the environmental factors, so I changed the weight of the general environment to 50% and two other criteria to 25% to investigate whether we could get a better result more closely to the reality.

The result can be seen in figure 4-20. Comparing the result of new created map with the SMR map, we can see that central parts of the country still remained as low risk, in contrast to the northern parts.

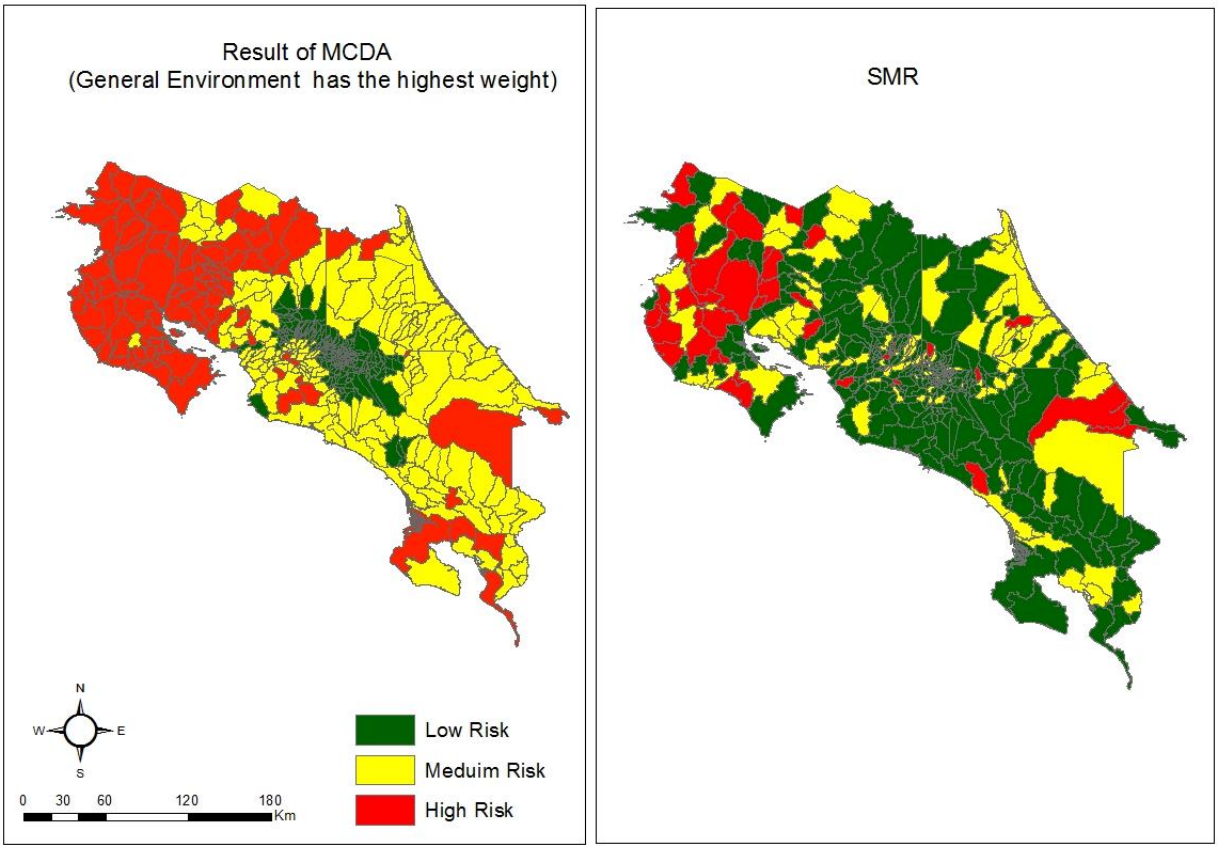


Figure 4-20: Comparison between MCDA and SMR (with "General Environment" as the highest weight)

Table 4-9: Cross tabulation and Kappa result

MCDA(Envi) * SMR Crosstabulation

			SMR			Total
			Low	Meduim	High	
MCDA(Envi)	Low	Count	167	50	6	223
	Meduim	Count	102	40	10	152
	High	Count	49	23	25	97
Total		Count	318	113	41	472

	Value	Approx. Sig.
Kappa	**.133**	.000

Table 4-9 compares the number of districts classified in low, medium or high risk in a new created map (i.e. weight of environment: 50%, other factors:25%) with the SMR map. The Kappa increased to 0.13(p<0.05)which showed a better agreement with the reality in comparison with the previous result (however it still showed a slight agreement), also the number of districts which were distinguished as high risk in both maps approximately tripled and reached to 25 districts.

5 DISCUSSION

This study – which is the first of its kind in Costa Rica – identified the hot spots of CKD and suggests that northern parts of Costa Rica deserve further CKD investigations to see what practical measures could better control CKD in those areas. Wesseling et al. (Wesseling et al. 2014) looked at geographical distribution of CKD mortality in Costa Rica and concluded that Guanacaste is a heterogeneous CKD "hot spot". This is consistent with our findings of geographical distribution. The results also confirmed the findings of previous studies that men are affected significantly more than women by this CKD epidemic (Cerdas 2005).

The study also showed significant associations between CKD mortality rate and environmental factors (temperature, permanent crops, and precipitation). These associations provide further evidence in support of the link between the current CKD epidemic and farming activities – in particular heat stress which has already been considered as a highly likely contributing factor by experts (Wesseling et al. 2013). These new-emerging factors have now been named in the literature as non-traditional risk factors against traditional risk factors of CKD (Almaguer et al. 2014).

The inconsistencies of the effects of temperature and precipitation in the GWR model in different locations is indicative that there should be another related causal factor (likely to be heat stress) in the exposure-outcome pathway. The consistencies in the effect of permanent crops in different parts of the country provide further evidence on the role of agricultural occupation in CKD (Almaguer et al. 2014). VanDervot et al. (VanDervort et al. 2014) concluded in their study that agricultural occupation is a risk factor in CKD. The association between permanent crops and CKD mortality rate is in line with the findings of VanDervort et al.

With respect to the last research objective, it was found that the expert's knowledge about the effect of the environmental factors to CKD in Costa Rica is probably not adequate. The current study found that experts believe environmental factors have the lowest effect on the CKD, due to assigning the lowest weight to it. After increasing the weight of the environmental factors, an improvement in the Kappa value was detected. Moreover, the model with the highest weight for the environmental factors could recognise the high risk districts better which confirms the effect of environmental factors to CKD in Costa Rica. This result is consistent with our findings in the regression model.

The findings of this study also provide objective evidence on the progressive nature of the current CKD problem in Costa Rica (i.e. steady increase in mortality rates and three times more risk of mortality in 2012 compared to 1980). Therefore, actions should be taken by those in charge, otherwise the problem is likely to continue becoming worse.

Several limitations to this study should also be acknowledged. In this study, the data regarding temperature, precipitation, annual crops and permanent crops go back to several years ago; so that there was no overlap between the study period and the variables of permanent crops and annual crops in the model. However, this is unlikely to affect the results due to the very slow progress of CKD which is a matter of 10 years from the beginning to end stage renal disease. Therefore, the exposure assessment of the risk factors could well look back to several years ago. From the medical point of view, once kidneys have been damaged due to exposure to risk factors, they may continue going downward for many years, even long after the exposure which has caused the damage has gone. Moreover, we do not expect significant variations over time for most of these variables (e.g. temperature).

Both in MCDA and regression model, all CKD risk factors recognised by the experts or mentioned in the literature review were not considered in the models due to lack of data.

Consequently, the models need improvements since they didn’t cover the whole aspects of CKD risk factors. However, in medical studies prediction has little role and it is more about associations to identify risk factors. In other words, the purpose of studies of this kind is not to predict how many people is going to die – but to find out which risk factors have been contributing to the illness in order to take proper actions to slow down the disease process or mortality rates. In this context, this study has been successful in providing further evidence on the possible role of heat stress and agricultural work in CKD mortality in Costa Rica.

Moreover, biological systems are usually too complex to be fully predicted and therefore it is not expected for medical models to provide high prediction of the situation – but it is expected for physical models.

With regard to the AHP questionnaire, useful comments were obtained from the participants concerning development of the questionnaire such as the questionnaire format or including/excluding some risk factors.

6 CONCLUSIONS

With regard to the first three objectives, the result showed a significant increase in CKD mortalities from 1980 to 2012. The results provide objective evidence on the progressive nature of the current CKD problem in Costa Rica (i.e. steady increase in mortality rates and three times more risk of mortality in 2012 compared to 1980). The results also confirmed the findings of previous studies that young men are affected significantly by this CKD epidemic. With regard to the objective four, mortality pattern of CKD, seven counties were identified as "hot spot" of CKD mortalities. Further studies in these counties, in particular Canas, are needed to find more evidence of causal factors of CKD in these areas. A field work in the hot spot area is recommended for gathering reliable data in a village level.

Considering the associations between environmental factors and CKD, significant associations were found between CKD mortality rate and temperature, permanent crops, and precipitation. These associations provide further evidence in support of the link between the current CKD epidemic with farming activities and heat stress. It should be mentioned that these associations were between SMR of the last period (2008-2012) and environmental factors. The definition of permanent crop in this study in unclear due to incomplete metadata. It is recommended that associations between CKD with different cultivated plants (sugarcane, coffee, etc.) will be investigated.

The results of this study need to be consulted with physicians who are experts in CKD and familiar with the region. The overall opinion of the physicians participated in this study showed they might have inadequate knowledge of environmental factors affecting CKD in Costa Rica.

In particular, the findings of this study cover two specific aspects. One relates to the newly emerging non-traditional risk factors for CKD (agricultural occupation, heat stress etc.) against traditional risk factors (diabetes mellitus, high blood pressure etc.). The study showed significant associations between CKD mortality and temperature, permanent crops, and precipitation. These associations provide further evidence in support of the link between the current CKD epidemic and farming activities (permanent crops) and heat stress (temperature & precipitation).

The second aspect relates to policy implications. Indeed, the findings of this study provided objective evidence on the progressive nature of the CKD problem in Costa Rica (i.e. steady increase in mortality rates over the study period; so that there was three times more risk of mortality in 2012 compared to 1980 as well as the geographically progressive nature of the problem over the time shown on the SMR maps).The identified hot spots in the northern parts of the country, in particular in Canas, warrants further investigations to see what practical measures could better control CKD in those areas.

Figure 6-1 demonstrates the key geographical areas which require further attention for intervention.

Geographic areas which require further attention for intervention

- County with the highest number of Mortality from 2008 to 2012:
  San Jose (115 people)

- County with the highest CKD Mortality Rate (MR) per 10000 people (2008 to 2012):
  Canas (22.2 – 95% CI: 17.07 – 28.9)

- County with the highest growth in CKD Mortality (1980 to 2012):
  Canas (Slope: 1.35 – 95% CI: 0.97 - 1.72)

- County with the highest CKD Standard Mortality Ratio (SMR) from 2008 to 2012:
  Canas (703.19 – 95% CI: 701.33– 705.05)

- Bagaces, Canas, Carrillo, La Cruz, Liberia, Santa Cruz in **Guanacaste province** and **Upala** in Alajuela province identified as hotspot areas.

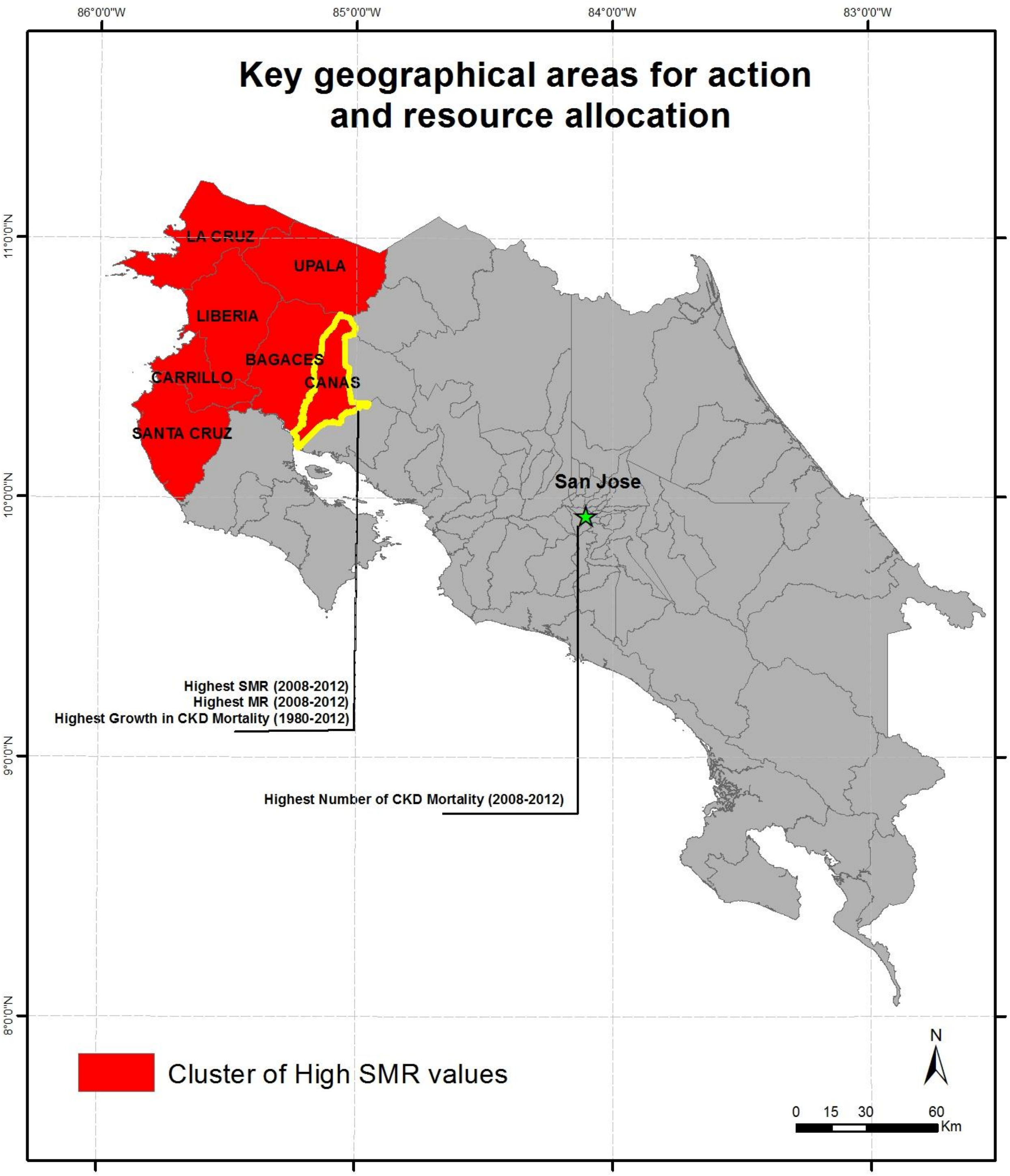


Figure 6-1: Geographical areas for action and resource allocation

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Appendix A: SMR, Mortality Rate (MR) and crude number of deaths

Table A-1: SMR and MR and total Number of death (2008-2012)

NCANTON	SMR	Lower95%CI	Upper95%CI	MR per 10000	Total No. of Death
ALAJUELA	93.37	93.17	93.57	3.00	85
ALFARO RUIZ	21.09	20.67	21.50	0.67	1
ATENAS	86.70	86.16	87.24	3.83	10
GRECIA	66.17	65.86	66.49	2.07	17
GUATUSO	159.74	158.55	160.92	4.27	7
LOS CHILES	159.64	158.53	160.75	3.87	8
NARANJO	126.02	125.46	126.59	4.19	19
OROTINA	73.30	72.65	73.94	2.66	5
PALMARES	35.32	35.01	35.63	1.31	5
POAS	155.35	154.53	156.16	4.47	14
SAN CARLOS	89.77	89.49	90.06	2.46	37
SAN MATEO	72.47	71.46	73.47	3.45	2
SAN RAMON	65.08	64.79	65.37	2.15	19
UPALA	179.07	178.26	179.88	5.21	19
VALVERDE VEGA	68.76	68.09	69.44	2.19	4
ALVARADO	130.29	129.15	131.43	3.65	5
CARTAGO	67.04	66.81	67.27	2.06	32
EL GUARCO	73.14	72.60	73.68	1.84	7
JIMENEZ	94.10	93.18	95.02	2.90	4
LA UNION	45.32	45.06	45.57	1.14	12
OREAMUNO	95.85	95.29	96.42	2.46	11
PARAISO	57.44	57.09	57.80	1.45	10
TURRIALBA	102.03	101.62	102.44	3.40	24
ABANGARES	163.22	162.21	164.23	5.95	10
BAGACES	458.31	456.62	460.01	14.71	28
CANAS	703.19	701.33	705.05	22.21	55
CARRILLO	338.45	337.34	339.55	11.94	36
HOJANCHA	156.29	154.76	157.82	6.06	4
LA CRUZ	425.12	423.30	426.94	12.10	21
LIBERIA	395.52	394.53	396.51	11.29	61
NANDAYURE	187.09	185.71	188.48	7.09	7
NICOYA	214.32	213.67	214.98	9.95	41
SANTA CRUZ	323.53	322.71	324.35	13.65	60
TILARAN	80.01	79.30	80.71	2.99	5
BARVA	149.32	148.61	150.03	4.35	17
BELEN	60.91	60.38	61.44	2.13	5
FLORES	155.23	154.26	156.19	5.68	10
HEREDIA	73.08	72.82	73.34	2.26	30
SAN ISIDRO	73.58	72.93	74.22	2.28	5
SAN PABLO	73.83	73.24	74.43	2.53	6
SAN RAFAEL	90.06	89.56	90.57	2.77	12
SANTA BARBARA	103.60	102.95	104.24	2.89	10
SANTO DOMINGO	91.42	90.92	91.92	3.47	13
SARAPIQUI	70.57	70.16	70.99	1.46	11
GUACIMO	151.46	150.76	152.16	3.78	18
LIMON	164.54	164.06	165.01	4.38	46

MATINA	98.09	97.51	98.67	2.33	11
POCOCI	89.24	88.93	89.55	2.12	32
SIQUIRRES	86.71	86.24	87.18	2.13	13
TALAMANCA	102.96	102.25	103.68	2.38	8
AGUIRRE	84.96	84.28	85.64	2.48	6
BUENOS AIRES	58.59	58.12	59.06	1.38	6
CORREDORES	96.97	96.37	97.57	3.05	10
COTO BRUS	103.94	103.29	104.58	2.83	10
ESPARZA	72.67	72.14	73.21	2.49	7
GARABITO	59.64	58.97	60.32	1.35	3
GOLFITO	155.58	154.79	156.36	5.01	15
MONTES DE ORO	76.62	75.87	77.37	3.03	4
OSA	145.77	144.87	146.68	4.72	10
PARRITA	0.00	0.00	0.00	0.00	0
PUNTARENAS	122.45	122.08	122.82	3.96	42
ACOSTA	42.70	42.22	43.19	1.55	3
ALAJUELITA	70.92	70.62	71.23	1.67	21
ASERRI	97.44	96.93	97.95	2.53	14
CURRIDABAT	81.13	80.76	81.51	2.48	18
DESAMPARADOS	66.37	66.19	66.55	1.88	55
DOTA	45.64	44.75	46.54	1.50	1
ESCAZU	53.69	53.37	54.01	1.81	11
GOICOECHEA	58.51	58.28	58.73	1.98	26
LEON CORTES	230.07	228.47	231.66	5.99	8
MONTES DE OCA	82.80	82.43	83.17	3.50	19
MORA	53.66	53.19	54.13	1.85	5
MORAVIA	42.58	42.28	42.87	1.46	8
PEREZ ZELEDON	82.70	82.41	82.99	2.37	31
PURISCAL	88.29	87.77	88.81	3.52	11
SAN JOSE	85.37	85.21	85.53	3.29	115
SANTA ANA	66.39	65.95	66.82	2.06	9
TARRAZU	42.72	42.13	43.32	1.21	2
TIBAS	135.34	134.86	135.81	5.02	31
TURRUBARES	130.74	128.93	132.56	4.31	2
VAZQUEZ DE CORONADO	107.20	106.76	107.63	2.83	23

Table A-2: SMR and MR and Total Number of death (2003 - 2007)

NCANTON	SMR	Lower95%CI	Upper95%CI	MR per 10000	Total No. of Death
ALAJUELA	121.36	121.11	121.61	3.55	92
ALFARO RUIZ	80.06	79.16	80.97	2.31	3
ATENAS	59.82	59.34	60.30	2.41	6
GRECIA	139.28	138.78	139.78	3.98	30
GUATUSO	133.05	131.89	134.22	3.30	5
LOS CHILES	108.34	107.39	109.29	2.42	5
NARANJO	193.6	192.91	194.43	5.88	25

	7				
OROTINA	69.39	68.71	70.07	2.28	4
PALMARES	84.79	84.26	85.31	2.88	10
POAS	52.96	52.45	53.48	1.39	4
SAN CARLOS	72.69	72.41	72.97	1.83	26
SAN MATEO	39.88	39.10	40.66	1.75	1
SAN RAMON	82.88	82.51	83.24	2.50	20
UPALA	216.50	215.60	217.41	5.81	22
VALVERDE VEGA	136.84	135.83	137.85	3.95	7
ALVARADO	116.41	115.27	117.55	2.99	4
CARTAGO	114.87	114.54	115.20	3.21	47
EL GUARCO	70.53	69.96	71.09	1.63	6
JIMENEZ	75.02	74.17	75.86	2.11	3
LA UNION	64.82	64.48	65.16	1.48	14
OREAMUNO	79.21	78.66	79.76	1.86	8
PARAISO	76.38	75.92	76.83	1.77	11
TURRIALBA	133.68	133.20	134.17	4.07	29
ABANGARES	178.12	177.01	179.22	5.91	10
BAGACES	432.18	430.42	433.95	12.76	23
CANAS	514.18	512.52	515.84	14.82	37
CARRILLO	357.04	355.84	358.24	11.54	34
HOJANCHA	210.93	209.08	212.78	7.48	5
LA CRUZ	308.21	306.60	309.83	8.06	14
LIBERIA	312.13	311.18	313.07	8.12	42
NANDAYURE	85.91	84.94	86.88	2.97	3
NICOYA	121.44	120.94	121.95	5.17	22
SANTA CRUZ	310.63	309.79	311.48	11.99	52
TILARAN	150.52	149.54	151.50	5.13	9
BARVA	133.69	132.96	134.41	3.55	13
BELEN	84.81	84.13	85.49	2.70	6
FLORES	108.04	107.17	108.90	3.58	6
HEREDIA	88.89	88.58	89.21	2.49	30
SAN ISIDRO	165.68	164.59	166.76	4.65	9
SAN PABLO	98.30	97.57	99.03	3.06	7
SAN RAFAEL	77.96	77.45	78.47	2.18	9
SANTA BARBARA	120.0	119.35	120.84	3.06	10

	9				
SANTO DOMINGO	62.72	62.28	63.15	2.16	8
SARAPIQUI	34.61	34.27	34.95	0.66	4
GUACIMO	41.05	40.65	41.45	0.94	4
LIMON	110.87	110.45	111.29	2.70	27
MATINA	77.92	77.35	78.50	1.70	7
POCOCI	98.71	98.35	99.08	2.16	28
SIQUIRRES	53.21	52.82	53.61	1.20	7
TALAMANCA	91.80	91.07	92.54	1.96	6
AGUIRRE	65.34	64.69	65.98	1.75	4
BUENOS AIRES	43.31	42.89	43.74	0.94	4
CORREDORES	58.63	58.16	59.10	1.70	6
COTO BRUS	51.99	51.53	52.44	1.31	5
ESPARZA	180.25	179.34	181.16	5.62	15
GARABITO	30.14	29.54	30.73	0.63	1
GOLFITO	197.74	196.85	198.63	5.88	19
MONTES DE ORO	22.07	21.64	22.50	0.80	1
OSA	141.95	141.07	142.83	4.23	10
PARRITA	81.32	80.40	82.24	2.37	3
PUNTARENAS	104.75	104.40	105.11	3.10	33
ACOSTA	15.43	15.13	15.73	0.51	1
ALAJUELITA	77.41	77.03	77.79	1.66	16
ASERRI	94.74	94.21	95.28	2.24	12
CURRIDABAT	73.61	73.23	74.00	2.05	14
DESAMPARADOS	92.43	92.19	92.67	2.38	57
DOTA	49.30	48.33	50.26	1.48	1
ESCAZU	78.71	78.30	79.13	2.41	14
GOICOECHEA	77.24	76.96	77.51	2.36	30
LEON CORTES	65.42	64.51	66.32	1.56	2
MONTES DE OCA	117.13	116.66	117.60	4.48	24
MORA	37.97	37.54	38.40	1.20	3
MORAVIA	53.96	53.61	54.31	1.67	9
PEREZ ZELEDON	67.51	67.24	67.79	1.78	23
PURISCAL	70.79	70.30	71.28	2.59	8
SAN JOSE	80.76	80.60	80.93	2.82	94
SANTA ANA	44.09	43.70	44.47	1.25	5
TARRAZU	98.72	97.75	99.68	2.53	4
TIBAS	106.10	105.67	106.52	3.57	24
TURRUBARES	0.00	0.00	0.00	0.00	0
VAZQUEZ DE CORONADO	59.81	59.44	60.18	1.43	10

Table A-3: SMR and MR and Total Number of death (1998 - 2002)

NCANTON	SMR	Lower95%CI	Upper95%CI	MR per 10000	Total No. of Death
ALAJUELA	115.18	114.91	115.45	3.14	70
ALFARO RUIZ	67.96	67.02	68.90	1.84	2
ATENAS	95.22	94.56	95.88	3.56	8
GRECIA	86.52	86.08	86.96	2.30	15
GUATUSO	67.35	66.41	68.28	1.53	2
LOS CHILES	24.46	23.98	24.94	0.51	1
NARANJO	94.15	93.56	94.73	2.66	10
OROTINA	62.12	61.42	62.82	1.91	3
PALMARES	64.23	63.72	64.75	2.02	6
POAS	115.24	114.38	116.09	2.83	7
SAN CARLOS	135.10	134.68	135.52	3.15	40
SAN MATEO	46.48	45.57	47.39	1.87	1
SAN RAMON	62.97	62.62	63.33	1.77	12
UPALA	63.88	63.37	64.39	1.59	6
VALVERDE VEGA	67.69	66.93	68.46	1.85	3
ALVARADO	102.12	100.97	103.28	2.44	3
CARTAGO	95.33	95.00	95.65	2.50	33
EL GUARCO	166.12	165.18	167.06	3.55	12
JIMENEZ	81.10	80.18	82.02	2.14	3
LA UNION	64.19	63.81	64.57	1.37	11
OREAMUNO	127.83	127.07	128.58	2.82	11
PARAISO	105.91	105.31	106.51	2.29	12
TURRIALBA	61.58	61.23	61.93	1.75	12
ABANGARES	158.57	157.47	159.67	4.92	8
BAGACES	253.04	251.54	254.53	6.89	11
CANAS	480.70	479.01	482.39	12.88	31
CARRILLO	403.84	402.46	405.22	12.09	33
HOJANCHA	138.05	136.49	139.61	4.59	3
LA CRUZ	252.96	251.39	254.53	6.06	10
LIBERIA	404.88	403.71	406.05	9.85	46
NANDAYURE	309.89	307.97	311.81	10.02	10
NICOYA	138.71	138.14	139.28	5.45	23
SANTA CRUZ	309.15	308.25	310.05	11.02	45
TILARAN	71.29	70.59	71.99	2.24	4
BARVA	99.93	99.24	100.62	2.47	8

BELEN	67.79	67.13	68.46	2.02	4
FLORES	85.34	84.51	86.18	2.66	4
HEREDIA	113.71	113.31	114.11	2.98	31
SAN ISIDRO	47.15	46.50	47.80	1.25	2
SAN PABLO	115.92	115.06	116.78	3.36	7
SAN RAFAEL	82.26	81.69	82.83	2.15	8
SANTA BARBARA	129.45	128.60	130.29	3.08	9
SANTO DOMINGO	133.53	132.85	134.20	4.32	15
SARAPIQUI	24.94	24.59	25.28	0.44	2
GUACIMO	80.97	80.32	81.62	1.72	6
LIMON	152.27	151.74	152.81	3.45	31
MATINA	74.76	74.11	75.42	1.51	5
POCOCI	81.99	81.60	82.38	1.65	17
SIQUIRRES	135.62	134.93	136.31	2.86	15
TALAMANCA	118.01	117.07	118.96	2.32	6
AGUIRRE	60.09	59.41	60.77	1.49	3
BUENOS AIRES	61.44	60.90	61.98	1.25	5
CORREDORES	90.15	89.56	90.74	2.41	9
COTO BRUS	53.57	53.10	54.03	1.25	5
ESPARZA	42.82	42.33	43.30	1.25	3
GARABITO	49.97	48.99	50.95	0.96	1
GOLFITO	128.08	127.36	128.81	3.55	12
MONTES DE ORO	80.27	79.36	81.18	2.69	3
OSA	125.57	124.75	126.39	3.48	9
PARRITA	91.24	90.21	92.27	2.48	3
PUNTARENAS	92.36	92.01	92.72	2.54	26
ACOSTA	52.03	51.44	52.62	1.61	3
ALAJUELITA	99.64	99.11	100.16	1.99	14
ASERRI	64.12	63.65	64.60	1.42	7
CURRIDABAT	82.15	81.70	82.59	2.14	13
DESAMPARADOS	85.97	85.70	86.24	2.07	40
DOTA	54.59	53.52	55.66	1.53	1
ESCAZU	107.14	106.62	107.67	3.06	16
GOICOECHEA	100.51	100.17	100.85	2.89	34
LEON CORTES	114.76	113.46	116.05	2.56	3
MONTES DE OCA	115.69	115.19	116.18	4.16	21
MORA	31.34	30.90	31.77	0.92	2
MORAVIA	47.33	46.98	47.68	1.39	7
PEREZ ZELEDON	56.86	56.59	57.13	1.39	17
PURISCAL	30.10	29.76	30.44	1.02	3
SAN JOSE	83.43	83.25	83.60	2.74	85
SANTA ANA	65.97	65.44	66.50	1.74	6

TARRAZU	116.58	115.44	117.73	2.82	4
TIBAS	74.77	74.42	75.13	2.36	17
TURRUBARES	0.00	0.00	0.00	0.00	0
VAZQUEZ DE CORONADO	80.03	79.53	80.52	1.80	10

TableA-4: SMR and MR and Total Number of death (1993 - 1997)

NCANTON	SMR	Lower95%CI	Upper95%CI	MR per 10000	Total No. of Death
ALAJUELA	104.01	103.73	104.29	2.78	54
ALFARO RUIZ	197.11	195.39	198.84	5.25	5
ATENAS	43.94	43.44	44.44	1.46	3
GRECIA	61.60	61.19	62.00	1.59	9
GUATUSO	107.90	106.40	109.39	1.76	2
LOS CHILES	149.25	147.94	150.56	2.60	5
NARANJO	54.03	53.56	54.50	1.49	5
OROTINA	66.28	65.53	67.03	2.09	3
PALMARES	13.87	13.60	14.14	0.39	1
POAS	53.24	52.64	53.84	1.39	3
SAN CARLOS	85.25	84.88	85.62	1.74	20
SAN MATEO	50.29	49.30	51.27	1.95	1
SAN RAMON	70.21	69.80	70.63	1.87	11
UPALA	111.62	110.85	112.40	2.13	8
VALVERDE VEGA	54.89	54.13	55.65	1.35	2
ALVARADO	172.96	171.27	174.66	3.54	4
CARTAGO	126.18	125.76	126.59	2.88	35
EL GUARCO	121.87	120.97	122.77	2.24	7
JIMENEZ	0.00	0.00	0.00	0.00	0
LA UNION	125.66	125.07	126.26	2.43	17
OREAMUNO	184.78	183.77	185.78	3.65	13
PARAISO	75.62	75.06	76.18	1.59	7
TURRIALBA	97.97	97.47	98.47	2.29	15
ABANGARES	121.58	120.52	122.65	3.19	5
BAGACES	500.10	497.79	502.41	12.68	18
CANAS	361.45	359.86	363.03	8.54	20
CARRILLO	319.6	318.41	320.97	9.44	24

	9				
HOJANCHA	65.76	64.47	67.05	1.56	1
LA CRUZ	291.35	289.33	293.37	5.14	8
LIBERIA	275.94	274.87	277.00	6.22	26
NANDAYURE	0.00	0.00	0.00	0.00	0
NICOYA	125.09	124.45	125.72	3.56	15
SANTA CRUZ	209.76	208.94	210.58	6.41	25
TILARAN	88.85	87.97	89.72	2.18	4
BARVA	94.31	93.56	95.07	2.07	6
BELEN	97.32	96.47	98.18	2.81	5
FLORES	80.39	79.48	81.30	2.19	3
HEREDIA	123.83	123.39	124.27	3.23	30
SAN ISIDRO	119.65	118.48	120.83	2.92	4
SAN PABLO	155.76	154.52	157.01	3.14	6
SAN RAFAEL	167.08	166.13	168.02	3.51	12
SANTA BARBARA	169.69	168.64	170.74	3.82	10
SANTO DOMINGO	66.67	66.14	67.20	1.81	6
SARAPIQUI	73.93	73.21	74.66	1.13	4
GUACIMO	32.95	32.50	33.41	0.69	2
LIMON	156.37	155.80	156.95	3.47	28
MATINA	95.60	94.84	96.37	2.26	6
POCOCI	105.52	105.00	106.04	1.94	16
SIQUIRRES	41.55	41.14	41.96	0.85	4
TALAMANCA	93.54	92.63	94.46	1.81	4
AGUIRRE	83.10	82.16	84.04	1.69	3
BUENOS AIRES	77.16	76.48	77.83	1.30	5
CORREDORES	90.86	90.19	91.54	1.71	7
COTO BRUS	57.20	56.64	57.76	0.95	4
ESPARZA	67.61	66.94	68.27	1.85	4
GARABITO	148.50	146.44	150.56	2.95	2
GOLFITO	219.32	218.24	220.39	4.51	16
MONTES DE ORO	79.50	78.40	80.60	2.00	2
OSA	67.56	66.90	68.22	1.40	4
PARRITA	85.97	84.77	87.16	1.74	2
PUNTARENAS	86.94	86.56	87.32	1.99	20
ACOSTA	91.27	90.38	92.17	2.20	4
ALAJUELITA	109.16	108.54	109.78	2.22	12
ASERRI	74.49	73.94	75.04	1.52	7
CURRIDABAT	49.50	49.10	49.89	1.08	6
DESAMPARADOS	95.13	94.80	95.45	1.99	33
DOTA	131.85	130.02	133.68	3.20	2

ESCAZU	42.83	42.46	43.21	1.05	5
GOICOECHEA	110.23	109.84	110.61	2.81	31
LEON CORTES	0.00	0.00	0.00	0.00	0
MONTES DE OCA	87.41	86.92	87.91	2.46	12
MORA	74.72	73.99	75.45	2.11	4
MORAVIA	95.62	95.03	96.21	2.07	10
PEREZ ZELEDON	106.74	106.31	107.17	2.08	24
PURISCAL	151.54	150.68	152.40	4.22	12
SAN JOSE	92.45	92.24	92.65	2.72	81
SANTA ANA	97.33	96.61	98.05	2.34	7
TARRAZU	38.77	38.01	39.53	0.78	1
TIBAS	59.77	59.42	60.12	1.38	11
TURRUBARES	85.87	84.19	87.56	2.02	1
VAZQUEZ DE CORONADO	68.50	67.99	69.00	1.57	7

Table A-5: SMR and MR and Total Number of death (1988 - 1992)

NCANTON	SMR	Lower95%CI	Upper95%CI	MR per 10000	Total No. of Death
ALAJUELA	126.69	126.30	127.08	2.48	41
ALFARO RUIZ	61.47	60.27	62.68	1.19	1
ATENAS	0.00	0.00	0.00	0.00	0
GRECIA	76.20	75.64	76.77	1.45	7
GUATUSO	425.72	421.99	429.46	5.40	5
LOS CHILES	45.51	44.62	46.41	0.60	1
NARANJO	138.59	137.63	139.55	2.75	8
OROTINA	0.00	0.00	0.00	0.00	0
PALMARES	66.18	65.43	66.93	1.35	3
POAS	0.00	0.00	0.00	0.00	0
SAN CARLOS	79.45	79.00	79.90	1.22	12
SAN MATEO	0.00	0.00	0.00	0.00	0
SAN RAMON	82.51	81.94	83.08	1.60	8
UPALA	41.38	40.80	41.95	0.59	2
VALVERDE VEGA	42.53	41.70	43.37	0.76	1
ALVARADO	0.00	0.00	0.00	0.00	0
CARTAGO	96.60	96.16	97.05	1.67	18
EL GUARCO	180.92	179.58	182.27	2.57	7
JIMENEZ	0.00	0.00	0.00	0.00	0
LA UNION	103.60	102.92	104.28	1.55	9
OREAMUNO	63.27	62.55	63.98	0.97	3
PARAISO	87.01	86.25	87.77	1.38	5
TURRIALBA	105.46	104.84	106.08	1.83	11
ABANGARES	36.97	36.25	37.70	0.69	1

BAGACES	403.89	401.25	406.53	7.35	9
CANAS	301.15	299.37	302.93	5.16	11
CARRILLO	428.74	426.86	430.62	8.84	20
HOJANCHA	0.00	0.00	0.00	0.00	0
LA CRUZ	430.30	427.32	433.28	5.82	8
LIBERIA	285.87	284.51	287.23	4.76	17
NANDAYURE	111.32	109.77	112.86	2.05	2
NICOYA	109.11	108.40	109.82	2.23	9
SANTA CRUZ	154.13	153.25	155.00	3.35	12
TILARAN	128.72	127.46	129.98	2.29	4
BARVA	121.40	120.33	122.46	2.02	5
BELEN	124.20	122.98	125.42	2.59	4
FLORES	210.52	208.68	212.37	4.24	5
HEREDIA	126.51	125.94	127.08	2.46	19
SAN ISIDRO	144.65	143.01	146.29	2.65	3
SAN PABLO	77.61	76.53	78.68	1.23	2
SAN RAFAEL	62.57	61.86	63.28	1.01	3
SANTA BARBARA	79.93	79.02	80.83	1.34	3
SANTO DOMINGO	66.59	65.94	67.25	1.34	4
SARAPIQUI	30.29	29.70	30.89	0.37	1
GUACIMO	56.11	55.33	56.89	0.87	2
LIMON	139.08	138.40	139.76	2.34	16
MATINA	55.62	54.85	56.39	0.96	2
POCOCI	67.31	66.77	67.84	0.94	6
SIQUIRRES	98.39	97.60	99.18	1.51	6
TALAMANCA	274.94	272.91	276.98	4.07	7
AGUIRRE	125.52	124.10	126.95	1.93	3
BUENOS AIRES	66.97	66.21	67.73	0.86	3
CORREDORES	107.75	106.89	108.61	1.55	6
COTO BRUS	175.67	174.52	176.81	2.28	9
ESPARZA	0.00	0.00	0.00	0.00	0
GARABITO	0.00	0.00	0.00	0.00	0
GOLFITO	150.58	149.53	151.62	2.33	8
MONTES DE ORO	303.93	301.26	306.59	5.72	5
OSA	202.12	200.80	203.44	3.10	9

PARRITA	184.48	182.40	186.57	2.83	3
PUNTARENAS	83.25	82.80	83.70	1.43	13
ACOSTA	99.06	97.94	100.18	1.77	3
ALAJUELITA	90.27	89.54	90.99	1.41	6
ASERRI	127.17	126.29	128.05	1.96	8
CURRIDABAT	76.42	75.81	77.03	1.29	6
DESAMPARADOS	109.24	108.82	109.67	1.77	25
DOTA	0.00	0.00	0.00	0.00	0
ESCAZU	26.05	25.69	26.41	0.48	2
GOICOECHEA	126.91	126.40	127.42	2.42	24
LEON CORTES	68.12	66.79	69.46	1.04	1
MONTES DE OCA	93.88	93.27	94.50	1.97	9
MORA	91.82	90.79	92.86	1.88	3
MORAVIA	41.13	40.67	41.60	0.70	3
PEREZ ZELEDON	99.34	98.83	99.84	1.48	15
PURISCAL	56.05	55.42	56.69	1.13	3
SAN JOSE	100.00	99.75	100.25	2.18	61
SANTA ANA	109.65	108.69	110.61	1.97	5
TARRAZU	58.69	57.54	59.84	0.90	1
TIBAS	58.55	58.14	58.95	1.04	8
TURRUBARES	122.90	120.49	125.30	2.08	1
VAZQUEZ DE CORONADO	100.36	99.56	101.17	1.73	6

Table A-6: SMR and MR and Total Number of death (1983 - 1987)

NCANTON	SMR	Lower95%CI	Upper95%CI	MortalityRate	DthTot
ALAJUELA	105.38	104.96	105.80	1.70	24
ALFARO RUIZ	165.25	162.96	167.54	2.61	2
ATENAS	94.25	93.18	95.31	1.82	3
GRECIA	90.33	89.61	91.05	1.42	6
GUATUSO	129.97	127.42	132.52	1.33	1
LOS CHILES	139.79	137.85	141.73	1.54	2
NARANJO	70.94	70.14	71.74	1.16	3
OROTINA	95.88	94.55	97.21	1.74	2
PALMARES	90.73	89.70	91.76	1.53	3
POAS	41.35	40.54	42.16	0.65	1
SAN CARLOS	141.92	141.20	142.64	1.79	15
SAN MATEO	0.00	0.00	0.00	0.00	0
SAN RAMON	57.28	56.72	57.84	0.91	4
UPALA	118.59	117.42	119.75	1.38	4
VALVERDE VEGA	229.72	227.47	231.98	3.39	4
ALVARADO	0.00	0.00	0.00	0.00	0
CARTAGO	43.96	43.60	44.31	0.62	6
EL GUARCO	73.36	72.34	74.37	0.86	2
JIMENEZ	52.58	51.55	53.61	0.78	1

LA UNION	87.43	86.66	88.19	1.08	5
OREAMUNO	267.33	265.58	269.08	3.37	9
PARAISO	49.45	48.76	50.13	0.65	2
TURRIALBA	75.72	75.12	76.33	1.09	6
ABANGARES	96.54	95.21	97.88	1.47	2
BAGACES	482.38	479.03	485.72	7.27	8
CANAS	187.44	185.79	189.08	2.63	5
CARRILLO	497.49	495.13	499.86	8.36	17
HOJANCHA	0.00	0.00	0.00	0.00	0
LA CRUZ	228.39	225.81	230.98	2.51	3
LIBERIA	308.53	306.85	310.21	4.19	13
NANDAYURE	67.12	65.80	68.43	1.00	1
NICOYA	106.83	106.04	107.62	1.78	7
SANTA CRUZ	133.10	132.18	134.03	2.37	8
TILARAN	85.71	84.52	86.90	1.25	2
BARVA	34.48	33.81	35.16	0.47	1
BELEN	43.47	42.61	44.32	0.75	1
FLORES	120.12	118.46	121.79	1.99	2
HEREDIA	50.62	50.18	51.07	0.81	5
SAN ISIDRO	137.98	136.07	139.89	2.10	2
SAN PABLO	115.57	113.97	117.17	1.50	2
SAN RAFAEL	146.81	145.52	148.09	1.96	5
SANTA BARBARA	0.00	0.00	0.00	0.00	0
SANTO DOMINGO	114.27	113.27	115.27	1.88	5
SARAPIQUI	93.00	91.71	94.29	0.94	2
GUACIMO	0.00	0.00	0.00	0.00	0
LIMON	137.11	136.30	137.92	1.89	11
MATINA	84.35	83.18	85.52	1.21	2
POCOCI	34.67	34.19	35.15	0.40	2
SIQUIRRES	96.72	95.77	97.67	1.23	4
TALAMANCA	127.01	125.25	128.77	1.58	2
AGUIRRE	108.38	106.88	109.89	1.39	2
BUENOS AIRES	30.96	30.36	31.57	0.33	1
CORREDORES	131.59	130.43	132.74	1.58	5
COTO BRUS	26.79	26.27	27.32	0.29	1
ESPARZA	37.45	36.72	38.18	0.61	1
GARABITO	0.00	0.00	0.00	0.00	0
GOLFITO	146.29	145.12	147.46	1.88	6
MONTES DE ORO	0.00	0.00	0.00	0.00	0
OSA	55.73	54.95	56.50	0.71	2
PARRITA	75.43	73.95	76.91	0.96	1
PUNTARENAS	104.48	103.89	105.07	1.47	12
ACOSTA	83.83	82.67	84.99	1.25	2
ALAJUELITA	88.69	87.82	89.56	1.14	4
ASERRI	68.68	67.90	69.45	0.87	3
CURRIDABAT	99.48	98.61	100.35	1.37	5
DESAMPARADOS	124.11	123.56	124.65	1.66	20
DOTA	127.20	124.70	129.69	1.86	1
ESCAZU	126.07	125.13	127.00	1.91	7
GOICOECHEA	94.14	93.63	94.65	1.47	13
LEON CORTES	0.00	0.00	0.00	0.00	0
MONTES DE OCA	121.66	120.86	122.45	2.11	9

MORA	128.27	126.81	129.72	2.16	3
MORAVIA	97.33	96.48	98.18	1.35	5
PEREZ ZELEDON	72.24	71.74	72.74	0.88	8
PURISCAL	96.80	95.85	97.75	1.59	4
SAN JOSE	133.28	132.95	133.61	2.39	63
SANTA ANA	30.90	30.29	31.50	0.46	1
TARRAZU	80.87	79.28	82.45	1.03	1
TIBAS	74.56	74.01	75.12	1.08	7
TURRUBARES	0.00	0.00	0.00	0.00	0
VAZQUEZ DE CORONADO	102.32	101.32	103.33	1.45	4

Appendix B: A sample of AHP Questionnaire

You are cordially invited to participate in a pilot study, for development of a questionnaire which explores expert opinions on potential risk factors for CKD in Central America.

Such risk factors may be tangible or intangible, carefully measured or roughly estimated, well or poorly understood—anything at all that might apply. By identification of the most important tentative risk factors for CKD in Central America (note; CKD, not MeN or CKDnT) future scientific studies as well as interventions can be better targeted.

We use an Analytic Hierarch Process (AHP) to identify and weight the risk factors. AHP is a Multi-Criteria Decision making Method that helps the decision-makers facing a complex problem with multiple conflicting and subjective criteria. The items in this questionnaire are deliberately not very specific, but relate to broad areas of concern.Your requested task is to:

A: fill in the questionnaire (part 1- 9)

B: give your comments (part 10) as to clarity of instructions, important items that are left out etc.

We hope that you can find time to answer the questionnaire **before Jan 30**, so that we can produce a final questionnaire to be sent to all CENCAM members already in March. Results will be presented at the 2nd International Workshop on MeN in Costa Rica, Nov 2015.

Further, the results of the pilot study will be used to produce a susceptibility map of CKD mortality in Costa Rica, using geographical information systems (GIS) and available spatially referenced data on potential risk factors, or indicators thereof.

Yours sincerely,

Ineke Wesseling

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In the AHP method each pair of criteria should be compared and weighted from 1 to 9 according to your view its influence on CKD. If, for example, you are comparing factor J with factor K and want to state that factor J is much more important than factor K then a value of 7 (very strongly preferred) should be checked at the J side, or if you think two factors are at the same level of importance you should check 1 (equally preferred) . The scale to use when comparing each pair of criteria is shown in Table 1.

Table 0-1: Values for the experts for pair wise comparison of criteria

Choice	***Importance Value***
Equally preferred	**1**
Moderately preferred	**3**
Strongly preferred	**5**
Very Strongly preferred	**7**
Extremely preferred	**9**
Values in between preferences	**2, 4, 6, 8**

In the present questionnaire factors associated with the incidence of **Chronic Kidney Disease (CKD) in Central America** are tentatively be grouped as:

1. Factors in the general environment
2. Factors related to land use, especially agriculture
3. Factors related to the work environment
4. Socio economic and demographic factors (individual level)
5. Socio economic and demographic factors (collective level)
6. Life-style factors
7. Medical and related conditions

This questionnaire is designed to perform a pair wise comparison of the available factors affecting the CKD, within each group, as follow:

1. Factors related to the general environment are:

- Temperature
- Altitude
- Rainfall
- Humidity
- Drinking water quality
- Air quality (particulate matter, PM)
- Housing proximity to crop land

With regard to the factor "Air quality", unlike the other factors, the association between this factor and CKD has not been investigated yet. So if you think that this factor is not relevant, please leave the comparisons which are between "Air quality" and other factors blank.

2. Factors related to land use are:

- Type of agricultural organization
- Pesticide use

3. Factors related to the work environment are:

- Physical work load
- Work environment temperature
- Exposure to pesticides
- Exposure to particles
- Piece work
- Informal employment (no formal contract, job insecurity, low income…)

4. Socioeconomic and demographic factors (individual level) are:

- Sex
- Age
- Family income
- Educational level
- Migrant status

5. Socioeconomic and demographic factors (collective level) are:

- Access to health care
- Social development Index

6. Life-style factors are:

- Tobacco smoking
- Alcohol use
- Use of illegal drugs
- Obesity
- Sugar intake
- Water intake

7. Medical and other conditions are:

- Metabolic syndrome and related diseases (diabetes, hypertension)
- Genetic predisposition
- Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)
- Regular use of pain-killers

- Recurrent urinary tract infections
- Use of nephrotoxic drugs and herbs

Your task: Please compare the relative importance of each pair of factors affecting the Chronic Kidney Disease using the scale below:

Part 1: Comparison of factors related to general environment

Extreme ◄······ Strong ······ Equal ······ Strong ······► Extreme

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	**Temperature**	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Altitude**
2	**Temperature**	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Humidity**
3	**Temperature**	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Rainfall**
4	**Temperature**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Drinking water quality**
5	**Humidity**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Altitude**
6	**Humidity**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Rainfall**
7	**Humidity**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Drinking water quality**
8	**Rainfall**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Altitude**
9	**Rainfall**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Drinking water quality**
10	**Drinking water quality**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Altitude**
11	**Air quality (particulate matter, PM)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Temperature**

		Extreme				Strong				Equal				Strong				Extrem	
		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
12	**Air quality (particulate matter, PM)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Altitude**
13	**Air quality (particulate matter, PM)**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Humidity**
14	**Air quality (particulate matter, PM)**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Rainfall**
15	**Air quality (particulate matter, PM)**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Drinking water quality**
16	**Housing proximity to cropland**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Temperature**
17	**Housing proximity to cropland**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Altitude**
18	**Housing proximity to cropland**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Humidity**
19	**Housing proximity to cropland**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Rainfall**
20	**Housing proximity to cropland**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Drinking water quality**
21	**Housing proximity to cropland**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Air quality**

Part 2: Comparison of factors related to land use

		Extreme				Strong				Equal				Strong				Extreme	
		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	**Pesticide use**	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Type of agricultural organization**

Part 3: Comparison of factors related to the Work Environment

		Extreme				Strong				Equal				Strong			Extreme		
		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	Physical work load	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Work environment temperature
2	Physical work load	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Exposure to pesticides
3	Physical work load	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Exposure to particles
4	Physical work load	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	Piece work
5	Physical work load	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Informal employment
6	Work environment temperature	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Exposure to pesticides
7	Work environment temperature	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Exposure to particles
8	Work environment temperature	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Piece work
9	Work environment temperature	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Informal employment
10	Exposure to pesticides	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Exposure to particles
11	Exposure to pesticides	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	Piece work
12	Exposure to pesticides	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Informal employment
13	Exposure to particles	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	Piece work

		Extreme				Strong				Equal				Strong				Extrem	
		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
14	Exposure to particles	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Informal employment
15	Piece work	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Informal employment

Part 4: Comparison of Socioeconomic and demographic factors (Individual level)

		Extreme				Strong				Equal				Strong				Extreme	
		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	Age	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Sex
2	Age	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Family income
3	Age	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Educational level
4	Age	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Migrant status
5	Sex	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	Family income
6	Sex	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	Educational level
7	Sex	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Migrant status
8	Family income	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Educational level

Extreme — Strong — Equal — Strong — Extreme

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
9	Family income	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Migrant status
10	Educational level	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Migrant status

Part 5: Comparison of Socioeconomic and demographic factors (collective level)

Extreme — Strong — Equal — Strong — Extreme

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	Access to health care	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	Social development index

Part 6: Comparison of life style factors

Extreme — Strong — Equal — Strong — Extreme

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	Tobacco smoking	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Alcohol use
2	Tobacco smoking	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Use of illegal drugs
3	Tobacco smoking	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	obesity
4	Tobacco smoking	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	Sugar intake

Extreme ◄······ Strong ······ Equal ······ Strong ······► Extreme

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
5	**Tobacco smoking**	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Water intake**
6	**Alcohol use**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Use of illegal drugs**
7	**Alcohol use**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**obesity**
8	**Alcohol use**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Sugar intake**
9	**Alcohol use**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Water intake**
10	**Use of illegal drugs**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**obesity**
11	**Use of illegal drugs**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Sugar intake**
12	**Use of illegal drugs**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Water intake**
13	**obesity**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Sugar intake**

		Extreme				Strong				Equal				Strong				Extreme	
		9	**8**	**7**	**6**	**5**	**4**	**3**	**2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
14	**obesity**	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Water intake**
15	**Sugar intake**	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Water intake**

Part 7: Comparison of factors related to Medical and other conditions

		Extreme			Strong					Equal				Strong				Extreme	
		9	**8**	**7**	**6**	**5**	**4**	**3**	**2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
1	**Metabolic syndrome and related diseases (diabetes, hypertension)**	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Genetic predisposition**
2	**Metabolic syndrome and related diseases (diabetes, hypertension)**	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)**
3	**Metabolic syndrome and related diseases (diabetes, hypertension)**	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Regular use of pain-killers**
4	**Metabolic syndrome and related diseases (diabetes, hypertension)**	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Recurrent urinary tract infections**
5	**Metabolic syndrome and related diseases (diabetes, hypertension)**	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Use of nephrotoxic drugs and herbs**
6	**Genetic predisposition**	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)**
7	**Genetic predisposition**	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Regular use of pain-killers**

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
8	**Genetic predisposition**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Recurrent urinary tract infections**
9	**Genetic predisposition**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Use of nephrotoxic drugs and herbs**
10	**Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Regular use of pain-killers**
11	**Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Recurrent urinary tract infections**
12	**Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Use of nephrotoxic drugs and herbs**
13	**Regular use of pain-killers**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Recurrent urinary tract infections**
14	**Regular use of pain-killers**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Use of nephrotoxic drugs and herbs**
15	**Use of nephrotoxic drugs and herbs**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Recurrent urinary tract infections**

Part 8: Which statement do you agree with regards to each factor?

General Environment	
Temperature	
People who are living in the high-temperature areas are more susceptible to CKD	☒
People who are living in the low-temperature areas are more susceptible to CKD	☐
Altitude (assumes there is no option for neither)?	
People who are living in the high altitude are more susceptible to CKD	☐
People who are living in the low altitude are more susceptible to CKD	☒
Rainfall	
People who are living in the areas with high precipitation are more susceptible to CKD	☐
People who are living in the areas with low precipitation are more susceptible to CKD	☒
Humidity	
People who are living in high humidity are more susceptible to CKD	☒
People who are living in low humidity are more susceptible to CKD	☐
Drinking water quality	
People who have insufficient water quality are more susceptible to CKD	☒
People who have good water quality are more susceptible to CKD	☐
Air quality (particulate matter, PM) (generic, not informed answer)	
People who are living in the air quality with the high level of PM are more susceptible to CKD	☒
People who are living in the air quality with the low level of PM are more susceptible to CKD	☐
Housing proximity to crop land	
People who are living close to cropland are more susceptible to CKD	☒

People who are living far from the cropland are more susceptible to CKD	☐
land use	
Type of agricultural organization	
People who are living in small-scale agricultural organization more susceptible to CKD	☐
People who are living in Plantations/monoculture agricultural organization are more susceptible to CKD	☒
Pesticide use	
People who are living in areas with high exposure to pesticides are more susceptible to CKD	☒
People who are living in areas with low exposure to pesticides are more susceptible to CKD	☐
work environment (some of these should offer option of NEITHER)	
Physical work load	
People with high physical work load are more susceptible to CKD	☒
People with low physical work load are more susceptible to CKD	☐
Work environment temperature	
People who are exposed to high temperature during the work are more susceptible to CKD	☒
People who are exposed to low temperature during the work are more susceptible to CKD	☐
Exposure to pesticides	
People who are exposed to high amount of pesticides at their work environment	☒
People who are exposed to low amount of pesticides at their work environment	☐
Exposure to particles	
People who are exposed to high amount of particles at their work environment are more susceptible to CKD	☒
People who are exposed to low amount of particles at their work environment are more susceptible to CKD	☐

Piece work	
People who have a piece work job are more susceptible to CKD	☒
People who don't have a piece work job are more susceptible to CKD	☐
Informal employment (no formal contract, no job insecurity, low income…)	
People with informal employment job are more susceptible to CKD	☒
People with formal employment are more susceptible to CKD	☐
Socioeconomic and demographic factors (Individual)	
Sex	
Men are more susceptible to CKD	☒
Women are more susceptible to CKD	☐
Age	
Young people are more susceptible to CKD	☐
Elderly people are more susceptible to CKD	☒
Family income	
People with low family income	☒
People with high family income	☐
Educational level	
People with low education level are more susceptible to CKD	☒
People with high education level are more susceptible to CKD	☐
Migrant status	
Immigrants are more susceptible to CKD	☒
Native people are more susceptible to CKD	☐

Socioeconomic and demographic factors (Collective)	
Social development Index	
People living in low Social development index areas are more susceptible to CKD	☒
People living in high Social development index areas are more susceptible to CKD	☐
Access to health care	
People who have a bad access to health care are more susceptible to CKD	☒
People who have a good access to health care are more susceptible to CKD	☐
Life-style (some answers Strong +; some really no difference)	
Tobacco smoking	
People who smoke tobacco are more susceptible to CKD	☒
People who don’t smoke tobacco are more susceptible to CKD	☐
Alcohol use	
People with a high alcohol consumption are more susceptible to CKD	☒
People with low alcohol consumption are more susceptible to CKD	☐
Use of illegal drugs	
People who use illegal drugs are more susceptible to CKD	☐
People who don’t use illegal drugs are more susceptible to CKD	☐
Obesity	
People with obesity are more susceptible to CKD	☒
People with no obesity are more susceptible to CKD	☐
Sugar intake	
People with high sugar intake are more susceptible to CKD	☒

People with low sugar intake are more susceptible to CKD	☐
Water intake	
People with high water intake are more susceptible to CKD	☐
People with low water intake are more susceptible to CKD	☒
Medical and other conditions	
Metabolic syndrome and related diseases (diabetes, hypertension)	
People with metabolic syndrome and related diseases (diabetes, hypertension) are more susceptible to CKD	☒
People with no metabolic syndrome and related diseases (diabetes, hypertension) are more susceptible to CKD	☐
Genetic predisposition	
People with genetic predisposition are more susceptible to CKD	☒
People with no genetic predisposition are more susceptible to CKD	☐
Exposure to infectious diseases transmitted by rodents (leptospira, hantavirus and others)	
People who have been exposed to infectious diseases transmitted by rodents (leptospira, hantavirus and others) are more susceptible to CKD	☒
People who have not been exposed to infectious diseases transmitted by rodents (leptospira, hantavirus and others) are more susceptible to CKD	☐
Regular use of pain-killers	
People who use pain killers regularly are more susceptible to CKD	☒
People who don't use pain killers regularly are more susceptible to CKD	☐
Recurrent urinary tract infections	
People who have recurrent urinary tract infections are more susceptible to CKD	☒
People who don't have recurrent urinary tract infections are more susceptible to CKD	☐

Use of nephrotoxic drugs and herbs	
People who use nephrotoxic drugs and herbs are more susceptible to CKD	☒
People who don't use nephrotoxic drugs and herbs are more susceptible to CKD	☐

Part 9: comparison of all 7 factors

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
1	**General environment**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Land use**
2	**General environment**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Work environment**
3	**General environment**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Socioeconomic and demographic (Individual)**
4	**General environment**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Life-style**
5	**General environment**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Medical and other conditions**
6	**Land use**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Work environment**
7	**Land use**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Socioeconomic and demographic (Individual)**
8	**Land use**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	**Life-style**
9	**Land use**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	**Medical and other conditions**
10	**Work environment**	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Socioeconomic and demographic**

		9	8	7	6	5	4	3	2	1	2	3	4	5	6	7	8	9	
																			(Individual)
11	**Work environment**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Life-style**
12	**Work environment**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Medical and other conditions**
13	**Socioeconomic and demographic (Individual)**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Life-style**
14	**Socioeconomic and demographic (Individual)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Medical and other conditions**
15	**Life-style**	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Medical and other conditions**
16	**Socioeconomic and demographic (Collective)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Life-style**
17	**Socioeconomic and demographic (Collective)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Medical and other conditions**
18	**Socioeconomic and demographic (Collective)**	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	**Work environment**
19	**Socioeconomic and demographic (Collective)**	☐	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	**Socioeconomic and demographic (Individual)**
20	**Socioeconomic and demographic (Collective)**	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	**General environment**

		9	**8**	**7**	**6**	**5**	**4**	**3**	**2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
21	**Socioeconomic and demographic (Collective)**	☐	☐	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Land use**

Part 10: Please, give your comments as to selection of groups and items – missing items, ambiguous wording, ……

The aim of the study was Suggestions for improvement:

□ 1 Very difficult to understand

□ 2

□ 3 Choice 3

□ 4

□ 5 Very easy to understand

The instructions for the questionnaire were Suggestions for improvement:

□ 1 Very difficult to understand

□ 2 Choice 2 Offer option of no answer

□ 3

□ 4

□ 5 Very easy to understand

It took approximately ……… minutes to answer the pilot questionnaire

30 minutes but due to on-line and needing to check each box using the double click and accept in Word. Not the best way. Interactive version would have been much easier

Comments on groups and items in the pilot questionnaire:

Some groups are fairly specific and others very general so choosing to rank along a continuum seemed impossible at times – Do you want to offer option to leave blank?

Missing groups and items:

Other comments:

Appendix C: Proposed Priorities from "MesoAmerican Nephropathy Report" for Exploring Hypotheses for Causes of CKD of unknown origin in Central America.

Highly Likely, High Priority to Investigate Further
Heat stress and dehydration (including electrolyte imbalances)
Non-steroidal anti-inflammatory drugs (NSAIDS)
Possible, High Priority to Investigate Further
Arsenic
Fructose intake
Nephrotoxic medications, including homeopathic medications
Leptospirosis and other endemic infections
Possible, High Priority but Logistically Difficult at this Time
Genetic susceptibility and epigenetics
Low birth weight and other prenatal, perinatal, and childhood exposures that increase susceptibility
Unlikely but strongly believed, Medium Priority to Investigate Further
Pesticides
Urinary tract diseases and sexually transmitted diseases (STDs)
Little Information, Medium Priority to Investigate Further
Calcium in drinking water, or water 'hardness'
Medication contamination and use of homeopathic medicines and non-approved drugs

Unlikely, Low Priority for Further Investigation
Lead
Mercury
Cadmium
Uranium
Aristolochic acid

Department of Physical Geography and Ecosystem Science

Master Thesis in Geographical Information Science (LUMA-GIS)

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2. *Rickard Hansen:* Daily mobility in Grenoble Metropolitan Region, France. Applied GIS methods in time geographical research. (2008).
3. *Emil Bayramov:* Environmental monitoring of bio-restoration activities using GIS and Remote Sensing. (2009).
4. *Rafael Villarreal Pacheco:* Applications of Geographic Information Systems as an analytical and visualization tool for mass real estate valuation: a case study of Fontibon District, Bogota, Columbia. (2009).
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