Interdisciplinary assessment of rodent-borne diseases and epidemic outbreak risks in the urban scale with the use of geographic information systems

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Abstract

This paper introduces an innovative system that combines spatial data and established epidemiological criteria to evaluate the risks of infectious disease spread in cities, particularly through rodent borne zoonoses. The system is based on GIS technology and generates an intuitive raster model displaying areas of major concern and potential risks. The system can be set up relatively quickly and to a low cost, provided the relevant data is available. This is especially interesting for developing countries, where funding is always an issue. The system can also provide a quick assessment platform for multidisciplinary exchange in case of emergencies.

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1. Introduction

1.1 Rationale

In recent years, global concern has arisen on the risks of infectious disease outbreaks that may easily and rapidly surpass regional and national borders. SARS, the influenza A virus subtype H5N1, Cholera and Ebola are only some of the most recent examples. Natural catastrophes and bioterrorism count also as possible outbreak causes.

Many analysts believe that nowadays large cities face the highest threat of transnational infectious disease epidemics since almost a century (Matthew, R.A. and McDonald, B., 1994). It has been observed that the growth of urban population leads to an increasing risk of disease spread by vectors (Meyer, 2003).

Pneumonic plague caused some of the worst pandemics in human history. Yet today, infected humans may spread the disease much quicker with modern transportation means, just as SARS and avian influenza. Plague is also regarded as a category A agent for Bio terrorism.

Terrorism has also been suggested as a potential starting point. In 2008 the US Congress released an alarming report on the threats of new terror attacks, which include the use of biological weapons (Pitzke, M., 2008).

Along with urban and population growth, infectious diseases also develop very dynamically. Taking Leptospirosis as an example of a disease spread by vectors, almost 300 serovars have been discovered, but this number still grows, as well as the number of hosts they can adapt to.

Control measures need to be made more efficient, including the seasonal and spatial context. Because Leptospirosis affects humans and farm animals, its economic impact in human and veterinary health sectors shouldn't be underestimated (Hartskeerl R., 2006).

The intergovernmental panel on climate change warned recently that infectious diseases can expand geographically with temperature rise. First long term studies that apply satellite remote sensing data of a time span of more than 30 years are suggesting the influence of climate change phenomena on epidemic outbreaks (Fritz & Samenow, 2014).

Advanced computer technologies like GIS and Database operated systems are being applied today in many countries for disease spread monitoring.

In North America, linking climate variables such as precipitation and temperatures as well as land cover and remote sensing data with zoonotic disease occurrences have lead to outstanding forecasts for Plague, Lyme Disease and Sin Nombre Hantavirus outbreaks (Enscore RE, et al., 2002).

However, and especially for developing countries, which contain most of the world's megacities, there is scarce data on the correlations of disease prevalence on humans and their environmental and socioeconomic aspects (Taylor P. J. et al., 2008)

1.2 Objectives

The system presented in this paper has been developed using a mathematical model linked to spatial data and parameters taken from findings of published studies on infectious disease spread by vectors, particularly rodent borne diseases.

The main objective of this paper is to test this model with the data of an existing study. The interpretation of the results may or may not support the assumptions made by the authors on the potential use of this approach for disease management and control strategies.

The objectives of the system are:

- To identify and analyse existing risks in the urban area on the spread and impacts of infectious disease

- To evaluate the vulnerability of urban areas in case of a major infectious disease event

- To identify areas which represent a hazard in case of disease outbreak

- To analyse the effects of urban renewal, when adequate measures are taken to minimize the risks

However, it is important to underline that while the model focuses its attention on rodents as vectors, the goal of disease control in general is not only to combat the spread of vectors, but to sum up measures to reduce disease spread and eventually to eliminate it. Due to the involvement of rodents in the spread of diseases, pest control measures, to which this approach is dedicated, are part of the strategy, but not the end goal.

2. Background

2.1 Other studies with this approach

This approach has been previously applied for urban management purposes, particularly to analyse potentials and constraints for infrastructure development. Case studies were carried out in the Glasgow Canals in Scotland (Schuett, 2006) and the metropolitan area of Warsaw, Poland (Schuett, 2008).

As mentioned before, computer based methods are being used today for similar purposes, but the use of this approach for rodent borne zoonoses studies has not been tried before by any of the authors.

Both case studies revealed that the approach is quite versatile in its possible purposes. The authors believe that when applying interdisciplinary experience, it is possible to identify the relevant variables required for the model, which if taken into account, may contribute to generate reliable information on hotspots for disease outbreak, vulnerability of endangered areas and potential strategies for disease control.

The authors believe that this approach can contribute to design more effective programmes for prevention, fighting and management of vector borne disease spread.

2.2   The RatZooMan Project

The RatZooMan project (Rodent Zoonoses Management) is an example of successful international and interdisciplinary cooperation for rodent borne disease research. Scientists from more than 20 countries working in Europe and Africa shared their expertise and knowledge in a project that lasted three and a half years (Taylor P. J. et al., 2008), obtaining valuable results for epidemiology and other disciplines and sciences.

The project had set two main objectives. The first one is to display and underline the risks that rodents cause to public health in rural and peri-urban areas of South East Africa and the second one is to develop risk management strategies using the information obtained from the research work.

The project as well observed aspects such as climate change, urbanisation, public hygiene and the closer interconnection between rural and urban areas due to (informal) urban growth and agriculture intensification.

One of the study sites, the city of Durban in South Africa, presents evidences of all these aspects and was considered ideal for the use of the model presented in this paper.

In Durban, the RatZooMan project focused on studying environmental conditions, soil conditions, socioeconomic and anthropological factors (Taylor P. J. et al., 2008). Additionally, three infectious diseases to which rodents contribute as vectors, namely Plague, Leptospirosis and Toxoplasmosis were considered.

To this end, data on all these factors was collected on site and recorded in a database. Rodents were trapped and its blood, serum and/or tissue tested for Plague, Leptospirosis and Toxoplasmosis. Also serum specimens of volunteer residents of Durban were tested.

According to one of the publications about the project, at least for the study site Durban, three core questions were formulated (Taylor P. J. et al., 2008):

(1) "Based on serological and polymerase chain reaction (PCR) tests for the three selected diseases in sampled rodents and humans, do urban pest rodents pose a real public health risk?"

(2) "Are there specific endemic disease areas ("hotspots") for rodents and humans? and what are the environmental and socioeconomic correlates of these?"

(3) "How can rodents be managed in urban (formal and informal) settings to minimize the sanitary risk to humans?"

The data collected in Durban was also georeferenced and displayed using a GIS. However, an analysis of links between the different datasets, especially between epidemiological tests and environmental setting needs additional research, as this was not part of the project (Thompson, R, 2006).

The authors of this paper believe that the model presented in this may contribute to establish these links and help to provide answers to the core questions.

At this point, the authors need to point out that they cannot to take any credit for the successful RatZooMan project, neither for its positive results and analysis. The authors are very thankful that the results were made available to the scientific community in papers, journals and Internet websites, for further studies like the one presented here to be possible.

Before describing the approach and model in detail, the authors consider necessary to describe roughly details and aspects about the vector and the city of Durban.

2.3 The rodent as vector of disease

Rodents may contribute to the transmission of more than 60 infectious diseases to humans. These infectious diseases may generally not be itself human-to-human contagious, like Leptospirosis and Toxoplasmosis or be usually human-to-human contagious, like Lassa fever or Pneumonic Plague (Belmain, S.R., 2006).

The transmission of diseases from rodents to humans may be direct through bites or ingestion of infected rat meat. Examples of indirect transmission are the ingestion, inhalation or penetration into the human skin of pathogens transmitted via ectoparasites and rodents' excreta. Without necessarily transmitting the pathogens themselves, rodents may also play an important role as intermediate hosts in a parasites life cycle (Belmain, S.R., 2006).

Amongst the diseases considered for the study in Durban, Leptospirosis is probably the most widespread and most prevalent zoonotic disease. According to Rudy Hartskeerl form the Royal Tropical Institute in The Netherlands (Belmain, S.R., 2006), the disease is mostly endemic in tropical countries, because environmental and socio-economic conditions are favourable for the survival of the pathogens. Leptospirosis is very easily transmitted to humans through contact with contaminated soil or water. Informal settlements may contribute to the spread due to the close contact of humans with contaminated water, particularly children when playing or women when washing clothes in contaminated water. Leptospirosis represents a life threat especially to humans with a weakened immune system, such as humans infected with AIDS, young children or elderly persons (Taylor P. J. et al., 2008).

Regarding Toxoplasmosis, the main host of the organism Toxoplasma Gondii is the cat, where it is able to sexually reproduce. When cat's faeces containing cysts are consumed by other animals, they are encapsulated by the animal's immune system, without sexually reproducing. Thereafter, when a cat eats this animal (generally a rodent) the cyst enters the cat's organism and is able to reproduce again, and this completes the cycle.

Because of this, the disease is unlikely to persist in an area where there are no cats. Human death because of infection is rare, and it is reported only in

persons with immunodeficiency, for example AIDS patients (Belmain, S.R., 2006).

When it comes to Plague, if humans get infected by the virus Yersinia pestis in direct contact with infected wild rodents or infective fleas, they can develop bubonic plague. Because the virus is unable to replicate outside the host, transmission is usually connected with encroachment of wild rodents into the habitat of domestic rodents or humans. Deforestation or destruction of wild rodents' habitat contributes to the above factor. This is suspected to have severely contributed to the recent Ebola outbreak in West Africa (Fritz & Samenow, 2014).

There are many unanswered questions concerning plague and reservoir hosts. It is unclear as to how or where the virus may survive and cause the resurgence of the disease after long periods of time. Neither is it clear if vectors other than fleas can be involved in human epidemics, and if so, which ones (Belmain, S.R., 2006).

According to the World Health Organisation, plague is endemic in many countries in Africa, the former Soviet Union, the Americas and Asia. In 2003, 2118 cases and 182 deaths were reported, around 99% of which came from Africa (WHO, 2005).

Other diseases spread directly or indirectly by rodents are Lassa Fever, Salmonellosis, Listeriosis, Cholera, Diarrhea (E. coli), the range of diseases caused by Campylobacter, Hantavirus disease, Dysentery, Cryptosporidiosis, etc. (Webster, JP and Macdonald DW, 1995; CDC, 2006).

2.4   Durban

Durban is the third largest city in South Africa in population. It is the largest city in the KwaZulu-Natal province as well in surface extension and has a lower population density than other cities in South Africa.

Durban's population today is close to 3.5 Millions, and consists of 68.3% Black Africans, 19.9% Asians or Indians, 8.98% Whites and 2.89% Coloureds.

The data of the 2001 demographic census revealed a percentage of unemployed people of 27.9% in Durban, of which 88.6% are Black Africans. In some areas of the metropolitan area, the percentage is higher. Around 10% of Durban residents aged 20 and above have not received schooling. 13.3% didn't finish primary school and 5.7% have completed only primary

school. Only 9.6% have had education after high school (Statistics of South Africa).

There are around 500 shack settlements (informal settlements) in Durban's municipal area, with around 156 500 households (Taylor P. J. et al. 2008).

Durban has a diversified economy, and is greatly influenced by its location as a sea port, with a significant manufacturing, transportation, finance and export bond sector.

Durban's container port is the busiest in South Africa and one of the busiest in the world. This was indeed the port of entry of the last Plague pandemic during the Anglo Boer war (1900-1901) (Taylor P. J. et al. 2008) and is considered a weak spot for vector borne disease invasion.

The port is not the only consideration for assessing zoonotic disease risk in Durban. Poverty, density, education and quality of infrastructure have to be considered for prevention measures and will be described later with the statistical data used in the model.

3   APPROACH

3.1   Short Description

The basic idea of this system is to read relevant environmental and socio-economic data recorded in the study site and to identify with the use of GIS calculations possible risk zones when considering the findings of similar studies about rodents and the epidemiology of the diseases they may transmit, in this particular case limited to Plague, Leptospirosis and Toxoplasmosis.

These indicators are translated into a simple mathematical model that is used to analyse the area. The model's results are later compared with the existent findings, hotspots, etc. These results, if valid, may be understood as possible correlations.

3.2   Data Input

In the case of Durban, the study site was limited to an area of 5150 Ha, which covers the commercial and business district, part of the harbour, part of the coastline and some residential areas (formal and informal).

The spatial data was collected from diverse sources including roads, land use (forests, parks), water systems and terrain topography. Additionally, locations of food stores and restaurants in the area were added. The latter data is not exhaustive, but it can be considered representative in some areas.

An important dataset was obtained from the database of the RatZooMan project and includes socioeconomic data from the areas considered in the case study. The data collected pertains to population, population density, accumulation of residents per household, type of education received, unemployment and income.

3.3   Data Processing

Numerical values were used to represent data in the study area in a standard way, with the purpose of representing "occurrence rate" of the datasets in a particular spot, area, district, etc, depending on the dataset in question. These values had a range between 0 (not valid) and 1 (fully valid) with intermediate values used as a quotient of the maximum value in the entire study area.

For example, the district with the highest density is represented by the value '1', and the district with the lowest density represented by a value in proportion to the highest density (n<1). Districts without population contain '0'. The same format was used for areas of influence of a particular dataset. The immediate area inside and around a forest receives the value '1', a buffer of 50m receives '0.8', a buffer of 100m gets '0.5', etc.

Distance values were based on the possible range of movement of a rodent. Studies have defined a range of 100-200m around a possible focus, depending on the topography (Belmain, S.R., 2006; Clay, Ch. A. 2008).

All data connectable to a location was quantified in this way, as precisely as the data accuracy allowed.

3.4   Setting Parameters and weighting factors

Weighting factors were used to determine with a factor the significance of the dataset to the habitat of rodents. The factors are in a range between -3 (very negative for the habitat of rodents) and +3 (very positive for the habitat of rodents). A value of '0' was set for datasets that are not relevant or not clearly significant.

Setting the weighting factors was associated to interpreting the findings of previous studies, particularly of the general conclusions of the RatZooMan studies in its several study sites. This task was rather clear for some datasets, and wherever no scientific reference was found by the authors, weighting factors.were set based on discussion and ad-hoc judgment.

To mention some of the parameters looked at, a relevant factor is the terrain topography. Outside the host, Leptospires spirochetes need damp soil and pH levels of 7.0-8.0 . This soil was typical in areas near rivers, areas with open discharge of waste water, along drainage canals or where pipes leak (Taylor P. J. et al., 2008). Thus, factor 3 was assigned to all locations in which the terrain is flat or has a low slope and is surrounded by gradient terrain. It is expected that these areas will keep soil humidity the longest, which is advantageous for rodents and the pathogens.

As said before, there is an increasing population of rodents due to human intervention. This includes urban growth, with increasing number and size of peri-urban slums and insufficient basic standards for urbanised infrastructure, deforestation, agricultural intensification, etc. For this reason, all areas spatially connected to forests and informal settlements were considered to contribute with a factor '3'.

There are at least five factors that contribute to an increasing spread of infection diseases, according to Herwig Leirs of the University of Antwerp, Belgium (Belmain, S.R., 2006):

(1) Deteriorated hygiene conditions like the ones in mega-cities,

(2) Expansion of human habitat and the contact with "new pathogens",

(3) Lowered immunocompetence in people, which is connected to AIDS,

(4) Devellopment of pathogens' resistance to treatment,

(5) Some reservoir species habitats may benefit from climate change.

From these five factors, at least (1) and (2) may be represented in a GIS, if applicable information is available. The socioeconomic data was interpreted accordingly.

3.5 Calculation

Once "occurrence rate" was defined and all "weighting factors" were set, the study site was divided in 20600 cells, each of which was given a value for the occurrence of each of the factors and these values were multiplied

by the respective weighting factor. That means, this operation was repeated 14 times in each cell, for each of the 14 datasets considered.

Finally, the sum of all the 14 products was obtained for each cell. In order to understand the obtained figures more easily, these were represented as a percentage of the value of the cell with the highest result.

The result represents a relative value of the factors occurring in that cell regarding its conditions as rodent habitat, in consideration of 14 factors, which are: Forest, Food outlet, Supermarket, terrain humidity, permanent water, city park, population density, medical care centre, accumulation of residents per household, education level, unemployment, 3 levels of income (under average, average and above average).

4   MODEL RESULTS

4.1   Observations and Interpretation

For an easier interpretation, as a last step before spatial representation, the range of cell results between 0 and 100 was translated into a range of yellows. The range goes in five degrees of natural brakes, which is a standard ArcView classification method that uses the Jenks optimization as statistical formula.
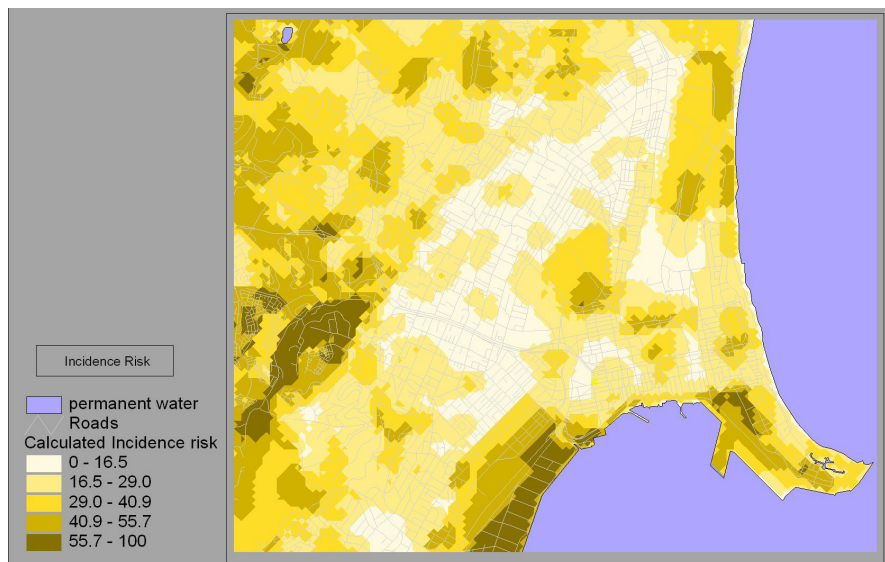

Fig. 1: Model results

Figure 1 shows the study site and the results displayed in the colour range. The darker the cells, the better the survival conditions for rodents (and therefore for the pathogens, if carried by the rodents).

In the area covered by the model presented here, the RatZooMan team had set up 58 trap sites, distributed in the commercial district, Cato Crest (a highly dense, low income settlement), the harbour and two isolated sites just north of the commercial district.

In a period of time of 19 moths, around 210 rodents were caught in this area. As it was said before, blood and tissue samples of these rodents were tested for antibodies or DNA of plague, Leptospirosis and Toxoplasmosis. Concerning the results, 26 rodents (12.4%) were seropositive of either Leptospirosis, Toxoplasmosis or both. No rodent was seropositive for Plague.
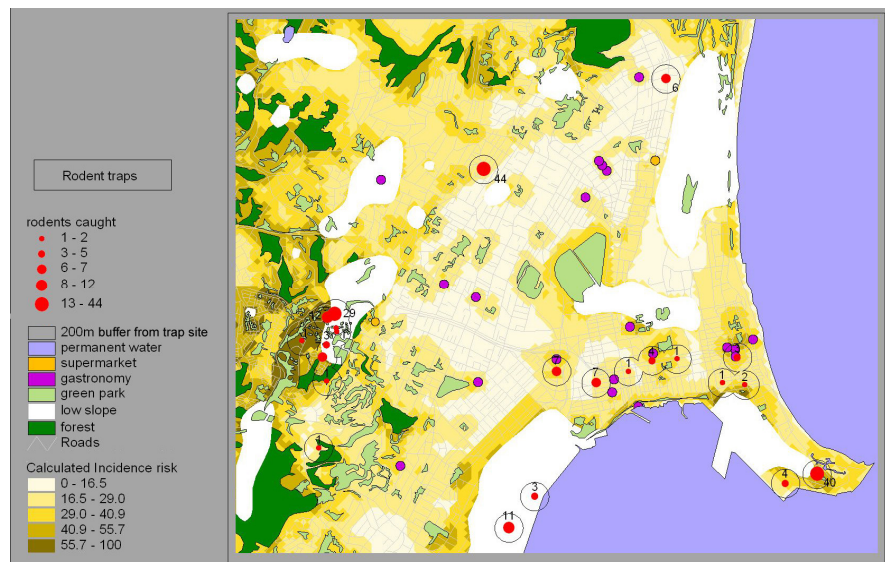

Fig. 2: Caught rodents

Figure 2 shows the model results and the locations of rodent traps in which rodents were caught during the RatZooMan project. The quantity displayed next to each red spot describes the number of rodents trapped there. Around each site, there is a buffer of 100m radius, that represents an average distance that a rodent is expected to move from its focus.

There are three possible hotspots calculated by the model: Part of the harbour on the south, an area between port stores and commercial buildings on the east side of the harbour and the Cato Crest neighbourhood on the west of the study site. The results are in part confirmed by the trap sites

graphic. Around 62% of the rodents caught had apparently their focus within areas of medium and high risk, whereas 57% within only areas of high risk. Rodents were also caught in other sites identified as of lower risk by the model.

There are also some areas considered of low risk in which rodents were caught. With one exception (site with n=44), the number of rodents caught there is low.
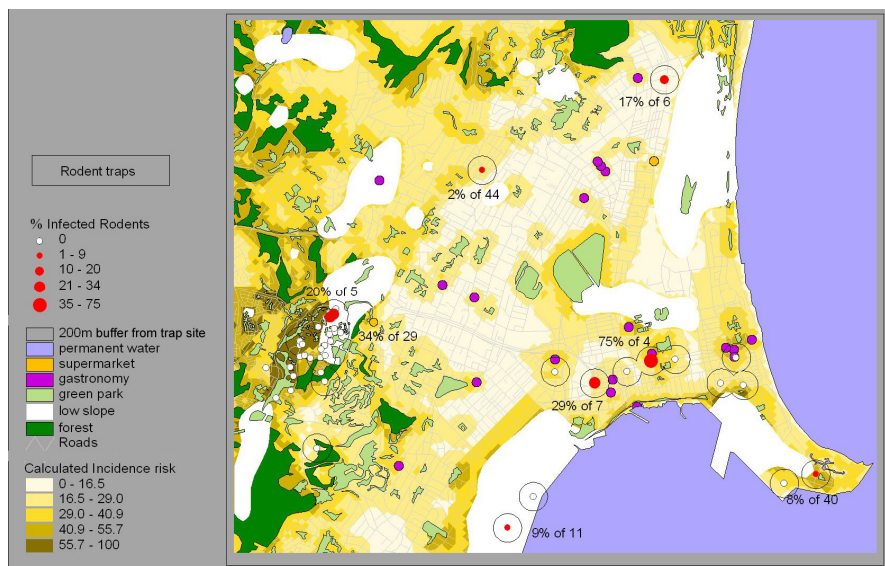

Fig. 3: Infected rodents

Finally, Figure 3 shows next to each trap site the percentage of infected rodents caught there. Only locations where more than four rodents were caught have been considered for this calculation.

This graphic also in part confirms the calculations of the model about areas of higher risk.

Two trap sites in areas calculated of low and lowest risk show a considerable percentage of infected rodents (29% and 17%, respectively).

The existence of spatially limited hotspots suggests that the spread of Leptospirosis and Toxoplasmosis is limited to the micro habitat of few rodents. This assumption, known as the "superspreader theory" or the "20/80 rule", was brought up by a study with wild deer mice in the Great Basin Desert, Utah, USA (Clay CH. A., 2008). The study suggested also that wherever rodents can get older easily, the danger of human infection is

higher. A high death rate of rodents reduces also the existence of super-spreaders and hence the rate of infections.

This assumption was also suggested by John Holt from the Natural Resources Institute, UK, and Stephen Davis, from the University of Antwerp, Belgium, reporting during the RatZooMan project on the results of mathematical models to prevent the spread of Leptospirosis in humans. These results suggest that reducing the number of rodents via trapping/ baiting may be more effective than reducing the suitability of the environment (Belmain, S.R., 2006).

The superspreader theory has also been applied to the spread of other infectious diseases like AIDS and SARS.

5   DISCUSSION AND CONCLUSIONS

It is difficult to place conclusive observations from analyses like the one presented here, because the matter is very complex and requires further study. The epidemiological literature often uses the phrase "correlation does not imply causation" (Bradford Hill, A., 1965). This is a true challenge for epidemiological studies.

According to a local survey, in Cato Crest, the informal settlement included in the study site, rodents were sighted outside houses regardless of their quality of construction (brick houses or houses built with recycled materials). Serological tests confirmed that the percentage showing sero-prevalence in Leptospirosis and Toxoplasmosis was 35% lower in humans living in electrified, council built houses (Taylor P. J. et al., 2008). However, the data also confirms that all inhabitants of Cato Crest are exposed to becoming seropositive, regardless of age, gender, or the areas where they live within Cato Crest, since seropositive persons belonged to all categories. This means that the proximity to a hotspot is an issue to be considered when designing campaigns.

A similar deduction was made after analysing the 2003 SARS epidemic in Hong Kong. The proximity to either effective health care services or to a disease focus were more relevant than high population density, which didn't seem to increase the spread. During the epidemic, lower case occurrence was recorded in areas of high density and resident accumulation, which were close to general hospitals, while newer districts with lower development densities registered higher disease occurrence, among them was

Mong Kok, where the Kwong Wah hospital is located, the starting point of the epidemic (Pun, K.S., 2004)

Adequate health services, infrastructure and funding are crucial to contain any type of disease spread. A recent cholera epidemic in Zimbabwe revealed a mortality of around 25%, while the mortality under normal treatment conditions worldwide is around 1% (Wernicke, C., 2008). In Zimbabwe the epidemic also had an origin in the political crisis in which the country is involved since years and this shows how many factors may play a role in epidemiology.
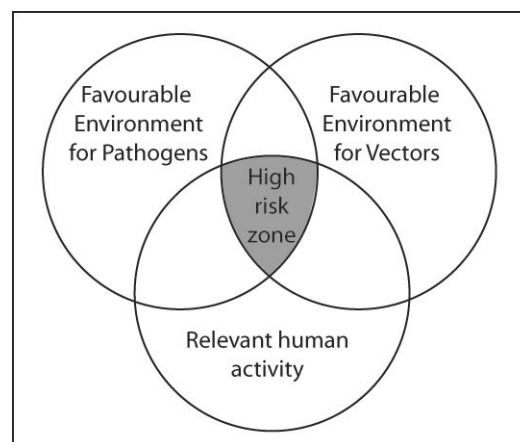

Fig. 4: Zoonoses risk scheme (Rolf Schütt)

The contradictory occurrence of rodents and also infected rodents in areas considered of low or no risk by the model results suggests that human influence is a variable that while very difficult to model, is a crucial key to forecast infection focuses. Probably, an effective model would require to narrow down vector habitat, pathogen habitat and relevant human influence into a mutual, spatially referenced field (Figure 4).

The RatZooMan project findings revealed a high connection between human behaviour, practices, beliefs or perceptions and the increase of disease spread, There is a lack of awareness about rodent borne diseases among the population in most of the study sites, especially among the population with a lower socio-economic status. The existence of traditional beliefs and practice of traditional healers was regarded as an important factor (Belmain, S.R., 2006). It must be added that in parts of Mozambique, Tanzania, Zimbabwe and Zambia, rodents are an important protein source and

are consumed by humans, which may increase the infection risk. This practice was not registered in Durban.

A previous pest control project undertaken in Boston in 1990 was used as a basis to design the disease management strategy in Durban. The Boston model included six key players, namely (1) pest control measures, (2) Authorities role, (3) Community participation, (4) Legal aspects, (5) Public Services and (6) Neighbourhood services (Colvin BA, Jackson WB, 1999; Taylor P. J. et al., 2008)

The RatZooMan project team suggested to apply the available keys of the Boston Model in Durban. It also suggested to focus on five practical issues: (1) understanding the dynamics of the disease; (2) knowledge of the rodent's behaviour and ecology, in particular the species involved; (3) Interdisciplinary cooperation; (4) use of control techniques; (5) funding.

The project also suggested to programme activities for disease control in three levels: A higher political level which provides integral programmes and funding; an intermediate community level to work on awareness raising and the improvement of basic services like water supply and garbage management; and an individual level lo improve self hygiene and focus on human practices that are part of disease transmission routes.

The suggested keys and activities in Durban would grab integrally the three key aspects displayed in the zoonoses risk scheme proposed above.

Regarding the core questions of the RatZooMan's study site Durban, shown in point 2.2, it can be assumed that the model presented here contributes to answer them. Because of the aspects explained when analysing the model results, it can be said that rodents pose a health risk for the public; that all 14 factors used to calculate incidence risk can be involved, although many others need to be identified, recorded and included; and that rodent borne disease management needs integral and interdisciplinary action, setting the human in the centre as both a weakness and a main weapon.

The actions to bring the 2014 Ebola outbreak in West Africa under control included restricting the movement of humans in areas with high incidence (schools were closed, city areas completely closed for transit), which reduced the interaction between potential virus carriers and healthy individuals. These measures have been so far fairly effective in reducing the incidence in a battle against an illness with a mortality rate above 90%. Vaccination and treatment methods are still on an experimental mode.

Last but not least, it has to be pointed out, that the model reported in this paper was made entirely with freely available data, either extracted from diverse public sources of Durban and South Africa or other sources like Google Maps, websites of open scientific and educational collaboration and the RatZooMan project website. This suggests that much more precise results may be achieved if more datasets with more exact and exhaustive data are included.

References

Belmain, S.R. (2006) Rats and Human Health in Africa. Proceedings of an international workshop on rodent-borne diseases and the RatZooMan research project. 3-6 May 2006, The Pestana Kruger Lodge, Malelane, Mpumalanga Province, Republic of South Africa. 46 pages. Natural Resources Institute, Chatham UK.

Bradford Hill, A. (1965) The Environment and Disease: Association or Causation. Proceedings of the Royal Society of Medicine, 58 (1965), 295-300.

CDC Centers for Disease Control and Prevention (USA) Diseases Directly Transmitted by Rodents, http://www.cdc.gov/rodents/diseases/direct_rodents.htm Published May 2006 [27 December 2008]

Clay, Ch. A. et al (2008) Contact heterogeneity in deer mice: implications for Sin Nombre virus transmission. Proceedings of the Royal Society B, DOI 10.1098/rspb.2008.1693

Colvin BA, Jackson WB (1999). Urban rodent control programmes for the 21st century. Ecologically-Based Management of Rodent Pests. Singleton G, Hinds LA, Leirs H, Zhang Z, eds. Australian Centre for International Agricultural Research monograph no. 59. ACIAR, Canberra, pp. 243-57.

Enscore RE, Biggerstaff BJ, Brown TL, et al. (2002) Modelling relationships between climate and the frequency of human plague cases in the south-western United States, 1960-1997. Am J Trop Med Hyg, 66(2), pp. 186-196. Online http://www.ajtmh.org/cgi/reprint/66/2/186 [7 January 2009]

Fritz, A. & Samenow, J., 2014. 'Will climate change worsen Ebola outbreaks?' *The Washington Post*. 5 August 2014. Available from: <http://www.washingtonpost.com/blogs/capital-weather-gang/wp/2014/08/05/will-climate-change-worsen-ebola-outbreaks/> [18 December 2014].

Hartskeerl R. (2006) Leptospirosis overview, see Belmain, S.R. (2006)

Matthew, R.A. and McDonald, B. (1994) Cities under Siege: Urban Planning and the Threat of Infectious Disease. Journal of the American Planning Association, Volume 72, Issue 1 March 2006 , pages 109 - 117, DOI: 10.1080/01944360608976728

Meyer A (2003). Urban commensal rodent control: fact or fiction. In: Rats, Mice and People: Rodent Biology and Management. Singleton G, Hinds LA, Krebs CJ, Spratt DM, eds. Australian Centre for International Agricultural Research monograph no. 96. ACIAR, Canberra, pp. 446-50.

Pitzke, M. (2008) Globale Bedrohung: US Kongress warnt vor Biowaffen-Terror. *Spiegel Online*, http://www.spiegel.de/politik/ausland/0,1518,druck-594117,00.html [03 December 2008]

Pun, K.S. (2004) Urban Planning For Healthy Physical Living Environment. Hong Kong Special Administrative Region. Proceedings of the International Housing Conference in Hong Kong 2004, Housing in the 21st Century: Challenges and Commitments. Web http://www.housingauthority.gov.hk/en/ihc/programme/0,3121,,00.html [15 October 2008]

RatZooMan official website: http://www.nri.org/projects/ratzooman/publications.htm [15 December 2008]

Schuett, R. (2007) GIS based planning support system in Glasgow. Case study: The Glasgow Canals regeneration. Proceedings of the 10th international conference on Computers in Urban Planning and Urban Management Da Silva, A. and De Souza, L., ed., University of Sao Paulo – Sao Carlos, Brazil

Schuett, R. (2008) Raster based GIS for urban management: a low-cost solution for developing countries - Case Study: Analysis of Constraints and Opportunities for Investment in the city of Warsaw, Poland. Proceedings of 44th ISOCARP International Congress: Urban Growth without Sprawl: A way towards sustainable urbanization, 19-23 September 2008 in Dalian, China

Statistics of South Africa, Website http://www.statssa.gov.za/census01/html/default.asp Publish date unknown, retrieved on Jan 06, 2009

Swaaf , K. F. de (2009) Gefärbte Mäuse verraten sich als Superspreader. Spiegel Online, http://www.spiegel.de/wissenschaft/natur/0,1518,druck-599783,00.html [7 January 2009]

Taylor P. J. et al. (2008) Understanding and managing sanitary risks due to rodent zoonoses in an African city: beyond the Boston Model. Integrative Zoology 2008; 3: 38-50 doi: 10.1111/j.1749-4877.2008.00072.x

Thompson, R, (2006) The ratzooman GIS, see Belmain, S.R. (2006)

Webster, J.P. and Macdonald, D.W. (1995). Parasites of wild brown rats (Rattus norvegicus) on UK farms. Parasitology 109: 37-43.

Wernicke, C. (2008) Cholera-Epidemie In Simbabwe, Die meisten sterben still und unbeachtet. Spiegel Online, web http://www.spiegel.de/politik/ausland/0,1518,druck-595873,00.html [12 December 2008]

WHO Website on Plague
http://www.who.int/mediacentre/factsheets/fs267/en published May 2005 [06 January 2009]