I am writing to be considered for a MRC LID studentship. I am currently on the MSc [removed] at [removed] due to complete in September 20XX. I have been successful on the course so far and am improving both my mathematical knowledge and study skills as the year progresses. I am applying for this project proposal that is relevant to my skills and experience and strongly appeals to me on “Spatial transmission of influenza and dengue fever in the Western Pacific”. This project will investigate spatial transmission of communicable diseases in the unique environment of the 23 countries of Western Pacific region.

Spatial transmission of influenza and dengue fever in the Western Pacific

Summary

- Study into the transmission of infectious diseases in a unique environment.
- Combining individual points of evidence into a network of disease transmission in the region.
- Mechanistic modelling to anticipate the future spread and calculate the original source of infections.
- Testing of these models using data from the region.

Background

Acute infections such as influenza and dengue fever carry a substantial disease burden in the Western Pacific. Recently the re-emergence of dengue virus serotype 3 in 2013 and the more recent spread of Zika virus to the Americas highlights the need to understand the routes of disease transmission.

The spread of infectious diseases from remote areas such as the Western Pacific to more populous areas has been long established. Warrilow et al. (2012) examined the causes of the importation of dengue virus to Queensland, Australia, 2002-2010. Through sequencing and genotyping the authors found evidence of increasing dengue outbreak over a 20-year period in Queensland reflecting the increase in international travel over the period with 21.4% of infected travellers returning from the Pacific Islands or Papua New Guinea (Warrilow et al., p. 1853). This trend is not unique to dengue fever as Roth et al. (2014) demonstrate with the increased epidemic wave of chikungunya and Zika virus in the Pacific 2012-2014 with 28 reported cases of these three mosquito-borne viruses affecting over 120,000 inhabitants (Roth et al., 2014, p. 1).

Helping to understand and limit the spatial transmission of these diseases will help facilitate response measures to mitigate the burden on the region’s health systems. This area is especially vulnerable to the spread of these diseases due to a lack of immunity in the region, the prevalence of competent vectors known to transmit these viruses and the large population mobility (Roth et al., pp. 5-6). The region is unique in its intra-regional links so should be studied in its own right as the system of island-to-island dependence for trade and commerce is dissimilar to most of the rest of the world.

Existing methods have been able to examine the path of specific viruses or strains of these viruses. This allows the authors to estimate the likely path of dengue fever serotype 3 to Queensland, for example, but of more statistical interest is the network of these disease transmissions. This would then allow investigation into the pattern of disease transmission to Queensland. This project aims to connect isolated individual analysis of rates of transmission into mapping the whole network in the Western Pacific.

Methods

Initial analysis will involve the use of existing methods on data specific to the region. The collaborators at the World Health Organisation (WHO) have a large amount of surveillance data including reports of influenza-like and dengue-like illness; virological confirmation and sequence data. The readiness and size of the existing data means that established methods can be applied swiftly. For example, the availability of sequence data allows for phylogenetic analysis to establish evolutionary relationships in the various pathogens.

This initial work would help map out transmission patterns for influenza and dengue fever in the region identifying common factors and sources for the outbreak. The project methodology would then need to extend into the construction and testing of mathematical models aimed at predicting the spatial transmission of these viruses in this region.

There already exists sophisticated models for probable propagation patterns of contagious diseases such as those drawn up by Brockman et al. (2013). The authors built a model to estimate disease arrival time from an original location was not determined by geographical distance but by “effective distance”, derived by including airline travel data with geographical distance. The authors were able to adjust the actual distance between countries to a more relevant distance that was determined by both geography and connectivity of countries. This reduces complex spatiotemporal patterns into a simple propagating wave where the disease path can be predicted through the most probable route based on effective distance.

This model is impressive in its complexity and effectiveness but is not thoroughly statistically tested in its accuracy. This project provides the opportunity to build similar models directly intended for application to the Western Pacific region. The availability of data from the region then would allow us to empirically test the models against historic disease transmission patterns in the region.

Objectives and Outputs

The initial output will be descriptive statistics of disease transmission in the region. Investigations of spatial synchrony should help identify patterns of how disease spreads in the region. This can be done across different pathogens to test whether influenza, dengue fever and other diseases have differing spatial transmission patterns. This can be expanded with sequence relatedness tests to determine the genetic similarities between several pathogens including novel emerging pathogens.

After mapping out disease transmission trends the next step would be to build mechanistic models using travel data to and from the region to estimate the speed with which disease is transmitted and to where. Incorporating flight data into similar models has been shown to increase predictive accuracy and could be applied in this setting. The advantage of these models is that they can be reversed to determine the most likely source of the disease as well as its most probable next location.

The key with this project is that these models should not be standalone experiments in model building but should be thoroughly tested in this specific setting using the rich resource of data available. This will help determine the validity of the models and their appropriateness in use on future disease outbreaks.

This work will firstly benefit the collaboration partners of WHO Division of Pacific Technical Support. The team have a valuable and extensive amount of data but a lack of resources to fully exploit these data. Crucially, successful investigations of disease transmission patterns in the region will benefit the local health systems if conclusions can be drawn about how to facilitate response measures to mitigate the burden on the region’s health systems. If the impact of future viruses can be reduced through the project, then this not only has health benefits for mortality and quality of life but also major economic benefits for the region.

From a UK perspective, we are not isolated from these viruses as shown this week with three UK travellers diagnosed with Zika. Knowledge of the origins and transmission patterns of these viruses will help protect the UK as well as the region of origin.

Experience and motivation

I studied Economics as an undergraduate at [removed] University but even when studying a social science, it was the statistical component of econometrics that interested me most. I was most engaged at the end of my final year at [removed] when we built a linear predictive model for the behaviour of the FTSE stock market using a variety of economic factors as covariates. The project also gave me my first experience with programming and handling large data sets which was greatly extended when I got my first graduate job at the [removed]. I had a very successful two years at the [removed], securing a promotion within four months due to my efficiency, attitude and ability to work collaboratively with others. In my time at [removed] I was trained in the use of SAS as a processing tool for very large survey data sets that were then used to calculate estimates for the UK economy’s Balance of Payments with the rest of the World. Again I greatly enjoyed the use of statistical programming on computers and handling large data sets.

A week’s work experience with a health economist at [removed] University made me aware of the possibility to apply these skills in a field I found far more exciting. I was awarded one of four [removed] studentships to study MSc [removed] in [academic year removed] and have found it to be a great experience. The teaching quality and my enthusiasm for the subject has led to a far greater grounding in the fundamentals of statistics covering probability distributions, statistical inferences and regression as well as their application in health settings. It is the regression techniques and model building that interests me most as this is an extension of pre-existing knowledge and because of its potential for application in research settings.

I have enjoyed the course and being back in an academic setting compared to working at [removed] as well as the environment at [removed]. This has led me to seek a PhD to continue my studies and develop my own research. Both projects listed appeal but especially the chance to develop a new skill in the building of mathematical models to predict spatial transmission, as a natural extension of a pre-existing skillset with regression techniques.

References:

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