Introduction to Infectious Disease Modelling and its Applications

Course Description

Intensive course: 19th – 30th June, 2017

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Public Health England




Introduction

Infectious diseases remain a leading cause of morbidity and mortality worldwide, with HIV, tuberculosis and malaria estimated to cause 10% of all deaths each year. Outbreaks of Ebola in recent years have led to unprecedented numbers of deaths and cases. New pathogens continue to emerge in animal and human populations, as demonstrated by the emergence of SARS in 2003, of Highly Pathogenic Avian Influenza (HPAI) in poultry and humans in 2004/2005, swine flu in 2009, MERS CoV in 2013 and Zika in 2016.

Mathematical models are being increasingly used to understand the transmission of infections and to evaluate the potential impact of control programmes in reducing morbidity and mortality. This two week intensive course is intended to introduce professionals with an interest in infectious diseases in either developing or developed countries or in veterinary questions to this exciting and expanding area. The emphasis will be on developing a conceptual understanding of the basic methods and on their practical application rather than the manipulation of mathematical equations.

The level of difficulty is appropriate for people with high school level of mathematics and is similar to that of the book "An Introduction to Infectious Disease Modelling", published in 2010, which was written by two of the course organizers (Emilia Vynnycky and Richard White). The book is based on material from this popular and successful course. For further details about the book, see www.anintroductiontoinfectiousdiseasemodelling.com.

Course structure

The course comprises 4 sections, as follows:

Section 1: Basic methods and motives for developing infectious disease models

This section is designed to introduce participants both to the basic methods for developing models of the transmission dynamics of infectious diseases and to the applications of these models. It starts with an introduction to the major concepts used for studying the epidemiology of infectious diseases (the basic reproduction number, incubation periods, serial intervals, herd immunity) and continues with an introduction to the main types of models that can be employed.

Participants learn about the basic methods for setting up deterministic models (difference and differential equations) and will gain practice and confidence in setting up simple models using spreadsheets and a specialist, user-friendly modelling package (Berkeley Madonna). Examples of diseases discussed in this section include influenza, measles, mumps and rubella. Participants will gain an understanding of the insights into infectious disease dynamics that models can provide, such as the factors influencing the periodicity of disease incidence for immunizing infections (e.g. the incubation period, basic reproduction number, seasonal transmission, vaccination and control programmes) and how the models can be applied to determine optimal control strategies for outbreaks involving new pathogens as well as for endemic infections.

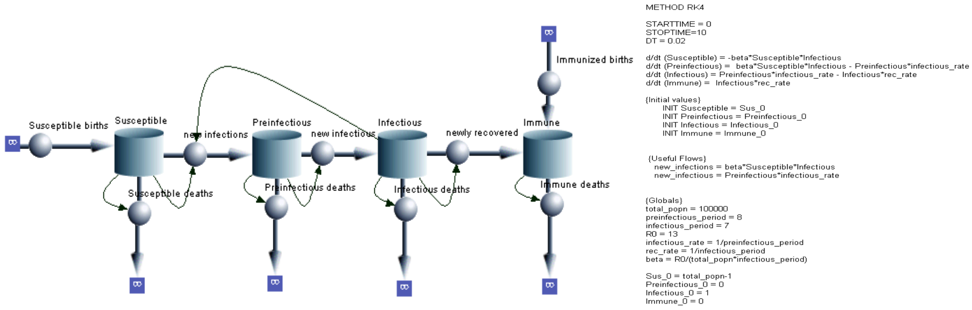

Figure 1: Example of different approaches which can be used to set up models using Berkeley Madonna. Models can be set using either flow diagrams or equations. Participants can work with the approach that they prefer during the course.

Section 2: Analysis of data and applications of modelling of seroprevalence data

Section 2 deals with the methods for analysing seroprevalence or other data on past infection, how they can be used for elucidating past trends in infection incidence and for studying the transmission dynamics and predicting the control of infections. The section starts with a lecture on how to analyse and interpret seroprevalence data, which is followed by a second lecture describing different fitting methodologies. During the subsequent practicals, participants will examine different data sets and estimate (age-dependent) infection incidences ("forces of infection") for high and low infection transmission settings, using rubella as an example.

These estimates are then used to analyse how control policies can lead to reductions in transmission but increases in infection incidence in adult life (and other unexpected events), depending on the study setting. Participants will also study how seroprevalence data can be used to estimate mixing patterns of subgroups in given populations and how different contact patterns between individuals affect the impact of control.

The section includes sessions which are part of a groupwork exercise, whereby participants use modelling to analyse data for influenza or Ebola and predict the impact of different interventions, including school closures and vaccination for influenza, and exposure to infectious people for Ebola.

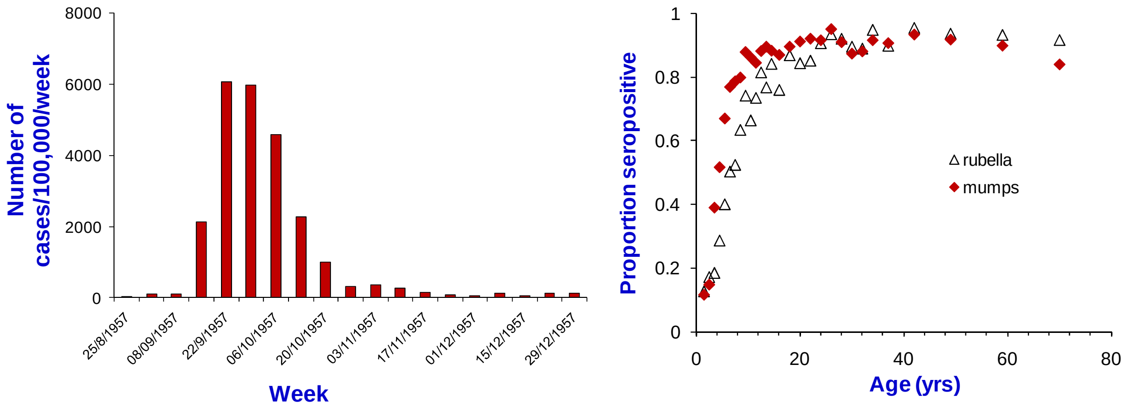

Figure 2: Examples of the kinds of datasets that course participants learn to analyse and use in models in this section. A. Data on the epidemic curve for influenza (from an outbreak during the 1957 influenza pandemic) B. Age-specific serological data for mumps and rubella.

Section 3: Additional methods and dynamics - stochastic and network modelling, health economics and sensitivity analyses

This section provides an introduction to several methodological aspects of modelling, namely stochastic and network models, health economics and sensitivity analyses.

Stochastic models are often used to describe the transmission dynamics of infections in small populations, for example, for predicting the course of outbreaks and critical population sizes for the persistence of infection. This section introduces participants to the basic methods for setting up stochastic models of outbreaks and the long-term dynamics of directly transmitted infections. It also illustrates how distributions of outbreak sizes may be used to infer the success of elimination programmes and extent of ongoing transmission (for example, for pandemic influenza or measles) and the application of stochastic models in describing nosocomial transmission.

The success of control programmes greatly depend on the extent to which different individuals are connected, for example, the individuals that each person contacts and the contacts of those persons. These issues are illustrated in a lecture and practical on network models, which try to capture such detailed contact patterns and have been used in modelling the transmission and control of sexually transmitted infections and Foot and Mouth Disease.

Modelling studies are increasingly including health economics analyses, for example, to estimate the cost-effectiveness of an intervention and such estimates can often be persuasive when making health policy decisions. Modelling studies also need to use sensitivity analyses to determine the effect of different assumptions or inputs on predictions of the incidence or control of an infection. In this section of the course, the basic principles of health economic analyses and sensitivity analyses are introduced in a lecture and practical.

An optional lecture discussing methods for fitting models to data and methods for sensitivity analyses is also scheduled.

Section 4: Applications of modelling

The lectures in this section are designed to illustrate several major current areas of applications of mathematical models, namely real-time modelling, the transmission of sexually transmitted infections (STIs) and HIV, tuberculosis, zoonoses and other veterinary diseases. Most of the sessions on the applications of modelling comprise two parallel streams and participants can attend sessions from either stream at any time.

The first stream starts with a lecture and practical on modelling sexually transmitted infections, covering the early mathematical models for STIs and the role of core groups in sustaining infections in populations. This is followed by a lecture covering the development of models to understand the spread and control of HIV. The stream concludes with a lecture and practical on modelling *M tuberculosis* transmission and predicting the impact of control.

The second stream starts with a lecture discussing the general issues relating to modelling problems in veterinary epidemiology, and is followed by a practical illustrating the principles using avian influenza in the UK. This is followed by a lecture and practical describing the transmission of malaria and the Ross Macdonald model. The stream concludes with a lecture on the uses of real-time modeling, which, as was the case during the 2009 swine flu pandemic, is used for monitoring the extent of ongoing transmission at regular intervals (e.g. daily) during the course of an outbreak.

The section includes a lecture and practical introducing the application of the rapidly growing area of phylodynamics, in which modelling is used, in conjunction with molecular data to track the evolution and course of outbreaks.

Teaching methods

Lectures and practicals

A typical day lasts during 9.00-5.30 (with breaks for lunch and coffee/tea), with each half-day session consisting of a lecture and an accompanying practical. There will also be review lectures on Wednesday morning of week 1 and on Monday morning of week 2, which are designed to help consolidate the material covered until then. Attendance at these sessions is optional.

Guest Lectures

Lunch-time and evening guest seminars by modellers from outside LSHTM are scheduled during the course. Speakers in the past have included Neil Ferguson (Imperial College), Hans Heesterbeek (University of Utrecht), Roy Anderson (Imperial College, London), Geoff Garnett (Imperial College, London), Robert May (University of Oxford), Eduardo Massad (University of Sao Paulo), Brian Williams (WHO), Jon Read (Warwick University), Liz Miller (Public Health England), Angela Maclean (University of Oxford), Raymond Hutubessy (World Health

Organization). These seminars are designed to provide further perspectives on the areas of application of modelling and attendance is entirely optional.

Paper discussions

A paper discussion is scheduled on Friday of week 1, which is designed to familiarize participants with the mathematical modelling literature and to introduce some of the areas of applications of modelling. The topics covered in these papers include tuberculosis, rinderpest and Ebola.

Groupwork/Problem–based learning exercise

During the course, there is a problem-based learning exercise, which is designed to highlight the way modelling methods may be used to solve "real" problems and to give practice in thinking about how models are designed and used to make policy decisions. Participants will be divided into small groups and will work on a problem relating to pandemic influenza or epidemics of Ebola. Participants are required to discuss and work on the problem in these groups during allocated sessions. The exercise culminates with a poster presentation on the final day.

Modelling clinic

Tutors are available during the course to discuss questions that participants may have on the course material. In addition, a short "clinic" is scheduled during several lunch-times of the second week of the course, during which tutors meet one-to-one with students to discuss questions relating to the participants' own work in more depth.

Social arrangements

Finally, there are several opportunities for social interaction during the course, including a reception on the first day, a guided walk around the sites of special medical interest in London, a quiz, a meal and a trip on the London Eye and a theatre outing.

Backgrounds of previous students

The course aims to bring a conceptual understanding of mathematical modelling and its applications in infectious disease research to individuals who have not had any advanced training in mathematics. It is also suitable for individuals with a background in mathematical disciplines who wish to obtain an understanding of the broad range of applications of mathematical models in

Figure 3: Illustration of the backgrounds of past course participants.

infectious disease epidemiology and who may wish to specialize in this area in the future.

The diversity of academic backgrounds catered for in this course is illustrated by the course photo from recent years, shown above and from the feedback from students (see below). Each individual in the photo is shaded according to his or her academic background and region of origin. For example, medical doctors are shaded in yellow, vets are in purple, etc.

Feedback from previous students

General

- 'Great course! It's hard to bring people from different levels of knowledge together, but this course succeeded in doing so.'
- 'It would help infectious diseases doctors to develop a higher level of comprehension of how epidemics spread.'
- 'Many MDs working in tropical areas badly need these concepts...'
- 'One of the few courses where I really feel I learnt something useful.'
- ‘I would say it is a must for infectious disease epidemiologists.’
- ‘One of best courses I have taken.’
- ‘Very good. The LSHTM should continue this course at least next 20 years.’
- ‘It was relevant, compact, intensive.’
- ‘The course is an excellent introduction to the field. It covers all the basics and I know enough to go away and work on the aspects I'd like to develop further.’
- ‘I think the subject is relevant to anyone in healthcare, not just decision makers. Gives different ways of looking at diseases.’
- ‘It is an excellent starting point for disease modelling.’
- I would like to just thank the faculty and tutors for an excellent course - it was very well-worth my time and the teaching and organization of the material/resources was really exemplary.

Course content and structure

- 'Really helps reinforce basic epidemiology and how that is applied and taken further.'
- 'We have lectures covering basic concepts and following that there are practicals to further digest them, that is so like me!'
- 'Is a really good course, where you really get useful outputs! Beautiful course to get in touch with modelling.'
- 'Lots of practicals for each session, lots of examples based on diseases: wide spectrum for applications.'
- ‘It gives a good picture of the problem. It is not too technical and therefore people with different backgrounds can follow and understand.’
- ‘Very rich content, did very well to get so much into such a short time.’
- This is one of the best short courses I've taken during my studies - I learned what I expected to learn and the course materials will be an excellent resource in the future.

Level of difficulty

- 'Very good for a totally 'blur' person like me on modelling - I saw the light.'
- 'Just right; could even have been more difficult (but it would take more time to explain the maths; so this might not be feasible).'
- 'Challenging but very well presented.'

- ‘This course provided a great introduction to modelling for non-mathematicians, making this important discipline accessible.’
- ‘Just the right amount of challenging content.’
- ‘It gives a good introduction to mathematical modelling for people without strong mathematical background to understand.’

Organization and teaching

- ‘It is very well organised. Every detail seems to have been covered.’
- 'Complete use of all our time - I certainly got 'my moneys' worth! Mix of fellow students was excellent, majority of lectures were to a really high standard, as you would hope from world famous LSHTM!'
- 'Excellent teachers, very good division of time between activities.'
- I thought the course was incredibly well organized.
- I appreciated how carefully the instructors built our understanding of concepts over the course. It was clear that the lectures had been planned in a very careful sequence and all faculty lecturers were aware of how far we had come in our understanding.
- 'I learnt a lot more from this course (LSHTM) than another modelling course I attended. First the lecture notes are really good. Second each lecture was followed by a practical session and is really fantastic. This helps students to consolidate the ideas from lecture and put the theory into practice. On the whole FANTASTIC. Thank you!'

Final word

The course has been developed in collaboration between modellers, epidemiologists and statisticians at the London School of Hygiene & Tropical Medicine, Public Health England, and the University of Sao Paulo, Brazil. The course aims to bring a conceptual understanding of mathematical models and their applications in infectious disease research to individuals who have not had any advanced training in mathematics. It is also suitable for individuals with a background in mathematical disciplines who wish to obtain an understanding of the broad range of applications of mathematical models in infectious disease epidemiology and who may wish to specialize in this area in the future.