Imperial College London

SPH017 Infectious Disease Modelling

Module Handbook 2018/19

Autumn (Term 1)

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TIMETABLE

*Please note these lectures and practical will run until 4.30pm

Date	Time	Session type	Session Title	Lecturer
WEEK 1:	9.30	Lecture	Why model?	Nim Arinaminpathy
12th Oct	11.00	Lecture & practicals*	Introduction to designing infectious disease models	Peter White
WEEK 2:	9.30	Practical	Implementing a model using a computer	Tom Churcher
19th Oct	14.30	Q&A	Q&A for students	Nim Arinaminpathy
WEEK 3:	9.30	Lecture & practicals	R0 from first principles	Romain Silhol
26th Oct	13.00	Practical	Estimating R0: influenza practical part 1	Ada Yan
WEEK 4:	9.30	Lecture	Individual heterogeneity, non-random mixing and contact networks	Nicholas Grassly
2nd Nov	11.00	Lecture & practicals*	Compartmental models with heterogeneous mixing	David Haw
WEEK 5:	9.30	Lecture	Parameters, models and data	Christl Donnelly
9th Nov	13.00	Practicals	Model fitting: part 2 of influenza practical	Ada Yan
WEEK 6:	9.30	Lecture	Stochasticity, sensitivity and uncertainty analysis	Juan Vesga
16th Nov	13.00	Practicals	Implementing stochastic models using a computer	Joanna Lewis
WEEK 7:	9.30	Lecture	Modelling vaccination	(TBC)
23rd Nov	11.00	Lecture	Modelling complex interventions	Peter Winskill
	13.00	Practicals	Design a model to answer a public health question	Patrick Walker & Hannah Slater
WEEK 8: 30th Nov	9.30	Practicals	Design a model to answer a public health question	Patrick Walker & Hannah Slater
WEEK 9:	9.30	Group discussion	Critical analysis of an article	Nim Arinaminpathy
7th Dec	11.00	Lecture & practicals*	Modelling vector-borne diseases	Maria-Gloria Basanez
WEEK 10:	9.30	Assessment	Multiple choice test on model building and analysis	Nim Arinaminpathy
14th Dec	13.00	Lecture	The application of infectious disease models: past, present and future	Steven Riley
	14.30	Q & A	Final module Q & A session	Nim Arinaminpathy

LOCATION

All teaching takes place at St Mary's Campus. Consult the module's page on Blackboard and the online timetable/calendar to see where sessions will take place.

MODULE OUTLINE

MODULE AIMS AND CONTENT

This module provides an overview of infectious disease modelling and develops skills in designing and analysing infectious disease models for public health policy. Students will be taught how to represent the characteristics of an infectious disease using a mathematical model, how to simulate that model using a computer, and how to analyse that model. Students will also learn how models have been applied in public health policy, and how models are designed to address a research question. The module also includes a long practical, involving groupwork to develop a research question; design and program the model; and analyse the results from the model.

OVERALL LEARNING OBJECTIVES

By the end of the module students should be able to:

- Generate valid mathematical models from knowledge of the biology of infectious diseases;
- Generate analytical expressions for key parameters from these equations, for example the basic reproduction number, $R_{0;}$
- Conduct a preliminary critical assessment of infectious disease modelling publications;
- Formulate a research question in infectious disease epidemiology and address it using a mathematical model

MODULE STRUCTURE

The majority of the sessions in *Infectious Disease Modelling* are lecture-based, some sessions will have group work and seminars to help demonstrate the concepts involved.

The following breakdown of learning and teaching hours are scheduled for this module, including the expectation of independent study hours you must undertake through self-directed study.

Learning & Teaching Hours	Independent Study Hours	Placement Hours	Total Hours
42	145.5	0	187.5
ECTS Credit	7.5	CATS Credit	15

ASSESSMENT

This module will be assessed through written examination in January 2019, and with a 'research abstract' on the practical work conducted in weeks 7 and 8 (Submission deadline: Monday, 17th December). These components will account for 75% and 25% respectively, of the final mark. There will be also be a formative assessment on Friday 14th December in the form of a multiple choice test followed by a lecture going through the questions and giving feedback on the answers. This will be an opportunity to assess your technical skills in formulating and analysing mathematical models.

RECOMMENDED GENERAL BACKGROUND READING

The following reading list is intended to provide students with a background to some of the topics covered in the lectures. ***Additional readings are highlighted for each week, and in lectures.***

Journal articles:

- Grassly NC & Fraser C *Mathematical models of infectious disease transmission.* Nat Rev Microbiol 2008;6:477-487.
- Hollingsworth, TD *Controlling infectious disease outbreaks: Lessons from mathematical modelling*. J Public Health Policy 2009. 30:328-341

Textbooks:

There are a number of related textbooks, each of which contains useful information. However, no single textbook follows the approach in this module and so none of them are an essential companion to the course. Relevant chapters are highlighted in the suggested reading for particular lectures.

Keeling M & Rohani P. *Modelling infectious diseases in humans and animals*. Princeton University Press 2007.This book has several relevant chapters for this course although it presents the material in a slightly more mathematical manner. Chapter 1 and the code from the simulations in the book can be found at:

http://press.princeton.edu/titles/8459.html

Anderson RM & May RM *Infectious disease of humans: dynamics and control*. Oxford University Press 1991.

Although it is now over 20 years old, this book describes core insights from infectious disease modelling across a large range of infectious diseases. It can be read throughout the course to give a broader context to the material taught in lectures.

White RC & Vynnycky E. *An introduction to infectious disease modelling* Oxford University Press, 2010.

This book is aimed at the novice infectious disease modeller and lays out many of the concepts which are taught within this module and so can be a very useful textbook.

Diekmann and Heesterbeek *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation.* Wiley, 2000

This book outlines a formal mathematical framework for mathematical modelling of infectious diseases, most of which is beyond the scope of this module. It may be of interest to the more mathematically experienced students.

SESSION OUTLINES AND WEEKLY READING

SECTION 1: Introduction and core concepts

LECTURE 1 Why model?

Dr Nim Arinaminpathy

Learning Objectives:

After this session students should be able to:

- Describe the role of mathematical modelling in understanding the transmission dynamics of infectious diseases
- Describe the use of models to inform the control of infectious diseases
- Describe the types of data needed to parameterise infectious disease models
- Describe instance where infectious disease modelling has affected public health policy in the UK and internationally.

Core Readings:

Fraser C et al (2009). *Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings.* Science. 324:1557-1561

Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley S, Meeyai A, Iamsirithaworn S, Burke DS. *Strategies for containing an emerging influenza pandemic in Southeast Asia.* Nature. 2005 Sep 8;437(7056):209-14. Epub 2005 Aug 3. PMID: 16079797

Cauchemez S, Fraser C, Van Kerkhove MD, Donnelly CA, Riley S, Rambaut A, Enouf V, van der Werf S, Ferguson NM, *Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance biases, and transmissibility*, Lancet Infectious Diseases. 2014, 14: 50-56

Suggested Further Readings:

Geoffrey P Garnett, Simon Cousens, Timothy B Hallett, Richard Steketee, Neff Walker *Mathematical models in the evaluation of health programmes.* Lancet (2011) 378:515

Synopsis

This lecture will give an overview of the role of infectious disease modelling in informing and designing public health policy, principally using examples from a range of infectious disease outbreaks (e.g. pandemic flu, SARS, Ebola). I will discuss the uses, and data needs and limitations of models and the importance of modelling for the future.

LECTURE 2 & PRACTICAL 1 Introduction to designing infectious-disease models

Dr Peter White

Learning objectives

After this session students should be able to:

- Explain why we need models specifically designed for the transmission dynamics of infectious diseases;
- Construct a compartmental model for a microparasitic infectious disease;
- Construct a differential equation model for a microparasitic infectious disease;
- Derive the mathematical formulation of the transmission rate of a directly-transmitted (i.e. person-to-person) microparasitic infectious disease;
- Understand the difference between a parameter and a variable;
- Understand the time-course of an epidemic of an acute immunising microparasitic infection such as influenza.

Core readings

For a good overview of fundamental theory, see Chapters 1-3 of Anderson RM & May RM. 1992. Infectious Diseases of Humans: Dynamics and Control. Oxford University Press; ISBN: 019854040X. (hardback 1991, ISBN: 0198545991).

For a gentle introduction to the mathematical concepts, see Chapters 1-3 of Scott ME & Smith G (editors). 1994. Parasitic and Infectious Diseases: Epidemiology and Ecology. Academic Press; ISBN: 0126333254.

Suggested further readings

Garnett GP *An introduction to mathematical models in sexually transmitted disease epidemiology*. Sex Transm Infect 2002;78:7-12 (This paper is concerned with models of sexually-transmitted infections, but explains some basic concepts clearly).

To my knowledge, there are no good introductory textbooks on solving ordinary differential equations and linear algebra specifically targeted for practical modelling. There are lots of good introductions to modelling population dynamics that carefully introduce the maths required here, such as:

Case TJ. An illustrated guide to population ecology. Oxford University Press, 2000.

For much more advanced maths, see :

Murray JD. Mathematical biology. Springer Verlag, 1989 and subsequent editions.

The following papers provide examples of different compartmental model structures; there are many others.

Garnett GP et al. *The transmission dynamics of gonorrhoea: modelling the reported behaviour of infected patients from Newark, New Jersey.* Phil.Trans. R. Soc. Lond. B 1999;354:787-797.

White PJ et al. *Vicious and Virtuous Circles in the Dynamics of Infectious Disease and the Provision of Health Care: Gonorrhea in Britain as an Example*. J Infect Dis 2005;192:824–836.

Garnett GP et al. *The natural history of syphilis - Implications for the transmission dynamics and control of infection.* Sex Transm Dis 1997;24(4):185-200.

Murray CJL & Salomon JA. *Modeling the impact of global tuberculosis control strategies*. PNAS 1998;95:13881–13886.

Synopsis

Infectious disease modelling requires a specific set of mathematical tools that reflect the biological processes involved in disease transmission.

The key difference between the spread of an infectious disease such as measles and a non-infectious disease such as lung cancer is that the potential for people to acquire an infectious disease depends on the number of people who are currently infectious, so that the risk for an individual person of acquiring the disease is a dynamic (variable) feature of the state of the population as a whole.

For this reason, the mathematics of disease spread are intimately related to those of interacting populations and ecology. Disease spreading is modelled using differential equations that relate sizes of population subgroups (e.g. the number of people infected) to rates of change in the sizes of those subgroups over time (e.g. the incidence of infection).

This lecture describes how compartmental mathematical models of microparasitic (viral, bacterial) infectious disease transmission are developed. Topics covered include how the structure of models is developed to reflect the natural history of infection (e.g. latency, progression through stages of infection, symptomatic and asymptomatic infection) and the fundamental assumptions of mathematical models.

The concepts introduced in this lecture will be consolidated in the practical that follows.

PRACTICAL 2 Implementing a model using a computer: introducing Berkeley Madonna and the basic reproduction number, R0

Dr Tom Churcher

Learning objectives

After this session students should be able to:

- Explain the concept of R0 and its effect on the speed and final size of an epidemic;
- Understand the influence of the generation time on the behaviour of an epidemic;
- Describe the effects caused by the introduction of different population and biological factors to infectious disease models, including births, deaths , immunity, and latent periods;
- Use Berkeley Madonna for numerical integration of infectious disease models with a variety of structures and output key quantities over time, such as the number of individuals infected, the prevalence and incidence in the simulated population, R0 and the cumulative epidemic size;
- Use Berkeley Madonna to do parameter plots and batch runs to explore the role of various parameters on infectious disease dynamics.

Core readings

Chapters 2-3 of Anderson RM & May RM. 1992. Infectious Diseases of Humans: Dynamics and Control. Oxford University Press; ISBN: 019854040X. (hardback 1991, ISBN: 0198545991). A general overview emphasising the points made in the LECTURE 2.

Suggested further readings

Chapters 4-6 of Anderson RM & May RM. 1992. Infectious Diseases of Humans: Dynamics and Control. Oxford University Press; ISBN: 019854040X. (hardback 1991, ISBN: 0198545991). For more detail on the SIR model and variations upon it.

Keeling, M.J. and Rohani, P. (2007) Modeling Infectious Diseases in Humans and Animals. Princeton University Press. Chapter 2.

Anderson RM & May (1982) *Directly transmitted infectious diseases: control by vaccination.* Science 215: 1053-60

Fine PEM & Clarkson JA (1982) *Measles in England and Wales I – an analysis of factors underlying seasonal patterns*. Int J Epidemiol 11(1): 5-14

Shulgin B, Stone L & Agur Z (1998) Pulse vaccination strategy in the SIR epidemic model. Bull. Math. Bio. 60: 1123-48.

Capasso V & Serio G (1978) *A generalization of the Kermack-McKendrick deterministic epidemic model.* Math. Biosci. 42: 43-61.

Online resources

Macey R, Oster G & Zahnley T (2000) Berkeley Madonna User's Guide. Available at: http://www.berkeleymadonna.com/BM%20User%27s%20Guide%208.0.pdf

Synopsis

This session will combine a lecture and practical to introduce students to common types of infectious disease models and the concept of R0, the basic reproductive number. We will learn how to use Berkeley Madonna software for numerical integration of an SIR (Susceptible-Infectious-Recovered) model and variations upon this.

The *R0* and the generation time of an infectious disease agent are key quantities in determining epidemic behaviour, including the magnitude of the peak in numbers of infected individuals and the final size of the epidemic. The effective reproductive number *R*, determines whether and how the epidemic will proceed once some of the population are immune due to previous exposure or after the implementation of control measures.

Several variations on the SIR model are appropriate for different diseases. An open SIR model includes births and deaths in the population, which can be important for diseases which usually cause lifelong immunity such as measles, since the birth of new susceptible individuals and death of immune individuals allows recurring epidemics. Some infections induce only short term or ineffective immunity and infection prevalence can reach a steady state known as an endemic equilibrium, which is modelled using SIRS (Susceptible-Infectious-Recovered-Susceptible) or SIS (Susceptible-Infectious-Susceptible) model structures. A latent period during which an individual is infected but not yet infectious can alter the time course of transmission and is often captured by including an extra state, for example a SEIR structured model (Susceptible-Exposed-Infectious-Recovered).

LECTURE 3 R_0 from "first principles"

Dr Romain Silhol

Learning Objectives:

After this session students should be able to:

- Describe and explain the components that go into the basic reproduction number, R_0
- Explain how the components can be estimated for influenza and HIV
- Explain how variable infectiousness and duration of infection affect transmission of HIV
- List the limitations in trying to estimate R_0 from separate studies of its components
- Derive the mathematical formula for R_0 for a simple compartmental mathematical model with homogenous mixing

Core Readings

Fraser C; Hollingsworth TD; Chapman R; de Wolf F; Hanage WP. (2007). *Variation in HIV-1 set-point viral load: epidemiological analysis and an evolutionary hypothesis.* PNAS. 104:17441-17446.

Edmunds, Kafatos, Wallinga and Mossong (2006) *Mixing patterns and the spread of close-contact infectious diseases*. Emerging Themes in Epidemiology 3:10.

Suggested further readings

Carrat, Vergu, Ferguson, Lemaitre, Cauchemez, Leach and Valleron (2008) *Time lines of infection and disease in human influenza: A review of volunteer challenge studies*. American Journal of Epidemiology 167(7): 775-785.

Mellors, Rinaldo, Gupta, White, Todd and Kingsley (1996) *Prognosis in HIV-1 Infection Predicted by the Quantity of Virus in Plasma*. Science 272:1167.

Gregson, S. et al. *Sexual mixing patterns and sex-differentials in teenage exposure to HIV infection in rural Zimbabwe*. Lancet 359, 1896-903 (2002).

Wallinga, J., Edmunds, W. J. & Kretzschmar, M. *Perspective: human contact patterns and the spread of airborne infectious diseases.* Trends Microbiol **7**, 372-7 (1999).

For further discussion of variability in R_0:

Lloyd-Smith, J. O., Schreiber S. J., Kopp P. E. and Getz W. M. (2005) *Superspreading and the effect of individual variation on disease emergence*. *Nature,* 438, 355-9.

Grassly and Fraser (2008) *Mathematical models of infectious disease transmission* Nature Reviews Microbiology 6:477-497

Synopsis

R_0 is made up of a combination of factors, infectiousness, contact patterns and duration of infection. In theory therefore, we should be able to calculate it from studies which measure different parts of this quantity. This may be called calculating R_0 "from first principles" since it is built up from the simpler steps. The main reason this method of estimation is rarely used is because is it difficult, and in many cases impossible, to gather the right data. Other problems include interpreting available data, variability between patients and infectiousness changing over time. In addition, R_0, the mean number of new infections cannot be calculated as the mean value of β multiplied by the mean value of D, since this would require that they were independent. Infectiousness and duration of infection are often linked, for example a patient who has severe disease may be more infectious but may die more quickly, or conversely, may remain ill for longer. Therefore the distributions of these parameters, their values for different patients, are usually required for calculating R_0 from first principles.

In this lecture we show that calculating R0 from first principles requires good, detailed data, under controlled conditions. For overall estimates, it is usually preferable to estimate R0 indirectly. However, 'first principles' estimation is useful to understand contributions of different factors to R0. In particular we show how estimating it for HIV gives insights on how HIV is transmitted, and how interventions which change HIV viral loads may impact the epidemic.

PRACTICAL 3 R_0 for compartmental models with homogeneous mixing

Dr Romain Silhol

Learning Objectives

After this session students should be able to:

- Calculate R_0 for any model with homogeneous mixing and a single risk group, but with multiple infectious stages
- Explain how variable infectivity affects R_0

Core Readings

This simple recipe is not spelled out clearly in the literature. It is mentioned on Section 2.6, page 44-45 of Keeling and Rohani *Modelling infectious diseases*,

Suggested Further Readings

- Diekmann and Heesterbeek. Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation. Wiley, 2000 (Chapter 5 gives a more mathematical explanation of how to derive R_0 for multiple risk groups as well as multiple infectious states. Only advised for the more mathematically advanced student at this stage in the course).

Synopsis

This practical outlines a recipe for calculating R_0 for a model structure with multiple boxes. The method will be illustrated for a range of model structures including SIR and SEIR.

PRACTICAL 4 Estimating R_0 : part 1 of influenza practical

Dr. Ada Yan

Learning objectives

After this session students should be able to:

- Explain the relationship between the reproduction number, the generation time and the exponential growth rate in an epidemic;
- Estimate the exponential growth rate, the doubling time and the reproduction number in an epidemic; and understand sensitivities associated with these estimates;

Core reading

- Wallinga J, Lipsitch M (2007). *How generation intervals shape the relationship between growth rates and reproductive numbers*. Proc Biol Sci 274: 599-604.
- Mills CE, Robins JM, Lipsitch M (2004).*Transmissibility of 1918 pandemic influenza.* Nature 432: 904-906.

Synopsis

Pandemics of influenza arise when a new strain capable of human-to-human transmission emerges that is sufficiently distinct from circulating strains that population immunity is low or nil. The potential for pandemic influenza to cause significant mortality was illustrated by the 1918-20 H1N1 'Spanish flu' which is estimated to have killed at least 20,000,000 worldwide. Note however that the much lower mortality caused by the 1957 H2N2 'Asian flu', the 1966 H3N1 'Hong Kong flu' or the 2009 H1N1 pandemics shows that devastation is not an inevitable result of a pandemic, but depends on the biology of each new strain. Preparedness is greatly helped by knowledge of the epidemiological determinants of influenza spread such as the basic reproduction number R_0, the duration of latency, and the duration of infectiousness. The aim of this practical is to estimate some of these quantities.

From a methodological perspective, the practical will introduce students to the methods and issues surrounding parameter estimation in epidemic models. Students will use different methods to estimate the reproduction number from epidemic data; and assess the sensitivities/limitations associated with each method. We will make use of data on excess pneumonia and influenza mortality during the great 1918 H1N1 "Spanish flu" pandemic in New York City (Mills et al, Nature, 2004).

SECTION 2: More complex models

LECTURE 4 Individual heterogeneity, non-random mixing and networks

Prof Nicholas Grassly

Learning Objectives:

After this session students should be able to:

- Define the generation time and offspring distributions for infectious disease transmission
- Explain why the SIR model implies a geometric offspring distribution and relate this to known offspring distributions
- Describe how to estimate the generation time and offspring distribution
- Explain the impact of non-random versus random patterns of contact on epidemic dynamics
- Describe the different approaches available for modelling individual heterogeneity and non-random mixing

Core Readings

Grassly NC, Fraser C. Mathematical models of infectious disease transmission. Nat Rev Microbiol. 2008;6:477-487

Suggested further readings

O. Diekmann, J. A. P. Heesterbeek, Mathematical epidemiology of infectious diseases: Model building, analysis and interpretation. (Wiley, Chichester, 2000). [chapter 4]

R. M. Anderson, R. M. May, Infectious diseases of humans: dynamics and control. (Oxford University Press, Oxford, 1991). [esp. chapters 8 – 12]

Riley S. Large-Scale Spatial-Transmission Models of Infectious Disease. Science 2007;316:1298-1301

Synopsis

The patterns of contact that lead to infectious disease transmission are extremely complex, with transmission depending on behavioural, geographic, biological and environmental processes. Yet often infectious disease dynamics can be described by quite simple mathematical models. In some cases, however, these simple models fail to capture the emergent dynamics of infections, and this can lead to inaccurate inferences about disease processes and control. This lecture addresses the problem of how to represent contact patterns; when such representation is necessary; and how the dynamics of infectious diseases change as a result.

LECTURE 5 and PRACTICAL 5 Compartmental models with heterogeneous mixing

Dr. David Haw

Learning objectives:

After this lecture the students should:

- be aware of different forms of heterogeneity in risk of transmission of infectious diseases
- understand how heterogeneity in sexual risk behaviour influences transmission of Sexually Transmitted Infections (STI's)
- understand the implications of heterogeneity on the impact of interventions for STIs
- be able to define a mixing matrix mathematically
- understand how different patterns of sexual mixing can be incorporated in a model

Core readings

For a comprehensive introductory text, see Chapter 3: Host heterogeneities. In "Modeling Infectious Diseases in Humans and Animals". M.J. Keeling and P. Rohani. Princeton University Press (2008). This chapter includes detailed technical discussions of incorporating risk structure in models of sexually transmitted diseases, modelling age structure for childhood infections and dependence on time since infection, as well as presenting the corresponding equations and technical details of the models.

For a detailed mathematical discussion of the literature regarding incorporating heterogeneity in models (up to the mid-1990s), see: Modeling Heterogeneous Mixing in Infectious Disease Dynamics. H.W. Hethcote. In "Models for Infectious Human Diseases. Their Structure and Relation to Data." V. Isham and G. Medley (eds.). Cambridge University Press (1996).

A seminal paper presenting empirical data for several infectious agents illustrating heterogeneities in transmission and a good theoretical discussion of the implications for interventions is: Heterogeneities in the transmission of infectious agents: Implications for the design of control programs. M.E.J. Woolhouse et. al. PNAS (1997) 94, 338-342.

A classic paper presenting an age and sexual risk structured model: Factors controlling the spread of HIV in heterosexual communities in developing countries: patterns of mixing between different age and sexual activity classes. G.P. Garnett and R.M. Anderson. Phil. Trans. R. Soc. Lond. B (1993) 342, 137-159. The model is considerably more advanced than the material covered in the lecture, but the principles are the same.

Suggested further reading

A model of gonorrhoea with eight risk groups: Gonorrhea Transmission Dynamics and Contol. H.W. Hethcote and J.A. Yorke (1984) Lecture Notes in Biomathematics 56. Springer-Verlag.

An early modelling paper which includes considerations for vaccination strategies: Epidemiological models for heterogeneous populations: Proportionate mixing, parameter estimation and immunization programs. H.W. Hethcote and J.W. Van Ark (1987) Math. Biosci. 84; 85-118.

Online resources

For those familiar with the programming languages C++, Fortran or Matlab - the code for each of the models in “Modeling Infectious Diseases in Humans and Animals” can be found here: http://www.modelinginfectiousdiseases.org/

Synopsis

Individuals in a population do not have equal risk of acquiring infection. The transmission of infections agents in a host population is influenced by many forms of heterogeneity.

Two forms of heterogeneity are covered in the first part of this lecture:

- age and its importance for modelling childhood infections
- sexual behaviour and its importance for sexually transmitted infections

Given that certain characteristics affect transmission of certain infections it is important to include such variation in mathematical models in order to more accurately represent transmission. Introducing heterogeneity in risk in a model changes the dynamics of how the model behaves. The influence of heterogeneity and different patterns of mixing (i.e. contacts) between individuals on the spread of infection are discussed.

The second part of the lecture focuses on how a mixing matrix can be defined and expressed mathematically.

The concepts introduced in this lecture will be consolidated in the practical that follows.

SECTION 3: Fitting models to data

LECTURE 6 Estimating parameters from data

Prof Christl Donnelly

Learning Objectives:
After this session students should be able to:

- Define likelihood
- Explain the logic of a likelihood equation
- Construct a simple likelihood equation

Core Reading:

Williams B. G. & Dye C. Maximum likelihood for parasitologists. *Parasitology Today* (1994) 10:489-493.

Suggested Further Reading:

Mutapi F. & Roddam A. P values for pathogens: statistical inference from infectious-disease data. *Lancet Infectious Diseases* (2002) 2:219-230.

Synopsis:

We observe data, although sometimes incompletely and sometimes with errors. The parameters of interest, however, are not directly observed.

In order to estimate them, we must describe (precisely and mathematically) the process we believe generated the data. If the equations describing the process contain the parameter(s) of interest, then we can usually use the data to obtain an estimate of the parameter(s). This is the case whether we started by writing down the model which describes the process and then collected the data or we collected the data (or obtained them from others) and subsequently wrote down the model.

One approach to parameter estimation is based on maximum likelihood. The likelihood is an equation which describes the probability of the observed data as a function of model parameters. This can be of simple (for example y=a+bx) or highly complex in form depending on the particular situation. The likelihood profile or surface can be used to obtain both parameter estimates and confidence bounds, the latter providing information on the level of uncertainty associated with the parameter estimate.

LECTURE 7 Comparing models to data: the iterative process of model acceptance, rejection & refinement

Prof Christl Donnelly

Learning Objectives:
After this session students should be able to:

- Perform and interpret a likelihood ratio test to compare two models
- Perform and interpret a goodness of fit test

Core Reading:

Wilson K. & Grenfell B. T. Generalized linear modelling for parasitologists. *Parasitology Today* (1994) 10:489-493.

Suggested Further Reading:

Mutapi F. & Roddam A. P values for pathogens: statistical inference from infectious-disease data. *Lancet Infectious Diseases* (2002) 2:219-230.

Synopsis:

H. L. Mencken wrote “For every problem, there is a solution that is simple, neat, and wrong.” Similarly, for nearly every dataset, there is a model that is simple, neat and wrong.

In many cases researchers stop their statistical analysis once they have obtained their parameter estimates (and associated confidence bounds). However, an important next step is for the researcher to assess whether the model described (and used to estimate parameters) could have generated the observed data. Inadequate model fit can suggest the need for model refinement, which in turn might require further data to be collected. Thus, the process is iterative.

Even if a model is shown to provide an adequate fit to the data, the model cannot be assumed to be ‘true’. We can only conclude that this model could have generated the observed data. (Further data collection might well highlight differences between model expectations and the observed data.)

PRACTICAL 6 Model fitting: part 2 of influenza practical

Dr Ada Yan

Learning objectives

After this session students should be able to:

- Fit a model of infectious disease transmission to time-series data using least-squares estimation in Berkeley Madonna
- Estimate model parameters and the effectiveness of interventions from time-series data in Berkeley Madonna
- Perform sensitivity analyses of parameter estimates to key assumptions
- Describe alternative methods of estimation and their strengths and weaknesses

Core reading

Cauchemez S, Bhattarai A, Marchbanks TL, Fagan RP, Ostroff S, et al. (2011) Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza. *Proc Natl Acad Sci USA* 108: 2825-2830.

Suggested further reading

King AA at al. Inapparent infections and cholera dynamics. *Nature* 454: 877

Ionides EL et al. Inference for nonlinear dynamical systems. *Proc Natl Acad Sci USA* 103: 18438-18443

Synopsis

In this practical session you will fit a simple deterministic mathematical model of influenza transmission to data from an outbreak in a school in Pennsylvania during the 2009 pandemic. You will be provided with the data and model code. You will be given the opportunity to experiment with different approaches to model fitting and asked to draw conclusions about the impact of school closure on the size of the epidemic. Subsequently we will consider approaches to fitting stochastic models of disease transmission to data.

SECTION 4: Dealing with uncertainty

LECTURE 8 and 9 Stochasticity, sensitivity and uncertainty analysis

Dr Juan Vesga

Learning objectives

After this session students should be able to:,

- Describe the intrinsic uncertainty in parameter values and how these uncertainties are reflected in the behaviour of models and the results they generate;
- Describe how to calculate means and variances for model outcomes using prior distributions for parameter values;
- Define the basis of the Latin Hypercube method;

Core reading

S.M. Blower and H. Dowlatabadi, Sensitivity and uncertainty analysis of complex models of disease transmission: and HIV model, as an example, International Statistical Review (1994), 62, 2, pp 229-243.

Melissa A. Sanchez and Sally M. Blower, Uncertainty and Sensitivity Analysis of the Basic Reproductive Rate: Tuberculosis as an Example, Am J Epidemiol, (1997), 145, pp 1127-1137.

Suggested further reading

Jeremy E. Oakley and Anthony O'Hagan, Probabilistic sensitivity analysis of complex models: a Bayesian approach, J. R. Stat. Soc. B (2004), 66, pp 751-769.

S. Riley et al., Transmission dynamics of the etiological agent of SARS in Hong Kong: Impact of public health interventions, Science (2003), 300, p1961.

Delta method and its applications, *www.math.umt.edu/patterson/549/Delta.pdf.*

Synopsis

The models examined in the course so far have been *deterministic* – i.e. they have not accounted for the inherent randomness of epidemiological processes. Stochastic models simulate this random behaviour in order to further understand the range of outcomes that may arise and their dependence on the parameters of the infection. However, stochastic models are much harder to analyse algebraically and require much more computing power.

Stochasticity is particularly important when there are small numbers of infected or susceptible individuals. When the number of infected individuals becomes very small, there is a finite

probability that the infection will become extinct. In deterministic models this is reflected by a very small number of infected individuals. Stochastic models allow us to quantify the probability of extinction. We discuss the critical community size for seasonal diseases and persistence criteria for the SIR and SIS models.

Moreover, all but the simplest models require a number of parameters in order to calibrate the epidemiological mechanisms they contain. For example, SIR models require rates of recovery from infection and infectious contact rates. However, parameter values are always subject to a degree of uncertainty.

Many parameters can have a range of credible values. This uncertainty in input parameters will be reflected in uncertainty in the model outcomes we are interested in. For stochastic models, this effect is compounded with the naturally randomness in the model itself.

The second lecture shows how to deal with uncertainty in model parameters through the use of sensitivity and uncertainty analysis. We examine the strengths and weaknesses of several ways of exploring parameter value ranges, including latin hypercube and Monte Carlo Markov chain simulation, and show how these techniques can be used to calculate means, variances and confidence intervals for model outcomes. We discuss how information on model sensitivity can be fed back into better model and experimental design.

The ideas discussed in the lecture will be consolidated in the practical which follows.

PRACTICAL 7 Stochasticity

Dr Joanna Lewis

Learning objectives

After this session, students should be able to:

- Describe the concept of stochasticity within the context of epidemiological models and how it arises;
- Define the relationship between stochastic and deterministic models;
- Describe what new types of phenomena arise in stochastic models as opposed to their deterministic counterparts and under what circumstances these phenomena are important;
- Implement a stochastic model on a computer.

Core reading

Keeling and Rohani *Modelling Infectious Diseases* Chapter 6 and Vynnycky and White *An introduction to Infectious Disease Modelling* Chapter 6 cover stochastic models of different types and give more detail on some alternative ways to formulate them.

Suggested further reading

Books:

Daley & Gani is a good introduction to stochastic models applied to epidemics.

Renshaw is a fairly high-level book that describes stochastic mathematical models.

Bailey, N.T.J., *The mathematical theory of infectious diseases and its applications*, 2nd edition, Griffin, 1975

Daley GJ & Gani J. Epidemic modelling: an introduction. Cambridge University Press, 1999. ISBN 9-780521-014670.

Renshaw, E., *Modelling biological populations in space and time*, Cambridge Univ. press, 1991

Papers:

Bartlett, M. S. (1957). "Measles periodicity and community size." J. Roy. Stat. Soc. A **120**: 48-70.

Bolker, B. M. and B. T. Grenfell (1995). "Space, persistence and dynamics of measles epidemics." Proc. Roy. Soc. Lond. B **348**: 308-320.

Jansen, V. A. A., N. Stollenwerk, et al. (2003). “Measles outbreaks in a population with declining vaccine uptake." Science 301(5634): 804-804.

Synopsis

Infectious disease transmission is a discrete event: when a susceptible individual encounters an infectious individual, a transmission event either occurs or it does not. Other changes of ‘state’ may also be discrete events – e.g. commencing treatment, being isolated, dying. These discrete events occur randomly, but with particular probabilities – e.g. the more infectious an individual is, the greater the probability that a transmission event will occur when that individual encounters a susceptible individual.

This practical gives the students a chance to see these models in action and to test some of the concepts covered in the lecture, such as extinction and critical community size.

LECTURE 10 Modelling Vaccination

(Lecturer TBC)

Learning Objectives

After this session students should be able to:

- Describe how mathematical models of infectious diseases can be useful to understand the effect of vaccination and list examples of questions that can be addressed using these models;
- Define vaccine efficacy, immunogenicity and seroprevalence;
- Construct an SIR model which includes vaccination, write the differential equations for this model and define the critical vaccination threshold;
- Describe how the mean age of infection can be used to estimate R_0 and hence the critical vaccination threshold, and list caveats for which this relationship does not hold true;
- Calculate the mean age of infection after vaccination and explain with examples why this shift can be an adverse effect of vaccination for certain diseases;
- Describe how the introduction of vaccination will perturb the endemic equilibrium and may result in oscillations in the number of infected individuals before a new equilibrium is reached;
- Describe extensions to the SIR model with vaccination that capture different assumptions in immunity or transmission heterogeneities.

Core reading

Anderson, R. M. & May, R. M. 1991. *Infectious diseases of humans: dynamics and control* (Oxford University Press, Oxford). Chapters 5, 7, 12 (pages 307 – 315)

Gomes, M. G. M., L. J. White, et al. (2004). "Infection, reinfection, and vaccination under suboptimal immune protection: epidemiological perspectives." J Theor Biol 228(4): 539-549.

Suggested further readings

Anderson, R. M. & May, R. M. 1991. *Infectious diseases of humans: dynamics and control* (Oxford University Press, Oxford). Appendix C

Longini IM Jr, Nizam A, Ali M, Yunus M, Shenvi N, et al. (2007) Controlling Endemic Cholera with Oral Vaccines. PLoS Med 4(11): e336. doi:10.1371/journal.pmed.0040336

Van de Velde N, Brisson M & Boily, M-C (2010) Understanding differences in predictions of HPV vaccine effectiveness: A comparative model-based analysis. Vaccine 26;28(33):5473-84

Brisson M & Edmunds WJ (2003) Varicella vaccination in England and Wales: cost-utility analysis. Arch Dis Child. 88(10):862-9

Pitzer VE, Atkins KE, de Blasio BF, Van Effelterre T, Atchison CJ, et al. (2012) Direct and Indirect Effects of Rotavirus Vaccination: Comparing Predictions from Transmission Dynamic Models. PLoS ONE 7(8): e42320. doi:10.1371/journal.pone.0042320

Synopsis

Incorporating vaccination into mathematical models of infectious diseases is a powerful tool to understand the impact of a given vaccination strategy. Insights can be made on the appropriate coverage, which populations should be targeted and whether transmission can be feasibly eliminated.

Definitions of vaccine efficacy, immunogenicity, and seroprevalence will be revised in this lecture, along with how to incorporate vaccination into a simple SIR model.

Where there are data on the mean age of infection for a given infectious disease and the average life expectancy of a population, it is possible to calculate R_0 using these two quantities and hence calculate the critical vaccination threshold. Vaccination can result in a shift in the mean age of infection. This shift can be a detrimental effect of vaccination for infections where the disease severity increases with age.

Introduction of vaccination perturbs the endemic equilibrium and can result in oscillations in the number of infected individuals before the new-post vaccination endemic equilibrium is reached. It is possible to estimate the period of these oscillations using the mean age of infection and the duration of infection.

Using an SIR model to model the impact of vaccination is a simplistic representation of the transmission and vaccination processes. Extensions can be incorporated into the model such as allowing for waning immunity, partially protective immunity or including spatial heterogeneity of transmission, all of which have important implications for vaccination.

LECTURE 11 Modelling complex interventions

Dr Peter Winskill

Learning objectives

After this session students should be able to:

- Describe how a range of interventions can be incorporated into models of directly transmitted pathogens;
- Describe the effect of interventions on the basic reproduction number and define the effect size;
- Implement combinations of vaccination, quarantine and contact tracing in SIR models;
- Understand how models can be extended to capture space;

Core reading

Chowell et al. 2004 The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. J Theor Biol 229:119-126.

This paper develops a simple compartmental model for Ebola and incorporates multiple interventions in a manner similar to the material covered in the lecture for smallpox. It therefore complements the lecture material well as well as being highly topical!

Suggested further reading

Ferguson NM et al. 2003. Planning for smallpox outbreaks. Nature 425: 681-685.

This paper reviews the ways in which models for smallpox have been used in planning.

Gething PW et al. 2010. Climate change and the global malaria recession. Nature 465: 342-345.

This paper introduces the concept of the effect size for interventions in relation to malaria.

Synopsis

In this lecture we will begin by considering how interventions combine to impact on the basic reproduction number and introduce the concept of an effect size. We will then use smallpox as a case example to build a model with multiple interventions. Finally we will consider how models can be simply extended to include spatial variation, introducing the concept of a meta-population model and spatial kernel.

PRACTICAL 8 Design a model to answer a public health question

Dr. Patrick Walker and Dr Hannah Slater

Learning objectives

After this session students should be able to:

- Describe the ways in which models can be used to assess and guide the impact of public health policies;
- Independently construct a mathematical model of the dynamics of infectious disease, tailored to a specific context;
- Consider the different ways in which an intervention can be incorporated into a model and the effect this has upon its projected impact;
- Monitor and understand the assumptions made whilst developing a mathematical model and to assess the impact this is likely to have upon obtained results;
- Critically appraise mathematical models developed by others.

Core readings

Keeling MJ & P Rohani, 2008, Modelling Infectious Disease in Humans and Animals. Princetion University Press; ISBN: 9780691116174(For useful examples of public health interventions and the implications of the different ways they are often incorporated into a model, chapter 8)

Suggest further readings

The following papers provide good examples of models of the public health effects of interventions, including analyses of the effect of different assumptions:

Jamie T Griffin et al., "Reducing Plasmodium Falciparum Malaria Transmission in Africa: a Model-based Evaluation of Intervention Strategies.," PLoS Medicine (2010) 7, http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2919425&tool=pmcentrez&rendertype=abstract**.**

Geoffrey P Garnett et al., "Chapter 21: Modelling the Impact of HPV Vaccines on Cervical Cancer and Screening Programmes.," *Vaccine* 24 Suppl 3, no. null (August 31, 2006): S3/178–86, http://dx.doi.org/10.1016/j.vaccine.2006.05.116.

Jeffrey W. Eaton et al., "HIV Treatment as Prevention: Systematic Comparison of Mathematical Models of the Potential Impact of Antiretroviral Therapy on HIV Incidence in South Africa," ed. John Bartlett, *PLoS Medicine* 9, no. 7 (July 10, 2012): e1001245, http://dx.plos.org/10.1371/journal.pmed.1001245.

(A review of the structure and results of different models all designed to answer the same public health control policy question)

Edwin Michael et al., “Mathematical Modelling and the Control of Lymphatic Filariasis.,” *The Lancet Infectious Diseases* 4, no. 4 (April 2004): 223–34, http://dx.doi.org/10.1016/S1473-3099(04)00973-9.

Synopsis

Mathematical models provide us with a rigorous, quantitative framework that can be used to understand how the biological processes of disease transmission and progression lead to dynamics at the population level. Such models can also serve as valuable tools for providing insight into how the effects of an intervention upon the course of infection in individuals translate into population-level effectiveness and public health benefits.

However, in order to provide useful and reliable conclusions, the structure of the model must be suitable for the disease context to which it is to be applied. This context comprises factors such as the pathogen involved, the structure of a population, any existing interventions and the availability of data. This context is also likely to determine what aspects of the relationship between individual effect and population effectiveness a model can inform. For example, if we know the efficacy of a vaccine we may wish to predict the effect this has upon disease prevalence within a population. Alternatively, if we know the prevalence of disease in a population-based trial of a vaccine, we may wish to use this to obtain an estimate of individual-level efficacy.

Moreover, conclusions based upon a model can only be reliable if the degree of uncertainty inherent within the model estimate is known. Some of the main contributors to model uncertainty are the assumptions which are necessarily made in order to model a disease. These include assumptions about the structure of the model, which can never be fully accurate descriptions of the true complexities of disease transmission. Chosen parameter values are also likely to be subject to a degree of uncertainty due to the possibility of misspecification and measurement error. As a result, understanding the assumptions made when modelling an infectious disease and, where possible, conducting sensitivity analyses upon the effect these have upon estimates are crucial aspects of using models to address real-life control policy issues.

In this practical, participants will be taken through the process of developing a model to answer a public health policy question. This will involve identifying a suitable research question for a chosen disease that can be investigated using a mathematical model. Using the knowledge and techniques acquired throughout the module, participants will then develop a model to best reflect their chosen disease context and use this as the basis to investigate their intervention in order to address this question. Throughout the practical participants will be encouraged to consider the assumptions they are making while developing their model and to identify and examine factors which have the potential to affect their results. At the end of the practical participants will present their model and conclusions to the group.

LECTURE 12 Critical analysis of an article

Dr Nim Arinaminpathy

Learning objectives

After this session students should be able to:

- Critique a modelling study, in the style of a peer-review
- Describe strengths and limitations of a given modelling approach to a given research question

Core readings

Granich et al (2009), 'Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model.' Lancet. 2009 Jan 3;373(9657):48-57

Please study both the paper and the supplementary material, both available on Blackboard.

Suggested further readings

Some of the debate was captured in a series of letters published by the Lancet that you can access via this weblink: http://goo.gl/GlXVvp

You can access slides presented by Reuben Granich here: http://goo.gl/p9U8kD

Synopsis

In preparing for this discussion, you may wish to ask yourself the following questions.

1. Have you read this paper before? Is there any evidence that it has been influential, and in what way?
2. Do you understand the model(s)?
3. Would you be able to reproduce the findings of the paper?
4. Try to classify the model according to the criteria presented in the 'Different types of models' lecture.
5. What is the main proposition made in the paper?
6. Is there enough evidence presented here to support the proposition? If not, what additional evidence would you need to believe the proposition?
7. With the benefit of hindsight, what do you think could have been done **differently** in the model or analysis (i.e. without adding detail or complexity)?
8. What do you think could have been **presented** differently?
9. How would you **extend** the model, or analysis (i.e. what details or complexity would you add?
10. Why do you think this paper provoked the debate it did, and what has been the influence of the paper?

LECTURE 13 & PRACTICAL 9 Introduction to modelling vector-borne diseases

Prof. María-Gloria Basáñez and Dr. Martin Walker

Learning Objectives

After this session, students should be able to:

- Translate the basic biology of infections transmitted by dipteran insects (with particular reference to malaria) into differential equations for the prevalence of infection in humans and vectors;
- Identify the malaria models of Ronald Ross, George Macdonald, and subsequent modifications by C. Garrett-Jones and others;
- Discuss the importance and mathematical formulations of vector survival and incorporation of delays in equations for vector-borne disease models;
- Examine the notion and components of *vector competence* and its relationship with *vectorial capacity* and the basic reproduction ratio (R_0) of vector-borne infections in the context of control interventions;
- Introduce the use of phase-plane diagrams as a tool for the analysis of model solutions;
- Discuss new developments of malaria modelling such as the role of parasite density in vectors and humans; the role of immunity and disease; the population dynamics of vectors; the age-dependency in vector mortality rate; the role of (spatial) heterogeneity (among others);
- Discuss the role of VBD modelling in general and malaria in particular in the current agenda(s) for control and elimination.

Core Readings

A key reference is Chapter 14 (Indirectly transmitted microparasites) of Anderson RM & May RM. 1992. Infectious Diseases of Humans: Dynamics and Control. Oxford University Press; ISBN: 019854040X. (hardback 1991, ISBN: 0198545991).

An excellent text on mathematical models of malaria is:

Bailey, N.T.J. (1982). The Biomathematics of Malaria. London: Charles Griffin & Co.

Suggested Further Readings

The following references discuss Vectorial Capacity:

Garrett Jones, C. (1964a). The human blood index of malaria vectors in relation to epidemiological assessment. *Bull World Health Organ* 30, 241-261.

Garrett Jones, C. (1964b). Prognosis for the interruption of malaria transmission through assessment of the mosquito's vectorial capacity. *Nature* 204, 1173-1175.

Garrett Jones, C. and Shidrawi, G. (1969). Malaria vectorial capacity of a population of *Anopheles gambiae*. An exercise in epidemiological entomology. *Bull World Health Organ* 40, 531-545.

The following are good introductions to models for VBDs:

Rogers, D.J. (1988). The dynamics of vector-transmitted diseases in human communities. *Phil Trans R Soc Lond B* 321, 513–539.

Dye, C. (1990). Epidemiological significance of vector-parasite interactions. *Parasitology* 101, 409–415.

Dye, C. (1992). The analysis of parasite transmission by bloodsucking insects. *Ann. Rev. Entomol.* 37, 1–19.

Dye, C. (1994). The epidemiological context of vector control. *Trans R Soc Trop Med Hyg* 88, 147–149.

Smith DL, McKenzie FE (2004). Statics and dynamics of malaria infection in *Anopheles* mosquitoes. *Malar J* 3, 13.

The following references present more complex models linked to epidemiological data and interventions:

Smith DL, Dushoff J, McKenzie FE (2004). The risk of a mosquito-borne infection in a heterogeneous environment. *PLoS Biol* 2, e368.

Smith DL, Dushoff J, Snow RW, Hay SI (2005). The entomological inoculation rate and *Plasmodium falciparum* infection in African children. *Nature* 438, 492–495.

Smith DL, McKenzie FE, Snow RW, Hay SI (2007). Revisiting the basic reproductive number for malaria and its implications for malaria control. *PLoS Biol* 5, e42.

Griffin JT, Hollingsworth TD, Okell LC, Churcher TS, White M, Hinsley W, Bousema T, Drakeley CJ, Ferguson NM, Basáñez MG, Ghani AC (2010). Reducing *Plasmodium falciparum* malaria transmission in Africa: a model-based evaluation of intervention strategies. *PLoS Med* 7, e1000324.

White MT, Griffin JT, Churcher TS, Ferguson NM, Basáñez MG, Ghani AC (2011). Modelling the impact of vector control interventions on *Anopheles gambiae* population dynamics. *Parasit Vectors* 4, 153.

Websites

http://www1.imperial.ac.uk/medicine/about/institutes/outbreaks/research/projects/malaria

Synopsis

Models for vector-borne diseases are based on the pioneer frameworks developed for the study of malaria transmission by Ronald Ross (1911) and George Macdonald (1950s), the so-called Ross-Macdonald model of malaria. In this lecture we discuss how to incorporate the building blocks described in the lecture on VBD epidemiology into simple mathematical equations describing the rate of change with respect to time of the prevalence of infection in humans and vectors. We also discuss the simplifying assumptions that are made in the formulation of these expressions, and describe the components of the force of infection operating on susceptible humans and mosquitoes in terms of the biting rate per mosquito on humans, the vector to host ratio, and the proportion of infected/infective mosquitoes and humans. We relate these concepts to field measures of transmission intensity such as the 'entomological inoculation rate (EIR)', and introduce additional complexities such as the incorporation of the extrinsic incubation period, and the analysis of null isoclines as a tool to obtain model solutions at equilibrium. Finally, we discuss the ways in which these foundation models could be modified for added realism and biological complexity in key aspects of the population biology of vector-borne diseases that are crucial for the application of models to guide ongoing interventions.

The aims of this session are to introduce the Ross-Macdonald model of malaria as the fundamental model for vector-borne infections, emphasizing its scope and limitations as the basis for subsequent modifications; to understand how the vector to host ratio, the biting rate, the proportion of bloodmeals taken on humans, the extrinsic incubation period, the human recovery rate, and the competence and mortality rate of vectors are incorporated into expressions describing the rates of change of infection prevalence in vertebrate hosts and vectors; to discuss novel developments inVBD modelling and their contemporary applications.

The concepts introduced in this lecture will be consolidated in the practical(s) that follow.

SECTION 5: Formative assessment and wrap-up

FORMATIVE ASSESSMENT Multiple choice test on model building and analysis

Dr Nim Arinaminpathy

Learning Objectives

After this session students should be able to:

- Assess their technical skills in model building and analysis.

Synopsis

This formative assessment will take the form of a multiple choice test. The test will be marked during the break and the test will be followed by a lecture and discussion of the answers to the test, and a review of the key learning points.

The skills being assessed will include:

- Selecting the correct model flow diagram from a description of the epidemiology of an infection
- Interpreting the parameters from the epidemiology of the infection (e.g. translating a mean duration into a rate)
- Calculating some emergent properties, such as the proportion of cases which get treated before recovering.
- Calculating R_0 for a homogeneously mixing model

LECTURE 14 The application of infectious disease models, past present and future: influenza as a case study

Dr. Steven Riley

Learning objectives

After this session students should be able to:

- Identify the type of model used to answer an important question
- Assess the degree to which results from the model have been related to available data
- Rate the data itself in terms of potential biases and generalizability
- Suggest trends that are likely to occur in disease dynamic studies that draw on evidence from models

Core readings

I will use the following papers as case studies for this talk to illustrate how trends have changed:

Riley S, Wu JT, Leung GM. Optimizing the dose of pre-pandemic influenza vaccines to reduce the infection attack rate. PLoS Med. 2007 Jun;4(6):e218. PMID: 17579511

Mills CE, Robins JM, Lipsitch M. Transmissibility of 1918 pandemic influenza. Nature. 2004 Dec 16;432(7019):904-6. PMID: 15602562

Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley S, Meeyai A, Iamsirithaworn S, Burke DS. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature. 2005 Sep 8;437(7056):209-14. Epub 2005 Aug 3. PMID: 16079797

Wallinga J, Teunis P, Kretzschmar M. Using data on social contacts to estimate age-specific transmission parameters for respiratory-spread infectious agents. Am J Epidemiol. 2006 Nov 15;164(10):936-44. Epub 2006 Sep 12. PMID: 16968863

Suggested further readings

Riley S, Kwok KO, Wu KM, Ning DY, Cowling BJ, Wu JT, Ho LM, Tsang T, Lo SV, Chu DK, Ma ES, Peiris JS. Epidemiological characteristics of 2009 (H1N1) pandemic influenza based on paired sera from a longitudinal community cohort study. PLoS Med. 2011 Jun;8(6):e1000442.

Lessler J, Riley S, Read JM, Wang S, Zhu H, Smith GJ, Guan Y, Jiang CQ, Cummings DA. Evidence for antigenic seniority in influenza A (H3N2) antibody responses in southern China. PLoS Pathog. 2012;8(7):e1002802

Synopsis

Infectious disease modelling designed to improve public health decisions has developed in recent years. Trends have emerged in the design of the models, the way those models use data and in the quality of the data that are available. More powerful models, parameterized using good available data are now able to give more robust evidence than was possible previously. I will examine these trends using influenza as a case study, and attempting to be systematic in appraising evidence in the example papers. I will then suggest that the future of modelling will be even closer integration with data. I will use examples from current studies of influenza that have been designed from the ground up as disease dynamic studies with both empirical and theoretical components. From there, I will comment on the aspects of model design that I think deserve the most effort in coming years: using genomic data effectively, coping with repeat measures from individuals, using all spatial data, and testing the sensitivity of results across different model structures. In the last section, I will also motivate my suggestions with examples from other disease topics.

STAFF PROFILES

Dr Nimalan Arinaminpathy (Department of Infectious Disease Epidemiology)

Dr Arinaminpathy trained in applied mathematics at the University of Cambridge (BSc), and at Oxford (D.Phil). He trained in mathematical epidemiology at Princeton University, USA, where he focused on the spread and control of human respiratory infections. Now senior lecturer at the department of infectious disease epidemiology, his research is primarily on the spread and control of human tuberculosis, with a focus on South- and South-East Asia. Carrying out mostly policy-focused work, he and his group collaborate regularly with national TB programmes, as well as the World Health Organisation and the US Centers for Disease Control.