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Statistical Epidemiology

Group leader: Prof Christl Donnelly

We use statistical principles and tools to tackle epidemiological challenges.

We develop and seek to answer interesting and important questions like how common diseases are, which groups are most likely to be affected and how transmission might be best controlled. In doing so, we collaborate with a wide range of colleagues including physicians, public health professionals, ecologists, veterinarians, field workers, laboratory scientists, mathematicians and economists.

We are members of the <u>MRC Centre for Outbreak Analysis and Modelling</u>. Current topics of interest for our research group include: Influenza; TB in Cattle and Badgers; Rabies and Distemper; Surveillance and Policy Evaluation.

Selected topics

- TB in Cattle and Badgers
- Real-time analysis of outbreaks (including H1N1 pandemic influenza, SARS and FMD)
- Surveillance and Policy Evaluation
- Influenza in Pigs
- Rabies and Distemper
- Tasmanian Devil Facial Tumour Disease

Group members

- Prof Christl Donnelly, head of group
- Dr Artemis Koukounari, MRC-funded research fellow (from September 2010)
- Dr Flavie Vial, Defra-funded research assistant, TB in Cattle and Badgers
- <u>Helen Jenkins</u>, MRC-funded postgraduate student, Polio (Defra-funded project consultant, TB in Cattle and Badgers)
- (To Be Confirmed), BBSRC-funded postgraduate student, Badgers (from October 2010)

Former associated staff and students with whom I still work:

• Dr Tom Johnston, Defra-funded project consultant, TB in Cattle and Badgers

Also involved in the supervision of

• Sitali Simwami, postgraduate student

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- Hannah Clapham, postgraduate student
- Sandy Wai-Yee Lam, postgraduate student

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TB in Cattle and Badgers



Independent Scientific Group on Cattle TB: (Front Row) Christl Donnelly, John Bourne, Sir David Cox; (Back Row) Andrea Le Fevre (ISG RA), John McInerney, Rosie Woodroffe, Ivan Morrison, Tom Johnston (ISG RA), Steve Coleman (Defra), George Gettinby

Prof Christl Donnelly was deputy chair of the <u>Independent Scientific Group on Cattle TB</u> (1998 to 2007), through which she was jointly responsible for the design and analysis of the randomized study of badger culling strategies, a field trial conducted over 3,000km² costing roughly £7million per annum. Statistical epidemiological research is key to the development of an increasingly robust scientific body of evidence to underpin policies to limit the transmission of *Mycobacterium bovis*, the infectious agent of bovine TB.

Helen E. Jenkins, Rosie Woodroffe and Christl A. Donnelly. <u>The Duration of the Effects of</u> <u>Repeated Widespread Badger Culling on Cattle Tuberculosis Following the Cessation of Culling</u>. *PLoS ONE* 5(2): e9090, 2010. DOI:10.1371/journal.pone.0009090

Helen E. Jenkins, Rosie Woodroffe and Christl A. Donnelly. <u>The effects of annual widespread</u> <u>badger culls on cattle tuberculosis following the cessation of culling</u>. *International Journal of Infectious Diseases* 12, 457-465, 2008. Published online 27 May 2008. DOI: 10.1016/j.ijid.2008.04.001

Christl A. Donnelly, Gao Wei, W. Tom Johnston, David R. Cox, Rosie Woodroffe, F. John Bourne, Chris L. Cheeseman, Richard S. Clifton-Hadley, George Gettinby, Peter Gilks, Helen E. Jenkins, Andrea M. Le Fevre, John P. McInerney and W. Ivan Morrison. <u>Impacts of widespread badger</u> <u>culling on cattle tuberculosis: concluding analyses from a large-scale field trial</u>. *International Journal of Infectious Diseases* 11, 300-308, 2007. Published online 22 June 2007. DOI: 10.1016/j.ijid.2007.04.001

Christl A. Donnelly, Rosie Woodroffe, David R. Cox, F. John Bourne, Chris L. Cheeseman, Richard S. Clifton-Hadley, Gao Wei, George Gettinby, Peter Gilks, Helen Jenkins, W. Tom Johnston, Andrea M. Le Fevre, John P. McInerney and W. Ivan Morrison. <u>Positive and negative</u> <u>effects of widespread badger culling on tuberculosis in cattle</u>. Nature 439, 843-846, 2006.

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Donnelly CA, Woodroffe R, Cox DR, Bourne J, Gettinby G, Le Fevre AM, McInerney JP, Morrison WI. Impact of localized badger culling on tuberculosis incidence in British cattle. *Nature*, 426, 834-837, 2003.

[other TB publications]

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Real-time analysis of outbreaks (including H1N1 pandemic influenza, SARS and FMD)

Research on outbreaks of novel and emerging infectious diseases (such as H1N1 pandemic influenza, Severe Acute Respiratory Syndrome, SARS, and Foot and Mouth Disease, FMD) is an important focus of statistical epidemiology research.

H1N1 Pandemic Influenza

In 2009 members of the MRC Centre for Outbreak Analysis and Modelling worked together to provide timely and robust epidemiological assessments of the H1N1 pandemic as it unfolded. The first stage of the work was within the context of the WHO Rapid Pandemic Assessment Collaboration and resulted in a paper published online in Science on the 14th of May 2009:

Fraser C[†], Donnelly CA[†], Cauchemez S, Hanage WP, Van Kerkhove MD, Hollingsworth TD, Griffin J, Baggaley RF, Jenkins HE, Lyons EJ, Jombart T, Hinsley WR, Grassly NC, Balloux F, Ghani AC, Ferguson NM, Rambaut A, Pybus OG, Lopez-Gatell H, Alpuche-Aranda CM, Chapela IB, Zavala EP, Guevara DME, Checchi F, Garcia E, Hugonnet S, Roth C: The WHO Rapid Pandemic Assessment Collaboration. <u>Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings</u>. *Science* 324, 1557-1561, 2009. (†These authors contributed equally to the work.) DOI:10.1126/science.1176062.

Members of the MRC Centre for Outbreak Analysis and Modelling provided scientific advice in both national and international settings. Here is a paper on the challenges which arise in the assessment of severity of a new influenza virus.

Garske T, Legrand J, Donnelly CA, Ward H, Cauchemez S, Fraser C, Ferguson NM and Ghani AC. <u>Assessing the severity of the novel influenza A/H1N1 pandemic</u>. *BMJ* 339, 220-224, 2009. Published 14 July 2009, doi:10.1136/bmj.b2840

Neil Ferguson, Simon Cauchemez, Christl Donnelly and Christophe Fraser all visited the US Centers for Disease Control and Prevention (CDC) during the pandemic. Here is a paper describing the results of one of the collaborative projects developed during these visits:

Cauchemez S, Donnelly CA, Reed C, Ghani AC, Fraser C, Kent CK, Finelli L and Ferguson NM. <u>Transmission of novel Influenza A(H1N1) virus in households in the USA</u>. *New England Journal of Medicine* 361, 2619-27, 2009.

SARS

In 2003 Christl Donnelly and colleagues (including Roy Anderson, Neil Ferguson, Christophe Fraser and Azra Ghani) closely collaborated with colleagues from Department of Community Medicine, University of Hong Kong to analyse the Hong Kong SARS epidemic as it unfolded.

Subsequently, Roy Anderson and Christl Donnelly were joint coordinators of the EU-funded SARSTrans project. The full project title was: SARSTRANS: Control policy optimisation for SARS and other emerging infections - characterising transmission dynamics and estimating key epidemiological parameters

The project is internationally collaborative with teams from:

- Imperial College London, UK
- Institut National de la Santé et de la Recherche Médicale, France
- Faculty of Veterinary Medicine, University of Utrecht, Netherlands
- Department of Community Medicine, University of Hong Kong, Hong Kong
- National Health Research Institutes, Taiwan, ROC
- Laboratory of Respiration Department, General Hospital of PLA 301 Hospital, Beijing, China
- IC Consultants Ltd, UK

Although much of the research was focused on SARS, the overall aims included the development of a mathematical and statistical framework to facilitate general analyses. The framework facilitates assessment of how best to control the spread of infectious agents of a given type (i.e. given incubation and infectious period distributions) in defined local, national, or global settings.

Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, Abu-Raddad LJ, Ho L-M, Thach T-Q, Chau P, Chan K-P, Lam T-H, Tse L-Y, Tsang T, Kong JHB, Cheung N-T, Lo S-V, Lau EMC, Ho W, Ferguson NM, Anderson RM. Epidemiological determinants of the spread of the causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet*, 361, 1761–1766, 2003.

Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ, Leung GM, Ho L-M, Lam T -H, Thach T-Q, Chau P, Chan K-P, Lo S-V, Leung P-Y, Tsang T, Ho W, Lee K-H, Lau EMC, Ferguson NM, Anderson RM. <u>Transmission dynamics of the etiological agent of SARS in Hong</u> <u>Kong: Impact of public health interventions.</u> *Science,* 300, 1961-1966, 2003.

[other SARS publications]

Foot-and-Mouth Disease (FMD)

Roy Anderson, Neil Ferguson and Christl Donnelly were involved in the analysis of the British 2001 outbreak of foot-and-mouth disease (FMD). They were members of the Foot-and-Mouth Disease Official Science Group, chaired by the Chief Scientific Advisor Professor (now Sir) David King, which advised on the spread of foot and mouth disease and the effects of potential control policies.

Ferguson NM, Donnelly CA and Anderson RM. <u>The foot-and-mouth epidemic in Great Britain:</u> <u>Pattern of spread and impact of interventions.</u> *Science*, 292, 1155-1160, 2001.

Ferguson NM, Donnelly CA and Anderson RM. <u>Transmission intensity and the impact of control</u> policies on the foot and mouth disease epidemic in Great Britain. *Nature* 413, 542-548, 2001.

[other FMD publications]

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Evaluation of Interventions and Diagnostics of Neglected Tropical Diseases

Research Fellow: Dr Artemis Koukounari (from September 2010)

Funding Source: MRC fellowship

This research will focus on schistosomiasis and trachoma; they are among the most prevalent of the socalled "Neglected Tropical Diseases (NTDs)", an umbrella term encompassing a group of parasitic, bacterial, and viral infections collectively imposing a similar disease burden to that of malaria and HIV. Decisions on Mass Drug Administration (MDA), estimates of the burden of morbidity, infection prevalence and intensity of infection and evaluation of control measures, all depend on the results from diagnostic tests.

The proposed research aims to use advanced biostatistical analysis (including latent variable models) to further understanding of the effect upon the prevalence and intensity of schistosomiasis and of the ocular bacteria causing trachoma, and the likelihood of their elimination, of interventions based on MDA,

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as well as to evaluate the performance of the diagnostic tools currently used for the Monitoring and Evaluation (M&E) of these two infections.

The main data sources are:

- annual longitudinal surveys from the Monitoring and Evaluation (M&E) of National Schistosomiasis Control Programmes in Niger and Tanzania
- monthly longitudinal trachoma studies conducted in The Gambia and Tanzania.

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Influenza in pigs

In November 2009, <u>UK research funders [the Medical Research Council (MRC)</u>, Wellcome Trust, Biotechnology and Biological Sciences Research Council (BBSRC), Department of Health and Department for Environment, Food and Rural Affairs (Defra)] announced the coordinated funding of £7.5 million aimed at understanding the development and spread of pandemic influenza.

We are part of the multidisciplinary team alongside researchers from Cambridge, Oxford, Edinburgh and London studying the spread and evolution of influenza in British pig herds and farm workers, in a project led by Professor James Wood, Cambridge. This project is complemented by one led by Professor Ian Brown, Veterinary Laboratories Agency (VLA), Weybridge, on transmission, infection dynamics and immunopathology of H1N1 in pigs. Together these projects form the Combating Swine Influenza (COSI) Initiative.

The newly funded research initiative is intended to develop a new understanding of how the pandemic H1N1 virus behaves in pig populations and how interactions between pigs and farm workers could help it to evolve and spread. With this information, it should be possible to inform effective strategies to limit the spread of the virus in both pig herds and the human population.

The intention is for the results to feed directly into wider policy analysis on dealing with pandemics, for the long-term benefit of human and animal health. '*This is amongst the fastest I have ever seen the UK science community react to an emerging disease threat. Turning around a funding initiative in a matter of months while ensuring we are supporting the best science has been a huge achievement by the scientific community and the funders.*' Professor Douglas Kell, BBSRC Chief Executive, commenting on four new collaborative projects being funded across the UK, including the Combating Swine Influenza (COSI) Initiative.

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