Edinburgh Infectious Diseases

Leading infectious disease research and training

2014 Annual Report

By Prof Rick Maizels (Director)

and

Dr Hilary Snaith (Executive Manager)

April 2015

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Annual Report of *Edinburgh Infectious Diseases,* 2014

Executive Summary

- The mission of *Edinburgh Infectious Diseases* is to **build a world-leading consortium in infectious disease sciences** across the University of Edinburgh and neighbouring Institutions with the following specific aims:
  1. Represent the strengths and promise of infectious disease science in Edinburgh through our symposia, workshops, outreach activity and digital profile;
  2. Maintain strategic oversight of infectious disease research in Edinburgh, to maximise synergy between established groups and promote new avenues for investigation;
  3. Foster infectious disease teaching and training at all levels within the University, including the development of new postgraduate initiatives.

- *Edinburgh Infectious Diseases* now comprises **over 160 academics** from the 3 Colleges of the University of Edinburgh, as well as Heriot-Watt University, Edinburgh Napier University, NHS Lothian and associated Institutes including the Moredun Research Institute and Scotland's Rural College). Together with the researchers working with each Principal Investigator, **over 700 staff** are involved in this sector across the city, **over 90 of whom were included in the University of Edinburgh's 2014 Research Excellence Framework (REF) submission**.

- In the academic year 2013-2014, our annual audit of external income and outputs revealed that **a total of £29m in research funding was secured within the University of Edinburgh alone**, over 10% of the total University income. Among the external funding successes are high-profile competitive awards from BBSRC, MRC and the Wellcome Trust, and many collaborative awards linking different groups across the city.

- We organised a series of successful events including our **Annual Symposium at the Royal College of Physicians** addressed by an internationally renowned keynote speaker; several Edinburgh-wide workshops on respiratory viruses, vaccine development, and noncommunicable diseases; and a public Winter Lecture at the Playfair Library in Old College.

- We have extended our **Outreach Programme** including a highly-accessed website (www.eid.ed.ac.uk), visits to schools and stands at the Edinburgh International Science Festival.

- We support the undergraduate programme in infectious diseases, and provide a portal for interested Master's and PhD student applicants to the University. Our bid for a Wellcome Trust funded 4-year PhD programme in "***Hosts, Pathogens and Global Health***" was selected to go forward for submission in April 2015.

Edinburgh Infectious Diseases : Strategy Statement

Our long-term strategy is to establish leadership in infectious disease research and training at the UK/European level and to be in the top tier worldwide. We will achieve this by :

- Capturing existing strengths in numbers and in depth to present a coherent external face to academia, industry and the public;
- Building by recruitment of key individuals in key areas;
- Minimising barriers between units and institutions in the city;
- Promoting collaboration between researchers and identifying areas of synergy for funding bids;
- Anticipating opportunities for breakthroughs in fundamental and translational research;
- Providing a suite of outstanding training programmes including PhD schemes.

Specific aims to support this strategy are

- Form closer liaison across the community, in particular between CHSS infectious disease researchers and those in the CSE and CMVM, and further strengthen links with other leading institutions in the city such as Moredun Research Institute, Scotland's Rural College, Heriot-Watt University and Edinburgh Napier University.
- Bridge between the academic and clinical infectious diseases community through closer links with clinicians in NHS Lothian.
- Build on *Edinburgh Infectious Diseases* activity (symposia, seminars, website, outreach) that bring investigators from different sites together.
- Promote joint external funding bids for PhD schemes, equipment and facilities, adding value rather than competing internally for existing funds.
- Expand overseas links, especially with developing countries, in concert with the University's Global Academies, particularly the *Global Health Academy.*
- Develop more extensive collaboration with pharmaceutical and other industry partners on translational outputs.
- Contribute to development of undergraduate teaching provision at the University, both to promote infectious disease sciences and as a further bond between academics from different units
- Publicise the impact of *Edinburgh Infectious Diseases* through continued website development and local outreach including events open to the public.

Annual Report of *Edinburgh Infectious Diseases,* 2014

Organisation

Edinburgh Infectious Diseases is organised by an Executive Manager (Dr Hilary Snaith) and Director (Professor Rick Maizels), through the following Executive Committee:

Member	Affiliation
Professor Judith Allen	Institute of Immunology & Infection Research, Ashworth Laboratories, King's Buildings
Dr Till Bachmann	Division of Infection and Pathway Medicine, Royal Infirmary of Edinburgh, Little France
Prof Harry Campbell	Centre for Population Health Sciences, Teviot Place
Dr Bernadette Dutia	The Roslin Institute, Easter Bush
Prof Gary Entrican	The Moredun Research Institute
Prof Clifford Leen	Department of Infectious Diseases, Western General Hospital
Prof Rick Maizels	Institute of Immunology & Infection Research, Ashworth Laboratories, King's Buildings
Prof Keith Matthews	Institute of Immunology & Infection Research, Ashworth Laboratories, King's Buildings
Prof Jürgen Schwarze	Centre for Inflammation Research, Queen's Medical Research Institute, Little France
Dr Hilary Snaith	*Edinburgh Infectious Diseases*, Ashworth Laboratories, King's Buildings
Prof Mark Stevens	The Roslin Institute, Easter Bush
Dr Alice Street	School of Social and Political Science, George Square
Prof Sue Welburn	Division of Infection and Pathway Medicine, Royal Infirmary of Edinburgh, Little France
Prof Jose Vazquez-Boland	School of Biomedical Sciences and Roslin Institute, Easter Bush

Membership of *Edinburgh Infectious Diseases* grew to over 160 academics during 2014, drawn from the University of Edinburgh, Heriot Watt and Edinburgh Napier Universities, NHS Lothian and associated Institutes including the Moredun Research Institute and Scotland's Rural College (formerly Scottish Agricultural College). A complete listing is on the *Edinburgh Infectious Diseases* website: http://www.eid.ed.ac.uk/members. In our annual census carried out in January 2015 there were also over 250 PhD students and almost 200 post-doctoral researchers so that together with technicians, technology specialists and externally-funded research fellows, **over 850 individuals participate in *Edinburgh Infectious Diseases*.**

A significant development in the past 12 months has been strengthening links with members of the College of Humanities and Social Sciences at the University of Edinburgh, with greater focus on social policies and healthcare dynamics in infectious disease control. Reflecting this, Dr Alice Street of the School of Social and Political Science has joined the Executive Committee, and we have two of the speakers at this year's Annual Symposium are from this College. We are also working to develop our website to highlight the impact of social science research to better reflect its influence throughout biological science and clinical infectious disease research.

We continue to work closely with the Global Health Academy, co-organising a successful workshop exploring the Interface Between Communicable and Non-Communicable Diseases in May 2014. Later this year we will jointly host the visit of Dr John Reeder from the WHO-Tropical Diseases Research (TDR) organisation to Edinburgh in September 2015.

We are forging links with the Innogen Institute, and they will be contributing to our cross-University workshop on Antimicrobial Resistance, Diagnostics and Drug Discovery, which we will hold later this year.

As part of building stronger connections with other institutions, and to facilitate future applications EU funding awards, we have set up a self-funded summer studentship exchange programme with Leiden University Medical Center. Under the scheme two students from the Infectious Diseases Honours class of 2014/15 worked in Leiden over the summer of 2014, and for 2015 we will extend to hosting two Leiden students in Edinburgh laboratories.

A new focus developed in 2014 has been to improve integration of clinicians working in infectious diseases research with their academic colleagues. For example, we plan local networking workshops to bring together the clinicians in the Department of Infectious Diseases at the Western General and microbiologists working at the Royal Infirmary of Edinburgh. Related to this is the imminent launch of new Division of Infection and Pathway Medicine, and the envisaged maturation of this Division into a new Centre for Infection Medicine based primarily at Little France.

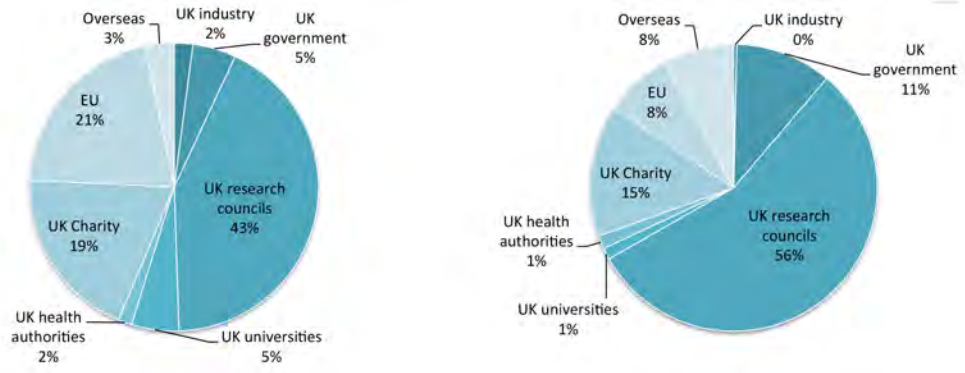
Research Funding

Very substantial resources are invested in infectious disease research across the UK, estimated at £200M per annum, by BBSRC, MRC and the Wellcome Trust, the European Commission and international agencies such as the Bill and Melinda Gates Foundation. The total funding awarded to infectious disease researchers within the University of Edinburgh in the Financial Year 2013/2014 was over £29M, representing over 10% of the University's total of £270M. While mostly from public and charitable sources, £1.4M funding was also secured from industrial sponsors and collaborators.

In addition, the Moredun Research Institute received £3.3M from the BBSRC in research funding, including three grants in partnership with the University of Edinburgh, so that we estimate over 15% of nationwide infectious disease funding has been brought to the city.

This high rate of funding has continued into the current financial year, with a further £10M awarded in the first half of FY 2014/15.

Research funding sources for University of Edinburgh overall (L)
and *Edinburgh Infectious Diseases* (R)

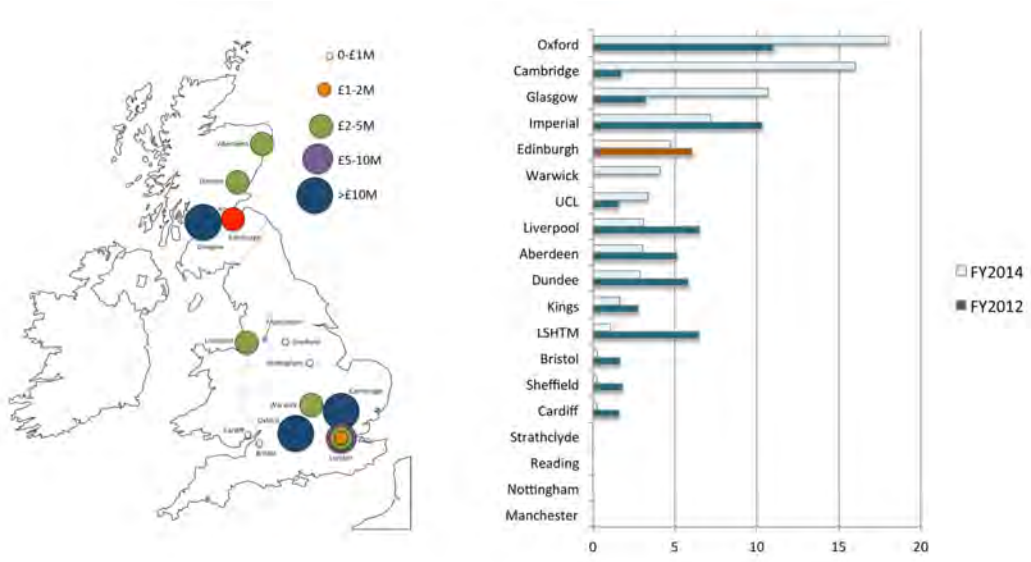


Research awards over £0.5M made to members of *Edinburgh Infectious Diseases* are listed below.

Researcher	Funding body	Amount
Achim Schnaufer Inst. for Immunol. & Infection Res.	Medical Research Council	£2,813, 545
Malcolm Walkinshaw Institute of Structural and Mol. Biol.	Wellcome Trust	£2,485,358
David Gally Roslin Institute	Food Standards Agency	£2,049,534
Clare Blackburn Institute for Stem Cell Research	European Commission	£1,216,874
David W Burt Roslin Institute	Biotechnology and Biological Sciences Research Council	£1,102,142
Kenneth Baillie Roslin Institute	Wellcome Trust	£986,082
Ivan Morrison Roslin Institute	Bill and Melinda Gates Foundation	£909,091
Elizabeth Glass Roslin Institute	Biotechnology and Biological Sciences Research Council	£903,900

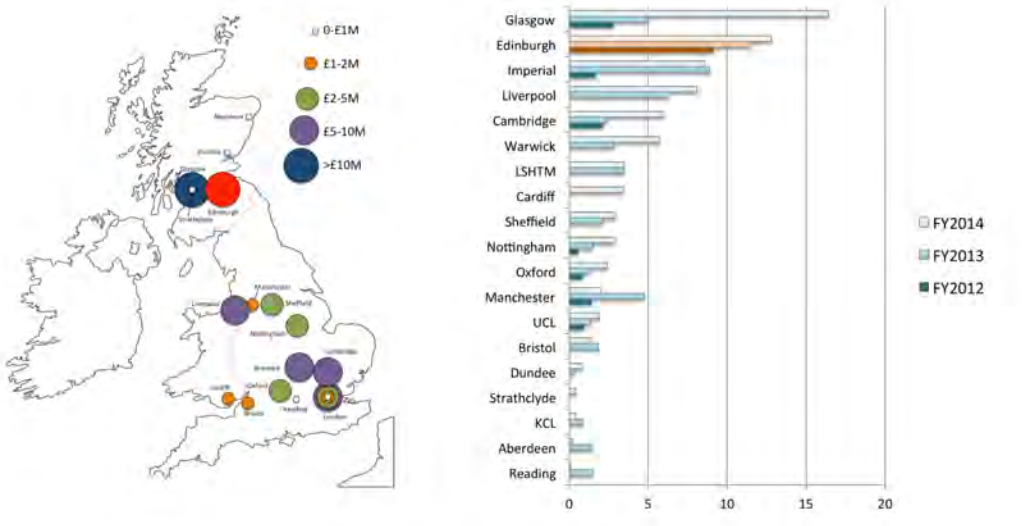
David Longbottom Moredun Research Institute	Biotechnology and Biological Sciences Research Council	£768,000
David Griffiths Moredun Research Institute	Biotechnology and Biological Sciences Research Council	£716,000
Stephen Jenkins Centre for Inflammation Research	Medical Research Council	£600,647
Jürgen K Schwarze Centre for Inflammation Research	Medical Research Council	£596,220
Alastair Nisbet Moredun Research Institute	Biotechnology and Biological Sciences Research Council	£503,000

Funding from the Wellcome Trust for Infectious Diseases



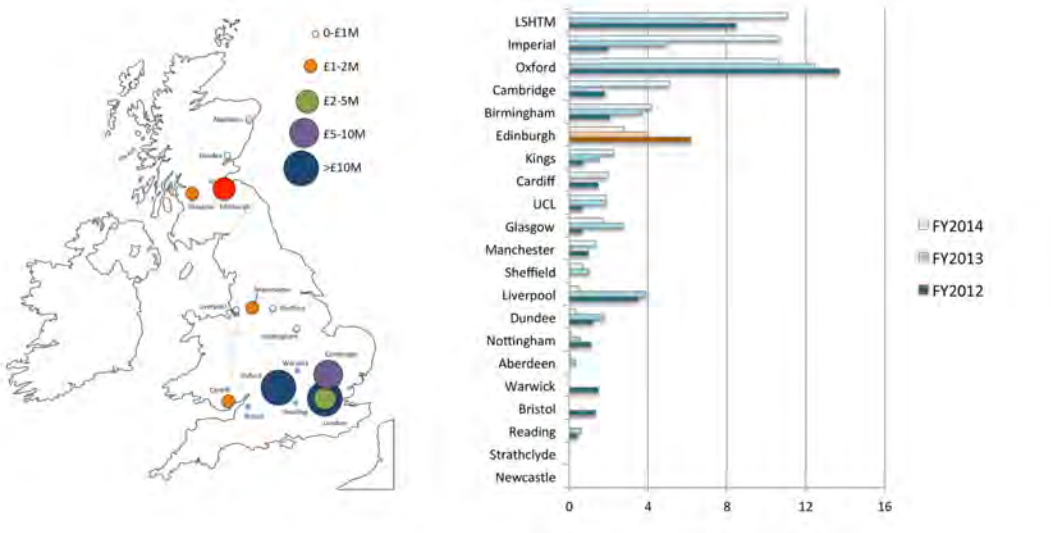
(L) Total funding received from the Wellcome Trust for Infectious Diseases research in 2014. (R) Total funding received for Infectious Diseases in FY 2011/12 and FY 2013/14; data is sorted on the 2014 funding totals.

Funding from the Biotechnology and Biological Sciences Research Council for Infectious Diseases



(L) Currently active grants from the Biology and Biotechnology Research Council for Infectious Diseases research in December 2014. (R) Value of active grants from the BBSRC in December 2012, 2013 and 2014. Note that data for 2012 is presented for Imperial College, University College London, and the Universities of Cambridge, Edinburgh, Glasgow, Manchester, Nottingham and Oxford only. Data is sorted on the 2014 totals.

Funding from the Medical Research Council for Infectious Diseases



(L) Total funding received from the Medical Research Council for Infectious Diseases research in 2014. (R) Total funding received for Infectious Diseases in FY 2011/12, FY 2012/13 and FY 2013/14; data is sorted on the 2014 funding totals.

Major awards so far in Financial Year 2014/2015

Researcher	Funding body	Amount
Keith Matthews Inst. for Immunol. & Infection Res.	Wellcome Trust (Investigator Award)	£2,365,413
Rick Maizels Inst. for Immunol. & Infection Res.	Wellcome Trust (Investigator Award)	£2,039,266
Peter Simmonds Roslin Institute	Biotechnology and Biological Sciences Research Council	£1,100,513
Mark Woolhouse Institute of Evolutionary Biology	Medical Research Council	£522,988

Research Excellence Framework (REF) : Impact and engagement

The 2014 Research Excellence Framework (REF) proved to be highly successful for the University of Edinburgh. Many members of *Edinburgh Infectious Diseases* were instrumental in this, with over 120 staff making significant contributions to the Units of Assessment in Clinical Medicine, Biological Sciences, Agriculture, Veterinary and Food Science and Anthropology and Development Studies. Scotland's Rural College submissions were successfully included with the University's Agriculture, Veterinary and Food Science return.

Summary of University of Edinburgh REF2014 performance, highlighting the Units of Assessment with >4 members of *Edinburgh Infectious Diseases returned*

Unit of Assessment	FTE staff	*EID* staff	4* (%)	GPA	Research power	Power rank	Impact rank	GPA rank
All UoE	1753	121	38	3.2	5575	4	13	11
Clinical Medicine	207	18	44	3.3	683	4	13	6
Biological Sciences	110	44	56	3.4	377	5	3	3
Agriculture, Veterinary and Food Science	123	50	42	3.1	384	1	14	11
Anthropology and Development Studies	34	4	33	3.0	104	4	4	7

FTE – Full time equivalent staff submitted; number of *Edinburgh Infectious Diseases* members submitted, % 4* research activity; GPA – grade point average; research power; overall ranking based on research power, impact and GPA

Edinburgh Infectious Diseases staff also contributed **15 Impact Case Studies** out of the 193 submissions made in total. *Edinburgh Infectious Diseases* has also contributed to producing summaries of the Impact Case Studies that will be used to inform both members of the University and members of the public about the significant impact generated by our research. Examples of these impact case study summaries are presented in Appendix 1.

Impact case studies

- **Accurate epidemiological pneumonia incidence and mortality estimates have influenced child health policy to reduce global child pneumonia mortality**
  - Harry Campbell, Centre for Population Health Sciences, University of Edinburgh
- **Blood donations are screened for malaria exposure with an immunoassay**
  - David Cavanagh, Institute of Immunology and Infection Research, University of Edinburgh
- **Bovine Neonatal Pancytopenia (BNP), a newly recognised disease of calves, is caused by colostral transfer of cross-reactive alloantibodies induced in dams by PregSure Bovine Viral Diarrhoea (BVD) vaccine**
  - Neil Sargison, R(D)SVS and Ivan Morrison, Roslin Institute, University of Edinburgh

- **Breeding a scrapie resistant international sheep flock**
    - Nora Hunter and Wilfred Goldmann, Roslin Institute, University of Edinburgh
- **Community-directed delivery of doxycycline in Cameroon demonstrates effectiveness as a treatment for onchocerciasis (river blindness) in Africa that avoids adverse effects associated with ivermectin**
    - David Taylor, Division of Infection and Pathway Medicine, University of Edinburgh
- **Controlling bovine TB in the UK by controlling badger numbers**
    - Ivan Morrison, Roslin Institute, University of Edinburgh
- **Diagnostic criteria for human prion disease enable case ascertainment and underpin international policy on prion disease**
    - Robert Will and James Ironside, National CJD Research and Surveillance Unit, University of Edinburgh
- **Eliminating trypanosome carriage in Ugandan cattle prevents sleeping sickness in humans, stimulating the formation of "Stamp Out Sleeping Sickness (SoS)" a Public Private Partnership that is eliminating the disease from Uganda**
    - Sue Welburn, Division of Infection and Pathway Medicine, University of Edinburgh
- **Identification of transmission risk of variant Creutzfeldt-Jakob disease (vCJD) via blood and blood products defines critical changes to health policy**
    - James Ironside and Robert Will, National CJD Research and Surveillance Unit, University of Edinburgh
- **Marker-assisted selection to breed for resistance to Infectious Pancreatic Necrosis in salmon**
    - Stephen Bishop and Ross Houston, Roslin Institute, University of Edinburgh
- **Phylogenetic analysis software BEAST informs public health responses to infection**
    - Andrew Rambaut, Institute of Evolutionary Biology, University of Edinburgh
- **Pre-school children are now included in schistosomiasis prevention programmes**
    - Francisca Mutapi, Institute of Immunology and Infection Research, University of Edinburgh
- **Promoting public and policy-maker understanding of the benefits of genetic modification (GM) technology in chickens; transgenic birds that do not transmit avian influenza**
    - Helen Sang, Roslin Institute, University of Edinburgh
- **Statistical methods are helping to control the spread of epidemics**
    - Ian Poxton, Royal Infirmary of Edinburgh; Gavin Gibson, Maxwell Institute, Heriot Watt University, University of Edinburgh
- **Tuberculosis Control in South Asia**
    - Ian Harper, School of Social and Political Science, University of Edinburgh

REF2014
Research Excellence Framework

BBSRC Activating Impact Award

Edinburgh Infectious Diseases has been actively working with Edinburgh Research and Innovation to increase the impact that our research to increase the impact of our research through collaboration with industrial partners. During 2014 this was greatly facilitated by the award of £50,000 from the BBSRC in the "Activating Impact" competition designed to promote conversion of BBSRC-supported bioscience into real-life applications.

As part of this scheme in September 2013 we appointed three **Technology Scouts –** Alex Corbishley and Adrian Muwonge from the Roslin Institute and Balazs Szoor, from the School of Biological Sciences. The Scouts were tasked with identifying commercial opportunities within *Edinburgh Infectious Diseases* and establishing links with potential industrial collaborators. The project ran from October 2013 to October 2014 during which time the Scouts identified three major areas of particular interest and to assess the current commercial landscape and connect academic researchers with potential industrial collaborators. The topics chosen were based on identified areas of strength within *Edinburgh Infectious Disease*s, namely (i). Vaccinology, (ii). Anti-microbials, and (iii). Treatment of inflammatory, allergic, autoimmune and neglected tropical diseases.

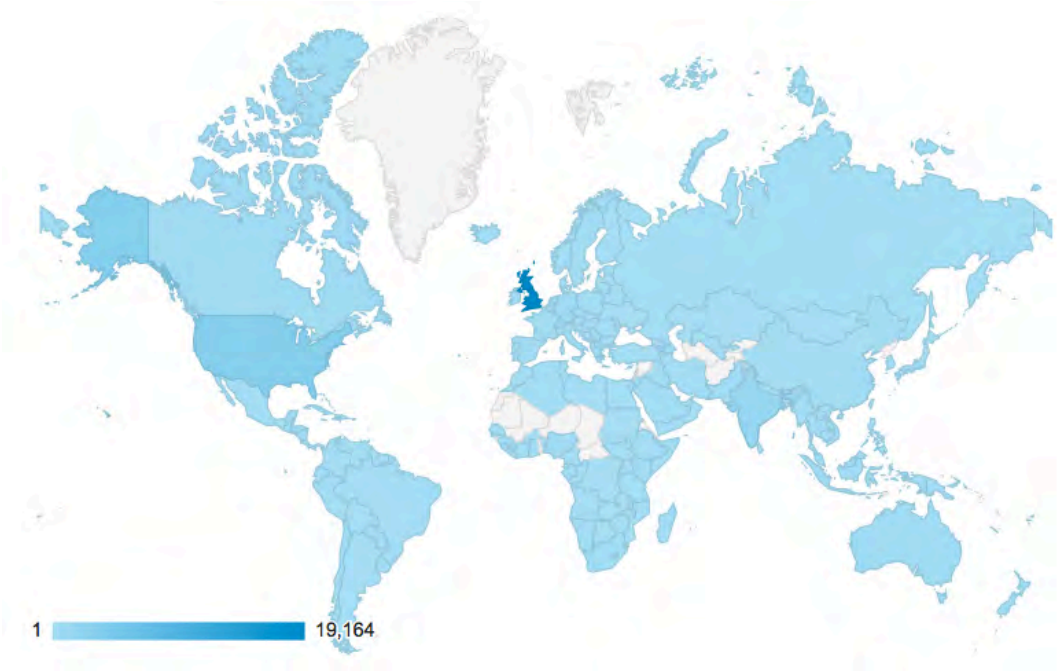
The *Scouts* carried out detailed interviews with members of *Edinburgh Infectious* Diseases, to prepare a portfolio of research strengths within the network. They then attended national, government sponsored networking events with local companies (mainly SMEs) in Edinburgh and Glasgow, where the capabilities of *Edinburgh Infectious Diseases* were pitched. The *Technology Scouts* also travelled to international partnering events (World Vaccine Congress in Washington DC, BioPharma Asia Convention 2014 in Singapore and BIO-Europe Spring 2014, Turin) to establish links with further companies and to ascertain the current priorities of big pharma companies and their interests in building academic collaborations in Edinburgh. These meetings have helped to draw the attention of several companies to the ongoing research at *Edinburgh Infectious Diseases* and initiated several discussions between pharmaceutical companies and PIs.

The *Scouts* have presented their findings at several meetings and workshops (including *Creating Impact in the Biological Sciences* and *Edinburgh Infectious Diseases* Vaccinology Workshop) and have used their knowledge of the members expertise and understanding of their technologies to suggest researchers of potential interest to the Edinburgh Research and Innovation business development executives, following specific enquiries from companies.

In summary, the *Technology Scouts* Initiative provided a very useful stepping stone towards identifying potential new opportunities for industrial collaboration. It also gave the Technology Scouts themselves valuable insight into the commercial research landscape. Together the Scouts generated an up-to-date database of translatable research projects within *Edinburgh Infectious Diseases* and more importantly, a list of possible industrial partners with named key personnel in the majority of cases. The project generated the essential knowledge base that will be used by the Roslin Institute and the School of Biological Sciences to pursue links with industrial partners in the future.

Outreach and public visibility

One of the key aims of *Edinburgh Infectious Diseases* is to increase the profile of our research and activity both within and outwith the University. We actively work with the University Press Office to identity and promote research for press releases, and ensure that these stories are published on our website. Members of *Edinburgh Infectious Diseases* were covered extensively in the local, national and international press, with several stories features on the BBC News, Radio 4, The Times, The Herald, The Scotsman, The Wall Street Journal, and The New York Times, amongst many others. In particular Clare Blackburn's report of thymus regeneration from reprogrammed fibroblasts and Mark Woolhouse's contributions to debates on antimicrobial resistance were carried around the world. More details are provided in **Appendix 3**.



We continue to manage our comprehensive, and expanding, website (http://www.eid.ed.ac.uk), which now receives **almost 3000 hits per week** with **>45%** of visitors from outwith the UK. In 2014 we had visitors from virtually every country in the world (see map above). Feedback from users surveyed on the site has been uniformly positive, with over 90% of respondents finding it easy to navigate the site and find the information they were looking for. In addition to this we maintain an active twitter feed now followed by over **850** people (http://www.twitter.com/edin_eid).

We manage a range of visits to external organisations and events. Including public lectures, Doors Open days and science festivals.

- *Edinburgh Infectious Diseases* has developed an outreach project for primary and lower secondary school aged children using the Ashworth Natural History Collection to explore the interaction between hosts and pathogens – the "Bones and Bugs". This project has proved very popular with children and continued to grow during 2014: we have now held workshops in 10 primary schools across Edinburgh, East Lothian and Midlothian, for over 400 children. We have taken the project to the Royal Blind School, Edinburgh, where it had a direct impact helping partially sighted children understand vertebrate anatomy. The project has also been part of the Dunbar, Midlothian and Edinburgh

International Science Festivals. There are plans to take the project to the Borders and Dundee Science festivals later in 2015.

- Members of *Edinburgh Infectious Diseases* manned an interactive display at the Edinburgh International Science Festival demonstrating how research into parasitic worms is helping to understand asthma.

- We are collaborating with colleagues across the University to develop the Impact Case Studies submitted for REF2014 into engagement tools for public displays and events, including the EU Researchers Night Explorathon in September 2015.

Research Publications

In the calendar year 2014, a over 400 research papers were published by members of *Edinburgh Infectious Diseases*, including a substantial number submitted in various REF Units of Assessment. Among the high profile publications, there are four papers published each in Nature, Science and Nature Genetics, and two in the Lancet, as well as one in Nature Cell Biology, seven in Proc Natl Acad Sci, five in Nature Communications, two in Lancet Infectious Diseases, four in PLoS Pathogens and eight in PLoS Neglected Tropical Diseases.

- **Bredenkamp, N., S. Ulyanchenko, K. E. O'Neill, N. R. Manley, H. J. Vaidya, and C. C. Blackburn.** 2014. An organized and functional thymus generated from FOXN1-reprogrammed fibroblasts. Nat Cell Biol **16:**902-908.

- **Ciccolini, M., T. Donker, H. Grundmann, M. J. Bonten, and M. E. Woolhouse.** 2014. Efficient surveillance for healthcare-associated infections spreading between hospitals. Proc Natl Acad Sci U S A **111:**2271-2276.

- **Faria, N. R., A. Rambaut, M. A. Suchard, G. Baele, T. Bedford, M. J. Ward, A. J. Tatem, J. D. Sousa, N. Arinaminpathy, J. Pepin, D. Posada, M. Peeters, O. G. Pybus, and P. Lemey.** 2014. HIV epidemiology. The early spread and epidemic ignition of HIV-1 in human populations. Science **346:**56-61.

- **Gire, S. K., A. Goba, K. G. Andersen, et al.** 2014. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. Science **345:**1369-1372.

- **Mableson, H. E., A. Okello, K. Picozzi, and S. C. Welburn.** 2014. Neglected Zoonotic Diseases-The Long and Winding Road to Advocacy. PLoS Negl Trop Dis **8:**e2800.

- **Mackenzie, K. J., D. J. Nowakowska, M. D. Leech, A. J. McFarlane, C. Wilson, P. M. Fitch, R. A. O'Connor, S. E. Howie, J. Schwarze, and S. M. Anderton.** 2014. Effector and central memory T helper 2 cells respond differently to peptide immunotherapy. Proc Natl Acad Sci U S A **111:**E784-793.

- **Mandal, P., J. D. Chalmers, C. Graham, C. Harley, M. K. Sidhu, C. Doherty, J. W. Govan, T. Sethi, D. J. Davidson, A. G. Rossi, and A. T. Hill.** 2014. Atorvastatin as a stable treatment in bronchiectasis: a randomised controlled trial. Lancet Respir Med **2:**455-463.

- **McNally, L., M. Viana, and S. P. Brown.** 2014. Cooperative secretions facilitate host range expansion in bacteria. Nat Commun **5:**4594.

- **Smith, C. L., P. Dickinson, T. Forster, M. Craigon, A. Ross, M. R. Khondoker, R. France, A. Ivens, D. J. Lynn, J. Orme, A. Jackson, P. Lacaze, K. L. Flanagan, B. J. Stenson, and P. Ghazal.** 2014. Identification of a human neonatal immune-metabolic network associated with bacterial infection. Nat Commun **5:**4649.

- **Theodoratou, E., D. A. McAllister, C. Reed, D. O. Adeloye, I. Rudan, L. M. Muhe, S. A. Madhi, H. Campbell, and H. Nair.** 2014. Global, regional, and national estimates of pneumonia burden in HIV-infected children in 2010: a meta-analysis and modelling study. Lancet Infect Dis **14:**1250-1258.

- **Tree, J. J., S. Granneman, S. P. McAteer, D. Tollervey, and D. L. Gally.** 2014. Identification of Bacteriophage-Encoded Anti-sRNAs in Pathogenic Escherichia coli. Mol Cell **55:**199-213.

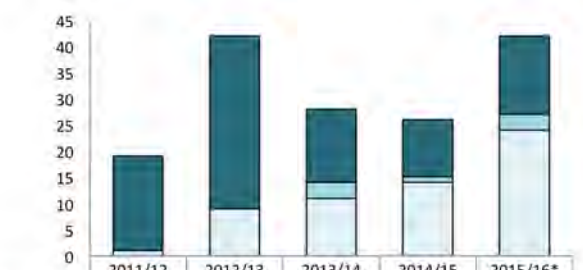
- **von Wissmann, B., J. Fyfe, K. Picozzi, L. Hamill, C. Waiswa, and S. C. Welburn.** 2014. Quantifying the Association between Bovine and Human Trypanosomiasis in Newly Affected Sleeping Sickness Areas of Uganda. PLoS Negl Trop Dis **8:**e2931.

- **Worobey, M., G. Z. Han, and A. Rambaut.** 2014. A synchronized global sweep of the internal genes of modern avian influenza virus. Nature **508:**254-257.

Training and Teaching

Although *Edinburgh Infectious Diseases* has no formal responsibility for undergraduate teaching, we offer significant added value to the student courses in Infectious Diseases. We continue to expand the information available to students on our website, and provide a portal for students seeking information on the range of courses at the University which have an infectious disease components, from undergraduate courses, through on-line and on-campus-Masters to PhD programmes. This now also includes the range of options for infectious diseases clinicians who would like to get more actively involved in research.

- Student numbers on the Infectious Diseases Honours programme are continuing to trend upwards, with an increasing popularity of this course among intercalating medical and veterinary students. We anticipate further expansion once all clinical students are required to take a B.Sc. after their second year. The larger class sizes will put increasing pressure on members of *Edinburgh Infectious Diseases*, both in terms of teaching and also provision of research projects in the second semester.



	2011/12	2012/13	2013/14	2014/15	2015/16*
Scientist	18	33	14	11	15
Vet	0	0	3	1	3
Medic	1	9	11	14	24

- *Edinburgh Infectious Diseases* Executive Manager gave a "Welcome" presentation to the 4th year students on the Infectious Diseases Honours course during the first week of term.

- Senior Honours students receive the weekly *Edinburgh Infectious Diseases* newsletter, keeping them up to date with all relevant seminars and news from across the Network. They are also invited to all workshops and other events we organise, and given opportunities to take part in public engagement events.

- During 2014 we initiated a Summer Student Exchange Programme for students who would be progressing into Infectious Diseases Senior Honours for 2014 /15. The two students selected for the programme spent two months in the Leiden University Medical Center, gaining important research experience (as described in the section above). Their experiences were uniformly positive, and they wrote very enthusiastically about their time in the Netherlands: http://www.eid.ed.ac.uk/news/student-summer-projects-lumc. We will be repeating the exchange for students in the class of 2015 / 16, with two students working in Leiden this summer.

- *Edinburgh Infectious Diseases* also gave the Honours students the opportunity to invite a speaker of their choice to allow them to explore in more detail aspects of their course. Three students from the class took on the task of coordinating their classmates to invite David Denning from the University of Manchester, and then to host him during his visit to Edinburgh. They have written about their experiences with David at http://www.eid.ed.ac.uk/news/david-denning-visit.

Scientific Events during 2014

Edinburgh Infectious Diseases organised a number of events, which brought together members of the Network working in specific themes or units, as well as attracting audiences from the whole organisation. The events were organised in a range of venues covering each of the major centres.

Events held in 2014

Date	Event	Venue
4 April	Workshop on Imaging Infection	Ashworth Laboratories, Kings Buildings
21 May	Annual Symposium	Audience of 200 persons at Royal College of Physicians (42 posters, 10 speakers, from within Edinburgh, and 5 external commercial exhibitors)
22 May	Workshop exploring Interface between Communicable and Non-Communicable Diseases	Ashworth Laboratories, Kings Buildings
Weekly	Edinburgh Virology Group	Regular seminar series at the Roslin Institute
8 October	Workshop on Vaccinology	Moredun Research Institute
5 November	Public Winter Lecture by Johannes Krause, MPI Jena	Playfair Library, Old College

- The half-day workshop on "*Imaging Infection"* brought together 40 researchers from across the Universities of Edinburgh and Heriot Watt to learn about the microscopy facilities available in Edinburgh for imaging pathogens.
- *Edinburgh Infectious Diseases* collaborated with the Global Health Academy to organise the workshop "*Exploring the interface between communicable and non-communicable diseases"* for 80 participants. The half-day event facilitated understanding of common ground in societal and technomedical solutions in this complex field. The workshop was chaired by Richard Smith, former editor of the British Medical Journal, with speakers including Sally Smith from UNAIDS and Sue Kinn from DfID, and a number of Edinburgh-based researchers. The event has provided a springboard to further enhance links between researchers in social, clinical and biological sciences across the Network.
- The Annual Symposium was a highlight of the year. Once again we were hosted by the Royal College of Physicians, where over 200 participants enjoyed a full day of talks, poster session and networking opportunities. We were delighted that the keynote lecture was given by Philippe Sansonetti from the Institut Pasteur in Paris.

- To conclude the Activating Impact Technology Scout project *Edinburgh Infectious Disease* organised a workshop specifically exploring the Vaccinology theme. The event was held at the Moredun Research Institute where 60 attendees heard from a number of external speakers, as well as presenters from across the *Edinburgh Infectious Diseases*. There was also a useful opportunity to discuss strengths in this field in Edinburgh and how to facilitate increase collaboration. It

was agreed that the formation of the "*Edinburgh Vaccinology Forum*" would contribute to greater cohesion between researchers.

- Our Winter Lecturer, Prof Johannes Krause, Director of the Max Planck Institute for History and the Sciences in Jena from was an extremely engaging speaker. His seminar "*Ancient Pathogen Genomics - What we Learn from Historical Epidemics*" was very accessible to a wide audience and enabled us to connect researchers across the whole spectrum of infectious diseases, from osteoarchaeologists to epidemiologists and evolutionary biologists. The German Consul General and representatives for the National Library of Scotland attended the lecture, allowing further opportunities for network building during the drinks reception that followed.
- Professor David Denning from the University of Manchester was invited by the undergraduate students from the 2014 / 15 Honours class in Infectious Diseases to speak about the large, but often hidden, burden of fungal infections.

Events so far planned for 2015 include:

Date	Event	Venue
3 March	Honours student lectures by David Denning (University of Manchester)	Queen's Medical Research Institute and Ashworth Laboratories, Kings Buildings
3 April	Ker Memorial Prize	Close of Nominations
23 April	Workshop on Antimicrobial Resistance	Grant Institute, Kings Buildings
20 May	Annual Symposium	Royal College of Physicians, Queen Street
27 May	Visit of Chris Morgan, Burnet Institute, AUS	Chancellor's Building, Little France
21/22 September	Visit of John Reeder (WHO-TDR)	50 George Square
19 November	Winter Public Lecture by Ramanan Laxminarayan (CDDEP)	Playfair Library, Old College

Appendix I: Summary of accounts for 2013/14

Summary of *Edinburgh Infectious Diseases* accounts for FY 2013 / 14		
Details 2013/14	**Income (£)**	**Expenditure (£)**
Support staff		31,178
Event organisation		5,395
Meeting support		1,102
Symposium 2014		3,703
Vacation study grants		3,200
Organisational support		950
Office supplies		605
Printing		1,103
Travel support		309
Prizes		100
University income	50,000	
Symposium 2014 sponsorship income	2,400	
Total	52,400	47,645

Activating Impact : BBSRC grant awarded in 2013 to *Edinburgh Research and Innovation* to embed Knowledge Exchange and Commercialisation within *Edinburgh Infectious Diseases*		
	Income (£)	**Budget(£)**
Technology Scouts (buy-out of time and honoraria for Alex Corbishley, Adrian Muwonge and Balazs Szoor)		19,500
Travel and entrepreneurial training for Technology Scots		7,500
Mini-secondments to industry and other external institutions, scoping workshops and other networking activities		24,000
Total	50,000	50,000

Appendix II: Publications from *Edinburgh Infectious Diseases* for 2014

1. **Abdelbary, M. M., A. Wittenberg, C. Cuny, F. Layer, K. Kurt, L. H. Wieler, B. Walther, R. Skov, J. Larsen, H. Hasman, J. R. Fitzgerald, T. C. Smith, J. A. Wagenaar, A. Pantosti, M. Hallin, M. J. Struelens, G. Edwards, R. Bose, U. Nubel, and W. Witte.** 2014. Phylogenetic Analysis of Staphylococcus aureus CC398 Reveals a Sub-Lineage Epidemiologically Associated with Infections in Horses. PLoS One **9:**e88083.
2. **Abuzaid, A. A., and S. G. Amyes.** 2014. The genetic environment of the antiseptic resistance genes qacEDelta1 and cepA in Klebsiella pneumoniae. J Chemother**:**1973947814Y0000000181.
3. **Achcar, F., A. Fadda, J. R. Haanstra, E. J. Kerkhoven, D. H. Kim, A. E. Leroux, T. Papamarkou, F. Rojas, B. M. Bakker, M. P. Barrett, C. Clayton, M. Girolami, R. L. Krauth-Siegel, K. R. Matthews, and R. Breitling.** 2014. The silicon trypanosome: a test case of iterative model extension in systems biology. Adv Microb Physiol **64:**115-143.
4. **Al-Shahi Salman, R., P. M. White, C. E. Counsell, J. du Plessis, J. van Beijnum, C. B. Josephson, T. Wilkinson, C. J. Wedderburn, Z. Chandy, E. J. St George, R. J. Sellar, and C. P. Warlow.** 2014. Outcome after conservative management or intervention for unruptured brain arteriovenous malformations. Jama **311:**1661-1669.
5. **Albers, A., E. Sartono, S. Wahyuni, M. Yazdanbakhsh, R. M. Maizels, U. Klarmann-Schulz, K. Pfarr, and A. Hoerauf.** 2014. Real-time PCR detection of the HhaI tandem DNA repeat in pre- and post-patent Brugia malayi Infections: a study in indonesian transmigrants. Parasit Vectors **7:**146.
6. **Allebrandt, K. V., M. Teder-Laving, T. Kantermann, A. Peters, H. Campbell, I. Rudan, J. F. Wilson, A. Metspalu, and T. Roenneberg.** 2014. Chronotype and sleep duration: The influence of season of assessment. Chronobiol Int **31:**731-740.
7. **Allen, R. C., R. Popat, S. P. Diggle, and S. P. Brown.** 2014. Targeting virulence: can we make evolution-proof drugs? Nat Rev Microbiol **12:**300-308.
8. **Alsultan, A. A., E. Aboulmagd, B. A. Evans, and S. G. Amyes.** 2014. Clonal diversity of Acinetobacter baumannii from diabetic patients in Saudi Arabian hospitals. J Med Microbiol **63:**1460-1466.
9. **Anbazhagan, P., R. K. Harijan, T. R. Kiema, N. Janardan, M. R. Murthy, P. A. Michels, A. H. Juffer, and R. K. Wierenga.** 2014. Phylogenetic relationships and classification of thiolases and thiolase-like proteins of Mycobacterium tuberculosis and Mycobacterium smegmatis. Tuberculosis (Edinb) **94:**405-412.
10. **Andersson, R., C. Gebhard, I. Miguel-Escalada, I. Hoof, J. Bornholdt, M. Boyd, Y. Chen, X. Zhao, C. Schmidl, T. Suzuki, E. Ntini, E. Arner, E. Valen, K. Li, L. Schwarzfischer, D. Glatz, J. Raithel, B. Lilje, N. Rapin, F. O. Bagger, M. Jorgensen, P. R. Andersen, N. Bertin, O. Rackham, A. M. Burroughs, J. K. Baillie, Y. Ishizu, Y. Shimizu, E. Furuhata, S. Maeda, Y. Negishi, C. J. Mungall, T. F. Meehan, T. Lassmann, M. Itoh, H. Kawaji, N. Kondo, J. Kawai, A. Lennartsson, C. O. Daub, P. Heutink, D. A. Hume, T. H. Jensen, H. Suzuki, Y. Hayashizaki, F. Muller, A. R. Forrest, P. Carninci, M. Rehli, and A. Sandelin.** 2014. An atlas of active enhancers across human cell types and tissues. Nature **507:**455-461.
11. **Appleby, L. J., N. Nausch, L. Erskine, C. D. Bourke, N. Rujeni, N. Midzi, T. Mduluza, and F. Mutapi.** 2014. CD16 Expression on Monocytes in Healthy Individuals but Not Schistosome-Infected Patients Is Positively Associated with Levels of Parasite-Specific IgG and IgG1. PLoS Negl Trop Dis **8:**e3049.
12. **Arking, D. E., S. L. Pulit, L. Crotti, P. van der Harst, P. B. Munroe, T. T. Koopmann, N. Sotoodehnia, E. J. Rossin, et al.** 2014. Genetic association study of QT interval highlights role for calcium signaling pathways in myocardial repolarization. Nat Genet **46:**826-836.
13. **Armitage, A. E., K. Deforche, J. J. Welch, K. Van Laethem, R. Camacho, A. Rambaut, and A. K. Iversen.** 2014. Possible footprints of APOBEC3F and/or other APOBEC3 deaminases - but not APOBEC3G - on HIV-1 from patients during acute/early and chronic infection. J Virol **88:**12882-12894.
14. **Armstrong, S. D., S. A. Babayan, N. Lhermitte-Vallarino, N. Gray, D. Xia, C. Martin, S. Kumar, D. W. Taylor, M. L. Blaxter, J. M. Wastling, and B. L. Makepeace.** 2014. Comparative Analysis of the Secretome from a Model Filarial Nematode (Litomosoides sigmodontis) reveals Maximal Diversity in Gravid Female Parasites. Mol Cell Proteomics **13:**2527-2544.
15. **Arnot, D. E.** 2014. How malaria parasites avoid running out of ammo. PLoS Genet **10:**e1004878.
16. **Arthur, C., K. Watt, D. H. Nussey, J. M. Pemberton, J. G. Pilkington, J. S. Herman, Z. L. Timmons, D. N. Clements, and P. R. Scott.** 2014. Osteoarthritis of the temporo-mandibular joint in free-living Soay sheep on St Kilda. Vet J **203:**120-125.
17. **Asher, A. K., G. M. Santos, J. Evans, E. K. Dokubo, T. H. Lee, J. N. Martin, S. G. Deeks, L. H. Tobler, M. Busch, P. W. Hunt, and K. Page.** 2014. A closer look at hepatitis C clearance in HIV controllers: a response. Aids **28:**1241-1242.
18. **Atkinson, N. J., J. Witteveldt, D. J. Evans, and P. Simmonds.** 2014. The influence of CpG and UpA dinucleotide frequencies on RNA virus replication and characterization of the innate cellular pathways underlying virus attenuation and enhanced replication. Nucleic Acids Res **42:**4527-4545.

19. **Bachofen, C., D. M. Grant, K. Willoughby, R. N. Zadoks, M. P. Dagleish, and G. C. Russell.** 2014. Experimental infection of rabbits with bovine viral diarrhoea virus by a natural route of exposure. Vet Res **45:**34.
20. **Balic, A., C. Garcia-Morales, L. Vervelde, H. Gilhooley, A. Sherman, V. Garceau, M. W. Gutowska, D. W. Burt, P. Kaiser, D. A. Hume, and H. M. Sang.** 2014. Visualisation of chicken macrophages using transgenic reporter genes: insights into the development of the avian macrophage lineage. Development **141:**3255-3265.
21. **Balogun, E. O., D. K. Inaoka, T. Shiba, Y. Kido, C. Tsuge, T. Nara, T. Aoki, T. Honma, A. Tanaka, M. Inoue, S. Matsuoka, P. A. Michels, K. Kita, and S. Harada.** 2014. Molecular basis for the reverse reaction of African human trypanosomes glycerol kinase. Mol Microbiol **94:**1315-1329.
22. **Barlow, P. G., E. G. Findlay, S. M. Currie, and D. J. Davidson.** 2014. Antiviral potential of cathelicidins. Future Microbiol **9:**55-73.
23. **Barr, L. C., M. Brittan, A. C. Morris, D. F. McAuley, C. McCormack, A. M. Fletcher, H. Richardson, M. Connell, D. Patel, W. A. Wallace, A. G. Rossi, D. J. Davidson, L. Manson, M. Turner, N. Hirani, T. S. Walsh, N. H. Anderson, K. Dhaliwal, and A. J. Simpson.** 2014. Reply: The alveolar macrophage and acute respiratory distress syndrome: a silent actor? Am J Respir Crit Care Med **189:**500-501.
24. **Barria, M. A., A. Balachandran, M. Morita, T. Kitamoto, R. Barron, J. Manson, R. Knight, J. W. Ironside, and M. W. Head.** 2014. Molecular barriers to zoonotic transmission of prions. Emerg Infect Dis **20:**88-97.
25. **Barria, M. A., J. W. Ironside, and M. W. Head.** 2014. Exploring the zoonotic potential of animal prion diseases: In vivo and in vitro approaches. Prion **8**.
26. **Barros-Alvarez, X., A. J. Caceres, P. A. Michels, J. L. Concepcion, and W. Quinones.** 2014. The phosphoglycerate kinase isoenzymes have distinct roles in the regulation of carbohydrate metabolism in Trypanosoma cruzi. Exp Parasitol **143:**39-47.
27. **Barros-Alvarez, X., M. Gualdron-Lopez, H. Acosta, A. J. Caceres, M. A. Graminha, P. A. Michels, J. L. Concepcion, and W. Quinones.** 2014. Glycosomal targets for anti-trypanosomatid drug discovery. Curr Med Chem **21:**1679-1706.
28. **Bauer, M. P., P. H. Nibbering, I. R. Poxton, E. J. Kuijper, and J. T. van Dissel.** 2014. Humoral immune response as predictor of recurrence in Clostridium difficile infection. Clin Microbiol Infect **20:**1323-1328.
29. **Baumert, J., J. Huang, B. McKnight, M. Sabater-Lleal, M. Steri, A. Y. Chu, S. Trompet, L. M. Lopez, M. Fornage, et al.** 2014. No evidence for genome-wide interactions on plasma fibrinogen by smoking, alcohol consumption and body mass index: results from meta-analyses of 80,607 subjects. PLoS One **9:**e111156.
30. **Beale, R., H. Wise, A. Stuart, B. J. Ravenhill, P. Digard, and F. Randow.** 2014. A LC3-Interacting Motif in the Influenza A Virus M2 Protein Is Required to Subvert Autophagy and Maintain Virion Stability. Cell Host Microbe **15:**239-247.
31. **Beard, P. M., S. J. Griffiths, O. Gonzalez, I. R. Haga, T. Pechenick Jowers, D. K. Reynolds, J. Wildenhain, H. Tekotte, M. Auer, M. Tyers, P. Ghazal, R. Zimmer, and J. Haas.** 2014. A Loss of Function Analysis of Host Factors Influencing Vaccinia virus Replication by RNA Interference. PLoS One **9:**e98431.
32. **Beaumont, P. E., B. McHugh, E. Gwyer Findlay, A. Mackellar, K. J. Mackenzie, R. L. Gallo, J. R. Govan, A. J. Simpson, and D. J. Davidson.** 2014. Cathelicidin Host Defence Peptide Augments Clearance of Pulmonary Pseudomonas aeruginosa Infection by Its Influence on Neutrophil Function In Vivo. PLoS One **9:**e99029.
33. **Bedford, T., M. A. Suchard, P. Lemey, G. Dudas, V. Gregory, A. J. Hay, J. W. McCauley, C. A. Russell, D. J. Smith, and A. Rambaut.** 2014. Integrating influenza antigenic dynamics with molecular evolution. Elife **3:**e01914.
34. **Bedi, P., M. K. Sidhu, L. S. Donaldson, J. D. Chalmers, M. P. Smith, K. Turnbull, J. L. Pentland, J. Scott, and A. T. Hill.** 2014. A prospective cohort study of the use of domiciliary intravenous antibiotics in bronchiectasis. NPJ Prim Care Respir Med **24:**14090.
35. **Belluti, F., E. Uliassi, G. Veronesi, C. Bergamini, M. Kaiser, R. Brun, A. Viola, R. Fato, P. A. Michels, R. L. Krauth-Siegel, A. Cavalli, and M. L. Bolognesi.** 2014. Toward the Development of Dual-Targeted Glyceraldehyde-3-phosphate Dehydrogenase/Trypanothione Reductase Inhibitors against Trypanosoma brucei and Trypanosoma cruzi. ChemMedChem **9:**371-382.
36. **Benezech, C., S. Nayar, B. A. Finney, D. R. Withers, K. Lowe, G. E. Desanti, C. L. Marriott, S. P. Watson, J. H. Caamano, C. D. Buckley, and F. Barone.** 2014. CLEC-2 is required for development and maintenance of lymph nodes. Blood **123:**3200-3207.
37. **Berenos, C., P. A. Ellis, J. G. Pilkington, and J. M. Pemberton.** 2014. Estimating quantitative genetic parameters in wild populations: a comparison of pedigree and genomic approaches. Mol Ecol **23:**3434-3451.
38. **Bermingham, M. L., S. C. Bishop, J. A. Woolliams, R. Pong-Wong, A. R. Allen, S. H. McBride, J. J. Ryder, D. M. Wright, R. A. Skuce, S. W. McDowell, and E. J. Glass.** 2014. Genome-wide association study identifies novel loci associated with resistance to bovine tuberculosis. Heredity (Edinb) **112:**543-551.

39. **Bettridge, J. M., S. E. Lynch, M. C. Brena, K. Melese, T. Dessie, Z. G. Terfa, T. T. Desta, S. Rushton, O. Hanotte, P. Kaiser, P. Wigley, and R. M. Christley.** 2014. Infection-interactions in Ethiopian village chickens. Prev Vet Med **117:**358-366.
40. **Bielejec, F., P. Lemey, G. Baele, A. Rambaut, and M. A. Suchard.** 2014. Inferring heterogeneous evolutionary processes through time: from sequence substitution to phylogeography. Syst Biol **63:**493-504.
41. **Bielejec, F., P. Lemey, L. M. Carvalho, G. Baele, A. Rambaut, and M. A. Suchard.** 2014. piBUSS: a parallel BEAST/BEAGLE utility for sequence simulation under complex evolutionary scenarios. BMC Bioinformatics **15:**133.
42. **Blackburn, E. A., F. A. Fuad, H. P. Morgan, M. W. Nowicki, M. A. Wear, P. A. Michels, L. A. Fothergill-Gilmore, and M. D. Walkinshaw.** 2014. Trypanosomatid phosphoglycerate mutases have multiple conformational and oligomeric states. Biochem Biophys Res Commun **450:**936-941.
43. **Bolton, J. L., C. Hayward, N. Direk, J. G. Lewis, G. L. Hammond, L. A. Hill, A. Anderson, J. Huffman, J. F. Wilson, H. Campbell, I. et al.** 2014. Genome Wide Association Identifies Common Variants at the SERPINA6/SERPINA1 Locus Influencing Plasma Cortisol and Corticosteroid Binding Globulin. PLoS Genet **10:**e1004474.
44. **Bont, L., E. Baraldi, B. Fauroux, A. Greenough, T. Heikkinen, P. Manzoni, F. Martinon-Torres, H. Nair, and N. G. Papadopoulos.** 2014. RSV - still more questions than answers. Pediatr Infect Dis J **33:**1177-1179.
45. **Borges, A. H., J. D. Lundgren, A. Ridolfo, C. Katlama, F. Antunes, A. Grzeszczuk, A. Blaxhult, V. M. Mitsura, M. Doroana, M. Battegay, P. Gargalianos, and A. Mocroft.** 2014. Thrombocytopenia is associated with an increased risk of cancer during treated HIV disease. Aids **28:**2565-2571.
46. **Bouckaert, R., J. Heled, D. Kuhnert, T. Vaughan, C. H. Wu, D. Xie, M. A. Suchard, A. Rambaut, and A. J. Drummond.** 2014. BEAST 2: A Software Platform for Bayesian Evolutionary Analysis. PLoS Comput Biol **10:**e1003537.
47. **Bourke, C. D., N. Nausch, N. Rujeni, L. J. Appleby, F. Trottein, N. Midzi, T. Mduluza, and F. Mutapi.** 2014. Cytokine Responses to the Anti-schistosome Vaccine Candidate Antigen Glutathione-S-transferase Vary with Host Age and Are Boosted by Praziquantel Treatment. PLoS Negl Trop Dis **8:**e2846.
48. **Bradford, B. M., P. R. Crocker, and N. A. Mabbott.** 2014. Peripheral prion disease pathogenesis is unaltered in the absence of sialoadhesin (Siglec-1/CD169). Immunology **143:**120-129.
49. **Bradford, B. M., P. Piccardo, J. W. Ironside, and N. A. Mabbott.** 2014. Human prion diseases and the risk of their transmission during anatomical dissection. Clin Anat **27:**821-832.
50. **Bredenkamp, N., C. S. Nowell, and C. C. Blackburn.** 2014. Regeneration of the aged thymus by a single transcription factor. Development **141:**1627-1637.
51. **Bredenkamp, N., S. Ulyanchenko, K. E. O'Neill, N. R. Manley, H. J. Vaidya, and C. C. Blackburn.** 2014. An organized and functional thymus generated from FOXN1-reprogrammed fibroblasts. Nat Cell Biol **16:**902-908.
52. **Bridle, H., B. Miller, and M. P. Desmulliez.** 2014. Application of microfluidics in waterborne pathogen monitoring: A review. Water Res **55C:**256-271.
53. **Briggs, R., K. Templeton, and I. Fernando.** 2014. Comparing HIV viral load assays and frequency of low level virological rebound in clinical practice. Int J STD AIDS **25:**1029-1034.
54. **Brimacombe, K. R., M. J. Walsh, L. Liu, M. G. Vasquez-Valdivieso, H. P. Morgan, I. McNae, L. A. Fothergill-Gilmore, P. A. Michels, D. S. Auld, A. Simeonov, M. D. Walkinshaw, M. Shen, and M. B. Boxer.** 2014. Identification of ML251, a Potent Inhibitor of T. brucei and T. cruzi Phosphofructokinase. ACS Med Chem Lett **5:**12-17.
55. **Brittan, M., L. C. Barr, N. Anderson, A. Conway Morris, R. Duffin, J. A. Marwick, F. Rossi, S. Johnson, K. Dhaliwal, N. Hirani, A. G. Rossi, and A. J. Simpson.** 2014. Functional characterisation of human pulmonary monocyte-like cells in lipopolysaccharide-mediated acute lung inflammation. J Inflamm (Lond) **11:**9.
56. **Brown, K. L., and N. A. Mabbott.** 2014. Evidence of sub-clinical prion disease in aged mice following exposure to bovine spongiform encephalopathy. J Gen Virol **95:**231-243.
57. **Brown, T. I., D. S. Collie, D. J. Shaw, N. M. Rzechorzek, and J. M. Sallenave.** 2014. Sheep lung segmental delivery strategy demonstrates adenovirus priming of local lung responses to bacterial LPS and the role of elafin as a response modulator. PLoS One **9:**e107590.
58. **Bryson, K. J., A. A. Nash, and M. Norval.** 2014. Does vitamin D protect against respiratory viral infections? Epidemiol Infect **142:**1789-1801.
59. **Bull, T. J., C. Vrettou, R. Linedale, C. McGuinnes, S. Strain, J. McNair, S. C. Gilbert, and J. C. Hope.** 2014. Immunity, safety and protection of an Adenovirus 5 prime - Modified Vaccinia virus Ankara boost subunit vaccine against Mycobacterium avium subspecies paratuberculosis infection in calves. Vet Res **45:**112.

60. **Busin, V., F. Kenyon, T. Parkin, D. McBean, N. Laing, N. D. Sargison, and K. Ellis.** 2014. Production impact of a targeted selective treatment system based on liveweight gain in a commercial flock. Vet J **200:**248-252.
61. **Callaby, R., O. Hanotte, V. A. N. W. I. Conradie, H. Kiara, P. Toye, M. N. Mbole-Kariuki, A. Jennings, S. M. Thumbi, J. A. Coetzer, C. B. B. M. de, S. A. Knott, M. E. Woolhouse, and L. E. Kruuk.** 2014. Variation and covariation in strongyle infection in East African shorthorn zebu calves. Parasitology**:**1-13.
62. **Campbell, H., and H. Nair.** 2014. Humanitarian crises due to natural disasters and armed conflict. J R Coll Physicians Edinb **44:**216-217.
63. **Campopiano, D. J.** 2014. ACP-AasS You Like It. Chem Biol **21:**1257-1259.
64. **Canton, G. J., F. Katzer, S. W. Maley, P. M. Bartley, J. Benavides-Silvan, J. Palarea-Albaladejo, Y. Pang, S. H. Smith, M. Rocchi, D. Buxton, E. A. Innes, and F. Chianini.** 2014. Cytokine expression in the placenta of pregnant cattle after inoculation with Neospora caninum. Vet Immunol Immunopathol **161:**77-89.
65. **Canton, G. J., F. Katzer, S. W. Maley, P. M. Bartley, J. Benavides-Silvan, J. Palarea-Albaladejo, Y. Pang, S. H. Smith, M. S. Rocchi, D. Buxton, E. A. Innes, and F. Chianini.** 2014. Inflammatory infiltration into placentas of Neospora caninum challenged cattle correlates with clinical outcome of pregnancy. Vet Res **45:**11.
66. **Cape, E., R. J. Hall, B. C. van Munster, A. de Vries, S. E. Howie, A. Pearson, S. D. Middleton, F. Gillies, I. R. Armstrong, T. O. White, C. Cunningham, S. E. de Rooij, and A. M. MacLullich.** 2014. Cerebrospinal fluid markers of neuroinflammation in delirium: A role for interleukin-1beta in delirium after hip fracture. J Psychosom Res **77:**219-225.
67. **Cardenas-Maestre, J. M., A. M. Perez-Lopez, M. Bradley, and R. M. Sanchez-Martin.** 2014. Microsphere-Based Intracellular Sensing of Caspase-3/7 in Apoptotic Living Cells. Macromol Biosci **14:**923-928.
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69. **Casaravilla, C., A. Pittini, D. Ruckerl, P. I. Seoane, S. J. Jenkins, A. S. MacDonald, A. M. Ferreira, J. E. Allen, and A. Diaz.** 2014. Unconventional maturation of dendritic cells induced by particles from the laminated layer of larval Echinococcus granulosus. Infect Immun **82:**3164-3176.
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72. **Chalmers, J. D., P. Goeminne, S. Aliberti, M. J. McDonnell, S. Lonni, J. Davidson, L. Poppelwell, W. Salih, A. Pesci, L. J. Dupont, T. C. Fardon, A. De Soyza, and A. T. Hill.** 2014. The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med **189:**576-585.
73. **Chandra, A., D. Mitry, A. Wright, H. Campbell, and D. G. Charteris.** 2014. Genome-wide association studies: applications and insights gained in Ophthalmology. Eye (Lond) **28:**1066-1079.
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Appendix III: Selected national and international press coverage of *Edinburgh Infectious Diseases* in 2014

News story	Coverage
Dr Richard Allen develops drug to address problem of antibiotic resistance	INDIA INFO LINE NEWS SERVICE, PRESS TRUST OF INDIA, BUSINESS STANDARD (India) MEDICAL XPRESS, PHYSORG.COM (USA), EDINBURGH EVENING NEWS
Edinburgh team led by **Prof Clare Blackburn** successfully regenerated a thymus in a mouse	**BBC NEWS**, THE SCOTSMAN, THE HERALD, EDINBURGH EVENING NEWS, SCOTTISH DAILY MAIL, BUSINESS STANDARD, THE ECONOMIST MRC, YAHOO CANADA, RADIO CANADA (Canada), LINCOLN DAILY NEWS, NANOPATENTS AND INNOVATIONS, MEDICAL DAILY , MEDICAL EXPRESS, INTERNATIONAL BUSINESS TIMES, THE DAILY BEAST, THE VERGE, WOMENS HEALTH, POPULAR SCIENCE, PHYS ORG, SCIENCE DAILY, GIZMODO (USA), REUTERS INDIA, ASIAN NEWS INTERNATIONAL, BUSINESS STANDARD, HEALTH DAILY STANDARD, WEBINDIA123, FINANCIAL EXPRESS (India), EUROPA PRESS, REUTERS SPAIN, IAINFORACIAN, LA VANGUARDIA, INTERBUSCA (Spain), ESPRESSO (Ecuador), LA TERCI, LA TERCERA, EMOL.COM (Chile), PAKISTAN OBSERVER, THE DAILY POST (Pakistan), EL IMPARCIAL, FRONTERA, TABASCO HOY, EL MEXICANA EL INFORMADOR, UNIVERSAL NEWS SERVICE, EL UNIVERSAL (Mexico), IRISH INDEPDENDENT (Ireland), PRESS TV, IRAN DAILY, FARS NEWS AGENCY (Iran), THE TIMES, PRETORIA NEWS, THE MERCURY, HEALTH 24, CAPE TIMES (South Africa), FUTURA SCIENCES, INFO HIGH TECH (France), PHILLIPINES NEWS AGENCY (Philippines), GIZMAG (Australia), YAM NEWS, UNITED DAILY NEWS, CNA (Taiwan), SHANGHAI DAILY, YAM NEWS, XINHUA, SINA, CHINA NET INTERNATIONAL, GLOBAL TIMES, SOUND OF HOPE, XINJIANG NEWS, CHONGQUING EVENING NEWS, SOHU, HONG KONG NEWS NETWORK, YANGCHENG EVENING NEWS, SCIENCE NET, GUANGXI BAGUI NET, (China), DAILY THE PAK BANKER (Pakistan), LA BRUJULA VERDE (Spain), FINANCIAL EXPRESS (India), PHYS ORG, MEDICAL DESIGN ONLINE (USA), LE NOUVAL OBSERVATEUR (France), CHINA SCIENCE AND TECHNOLOGY NET, CHINA PHARMACEUTICAL NEWS (China), DAILY TELEGRAPH, THE INDEPENDENT, DAILY MAIL, THE GUARDIAN, THE TIMES, THE SUN, DAILY EXPRESS, DAILY RECORD, THE SCOTSMAN, TH HERALD, DAILY MIRROR, YORKSHIRE POST, EDINBURGH EVENING NEWS, GLASGOW EVENING TIMES,BBC ONLINE, BBC RADIO 4, BBC RADIO SCOTLAND, THE AUSTRALIAN, SCIENCE ALERT, THE ADVERTISER (Australia), FIJI BROADCASTING CORP (Fiji), INDO-ASIAN NEWS SERVICE, PRESS TRUST OF INDIA, THE TIMES OF INDIA, THE STATESMEN (India), VIVA, JURNAL NASIONAL (Indonesia), REGINA LEADER POST, SUN NEWS NETWORK, OTTAWA CITIZEN, EDMONTON JOURNAL, TVA NOUVELLES (Canada), IRISH DAILY MAIL, IRISH TIMES (Ireland), MEDICAL DAILY, WALL STREET JOURNAL VIDEO, MEDICAL DESIGN ONLINE (USA), INGERIOREN (Denmark), EL COMOMBIANO EL ESPECTADOR (Colombia), INFOBAE DIARIO (Argentina), INNOVATIONS REPORT (Germany), TARANAKI DAILY NEWS (New Zealand), L'HUMANITE (France), CORREA DEL ORRINOCO (Venezuela), THE PATRIOT (Pakistan), EL DEBER (Bolivia), THE STANDARD (Kenya), ORIENTAL DAILY NEWS, SIN CHEW DAILY (Malaysia), XINHUA, CHINA TAIWAN.NET, GLOBAL TIMES, SEE HUA, LIBERTY TIMES, CHINA WOMAN, GUANGZHOU DAILY, CHINA.COM, CHINA NATIONAL RADIO, GUANGMING.NET, DAILY GANSU, CHINA ECONOMIC NET, CHONGQUING EVENING NEWS, CHINA TAIWAN NET, GUANGXI BAGUI NET, CHINA ECONOMIC TIMES (China), THE SUN, ORIENTAL DAILY NEWS, APPLE DAILY (Hong Kong), REMEDIUM.RU (Russia) HEALTHCARE PURCHASING NEWS, VOICE OF AMERICA, THE DISCOVERY

	CHANNEL (USA) YAHOO! FRANCE, FUTURA-SCIENCES (France) EL ESPECTADOR (Colombia) THE DAILY POST (N Zealand) GIZMAG (Australia) ONLINE ATHENS (Greece) MAIL & GUARDIAN (S Africa) LA REPUBLICA (Uruguay) WEB OF SCIENCE (China), LA REPUBLICA (Uruguay), DIGITAL JOURNAL (Canada)
Dr Sam Brown leads study into how bacteria "talk" to each other	BBC NEWS, TIMES OF MALTA, IRISH EXAMINER, TIMES, SCOTTISH DAILY MAIL, HERALD, SCOTSMAN, NOTTINGHAM POST, IRISH EXAMINER, IRISH INDEPENDENT
Dr David Cavanagh takes step towards malaria vaccine	MEDICAL EXPRESS, SCIENCE DAILY (US), AGENZIA ITALIA (Italy), DAILY MAIL, DAILY RECORD, THE HERALD, THE SCOTSMAN, EDINBURGH EVENING NEWS, PHARMA MIRROR (Bangladesh)
Prof Ross Fitzgerald says whole-genome sequencing can aid infection control in hospitals	THE GUARDIAN
Prof Peter Ghazal finds new-born babies' genetic code can send an infection distress signal	THE SCOTSMAN, THE TIMES, DAILY EXPRESS, METRO, INNOVATIONS REPORT (Germany) PHYSORG.COM, MEDICAL XPRESS (USA) INDO-ASIAN NEWS SERVICE, BUSINESS STANDARD, WEB INDIA123.COM, NET INDIA123.COM, YAHOO! INDIA (India) YAHOO! SINGAPORE (Singapore), SCOTTISH TELEVISION
Prof Liz Glass uncovers genetic clues that might lead to cattle that are more resistant to TB	AGWEB (US), MEDICAL EXPRESS, SCIENCE DAILY (US), THE HERALD, THE SCOTSMAN, ABERDEEN PRESS AND JOURNAL. THE CONVERSATION (Australia)
Prof Jurgen Haas helps explain spread of herpes simplex virus	DAILY MAIL
Prof James Ironside hails breakthrough in bid to detect CJD in humans	THE HERALD, THE SCOTSMAN, THE METRO, THE DAILY RECORD, THE SCOTTISH DAILY MAIL, THE YORKSHIRE POST, INFECTION CONTROL TODAY, NEWSWISE, MEDICAL XPRESS (USA), EDINBURGH EVENING NEWS, WEBNEWSWIRE (India), THE CONVERSATION (Australia)
Dr Liam Keegan finds new hope for sufferers of autoimmune diseases in gene research	THE HERALD, EDINBURGH EVENING NEWS
Dr Luke McNally finds that bacteria with lots of genes can spread infection more easily	BBC RADIO SCOTLAND, EDINBURGH EVENING NEWS, DAILY EXPRESS
Dr Henry McSorley finds parasites could curb lung damage in asthmatics	DAILY MAIL, EDINBURGH EVENING NEWS, LA TRIBUNA (Spain)
Study led by **Dr Harish Nair** finds pneumonia risk far higher for HIV-positive children	MEDICAL XPRESS, SCIENCE NEWSLINE, SCIENCE DAILY, EUREKALERT, MEDICAL EXPRESS, JERSEY TRIBUNE, UNIVERSITY HERALD, SCIENCE DAILY, SCIENCE NEWSLINE (USA), TIMES HIGHER EDUCATION SUPPLEMENT, VOICE OF AMERICA (USA), BUSINESS TO COMMUNITY (USA), THE SCOTSMAN, NEWS MEDICAL NET (Australia)
Prof Andrew Rambaut finds evolutionary tree of flu viruses can help assess health risks	SPEKTRUM DER WISSENSCHAFT (Germany)
Prof Andrew Rambaut finds those with strongest immune system were at greatest risk in 1918 flu pandemic	NEW YORK TIMES (USA)
Science paper co-authored by **Prof Andrew Rambuat** and **Gytis Dudas** on Ebola virus has input from Edinburgh researchers	SINA NEWS, CRI ONLINE, CHINA TAIWAN NETWORK, CHINA NETWORK NEWS, CHINA.COM.CN, CHINA YOUTH DAILY, TEN CENT NEWS, CHINA INTERNATIONAL CENTER NETWORK, PEOPLE'S DAILY, GLOBAL TIMES, SOUND OF HOPE (China), EMAXHEALTH (USA)
Study by **Prof Adriano Rossi** offers hope of improved treatment for lung diseases	THE HERALD, METRO, PRESS AND JOURNAL, EDINBURGH EVENING NEWS, SPECIAL BROADCASTING SERVICE (Australia), TIMES OF MALTA (Malta)
Prof Paul Sharp traces common form of human malaria to African apes	TIMES OF INDIA, BBC RADIO SCOTLAND, EDINBURGH EVENING NEWS (UK), NEWSWISE, SCIENCE DAILY, USAG.NET, TERRA DAILY (US), THE TIMES OF INDIA, MED INDIA (India)
Roslin Institute's **Prof Peter Simmonds** co-authors study into diseases carried by rats of New York	INFECTION CONTROL TODAY, BIOSPACE (USA)
Prof James Smith writes about sleeping sickness in Uganda and risk posed by Ebola	THE CONVERSATION (Australia)

Dr Hilary Snaith says University can play a key role in solving the current Ebola crisis	THE SCOTSMAN
Dr Devi Sridhar voices concern isolated Ebola cases returning to UK will stop volunteers to affected countries	THE SUNDAY HERALD
Dr Pedro Vale cautiously welcomes alternatives to antibiotics	THE TIMES OF INDIA, THE HERALD, THE SCOTSMAN, TOP NEWS.IN (India), THE TIMES OF INDIA, INDIA INFOLINE NEWS SERVICE, INDO ASIAN NEWS SERVICE, BUSINESS STANDARD, NET INDIA 123.COM, YAHOO! INDIA, APN NEWS, INDIA EDUCATION DIARY, POPBUZZ.COM, EDUCATIONJUNGAL.COM, THE ASIAN AGE (India) PHARMACY CHOICE (USA) YAHOO! MALAYSIA
Prof Malcolm Walkinshaw leads bid with Selcia to develop sleeping sickness drug	PHARMACEUTICAL BUSINESS REVIEW, NEWS-MEDICAL.NET, THE HERALD, EDINBURGH EVENING NEWS
Prof Malcolm Walkinshaw discovers enzyme that could be targeted to block infection	THE TIMES, DAILY RECORD
Dr Melissa Ward finds some MRSA bugs linked with livestock in hospitals	BBC NEWS, THE TIMES, THE SCOTSMAN, THE HERALD, DAILY MAIL, DAILY EXPRESS, DAILY STAR, COURIER AND ADVERTISER, INFECTION CONTROL TODAY, MEDICAL XPRESS, PHYSORG.COM, EXAMINER, SCIENCE DAILY, SCIENCE 2.0, US NEWS & WORLD REPORT, HEALTH DAY, MEDBROADCAST, INTELIHEALTH, KLFY, WOCTV, KCEN TV NBC 6, FOOD SAFETY NEWS, WLNS, WSFA, NEWS CHANNEL 10, UNIVISION.COM, MEDICINE NET, EMEDICINE HEALTH (USA), BIOLOGY NEWS NET (Canada), FOREIGNAFFAIRS.CO.NZ (New Zealand), DIGITAL JOURNAL (Canada), HERENCIAGENETICAYENFERMEDAD (Argentina), FLEISCHWIRTSCHAFT (Germany), PHARMACY CHOICE (USA)
Prof Sue Welburn leads study of neglected zoonotic diseases.	PHYSORG.COM, SCIENCE DAILY, EXAMINER, INFECTION CONTROL TODAY, TERRA DAILY (USA) MED INDIA, INDO ASIAN NEWS SERVICE, BUSINESS STANDARD, NET INDIA123.COM, YAHOO! INDIA (India) THE PATRIOT (Pakistan).
Prof Mark Woolhouse warns of growing problem of antibiotic resistance	THE OBSERVER, INDO ASIAN NEWS SERVICE, PRESS TRUST OF INDIA, DOMAIN-B, THE HINDU (India), INGENIOREN (Denmark), CANADIAN BROADCASTING CORP (Canada), INTERBUSCA (Spain), NU.NL (Netherlands), CHINA SCIENCE AND TECHNOLOGY NETWORK, SOHU (China), BBC RADIO 4 'TODAY PROGRAMME', BBC SCOTLAND 'GOOD MORNING SCOTLAND', STV NEWS, INDEPENDENT, REUTERS, PRESS ASSOCIATION, IANS (INDIA), ASIAN NEWS INTERNATIONAL, TIMES, THE GUARDIAN, TELEGRAPH.CO.UK , INDEPENDENT, HERALD SCOTLAND, SCOTSMAN, STV NEWS, HUFFINGTON POST, FORBES (US), SALON, THE EDINBURGH REPORTER, FARMERS GUARDIAN, PHARMA TIMES, CANOE, VIEWS TIMES, INTERNATIONAL BUSINESS TIMES UK, THEHEALTHSITE MEDICAL XPRESS, WORLDBULLETIN.NET, BUSINESS INSIDER, TECHSONIA, REDORBIT, NEWS-MEDICAL.NET, YAHOO NEWS, SCIENCE CODEX, BUSINESS INSIDER AUSTRALIA, THE GLOBE AND MAIL (CANADA), CBC.CA (CANADA), TORONTO SUN (CANADA), VANCOUVER DESI (CANADA), THE JAPAN TIMES, BUSINESS STANDARD (INDIA), ECONOMIC TIMES (INDIA), ZEE NEWS (INDIA), MIZO NEWS (INDIA), FREE PRESS JOURNAL (INDIA), INDIA EDUCATION DIARY, DELHI DAILY NEWS (INDIA), NEWSTRACK INDIA, TIMES OF MALTA, NEW ZEALAND HERALD, NEWS24 (SOUTH AFRICA), BALTIMORE SUN (USA), CHICAGO TRIBUNE (USA), EAST IDAHO NEWS (USA), NEWSROOM AMERICA (USA), GLOBALPOST (USA), KFGO-22 (USA), KDAL-22 (USA), KMBZ (USA), 610KVNU (USA), WKZO-22 (USA), WHBL SHEBOYGAN (USA), WTAQ-22 (USA)
US antibiotic discovery exciting and vital, says **Prof Mark Woolhouse**	BBC NEWS, THE INDEPENDENT, THE DAILY TELEGRAPH, THE TIMES
Study by **Profs Mark Woolhouse** and **Jeremy Farrar** explores antibiotic development and licensing.	SACHSISCHE ZEITUNG (Germany), GENERAL ANZEIGER (Germany)

Appendix V: *Edinburgh Infectious Diseases* news featured on our website (hyperlinked – http://www.eid.ed.ac.uk/newsdb)

1. Researchers at the Roslin and Moredun Research Institutes have received £2.7M boost to improve the health of livestock around the world
2. Biological scientists at the University of Edinburgh secure £25.7m to create powerhouse of research
3. On World Tuberculosis Day: Why you need to know your enemy when it comes to eradicating TB
4. Infectious Diseases Honours students recently invited David Denning, prominent expert in fungal infections, to visit them in Edinburgh
5. Cattle parasite study from Centre for Immunity, Infection and Evolution, suggests new ways to combat infectious diseases
6. Children under five living in sub-Saharan Africa are at greater risk than older children of developing a long-term parasitic disease
7. Soil study led by Edinburgh researchers helps unearth vital clues in search for infection treatments
8. Three members of Edinburgh Infectious Diseases elected to the Royal Society of Edinburgh
9. Edinburgh study shows that garlic extract could help cystic fibrosis patients fight infection
10. New study from the Roslin Institute shows how easy it can be for bacteria to jump species
11. Edinburgh Infectious Diseases members at Edinburgh Napier University win grant to investigate novel drugs to treat Rhinovirus infection
12. Recent study shows that co-infected plants cause more severe epidemics
13. Crohn's study at University of Edinburgh seeks to find causes of the disease
14. New micro-residency teaming artists and researchers in infectious diseases starts at the University of Edinburgh
15. Research at University of Edinburgh shows that infection risk could be cut with new coatings for surgical devices
16. Pneumonia risk far higher for HIV-positive children, finds new study from Centre for Population Health Sciences
17. Research rankings reaffirm Edinburgh's place as global leader - now ranked 4th in research power across UK
18. Many congratulations to all winners of the Recognising Excellence Awards in the School of Biological Sciences!
19. Research Professional has featured Malcolm Walksinshaw: "Top PI - Following the Opportunity"

20. The BBSRC launches the UK Veterinary Vaccinology Network to help fight infectious diseases in animals

21. Researchers at the MRC Human Genetics Unit discover gene mutation that helps explain some autoimmune diseases

22. New paper from Amy Buck's and Rick Maizels' labs shows how parasites use subterfuge to manipulate the immune system of their hosts

23. Understanding the long-term consequence of deworming programmes - by Francisca Mutapi

24. New study from researchers in Edinburgh Infectious Diseases shows farm animal link to hospital MRSA bugs

25. Work on Ebola from Andrew Rambaut and Gytis Dudas (Inst. Evolutionary Biology) featured in Scotsman article

26. A new study from the University of Edinburgh into the bacterium Escherichia coli suggests that bacteria are hard-wired for survival

27. Animal experts in Edinburgh aim to keep Europe safe from infection threat

28. Two Edinburgh students report back on their experiences at Leiden University Medical Centre in summer 2014

29. An enzyme found in all living things could hold the key to tackling deadly diseases caused by parasites, such as sleeping sickness, a study suggests.

30. Edinburgh researchers help analyse Ebola genome sequences from current outbreak in West Africa

31. Researchers in the Division of Pathway Medicine and the Roslin Institute call for better understanding of the genetic basis of susceptibility to infectious disease

32. Edinburgh Infectious Diseases: September 2014 Lab of the Month - The PROTEUS Project

33. Many congratulations to Pedro Vale, who has been made a Branco Weiss Fellow by Society in Science

34. Researchers from the MRC Centre for Regenerative Medicine in Edinburgh are first to grow organ in animal from cells created in lab

35. Newborns' genetic code sends infection distress signal, finds new study from Division of Pathway Medicine

36. CJD urine test could be effective screening tool, shows study carried out in conjuction with University of Edinburgh

37. New study from University of Edinburgh shows that social networking is key to helping bugs spread

38. Tropical farmers' plight is focus of animal research initiative at Easter Bush campus

39. World Hepatitis Day 28 July 2014 – Hepatitis E virus - an emerging infection in Scotland?

40. Professor Sarah Reece - many congratulations on the award of a Chair in Evolutionary Parasitology!

41. Congratulations to Vincenzo Lorusso on award of prestigious travel grant from Society for Tropical Veterinary Medicine

42. "Bugs and Bones" go to the Edinburgh International Science Festival

43. Julie Fitzpatrick, Director of Moredun Research Institute and member of Edinburgh Infectious Diseases strategic board, awarded OBE

44. Researchers associated with the Edinburgh-based ICONZ project have three papers in the May edition of PLOS NTD

45. Mutapi lab featured in newsletter from African Paediatric Infectious Diseases Society

46. Report on productive Edinburgh workshop exploring the interface between communicable and non-communicable diseases

47. Successful Edinburgh Infectious Diseases symposium 2014 held on 21 May

48. Many congratulations to Peter Keightley, FRS, Institute of Evolutionary Biology, on his recent election to Fellowship of the Royal Society

49. Ker Memorial Prize for best PhD thesis in infectious diseases awarded to Chris Lucas

50. Rambukkana leprosy paper is one of Cell's "Best of 2013"

51. New synthetic biology research facility in the School of Biological Sciences at the University of Edinburgh receives £1.8 M from the BBSRC

52. New study from Edinburgh researchers in the Lancet shows statins could bring cough relief for lung disease patients

53. Team from Edinburgh Infectious Diseases take the "Understanding Bilharzia Programme" to school children in Zimbabwe

54. New class of drug could curb antibiotic resistance, new study suggests

55. New paper from Amy Pedersen (IEB) shows that parasites in humans influence each other via shared food sources

56. Interpreting bacteria's complex language could aid infection fight

57. 5 members of Edinburgh Infectious Diseases elected as Fellows of the Royal Society of Edinburgh

58. New paper in Nature from Andrew Rambaut (Inst. Evolutionary Biology) that reconstructs the evolutionary tree of influenza viruses

59. New study in Nature Communications shows that common form of malaria originated in Africa

60. Professor Alex Rowe, Institute of Immunology and Infection Research, wins C.A. Wright Memorial Medal

61. Researchers from Edinburgh Infectious Diseases have made vital steps forward in malaria vaccine development that pave way for protective therapy

62. Steven Spoel in the Institute of Molecular Plant Sciences awarded the Bayer Prize for Excellence

63. Genetic clues to TB-resistant cattle from researchers at the Roslin Institute

64. £4m investment secured for Edinburgh Molecular Imaging

65. £2.5 M joint initiative between the University of Edinburgh and Selcia to develop new drugs to target sleeping sickness

66. Edinburgh Infectious Diseases members win awards in NC3Rs CRACK IT Challenges to reduce use of animals in research

67. Global Health Academy, University of Edinburgh recognised by Ugandan government for contribution to eliminating sleeping sickness

68. Drug alternatives to antibiotics may not be perfect, study shows

69. Continued funding of Centre for Translational and Chemical Biology facilities by Wellcome Trust

70. New MRC grant awarded to Jurgen Schwarze, Rick Maizels and Donald Davidson to study helminth induced antiviral immunity to RSV

71. Many congratulations to Edinburgh researchers in the New Years Honours list!

Summaries of REF2014 Impact Case Studies

- Beast: Understanding the spread of global pandemics
- Bovine neonatal pancytopenia: a new disease of calves
- Breeding salmon for resistance to infectious pancreatic necrosis
- Breeding a scrapie resistant international sheep flock
- Combatting neglected tropical diseases – Schistosomiasis
- Controlling Tuberculosis in South East Asia
- GM chickens: therapeutics production and diseases resistance
- Testing International blood donations for malaria

TESTING INTERNATIONAL BLOOD DONATIONS FOR MALARIA

Malaria is one of the world's most prevalent diseases, affecting over 200 million people and is a major cause of morbidity and mortality. According to WHO, in 2013, there were 104 countries in which malaria was considered endemic. Globally, an estimated 3.4 billion people are at risk of malaria and WHO estimates that in 2012 there were 207 million cases of malaria and 627,000 deaths. Most cases (80%) and deaths (90%) occurred in Africa and most deaths (77%) were in children under 5 years of age (WHO, World Malaria Report 2013).

Malaria is caused by Plasmodium protozoan parasites. There are four species of Plasmodium causing human malaria: *P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*. These parasites are injected into the human bloodstream by the bite of an infected female Anopheles mosquito. Direct transmission from one human to another can also be caused via the transfusion of infected blood. Of the four species, *P. falciparum* is the most common and virulent strain, causing most malaria-related deaths worldwide. *P. vivax* is a particular problem in South-east Asia and South America.

TRAVEL-RELATED MALARIA IN THE UK

The UK has the highest incidence of travel-related malaria compared to other non-endemic countries; several thousand cases are imported into the UK every year. This constitutes an on-going risk of transfusion-transmitted malaria. Because of this, most blood transfusion services have a policy of deferring 'at risk' donors. In 2002 approximately 3% of all donations in England and Wales were lost as a result of the lengthy deferral period of malaria-risk blood donors, and led to challenges in maintaining a sufficient blood supply.

In 2001 researchers at the University of Edinburgh started working with Newmarket Laboratories Ltd to develop a screening assay that would be sensitive enough to identify all infected donations and have high specificity. It also had to be low cost and straightforward to perform routinely in the laboratory

TESTING FOR MALARIA IN ALL BLOOD DONATIONS ACROSS THE UK

Work carried out in Jana McBride's and David Cavanagh's labs during the 1990s identified four particular antigens from Plasmodium that led to production of malaria-specific antibodies in infected people – 2 from each of the MSP-1 and MSP-2 proteins. McBride and Cavanagh demonstrated that detection of antibodies against MSP-1 and MSP-2 could be used be used in a screening assay to reliably identify malaria-positive blood donations.

The new Malaria Enzyme ImmunoAssay (EIA) developed by Newmarket Laboratories detects all four human malaria strains, and is highly specific and sensitive (98%) for P. falciparum and P. vivax. Following successful trials of the assay at the English National Transfusion Microbiology Reference Laboratory in 2004, all blood donations in England and Wales are been screened using the Malaria EIA. It is also in use as the primary screening assay in Scotland and in several other European countries and was adopted by Australia and New Zealand in 2005.

WORLD-WIDE IMPACT OF MALARIA TEST

Development of this new test has had significant ongoing impact: between 2008-13 in the UK alone more than 345,000 blood donations were retained by the early re-admittance of donors – approximately 3% of all donations made. Use of the assay in Australia and New Zealand has led to the clearance of 250,000 donations during the same period.

Impact on commerce:

Since July 2013 Trinity Biotech has marketed the Malaria EIA worldwide, with ongoing sales of over 2.5 million assays since 2008.

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THE UNIVERSITY of EDINBURGH

BOVINE NEONATAL PANCYTOPENIA: A NEW DISEASE OF CALVES

Bovine Neonatal Pancytopenia (BNP), a newly recognised disease of calves, is caused by antibodies in the cow's first-milk (colostrum) which damage the calf's bone marrow when it suckles. The harmful alloantibodies are induced in the cow after vaccination with a particular vaccine (Pregsure BVD).

It was scientists at the University of Edinburgh and SRUC who were the first to describe this unexplained haemorrhagic disease of calves, with profound depletion of white blood cells and platelets. Our subsequent research enabled recognition of BNP as a truly novel disease and characterised the clinical, haematological and pathological findings.

While the numbers of cases of BNP on each farm is usually small, most affected calves die, with some farms loosing up to 5% of their calves. Between 2009 and 2010 more than 4,500 cases were confirmed across Europe, and the disease has also been seen in New Zealand. Our recent studies have suggested many more calves may be affected by a milder form of the condition.

EASTER BUSH RESEARCH CONSORTIUM

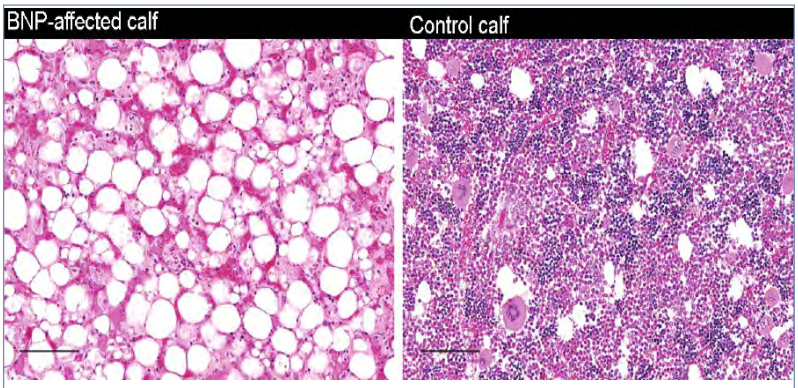
The Easter Bush Research Consortium (EBRC) brings Animal Sciences researchers from the University of Edinburgh's Roslin Institute and Royal (Dick) School of Veterinary Studies together with counterparts from Scotland's Rural College (SRUC) and the Moredun Research Institute. In collaboration teams from all EBRC organisations identified BNP as a new disease entity, elucidated the cause and developed strategies to reduce the incidence. The outcome was that the vaccine associated with emergence of BNP was withdrawn from sale.

BBSRC bioscience for the future

EXCELLENCE WITH IMPACT

ROSLIN

W ITHDRAWL OF BVD VACCINE AND INCREASING MONITORING



In BNP the calf's bone marrow is damaged (left), compared to a normal calf (right)

Early observations suggested a role for colostrum in the development of BNP and research at the University of Edinburgh and SRUC demonstrated that the disease could be prevented by colostrum substitution. These findings were subsequently confirmed by an experimental feeding trial conducted in collaboration with the Moredun Research Institute.

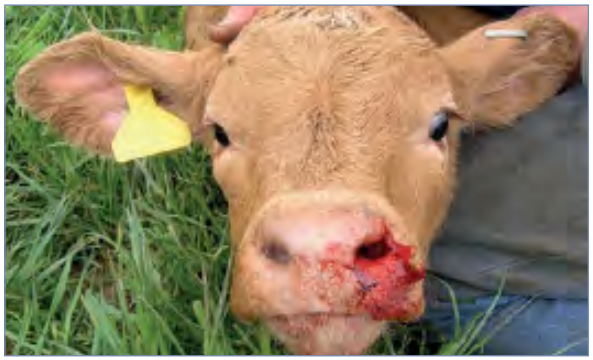
Subsequent studies demonstrated that the harmful alloantibodies produced by vaccinated cows react with the proteins from the cell line used to manufacture Pregsure vaccine. An association between BNP and Pregsure was also confirmed by a Defra epidemiological study, with input from the University of Edinburgh. On-going work at Roslin has offered insight into the exact nature of the problem with this particular vaccine, and provided a means to test future vaccines to ensure that they don't cause similar problems.

The immediate impact of this research was the acknowledgment by Pfizer Animal Health (now Zoetis) of the connection between BNP and vaccination of cows with Pregsure. This led to the precautionary withdrawal of the vaccine from Europe in 2010 and the retraction of market authorisation by the European Medicines Authority. Despite this, cases of BNP continue to be seen in calves born to dams that have been historically vaccinated. However, even with increased awareness of the disease, the number of cases diagnosed at post-mortem by SRUC fell by 42% from 2012 to 2013, suggesting that the withdrawal of Pregsure vaccine will gradually reduce cases of BNP.

PREVENTION THROUGH COMMUNICATION

Rapid transfer of information about the clinical features of the disease to vets and farmers allowed prompt recognition and investigation of cases, which helped investigations into the cause. Results contributed to the Defra BNP working group which generated a case definition for the disease that was used in further large-scale epidemiological studies.

Our finding that BNP can be prevented by colostrum substitution was rapidly disseminated to the veterinary profession and farming community which helped to prevent many further cases of the disease.



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THE UNIVERSITY of EDINBURGH

BREEDING A SCRAPIE RESISTANT INTERNATIONAL SHEEP FLOCK

Scrapie is a transmissible spongiform encephalopathy (TSE) of sheep and goats. It is a disease of considerable economic consequence to the small ruminant farming industry. In the EU, scrapie is a notifiable disease with affected farms facing severe trading restrictions and loss of animals. Scrapie is also a listed disease in the OIE Terrestrial Animal Health Code (2008) and as such affects wider international trade.

Selection of sheep for classical scrapie resistance became a possibility after pioneering work by Professor Nora Hunter and Dr Wilfred Goldmann, of the University of Edinburgh's Roslin Institute, demonstrated strong association between prion protein (PrP) genotype (PRNP) and scrapie susceptibility. Extended linkage information and epidemiological studies consolidated this association for natural scrapie outbreaks.

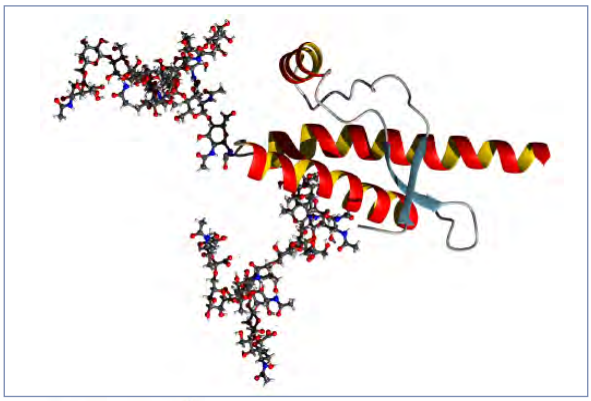
They showed that sheep with PRNP genotype VRQ/VRQ are highly susceptible to classical scrapie, whereas ARR/ARR animals are resistant.

The findings led directly to the implementation of the UK National Scrapie Plan, which ran from 2001 to 2009 and to similar programmes throughout the EU. These strategies were implemented with the twin aims of controlling classical scrapie and protecting the consumer from the exposure to BSE via sheep meat, should the national flock have become infected.

IMPACT ON THE ECONOMY

UK sheep meat exports are worth >£380million (2011 figures). Breeding for resistance to scrapie and BSE, and the fact that it was being carried out, undoubtedly protected the sheep industry from similar damage to that inflicted by BSE on cattle and the UK economy. WHO estimates US$6 billion losses to the UK and in addition, EU paid out 4.7 billion euros in control measures for cattle BSE.

In June 2013, the USDA followed the example of UK and the EU and implemented a Scrapie Free Flock Certification Program.



IMPROVING SHEEP WELFARE THROUGH GENETIC SELECTION

The National Scrapie Plan, funded by the UK government, provided free genotyping of 1.8 million sheep in 11,000 flocks in an effort to control all TSEs. Sheep breeders both within and outside the EU (Directive 91/68/EEC) require genotyping and health certificates in order to trade their sheep (OIE Terrestrial Animal Health Code, 2008). Trade in affected animals or animals coming from a flock known to have had scrapie in the last two years is prohibited.

Selection for TSE resistance by PRNP genotyping has reduced the reported incidence of scrapie in sheep as a result of profound impact on the genetic structure of the entire UK sheep industry: between 2002 and 2006 the frequency of the susceptible VRQ allele decreased in ram lambs by 60% and the frequency of the ARR allele rose by 37% and as a direct result, the reported prevalence of sheep with scrapie has also decreased from 0.22% in 2003 to 0.04% in 2008. Voluntary PRNP genotyping continues, through the industry-funded Scrapie Monitoring Scheme (since January 2009), which issues certificates of sheep genotype for trading purposes.

Sheep welfare has been improved by selection against PRNP genotypes linked to susceptibility to scrapie and subsequent reduction in incidence of disease. There is under-reporting of scrapie but nevertheless, Defra statistics indicate over 200 classical scrapie sheep were reported to them in 2002, and three in 2011.

Our work that established the genetic basis of scrapie resistance has ensured continuous maintenance of the UK (and international) sheep flocks in the face of potential disease outbreaks.

SCRAPIE RESISTANT GOATS

Based on the success in the reduction of sheep scrapie following the implementation of the various sheep breeding strategies, EU and UK research effort in ruminant TSEs since 2006 has focused on goat scrapie genetics. This has led recently to the discovery of new resistant goat PRNP alleles (e.g. IRK), which are currently being tested in collaboration with the goat industry for their potential in breeding programs on commercial farms. Dr Goldmann is a member of the EU (UK) management team that has overseen the goat scrapie genetics.

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BREEDING SALMON FOR RESISTANCE TO INFECTIOUS PANCREATIC NECROSIS

The viral disease infectious pancreatic necrosis (IPN) has been a major constraint on salmon aquaculture. BBSRC-funded research led by Professors Stephen Bishop, John Woolliams and Chris Haley at the University of Edinburgh's Roslin Institute demonstrated that host resistance is a heritable trait and that observed genetic differences are almost entirely due to variation in a single quantitative trait locus (QTL) of the salmon genome. The large effect of the QTL on resistance was consistent in seawater cages and in controlled freshwater disease-challenge experiments. Fish inheriting two copies of the resistant variant of the QTL from their parents have negligible mortality, whereas those receiving the susceptible variant from both parents have mortality levels higher than 50% during epidemics. The disease resistance effect does not appear to show any negative correlations with other economically important production traits.

Dr Ross Houston has continued the research using high-throughput sequencing technology to study differences in DNA and RNA sequence between salmon carrying resistant alleles and those carrying susceptible alleles. This has enabled detection of more closely linked single nucleotide polymorphism (SNP) markers that show association with resistance to the IPN virus at the population level.

Incorporation of these improved markers into industry selective breeding programmes has further improved the accuracy and simplicity of genetic tests that enable the identification of IPN-resistant fish at an early stage.

IMPACTING SALMON FARMING WORLDWIDE

Infectious pancreatic necrosis (IPN) outbreaks can affect salmon farms in Scotland, Norway, Chile and other salmon-producing countries. Typical mortality levels in an epidemic are ~25%, and severe outbreaks are known to kill as many as 80-90% of farmed fish. No vaccine is effective in very young fish.

As a result of the University of Edinburgh's research, genetic markers have been identified that enable selection of salmon lines with improved IPN virus resistance, which is estimated to be worth ~£26 million/annum GVA to the UK economy.

BBSRC bioscience for the future

EXCELLENCE WITH IMPACT

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ECONOMIC BENEFIT TO THE SALMON FARMING INDUSTRY

In 2008 the salmon-breeding company Landcatch Natural Selection (LNS) Ltd, implemented marker-assisted selection (MAS) for IPN resistance when selecting its elite and commercial salmon populations. This is one of the first successful documented example of MAS in any aquaculture species. A license agreement between The Roslin Institute and LNS enabled a molecular genetic test for IPN resistance incorporating the QTL resistance markers to be sold internationally to aquaculture companies.

IPN resistance, using MAS, can reduce IPN mortality by 25% (i.e. from ~25% on average to virtually zero). After taking account of the market share of LNS for the eggs and smolts required by UK salmon industry, this equates to an economic impact of £26.4 million GVA (comprising reduced costs and losses, as well as greater output of marketable salmon) and between 360 and 450 jobs across the UK. As LNS also supplies 15%-20% of the eggs and smolts required by the global salmon farming industry, similar impacts can be documented overseas.

Salmon farming is heavily concentrated in the Scottish Highlands and Islands, and therefore provides employment in some of the remotest communities in the UK where few alternative opportunities exist. Severe outbreaks of IPN are potentially devastating for such communities; hence this research supports these fragile rural communities.

Implementation of the findings also reduces the ecological impact of salmon farming as IPN is an endemic infectious disease that affects both wild and farmed salmon.

FISH N [SNP] CHIPS

The research translation process has served as a paradigm for other economically important diseases. LNS Ltd received funding from the TSB / BBSRC Genomes UK: Exploiting the Potential of High-Throughput Sequencing competition to develop a high-density salmon SNP chip, which will be a key tool for improving the competitiveness and sustainability of the UK salmon farming industry. These SNP arrays are now being utilised to select salmon for increased resistance to sea louse infestations. Both the SNP chip and the IPN resistance research has involved several collaborators including Edinburgh Genomics, the Universities of Stirling and Glasgow, and industry partners Landcatch Natural Selection and Affymetrix Ltd.

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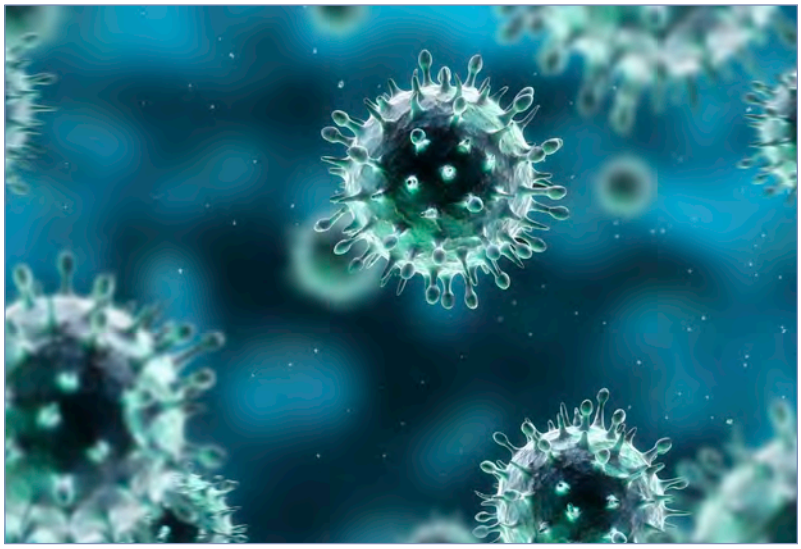
BEAST: UNDERSTANDING THE SPREAD OF GLOBAL PANDEMICS



BEAST is powerful computer software that has been used to understand the spread of, and to inform the response to, global pandemics such as H1N1 swine-flu. It has been also used to investigate disease origin and transmission routes in defined medical or criminal situations.

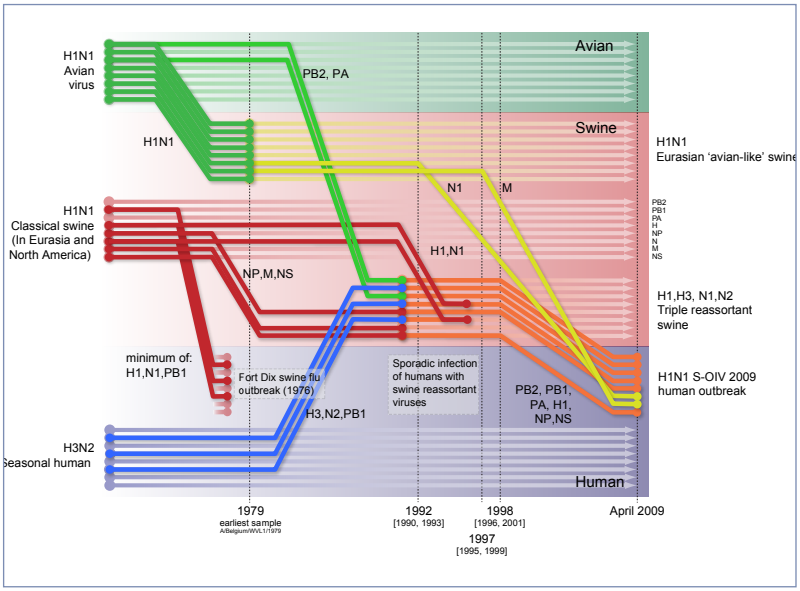
The BEAST (Bayesian Evolutionary Analysis Sampling Trees) software was developed by Andrew Rambaut at the University of Edinburgh, with his collaborator, Alexei Drummond, now at the University of Auckland, New Zealand. In essence it allows the reconstruction of evolutionary relationships and the testing of evolutionary models baed on molecular sequence data.

The key insight made by Rambaut and Drummond is that many intracellular pathogens such an viruses, evolve at a sufficiently rapid rate that genetic mutations accumulated during an epidemic, record information about the epidemiological processes that occurred during that same outbreak. This allows researchers to obtain accurate information about the location and the rate of spread of an epidemic while it is still on-going. The data can then inform decisions on the public health measures that may need to be implemented.

HIGH IMPACT PUBLICATIONS USING BEAST SOFTWARE

- Understanding the global movement of influenza virus and the seeding of Northern and Southern hemisphere winter epidemics by strains in non-temperate areas.
- Demonstrating that an outbreak of HIV and hepatitis C virus amongst children in a Libyan hospital was nosocomial, thereby exonerating the foreign medical workers who had been accused of deliberate infection and sentenced to death.
- Revealing the zoonotic origins and genetic architecture of the 2009 H1N1 influenza A pandemic virus. This last example, in particular, demonstrates the power of the software because, by the time the virus had been discovered in California, it had had already spread extremely widely unnoticed and would have been impossible to trace by conventional epidemiological means. Genetic data combined with the statistical models implemented in BEAST based on data from the initial outbreak in Mexico allowed the reconstruction of the hidden early history of the pandemic.
- Tracking down the epidemiological source of the 1918 pandemic influenza outbreak which killed approximately 75 million people worldwide.
- Understanding the spread, circulation, and evolution of the Middle East respiratory syndrome coronavirus (MERS-CoV).

WIDELY AVAILABLE OPEN SOURCE SOFTWARE FOR MANY APPLICATIONS



An important feature of BEAST is that the source code is highly modular allowing other developers to easily add new modules in almost unlimited permutations allowing the construction of complex models to describe particular infectious diseases or epidemics. This has also allowed the software to be used for a large number of applications - to date there have been over 1500 different users - with more than 5000 citations in diverse fields of research and study.

Impact on public policy and services:

BEAST is now widely used by the Centers for Disease Control and Prevention in Atlanta, GA for public health assessment.

Influence on public health policy and advisory committees:

BEAST was extensively used to inform public health assessments and approaches taken by the World Health Organization (WHO) during and after the 2009 human influenza (H1N1 'swine flu') pandemic. Crucially, BEAST data was key to the WHO assessment of the severity of the outbreak and to their susbsequent advice to international governments on responses to the threat from the pandemic virus.

USE OF RESEARCH IN LEGAL CASES

Analysis using the BEAST software has been used in international court cases.

An expert report for a large criminal case in Valencia, Spain, used BEAST to determine the likely nature and timing of hepatitis C infection in hundreds of patients treated by an anaesthetist, who was subsequently convicted of transmitting the infection.

BEAST analysis was also used in expert witness testimony in a patent dispute brought in Norway for fish virus vaccines between Intervet International and Pharmaq AS. The use of BEAST demonstrated the genetic separation of two virus strains at the core of the case.

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COMBATTING NEGLECTED TROPICAL DISEASES - SCHISTOSOMIASIS

Schistosomiasis is a disease of poverty that leads to chronic ill-health. Infection is acquired when people come into contact with fresh water infested with the larval forms of parasitic worms, known as schistosomes. The adult worms live in the veins draining the urinary tract and intestines. Some of the eggs they lay are trapped in the tissues and it is the body's immune reaction to them that can cause severe damage.

Urogenital schistosomiasis (also known as bilharzia) is caused by *Schistosoma haematobium* and affects more than 100 million people across Africa, including in Zimbabwe. After malaria, schistosomiasis is the second most important parasitic infection of public health concern in that region, with children being most at risk of infection and disease. In affected populations, children carry the heaviest burden of disease, often suffering from haematuria, anaemia, nutritional deficiencies, growth retardation and poor educational attainment.

Furthermore, untreated schistosome infections acquired in childhood can lead to kidney and bladder disease, bladder cancer, reduced fertility and susceptibility to HIV infection in adulthood.

INFLUENCING PUBLIC POLICY IN AFRICA

Francisca Mutapi at the University of Edinburgh has studied the immunological consequences of urogenital schistosomiasis for several years. Her team has focused on determining the host and parasite factors that influence patterns of infection and disease in human populations.

In particular, her research has shown that the drug Praziquantel (PZQ) - the only control measure currently available - accelerates the development of acquired schistosome-specific immunity favouring responses associated with protection against re-infection with the parasites.

The data has been extensively used to inform vaccine development and optimization of drug intervention strategies in Africa, including mass drug administration (MDA) programmes in Zimbabwe.

PUTTING RESEARCH INTO ACTION - SCHISTOSOMIASIS TREATMENT FOR UNDER 5s

Previous MDA programmes using Praziquantel (PZQ), the only control measure currently available, were restricted to school age children and adults. These programmes excluded under 5s partly because the efficacy of PZQ treatment in this age-group had not been evaluated, and also because it was thought that such young children only carried a low worm burden. This potentially exposed several million very young children in Africa to infection with schistosomes and associated diseases.

However research from Francisca Mutapi and her team working with collaborators at the University of Zimbabwe, and others elsewhere in Mali and Sudan, demonstrated that schistosome infection rates in the under-5s are actually higher than in adults already enrolled in MDA programmes. Their data also showed that not only is PZQ safe for pre-school children, it is as effective at treating schistosome infection in this age-group as it is in older children.

The results obtained by Francisca's team in Zimbabwe were presented alongside those from other regions of African to a workshop at the World Health Organisation in September 2010. In September 2012, a new MDA programme was begun in Zimbabwe, which has already treated almost 350,000 pre-school children for the first time. The University of Edinburgh is now leading a monitoring and evaluation survey that has shown that the new MDA programme has been extremely successful in reducing *S. haematobium* infection in pre-school children, and is significantly reducing the risk of long-term morbidity.

PRAZIQUANTEL DOSE POLE EXTENSION

The University of Edinburgh was also instrumental in the extended validation of a dose pole for use in the field when treating pre-school children with Praziquantel. PZQ doses to children are calculated based on patient weight. However, in the field, correct dosages of PZQ need to be administered quickly to large groups of children with minimal equipment.

The Mutapi lab contributed data to a study analysing results from several developing countries, which showed that a child's height can used as a simple but accurate proxy for weight when calculating the correct dose for pre-school children as occurs in primary school children and adults.

The modified dose pole is now deployed across the developing world for PZQ administration.

The Chair of the 2010 WHO workshop on schistosomiasis said:

"This on-going programme and evaluation study in Zimbabwe will help many thousands of children in the short term and several million in the long term."

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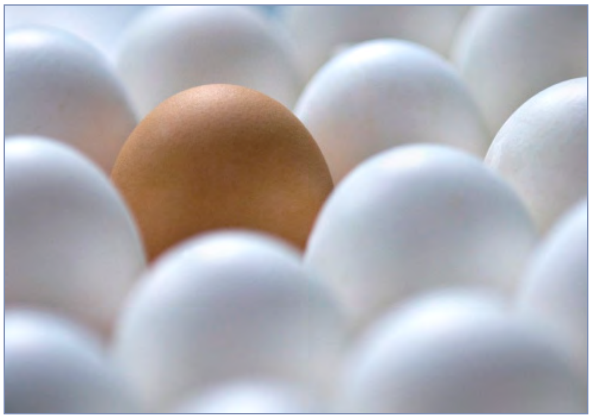
GM CHICKENS; THERAPEUTICS PRODUCTION AND DISEASE RESISTANCE

The chicken industry is worth £2 billion per annum in the UK alone. GM technology offers increased productivity, biosecurity and welfare as well as biotechnology applications in production of protein therapeutics.

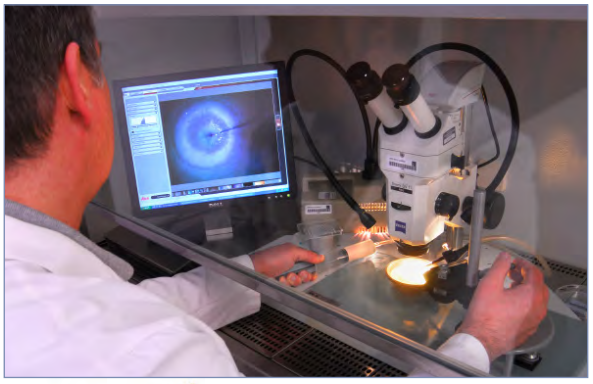
The production of transgenic chickens is technically challenging because embryonic development occurs on the surface of the egg yolk and development to hatch requires incubation in a shelled egg. Professor Helen Sang and colleagues at the University of Edinburgh's Roslin Institute developed a host egg culture system that enabled hatching of embryos after genetic manipulation and constructed lentiviral vectors capable of delivering transgenes to early chick embryos, which were subsequently hatched as healthy chicks.

Chick embryos are valuable models for investigating vertebrate development: they are accessible in the incubated egg and can be manipulated in functional experiments. Professor Sang and colleagues developed a transgenic chicken line ubiquitously expressing green fluorescent protein (GFP) and demonstrated that cells from GFP embryos could be transplanted to normal chick embryos to investigate the fate of transplanted cells, including identifying stem cell populations. This technique was utilised further in collaboration with Roslin colleague Dr Mike Clinton to demonstrate that somatic sex identity is cell autonomous in the chicken.

EGGS AS BIOREACTORS FOR DRUG PRODUCTION



From 2004-2006 Professor Sang and colleagues optimised expression vectors in order to direct synthesis of foreign proteins specifically to the oviduct of laying hens, resulting in incorporation of the protein in egg white. This advance paved the way for expression of biologically active, therapeutic proteins that are expressed exclusively in the oviduct during egg formation and can be extracted from egg white.



PRODUCTION OF GM CHICKENS THAT ARE RESISTANT TO AVIAN INFLUENZA

Genetic modification in the chicken has potential to improve productivity of domestic poultry. Professor Sang and Dr Laurence Tiley (University of Cambridge) undertook a proof-of-principle study, describing generation of transgenic chickens that do not transmit avian influenza when infected with H5N1 virus. Chickens were genetically modified to produce a synthetic decoy RNA derived from a sequence present in all strains of avian influenza, and which interferes with virus replication.

Development of bird flu resistance is being advanced through a BBSRC Industrial Partnership Award and collaboration with a poultry breeding company. The investment is a reflection of awareness by major breeding companies that the technology has potential to deliver genetic improvements in disease resistance that cannot be achieved by conventional breeding. The potential of the GM approach to control avian influenza virus will be assessed while developing the business strategy and investigating the regulatory and public acceptance issues inherent in introducing genetic modification into food production.

Poultry meat is currently the second largest (34%) meat market after pork. Industry experts believe that flu resistant birds would command a premium price in markets in South East Asia where bird flu is endemic.

POLICY AND SOCIAL IMPACT

Sang and colleagues have used numerous opportunities to explain, discuss and debate GM technologies and issues. Forums have included presentations and discussions with school children, public lectures, e.g. meetings of Café Scientifique, and science and arts festivals events.

The generation of birds that cannot transmit avian flu received national and international press coverage. For example, the transgenic birds resistant to influenza were featured on the BBC1 show Countryfile in 2013 with additional articles featuring in BBC Radio Four and BBC World Service programmes demonstrating the mainstream interest in the birds' production.

In addressing the issues of safety, licensing and public acceptance that applications of genetic modification in poultry breeding and production raise, Professor Sang has been an advisor to policy development providing information to the Centre for Veterinary Medicines of the US Federal Drug Administration and the European Food Safety Authority GMO panel.

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CONTROLLING TUBERCULOSIS IN SOUTH EAST ASIA

In 2015 WHO has achieved the 2015 Millennium Goal of halting and reversing the incidence of the Tuberculosis. Despite this great acheivement, in 2013 alone the WHO recorded 9 million new cases of TB, and one a half a million people died of the disease. Tuberculosis remains the second leading cause of death from infectious diseases worldwide, the overwhemling majority of deaths (95%) occurring in the developing world.

The disease is mainly caused by infection in the lung with the bacterium *Mycobacterium tuberculosis*, and is spread through the air when an infected patient coughs or sneezes. Following infection the symptoms of the disease may be mild for several months, which can often delay patients from seeking medical care, and allowing continued transmission of the bacteria to others in the community.

However Tuberculosis is a treatable and cureable disease. Active drug-sensitive disease can be treated with a standard six-month course of antimicrobial drugs that are provided to the patient by a trained healthcare worker.

Nevertheless without appropriate support and supervision patients often find it hard to adhere to the treatment regimen thus allowing further disease spread and continued.

THE IMPORTANCE OF SOCIAL CONTEXT IN TUBERCULOSIS CONTROL

Work at the University of Edinburgh has had a major impact on the way TB is managed and controlled across South East Asia. **Professor Ian Harper** in the School of Social and Political Science has combined long-term research into TB control and community health, with direct engagement at the level of policy and practice in the National TB Programme in Nepal.

In particular Ian's research has highlighted the importance of **context-specific** social and political factors in understanding how the disease is controlled, how patients respond to treatment, and how drugs are made available.

DEVELOPMENT OF REGION-SPECIFIC GUIDELINES FOR TREATMENT AND CONTROL OF TB

Desk-manuals for healthcare professionals in Nepal

Policy-makers and programme-implementers often think of TB as simply a technical or medical problem. However research at the University of Edinburgh has provided strong empirical evidence for the importance of social context in influencing the ways in which TB control mechanisms are implemented and take effect.

In particular Ian directly contributed to the content the Tuberculosis Case Management Guideline for Health Workers and Doctors, for all health workers dealing with TB in Nepal. This desk manual is now used all the more than 4000 health institution in that country, and ensures that medical staff follow a 'patient-centred' approach, taking into account how tuberculosis impacts on patient's lives in diverse and complex ways.

Programme Managment Unit for Nepali Tuberculosis control

In 2008, the Global Fund to Fight AIDS, TB and Malaria (GFATM), which channels 82% of all global financing to TB control, offered support to the Nepal Government. One of the conditions of the grant was the creation of appropriate local structures for implementation and monitoring.

Due to his considerable expertise, Ian was invited jointly by the Nepali Government and the WHO to design the **Programme Management Unit,** which would assess the impact of TB control mechanisms in Nepal. Ian developed the structure, wrote the job descriptions, and created the assessment manuals. He was also directly involved in planning for the procurement of TB drugs for the Nepali national TB programme.

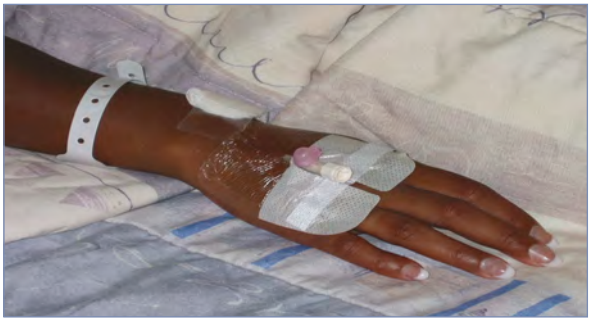
As a result of Ian's work on this key monitoring project, **$3.5m** funding for TB control was obtained, thus setting in place ongoing national mechanisms for monitoring the effectiveness of TB control programmes.

Ian has also advised the Indian Revised National TB control Programme on their monitoring and evaluation plan, again stressing the importance of context-specific assessment when evaluating treatment TB control measures. This work was another prerequisite for the release of a **$90m** GFATM grant.

INCREASING CAPACITY FOR TUBERCULOSIS CONTROL IN SE ASIA

Through his research Ian has played a central role in increasing the significance of, and capacity for the use of qualitative evidence in the assessment of TB prevention strategies, both in Nepal and more globally:

- worked to allow more responsive planning for targeted interventions in the provision of TB medications and support;
- increased the professional recognition given to qualitative research by medical practitioners;
- raised the global profile on qualitative research in assessing the impact of TB control programmes, and set new guidelines for scientific standards in qualitative research into TB.



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