Institution: University of Strathclyde

Unit of Assessment: 10

Title of case study: Health and cost benefits of monitoring infectious diseases using novel statistical methods.

1. Summary of the impact (indicative maximum 100 words)

Research on novel statistical methods for disease surveillance and influenza vaccine effectiveness has led to the development of a suite of automatic systems for detecting outbreaks of infectious diseases at Health Protection Scotland (HPS). This work has improved the public health response and helped to reduce costs in Scotland and also in the wider UK and EU by providing real-time early warning of disease outbreaks and timely estimates of the effectiveness of the influenza vaccine. This research, commissioned by the Scottish Government, through HPS, and also the UK National Institute for Health Research (NIHR) and the European Centres for Disease Control (ECDC), but used in a wider context by many others, formed the basis for the HPS response to the H1N1 Influenza Pandemic and monitoring of the effects of Influenza Vaccines.

2. Underpinning research

Context: Health Protection Scotland is the NHS agency concerned with protecting the population of Scotland from the effects of infectious diseases and outbreaks that are a major public health problem. It is also responsible for assessing the impact of vaccination programmes on health. The seasonal influenza vaccination programme is estimated to cost in excess of £15 million annually (the cost was £14M in 2008) and it is necessary to establish that the vaccine used is effective. Diminishing resources and a large number of diseases means that little time can be allocated to any one disease. Consequently, research into the use of sophisticated statistical techniques to process automatically large volumes of data was carried out in close collaboration with consultants and epidemiologists at HPS.

Key Findings: Statistical models based upon Poisson regression techniques were developed for statistical exception reporting [1]. These models were extensions of research critically reviewed in [2] and led to the development of a syndromic surveillance system for Scotland based upon daily data provided by NHS24, the out of hours telephone service for medical advice [1]. Methods for modelling these data were developed and existing algorithms for signalling an exception were modified and compared using real and simulated data. The initial research was carried out in 2006-07, based upon earlier work in the PhD thesis of G. McCabe. Further research has considered both spatial and temporal effects [3], which permits HPS to provide epidemiological guidance at sub national (Health Board) level and thus increase the specificity of the HPS response. The research demonstrated that these surveillance systems detect outbreaks early and are important in monitoring disease activity.

Competitive research grants funded by ECDC (EpiConcept), the Chief Scientist's Office (CSO), NIHR, and HPS have permitted the utilisation of HPS data to develop statistical methods for the estimation of vaccine effect, particularly for seasonal and pandemic influenza, and the Human Papilloma Virus (HPV) vaccine. Information on cohorts of patients was assembled and linked with other health related details available in Scotland, such as laboratory and hospital data and cause of death statements. Statistical models for the estimation of vaccine effectiveness were produced and compared. Over and above the novelty of the epidemiological research, the novel statistical aspects of this research are in the application of state-of-the-art statistical models and methods for the control of confounding, such as instrumental variables, propensity scores and negative confounders imbedded within time dependent Cox models, with a correlated error structure to account for the clustering of patients within GP practices in the cohorts. The research provided timely estimates of the effect of the influenza vaccine in Scotland, as well as an understanding of the effect of the influence of the methodology. [4, 5]

Key Researchers: Research was, carried out by the Epidemiology and Population Modelling

group at Strathclyde:
Chris Robertson (Professor, 2002-) supported by D Greenhalgh (Reader, 1990-) and G Gettinby (Professor, 1978 -), undertook the initial research into the surveillance systems.
C Robertson undertook the research on statistical methods for estimating vaccine effectiveness in association with Dr J McMenamin (Health Protection Scotland), Dr R Pebody and Dr N Andrews at Public Health England, Dr D Fleming at Royal College of General Practitioners, Birmingham, Dr C Simpson, Dr N Lone and Prof A Sheik (Edinburgh University), and Prof L Ritchie (Aberdeen University). The key researchers in this project were Prof C Robertson, Dr McMenamin and Dr Lone who provided the medical background, and Dr Simpson who was PI on 2 NIHR grants and is an expert on data systems.

3. References to the research (indicative maximum of six references)
References 1, 3 and 5 best exemplify the quality of the body of research. References1, 4 and 5 are part of the REF2014 submission

1. Kavanagh. K., Robertson, C., Murdoch, H., Crooks, G., McMenamin, J. Syndromic surveillance of influenza-like illness in Scotland during the Influenza A H1N1v pandemic and beyond. Journal of the Royal Statistical Society Series A: Statistics in Society, 2012, 175 (4) pp.939-958
2. Unkel, S., Farrington, C., Garthwaite, P. H., Robertson, C., & Andrews, N. Statistical methods for the prospective detection of infectious disease outbreaks: a review. Journal of the Royal Statistical Society: Series A (Statistics in Society), 2012, 175(1), 49-82.
3. Wagner A.P., McKenzie E., Robertson C., McMenamin J., Reynolds A., Murdoch H. Automated mortality monitoring in Scotland from 2009. Euro Surveillance, 2013, 18(15),pii=20451.Available online:: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20451
4. Kavanagh K., Robertson C., McMenamin J. Assessment of the Variability in Influenza A(H1N1) Vaccine Effectiveness Estimates Dependent on Outcome and Methodological Approach. PLoS ONE, 2011, 6(12): e28743. doi:10.1371/journal.pone.0028743
5. Simpson C.R., Ritchie L.D., Robertson C., Sheikh A., McMenamin J. Effectiveness of H1N1 vaccine for the prevention of pandemic influenza in Scotland, UK: a retrospective observational cohort study. Lancet Infect. Dis., 2012, Sept, 12(9),696-702. Epub 2012 Jun 26.

Other evidence for quality of research:
18 grants with a total value of over £2.4M were awarded by HPS, HPA, ECDC, CSO, NIHR, SEHD, EPSRC since 2003. Examples are

1. Simpson C.R., Lone N., Ritchie L.D., Robertson C., Sheikh A., McMenamin J. Early estimation of pandemic influenza Antiviral and Vaccine Effectiveness (EAVE) - use of a unique community and laboratory national linked dataset. 2012-15, NIHR, £215,000.
2. Simpson C.R., Lone N., Ritchie L.D., Robertson C., Sheikh A., McMenamin J. Seasonal Influenza Vaccine Effectiveness (SIVE), 2010-12, NIHR, £104,000.
3. Cruickshank M., Campbell C., Choi Y., Cubie H., Cushieri K., Donaghy M., Imrie J., Robertson C., Sullivan F., Weller D. The Scottish Cervical Cancer Prevention Programme: Assessing And Modelling The Impact Of HPV 16/18 Immunisation, 2010-15, CSO, £450,000.

4. Details of the impact (indicative maximum 750 words)
Process from research to impact:
C Robertson has a joint appointment with Health Protection Scotland and this close working relationship between the researchers based in Mathematics and Statistics at Strathclyde and those at Health Protection Scotland enables the timely identification and investigation of important health research areas. Implementation of the research outputs comes through the contribution of university staff to core HPS strategy and planning groups, such as HPV Surveillance in Scotland, the MRSA Screening Programme Board, Pandemic Influenza, and the Olympic and Commonwealth Games Surveillance Group (Source1). Wider dissemination takes place through reports to Government and HPS study reports (Source 2). Consequently, the results of Strathclyde's research are often transferred to and implemented by HPS before publication in journals.

Preparatory research at the university led to the establishment of a national surveillance system for the weekly "organism report" around the time of the G8 summit in Gleneagles in July 2006. At this time, HPS had no facility for processing large amounts of varied, daily produced data within a unified surveillance system and the university research led directly to the establishment of such systems. A review of the surveillance strategy by HPS in the aftermath of the G8 conference concluded that statistical methods for the automatic scanning of a large amount of daily data were crucial to its operational effectiveness. In the period 2008-13, at least 5 separate data analysis systems have been developed and tested, based on adoption of Strathclyde's research.

Types of Impact

Monitoring Influenza Pandemic:

During the H1N1v Influenza Pandemic, HPS systems based on Strathclyde's research were instrumental in successfully monitoring the evolution of the pandemic, estimation of the transmission dynamics of the virus, monitoring the numbers of people dying in relation to those expected to succumb; and development of a national system for surveillance of GP consultations, including the use of NHS24. HPS placed, and continues to place, a huge reliance on these systems so that it can function effectively (Source 3).

Outputs derived from the university research, were regularly used by government, health officials, and health protection agencies. Reports were prepared for the both the UK Government's Scientific Advisory Group for Emergencies (SAGE) and the Scientific Pandemic Influenza Subgroup on Modelling (SPI-M),which monitored the course of the pandemic(Source 4). Without the university research, HPS would not have had advanced syndromic surveillance systems, nor would it have had as sophisticated a response to pandemic influenza surveillance (Source 5). The benefits to HPS, and consequently the general population, have been apparent throughout the period 2008-13, with greatest impact in the period April 2009-June 2010. The Clinical Director at HPS during this period (Source 1) states "This research had a great impact at HPS in helping to mitigate the increased workload and pressures on the organisation associated with managing a national outbreak and reporting, each day, on a wide range of issues".

Vaccination programmes:

Vaccination is the main way of protecting the population against some infectious diseases and HPS monitors the impact of the national vaccination programmes. The university's research on vaccine effectiveness is carried out in conjunction with colleagues at HPS (Dr Jim McMenamin) , Edinburgh University (Dr Colin Simpson, Dr Nazir Lone, Prof Aziz Shiekh) and Aberdeen University (Prof Lewis Ritchie). A successful HTA grant during the H1N1v pandemic yielded one of the first publications on the effectiveness of the pandemic vaccine, demonstrating that the vaccination programme had prevented infection, hospitalisations and death. This group has also worked on Seasonal Influenza Vaccine Effectiveness (HTA grant 2011-12) and preparatory work to develop data systems for pandemic preparedness (EAVE, HTA 2013-2015). As a result of this research HPS has published mid-season and end-of-season estimates of the effect of the influenza vaccines since 2009. These results are communicated to (a) Scottish Government through reports and meetings, (b) Public Health England and, hence, the UK Government, and (c) the I-Move network through meetings and reports, where the results have assisted in guiding public vaccination policy at national and European level.

Improved effectiveness of Health Protection Scotland:

Strathclyde's research working in partnership with HPS, has permitted the demonstration of a positive health impact of the influenza vaccination programme on the health of the UK population, with the added benefits of improving the effectiveness of HPS in carrying out its responsibilities. The surveillance systems provide HPS with the ability to monitor disease levels in relation to expected levels and to detect outbreaks of infectious diseases in a timely fashion. When combined with appropriate interventions, a reduction in the magnitude of the outbreaks can be achieved, with a reduction in the time in which they can be controlled. Furthermore, there is a workforce impact as epidemiologists are freed from routine surveillance, leading to a more efficient deployment of staff within HPS. A conservative estimate of the savings is one staff per year since 2009 at £50,000 per annum (Source 6).

Reach and Significance: The results of the research on influenza vaccine effectiveness have been presented annually at a European network on vaccine effect, I-Move, which reports to ECDC and WHO (Source 7). This regular reporting has influenced other national programmes demonstrating a global reach. Early estimates of the effect of the current seasonal flu vaccine are crucial for the planning of the next year's flu vaccine. As a result of the university research, HPS, in conjunction with Public Health England (PHE), are better able to provide timely estimates for the UK (Source 8) placing HPS/Strathclyde University amongst the leaders in the early estimation of influenza vaccine effect in Europe.

A consultant epidemiologist at HPS has confirmed "This research is carried out at Strathclyde University but has a national, European and international impact. Since 2009 we have developed a system of linked datasets which, with complex statistical modelling, can be used to provide timely estimates of the effectiveness of the seasonal influenza vaccine. The results of this research have an impact at national level, where they are communicated to Scottish Government, through reports and meetings and to Public Health England and thence the UK Department of Health. Furthermore, the impact is wider through the contribution of HPS in a European network of researchers and public health officials from European Centre for Disease Control. This data allows in-season estimation of the severity of influenza as it impacts the public health and the success or otherwise of public health measures to limit its impact. The network regularly contributes to the World Health Organisation influenza vaccine strain selection meeting where the composition of the seasonal influenza vaccine for the next season is decided" (Source 6).

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. Statement from Clinical Director, HPS will corroborate that the university research is crucial to workings of HPS and that university researchers are a vital part of HPS working groups.
2. http://www.documents.hps.scot.nhs.uk/respiratory/swine-influenza/outbreak-report/flu-a-h1n1-hp-response-2010-12.pdf
   will corroborate that university research is published in reports by Health Protection Scotland and which are then submitted to Scottish Government
3. http://www.documents.hps.scot.nhs.uk/respiratory/seasonal-influenza/flu-update/2012-11-29.pdf and Elliott, A. J., N. Singh, P. Loveridge, S. Harcourt, S. Smith, R. Pnaiser, K. Kavanagh et al. "Syndromic surveillance to assess the potential public health impact of the Icelandic volcanic ash plume across the United Kingdom, April 2010." Eurosurveillance 15, no. 23 (2010).will support the claim that the results of the university research continue to have an impact
4. HPS Report to SAGE Committee. HPS_School_Closures_Scotland 23 July 2009 and HPS Report to SAGE Committee. SAGE paper impact of schools in Scotland Opening after summer break Sept 2009 will support the claim that University research contributed to SAGE committee during pandemic
5. http://www.straightstatistics.org/article/monitoring-hidden-deaths-swine-flu will support the claim that the Scottish response to H1N1v was sophisticated
6. Statement from Consultant Epidemiologist at HPS will affirm that university research is crucial for influenza surveillance in Scotland and improves efficiency at HPS
7. Valenciano M, Ciancio BC. I-MOVE: a European network to measure the effectiveness of influenza vaccines. Euro Surveill. 2012;17(39):pii=20281. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20281 demonstrates influenza surveillance in Scotland and vaccine effectiveness estimates from UK are timely and are used to inform the development of next season's vaccine.
8. Pebody, Richard, P. Hardelid, D. Fleming, J. McMenamin, N. Andrews, C Robertson, D. Thomas et al. "Effectiveness of seasonal 2010/11 and pandemic influenza A (H1N1) 2009 vaccines in preventing influenza infection in the United Kingdom: mid-season analysis 2010/11." Euro Surveill 16, no. 6 (2011): 19791. Supports the claim that university research is crucial for influenza surveillance in Scotland and that this research is timely and is used to inform the development of next season's vaccine.