

Institution: University of Strathclyde		
Unit of Assessment: B10 Mathematical Sciences		
Title of case study: Informed management strategies and vaccination programmes for influenza, Human Papilloma Virus and COVID-19		
Period when the underpinning research was undertaken: 2010 - 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Chris Robertson	Role(s) (e.g. job title): Professor	Period(s) employed by submitting HEI: 01/01/2002 - present
Period when the claimed impact occurred: August 2013 – December 2020		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact		
<p>As a long-standing recognised expert in statistical epidemiology, Robertson's advice and evidence has informed government policy across many domains including planning for influenza pandemics, surveillance and vaccination programmes for seasonal flu, Human Papilloma Virus (HPV) immunisation (saving GBP500,000 annually) and management of the COVID-19 pandemic. He has a significant role on many health-related national and international committees, including the Scottish Government COVID-19 Advisory Group and the Scientific Pandemic Influenza Group on Modelling (SPI-M) which feeds directly into the UK Scientific Advisory Group for Emergencies (SAGE). Additionally, through Robertson's joint appointment as Head of Statistical Research with Health Protection Scotland (HPS), Strathclyde has directly informed strategy for managing infectious diseases in Scotland.</p>		
2. Underpinning research		
<p>Context: Infectious diseases and vaccination have been a critical concern for the UK and devolved Scottish governments dealing with such threats as pandemic and seasonal influenzas, COVID-19 and a resurgence of measles. Surveillance is a key factor in early detection of outbreaks and guiding public health policy. Availability of quality data and advanced statistical analysis are crucial in addressing the response to infection threats as well as addressing long-term vaccination strategies for diseases like HPV.</p> <p>Health Statistics research in the Department of Mathematics and Statistics at the University of Strathclyde has long focused on infectious disease surveillance, prediction and control. Robertson has had significant and continuing influence in this field over decades, including surveillance of seasonal influenza, pandemic influenza and COVID-19, and providing essential analysis for the evaluation of vaccine efficiency for influenza, HPV and COVID-19.</p> <p>Key areas of research:</p>		
Infection rate surveillance and prediction		
<p>Statistical models based on Poisson regression techniques were developed by Robertson and colleagues for a syndromic surveillance system for infectious diseases in Scotland, including pandemic and seasonal influenza [R1]. This surveillance approach was extended by incorporating the Moving Epidemic Method and demonstrating its ability to predict the time of peak seasonal influenza, and has been fundamental in establishing a rapid response to the COVID-19 pandemic throughout 2020 including formulation of a protocol for evaluation and surveillance [R2]. Furthermore, underpinning research by Robertson for identifying spatio-temporal disease trends, using a novel Bayesian hierarchical mixture model with inference based on a Metropolis-coupled</p>		

Markov chain Monte Carlo simulation [R3], has enabled the development of a spatio-temporal syndromic surveillance tool for COVID-19 in Scotland.

Vaccine effectiveness

Influenza: Modelling assessment of impact of influenza vaccine on seasonal influenza.

Robertson conceived and developed statistical methods for the estimation of vaccine effect for seasonal and pandemic influenza. The approach utilised state-of-the-art statistical models and methods for the control of confounding factors, such as instrumental variables and 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 different cohorts [R4]. Two Poisson regression models were developed by Robertson, using weekly counts of all-cause mortality, cause-specific mortality and emergency hospitalisations, and Robertson also played an important role in investigating the issue of within-season waning of the efficacy of the flu vaccine against virus subtypes [R5].

HPV: Modelling and statistical analysis of the reduction of cervical disease and precancerous disease owing to the Human Papilloma Virus (HPV) vaccine.

To assess the impact of the vaccine on HPV infection rates, Robertson (in collaboration with the HPV surveillance group at Health Protection Scotland) designed a programme of national surveillance to annually collect individual vaccination, screening and HPV testing records, as well as HPV genotyping of women attending their first cervical screening at age 20. By linking and analysing these data, Robertson and colleagues demonstrated the effectiveness of the HPV vaccine and showed that the vaccine-specific HPV types (16/18) and the cross-protective types (31/33/45) have almost disappeared among women who were not vaccinated seven years after the introduction of the vaccine [R6]. By combining data analysis with modelling, this research provided evidence of herd immunity for these HPV types.

3. References to the research (Strathclyde affiliated authors in bold)

- R1** K. Kavanagh, C. Robertson, H. Murdoch, G. Crooks, J. McMenamin (2012) 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*, 175 (4): 939-958. <https://doi.org/10.1111/j.1467-985X.2012.01025.x> [REF2 in 2014]
- R2** C.R. Simpson, C. Robertson, E. Vasileiou, J. McMenamin, et al. (2020) Early pandemic evaluation and enhanced surveillance of COVID-19 (EAVE II): protocol for an observational study using linked Scottish national data, *BMJ Open* 10: e039097 (13 authors). <http://dx.doi.org/10.1136/bmjopen-2020-039097>
- R3** G. Napier, D. Lee, C. Robertson, A. Lawson (2019) A Bayesian space-time model for clustering areal units based on their disease trend, *Biostatistics* 20(4): 681-697. <https://doi.org/10.1093/biostatistics/kxy024>
- R4** K. Kavanagh, C. Robertson, J. McMenamin (2011) Assessment of the variability in influenza A(H1N1) vaccine effectiveness estimates dependent on outcome and methodological approach, *PLoS ONE*, 6(12): e28743. <https://doi.org/10.1371/journal.pone.0028743>
- R5** E. Kissling, B. Nunes, C. Robertson, M. Valenciano, et al. (2016) I-MOVE multicentre case-control study 2010/11 to 2014/15: Is there within-season waning of influenza type/subtype vaccine effectiveness with increasing time since vaccination?, *Euro Surveillance*, 21(16): 30201 (23 authors). <https://doi.org/10.2807/1560-7917.ES.2016.21.16.30201>
- R6** R.L. Cameron, K. Kavanagh, J. Pan, J. Love, K. Cuschieri, C. Robertson, S. Ahmed, T. Palmer, K.G.J. Pollock (2016), Human papillomavirus prevalence and herd immunity after introduction of vaccination program, Scotland, 2009-2013, *Emerging Infectious Diseases* 22 (1): 56-64. <https://dx.doi.org/10.3201/eid2201.150736>

Notes on the quality of research: All outputs are published in peer-reviewed journals. The research has been supported with competitively-awarded funding, including but not limited to:

- Robertson (PI) and Corson (CI), Influenza and Pneumococcal Vaccine Effects (IMove, IMove+, SpiDnet), Health Protection Scotland, 01/04/15-30/11/18, GBP106,164;
- Robertson (PI), Chief Scientist's Office, Scottish HPV Research Programme - Health Service Research, 01/04/10-30/03/16, GBP171,695; and
- Robertson (PI), COVID-19: Early Assessment of COVID-19 epidemiology and Vaccine/anti-viral Effectiveness (EAVE II), Medical Research Council, 01/04/20-30/09/21, GBP100,414.

4. Details of the impact

Through the above body of research, Robertson is widely recognised as an expert statistical epidemiologist who has had a significant influence on many health-related, national and international committees, through active membership, provision of evidence and referencing of his work. His influence and expertise have contributed to advice provided to government across a range of epidemiological domains, including planning for influenza pandemics and vaccination programmes for seasonal flu, COVID-19 and HPV. This is reflected in correspondence from the UK Government Chief Scientific Advisor who expressed thanks for: *'the continuing contribution of Professor Chris Robertson...to the work of SAGE'* [S1].

Informing advice to government on plans to deal with influenza pandemics and immunisation programmes for seasonal influenza

Robertson has been a full member of the Scientific Pandemic Influenza Group on Modelling (SPI-M) since 2009 [S2]. This group gives expert advice on influenza pandemics, based on disease modelling, to the Department of Health and Social Care, and also currently reports directly to the UK Scientific Advisory Group for Emergencies (SAGE).

As a recognised expert Robertson has co-authored annual mid-season and end-of-season reports on surveillance of seasonal (as opposed to pandemic) influenza since 2013 [S3 is an example]. As well as shaping immunisation advice given to UK health departments by the Joint Committee on Vaccination and Immunisation (JVCI), these reports have informed Public Health England's weekly national reports on influenza and provided surveillance data to enable effective flu vaccine planning for the following year. The value of these reports has been widely recognised, being cited in both the European Centre for Disease Prevention and Control's *Annual epidemiological report for 2015: Seasonal influenza* and the WHO report *Improving influenza vaccine virus selection* (WHO 2015). Furthermore, twice yearly meetings of the WHO decide on the composition of the flu vaccine, taking account of these reports as relevant to vaccine effectiveness.

Robertson's published work on vaccine waning [R5], which is a critical factor in relation to the efficacy of seasonal flu vaccines as the flu season develops, has been referenced by several health agencies around the world, and explains why there is often a late flu season even in countries with high vaccine coverage. This includes references in the official guidelines and reports of USA's Centres for Disease Control and Prevention (CDC), advising that the timing of the start of flu vaccinations each year should be carefully chosen taking waning into account [S4a]. R5 is also cited in the 2017 World Health Organization (WHO) guide to evaluating flu vaccine effectiveness [S4b], and a 2019 influenza vaccination report by the National Institute for Public Health and the Environment (RIVM) in the Netherlands which provides independent scientific advice on public health [S4c]. In both cases the need for further research is thereby recommended. This research also received global media coverage [S5], helping to raise public awareness of flu vaccines and their efficacy.

Epidemiological surveillance influencing measures to control COVID-19 and securing vaccinations for influenza and COVID-19.

Robertson has been a full member of the following key COVID-19 committees, as a scientific advisor, since their inception.

- **Scottish Government COVID-19 Advisory Group:** The group informs decisions about COVID-19 in Scotland. It reports through the Chief Medical Officer (Scotland). Robertson has submitted written papers and oral reports to the group on spatial surveillance, forecasting hospitalisations and deaths, estimating the impact of interventions on the course of the epidemic, and the consequences of new variants. Inputs contributed to decision making on the phased exit from the first COVID-19 lockdown, on opening schools, monitoring infection rate changes and assessing the success of restriction measures in reducing rates. The Cabinet Secretary for Health and Sport wrote to Robertson expressing personal thanks *‘for the time you have devoted and the dedication you have shown since joining the Scottish Government Covid-19 Advisory Group’* and *‘in particular for the comments you have provided on draft Scottish Government measures, such as the transmission reduction measures for the central belt in early October’* [S6].
- **COVID-19 Nosocomial Review Group (CNRG):** The group advises on the COVID-19 potential impacts in hospitals in Scotland, reporting to the Chief Nursing Office (CNO) and Chief Medical Officer’s Scientific Advisory Group (CMO AG). Robertson has presented to the committee on the state of the epidemic in Scotland, as well as health care associated COVID-19 infection and hospitalisations.
- **COVID-19 Vaccines Safety Surveillance Methodologies Expert Working Group** of the Commission of Human Medicines (CHM), whose role is to expedite development of effective medicines and vaccines. The group of ten members was formed especially for COVID-19 with Robertson providing expertise in statistical analysis and working on studies to capture near real-time information on COVID-19 vaccine effectiveness and safety as well as advising on the range of other aspects of the groups work [S7].
- **COVID-19 Vaccines Benefit Risk Expert Working Group of CHM:** Robertson is one of 19 members coordinating safety evaluation of COVID-19 vaccine trials with the expert group on clinical trials as well as advising CHM on the quality, safety and efficacy of the vaccines and on the balance of benefit and risks prior to authorisation [S7].

As mentioned above, Robertson is also a long standing member of the Scientific Pandemic Influenza Group on Modelling (SPI-M), which, in addition to its original remit to cover influenza, is also currently providing advice on COVID-19 and reporting directly to SAGE. In particular, Robertson has submitted papers to the SPI-M committee covering the potential impact of school closures in Scotland, hospital-acquired COVID-19, and forecasting hospitalisations and deaths in Scotland. The Deputy Director at the Department of Health and Social Care writes *‘Robertson has played a critical role in the ongoing provision of hospital data from Scotland to SPI-M’* [S2].

Additionally, as Head of Statistical Research at Health Protection Scotland (a part-time role alongside his Strathclyde Professorship) during the COVID-19 pandemic Robertson has advised Public Health Scotland on the production of weekly reports entitled *Enhanced Surveillance of COVID-19 in Scotland*. Commissioned by the Scottish Government, these were disseminated to Directors of Public Health in Scotland to help them with local management of the pandemic [S8].

Changes to national HPV screening and vaccinations programmes

From 2014 to 2016 a range of Strathclyde research led by Robertson [R6] was presented to and discussed by the UK Joint Committee on Vaccination and Immunisation (JCVI), an advisory body to the Secretary of State on the provision of vaccination and immunisation in the UK. The research demonstrated the impact of vaccination, determined the performance and role of HPV testing, assessed biomarkers of HPV, and developed enhanced HPV surveillance. In particular, results demonstrating that the vaccine virtually eliminated the types of HPV that the vaccine targeted, with cross protection to other types, and that herd immunity developed in those of a similar age but not vaccinated, were used by the JCVI to provide advice to the UK Government [S9]. In June 2016 a review panel, citing Strathclyde research, changed the age range for cervical screening from 20-60 to 25-64 on account of the low predictive value of cytology screening for women aged 20-25.

By reducing the number of unnecessary screenings for low risk young women, the annual saving to NHS Scotland is estimated to be approximately GBP500,000 [S10].

Collaboration with Health Protection Scotland

In addition to his position at Strathclyde, Robertson has a part time position as Head of Statistical Research at Health Protection Scotland (HPS), by virtue of his academic credentials exemplified by the above body of work and in particular his work on enhanced surveillance of infectious diseases in Scotland [R1, R2, R4]. HPS is part of the Public Health Scotland (PHS) and plans and delivers national services for protecting Scotland's population from infectious disease. Research collaboration between Strathclyde and HPS resulting from this partnership [S8] includes the statistical modelling of effectiveness of Scotland's vaccination programmes for seasonal influenza, pandemic influenza and HPV. Acknowledging the value of this, the Interim Clinical Director of PHS notes, 'Research at the university has made an enormous contribution to the functioning of PHS. On a day-to-day basis, the work of Professor Robertson enables the use of accurate surveillance techniques of infectious diseases, and has been invaluable in assisting the organisation to practically manage a national emergency' [S8].

5. Sources to corroborate the impact

- S1** Factual statement from UK Government Chief Scientific Advisor, acknowledging the work of Robertson, dated 12 June 2020.
- S2** Factual statement from Deputy Director, COVID-19 and Health Protection Analysis, Department of Health and Social Care, dated 19 March 2021.
- S3** Pebody R, et al. (2019) [End of season influenza vaccine effectiveness in adults and children in the United Kingdom in 2017/18](#), *Euro Surveill.*, Vol. 24 (31).
- S4** Citations on waning:
- [CDC Influenza Division Summary & Technical Key Points](#), 19 October 2018.
 - World Health Organization (2017) [Evaluation of influenza vaccine effectiveness: a guide to the design and interpretation of observational studies](#)
 - National Institute for Public Health and the Environment (2019) [Influenza vaccination in the Netherlands. Background information for the Health Council of the Netherlands](#), RIVM Letter report 2019-0002.
- S5** Selected media references to publication on vaccine waning:
- New Zealand Herald, ['Have you had a flu vaccination? It's more important than you think'](#), 11 June 2017.
 - Ian Mackay and Katherine Arden, ['Here's why the 2017 flu season was so bad'](#), The Conversation, 2 November 2017.
- S6** Factual statements from Cabinet Secretary for Health and Sport, Scottish Government, recognising Robertson's contributions, dated 30 September 2020 and 4 November 2020.
- S7** Factual statement from Chair and Principal Assessor, Commission on Human Medicines, dated 17 March 2021.
- S8** Factual statement, Interim Clinical Director, Public Health Scotland, dated 4 March 2021.
- S9** JVCI discussions:
- HPV Sub-committee of the Joint Committee on Vaccination and Immunisation, [Minute of the meeting held 26 February 2016](#).
 - HPV Sub-committee of the Joint Committee on Vaccination and Immunisation, [Minute of the meeting held 20 January 2014](#)
 - Letter from Director of HPV Reference Laboratory, NHS Lothian, dated 20 January 2018.
- S10** Factual statement from Clinical Lead for Cervical Screening in Scotland, dated 15 October 2019.