

Institution: University of Oxford

Unit of Assessment: 10: Mathematical Sciences

Title of case study: Understanding the transmission and control of COVID-19

Period when the underpinning research was undertaken: 18 January 2020 – 31 December 2020

 Details of staff conducting the underpinning research from the submitting unit:

 Name(s):
 Role(s) (e.g. job title):
 Period(s) employed by submitting HEI:

 Christl Donnelly
 Professor of Applied Statistics
 2018 – present

Period when the claimed impact occurred: 1 March 2020 – 31 December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

University of Oxford Professor Christl Donnelly, as a senior member of a large inter-disciplinary COVID-19 Response Team primarily based at Imperial College, played a key role in the statistical design, conduct and interpretation of studies which have transformed our understanding of the epidemiology of COVID-19 and the measures required to protect public health. Moreover, Donnelly was a key architect of the REACT study, whose results continually inform evolving British Government COVID-19 policy.

The results of these studies have been considered by SAGE (the UK's Scientific Advisory Group for Emergencies) and have informed policy decisions, such as the rule-of-six introduced in September 2020 and the decision, taken on 30 December 2020, to delay the return of secondary school pupils. As an example of commercial impact, Donnelly's advice informed mitigations taken by theatre leaders within the UK. Internationally, the results have informed policymakers in Europe and the US.

2. Underpinning research

Professor Christl Donnelly FRS FMedSci CBE moved from Imperial College to the University of Oxford in August 2018. Since that time she has held a 0.8FTE position as the Professor of Applied Statistics in the University of Oxford Department of Statistics, and a 0.2FTE position at Imperial College as one of four Associate Directors of the MRC Centre for Global Infectious Disease Analysis, headed by Professor Neil Ferguson. The team at the MRC Centre is highly inter-disciplinary; Donnelly is the lead statistician providing both academic leadership and technical input on the diverse statistical aspects of the team's research.

The MRC Centre team formed a COVID-19 Response Team in January 2020. This grew rapidly as the seriousness of the impact of COVID-19 became apparent and, from 18 January 2020, Donnelly devoted all her time (both in her University of Oxford and Imperial College London capacities) to the national response to COVID-19, as attested to by Ferguson [A].

Donnelly, in collaboration with Imperial College Senior Lecturers Flaxman and Bhatt, developed the Bayesian model linking shared intervention effects with transmission and biological delay distributions (including the serial interval distribution) to model infections and resulting deaths. This was a key component of [1] (first published on the Imperial College website on 30 March 2020). For this paper, Donnelly also developed methods for evaluating the robustness of the key policy-relevant conclusions regarding the impact of social distancing measures both in terms of their impact of transmission (characterised using the effective reproduction number) and the number of individuals infected in the first COVID-19 wave in Europe. In collaboration with Imperial College Lecturer Dorigatti, Donnelly developed and validated both the transmission

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model and the reconstruction of transmission chains which appears in [2] (first published on MedRxiv on 18 April 2020). Working again with Flaxman and Bhatt, Donnelly adapted and refined the dynamical model used in [1] to link real-time movement data to the incidence of COVID-related deaths in the US leading to [3] (first published on the Imperial College website on 28 May 2020). In addition, the COVID-19 Response Team reports provided estimates (and uncertainty bounds) for the parameters within the Imperial College epidemiological model employed by the key groups such as SAGE and the Scottish government.

Donnelly played a key role in the study design (sampling and statistical analysis) of the REaltime Assessment of Community Transmission (REACT) Study [4,5,6], a major programme of home testing, involving over 1,000,000 individuals between May and December 2020, to track SARS-CoV-2 across England - commissioned by the UK Department of Health and Social Care. In collaboration with the REACT team, she developed and honed further analyses in response to emerging results.

3. References to the research

- Flaxman, S., et al. (including Donnelly, C.A.) (2020) "Estimating the effects of nonpharmaceutical interventions on COVID-19 in Europe". *Nature* 584, 257-261. DOI: <u>10.1038/s41586-020-2405-7</u>
- [2] Lavezzo, E., et al. (including Donnelly, C.A.) (2020) "Suppression of SARS-CoV-2 outbreak in the Italian municipality of Vo' ". *Nature* 584, 425-429. DOI: <u>10.1038/s41586-020-2488-1</u>
- [3] Unwin, H.J.T., et al. (including Donnelly, C.A.) (2020) "State-level tracking of COVID-19 in the United States". *Nature Comms*, 11, 6189. DOI: <u>10.1038/s41467-020-19652-6</u>
- [4] Riley, S., et al. (including Donnelly, C.A.) (2020) "Resurgence of SARS-CoV-2 in England: detection by community antigen surveillance". Published 13 September 2020 in MedRxiv, DOI: <u>10.1101/2020.09.11.20192492</u>
- [5] Ward, H., Cooke, G., Atchison, C., et al. (including Donnelly, C.A.) (2020) "Declining prevalence of antibody positivity to SARS-CoV-2: a community study of 365,000 adults". Published 27 October 2020 in MedRxiv. DOI: <u>10.1101/2020.10.26.20219725</u>
- [6] Riley, S., et al. (including Donnelly, C.A.) (2020) "REACT-1 round 7 updated report: regional heterogeneity in changes in prevalence of SARS-CoV-2 infection during the second national COVID-19 lockdown in England". Published 16 December 2020 in MedRxiv. DOI: <u>10.1101/2020.12.15.20248244</u>

References [1] and [3] were originally published by Imperial College London on the COVID-19 Response Team website <u>https://www.imperial.ac.uk/mrc-global-infectious-disease-</u> <u>analysis/covid-19/</u> which lists more than 40 preprints/reports (most with Donnelly as a co-author) including online planning tools published over the course of the COVID-19 pandemic. References [4], [5], [6] are part of a sequence of REACT Study reports first published on <u>https://www.imperial.ac.uk/medicine/research-and-impact/groups/react-study/real-time-</u> <u>assessment-of-community-transmission-findings</u> before going onto MedRxiv.

4. Details of the impact

The primary impact of the statistical research undertaken by Donnelly has been on improved public health policy and actions in England and Scotland during the management of the COVID-19 pandemic. In addition, there are wider public health contributions in Europe and the US, and economic benefits are identified in one specific area through the provision of advice directly to theatre leaders.

Pathway to Impact

The reports and papers written by the COVID-19 Response Team and the REACT Study Team have been very widely read by key policy-makers in the UK, Europe and the US. Throughout the pandemic, the information flow to SAGE was facilitated by Donnelly's colleagues who were/are members of SAGE and SPI-M, the SAGE subgroup on modelling (including Prof Neil Ferguson until May 2020 and Prof Steven Riley throughout).

Impact: UK public health

Paper [1], in its Imperial College pre-print version known as Report 13, and the accompanying computer model, have been used extensively by the English and Scottish governments to model the development of the pandemic and the impact of different public health measures, such as lockdowns. Report 13 is reviewed on a webpage of the UK Parliamentary Office of Science and Technology [B], and a SPI-M report from 16 April 2020 [C] cites both Report 13 and the pre-print version of [2] in discussing the role of children in COVID-19 transmission, and the implications for possible school closures.

The impact on public health in Scotland is indicated by the model and computer code from [1] being used by the Scottish Government in a sequence of 32 reports in 2020, the first of which [D] says: "Scottish Government uses the publically available Imperial model as reported in their Report 13 to help understand the Covid-19 epidemic in Scotland over the longer term and what the reproductive rate at a point in time (Rt) is for Scotland."

The REACT programme [4,5,6] has been used extensively to inform the deliberations for SAGE and its sub-committees during 2020. According to the UK Government press release on 29 April 2020 [E i)], REACT "forms part of Pillar 4 of the Government's COVID-19 testing strategy, to conduct UK-wide surveillance testing to learn more about the spread of the disease and inform the development of new tests and treatments." At the launch, Health Minister Lord Bethell said [E i)]: "Understanding more about the current spread of coronavirus and the prevalence of antibodies is a vital part of our ongoing response to this pandemic."

The REACT results [4], summarised in a Government press release on 11 Sept 2020 [E ii)], showed that infections in the UK were doubling every 7 to 8 days. These results led to the introduction of the so-called rule-of-six, with Health Secretary Matt Hancock saying in the same press release [E ii)] *"It's so important that everyone abides by the law and socialise in groups up to 6, make space between you and those outside your household, get a test and self-isolate if you develop symptoms and wash your hands regularly."* Following this, on 21 Sept 2020 in a Downing Street briefing, Sir Patrick Vallance said [F]: "*The challenge therefore is to make sure the doubling time does not stay at seven days. There are already things in place which are expected to slow that, and to make sure that we do not enter this exponential growth and end up with the problems that you would predict as a result of that. That requires speed, it requires action."*

The later REACT results [5] from testing over 365,000 volunteers, the world's largest home SARS-CoV-2 antibody testing programme, were summarised in a Government press release on 27 Oct 2020 [E iii)] in which Health Minister Lord Bethell said: "*This study … is a critical piece of research, helping us to understand the nature of COVID-19 antibodies over time, and improve our understanding about the virus itself. We rely on this kind of important research to inform our continued response to the disease, so we can continue to take the right action at the right time.*"

The most recent REACT results [6] were summarised in a Government press release on 15 Dec 2020 [E iv)] which stated "The study findings demonstrate a rise in infections among secondary school age children. To tackle this rise in London and surrounding areas, additional mobile testing units will be deployed in or near schools for staff, students and their families ..." Two days later a report to SAGE on children, schools and transmission [G] cited [6] saying "REACT-1 data between 13th Nov and 3rd Dec ... show the highest prevalence in children aged 13-17 years



(high confidence)". On 30 Dec 2020, the Government in a press release [E v)] "responded to rapidly rising case rates due to the new, more transmissible variant of coronavirus by triggering the education contingency framework and pushing back the staggered return for secondary schools and colleges by one week". Having previously committed to keeping schools open, the Prime Minister explained at the 30 Dec 2020 coronavirus press conference [H] "But we must face the reality that the sheer pace of the spread of this new variant requires us now to take even tougher action in some areas and that does affect schools."

Impact: Commercial

The COVID-19 Response Team was contacted by various industry and commercial groups for advice and guidance. For example, Donnelly was asked for advice by a group of leading theatre producers, directors and CEOs representing major theatres in the UK and US, and directly communicated the implications of her findings for indoor live performances in the UK and the US. They were able to anticipate that the ban on full-capacity indoor live performances would last for many months and, as explained by the group [I]: "*Thus, we used Prof Donnelly's research to inform production schedules and investments to reduce avoidable losses incurred by preparing productions that then could not go ahead.* ... The size of the risks to subsidised and commercial theatre production of making the wrong decision as to when to reopen are, within each specific context, immense. In the case of a major art house theatre such as Sadler's Wells or The National Theatre with an annual turnover in the 10s of millions [GBP10,000,000 per year], had they gone into production with the aim of re-opening with a full season in July, or even September, and then had to cancel for a second time, this might have brought the company to the verge of bankruptcy."

Impact: Europe and US public health

Within Europe, the European Centre for Disease Prevention and Control [ECDC] plays a coordinating role in issuing advice to member states during pandemics. ECDC reports between April and September 2020 drew extensively on [1, 2]. In the sample of six reports provided [J], three cite [1],and five cite [2]. Public health policy documents from both the EU Commission and individual European governments cite both the ECDC reports and [1, 2] directly. Source [K] contains three examples: a) "Joint European Roadmap towards lifting COVID-19 containment measures" from the EU Commission (17 April 2020) cites [1]; b) "Plan de Respuesta Temprana en un Escenario de Control de la Pandemia por COVID-19" ("Early Response Plan in a COVID-19 Pandemic Control Scenario") from the Spanish government (16 July 2020) also cites [1], and c) "Operational guidance for the management of SARS-CoV-2 cases and outbreaks in schools and kindergartens" from the Italian government (28 Aug 2020) cites [2].

In the US, leadership on the public health response to COVID-19 has been provided by the state governors. New York State was particularly badly hit, and Governor Cuomo and his officials paid close attention to [3] on the state-level tracking of COVID-19 within the US. One of the authors of [3] was involved in a virtual press conference on the day of its publication, at which the governor discussed plans to re-open the state and drew attention to the state's use of the modelling and analyses undertaken in [3] saying [L]: "In a State like New York, what the people did dramatically changed that curve so it affected the projections. The Imperial College model, as we've been following this for weeks, was the best, most accurate model. And therefore, I think Dr. Bhatt [co-author of [3]] deserves all our thanks because they really helped us all through this to date, and I want to thank him very much for taking the time to advise us, not just on how we constructed our model to date but what happens going forward as we increase the economic activity and we start to see numbers change."

5. Sources to corroborate the impact

[A] Letter from Prof Neil Ferguson (1 Dec 2020)



[B] Parliamentary Office of Science and Technology webpage (2020) with review of [1]: <u>https://post.parliament.uk/models-of-covid-19-part-3/</u>	
[C] <u>SAGE 26 report</u> on "The role of children in transmission" (16 April 2020), citing [1,2]	
[D] Scottish Government report, "Coronavirus (COVID-19): modelling the epidemic", 21 I December 2020. First of 32 reports available from <u>https://www.gov.scot/collections/coronavirus-covid-19-modelling-the-epidemic/</u>	May —
 [E] Press releases from: UK Department of Health and Social Care: Major home testing programme for coronavirus will track levels of infection in the community (29 April 2020) UK Department of Health and Social Care: Largest testing programme for corona reinforces need for vigilance (11 Sept 2020) UK Department of Health and Social Care: Largest COVID-19 antibody testing programme publishes findings on antibody response over time (27 Oct 2020) UK Department of Health and Social Care: November 2020 findings from COVID study published (15 Dec 2020) UK Department for Education and Gavin Williamson MP: School contingency planting implemented as cases rise (30 Dec 2020). 	<u>-19</u>
[F] BBC report on "Covid-19: UK could face 50,000 cases a day by October without action Vallance" (21 Sept 2020). <u>https://www.bbc.co.uk/news/uk-54234084</u>	on —
[G] <u>Children's Task and Finish Group: update to 4th Nov 2020 paper on children, schools</u> <u>transmission (17 Dec 2020).</u>	<u>s and</u>
[H] Public statement by the Prime Minister on COVID-19 (30 Dec 2020) <u>https://www.gov.uk/government/speeches/prime-ministers-statement-on-coronavirus- 19-30-december-2020</u>	-covid-
[I] Letter from theatre producers, directors and CEOs (28 Oct 2020)	
 [J] Reports from the European Centre for Disease Prevention and Control (2020): i) <u>"Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK – ninth update 2020)</u> cites [1] and [2] ii) <u>"Paediatric inflammatory multisystem syndrome and SARS-CoV-2 infection in chi</u> 	
 (May 2020) cites [2] iii) <u>"Methodology for estimating point prevalence of SARS-CoV-2 infection by pooled</u> <u>PCR testing" (May 2020)</u> cites [2] iv) "Guidance on the provision of support for medically and socially vulnerable popul 	
 v) <u>Guidance on the provision of support for medically and socially vulnerable population in EU/EEA countries and the UK during the COVID-19 pandemic" (Jul 2020) cites [7]</u> v) <u>"Infection prevention and control and surveillance for coronavirus disease (COVID prisons in EU/EEA countries and the UK" (July 2020) cites [2]</u> 	1]
 vi) <u>"Guidelines for the implementation of non-pharmaceutical interventions against C 19" (Sept 2020)</u> cites [1] and [2] 	OVID-
 [K] European public health guidance documents citing [1] and [2]. (2020) i. "Joint European Roadmap towards lifting COVID-19 containment measures", EU Commission (17 April 2020) 	
 ii. "Plan de Respuesta Temprana en un Escenario de Control de la Pandemia por C 19", Spanish government (16 July 2020) iii. "Operational guidance for the management of SARS-CoV-2 cases and outbreaks 	
schools and kindergartens", Italian government (28 Aug 2020) [L] Governor Cuomo press statement. (18 May 2020) <u>https://www.governor.ny.gov/news</u>	
ongoing-covid-19-pandemic-governor-cuomo-announces-state-bringing-international	-experts