Institution: Imperial College London

Unit of Assessment: 10 – Mathematical Sciences

Title of case study: B10-1 A new statistical framework impacted millions during the COVID-19 pandemic

Period when the underpinning research was undertaken: March 2020 – 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:
Dr Samir Bhatt Dr Seth Flaxman Professor Axel Gandy Dr Swapnil Mishra Dr Juliette Unwin	SB: Senior Lecturer in Geostatistics SF: Senior Lecturer in Statistical Machine Learning AG: Chair in Statistics SM: Research Associate JU: Research Fellow	SB: 2016-present SF: 2017-present AG: 2006-present SM: May 2019-present JU: August 2019-present

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

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

1. Summary of the impact

Imperial researchers developed a new statistical framework to model the COVID-19 pandemic which has been used to inform the decisions of policy makers worldwide, for example, in the UK and the US, affecting the lives of millions. From the early stages of the first wave of the epidemic, the framework allowed quantification of the effectiveness of non-pharmaceutical interventions, especially lockdowns, contributing to worldwide understanding of the effect of such measures. This helped public health authorities communicate about, and maintain public support for, social distancing measures. After the first wave, the modelling framework was further developed and taken up by health authorities, e.g., in Scotland and New York, to guide ongoing policy decision-making during subsequent waves. The framework was also a key component in determining the speed of the spread of a new variant of SARS-CoV-2 (the 'Kent variant') detected in England, supporting the evidential basis which led to the introduction of Tier 4 measures in England in December 2020.

2. Underpinning research

On 11 March 2020, the World Health Organization declared a pandemic: SARS-CoV-2, the virus that causes COVID-19, had spread far and wide around the world. After the initial outbreak in China, the epicentre shifted to Europe, where countries were considering drastic strategies to control the epidemic, from banning public events to closing schools to lockdowns.

During this first wave of COVID-19, and due to limited testing and asymptomatic spread, reports of case numbers were not a reliable measure of the spread of SARS-CoV-2. This meant that existing approaches to quantifying R_0, the basic reproduction number, and R(t), the time-varying reproduction number, were inadequate to answer the pressing questions facing public health authorities worldwide: How far had SARS-CoV-2 spread? Were control measures effective and, in particular, did they bring R below 1?

A group of Imperial academics, with expertise in epidemiology, statistics, and machine learning, led by Drs Flaxman, Mishra, Bhatt, Unwin, and Prof Gandy (Flaxman and Gandy are in the Department of Mathematics), started work on a new semi-mechanistic statistical modelling framework to understand the extent of the spread of SARS-CoV-2 infections in real-time, and to infer the effect of government interventions. The framework developed at Imperial relied on the following innovative approaches: 1) A novel fully Bayesian statistical model that accurately

incorporates the time-delays between subsequent infections and between infections and observations (both cases detected and death numbers). 2) Leveraging of observations from multiple countries and regions, which previously existing epidemiological models did not do. 3) Open-source implementation in a probabilistic programming language (Stan) to enable widespread dissemination and reproducibility of the modelling approach.

The first results and the first model description were released as a preprint ("Report 13") on 30 March 2020 (peer reviewed and updated in **[1]**) - Flaxman, Mishra, Gandy were joint first authors, Bhatt was last author, all with equal contributions. This works showed that lockdowns were beginning to be effective across Europe, in the sense of bringing the reproduction number below 1, at a time when death counts were still rising. It also estimated how many lives had already been saved through the non-pharmaceutical policy interventions.

From these methods and approaches, further research activity spawned at Imperial, including specific studies of the epidemic in Italy **[2]**, Brazil **[3]**, and the US **[4]**, each including key novelties in the statistical models. The Italy report **[2]** was a subnational analysis incorporating data on human mobility. Brazil **[3]** provided the first subnational analysis of the reproduction number in Brazil, finding that R(t)>1 in all states analysed, meaning that the epidemic was not under control in Brazil in May. The US report **[4]** correctly warned about the precarious position of many states in the US at a critical period after the first wave.

Based on the methodology developed in **[1-4]**, Imperial researchers developed an R package called "epidemia" **[5]**. In addition, the team also developed a local area model for the UK **[6],** made public on 3 September 2020, which provides projections of COVID-19 cases per 100,000 individuals at the local-authority (LTLA) level across all 4 nations of the UK. Daily updates to these projections are released on a public website. Estimates of R(t) from this model were essential to the rapid analysis of the increased transmissibility of the new B.1.1.7 variant of the virus in December 2020 **[7]**.

3. References to the research

[1] Flaxman S*, Mishra S*, Gandy A*, Unwin HJT, Mellan TA, Coupland H, Whittaker C, Zhu H, Berah T, Eaton JW, Monod M, Imperial College COVID-19 Response Team, Azra C. Ghani AC, Donnelly CA, Riley S, Vollmer MAC, Ferguson NM, Okell LC, Bhatt S*, *Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe*, Nature 584, 257–261(2020), doi:10.1038/s41586-020-2405-7.
Preprint on 30/03/2020 as "Report 13", doi:10.25561/77731. *=contributed equally

[2] Vollmer MAC, Mishra S, Unwin HJT, Gandy A, Mellan TA, …[53 authors]..., Donnelly CA, Ferguson NM, Dorigatti I, Flaxman S, Bhatt S (2020) "Report 20: Using mobility to estimate the transmission intensity of COVID-19 in Italy: A subnational analysis with future scenarios", medRxiv 2020.05.05.20089359, doi:10.1101/2020.05.05.20089359.

[3] Hawryluk I, Mellan TA, Hoeltgebaum H, Mishra S, Schnekenberg RP, Whittaker C, Zhu H, Gandy A, Donnelly CA, Flaxman S, Bhatt Samir (2020) *Inference of COVID-19 epidemiological distributions from Brazilian hospital data*, J. R. Soc. Interface.17:20200596, doi:10.1098/rsif.2020.0596. Preprint on 8/5/2020 as "Report 21", doi:10.25561/78872.

[4] Unwin HJT*, Mishra S*, Bradley VC*, Gandy A*, Mellan TA, …[43 co-authors]…,Ghani, AC, Ferguson NM, Riley S, Donnelly CA, Bhatt S, Flaxman S (2020) *State-level tracking of COVID-19 in the United States*, Nature communications, 11(1), p. 6189, doi:10.1038/s41467-020-19652-6.
Preprint on 21/5/2020 as "Report 23", doi:10.25561/79231. *=contributed equally

[5] Epidemia R package https://imperialcollegelondon.github.io/epidemia/index.html

[6] Mishra, S., J. Scott, H. Zhu, N. M. Ferguson, S. Bhatt, S. Flaxman, and A. Gandy. 2020. "A COVID-19 Model for Local Authorities of the United Kingdom." *medRxiv,* doi:10.1101/2020.11.24.20236661.
Previous versions of the website: https://doi.org/10.5281/zenodo.4400238.
Git repository with all versions: https://github.com/ImperialCollegeLondon/covid19local
Current version of Website: https://imperialcollegelondon.github.io/covid19local/

[7] Volz E*, Mishra S*, Chand M*, Barrett JC*, Johnson R*, …[22 co-authors]…, Flaxman S, Ratmann O, Bhatt S, Hopkins H, Gandy A*, Rambaut A*, Ferguson N*, "Report 42: Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: insights from linking epidemiological and genetic data," doi: 10.1101/2020.12.30.20249034, 31 December 2020.
*=contributed equally
The report was released on 31 Dec 2020 at https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-42-sars-cov-2-variant/; the above doi points to the MedRXiv Version which was made publicly available on 4 January 2021.

4. Details of the impact

The research of the Imperial team informed public and government understanding of the epidemic worldwide, was used by governments to justify maintaining restrictions, and had direct and extensive impact on policy decisions, particularly in Scotland (from April 2020) and New York State (from May 2020) and in the imposition of stronger restrictions in England in December 2020.

Public understanding and awareness: The research attracted strong public attention: At least **484** news stories from **332** outlets (e.g. BBC, Economist, Times, Financial Times, National Public Radio (US), Boston Globe, Washington Post) reported on **[1-7]**, see **[A]**. The Altmetric score of **[1]** is greater than 6300, putting it amongst the top 250 articles of more than 16 million articles tracked on Altmetric **[A]**. The website reporting updates from **[6]** had more than 750k visitors from 142 countries up to the end of 2020 **[A]**. The news coverage was helping public understanding by picking up several results from the research, e.g.: results from **[1]** were used to show how many lives had been saved through the interventions (Daily Telegraph, **[A]**), that more individuals than previously thought has been infected (Economist, **[A]**), and to describe the state of the epidemic around the time of the first lockdown and to compare it to other European countries (The Times, **[A]**); local newspapers used **[6]** to inform about the likely development of the epidemic in their local area (Google News search, **[A]**).

Policy makers and health authorities used [1,4] to assess and evidence the effectiveness of interventions:
The Scottish government's assessment of lockdown effectiveness highlights our impact within this area. The Chief Statistician of Scotland states that "[…] *these methods have been crucial in our assessment that the lockdown in March in Scotland was effective, giving us confidence to sustain it and to be able to communicate our decisions to the general public.*" **[C]**

Members of the French government (the Health Minister, the Directeur Général de la Santé, President Macron) used **[1]** to demonstrate that lockdowns were working and to encourage the public to stay at home, using the slogan "one life saved every 8 minutes" **[D]**.

The State of Michigan cited **[4]** in a legal case defending the legal basis of their public health measures, as well as on social media and in a press release, in the face of vehement opposition from a fringe (and violent) minority **[E]**.

Impact on policy decisions, the general population and saving lives
The **Scottish Government** used **[1,5,6]** extensively. The Chief Statistician of the Scottish Government writes **[C]**:

> *"Based on the source code released from Report 13, we developed a model for **Scotland** […]. This has been key in our decision making process throughout the epidemic. This model has been run on a weekly basis since the end of April 2020 […] Outputs from our model have also been **central to the Scottish Government's regular COVID-19 modelling updates, of key interest to members of the public**. […] This has been a **crucial input into ministerial decisions** on advice for the Scottish population, **including on whether to relax or to impose government restrictions**."*

From 29 October 2020, the Scottish government reports our local area estimates **[6]** and has been using them as criteria for areas transitioning between lockdown tiers **[C]**; 3 of the 5 criteria used are based on **[6]**.

Overall, there has been strong impact in Scotland; quoting **[C]:**

> *"[…] the methods developed by Imperial have been crucial in the Scottish Government's response to the COVID-19 pandemic. These methods have formed a crucial part in many of our decisions during the pandemic and thus have **had a profound impact on the entire Scottish population, helping to save many lives**."*

Based on **[1,4]**, the Imperial team developed a model for **New York State** (population ~19 million),

> *"whose results were discussed weekly […] in the state's determination of **when regions should begin easing restrictions** […] the modelling results have subsequently been used to assist in identifying hotspots and inform additional control strategies. The Imperial college team has been an important partner … in informing the state's COVID response."* **[F]**

New York State appointed a team of experts, including Dr Bhatt, "who, before giving a region the green light to move from one phase to the next, would review our data and then advise whether it was safe to continue the reopening of that region of the state" (Cuomo, **[F]**).

A model based on **[1]** has been influential in the **State of Tennessee**: "*We were able to construct our first model in one day, which we would never have been able to do without the work you shared. […] This model **helped solidify the value of such measures**, and safer-at-home in particular, **for several leaders at a critical point** in local decision making."* **[G]**

Tier 4 restrictions in England: On 19 December 2020, the UK government imposed stricter restrictions in several areas in England, due to the spread of a novel SARS-CoV-2 variant. The Prime Minister said: *"NERVTAG's early analysis suggests the new variant could increase R by 0.4 or greater. Although there is considerable uncertainty, it may be up to 70% more transmissible than the old variant."* **[H]** (NERVTAG is the "New and Emerging Respiratory Virus Threats Advisory Group" advising the UK government.)

The figures in the PM's statement are the result of analysis by Imperial scientists (a group including Professors Ferguson, Gandy, Drs Mishra and Volz), which was presented to NERVTAG on 18 December 2020 **[H]** and later published as **[7]**. The Imperial analysis was based on genomic data as well as on linking local estimates of the reproduction number **[6]** to estimates of the proportion of the new variant present. Based on these results plus two further pieces of evidence from other scientists concerning the amount of virus present in samples of the new variant (PCR Ct values, viral load from genomic analysis) NERVTAG reached its conclusion **[H].**

By 30 December, twenty million more people in England were subject to the toughest level of tier restrictions. Further consequences of these results were travel bans imposed e.g., by France and Germany, to stop the spread of the new variant of SARS-CoV-2.

Further Policy Impact: Policy documents from the African Union, the European Union and the World Bank cited **[1]**, see Altmetric, **[A]**. Prof Gandy gave evidence in the UK House of Commons based on **[6]** regarding the local spread of COVID-19 in the inquiry on "Lessons learnt from Covid-19" **[B].** Prof Gandy and Dr Bhatt were appointed to the SPI-M subgroup of SAGE (Scientific Advisory Group for Emergencies) from 30/10/2020, contribution to consensus statements, for example through modelling outputs about the effectiveness of the first UK tier system.

5. Sources to corroborate the impact

[A] Media Impact (Archived here):

- List of news reports
- https://nature.altmetric.com/details/83468934 for **[1]**
- Report of number of visits to website of **[6]**
- https://www.economist.com/graphic-detail/2020/04/01/covid-19-may-be-far-more-prevalent-than-previously-thought
- https://www.telegraph.co.uk/global-health/science-and-disease/coronavirus-lockdown-measures-may-have-saved-59000-lives-europe/amp/
- 23 May 2020 https://www.thetimes.co.uk/article/three-weeks-of-dither-and-delay-on-coronavirus-that-cost-thousands-of-british-lives-05sjvwv7g

- Google New Search on local newspapers using results from **[6]**

[B] Evidence to House Select Committee by Prof Gandy (Archived here)
https://committees.parliament.uk/event/2362/formal-meeting-oral-evidence-session/

[C] Impact in **Scotland** – Evidence pack

- Testimonial by the Chief Statistician of Scotland.
- Use of local model in tiering decisions: https://www.gov.scot/publications/coronavirus-covid-19-allocation-of-levels-to-local-authorities/

[D] Impact in **France** (Archived here):

- Tweets from the French Health minister on 31 March; (https://twitter.com/olivierveran/status/1244998753616084992)
- Link to the daily COVID-19 status update on 8 April from the "Directeur Général de la Santé" (https://dai.ly/x7t6lnx) - remark at 8:30.
- Tweet from the French President on 11 April. (https://twitter.com/emmanuelmacron/status/1249042840241479682)
- Newspaper articles (Le Parisien, Le Figaro) explaining the link to **[1]**

[E] Impact in **Michigan** (Archived here):

- Court Case: https://www.clearinghouse.net/chDocs/public/PR-MI-0002-0011.pdf.
- Social media (https://twitter.com/GovWhitmer/status/1271114225482706945)
- Press Release (https://www.michigan.gov/coronavirus/0,9753,7-406-98163-531728--,00.html).
- News article about opposition to lockdowns in Michigan https://www.nytimes.com/2020/10/11/us/whitmer-kidnapping-plot-michigan.html).

[F] Impact in **New York State**

- Testimonial from the Commissioner of the Department of Taxes and Finances of New York State, who was a member of the Governor's COVID-19 Task Force.
- Cuomo, Andrew. 2020. *American Crisis: Leadership Lessons from the Covid-19 Pandemic*. Random House Inc. ISBN 978-0593239261. Chapter "May11 | 1,660 New Cases| 7,226 Hospitalised| 161 Deaths"*, page 446.*

[G] Impact in **Tennessee:** Testimonials by a member of the COVID-19 Response Unit academics from the University of Memphis, the University of Tennessee

[H] Impact on Tier 4 Decisions in **England** (Archived here):

- "New evidence on VUI-202012/01 and review of the public health risk assessment" Report to NERVTAG meeting 18/02/2021 by Public Health England, with Imperial College, the University of Edinburgh, the University of Birmingham and the Wellcome Sanger Institute.
- Minutes of NERVTAG Meeting on 18/12/2020.
- Speech by the Prime Minister, Boris Johnson on 19/12/2020.