Institution: King's College London		
Unit of Assessment: 12 Engineering		
Title of case study: COVID Symptom Study App		
Period when the underpinning research was undertaken: 2014-2020		
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:**
Sebastien Ourselin	Professor of Healthcare Engineering	From 09/04/2018
Tim D. Spector	Professor of Genetic Epidemiology	From 01/09/2006
Emma L. Duncan	Professor of Clinical Endocrinology	From 04/05/2020
Claire J. Steves	Senior Clinical Lecturer	From 06/04/2009
M. Jorge Cardoso	Senior Lecturer	From 14/05/2018
Marc Modat	Senior Lecturer	From 14/05/2018
Cristina Menni	Lecturer	From 18/08/2011
Period when the claimed impact occurred: March 2020-December 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

In March 2020, as the global COVID-19 pandemic was declared, King's College London (King's) researchers together with ZOE Global rapidly engineered the COVID Symptom Study smartphone app. This was used to capture real-time data on known and potential symptoms of COVID-19 from residents of the UK, USA and Sweden. Endorsed by the Welsh, English and Scottish Governments, over 4,000,000 people signed up to the app globally, with 2,000,000 of those registering in the first two weeks it was available (24 March 2020). Analysis of the data generated led to:

1. The World Health Organisation (WHO), UK government and the UK Office for National Statistics updating their guidance on anosmia and delirium as key symptoms of COVID-19.
2. Identification of rate and location of new infections in real time, which informed the UK Government's national strategy for containing infection.
3. Helping the UK government identify hot-spots across the nation.
4. Identification of the symptoms and duration of Long COVID for the first time in a non-clinical population, informing UK government policy and NICE guidelines.

2. Underpinning research

At King's School of Biomedical Engineering & Imaging Sciences (BMEIS) we have been engineering methods and tools to deal with large scale imaging clinical trials and clinical studies. Ourselin, Modat, and Cardoso have led the development of computational platforms to host, curate and process imaging and associated clinical data for large-scale neurodegenerative studies. An exemplar is the deployment of a validated, unsupervised, automated algorithm in the Insight 46 study [R1]. Our know-how and research has contributed to the development and deployment of the Dementia Platform UK infrastructure and portal [R2]. This portal now hosts 3 million patients' data, completely curated, and enables researchers to access the combined information from over 40 dementia studies. Additionally, our combined research expertise in machine learning led to the development of some the most popular open-source toolboxes dedicated to the process of healthcare data analysis with machine learning techniques, NiftyNet [R3], and more recently MONAI.io, co-developed with NVIDIA.

Zoe Global is a health technology spin-out from King's, co-founded by Spector, that develops a mobile platform to gather nutrition data from its users. As the COVID-19 pandemic began, Zoe repurposed their platform to create a smartphone app that gathers self-reported data on COVID-19 from the general population, collaborating with clinicians and epidemiologists from the King's Department of Twins Research to analyse the data.

The COVID Symptom Study App was launched in three countries (UK, US, Sweden) on 24 March 2020. After more than 1.5 million users downloaded the app within days of its launch, several engineering challenges emerged that we solved because of our expertise in algorithm engineering and development and deployment of software at scale.

a. The sheer scale of the data generated by millions of users meant that researchers were not able to analyse it using the hardware and software available to them. With billions of rows of reports, the data from the COVID Symptom study became quickly too large to load and process on typical analysis software. We developed the open-source ExeTera software package [R4] based on our expertise. This open-source software package was designed to address scalability challenges and allows researchers to analyse large datasets, with billions of rows of data, without the need to load the full dataset into memory, taking care of the curation and imputation at scale to enable reproducible research.

b. The non-traditional acquisition of the data compared to classical epidemiological studies required the development of new analysis methods to extract insight from the rich, although non-curated, data produced by the study. New machine learning and statistical analysis algorithms were engineered and deployed in order to allow for insight to be extracted from the Symptom Study data. Traditional disease surveillance methods perform tests on many people to build an idea of disease levels in the population; we developed a novel approach that combines information from a small number of tests with predictive models applied to self-reported symptoms from a large number of app users to track the pandemic. While demonstrating similar accuracy as traditional methods, this approach allowed for greater geographic granularity, enabling notably the identification of emerging disease hotspots [R5]. The self-reported and voluntary nature of the study introduces potential bias that can undermine the validity of any insights extracted from it. To address this, we developed a number of selection processes that allow us to extract reliable insight from the data, leveraging its unique dense longitudinal nature, such as differential weighting, as some parts of the population are sampled with unequal probabilities of selection. Such techniques allowed us to develop robust predictive models, producing one of the earliest pieces of evidence that anosmia is a key symptom of COVID-19 [R6], that delirium is an important symptom in older patients, and enabling us to carry out one of the largest studies on Long COVID, significantly furthering our understanding of the disease and its presentation [R7].

3. References to the research

R1. Lane CA, et al. (2019) Associations between blood pressure across adulthood and late-life brain structure and pathology in the neuroscience substudy of the 1946 British birth cohort (Insight 46): an epidemiological study. Lancet Neurol. August;18(10):942-952, DOI: 10.1016/S1474-4422(19)30228-5

R2. Bauermeister S, Ourselin S et al. (2020). The Dementias Platform UK (DPUK) Data Portal, Eur. J Epidemiology, Jun; 35(6):601-611, DOI: 10.1007/s10654-020-00633-4

R3. The NiftyNet Consortium

R4. Accessible Data Curation and Analytics for International-Scale Citizen Science Datasets, arxXiv, (2020) November, Software available on GitHub

R5. Varsavsky T, Modat M, Jorge Cardoso M, Steves C, Spector T, Ourselin S et al. (2020). Detecting COVID-19 infection hotspots in England using large-scale self-reported data from a mobile application, Lancet Public Health, December;6(1):E21-E29, DOI: 10.1016/S2468-2667(20)30269-3

R6. Menni C, Jorge Cardoso M, Ourselin S, Steves C, Spector T et al. (2020). Real-time tracking of self-reported symptoms to predict potential COVID-19. Nat Med. July;26(7):1037-1040, Epub May 1, DOI:10.1038/s41591-020-0916-2

R7. Sudre C, Modat M, Jorge Cardoso M, Duncan E, Menni C, Ourselin S, Spector T, Steves C et al (2020). Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App (preprint first online October 2020) medRxiv, DOI: 10.1101/2020.10.19.20214494

4. Details of the impact

King's researchers leveraged their expertise in algorithm engineering, big data, and artificial intelligence to rapidly engineer the COVID Symptom Study App in response to the COVID-19 pandemic. Rapid deployment and analysis of the data generated key evidence which widened the understanding of core symptoms for COVID-19 worldwide, helped with the identification of hotspots in the UK, contributed to a better understanding of Long COVID-19 both in the UK and internationally, and supported the UK government and the public to navigate the pandemic.

Endorsements lead to widespread adoption of the app by UK public.

The Scottish and Welsh Governments and prominent health charities endorsed the COVID Symptoms Study App. The Welsh Government and NHS Wales [S1] were the first to make an appeal for the public to download and use the app. In April 2020, they released a press release where Welsh First Minister, Mark Drakeford, stated: "*Having a range of evidence and data is crucial in helping us build a clear picture of how the virus is behaving and affecting everyone's lives. Crucially this app can help us anticipate potential COVID hot spots and get our NHS services ready. I'm asking everyone in Wales to download the new COVID Symptom Tracker App, so you can help protect our workers and save lives* [S1a]." The Scottish Government also encouraged people to use the app in their official social media channels. They stated: "*The COVID Symptom Tracker is an app, approved by Scotland's top clinicians, designed to study the symptoms of #coronavirus and track how it spreads. We need as many people as possible to take part including people who are feeling well* [S2]*."* Several key health charities in the UK also urged members and the general public to use our app such as the British Heart Foundation, British Lung Foundation, National Rheumatoid Arthritis Society, and Stand Up to Cancer [S3]. **By July 2020, the app had been downloaded by over 4,000,000 users** [S11]. In August 2020, the UK government further recognised the importance of the app by awarding ZOE Global a GBP2,000,000 grant [S9]. They said [S9] the app is "*the largest public science project of its kind anywhere in the world*" and that it "*will help control the spread of the virus by providing vital new intelligence on the scale of local outbreaks, inform our understanding of the virus and how it affects different demographics."*

King's research on data collected from COVID Symptom Study App led the WHO and the UK Government to include anosmia in official COVID-19 symptoms lists. Data from our COVID Symptom Study App confirmed, for the first time in non-clinical patients, the loss of taste and smell as the most predictive symptom of COVID-19 - 10 times more so than the initial officially listed symptoms, fever or cough**.** As a result, the World Health Organisation (WHO) [S5] and UK Government [S6] added anosmia to the official list of COVID-19 symptoms. **This increased the medical community's diagnostic capability, and ensured the public recognised this symptom as a sign that they may have COVID and took appropriate action to protect themselves and their community**. [Text removed for publication], said [S5b]: "*Your [King's] work, particularly in relation to anosmia, was really important in informing the discussions behind this and is much appreciated.*" [Text removed for publication], confirmed that data from the app was one of the pieces of evidence reviewed which led to anosmia being added to the official case definition symptoms list for COVID-19 in May 2020. [Text removed for publication] [S6b]: "*As estimated by NERVTAG* (The New and Emerging Respiratory Virus Threats Advisory Group) *at the time, this will have helped pick up 93% of symptomatic cases, up from 91% previously, which may have led to significant benefit over time.*" [Text removed for publication] said "*These reports have been part of a range of information that is received, which has influenced the management of the COVID-19 pandemic in Scotland. …..estimated prevalence data has informed SARS-CoV-2 testing strategy; the app provided clear evidence of that anosmia was a cardinal symptom of COVID-19…..*" [S6c]

King's research led the UK Government to include delirium in the official COVID-19 symptoms list for the elderly. The COVID Symptom Study showed that delirium - a state of sudden confusion - is a key symptom of COVID-19 in older people**.** As a result, UK government updated its guidance, outlining the addition of delirium to the UK's official list of COVID-19 symptoms in the elderly, and advising doctors to test elderly people presenting with acute confusion for COVID-19 [S6a]. This helped healthcare professionals in diagnosis, and increased awareness amongst the public and in care homes to recognise this symptom and take appropriate action to test and avoid spread.

Research by King's allowed the UK government to identify hot spots across the nation. Thanks to over 4,200,000 people logging their symptoms and location in the app daily, our daily reports to the UK government were able to show the rates of infection in real time across the UK, allowing identification of areas where rates of infection were increasing rapidly. This information was used by the different government bodies in England [S6b], Wales [S1c] and Scotland [S2a], to inform policies intended to slow rates of infection and allow health services to cope. [Text removed for publication] stated [S6b]: "*(…) the app has been very useful in tracking the progress of the disease. Since March 2020* [Text removed for publication] *to identify hot spots across the nation showing the rates of infection in real time all over the UK, allowing identification of areas where rates of infection were growing rapidly. These data have also contributed to increased public awareness and facilitated better management of the disease, which has had an impact on the UK population, the NHS and COVID-19 patients.*"

King's research informed NICE and the UK government about Long COVID-19. Data from our COVID Symptom Study suggests that while most people recover from COVID-19 within two weeks, one in ten people will suffer symptoms after three weeks, and some may suffer for months**.** In December 2020, The National Institute for Health and Care Excellence (NICE) published guidelines on the management of long-term COVID [S7a] informed by King's research. [Text removed for publication]: "*COVID Symptom Study data was* [Text removed for publication] *at a critical moment in the development of the guideline, allowing the advisory panel to consider it when making recommendations on the identification and management of post COVID-19 syndrome* [S7b]."

[Text removed for publication] mentioned, *"In both of these roles I am grateful for the work of the COVID Symptom Study. Its data has informed early understanding of Long-COVID, being the first dataset to show the extent of the problem, and characterise the syndrome.* […] We have seen how the findings of the COVID Symptom Study App have had an important impact on our understanding of the natural history of COVID, both in the UK and internationally." [S5d]

Furthermore, the Health and Social Care Secretary Matt Hancock confirmed: "*The findings of the Covid Symptom Study are stark and this should be a sharp reminder to the public, including to young people, that COVID-19 is indiscriminate and can have long-term and potentially devastating effects* [S8]." The [Text removed for publication] data from the app will continue to help track the symptoms of those suffering from Long COVID, to help understand more about its course and the long-term impact of this disease on people's lives [S6b].

Members of the public have benefitted from using the app. The app is free of charge and has been available since March 2020. It's rated 4.7 out of 5 stars based on over 276,500 user ratings in the Apple [S10a] and Google Play App Store [S10b]. Anonymous reviews illustrate how well the app has been received by the public and what difference it has made in their lives while living through a pandemic. An anonymous review from April 2020 revealed [S10b]: "*In our isolation feels like we are helping to stop the spread of COVID-19 and the research into its spread with this app*."

Reviews have also shown the difference the app has made in people with Long COVID symptoms [S10a]: "*This app is very welcome both for its potential to enable better understanding of the illness, and for the fact that it makes those of us isolating with long term symptoms feel less alone."* (May 2020) "*My youngest daughter is showing signs of long COVID like myself, so this app is great for me to keep track of my symptoms and hers."* (November 2020).

5. Sources to corroborate the impact

S1. Sources corroborating Welsh Government and NHS Wales endorsing King's App:

a. Welsh Government Press Release, 11th April 2020
b. Tweet from Mark Drakeford's verified Twitter handle, 9th June 2020
c. [Text removed for publication]

S2. Sources that corroborate Scottish Government endorsing King's App (April 2020):

a. [Text removed for publication]
b. Tweet from Scottish government's verified Twitter handle, 10th April 2020
c. Post from Scottish government's verified Facebook page, 10th April 2020

S3. Sources that corroborate various health charities endorsing King's App:

a. British Heart Foundation
b. British Lung Foundation
c. National Rheumatoid Arthritis Society
d. StanduptoCancer

S4. Guidance COVID-19 surveillance Government UK Website Page

S5. Sources that corroborate claim of King's research influencing WHO adding anosmia to list of COVID symptoms:

a. WHO website COVID symptom list
b. [Text removed for publication]
c. WHO Technical Package
d. [Text removed for publication]

S6. Sources that corroborate claim of King's research influencing UK Government policy:

a. UK Government website COVID symptom list (items 2 and 3)
b. [Text removed for publication]
c. [Text removed for publication]

S7. Sources to corroborate:

a. NICE COVID-19 rapid guideline: managing the longterm effects of COVID-19 (NG188) (pages 4, 6, 8, 15, 43-45)
b. [Text removed for publication]

S8. BBC News Article 'Long Covid: Who is more likely to get it?', 21st October 2020

S9. Press release from the Department of Health and Social Care about GBP2,000,000 funding

S10. Sources that corroborate members of the public benefitting from the App:

a. Apple App Store reviews
b. Google Play App Store Reviews

S11. Zoe Global website celebrating 4 million app downloads