

Impact case study (REF3)

Institution: King's College London		
Unit of Assessment: 1		
Title of case study: COVID-19 Symptom Study App: Influencing global understanding and national government policy		
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:
Prof Tim Spector	Professor	1993-to date
Dr Claire Steves	Clinical Reader	2009-to date
Dr Cristina Menni	Lecturer	2011-to date
Dr Mario Falchi	Reader	2015-to date
Dr Sarah Berry	Reader	2006-to date
Dr Frances Williams	Professor	2007-to date
Prof Emma Duncan	Professor	2020 -to date
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

In March 2020 the coronavirus outbreak was declared a pandemic by the World Health Organization (WHO). That same month, King's researchers together with ZOE Global (a King's spinout) rapidly adapted a successful King's digital health App into the COVID Symptom Study 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 in the UK, with 2,000,000 of those registering in the first two weeks it was available. Analysis of the data generated led to:

1. The World Health Organisation, Public Health England 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. 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

Background: Since 2018, King's researchers leading the Wellcome funded Longitudinal Population Study with a large set of volunteers from the well-established King's adult twins registry (TwinsUK), which have pioneered the use of "digital cohort" App-based approaches to collect detailed longitudinal datasets on diet and health from large numbers of participants, in real time, and at low cost. We applied artificial intelligence to analyse profiles of the twins and identify and predict biological responses to food. When the COVID-19 pandemic emerged in 2020, little was known about the symptoms of the virus: King's researchers saw an opportunity to rapidly redirect their existing technology and scientific expertise, by shifting from logging information on diet and health, to collecting daily data about potential symptoms, risk factors and consequences of COVID-19 in real-time.

King's researchers combined AI technology with cohort data to look at ways to improve human health through precision personalised nutrition. Following the success of King's work in relating health to gut microbiome differences (**2, 3**), in 2018 King's spun out Health technology company ZOE Global and set up the largest in-depth nutrition study in the world: PREDICT. In collaboration with the Biomedical engineering department at King's, we used AI tools to show that

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people respond differently to food and that these differences could be predicted using several unique physiological and metabolic variables such as microbiome diversity and glucose levels (1). Most importantly, this breakthrough enabled us to develop App based tools to engage with the study participants in a new way, feeding back personalised insights on which foods may help that individual reduce dietary inflammation, improve gut health, and help users reach a healthy weight.

Based on this underpinning research, King's researchers responded to the COVID-19 pandemic: with insight into how App technology could reach the wider UK population and gather daily reports on symptoms, they used AI methods on time-series and geographical data to map the spread of disease. In early 2020, King's researchers designed the COVID Symptom Study App, collaborating with ZOE to put the content into a smart-phone based platform enabling rapid dissemination. Combining information/observations drawn from the clinical experience of treating COVID-19 patients of the team and their international network, King's researchers designed the App to accurately target key symptoms. The App was launched on 23rd March, and between 24th March and 21st April 2020 alone, 2,450,569 UK and 168,293 US individuals began reporting symptoms through the smartphone App (4, 5). Deepening the existing collaboration with King's School of Engineering enabled intensive, rapid development of software to use this huge dataset to understand and map COVID-19, and estimate national and local COVID-19 cases based on algorithmic prediction. The App was free and widely available for any UK resident to use and by December 2020, more than 4,000,000 people were using it. Participants were asked to log daily health updates and record a wide range of risk factors, symptoms (temperature, tiredness, coughing, breathing problems, headaches etc), whether or not they had tested positive for the virus and if so, the treatment they received. To encourage their ongoing participation, users had access to local data, latest research, information on risk factors, local and national trends, advice and the ability to keep track of self-isolation. King's researchers existing skills allowed them to continue to optimise the App in real time based on feedback from participants.

The COVID Symptom Study App allowed King's researchers to identify a number of symptoms of COVID-19. In total, by the end of 2020 King's researchers had contributed to 18 papers published in peer reviewed scientific journals on symptoms of COVID-19, and their relationship to clinical outcomes, with 511 citations in less than a year. The research uncovered:

Evidence that anosmia is a key symptom of COVID-19 (4). Over 2,000,000 participants had reported their potential symptoms of COVID-19 on our App since March 2020. Among the 18,401 who had undergone a SARS-CoV-2 test, the proportion of participants who reported a loss of smell and taste (also known as anosmia) was higher in those with a positive test result (4,668 of 7,178 individuals; 65.03%) than in those with a negative test result (2,436 of 11,223 participants; 21.71%). This formed the basis of our symptom-based predictive algorithm, which has been widely used throughout the world.

Evidence that Delirium can be the only presenting sign of infection in older adults (6). King's academics conducted research on COVID-19 by analysing the symptoms of a cohort of 322 hospitalised and 535 community-based older adults in the UK admitted to hospital between 1 March 2020 and 5 May 2020. The sample data came from the App, logged in by the participants themselves. The study found that delirium is a presenting symptom of COVID-19 in frail, older adults.

Evidence for Long-COVID (7). King's researchers analysed data from 4182 people with COVID-19 who logged their symptoms prospectively. 558 (13.3%) had symptoms lasting >28 days, 189 (4.5%) for >8 weeks and 95 (2.3%) for >12 weeks, which was significantly longer than controls who had viral symptoms but tested negative for COVID-19. Long-COVID was characterised by symptoms of fatigue, headache, dyspnoea, anosmia; and was more likely with increasing age, BMI and female sex, and was associated with experiencing more than five symptoms during the first week of illness. We generated a predictive model which enables identification of Long-COVID risk groups in the first week of illness.

King's monitored the spread of infection in the UK and identified COVID-19 hotspots (8). We analysed data from 2,873,726 App users living in England and showed that this triangulated closely with later national studies by the Office for National Statistics (ONS) and REACT (Real-

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time Assessment of Community Transmission Study). We used incidence rates to estimate the effective reproduction number, $R(t)$, modelling the system as a Poisson process and using Markov Chain Monte-Carlo. This enabled us to highlight regions with rapidly increasing case numbers – ‘hotspots’ – with geographically granular estimates. We detected 15 of the 20 geographic regions with highest incidence, according to subsequent government test data. This therefore demonstrated that using real-time data offered a route to rapidly identify emerging hotspots.

3. References to the research

1. Berry, S.E., et al. Human postprandial responses to food and potential for precision nutrition. *Nat Med* 26, 964–973 (2020). doi.org/10.1038/s41591-020-0934-0
2. Goodrich JK, et al. Human genetics shape the gut microbiome. *Cell*. 2014 Nov 6;159(4):789-99. doi: 10.1016/j.cell.2014.09.053.
3. Jackson MA, et al. Gut microbiota associations with common diseases and prescription medications in a population-based cohort. *Nat Commun*. 2018 Jul 9;9(1):2655. doi: 10.1038/s41467-018-05184-7.
4. Menni C et al. Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nat Med*. 2020 Jul;26(7):1037-1040. doi: 10.1038/s41591-020-0916-2.
5. Drew DA, et al. Rapid implementation of mobile technology for real-time epidemiology of COVID-19. *Science*. 2020 Jun 19;368(6497):1362-1367. doi: 10.1126/science.abc0473.
6. Zazzara MB, et al. Probable delirium is a presenting symptom of COVID-19 in frail, older adults: a cohort study of 322 hospitalised and 535 community-based older adults. *Age Ageing*. 2020 Sep 28;afaa223. doi: 10.1093/ageing/afaa223.
7. Sudre CH, et al. Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. medRxiv 2020.10.19.20214494; doi: doi.org/10.1101/2020.10.19.20214494
8. Varsavsky T, et al. Detecting COVID-19 infection hotspots in England using large-scale self-reported data from a mobile application: a prospective, observational study. *Lancet Public Health*. Published online Dec 2020; subsequently published Jan 2021;6(1):e21-e29. doi: 10.1016/S2468-2667(20)30269-3.

4. Details of the impact

King’s COVID Symptom Study App-based research generated key evidence which widened the core symptoms for COVID-19 testing, enabling contact tracing of infectious individuals world-wide, and thus limiting spread and ultimately global deaths from the disease. Moreover, through providing critically early geographical data on predicted cases in the UK, the App enabled localised policies to reduce the spread of the virus, preventing health services from being overwhelmed.

King’s App data led the WHO and the UK Government to include anosmia in official COVID-19 symptoms lists. Data from our COVID-19 Symptom Tracking 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 **(2)**. As a result, the World Health Organisation (WHO) **(E)** and UK Government **(F)** 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. Professor Peter Byass, advisor to WHO, said **(E.2)**: “Your [King’s] work, particularly in relation to anosmia, was really important in informing the discussions behind this and is much appreciated.” Sir Patrick Vallance, UK Government Chief Scientific Adviser (GCSA), 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. He added **(F.2)**: “As estimated by NERVTAG 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.”

King’s App data 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

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sudden confusion - is a key symptom of COVID-19 in older people **(3)**. Public Health England's (PHE) Chief Medical Officer, as a result, 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 **(F.2)**. 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 the 4,200,000 people logging their symptoms and location in the App daily, the machine learning model algorithm provided information that was used by the different government bodies in England **(F.2)**, Wales **(A.3)** and Scotland **(B.1)**, to inform policies intended to slow rates of infection and allow health services to cope. The UK Government Chief Scientific Adviser stated **(F.2)**: *"(...) the App has been very useful in tracking the progress of the disease. Since March 2020, the data provided by the App has been informing SAGE advice to the UK government on COVID-19. Research by King's helped the UK government 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 App data uncovered key information about Long COVID-19 informing the approaches of NICE and the UK government. 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 **(6)**. In December 2020, The National Institute for Health and Care Excellence (NICE) published guidelines on the management of long-term COVID **(G.1)** heavily informed by King's research. The Programme Director for NICE's Centre for Guidelines said: *"COVID Symptom Study data was made available to NICE 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 (G.2)."*

Furthermore, the Secretary of State for Health and Social Care 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 (H)."* The UK GCSA added that 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 **(F.2)**.

Data collected by the King's App has continued to support the UK Government's decision-making on the pandemic (D, F). The research conducted by King's supported by the data from the App remains one of only ten studies that support the Government's population surveillance programmes. These are essential to understand the rate of COVID-19 infection, and how the virus has spread across the country. They have helped the Government assess the impact of measures taken to contain the virus, to inform current and future actions, and to develop new tests and treatments. The insight generated from the App along with data from other studies made a significant contribution in helping strengthen the government's scientific understanding of COVID-19, inform their policy decisions and work across the testing programme. In August 2020, the UK government further recognised the importance of the App by awarding ZOE Global a GBP2,000,000 grant **(I)**. They said 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."*

The Scottish and Welsh Governments and prominent health charities have endorsed the COVID Symptoms Study App. The Welsh Government and NHS Wales **(A)** were the first to make an appeal for the public to download the App and log their data to help them understand and predict the developing situation of the disease in Wales. 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*

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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 (A.1)." The Scottish Government also encouraged people to use the App in their official social media channels which in combination reach over 543,000 people. 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 (B)." Several key health charities in the UK also urged members and the general public to use the King's App such as the British Heart Foundation, British Lung Foundation, National Rheumatoid Arthritis Society, and Stand Up to Cancer (C).

Members of the public have also benefitted from using the App. The App is free of charge and has been available since March 2020. It doesn't just collect data, it also provides freely-available, up to date information about COVID cases. It's rated 4.7 out of 5 stars based on over 276,500 user ratings in the Apple (J.1) and Google Play App Store (J.2). 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 (J.2): "In our isolation feels like we are helping to stop the spread of COVID-19 and the research into its spread with this app." Another from December 2020 stated: "I have used this app from the start and it's comforting to know that my entries are being recorded and used to advance the fight against COVID. It is continually developing as new information is recorded and I gain more insight from the app rather than the usual media sources (J.2)."

Reviews have also shown the difference the App has made in people with Long COVID symptoms (J.1): "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) "(...) for us the symptom tracker is very useful because it reveals the extent of the long-term suffering that even a mild case of COVID-19 can cause. Moreover in the absence of a proper response by the U.K. government this is much better than nothing." (April 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

A. Sources corroborating Welsh Government and NHS Wales endorsing King's App: A.1 [Welsh Government Press Release](#) **A.2** [Tweet from Mark Drakeford's verified profile](#) **A.3** [Testimonial from Welsh Government Representative \[PDF\]](#)

B. Sources that corroborate Scottish Government endorsing King's App (April 2020): B.1 [Testimonial from Scottish Government](#); **B.2** [Twitter post](#); **B.3** [Facebook post \[PDF\]](#)

C. Sources that corroborate various health charities endorsing King's App: C.1 [British Heart Foundation](#); **C.2** [British Lung Foundation](#); **C.3** [National Rheumatoid Arthritis Society](#); **C.4** [StanduptoCancer \[PDF\]](#)

D. Guidance COVID-19 surveillance Government UK Website Page [PDF]

E. Sources that corroborate claim of King's research influencing WHO adding anosmia to list of COVID symptoms: E.1 [WHO website COVID symptom list](#) **E.2** [Email from Prof Byass, WHO Advisor \[PDF\]](#); **E.3** [WHO Technical Package \[PDF\]](#)

F. Sources that corroborate claim of King's research influencing UK Government policy: F.1 [UK Government website COVID symptom list](#) (items 2 and 3); **F.2** [Testimonial from Professor Patrick Valance, UK Government Chief Scientific Adviser \[PDF\]](#)

G. Sources to corroborate G.1 [NICE COVID-19 rapid guideline: managing the longterm effects of COVID-19 \(NG188\)](#) (pages 4, 6, 8, 15, 43-45) **G.2** [Testimonial from NICE \[PDF\]](#)

H. BBC News Article 'Long Covid: Who is more likely to get it?' October 2020 [PDF]

I. Press release from the Department of Health and Social Care about £2M funding [PDF]

J. Sources that corroborate members of the public benefitting from the App: J.1 [Apple App Store reviews](#); **J.2** [Google Play App Store reviews \[PDF\]](#)