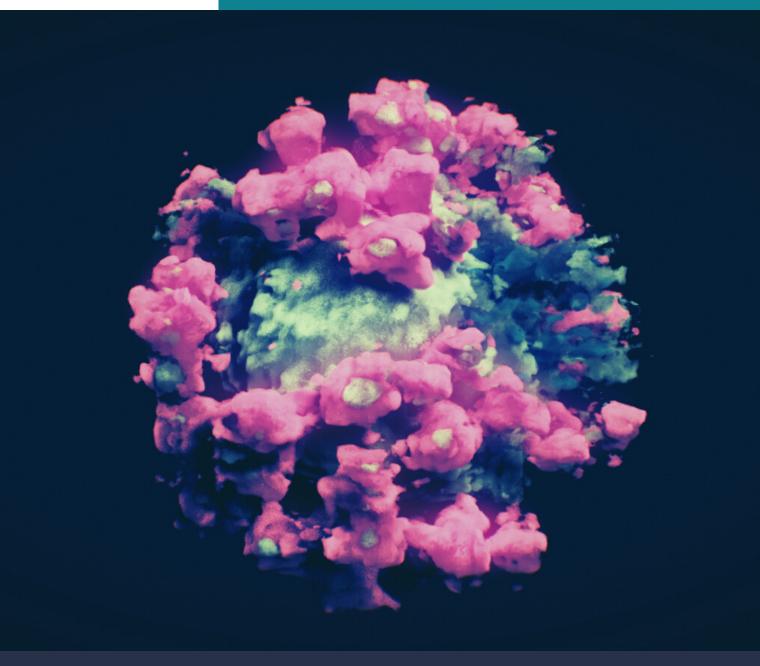
2020 2021

Imperial College COVID-19 Response Team

REPORT





Imperial College London





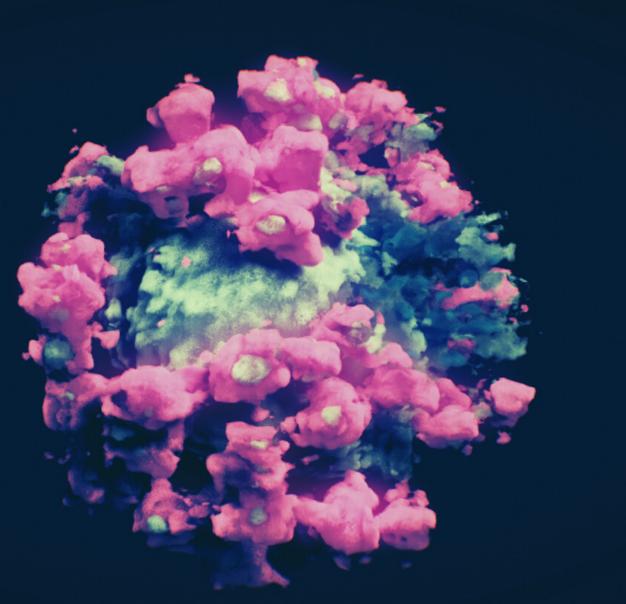
l Institute for f Disease and E Emergency Analytics

IMPERIAL COLLEGE Department of Mathematics

MORE INFORMATION



http://www.imperial.ac.uk/mrc-gida/ @MRC_Outbreak mrc.gida@imperial.ac.uk



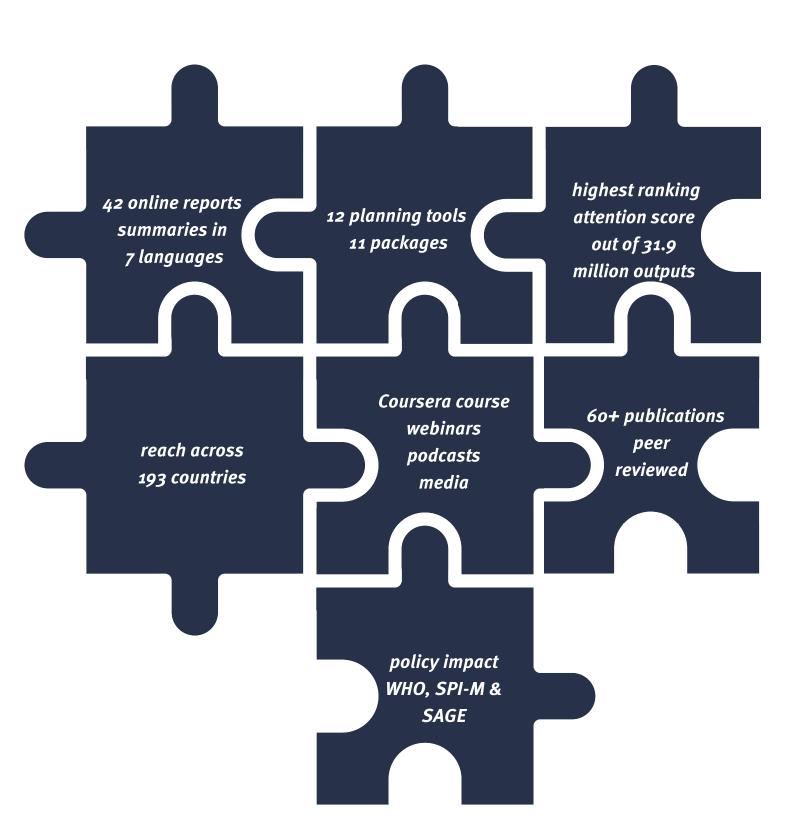
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Imperial College COVID-19 Response team WHO Collaborating Centre for Infectious Disease Modelling MRC Centre for Global Infectious Disease Analysis, Jameel Institute (J-IDEA) School of Public Health Imperial College London Norfolk Place, London, W2 1PG

COVID-19 Response

AT A GLANCE



Foreword

PROFESSOR NEIL FERGUSON



I first became concerned about the then 'novel Coronavirus' when the first case was announced in Thailand on January 13th, 2020. Four days later we released our first report on the outbreak, estimating there must have been 1700 cases in Wuhan by that time, some 40-fold more than reported. Three weeks later, with China already locked down, we released the first estimates of the lethality of SARS-CoV-2. I and my colleagues were sobered by the realisation that the combination of high transmissibility and an approximately 1% infection fatality ratio meant that the UK and the world were entering a difficult and likely tragic time.

I have been immensely proud of how my colleagues here at Imperial have responded – working incredible hours, coping with relentless pressure, being thrust into the public eye, and making a real difference. It has been a particular honour to work with the team in the MRC Centre for Global Infectious Disease Analysis, and collaborators in the wider School of Public Health, the Department of Mathematics, and the Imperial College Business School. Through their work to better understand the virus, how it spreads, its severity, and the potential impact of interventions, they have made a real difference to how the world has responded to the virus. I thank and salute them.

I'd like to particularly highlight the contributions of our PhD students, many of whom interrupted their studies to work on the pandemic, and of our software developers, technical, administrative and professional support staff. Their commitment was critical to our COVID-19 research, but also ensured all other critical work continued.

Our relationships with our external partners have also been more important than ever. In the UK, I would like to particularly note the contribution of the other UK academic groups feeding into SPI-M and SAGE, the amazing work done by PHE and NHS colleagues throughout this crisis, and our partners in the NIHR Health Protection Unit for Modelling and Health Economics at both the London School of Hygiene and Tropical Medicine and PHE. Internationally, our many friends and colleagues in the World Health Organization, other multilateral bodies and in many individual countries have worked tirelessly to help communities across the world better respond to the pandemic. Their often-challenging work has saved countless lives. Last, we are grateful to our funders to be given the flexibility to re-focus the attention to where it was most needed to support the COVID-19 outbreak response around the world.

The incredible scientific progress made during the pandemic, as highlighted by the speed of vaccine development, is cause for huge optimism especially as we see the advanced roll out of several COVID-19 vaccines. However, whilst for many high-income countries this year 2021 will return some level of normality, it is critical to ensure the fair and equitable access to COVID-19 vaccines for all.

This report provides an overview of the research of the Imperial College COVID-19 Response Team in the last 15 months and the impact this has had. As the world rolls out vaccination while facing the challenge posed by new virus variants, we are continuing our work to better understand the virus, its spread and how best to control it.

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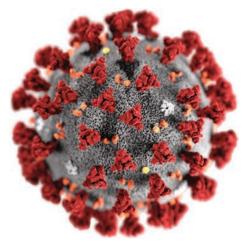
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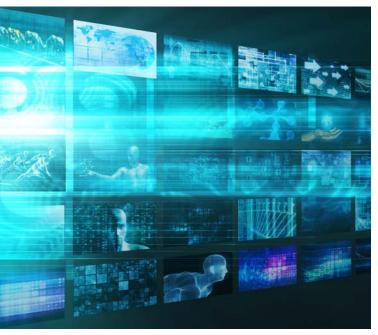
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Introduction

IMPERIAL COLLEGE COVID-19 RESPONSE TEAM



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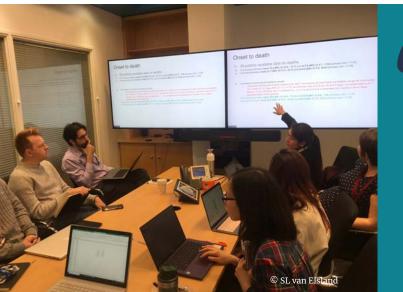
© Source: Twitter @WHO

NEW CORONAVIRUS

On the 31 December 2019, the People's Republic of China reported the first cases of a pneumonia of unknown cause in Wuhan City, Hubei. The outbreak sparked memories of the SARS epidemic 18 years earlier, according to the BBC's first report on the topic. The announcement of a cluster of pneumonia cases by the World Health Organization (WHO) triggered a rapid response from the global scientific community. Within a few days genetic sequences were identified and only weeks later PCR and serological assays were in use.

UNIQUE IN-HOUSE CAPACITY

Timely and robust epidemiological analysis is essential to inform policy responses to any emerging threats. This real-time epidemiological analysis and modelling is a core remit of the MRC Centre for Global Infectious Disease Analysis. The Centre's in-house capacity to respond to outbreaks such as the COVID-19 pandemic is unique within academia. This enabled us to provide rapid support to policy makers, including the secondment of Centre staff to WHO and the United Kingdom (UK) Government.

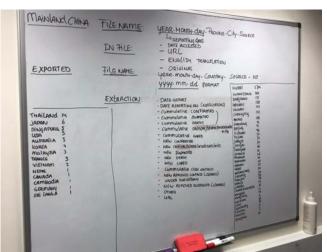


Professor Neil Ferguson

The MRC Centre was established 13 years ago to provide robust epidemiological support for policymakers managing infectious disease crises. Over that time we have developed methods of working and technical capacity which allowed us to rapidly respond to the new global threat posed by COVID-19.

Introduction

IMPERIAL COLLEGE COVID-19 RESPONSE TEAM



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EXPERTISE AND PARTNERSHIPS

In the early days of January 2020, a small group within the MRC Centre began work to understand the transmissibility and severity of the virus. This quickly grew to a team of over 80 staff and students including epidemiologists, statisticians, research software developers, clinicians and health economists. The Imperial College COVID-19 Response Team rapidly outgrew the Centre, as it encompassed new collaborations with colleagues from the Imperial College Department of Mathematics and Imperial College Business School.

The team's work built on extensive prior research and experience working on outbreaks such as Ebola, SARS and pandemic influenza. The MRC Centre is a WHO Collaborating Centre for Infectious Disease Modelling and, has close collaborative partnerships with public and global health agencies, governments and non-governmental bodies across the world. Under the umbrella of the newly established Jameel Institute (J-IDEA) within the School of Public Health, the team were also able to forge new collaborations across the College to further support the national and international response.

SUPPORT

Staff at all levels - including senior academics, postdoctoral researchers, PhD students and support staff - put their individual projects on hold to refocus their time and resources to respond to the pandemic. These extraordinary circumstances were supported by our funders allowing for the rapid scale up of the response. In-house MRC Centre capacity was boosted by additional UKRI funds and supplemented by Community Jameel and the Wellcome Trust to strengthen the impact and resilience of the team's efforts.

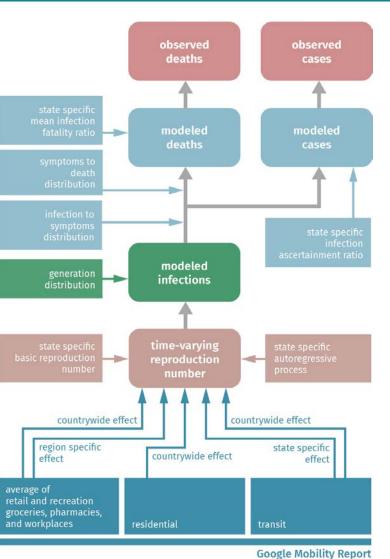


Professor Azra Ghani

I think perhaps sometimes we are viewed as mathematical modellers working in isolation from the wider public health community; when actually we're epidemiologists first, who happen to have a more quantitative background and we work quite closely across disciplines. We'll talk to an immunologist to understand how the immune response is working, we'll talk to the clinicians to understand the clinical processes.

Introduction

IMPERIAL COLLEGE COVID-19 RESPONSE TEAM



© Source: https://mrc-ide.github.io/covid19usa/#/



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MODELLING

With limited data available early in the epidemic, the team used simple models to estimate the potential scale of the epidemic in Wuhan, the transmissibility of the virus, and the potential epidemic trajectory. As we learned more about the virus and more data became available, the team developed more sophisticated models to capture patterns of transmission in different settings and to explore the potential impact of specific interventions.

This report gives an overview of the Imperial College COVID-19 Response Team's work in the United Kingdom (UK) and globally. In addition, it provides an insight into how the team has communicated its findings during the first year of the pandemic.



MRC Centre for Global Infectious Disease Analysis 🥥

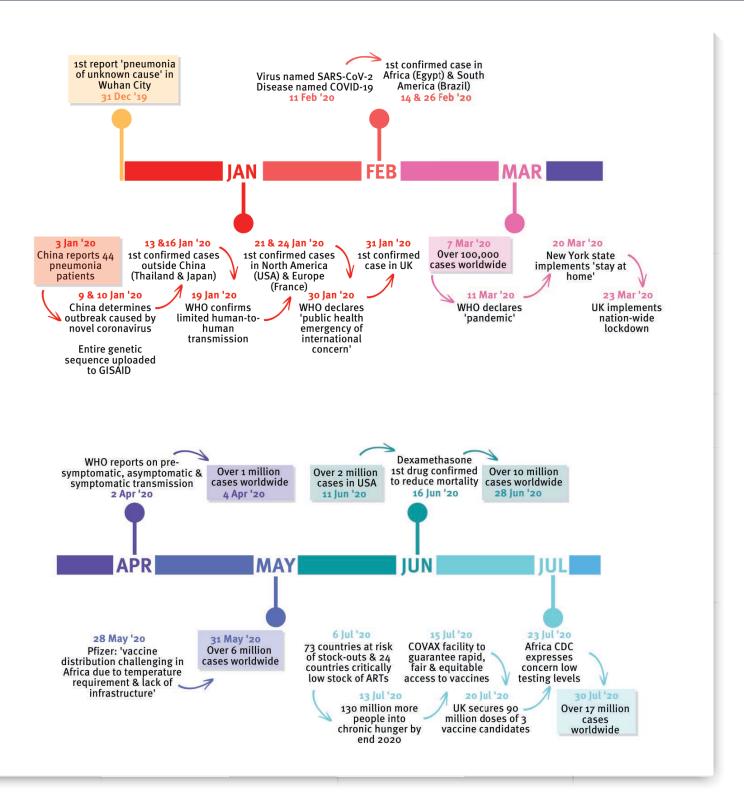
@MRC_Outbreak

World Health Organization (WHO) and 9 others

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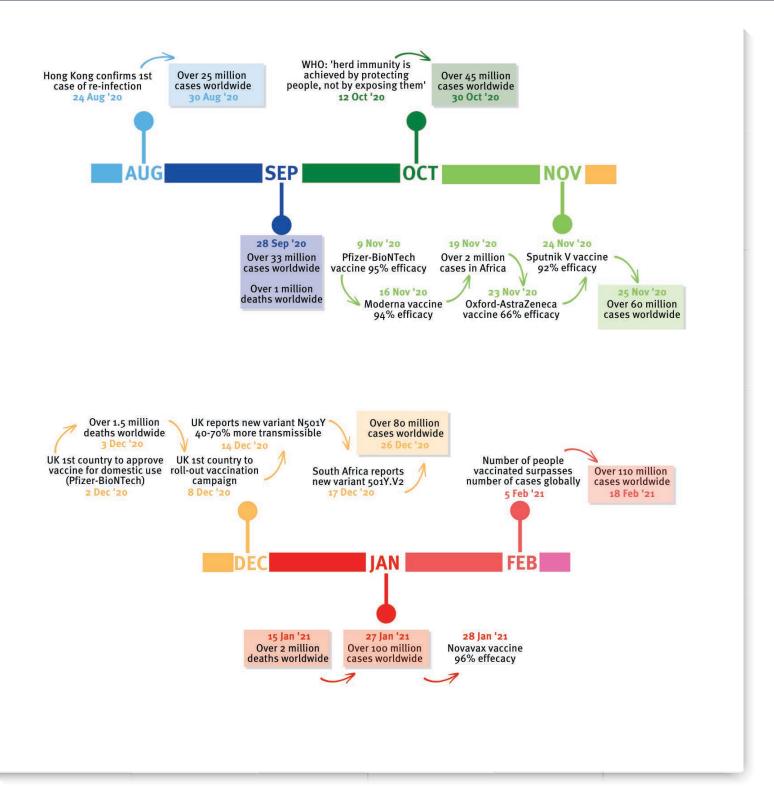
Timeline

COVID-19 PANDEMIC



Timeline

COVID-19 PANDEMIC



Characterising the threat

INFORMING THE GLOBAL RESPONSE



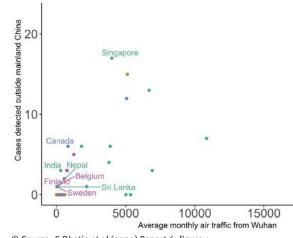
The Imperial College COVID-19 Response Team worked with governments around the world to help inform initial responses to the pandemic. In the early reports we estimated two critical quantities - the transmissibility of the virus and the infection fatality ratio. Using these estimates, we were able to provide early insight into the potential scale of the pandemic, with these reports helping to warn of the likely threat and thereby providing supporting evidence for the need to act.

© Source: Canva Pro

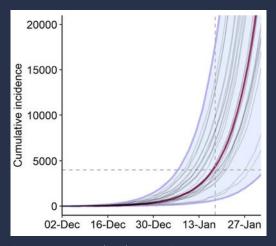
OUTBREAK SIZE & TRANSMISSIBILITY

The team's Report 1, published on 17 January 2020, was the first to estimate the scale of the emerging epidemic, with results suggesting that the outbreak was already considerably larger than detected at the time. Report 3 was the first to highlight that self-sustaining human-to-human transmission was the only plausible explanation of the scale of the outbreak in Wuhan City.

Further analysis of COVID-19 cases exported from mainland China revealed that more than half remained undetected worldwide, leaving sources of human-to-human transmission unchecked (Report 6). These findings were widely disseminated, demonstrating the need for heightened surveillance, prompt information sharing, and enhanced preparedness.



© Source: S Bhatia et al (2020) Report 6, figure 1



🏉 Dr Natsuko Imai

I remember so clearly the day we started working on this. Based on limited information we estimated that the epidemic in Wuhan City was already far larger than reported. I'm blown away by how far our scientific understanding has come since then thanks to the efforts of the entire research community.

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Characterising the threat

INFORMING THE GLOBAL RESPONSE



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SEVERITY

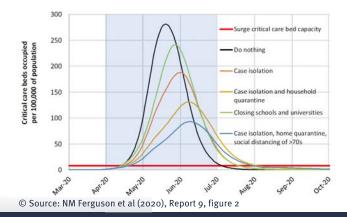
During a growing epidemic, it is important to understand how severe the disease is in all those who get infected, not just those that are symptomatic or detected during surveillance. In the face of rapidly changing data, the team provided robust estimates of the case fatality ratio and infection fatality (IFR) ratio in early February 2020 (Report 4, later published in Lancet Infectious Diseases). With an IFR more than ten-times higher than seasonal influenza, this work provided the first reliable estimates of the true scale of the threat.

INTERVENTION POLICY MODELLING & ASSESSMENT

The global spread of COVID-19 was rapid and over 200 countries reported cases by the end of March 2020. The world faced the challenge of balancing the implementation of policies that could curtail spread alongside the wider impact that these would inevitably have on livelihoods and economies.

Early work to understand the transmissibility and severity of SARS-CoV-2 underpinned Reports 9 and 12 and a later Science paper which showed that even the most developed health systems would be overwhelmed unless suppression strategies were adopted. This work also highlighted the inevitable resurgence of transmission once lockdowns were lifted and that intermittent lockdowns would be required until a vaccine was available.

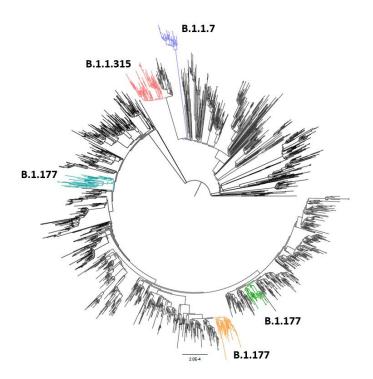
The analyses highlighted the challenging decisions faced by all governments and demonstrated the extent to which rapid, decisive, and collective action could save millions of lives. This work – together with parallel work by colleagues at LSHTM and several other universities – informed how the UK, Europe and the world responded to the pandemic in March of 2020.





Characterising the threat

INFORMING THE GLOBAL RESPONSE

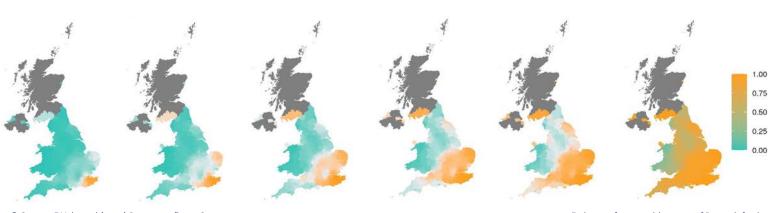


© E Volz, O Boyd and team (2021)

GENETICS

Early in the pandemic, the team demonstrated that the genetic diversity of COVID-19 was consistent with exponential growth with a doubling time of seven days and estimated the start of the pandemic to have occurred in early December 2019 (Report 5). Further analysis showed that early implementation of nonpharmaceutical interventions resulted in fewer COVID-19 cases and deaths.

The team has made further major contributions to the phylogenetic analyses of SARS-CoV-2 as part of the COVID-19 Genomics UK Consortium (COG-UK). COG-UK captures SARS-CoV-2 samples from COVID-19 infections from across the UK, provides weekly summaries on sequence coverage, and background context on mutation tracking.



© Source: E Volz et al (2020) Report 42, figure S1

Estimate of true positive rates of B.1.1.7 infection

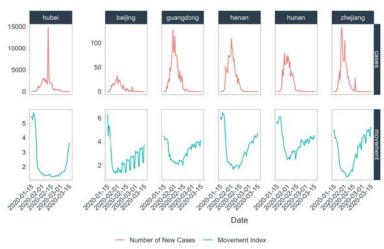
Dr Erik Volz



PANDEMIC & INTERVENTIONS

INTERVENTIONS

China was the first country to impose strict social distancing measures, impacting the country's economic productivity. By estimating the transmissibility of the virus from reported cases and within-city movement (as a proxy for economic activity), we showed that the intense social distancing resulted in containment of the virus (Report 11, later published in Wellcome Open Research). As a result, China was successful in opening society without a subsequent resurgence in cases.



© Source: K Ainslie et al (2020) Report 11, figure 1

By April 2020, the epicentre of the pandemic had shifted to Europe. Through a collaborative analysis with the Department of Mathematics we quantified the impact of non-pharmaceutical interventions in reducing transmission in multiple European countries. This work was used by several governments, including the French prime minister Emmanuel Macron, to inform their policy responses (Report 13, later published in Nature).



© Source: Canva Pro

In response to the growing pandemic, countries implemented strict curfews or restrictions on population movement. However, the team estimated that for many countries with sustained transmission in May 2020, few had sufficiently reduced mobility, a proxy measure for social contacts outside the home, to control the epidemic and bring the reproduction number below 1 (Report 26). In the UK at that time, mobility data showed that initial compliance with COVID-19 social distancing interventions was high and geographically consistent across regions (Report 24, later published in Wellcome Open Research).

Professor Axel Gandy

Imperial's research has informed policy worldwide - partly because we were able to deliver timely, reliable results this was only possible through the dedication and hard work of all researchers involved.



PANDEMIC AND INTERVENTIONS

In comparison to the blunt lockdown measures adopted by Europe, South Korea's approach relied heavily on case isolation, contact tracing, and self-quarantine of contacts. The swift scale up of testing capacity allowed them to maintain case-based interventions throughout the epidemic. The team cautioned that implementing a similar response in settings with larger, generalized epidemics might be difficult (Report 25).



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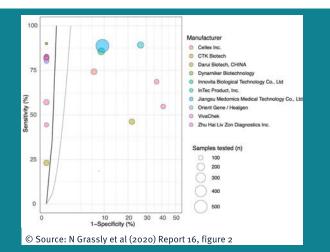
With the World Health Organization (WHO) calling for increased testing in response to the COVID-19 pandemic, the team developed a mathematical model of SARS-CoV-2 transmission to investigate the impact of different testing strategies, including regular asymptomatic screening and 'test and trace'. The results (Report 16, later published in Lancet Infectious Diseases) show that molecular testing can play an important role in prevention of SARS-CoV-2 transmission, especially among healthcare workers and other high-risk groups, but no single strategy will reduce the reproduction number (R) below 1. Immunity passports based on antibody tests or tests for infection face substantial technical, legal, and ethical challenges.

New tests are urgently needed to meet the huge unmet needs for testing worldwide. Members of the team supported the WHO's Access to COVID-19 Tools (ACT) Accelerator by developing an investment case for antigen rapid diagnostic test scale-up in low-income settings.



Professor Nicholas Grassly

Effective testing can contribute to control of the coronavirus pandemic. Test and trace can help reduce the R number but the coverage and speed of the programme in the UK during 2020 meant the impact on transmission was minimal.



PANDEMIC AND INTERVENTIONS

HEALTH IMPACTS

The impact of the COVID-19 pandemic in low-income countries may be more severe than high-income settings due to limited healthcare capacity and an inability to maintain highly restrictive lockdowns. Furthermore, across all settings, there exist unfair or avoidable differences in health among different groups in society – health inequities – that mean that some groups are particularly at risk from the negative direct and indirect consequences of COVID-19.

Early analysis of COVID-19 patients in China, Singapore, and Hong Kong – regions first affected by COVID-19 - showed geographic variation in symptoms, disease presentation and clinical progression likely caused by differences in surveillance, healthcare-seeking behaviour, population, and age distribution (Report 8).



© WHO UN Martine Perret

Differences were also found within the UK with the analysis of the very first COVID-19 patients admitted to Imperial NHS Healthcare Trust hospitals. The team characterized predictors of outcome for hospitalised COVID-19 patients. This work was one of the first studies to identify that being a male from an ethnic minority with preexisting conditions was associated with higher mortality (Report 17, later published in Clinical Infectious Diseases). Understanding healthcare seeking behaviour helps to inform healthcare planning and our analysis showed a drastic decrease in emergency attendance across England (Report 29). An online tool subsequently developed by the team tracking weekly COVID-19 and excess non-COVID-19 deaths (deaths that would not have happened without the COVID-19 pandemic) for England and Wales provides policy makers with useful insights for healthcare planning.

Working together with academics, healthcare providers and policy makers across the world, the team's analysis highlighted specific enhanced risks and key vulnerabilities – alongside the broader concerns surrounding displaced or conflict-affected populations. This work demonstrated the challenges that the most marginalised populations face during the ongoing COVID-19 pandemic (Report 22).

Dr Katharina Hauck

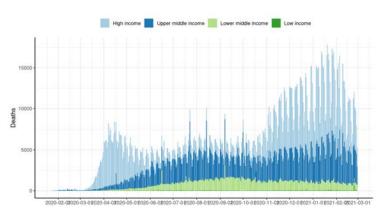
The pandemic confronts us with immensely challenging trade-offs between health, economic output, hospital capacity, and personal liberties. We need multidisciplinary approaches to give effective policy guidance on how to control pandemics.



PANDEMIC AND INTERVENTIONS



© Source: Canva Pro



© Source: https://mrc-ide.github.io/global-lmic-reports/



© Source: Canva Pro

Countries in the Middle East and Africa have reported substantially lower mortality rates than Europe and the Americas. The low number of cases and deaths reported in these countries may be due to a number of factors including underlying differences in the risks of the population as well as more limited surveillance and testing capacity. Using alternative reporting streams as indicators of the true epidemic, the team estimated that only a small percentage of deaths had been detected in Syria and Sudan (Reports 31 and 39). This work helped to inform the likely trajectory of the second wave.

Given this significant under-ascertainment of cases and deaths, the infection fatality ratio (IFR) remains a key statistic for estimating the true burden of COVID-19 from infection surveys. The team updated their IFR estimates using representative seroprevalence data accounting for test sensitivity and specificity, delays from infection to seroconversion and death, and antibody waning (Report 34). Unbiased estimates of the IFR continue to be critical for policy makers to inform their response.

TRANSMISSION PATTERNS

Transmission patterns of SARS-CoV-2 have varied widely across the world in part due to the differing responses taken by governments. This has meant that country-specific analyses were critical in understanding and informing responses to local epidemics.



Professor Christl Donnelly

We have worked on several interrelated COVID-19 research projects in parallel to provide insights into the transmission dynamics that led to the current situation and to explore possible futures depending on collective behaviour.



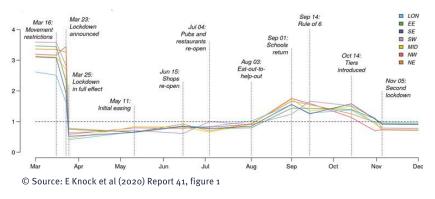
PANDEMIC AND INTERVENTIONS

Brazil is an epicentre for COVID-19 in Latin America. Whereas enforced lockdowns in Europe and Asia had successfully driven the reproduction number below one (meaning the epidemic is controlled), the team showed a very different picture in Brazil: although the reproduction number dropped in response to the virus, the epidemic was not controlled demonstrating that further action was needed (Report 21).



In the United States, Dr Samir Bhatt was appointed by the State of New York Governor, Andrew Cuomo, as a special advisor. In this capacity, the team were consulted on each step of the State's phased reopening, using a bespoke transmission model to provide short-term projections. Other states, including Michigan, used the team's work not only for decision making but also to legally substantiate the implementation of public health measures (Report 23, later published in Nature Communications).

Report 32, now published in Science, analysed age groups that sustain resurging COVID-19 epidemics in the USA at state level. Although most children experience clinically mild disease or remain asymptomatic, children's susceptibility to infection and onward transmissibility relative to adults remains unclear (Report 37). A systematic review by the team found that differences observed in transmissibility by symptom status of index cases and the potential for age-dependent effects have important implications for outbreak control strategies such as contact tracing, testing and rapid isolation of cases (Report 38, later published in Clinical Infectious Diseases).



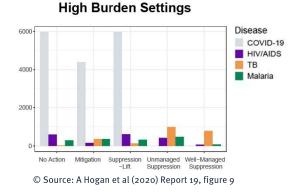
In the UK, an in-depth analysis of the first two waves in England found that only national lockdown measures consistently brought the reproduction number below one and underscored the huge burden of COVID-19 in care homes. With an estimated 4.8% of the population infected by 2 December 2020, it highlighted the long path to herd immunity whether by natural infection- or vaccineinduced immunity (Report 41).



PANDEMIC AND INTERVENTIONS

INDIRECT IMPACTS

COVID-19 can cause disruptions to health services in different ways; through the health system becoming overwhelmed with COVID-19 patients, through COVID-19 interventions inhibiting access to preventative services, and through supplies of medicine being interrupted. The team showed that HIV, TB, and malaria related deaths over 5 years could increase by up to 10%-36% in high burden settings, compared to if there were no COVID-19 pandemic.



This analysis highlighted the importance of maintaining the most critical prevention activities and healthcare services, demonstrating how this could significantly reduce the overall impact of the COVID-19 pandemic (Reports 18 and 19, later published in Nature Medicine and Lancet Global Health respectively). Working with the WHO South East Asia Regional Office (SEARO), a tuberculosis service disruption simulator was developed to help member states anticipate and prepare for disruptions to TB services due to COVID-19.

With a surge of COVID-19 patients requiring urgent life-saving treatments, hospitals face the unprecedented challenge of keeping up high-quality care for all patients. A hospital planner was developed to calculate which hospital interventions can increase critical care capacity most effectively and quickly (Report 15, later published in Journal of Medical Care).

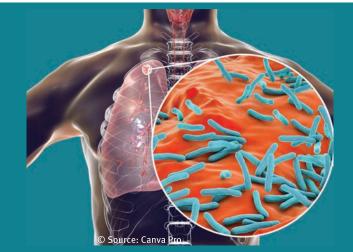


© Source: Canva Pro

Projections provide insight into the number of non-COVID-19 patients who can be admitted to hospital once occupancy of COVID-19 reaches a certain threshold (Report 27, later published in BMC Medicine). Once hospitals hit their capacity limits, difficult decisions must be made on how to prioritize scarce resources across all patients requiring life-saving care.

Dr Nimalan Arinaminpathy

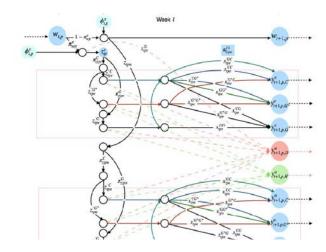
It takes several years for the elevated TB burden to come back to pre-lockdown levels. The more severe the lockdown, the more severe the impact is going to be on the TB burden.



PANDEMIC AND INTERVENTIONS

Expanding the team with experts from the Imperial College Business School, optimized admission schedules were developed to maximize life years gained during pandemic surges. The team found that optimized admission scheduling could gain up to 5.9 million life years in England over 12 months, and that schedules which prioritize non-COVID-19 patients are projected to gain more life years (Report 40). Tools developed by the team were made available to help the NHS and other countries to inform optimal hospital planning.

COVID-19 presents all countries with an agonizing trade-off between lives and livelihoods. Our epidemiologists and economists explored how control interventions can capture both public health and economic objectives. To project outcomes from control strategies and alternative vaccination scenarios, the team developed an economic-epidemiological model (DAEDALUS). This model was employed to describe which economic sectors need to close in order to keep schools and universities open in the UK and demonstrated that a targeted approach could increase economic output over six months by an estimated £193 billion compared with a blanket lockdown (Report 35).



© Source: J D'Aeth et al (2020) Report 40, figure A2



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Dr Marisa Miraldo, Imperial College Business School

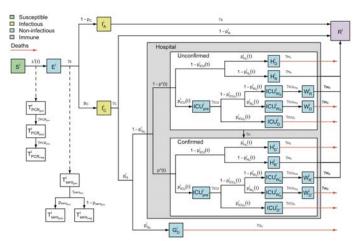
The pandemic has been the biggest challenge on the NHS since its inception. We provide evidence on what can work to mitigate the impact of capacity shortages on population health.



THE EVOLVING POLICY RESPONSE

The Imperial College COVID-19 Response Team provides the United Kingdom government with scientific evidence to support their policy response. Primarily this has occurred through research feeding into advisory committees such as SPI-M, NERVTAG and SAGE, but multiple members of the team have provided evidence in the House of Commons and the House of Lords in several inquiries and committee meetings.





© Source: E Knock et al (2020), Report 41, supplementary figure 2

We use a mixture of standardised and bespoke analyses to analyse the impact of COVID-19 on the healthcare system and clinical outcomes and to support policymaking. In addition to providing weekly estimates of the "R" value and projections of the trajectory of the epidemic in the next few weeks, we often respond to specific policy-specific commissions. The team also supports governments around the world with modelling requests and works with local collaborators to inform policy.

Several models have been developed to provide these analyses, ranging from advanced individual-based models to compartmental "SEIR" models of varying complexity. At this stage of the pandemic, three are routinely deployed: epidemia (for weekly UK estimates at local authority scale), sircovid (for UK regional estimates and simulation of policy options, including vaccination) and Squire (for global modelling).



Dr Marc Baguelin

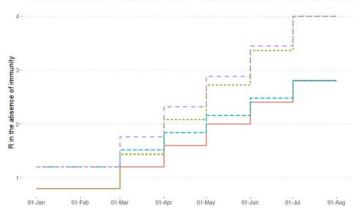
sircovid is unique in quantifying both community and care-home transmission of COVID and the interaction between the two. The results highlight how difficult it is to mitigate the impact of the epidemic on some of the most vulnerable people in society.

Support THE EVOLVING POLICY RESPONSE



© Source: Imperial College London

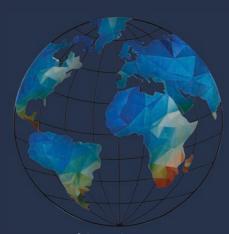
- R_excl_immunity_0.8_to_2.8 -- R_excl_immunity_0.8_to_4.0 - R_excl_immunity_1.2_to_2.8 - R_excl_immunity_1.2_to_4.0



© Source: L Whittles et al (2021) SAGE https://www.gov.uk/government/ publications/imperial-college-london-potential-profile-of-the-covid-19-epidemicin-the-uk-under-different-vaccination-roll-out-strategies-13-january-2021

The sircovid model integrates 8 distinct surveillance data streams to provide an immediate analysis of the current epidemic trajectory (SARS-CoV-2 transmission), severity, epidemic size, and evaluate the impact of interventions in the UK. Bespoke software pipelines and a team of research software engineers have built tools to efficiently manage the large and ever-changing data and allow efficient evaluation of epidemiological hypotheses and policy options. The outputs feed into SAGE and government via the UK SPI-M committee.

In addition to the standardised weekly analysis, the team regularly produces additional bespoke outputs. We have generated reasonable worst-case scenarios both directly for government planning but also to feed the Academy of Medical Sciences' report on the possible challenges that would be faced in the winter of 2020/21. We have also modelled policy options such as the strategy for exiting the first lockdown, the introduction of local measures in summer/autumn 2020 (tiers and local lockdowns), the need for and impact of the second lockdown and the potential effect of relaxation of social distancing rules over Christmas. Most recently, we have intensively modelled the likely impact of the rollout of vaccination, and different policy options for the roadmap out of the third England lockdown. This work has been highly influential in informing UK government policy.

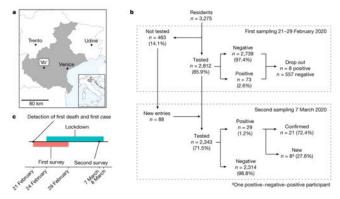


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THE EVOLVING POLICY RESPONSE

REACT

Imperial College London leads a major programme of home testing for COVID-19 to track the progress of infection across England. The REal-time Assessment of Community Transmission (REACT) Study was commissioned by the Department of Health and Social Care and is being carried out in partnership with Imperial College Healthcare NHS Trust and Ipsos MORI.



© E Lavezzo et al (2020) Nature, https://doi.org/10.1038/s41586-020-2488-1



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Professor Steven Riley

REACT is one of a number of studies that are feeding into decisionmaking and helping to ensure that public health measures are based on robust, current evidence. The REACT-1 study tracks current cases of COVID-19 in the community by testing randomly selected people each month over a two-week period. Volunteers take throat and nose swabs at home, which are then analysed in a laboratory by a technique called RT-PCR. REACT-2 looks at how many people in the population have had an immune response using antibody finger-prick tests to track past infections and monitor the progress of the pandemic, including antibody responses following vaccination.

The Imperial College COVID-19 Response Team collaborates with colleagues in the Department of Epidemiology and Biostatistics in the School of Public Health to conduct the REACT studies, in which well over a million people have taken part thus far. This provides a key data stream for the UK Government to track COVID-19 in real-time across England.

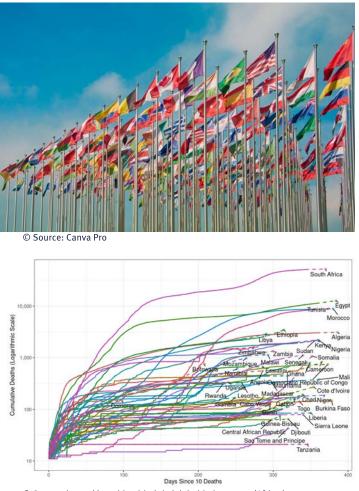
EUROPE

On 24 January 2020 France reported the first case in Europe. One of the first COVID-19 related deaths in Europe was reported in a small town near Padua, Italy in February 2020. The team have collaborated with the Italian National Institutes and Ministry of Health since the beginning of the epidemic in Italy to estimate the potential trajectory of SARS-CoV-2 and the impact of non-pharmaceutical interventions. Key findings were published in Nature describing the high proportion (40%) of asymptomatic infections, their infectivity and insight into the transmission dynamics.

THE EVOLVING POLICY RESPONSE

GLOBAL RESPONSE

Our early work in March 2020 focused on generating global model estimates of the potential scale and impact of the pandemic (Report 12, later published in Science).



© Source: https://mrc-ide.github.io/global-lmic-reports/Africa/



© WHO UN Martine Perret

In this, we explored the impact of factors that differ between countries - including demography, mixing patterns and health system provision - on the likely scale and impact of the pandemic. These early estimates were used extensively in policy reports by several United Nations agencies including WHO, the United Nations Humanitarian Commission for Refugees (UNHCR), the United Nations Development Programme (UNDP) and the World Food Programme. They were also used to advocate for and inform early allocation of funds to support preparedness by The World Bank, The International Monetary Fund and The Global Fund. Working closely with WHO, subsequent estimates that incorporated fits to the emerging pandemic were used to support the WHO Essential Supplies Forecasting Tool as well as for the basis of a WHO global costing (published in Lancet Global Health). The team also supported the WHO's Access to COVID-19 Tools (ACT) Accelerator by developing an investment case for antigen rapid diagnostic test scale-up in low-income settings.

To provide support to a range of countries, the team developed a dashboard showing the trajectory of the epidemic across low- and middle-income countries, model fits to data and short-term projections. The team also worked with academic partners, NGOs and health ministries in several countries spanning Latin America (Brazil, Columbia, Panama), Africa (Malawi, Nigeria, Senegal, Sudan, Zimbabwe) and Asia (India, Indonesia, The Philippines). These collaborations helped to support country responses to the pandemic during the early stages of the pandemic, providing short-term projections of healthcare demand.

THE EVOLVING POLICY RESPONSE

SOFTWARE & TOOLS

With the support of research software engineers, the team has improved the quality of coding continuously, and shared the code that was developed in the public domain. This includes innovative modelling tools for estimating the reproduction number and generating incidence projections (nationally and globally), as well as assessing the impact of control measures:

	CovidSim	models the transmission dynamics and severity of COVID-19 infections. It allows modelling of how intervention policies and healthcare provision affect the spread of COVID-19.
DUST	dust	provides a light interface to run models that are written in C++ in parallel from R.
	epidemia	allows researchers to flexibly specify and fit Bayesian epidemiological models.
	EpiEstim	is an R package used by public health agencies and ministries of health as part of monitoring and response to the COVID-19 epidemic.
ê	markovid	is a Markov Chain Monte Carlo (MCMC) package for carrying out preliminary fits of hospital progression parameters.
	mcstate	implements Monte Carlo methods for state-space models such as SIR models (Susceptible, Infectious, Recovered) in epidemiology.
	nimue	is an R package which implements a version of the squire model with functionality to capture the distribution, prioritisation and epidemiological impact of COVID-19 vaccines.
	orderly	is designed to help make analysis more reproducible. Its principal aim is to automate a series of basic steps in the process of writing analyses, making it easy to track all inputs, store multiple versions of analysis, track outputs and create analyses that depend on the outputs of previous analysis.
	PhyDyn	is a BEAST2 package which enables the user to simultaneously estimate epidemiological parameters and pathogen phylogenies.
SIRCOVID	sircovid	implements a series of mechanistic models to help model the transmission of the SARS-CoV-2 virus using stochastic compartmental models. sircovid also provides tools to perform Bayesian evidence synthesis from several surveillance data streams through the estimation of transmission parameters.
	Squire	enables users to simulate models of SARS-CoV-2 epidemics. This is done using

an age-structured SEIR model (Susceptible, Exposed, Infectious, Recovered)

that explicitly considers healthcare capacity and disease severity.

THE EVOLVING POLICY RESPONSE

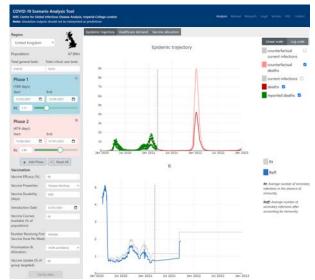
In addition to developing the range of technical modelling tools, the team has also generated a plethora of easy-to-use web-based tools for end-users in healthcare and governments:

The COVID-19 scenario analysis tool (covidsim.org) allows the user to make projections of the prevalence of infections each day and the expected number of people requiring hospitalisation and critical care facilities. This tool provides projections for every country and is currently used across the world, accessed by almost 200 different countries and territories.

The LMIC short term forecast dashboard provides future scenarios of the healthcare burden of COVID-19. Initially focused on Low- or Middle- Income countries, the dashboard synthesises these results for every country in the world into an easily digestible report which helps to improve situational awareness. Global short-term forecasts are weekly updated forecasts of the reported number of COVID-19 deaths in the week ahead and analysis of case reporting trends for countries with active transmission.



© Source: https://mrc-ide.github.io/covid19-short-term-forecasts/



© Source: https://covidsim.org/v4.20210310/

Nucleic acid tests (NAT) have been widely used in testing for COVID-19, however, they are not always readily available. Recently emerging antigen-detection rapid diagnostic tests (Ag-RDTs) could help to address these challenges, which are particularly acute in low- and middle-income settings. The COVID-19 NAT-RDT web tool helps to identify the optimal diagnostic testing strategy specific to any such setting.



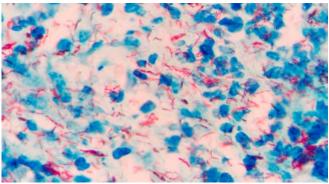
Dr Richard FitzJohn

Rigorous software engineering supports real-time modelling by providing well-tested tools to stay on top of ever-changing data.

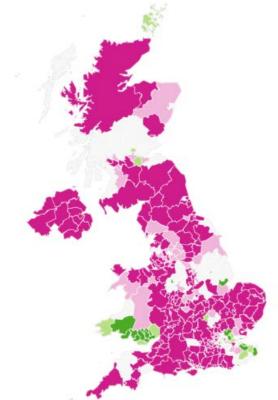
THE EVOLVING POLICY RESPONSE

Many countries have experienced significant weakening in tuberculosis (TB) services, widely signified through sharp drops in TB notifications and adherence to TB treatment has been threatened. The TB service disruption simulator is a web-based tool developed for the WHO and tailored to 11 countries of the South-East Asian Region to anticipate effects that disruptions due to COVID-19 could have, on TB incidence and mortality.

The COVID-19 UK local area website provide real-time estimates of the reproduction number of COVID-19 and projections of cases based on testing and mortality data. In addition, the tool provides a map of hotspots for England, Wales, Scotland and Northern Ireland. The Scottish government uses this model to inform the criteria for decision making of lockdown tiers. Both the Scottish and Welsh governments use the local area model in their reporting. On request, a parallel web tool was set up for Austria.



© Source: Canva Pro



 $\label{eq:source:https://imperialcollegelondon.github.io/covid19local/#map} \\ \end{tabular}$

Europe and USA web tools were developed at the start of the first wave and provided country and state-level estimates of the number of COVID-19 infections, rate of transmission, and the impact of changes in mobility on the rate of transmission in the absence of additional interventions.

The J-IDEA Pandemic hospital planner calculates the increase in capacity in terms of beds, staff and critical equipment when implementing healthcare provision interventions – cancelling elective surgeries, converting operating theatres to critical care wards, implementing emergency triage, upskilling staff, or changing staff-to-bed ratios. The tool supports decision-makers to deliver a fast, effective and coordinated response to extreme surges in demand for hospital care presented by the COVID-19 pandemic.

The Excess Deaths tracker for England and Wales provides weekly estimates of one of the most important health outcomes of the pandemic. It estimates excess deaths that are indirectly caused by the pandemic since March 2020. This tool helps decision makers assess the impact of the pandemic and control interventions on overall mortality in real time.

Looking to the future

VACCINES & NEW VARIANTS OF CONCERN



VACCINATIONS

The team have provided key modelling outputs and advice to the World Health Organization (WHO), other international partners and countries on the potential vaccine impact and optimal allocation strategies. In addition, the team have analysed the impact of COVID-19 on childhood vaccination programmes.

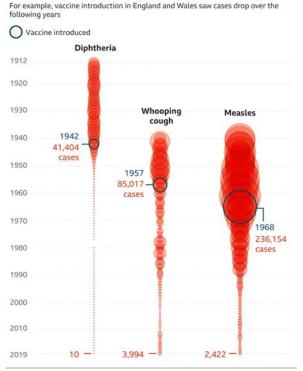
Over 200 candidate vaccines have been developed with candidates currently spanning the range of development stages. In November 2020, the first efficacy estimates from the leading vaccine candidates were announced demonstrated very high efficacy against COVID-19 disease. In early December 2020, the UK begun its roll-out of a national vaccination campaign, one of the earliest to do so. Across the globe the demand for doses is likely to exceed supply through 2021 due to constraints in manufacturing. Despite international initiatives, political and economic incentives for countries to prioritise national interest remain high.

Extending an epidemiological model of transmission to capture vaccination, the team explored the potential public health impact of different vaccine characteristics and population-targeting strategies (Report 33). Within a country, given a limited supply, the optimal strategy is to target the elderly and other high-risk groups. If the supply is larger, the optimal strategy switches to targeting key transmitters (working age population and children) to indirectly protect the elderly and the vulnerable. Allocating doses to countries in proportion to their population size was found to be close to optimal in averting deaths and aligns with ethical principles for pandemic preparedness.

This work informed the prioritization recommendations made by the WHO Strategic Advisory Groups of Experts on Immunization (SAGE). Professor Nick Grassly also directly supports the WHO SAGE COVID-19 Vaccine Modelling Group as its co-chair. The team also worked closely with the WHO European Office to develop the model to support vaccine introductions, including an extension of the covidsim.org software to enable countries to explore the impact different roll-out and prioritisation scenarios on their local epidemic.

Professor Azra Ghani

A vaccine will end the pandemic, it is just a question of when, and that's the hardest bit to anticipate because it is getting this vaccine out that is the biggest challenge.



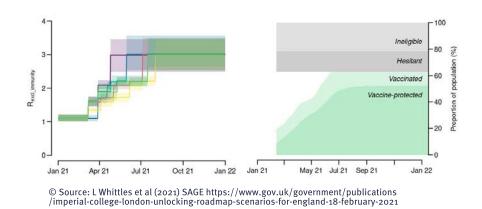
Mass vaccination has had a profound effect on some diseases

 $\ensuremath{\mathbb{C}}$ Source: BBC. Cases of notifiable infectious Diseases, Public Health England

Looking to the future

VACCINES & NEW VARIANTS OF CONCERN

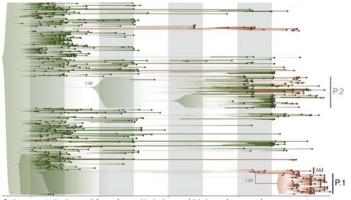
As the UK emerges from its third national lockdown, the Response Team modelled different exit plans for lifting non-pharmaceutical interventions under different vaccine roll-out speeds. This work has been critical in informing England's "roadmap" out of lockdown (SAGE reports).



NEW VARIANTS

The emergence of new coronavirus variants in the United Kingdom, Brazil, and South Africa has required countries to rapidly reassess their epidemic trajectories and control strategies. These variants of concern have evolved independently but share some similarities such as the N501Y and E484K mutations.

In the UK, the Team evaluated the relationship between transmission and the frequency of the new Variant of Concern (VOC) in England over time (Report 42). Critically, they estimated that the new variant was up to 70% more transmissible than the wild-type variant. This finding was crucial in informing the UK government's decision to implement a third national lockdown.



© Source: N Faria et al (2021), medRxiv https://doi.org/10.1101/2021.02.26.21252554

A collaborative study with colleagues in Brazil showed that the emerging lineage P.1 of the SARS-CoV-2, has driven a second wave of infections even in a region hit hard by the first wave such as Manaus, the largest city in the Amazon region. The team identified 17 mutations for this variant of concern and found that it is likely more transmissible than other variants and may have the ability to evade protective immunity.

Professor Ester Sabino, Universidade de São Paulo

Global collaborative efforts on rapid virus genome sequencing are allowing us to identify SARS-CoV-2 lineages of concerns in near real-time. Yet, uncertainty in the ways SARS-CoV-2 is changing and implications for vaccine design calls for much more sequencing and analysis of virus genomes globally.

Communication

OUTREACH & MEDIA ENGAGEMENT

Since the emergence of COVID-19, the Imperial College COVID-19 Response Team has adopted a policy of immediately sharing research findings on the developing pandemic. This includes public resources such as web tools, training, virtual Q&A's, webinars, seminars and media engagement.

TRAINING

Partnering with Coursera, the Patient Experience Research Centre (PERC) and colleagues across the college, the team offer a free Massive Open Online Course (MOOC) "Science Matters: Let's Talk About COVID-19" explaining the science behind coronavirus. Throughout the first year of the pandemic the course was continuously updated, with new assignments and materials for new modules added. With over 138,000 learners, the course was the most popular launched on Coursera in 2020 during Europe's first lockdown.

ACCESSIBILITY

All output including reports, planning tools, scientific and public resources and peer-reviewed publications are easily accessible on the website (www.imperial.ac.uk/mrc-globalinfectious-disease-analysis/covid-19/).



© SL van Elsland



© Source: Twitter @MRC_Outbreak





In most cases, the team initially published their research in the form of open-access online reports and preprints. To support more universal access to the work, each report's summary is provided in seven languages. Multiple major reports were accompanied by videos freely available on social media and YouTube, diving in deeper with the lead scientists to better understand the results and their implications.



Professor Helen Ward

Communication

OUTREACH & MEDIA ENGAGEMENT

In collaboration with Oxford Sparks, an animation was created explaining COVID-19 transmission, how different control measures work and answering questions on how scientists go about piecing together the puzzle and why modelling is so important.

Where most scientific research is reported in specialized scientific journals in a language often accessible only to adult scientists, it is critical that children are given the opportunity to better understand the COVID-19 pandemic and why, for example, schools have closed. Two of the team's major reports were adapted into Science Journal for Teens articles (Reports 9 and 19).



Understanding COVID-19 Transmission, Informing Control



© Source: Oxford Sparks





© Source: Jameel Institute (J-IDEA)

Through a partnership between PERC and Burnt Orange Theatre Company, the team engaged 20 young creatives in COVID-19 research, resulting in short films about Reports 1, 10, 13, 22 and 24 and their personal experience of the pandemic.

The team participated in a large number of podcasts, virtual seminars, webinars, and public Q&A sessions. The topics discussed range from life as a scientist in a global crisis response, experiences from a mathematical modelling team, how to model the spread of a virus, and how to use our web tools.

The annual flagship course which is taught be leading researchers who advise policymakers internationally, "Introduction to Mathematical Models of the Epidemiology & Control of Infectious Diseases" is taught by leading researchers who advise policymakers internationally. In 2020, this was replaced by a two-day webinar series with talks from top epidemiologists and mathematical modellers from around the world. The series focused on how epidemiological analysis and mathematical modelling has helped to inform the COVID-19 responses around the world.

Marking the one-year anniversary of the Jameel Institute (J-IDEA), a thought-provoking symposium with international experts was organised focusing on lessons learned so far, how to mitigate the social and economic impacts of the pandemic, and how we can better prepare for future pandemics. The live event reached over 800 attendees across the world.

Communication

OUTREACH & MEDIA ENGAGEMENT

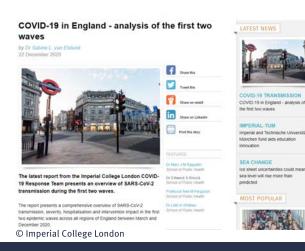
MEDIA & SOCIAL MEDIA

The COVID-19 pandemic has been an acute reminder of the importance of science communication. It can be a powerful tool, but ineffective communication, poor access to information and information overload can lead to concern, confusion and panic. With political reporters dominating the press and the many unanswered questions about the ever-changing pandemic, open and clear sharing of what we do and do not know is important.



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Our team have provided clear and consistent information to the media, explaining the research as it was made available. Facilitated by the Science Media Centre, the team was part of press briefings to provide accurate and evidence-based information about science through media to the public and policy makers. The team received close to 2000 interview requests from 49 countries, engaged with well over 1000 media queries and conducted interviews in a range of languages including Bahasa, Dutch, French, German, Italian, Japanese, Portuguese and Spanish. The Imperial College News pages covered the progress of the team's work with over 100 news items.



All research findings, publications and activities are shared on the team's social media platforms including YouTube, Twitter, LinkedIn, Instagram and Facebook. This messaging has massive reach with all tweets since the release of the team's first report receiving well over 14 million impressions (the tweet for the release of Report 42 on the new variant receiving close to 900,000 impressions alone, the release of Report 9 on the impact of nonpharmaceutical interventions was seen by close to half a million people).

Fiona Fox, Director Science Media Centre

It's almost impossible now to imagine how the public, policy-makers and journalists would have understood the full impact of the threat from this virus from mid-January without the data coming from the team of modellers at Imperial College London. The proactive communication of that evidence has been done brilliantly by the media team at Imperial College London and it's been a privilege to work with them on many press briefings including the one that took place on 16th March which will undoubtedly make the history books. Having a dedicated press officer embedded with the modelling team who is so familiar with the science and the scientists has been especially important and I think this is a model I would advocate where possible.

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IMPERIAL COLLEGE COVID-19 RESPONSE TEAM & CONTRIBUTORS (IN ALPHABETICAL ORDER)

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National Institute for Health Research (NIHR) Applied Research Collaborative North West London BRC Imperial College NHS Trust Infection & COVID themes HPRU in Emerging and Zoonotic Infections HPRU in Healthcare Associated Infections & AMR HPRU in Modelling and Health Economics Imperial Biomedical Research Centre Novartis Vaccine Efficacy Evaluation for Priority Emerging Diseases 02 Office of the President of Indonesia's Special Staff Panama Government Advisory Council for COVID-19 **Public Health England** Public Health Institute of Malawi (PHIM) Royal Infirmary of Edinburgh - Department of Clinical Biochemistry Science Media Centre Secretaría de Salud de Bogotá Singapore General Hospital Sree Chitra Tirunal Institute for Medical Sciences & Technology Sudan COVID-19 Research Group Sudan Youth Peer Education Network Translational Health Science & Technology Institute (THSTI), India Umeå University - School of Business Economics & Statistics United Kingdom Embassy in Colombia US CDC Nigeria Office, Nigeria Universidad Javeriana, Bogotá Universidade de São Paulo Universidade Federal do AB Universitat Jaime I - Facultad de Ciencias de la Salud Universiti Brunei Darussalam - PAPRSB Institute of Health Science University College Cork School of Public Health Irish Centre for Maternal & Child Health Research (INFANT) University of Bari - Interdisciplinary Department of Medicine University of Birmingham - Institute of Microbiology & Infection University of Copenhagen University of Edinburgh - Institute of Evolutionary Biology University of Oxford **Department of Statistics** Nuffield Department of Clinical Neurosciences Department of Zoology University of Padua University of Sussex - School of Life Sciences University of Warwick University of York - Centre for Health Economics Vektorraum Wellcome Sanger Institute West Bengal State Government, India World Health Organization (WHO) Zimbabwe Ministry of Health & Child Care

OVERVIEW

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J-IDEA Pandemic Hospital Planner. MRC Centre for Global Infectious Disease Analysis, Jameel Institute (J-IDEA), Imperial College London. https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-04-17-COVID19-Report-15hospital-planner.xlsm

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PACKAGES (IN ALPHABETICAL ORDER)

CovidSim. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/covid-sim dust. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/dust epidemia. Imperial College London. https://github.com/ImperialCollegeLondon/epidemia EpiEstim. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/EpiEstim markovid. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/markovid MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/mcstate mcstate. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/nimue nimue. orderly. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/vimc/orderly MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/PhyDyn PhyDyn. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/sircovid sircovid. MRC Centre for Global Infectious Disease Analysis, Imperial College London. https://github.com/mrc-ide/squire squire.

DISCLAIMER

Content was up to date to the best of our knowledge and understanding at the time of printing (22-03-2021). All staff captured in photographs strictly adhered to all local COVID-19 measures and regulations required at the time the pictures were taken. Views expressed in quotes are those of the individuals involved and do not reflect the opinions of their affiliate institutions.