

The Royal Society of Medicine

COVID-19: Two Years On A Research Timeline

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COVID-19: A Research Timeline

A research perspective on the pandemic

The volume and speed of research on the COVID-19 pandemic is unprecedented in the history of scientific and medical publishing. As soon as the SARS-CoV-2 virus was discovered, research groups worldwide investigated its biology, developed diagnostic tests or explored public health measures to control it. Researchers raced to find treatments and create vaccines that could bring the pandemic under control.

This timeline presents a research perspective on the pandemic with a selection of the key discoveries made month-by-month between January 2020 and March 2022.

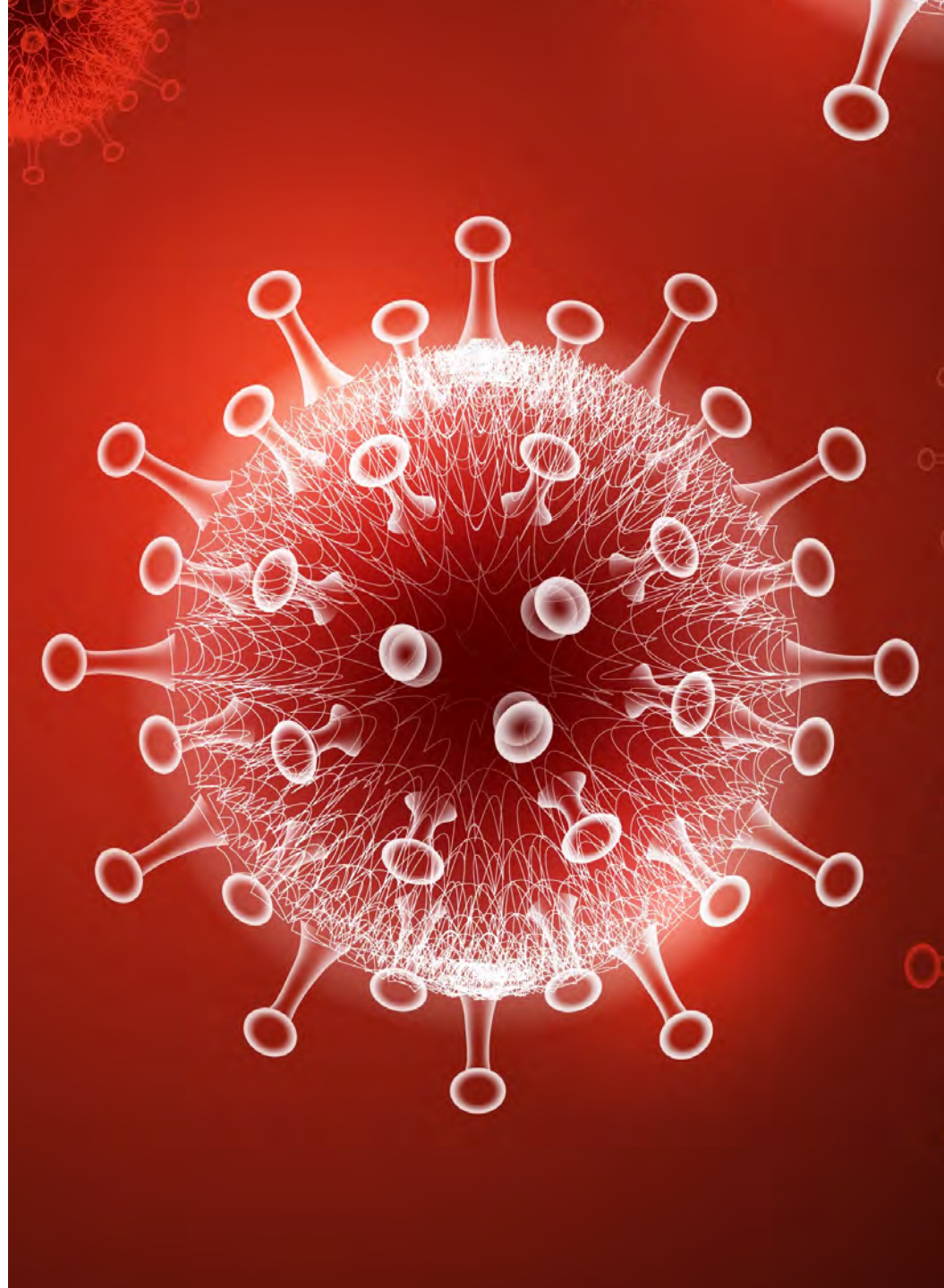
Research findings are presented by their earliest announcement in the press, as a news release, preprint or e-pub before print article. Where available, the final peer-reviewed publication details are provided in a separate [reference list](#).

For the timeline to flow coherently, earlier or later studies may be weaved into the narrative for some months. Clinical trials and studies still underway are not covered in this timeline.

All citation details and URL links are current to 18 March 2022.

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January 2020

A new virus SARS-CoV-2 is identified and its genome is mapped

The first cases of a pneumonia-like virus infecting patients in Wuhan are reported to the WHO China Country Office on 31 December 2019 ([Zhu 2020](#)). The virus later becomes known as 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2).

Less than 2 weeks later, the first draft of the complete genome of SARS-CoV-2 is made publicly available on GenBank ([Zhang 2020](#); [Wu 2020](#)), the world's largest database of genetic sequences. This leads rapidly to German virologists producing the first reverse transcriptase real-time polymerase chain reaction (RT-PCR) diagnostic test ([Corman 2020](#); [Corman 2020](#)), now considered the gold standard for laboratory diagnosis of an active SARS-CoV-2 infection.

The first description of the clinical characteristics, severity and mortality of the original 41 Wuhan patients is published on 24 January ([Huang 2020](#)). Common symptoms at disease onset are cough, fever, shortness of breath, myalgia and fatigue with all patients developing pneumonia.

Studies providing the first evidence of human-to-human transmission and asymptomatic (pre-symptomatic) infection are documented ([Chan 2020](#); [Rothe 2020](#)) and support a 14-day quarantine period for those exposed ([Li 2020](#)).

As Chinese scientists forecast a global pandemic ([Wu 2020](#)), the UK confirms its first case on 31 January.



February 2020

The disease is named COVID-19 and therapeutic targets are identified

WHO announces COVID-19 as the official name for the new disease caused by SARS-CoV-2 infection on 11 February ([WHO 2020](#)).

Early in February, the bat coronavirus is first reported as the possible early progenitor ([Zhou 2020](#)). An important early finding is that SARS-CoV-2 tightly latches on to angiotensin-converting enzyme 2 (ACE2) ([Letko 2020](#)), a protein receptor found on cell surfaces of many organs including the lungs, heart and gut, explaining the breadth of symptoms ([Gupta 2020](#)) and infectiousness of the virus.

Only 2 months after the first genome was released, researchers map the molecular structure of the spike protein which allows the virus to bind and invade human cells ([Wrapp 2020](#)).

This is followed quickly by structures of human ACE2 ([Hoffmann 2020](#)) bound to spike protein ([Yan 2020](#)), the SARS-CoV-2 nucleocapsid RNA-binding domain on the spike protein ([Kang 2020](#)), and the SARS-CoV-2 main protease ([Zhang 2020](#)).

All become important targets for potential vaccines and the development of treatments.



March 2020

WHO declares COVID-19 a pandemic as global lockdowns begin

Shortly after WHO declares COVID-19 a pandemic on 11 March, the first vaccine candidate begins a Phase I clinical trial – a mRNA vaccine targeting the spike protein (mRNA-1273) designed by the National Institutes of Health and Moderna ([ClinicalTrials.gov 2020](#)).

Neutralising antibody responses to the receptor-binding domain of the SARS-CoV-2 spike protein are identified in patients ([Ju 2020](#)). A serological assay to detect the production of antibodies in response to SARS-CoV-2 antigens in humans is made available ([Stadlbauer 2020](#)).

The first evidence is revealed of a lack of interferon responses to SARS-CoV-2 predicting sustained viral replication and leading to serious infection ([Blanco-Melo 2020](#)). The loss of smell and taste is first described in Milan, Italy as a common symptom of COVID-19 ([Giacomelli 2020](#)).

In mid-March, Imperial College publishes an influential epidemiological model of the impact of non-pharmaceutical interventions aimed at reducing viral transmission such as social distancing, home isolation, quarantine and school closures ([Ferguson 2020](#)).

As the first national lockdown is introduced in the UK on 23 March, another modelling study shows extended lockdowns can delay a second wave ([Prem 2020](#)).

Less than 2 weeks later, the Royal Society of Medicine (RSM) begin their [COVID-19 Series](#) of webinars.



April 2020

Lateral flow assays are developed and viral transmission is established

Epidemiologists advised that mass testing for SARS-CoV-2 diagnosis is the way out of the pandemic, spurring research teams worldwide to start devising new rapid tests for prior viral exposure, known as lateral flow assays ([Li 2020](#); [Broughton 2020](#); [Lassaunière 2020](#)).

Three separate research teams report that viral levels in a person's body peak at the onset of symptoms suggesting that the virus can be easily transmitted between people, even when symptoms are mild and can predict if they will develop more severe symptoms ([To 2020](#); [Zou 2020](#); [Liu 2020](#)).

Research establishes that wearing a surgical face mask reduces the spread of the virus ([Leung 2020](#)) and is supported the following month by findings showing that the nose could be the body's entry point for the virus ([Hou 2020](#)).

Other researchers find that illness severity increases with age ([Pan 2020](#)) and that cancer patients are nearly 3 times as likely to die of COVID-19 than non-cancer patients ([Dai 2020](#)). Children younger than 10 years old are not immune to SARS-CoV-2 after close contact with an infected person, indicating that such 'super-spreading' events could lead to large COVID-19 clusters ([Bi 2020](#)).

In the closing week of April, WHO launches the [Access to COVID-19 Tools \(ACT\) Accelerator](#), a global collaboration to support fast development, production and equitable access to COVID-19 diagnostic tests, treatments and vaccines (including the COVAX vaccine initiative for poorer countries) ([WHO 2020](#)).



May 2020

Concerns raised over high risks of COVID-19 death in specific groups

A study of 17+ million English residents shows COVID-19-related death is associated with greater age, being male, social deprivation, diabetes, asthma and other medical conditions. It also reveals that ethnic minorities are at substantially higher risk of dying from COVID-19, but this is only partially attributable to pre-existing health conditions and socio-economic factors, prompting an urgent need for measures to protect this population group from the disease ([Williamson 2020](#); [Mathur 2021](#)).

Autopsy studies find severe COVID-19 causes vascular damage in the lung ([Wichmann 2020](#)) but the virus also appears in the kidneys, heart, brain and other organs ([Puelles 2020](#)) supporting non-respiratory symptoms seen in some patients.

A study shows pre-existing cross-reactive T-cell responses to SARS-CoV-2 antigens are identified in around 30-50% of unexposed people ([Grifoni 2020](#)). Previous infection with SARS-CoV-2 or vaccination with spike protein protects monkeys from viral challenge indicating some immune protection ([Chandrashekar 2020](#); [Yu 2020](#)).

Pregnant women are not at greater risk of severe COVID-19 than other women but a majority who became ill were in their third trimester of pregnancy emphasising the importance of social distancing for this group ([Knight 2020](#)).

Children with COVID-19 are at lower risk of death than adults but the very youngest are most likely to be hospitalised ([Garazzino 2020](#)).

The month ends with the launch of England's COVID-19 contact tracing programme, NHS Test and Trace, on 28 May ([DHSC 2020](#)). The programme is complemented by the roll out of the NHS COVID-19 App weeks later following pilot trials ([DHSC 2021](#)).



June 2020

Dexamethasone is beneficial as a COVID-19 therapy and lockdowns prove effective

Results from the UK's RECOVERY trial, currently the world's largest randomised controlled clinical trial for COVID-19 treatments, suggest that the commonly used steroid dexamethasone is the first drug found to reduce mortality in hospitalised patients with respiratory complications of COVID-19 ([Horby 2021](#)).

Until May 2020, children infected with SARS-CoV-2 were thought to have only mild or asymptomatic infections but studies in Europe and the USA begin to emerge showing that a small subset of children who recovered from COVID-19 present with multisystem inflammatory syndrome ([Riphagen 2020](#); [Whittaker 2020](#); [Verdoni 2020](#); [Moraleda 2021](#); [Cheung 2020](#)).

Regeneron Pharmaceuticals show that monoclonal antibody therapies can drive escape mutants of SARS-CoV-2 but that this can be avoided by using antibody cocktails ([Baum 2020](#)). More than two-thirds of infected people never show classic respiratory symptoms or fever ([Poletti 2021](#)). For the first time, high blood levels of the stress hormone cortisol are shown to be a marker of the severity of COVID-19 ([Tan 2020](#)).

A Cochrane review shows antibody tests are most effective at detecting whether someone has had COVID-19 two or more weeks after their symptoms began ([Deeks 2020](#)). Contaminated surfaces might pose only a modest risk for household spread of COVID-19 suggesting direct transmission through exhaled droplets is probably the main route of infection ([Döhla 2020](#)).

National lockdowns and other distancing measures in several countries prove to be powerful tools at thwarting SARS-CoV-2, according to two independently conducted studies ([Flaxman 2020](#); [Hsiang 2020](#)). In contrast, bars, restaurants, concerts, karaoke and gyms can aid 'super-spread' of the virus ([Furuse 2020](#)).



July 2020

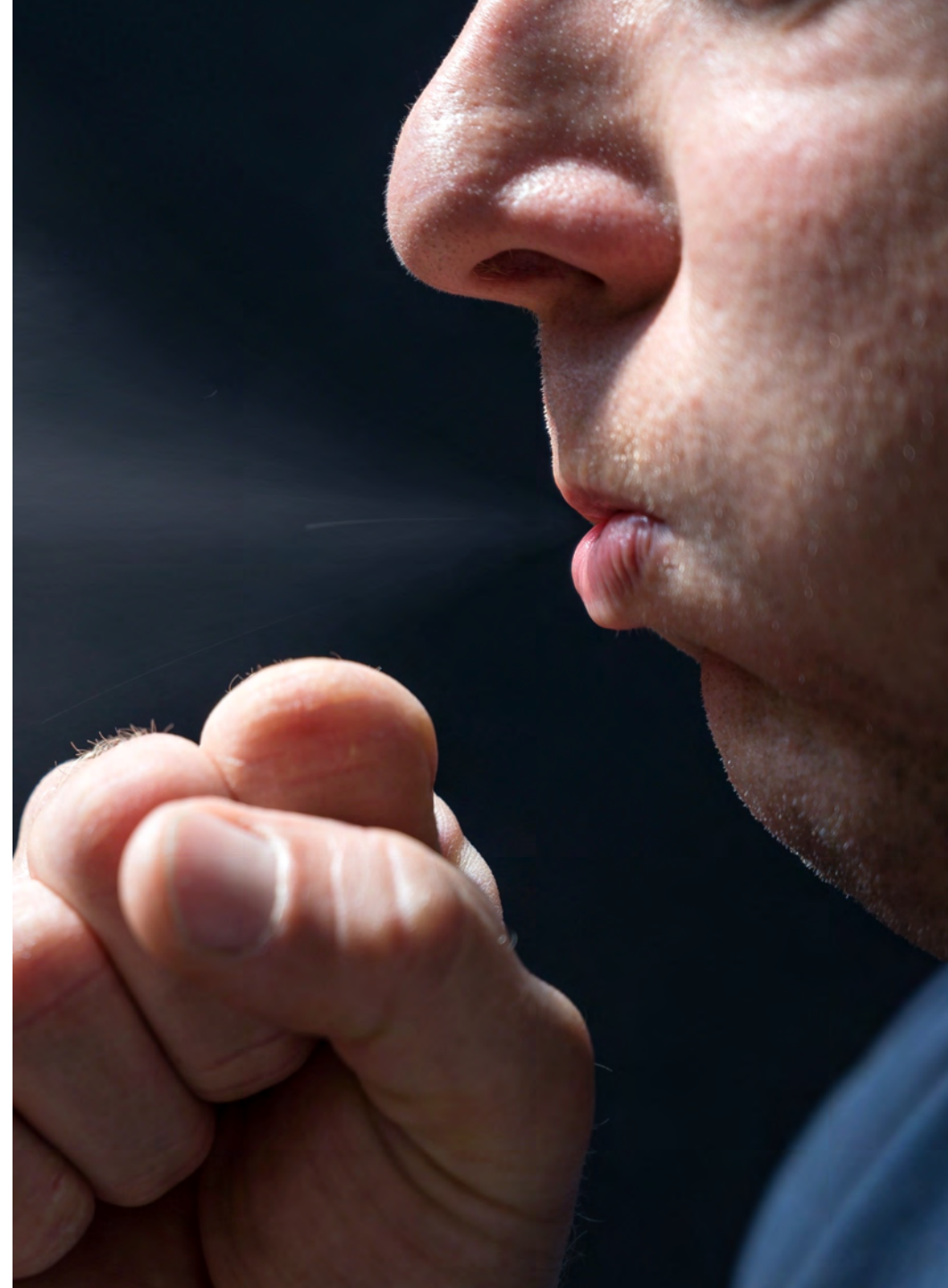
WHO confirms airborne transmission of SARS-CoV-2

WHO reviews evidence suggesting airborne viral transmission and emphasises the possibility of spread by asymptomatic individuals ([WHO 2020](#)) which may affect guidelines for indoor spaces such as mandatory mask wearing. Two days previously, a South Korean study proves that a massive contact-tracing effort found hundreds of cases linked to attending nightclubs ([Kang 2020](#)).

Several studies report varying levels of antibody protection against SARS-CoV-2 from 3-4 weeks to 3-5 months ([Seouw 2020](#); [Wajnberg 2020](#); [Crawford 2021](#); [Ibarrando 2020](#)) indicating that antibody resistance would be depleted within a year and questioning the durability of vaccines designed to promote the production of neutralising antibodies.

Immune T cells against the virus are found in unexposed people but it remains unclear whether these offer protection against SARS-CoV-2 infection ([Braun 2020](#)).

Those with severe COVID-19 exhibit a specific immune profile producing fewer interferons and more inflammatory molecules ([Hadjadj 2020](#)). Researchers conceive a 'cocktail' that uses antibodies targeting different regions of the viral spike protein which may treat or prevent COVID-19 ([Liu 2020](#)).



August 2020

Neutralising antibodies to SARS-CoV-2 protect against reinfection

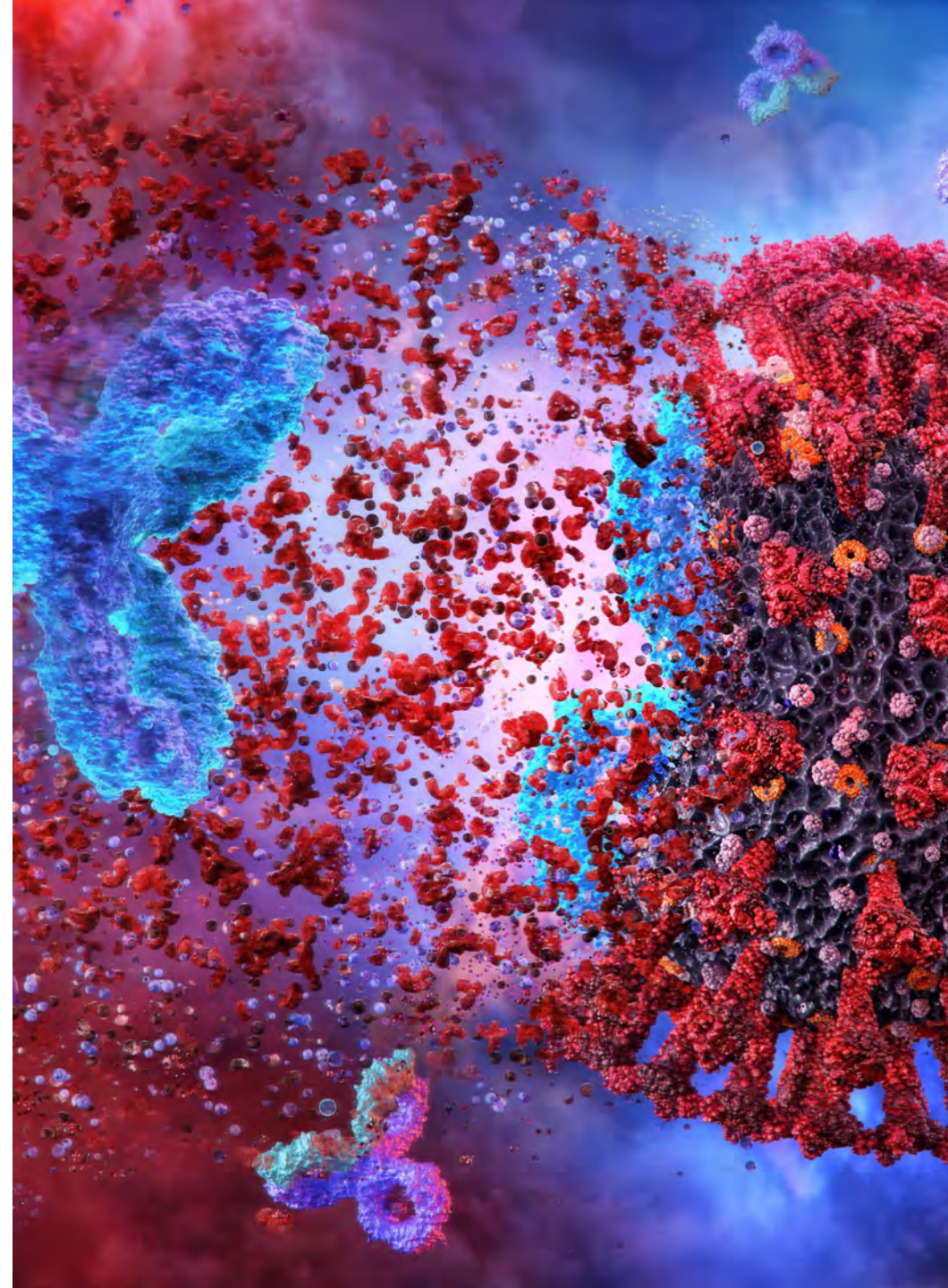
Individuals who had neutralising antibodies to SARS-CoV-2 were protected from reinfection during a COVID-19 outbreak with a high attack rate on a fishing boat, providing the first evidence for neutralising antibodies as a correlate of immune protection in humans ([Addetia 2020](#)).

Less than 2 weeks later, the first case of reinfection by a different variant of the virus is reported in Hong Kong supported by genetic evidence ([To 2021](#)).

For the first time, researchers map the 3D shape of spike proteins that are part of intact SARS-CoV-2 particles; earlier reported structures were gleaned from modified proteins expressed in cells ([Ke 2020](#)).

Severe obesity increases mortality risk from COVID-19 by exacerbating breathing issues brought on by the disease ([Tartof 2020](#)).

Gender differences in the immune response to COVID-19 might explain men's greater risk for severe disease ([Takahashi 2020](#)). The study finds that men have higher blood levels of the inflammation-causing proteins cytokines and chemokines whereas women tend to have a stronger response from immune T cells.



September 2020

Corticosteroid treatments lower deaths among critically ill COVID-19 patients

A meta-analysis of trials across 12 countries (including the REMAP-CAP study on hydrocortisone [Angus 2020](#)) reinforces evidence linking systemic corticosteroid treatment to improved survival rates among critically ill COVID-19 patients ([Sterne 2020](#)).

Regeneron announces positive results for its monoclonal antibody cocktail treatment REGN-COV2 ([Regeneron 2020](#)) and a front-runner COVID-19 vaccine (Moderna mRNA-1273) reports promising results in older people ([Anderson 2020](#)).

The Lab-in-Cartridge rapid testing device is proven highly accurate and is used across 8 London hospitals ([Gibani 2020](#)). Weekly surveillance testing may limit an outbreak even if the testing method is less sensitive than PCR tests ([Larremore 2021](#)).

The first cases of animal-to-human transmission are detected using genetic analysis at Dutch mink farms ([Oude Munnink 2021](#)). A survey in Iceland shows that antibodies against SARS-CoV-2 do not decline within 4 months after diagnosis, countering earlier evidence suggesting they quickly disappear ([Gudbjartsson 2020](#)).

Inborn mutations and neutralising antibodies that affect type I interferon signalling, predispose patients to life-threatening COVID-19 ([Zhang 2020](#); [Bastard 2020](#)). Higher plasma levels of neutrophils in infected people who later became critically ill could be used to predict severe COVID-19 ([Meizlish 2021](#)). The new 4C Mortality Score accurately predicts the risk of death from COVID-19 after hospital admission ([Knight 2020](#)).

UK researchers find nearly half of SARS-CoV-2 transmission is from people not yet feeling ill, underscoring the importance of mass testing, contact tracing and physical distancing to prevent transmission from pre-symptomatic people as well as self-isolation for at least 2 days at the first sign of symptoms, even if mild ([Ferretti 2020](#)).



October 2020

Living with long COVID

The NIHR Centre for Engagement and Dissemination publishes its first dynamic themed review of the scientific evidence and lived experience of long-term 'ongoing' COVID-19 – which becomes known as 'long COVID' ([NIHR 2020](#)).

Earlier in the month, a study finds that one in four pregnant women experience prolonged COVID-19 symptoms lasting for 8 weeks or longer after infection ([Afshar 2020](#)). Patients of black ethnicity have an increased risk of requiring hospital admission for COVID-19, while those of asian ethnicity have a higher risk of dying in hospital from COVID-19 ([Zakeri 2020](#)).

Antibodies against seasonal coronaviruses which cause the common cold offer little defence against SARS-CoV-2 ([Poston 2021](#)) and transmission is not slowed by warmer seasonal temperature changes unlike influenza viruses ([Poirier 2020](#)).

Two studies suggest blood type may play a role in the risk of becoming infected with COVID-19 or developing life-threatening complications but don't point to any single blood type being more protective or more vulnerable to the disease ([Barnkob 2020](#); [Hoiland 2020](#)).

A randomised controlled drug trial of tocilizumab, which mutes the body's immune response by interfering with interleukin-6 activity, found that it didn't prevent the deaths of people with moderate COVID-19 ([Stone 2020](#)). This study doesn't rule out the possibility that a larger trial with more statistical power could uncover a benefit.



November 2020

Vaccine clinical trials prove successful as WHO identifies an 'infodemic'

Days after England enters a second national lockdown on 5 November, and less than a year after the viral genome sequence was released, excellent results from vaccine Phase III clinical trials are announced via company press releases.

Pfizer-BioNTech's mRNA vaccine BNT162b2 is 95% effective following a two-dose regimen in 16+ year olds ([Polack 2020](#)), Moderna states final efficacy data of 94.1% for their vaccine mRNA-1273 ([Baden 2021](#)) and AstraZeneca-Oxford University report that their viral vector-based vaccine ChAdOx1 nCoV-19 (AZD1222) has an average efficacy of 70.4% across two different dose regimens ([Voysey 2021](#)).

The need to speed up the development and delivery of the vaccines has resulted in many clinical trial phases executed in parallel rather than sequentially; some developers have combined trial phases or started subsequent clinical phases before confirming the success of previous trials.

Positive results from the early phase trial of nebulised interferon beta-1a (SNG001) are published as the new inhaled antiviral drug moves to a much larger Phase III trial delivered across England in hospitalised COVID-19 patients ([Monk 2021](#)).

More than 60% of uninfected children aged 6-16 years have antibodies to SARS-CoV-2, possibly explaining why most infected children have mild or no illness ([Ng 2020](#)).

WHO identifies excessive COVID-19 pandemic-related misinformation on social media as a public health crisis, calling it an 'infodemic' ([WHO 2020](#)).



December 2020

Vaccines receive first approvals leading to a mass immunisation programme in the UK

The UK's authorisation of the Pfizer-BioNTech vaccine on 2 December makes history as the first international approval of a COVID-19 vaccine and the world's first non-trial approval of a mRNA vaccine ([MHRA 2020](#)). Less than a week later, on 8 December, the UK starts its nationwide COVID-19 immunisation programme.

The largest vaccine campaign in NHS history begins with 90-year-old grandmother Margaret Keenan becoming the first person in the world to receive the Pfizer-BioNTech vaccine jab ([NHS England 2020](#)). At the end of the year, the UK becomes the first to authorise the Oxford-AstraZeneca vaccine ([MHRA 2020](#)) and would go on to grant approval to the Moderna vaccine on 8 January 2021 ([MHRA 2021](#)).

Researchers discover five genes associated with the most severe form of COVID-19 involved in antiviral immunity and lung inflammation ([Pairo-Castineira 2021](#)).

Sporadic accounts of coronavirus reinfection and reports of rapidly declining antibody levels raised concerns that immunity to SARS-CoV-2 could dwindle within weeks of recovery from infection, but two US studies show that for most people, the immune system's memory of the virus persists for at least 6 months ([Dan 2021](#); [Gaebler 2021](#)).

The ZOE COVID Study is the first to demonstrate the use of mobile technology to provide national-level disease surveillance by rapidly identifying local infection hotspots in England needing targeted intervention ([Varsavsky 2021](#)).

The WHO Solidarity Trial fails to find significant changes in mortality rate or hospitalisation time in COVID-19 patients treated with four repurposed antiviral drugs – remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon beta-1a ([Pan 2021](#)).



January 2021

Global concern as virus variants are on the rise

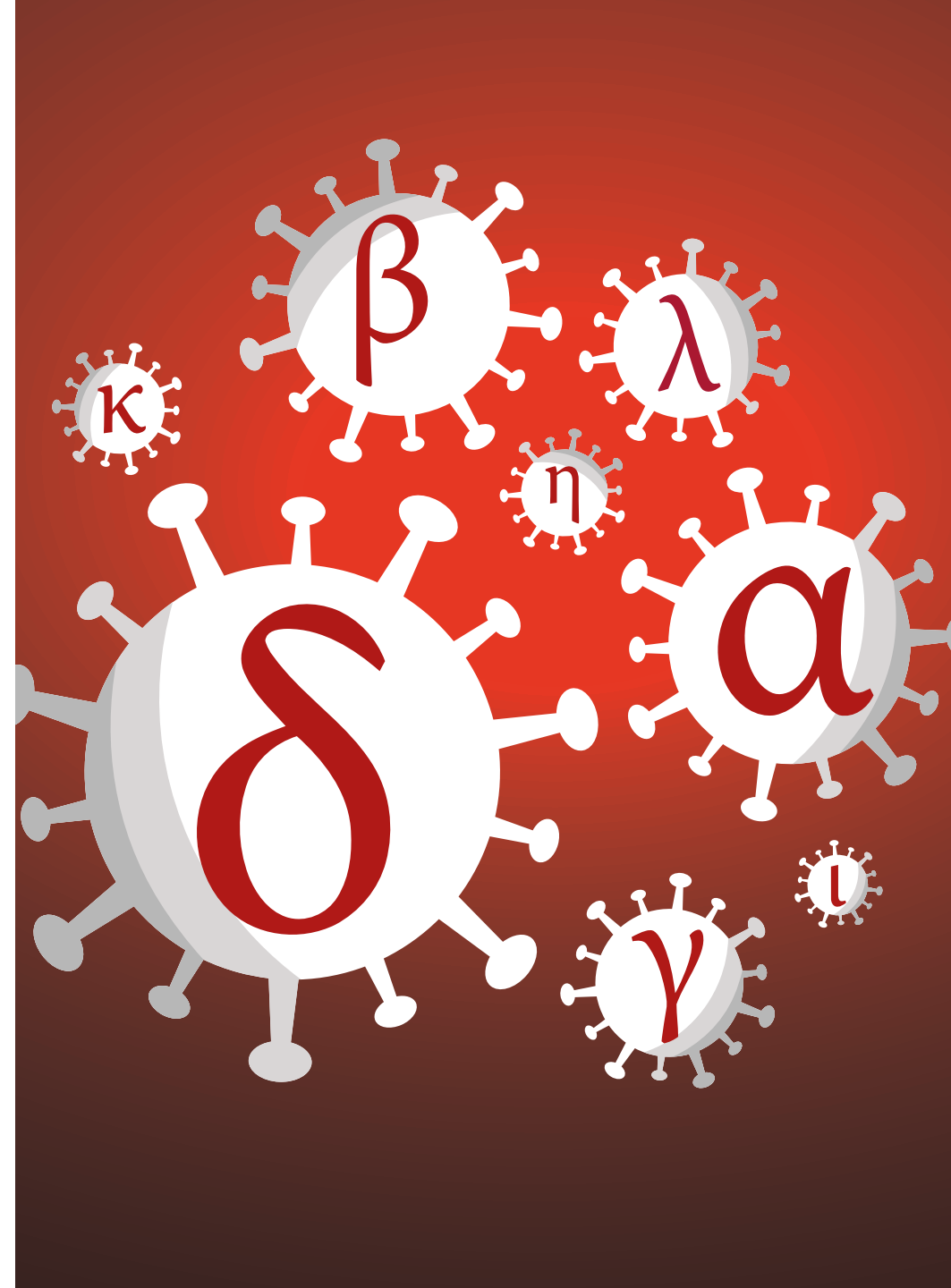
England begins its third national lockdown on 6 January amid growing concern over viral variants with increased infectivity, such as the UK-origin B.1.1.7 (Alpha) variant ([Volz 2021](#); [Walker 2021](#); [Davies 2021](#)), and enhanced disease severity and reduced vaccine efficacy, such as the South African-origin B.1.351 (Beta) variant ([Tegally 2021](#)).

WHO designates these as global 'variants of concern' on 18 December 2020 ([WHO 2022](#)) and they will be joined in subsequent months by Brazilian-origin B.1.1.28/P.1 (Gamma), Indian-origin B.1.617.2 (Delta) ([Thye 2021](#)) and B.1.1.529 (Omicron).

Two arthritis drugs – tocilizumab and sarilumab – are effective in improving survival in COVID-19 pneumonia patients admitted to intensive care ([Gordon 2021](#), prompting the UK to issue a therapeutic alert ([MHRA 2021](#)). The 4C Deterioration Score, a new online risk stratification tool, identifies hospitalised COVID-19 patients at highest risk of deterioration ([Gupta 2021](#)).

A mutation common to the South African and Brazilian viral variants, causes a steep drop in the potency of antibodies ([Greaney 2021](#)). A US study suggests that the Moderna and Pfizer-BioNTech vaccines might lose potency against the new Alpha, Beta and Gamma variants ([Wang 2021](#)) but less than a week later, Moderna indicates that their vaccine seems to work against the Alpha and Beta variants ([Wu 2021](#)).

In late January, Phase III trial results report that the Novavax recombinant spike vaccine NVX-CoV2373 is 89.3% effective ([Novavax 2021](#)), including against new variants of concern, and the first of its kind, the Johnson & Johnson Janssen single-shot vaccine Ad26.COV2.S shows 66% efficacy ([Johnson & Johnson 2021](#)).



February 2021

First real-world data studies prove vaccine efficacy

A landmark community study in Scotland is the first to report that vaccination links to a substantial reduction in COVID-19 hospital admissions ([Vasileiou 2021](#)).

The first real-world data studies show that the Pfizer-BioNTech vaccine is highly effective at preventing COVID-19 after one dose in the UK ([Hall 2021](#)) and after two shots in Israel ([Dagan 2021](#)). The Oxford-AstraZeneca vaccine is 81% effective if the second of its two doses are given more than 12 weeks after the first, supporting the UK's decision to space out the doses ([Voysey 2021](#)).

A single shot of either the Moderna or Pfizer-BioNTech vaccine provokes a strong immune response of about 1,000-fold against the Beta variant of SARS-CoV-2 ([Stamatatos 2021](#)).

People with high viral loads in their bodies are more likely to transmit SARS-CoV-2 to close contacts whether they have a cough or not, according to a Spanish study looking at how they become 'super-spreaders' ([Marks 2021](#)). This measure of an infected person's viral load is used to predict an outbreak's course ([Hay 2021](#)).

Preliminary findings suggest that the Alpha variant might be more transmissible because it spends more time inside its host than earlier variants do, warranting the need for longer quarantine periods ([Kissler 2021](#)).

Respiratory support, used to treat severe COVID-19 patients, is associated with less aerosol emission than breathing, speaking or coughing ([Hamilton 2022](#)).

Tocilizumab, an anti-inflammatory rheumatoid arthritis treatment, improves survival for COVID-19 hospitalised patients, shortens the time to discharge and reduces the need for mechanical ventilation ([RECOVERY Collaborative Group 2021](#)).



March 2021

Blood clotting – a vaccine side effect?

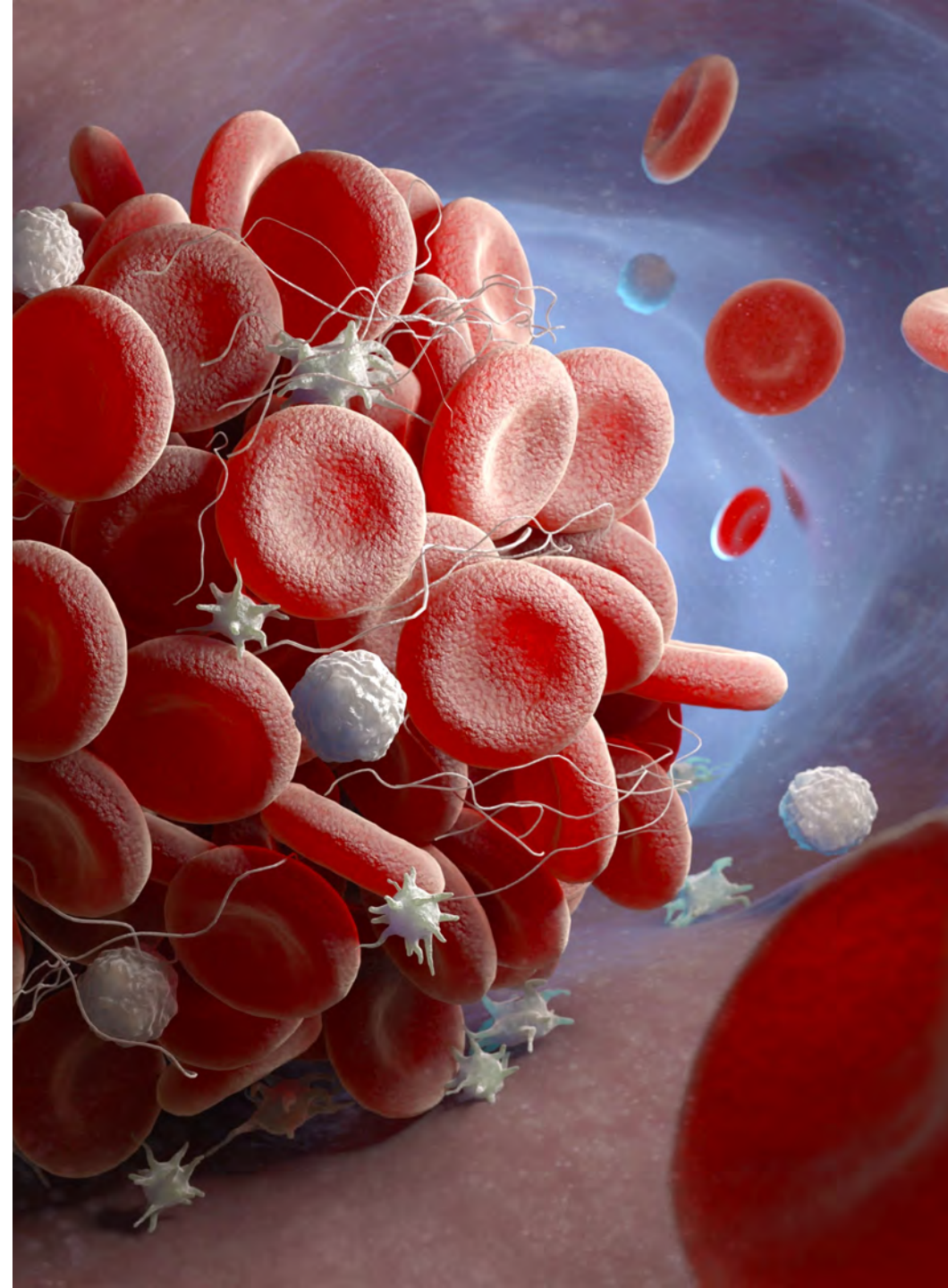
An investigation by the European Medicine Agency (EMA) concludes that the Oxford-AstraZeneca vaccine is not linked to an increased risk of blood clots after a small number of cases of the life-threatening condition were previously reported ([EMA 2021](#)). However, the following month, EMA recommends adding blood clots to the list of possible side effects whilst stressing that the vaccine is still considered safe and effective ([EMA 2021](#)).

A small trial reveals that the Oxford-AstraZeneca vaccine might offer only limited protection against the Beta variant ([Madhi 2021](#)), linking it to previous reports of reduced efficacy for the Novavax and Johnson & Johnson vaccines.

Emerging SARS-CoV-2 variants might not evade T cells which help to reduce infectious disease severity ([Tarke 2021](#)). People infected with the Alpha variant are at a higher risk of dying than those infected with other circulating variants, regardless of their age, gender and pre-existing health problems ([Grint 2021](#)).

A Danish study suggests that natural infection with SARS-CoV-2 protects against reinfection in most people, but protection is significantly weaker in those aged 65+, emphasising the need to prioritise vaccinations for this group ([Hansen 2021](#)).

The month ends with a WHO report concluding that animal-to-human transmission was the most likely origin of SARS-CoV-2 and spread to humans no more than a couple months before it was reported to WHO in December 2019 ([WHO 2021](#)).



April 2021

A common asthma drug could shave days off COVID-19 illness

A clinical trial in more than 4,600 people at risk of serious COVID-19 in the community finds that treatment with the widely available inhaled asthma drug, budesonide, shortens the duration of disease symptoms by about 3 days when taken twice daily for two weeks ([Yu 2021](#)).

The largest community-based survey of UK individuals shows for the first time the impact of vaccines in reducing the number of new infections, with the greatest benefit received after two doses, and against symptomatic and high viral burden infections ([Pritchard 2021](#)).

Another study shows that single doses of these vaccines cut a person's risk of transmitting SARS-CoV-2 to their closest contacts by 50% ([Harris 2021](#)). Antibodies triggered by the Moderna vaccine persist for at least 6 months after receiving a second dose ([Doria-Rose 2021](#)). Previous infections by viruses related to SARS-CoV-2 could reduce COVID-19 symptom duration due to the presence of T cells generated in response to past infections ([Gouma 2021](#)).

The most sensitive lateral flow tests can detect nearly 90% of SARS-CoV-2 cases that would lead to an infected contact, showing their value in preventing COVID-19 spread, based on a performance analysis of millions of tests ([Lee 2022](#)). Regular swabbing of a random sample of the population quickly detects the resurgence of infections, even at low levels of virus transmission, demonstrating the benefit of large-scale community testing ([Riley 2021](#)).

The national health protection functions of Public Health England (PHE) and NHS Test and Trace (NHSTT) are combined and formally established from April into a new UK Health Security Agency (UKHSA) ([DHSC 2021](#)).



May - June 2021

Vaccines fight against the Delta variant

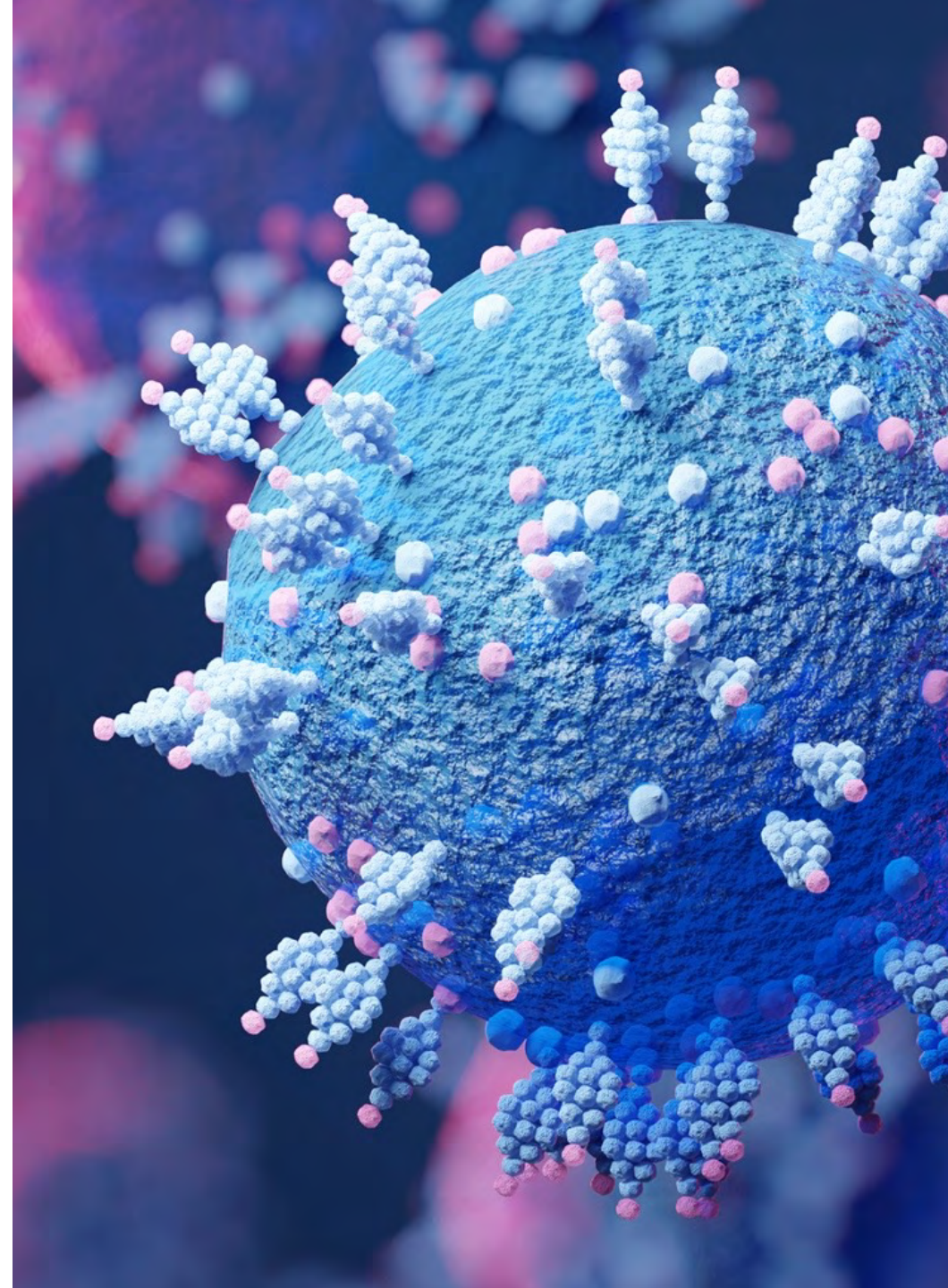
The new highly contagious Delta variant is now responsible for 90% of UK cases, becoming more prevalent than the Alpha variant ([Elliott 2021](#)). A new UK analysis shows that two doses of either the Pfizer-BioNTech or Oxford-AstraZeneca vaccines are highly effective against hospitalisation from the Delta variant, but it remains twice as likely to hospitalise people as the already more infectious Alpha variant ([Lopez Bernal 2021](#)).

A study by Oxford University of all available vaccines, including their own AstraZeneca vaccine, demonstrates protection against Delta and Kappa (B1.617.1) variants, both originating from India ([Liu 2021](#)). Moderna also reports its vaccine produces protective antibodies against the Delta variant ([Choi 2021](#)).

As the Delta variant begins its path to global dominance, critically ill patients in Africa are found to have the highest global mortality rate among COVID-19 patients ([Kirenga 2021](#)). A cutting-edge imaging method, hyperpolarised xenon MRI (XeMRI), identifies lung damage in COVID-19 patients more than 3 months after hospital discharge ([Grist 2021](#)). Up to one in three people who have had COVID-19 report long COVID symptoms, with older people and women more likely to be affected whereas ethnic minorities are at lower risk ([Whitaker 2021](#); [Thompson 2021](#)).

Pfizer-BioNTech report that their vaccine demonstrates 100% efficacy and robust antibody responses in adolescents aged 12-15 years, exceeding those recorded earlier amongst participants aged 16-25 years ([Frenck 2021](#)).

Alternating doses of the Oxford-AstraZeneca and Pfizer-BioNTech vaccines generates strong immune responses against COVID-19 when administered 4 weeks apart, indicating that all possible vaccination schedules could potentially be used in immunisation programmes ([Liu 2021](#)).



July - September 2021

The extent of long COVID is revealed and another vaccine side effect is reported

People who experience five or more symptoms of COVID-19 in the first week of infection are more likely to develop long COVID, according to a review which also identifies the 10 most common symptoms of the condition ([Aiyegbusi 2021](#)). A large study in September reveals over a third of COVID-19 patients are diagnosed with at least one long COVID symptom in the 3-6 months period after infection ([Taquet 2021](#)). Up to one in seven children and young people who had COVID-19 may have symptoms linked to the virus 15 weeks later, suggest preliminary findings from the world's largest study on long COVID in children ([Stephenson 2022](#)).

Concerns about side effects of vaccines against COVID-19 surface again in July when a WHO committee identifies 'a likely causal association' between mild myocarditis / pericarditis and mRNA vaccines, although such cases are rare ([WHO 2021](#)). The risk of severe COVID-19 leading to increased hospitalisations and deaths remains greater than the risk of vaccine side effects.

Pfizer report initial findings of its SARS-CoV-2 inhibitor, nirmatrelvir, the first orally administered compound to enter clinical trials which could lead to a preventative COVID-19 treatment ([Owen 2021](#)).

The QCovid tool accurately identifies people at greatest risk from severe COVID-19 despite being fully vaccinated ([Hippisley-Cox 2021](#)). This tool previously accurately estimated a person's risk of becoming seriously ill with COVID-19 ([Clift 2020](#)) which guided shielding policy decisions in February 2021.

The COVID-19 Psychological Wellbeing Study reports a negative impact on the mental health of adults during the first UK national lockdown emphasising the need for support interventions in the recovery phase ([McPherson 2021](#)).



September - October 2021

The NHS rolls out COVID-19 booster vaccination campaign

The UK COVID-19 booster vaccination campaign begins on 16 September ([NHS England 2021](#)) in line with advice from the Joint Committee on Vaccination and Immunisation (JCVI) set out just two days before ([DHSC 2021](#)). Key decisions made were informed by COV-BOOST, the first study in the world to provide data on the impact of a third vaccine dose on immune responses, favouring the Pfizer-BioNTech vaccine for the booster programme ([NIHR 2021](#)), and the ComFluCOV trial which shows that coadministration of influenza and COVID-19 vaccines is safe and effective ([Lazarus 2021](#)). Just 4 days later, the NHS starts to roll out the Pfizer-BioNTech vaccine jab to school children aged 12-15 years ([NHS England 2021](#)).

Two vaccine doses offer very high levels of protection against death from the Delta variant, according to the first study on the effectiveness of COVID vaccines against Delta using real-world data from an entire country, Scotland ([Sheikh 2021](#)). However, another large UK community-based study finds that while vaccination reduces new SARS-CoV-2 infections, effectiveness and protection against peak viral burden are reduced with the Delta variant ([Pouwels 2021](#)). Partial or full vaccination is effective against severe COVID-19 but vaccinated men, the elderly and those with underlying health conditions are still at risk ([Agrawal 2021](#)).

After receiving both doses of a mRNA vaccine, pregnant and lactating women's initially weaker immune response becomes as robust as the general populations' ([Ateyo 2021](#)). Another study finds that women carrying a male foetus not only have fewer antibodies after infection but also pass less across the placenta than those carrying a female foetus ([Bordt 2021](#)). The first study to look at reinfection following natural infection in the unvaccinated is published in October, and finds strong protection is short-lived after recovery and will become increasingly common as immunity wanes and new virus variants arise ([Townsend 2021](#)).



November-December 2021

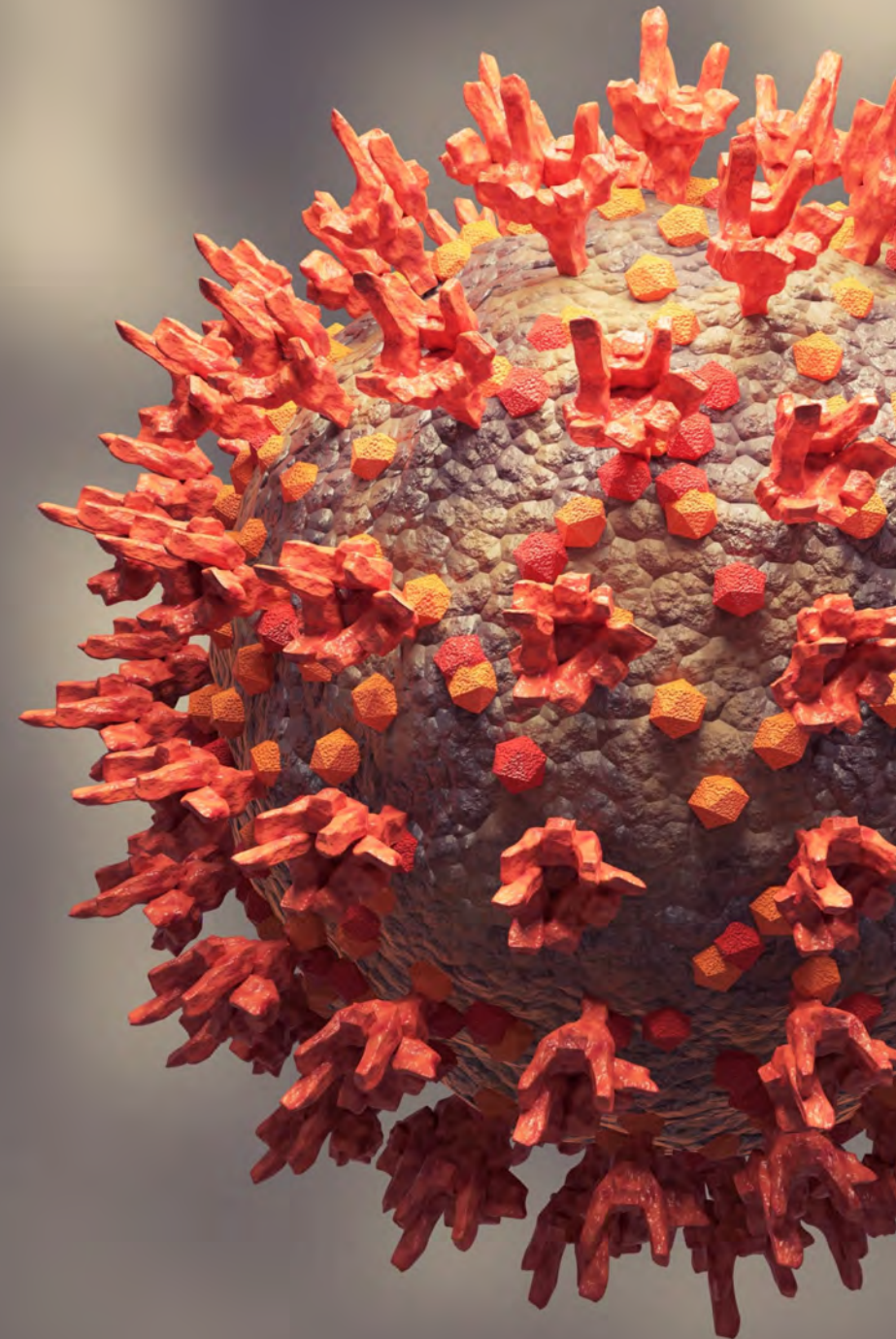
The Omicron variant is characterised

Within weeks of WHO designating B.1.1.529 (Omicron) as a variant of concern in November, it's reported in more than 67 countries driven by a larger number of mutations in the virus's spike protein, proposed to be associated with increased transmissibility and escape from protection conferred by vaccines and monoclonal antibodies ([VanBlargan 2022](#); [Torjesen 2021](#)).

An early study shows neutralising activity is decreased in sera from vaccinated patients but highlights the need for additional booster doses ([Garcia-Beltran 2022](#)). Angelique Coetzee, the doctor who first spotted the Omicron variant states that patients display mild symptoms ([BBC 2021](#); [CNN Health 2021](#)). Researchers in Hong Kong find Omicron multiplies 70 times faster than Delta in human airways but replicates less rapidly in human lung tissue ([HKUMed 2021](#)). These initial findings show that Omicron appears to be more contagious, but not more lethal.

In a world first, the UK authorises an oral antiviral drug molnupiravir for the treatment of mild-to-moderate COVID-19 ([MHRA 2021](#)), following interim results from Merck's Phase III clinical trial demonstrating a cut in the risk of hospitalisation or death by about 50% among high-risk adults ([Merck 2021](#)).

UK scientists identified a version of a gene that may be associated with double the risk of lung failure from COVID-19, providing new insights into why some people are more susceptible to severe illness ([Downes 2021](#)). Pfizer-BioNTech demonstrate the effectiveness and safety of their mRNA vaccine in children aged 5-11 years ([Walter 2022](#)). Children with poorly controlled asthma are up to 6 times more likely to be hospitalised with COVID-19 than those without the condition and should be considered a priority for vaccinations ([Shi 2022](#)).



December 2021

Vaccinating young children and 'mix-and-match' dosing for booster jabs in adults

Vaccine studies continue to dominate. Pfizer is studying their vaccine in a trial of children aged 2-11 years and another trial in infants 6 months-2 years ([Pfizer 2021](#)). The latest report from the ongoing REACT study reveals COVID-19 vaccination cuts infection risk by half in children aged 12-17 years who have received a single Pfizer-BioNTech dose ([Chadeau-Hyam 2021](#)).

The COV-BOOST study, key to shaping the UK booster vaccination programme, states that six COVID-19 vaccines when used as a third booster jab are safe and boost immunity for people who have had two doses of Oxford-AstraZeneca or Pfizer-BioNTech ([Munro 2021](#)). Another study finds that following up first doses of the Oxford-AstraZeneca or Pfizer-BioNTech vaccines with second doses of the Moderna or Novavax jabs generates robust immune responses against COVID-19 ([Stuart 2022](#)).

These results support 'mix-and-match' dosing and is expected to boost vaccine drives in poor and middle-income countries. The world's first plant-based COVID-19 vaccine from Medicago and GSK is 75.3% effective against preventing COVID-19 of any severity ([Medicago 2021](#)).

The year ends with two non-vaccine studies. Demographic and lifestyle factors drive difference in COVID-19 infection risk for healthcare workers from ethnic minority groups, according to the largest and most detailed study on the subject UK-REACH ([Martin 2021](#)). The latest data from the REACT study shows the highest-ever recorded numbers of daily SARS-CoV-2 infections in England due to a rapid rise in Omicron despite high levels of vaccination in the population ([Elliott 2022](#)).



January - February 2022

COVID-19's effects on fertility, pregnancy and children

Severe COVID-19 infection in pregnant women increases the risk of harmful outcomes for mothers and babies ([Vousden 2022](#)). A study by the National Institutes of Health shows no link between COVID-19 vaccines and infertility, but SARS-CoV-2 infection is associated with a short-term reduction in male fertility ([Wesselink 2022](#)).

A modelling study estimates at least 5.2 million children have lost a parent or caregiver due to COVID-19 ([Unwin 2022](#)). England's 14-days travel quarantine measures reduce COVID-19 spread and is particularly effective for travellers aged 16-20 years ([Aggarwal 2022](#)).

In a study of predominantly mild community-based infection, Omicron is associated with fewer lower and more upper respiratory tract symptoms ([Vihta 2022](#)). The UK's world-leading COVID-19 human challenge study is the first to provide detailed insights on the early phase of infection and supportive evidence that lateral flow tests reliably identify people likely to be infectious ([Killingley 2022](#)).

Concerns are raised again after two subvariants of Omicron, BA.1 and BA.2 emerge with substantially greater transmissibility than the original strain and with potential vaccine implications ([Lyngse 2022](#)).

Data from both an ongoing trial and a separate Phase IV trial shows that the Oxford-AstraZeneca vaccine increases antibody responses to several variants including Omicron, when given as a third dose booster, regardless of the primary vaccination schedules tested ([AstraZeneca 2022](#); [Costa Clemens 2022](#)).

The first results of an early trial of a multivalent vaccine booster, a self-amplifying mRNA second generation vaccine (samRNA), release positive data ([Manchester University NHS Foundation Trust 2022](#)).



February - March 2022

New antiviral drug treatments are investigated

An Israeli observational study reports that a fourth dose of the Pfizer-BioNTech vaccine lowers the rates of confirmed Omicron infection and severe illness compared to only three doses ([Bar-On 2022](#)), after Israel became the first country to administer a fourth dose to the elderly and high-risk populations on 2 January.

The UK approves Novavax NVX-CoV2372 (Nuvaxovid) as its first protein-based COVID-19 vaccine ([MHRA 2022](#)), based on a trial reported in June 2021 showing the vaccine 89.7% effective at preventing COVID-19, prior to the emergence of Omicron ([Heath 2021](#)).

Pfizer's oral antiviral drug nirmatrelvir when combined with ritonavir, results in 89% lower risk of progression to severe COVID-19 in non-hospitalised adults with the mild-to-moderate form of the disease ([Hammond 2022](#)).

Over 10,000 UK participants have now taken part in the PANORAMIC trial, the world's largest study into antiviral treatments in community care, with molnupiravir being the first antiviral drug currently being assessed ([NIHR 2022](#)). The RECOVERY trial finds the oral anti-inflammatory rheumatoid arthritis drug, baricitinib reduces deaths in COVID-19 hospitalised patients by around one-fifth ([Horby 2022](#)).

A study in Australia suggests that sotrovimab, a monoclonal antibody treatment for COVID-19, may cause the virus to acquire mutations that enable it to resist the drug ([Rockett 2022](#)).

The UK approves AstraZeneca's Evusheld (tixagevimab co-packaged with cilgavimab) as the first monoclonal antibody combination for pre-exposure prophylaxis against COVID-19 in immuno-compromised people licensed in the UK ([MHRA 2022](#)).



March 2022

The Royal Society of Medicine hosts the *COVID-19: Two Years On* conference

The world's largest study of the genetics of critical COVID-19 discovers 16 new genetic variants associated with severe COVID-19, including some related to blood clotting, immune response and intensity of inflammation ([Kousathanas 2022](#)). Imaging before and after infection by SARS-CoV-2 reveals substantial changes in the brain which could explain symptoms such as loss of smell and taste ([Douaud 2022](#)). Researchers in France identify a new hybrid variant 'Deltamicron', a recombinant virus of the Delta and Omicron strains ([Colson 2022](#)).

Children infected with SARS-CoV-2 are less likely than adults to produce antibodies against the virus, despite having similar symptoms and levels of virus in their bodies ([Toh 2022](#)) supporting an earlier study which showed that children mount a stronger and faster response to an infection ([Yoshida 2022](#)) – but it raises questions about how well protected children are to reinfection. A review concludes that transmission of SARS-CoV-2 from mother to baby is rare and suggests that preventive measures during delivery may make infection of newborns unlikely ([Allotey 2022](#)).

The 100th episode of the RSM's COVID-19 series of webinars is marked by a special conference *COVID-19: Two Years On* held on 31 March, two years after the start of the pandemic and the first UK lockdown ([RSM 2022](#)). It brings together leading authorities on COVID-19 to discuss the pandemic's impact, best approaches for managing the endemic stage and preparing for the next pandemic threat.



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