COVID-19: Preparing for the future

Looking ahead to winter 2021/22 and beyond

15 July 2021



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Executive summary

Immediate priorities

Despite a highly successful vaccination campaign in the UK, the coronavirus disease 2019 (COVID-19) pandemic is not over, and we are currently seeing rapidly rising infection rates. While there is an understandable and intense desire for 'normality' to return, we need to sustain our efforts to limit the transmission and impacts of the virus, particularly for the most vulnerable, for the longer term. To prepare for the winter period and beyond, the priorities over the summer period must be to:

- Maximise the speed and uptake of COVID-19 vaccination in all eligible age groups, and prepare for possible booster vaccines in priority groups and vaccination against influenza later in the year.
- Increase the ability of people with COVID-19 to self-isolate through financial and other support, with a particular focus on those in areas of persistent transmission and in the lowest socio-economic groups.
- Boost capacity in the NHS (staff and beds) to: build resilience against future
 outbreaks of COVID-19 and other infectious diseases, including through
 improving infection prevention and control (IPC), increasing vaccination and
 testing capacity for COVID-19 and influenza, adequately resourcing primary care,
 and reducing the backlog of non-COVID-19 care.
- **Provide clear guidance** about environmental and behavioural precautions (such as the use of face coverings, ventilation and physical distancing) that individuals and organisations can take to protect themselves and others, especially those who are most vulnerable from infection.

Underpinning principles for success

In working to achieve these priorities and addressing the challenges ahead, the following key principles must be applied to ensure the most successful and equitable outcomes:

- Reduce inequalities. The pandemic has had a disproportionate impact on certain groups, including individuals from poorer and disadvantaged backgrounds, ethnic minority groups and deprived regions, who have shown greater COVID-19 mortality rate and poorer outcomes. The economic impact of the pandemic and repeated lockdowns is likely to have longer-term negative health impacts for groups already experiencing structural inequalities. All measures implemented to address the pandemic and the UK's recovery must seek to halt and reverse the unequal impact of the pandemic on health and wellbeing. This will include prioritising those with the greatest need, ensuring that communication is appropriate and that access to prevention of infection and expert care is available to all.
- Effective engagement and communication. Communication should focus on enabling people to understand the latest evidence on symptoms, transmission and effective mitigation. To maximise their effectiveness and to ensure they do not exacerbate inequalities, preparations for this winter, longer term adaptation plans and communications must be informed by engagement with and involvement of patients, carers, the public and healthcare professionals. We

- support **co-development** where possible, which **should be properly resourced**, **inclusive**, **transparent and recognise power inequalities**.
- Empower and resource local public health capacity. As we see greater variability in COVID-19 transmission and outbreaks at a local level, there needs to be a collaborative partnership between central government who provide standards and consistency and local authorities who should lead outbreak investigation and control. Local responses should be co-designed with local communities and delivered through local public health teams and primary care.

The challenges for winter 2021/22 and beyond

In this report, we outline three key challenges that will be faced by the UK this winter and beyond:

- A resurgence of respiratory infectious diseases, including COVID-19, influenza and respiratory syncytial virus (RSV). Our modelling suggests that there will be a third peak of COVID-19 infections over the summer of 2021, although the timing and magnitude of the peak are uncertain. Mortality may be less severe than last winter but a rise in infections will put pressure on the health service and lead to higher levels of long COVID. The possibility of a further new variant is also of concern. Outbreaks of RSV in the autumn and influenza in the winter could be around twice the magnitude of a 'normal' year, and might overlap (at least partially) with a peak in COVID-19 infections.
- Wider health and wellbeing impacts of the pandemic, including long COVID, mental and physical deconditioning, and the impact of delays in diagnosis and disease management during the pandemic. During the winter months, non-communicable diseases (NCDs) such as asthma, chronic obstructive pulmonary disease (COPD), ischaemic heart disease, myocardial infarction and stroke are likely to be exacerbated.
- Continued disruption to health and social care service delivery, including
 managing the backlog of treatment and diagnosis, incorporating IPC measures,
 and the financial precariousness of social care. By the winter, staff across the
 sectors will have been responding to a prolonged pandemic for over 18 months,
 with many directly affected by COVID-19, thereby compounding issues of staff
 capacity and vacancies.

Added to these, **ongoing uncertainties remain** over the: duration of post-vaccination immunity in different groups (and safety in children); likelihood of and impact of new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, including the possibility of vaccine-resistant variants. This is in addition to the development and availability of treatments and prophylaxis for COVID-19; and prevalence, duration, severity and ability to treat, long COVID.

Addressing the pandemic and its impact

To address these challenges, we propose a series of prevention and mitigation measures. The key principles outlined above must be considered in developing and implementing these measures to maximise their impact and effectiveness.

Vaccination to reduce severity and incidence of disease

- COVID-19 vaccination must continue to be a priority, focusing on uptake of both vaccine doses in older adults, those who are vulnerable due to long-term conditions, the staff or family members who provide close personal care and amongst those living in areas of deprivation and persistent transmission of SARS-CoV-2. Specific consideration must be given to communication and engagement strategies to improve vaccine uptake in population groups with low coverage, including ethnic minorities and young adults.
- The proposed **COVID-19 vaccination booster campaign** should be informed by emerging evidence on the duration of immunity and expected timing of peaks in infection and prioritise those most likely to have waning immunity (e.g. the vulnerable and those vaccinated first).
- Children and adolescents remain susceptible to the infection and are experiencing high transmission rates resulting in further disruption of schooling. The Joint Committee on Vaccination and Immunisation (JCVI) should continue to consider the possibility of vaccinating secondary school aged children against COVID-19. This will need to consider safety data emerging from other countries; the balance of risks and benefits of both vaccination and natural infection at different ages; ethical issues; and other impacts including wider effects on education, transmission and general wellbeing.
- Maximising the uptake of influenza vaccination to close to universal coverage in eligible populations, including among health and social care staff, to minimise the impact of a possible influenza epidemic.
- To meet the need for vaccination against COVID-19 and influenza and to ensure routine childhood vaccinations are up to date, maintaining and potentially increasing the capacity for vaccine delivery is a priority.
- Support for global vaccination programmes is needed to control the pandemic, reduce the risk of the emergence of new variants, and reduce the need for travel restrictions.
- Efforts to develop and update vaccines against COVID-19 must continue, informed by the monitoring of emergent variants. International collaboration, data sharing and genome sequencing will remain essential tools in identifying global variants of concern.

Behavioural and environmental interventions¹

- Even with high vaccination levels, we will all need to take action to suppress the spread of virus, limit the emergence and spread of new variants, and reduce the likelihood of epidemics of other respiratory diseases like influenza.
- As identified above, self-isolation of infected people is the most effective means
 of preventing transmission by reducing the likelihood that those infected are
 interacting with others. Continued access to fast and accurate testing is
 needed to underpin this and must be accompanied by clear and up to date
 information on symptoms and effective reminders of the actions that

- **people need to take**. As the UK Government has recognised, **avoiding unnecessary self-isolation** will be essential to support education, the economy, health and wellbeing.
- The test, trace and isolate (TTI) programmes must prepare for an increased demand for tests as result of the expected increase in people with respiratory symptoms in autumn and winter and consider how to incorporate multiplex testing (see below).
- Given overlapping symptoms, routine multi-pathogen testing for SARS-CoV-2, influenza (and possibly other respiratory infections) is important for surveillance, treatment decisions (such as timely use of antivirals for influenza), minimising isolation times, and avoiding and reducing rates of transmission. We strongly support multiplex testing. However, if this is not feasible, well-evaluated and accurate point-of-care testing (POCT) for influenza should be deployed in hospitals, primary care settings, care homes and community pharmacies.
- More guidance is needed from Governments in all UK nations to prevent spread of the disease in households where someone is infected. This includes practical advice on how to isolate the infected person, and guidance around ventilation of the house, cleaning and hand and respiratory hygiene.²
- Within workplaces and public buildings there should be a focus on ventilation and hand and respiratory hygiene as baseline measures that can reduce transmission of SARS-CoV-2 and other viruses without significant restriction on individuals or business activities. Governments must ensure that organisational and community guidance, training and financial investment are available to ensure infrastructure interventions such as ventilation can be properly implemented.
- The use of measures such as **face coverings**, **physical distancing**, **and working from home** should continue to be implemented in situations **where the risk of transmission is high** (e.g. crowded indoor spaces, areas with high infection rates, etc.). Such interventions would reduce other respiratory viral infections, such as influenza.
- The next few months must be used to **co-develop** with communities and organisations **a comprehensive communication and engagement programme** to identify and implement acceptable, feasible and effective mitigation measures to reduce transmission of COVID-19 and other infections.
- We have highlighted above the importance of collaboration between central and local governments; similarly, sharing advice for the planning and delivery of services across the four nations is also a priority.

Managing the wider health and wellbeing impacts of the pandemic

Estimates of the number of adults, children and young people affected by long COVID varies. Symptoms ranging from mild to disabling, may affect a number of organ systems and occur in diverse patterns. The occurrence of symptoms severe enough to impact education and employment, with working age adults at higher risk reinforces the need to reduce the rates of infection. Ensuring equitable access now to long COVID clinics, including for children, is a priority. Research including control groups is needed to improve understanding of the prevalence, range, severity and duration of long COVID; to inform optimal clinical management; and support health service planning and delivery.

- An additional priority is to establish the population prevalence of physical and cognitive deconditioning resulting from immobility and isolation of people in their own homes and those living in care homes during the pandemic. These data should be used to plan and prioritise reablement and rehabilitation resources for those most in need. Control of infection in care homes will protect residents and staff but also allow safe visiting to improve quality of life and reduce isolation.
- Substantial expansion of Improving Access to Psychological Therapies (IAPT) programmes, and high-quality community mental health services for the young and old is urgently needed. Crisis and liaison services will need to be available and promoted all around the country.
- In the longer term, public health agencies across all UK nations must address the
 wider social determinants of health (environmental, educational, employment,
 etc.), with a focus on decreasing health inequalities to address the wider public
 health impacts of the COVID-19 pandemic, and improve the UK's resilience
 ahead of any future outbreaks or new threats.

Supporting health and social care settings to ensure that COVID-19 and routine care can take place in parallel

- As the vaccination programme reduces the incidence and severity of COVID-19, the healthcare system must ensure it has capacity to address and reduce the backlog of non-COVID-19 care. Robust processes should be in place to ensure clinical prioritisation of elective procedures (e.g. regular clinical reviews of waiting lists), and access to treatment should be prioritised by clinical need rather than by length of wait. Restoring hospital bed capacity that has been limited by IPC measures for example through use of the private sector capacity and other initiatives such as 'surgical hubs' will be vital to getting through the backlog as this is a major bottleneck.
- Vacancy rates in the health and social care workforce must be addressed to
 minimise risk of burnout, and improve staff conditions and health, through
 exploring transferring or sharing duties, retaining retired staff, rapid recruitment,
 accelerated training, and using private sector capacity. We expect the
 pressures on primary care to intensify not least due to its ongoing role in the
 vaccination effort; increasing numbers of COVID-19 patients being treated in the
 community (rather than in hospital); and delayed treatment causing worsening of
 chronic conditions. Primary care will need sufficient resourcing and support,
 particularly throughout winter.
- Infection prevention and control must remain a key priority in hospital and social care settings and needs to fully reflect emerging evidence of how the virus is transmitted, including airborne transmission. There is a need for full investigation of transmission and outbreaks, prompt and transparent reporting, and publicly available data on rates of hospital-acquired infection so that factors influencing transmission can be understood and mitigated.
- In the longer term, evidence generated on the effective control of COVID-19 in hospitals and other health and social care settings needs to **inform the next** generation of buildings, and enable renovations of existing spaces to make them respiratory-infection safe.

In this report, we set out our priorities for safeguarding the health and the wellbeing of the UK population for winter 2021/22 and beyond. Many of our priorities are the same as they were in our report 'Preparing for a challenging winter 2020/21', published a year ago.³ As before, we need to focus on promoting the resilience of communities, populations and the health and social care system. Approaches will need to be adaptable and flexible to deal with a changing and uncertain landscape for the foreseeable future. Reducing health inequalities and developing rigorous, evidence-based approaches that are co-developed with relevant communities will be critical to the design and delivery of a successful and equitable response to the challenges that face us.

1. Overview of the report

In July 2020, the Academy of Medical Sciences published its report, 'Preparing for a challenging winter 2020/21'. This year, at the request once again of the Government Chief Scientific Adviser, the Academy established an Expert Advisory Group chaired by Professor Sir Stephen Holgate CBE FMedSci to:

- Explore the health and social care challenges, including inequalities in health, that will be presented by winter 2021/22 in terms of COVID-19 and non-COVID-19 care.
- Develop a range of scenarios for winter 2021/22 and, where possible, model health outcomes to inform planning.
- Identify the priority areas for action and likely most effective interventions to manage these challenges, and stakeholders to address these.
- Determine outstanding uncertainties that will require further investigation, including research, ahead of winter.
- Explore the transition towards achieving lower circulation levels of SARS-CoV-2.

The deliberations of the Expert Advisory Group were informed by a Patient and Carer Reference Group, whose views and discussions underpinned our guidance on priorities and concerns for winter 2021/22 and beyond. A 'People's perspective' written by the Patient and Carer Reference Group – which focuses on the need for continued public involvement in designing services, mitigations and communications, and the necessity to provide support at a community level to tackle inequalities – is provided in Annex 1. The development of this report was also supported by early to mid-career researchers. The composition of the Expert Advisory Group, Patient and Carer Reference Group, and early to mid-career researchers is provided in Annex 2.

A series of public discussion workshops were also undertaken as part of this project to explore patient and public views on the challenges for winter 2021/22 and beyond. Ipsos MORI conducted five online workshops with a panel of thirty-two members of the public drawn from across the UK, including representatives of ethnic minority groups and those who had received shielding letters or cared for someone who had received one during the COVID-19 lockdown measures. Eight of these panel members were returning participants from the Academy's previous COVID-19 winter project in 2020. Fourteen young adults (18-24 years old) from the Academy's Planet DIVOC-91 Young Person UK panel also took part in Ipsos MORI workshops. A summary of findings is provided in Annex 3 and the full report can be downloaded from the Academy's website. The work of both our Patient and Carer Reference Group and the Ipsos MORI workshops were informed by an online workshop with The Health Foundation Inclusion Panel.

In addition, we consulted the Medical Royal Colleges to gain their insights into the challenges they anticipated facing this coming winter within their respective areas of practice, and how these could best be mitigated. A full list of respondents is listed in Annex 2.

The Academy is indebted to all those who contributed to this report and is particularly grateful to all those who also contributed to the development of our COVID-19 winter report last year.⁸

This report sets out a number of priorities for safeguarding the health and the wellbeing of the UK population for winter 2021/22 and beyond. Many of our priorities are the same as they were in our previous report. As before, we need to focus on promoting the resilience of communities, populations and the health and social care system. While there is an understandable and intense desire for 'normality' to return, approaches will need to be adaptable and flexible to deal with a changing and uncertain landscape for the foreseeable future. Reducing health inequalities and developing rigorous, evidence-based approaches that are co-developed with relevant communities will be critical to the design and delivery of a successful and equitable response to the challenges that face us.

While we know that winter climatic conditions and more time spent indoors will favour the spread of SARS-CoV-2 and other viruses this winter, there is still a lot of uncertainty about how the pandemic will evolve over the coming months. Many of the key determinants of future behaviour remain poorly understood, and the picture is likely to change as additional evidence emerges over the coming months. Throughout the coming year, as the SARS-CoV-2 and other respiratory virus epidemics unfold, it is imperative to use such information to prepare, adapt and refine planning to mitigate the likely risks. Knowledge exchange and co-ordination between the four nations will be vital. In addition, as we see greater variability in COVID-19 transmission and outbreaks at a local level, there needs to be a collaborative partnership between central and local government.

This report is a rapid review and provides a summary of the current research available at the time of writing (including those in pre-print which are clearly noted in the references) rather than an exhaustive literature review. It draws on the most recent evidence and has not been subject to formal peer-review. The report is the considered input of the Expert Advisory Group and does not necessarily represent the position of the Academy of Medical Sciences or the individual members of the group. This independent overview of the scientific evidence has been provided in good faith by members of the Expert Advisory Group and the Academy of Medical Sciences, who accept no legal liability for decisions made based on this evidence.

2. An uncertain and evolving pandemic

As the UK emerges from the challenging winter of 2020/21, the COVID-19 pandemic situation continues to evolve globally, and the focus remains on mechanisms to overcome and ultimately recover from the pandemic, while learning to live with the virus. Although the world is still in the midst of a pandemic, the situation the UK is facing is very different to that which it faced this time last year.

Last year, the UK population was highly susceptible to COVID-19 and no vaccinations were available. We currently have a much smaller susceptible population, resulting from a combination of widespread vaccination and natural infection. However, whilst whole groups of the population remain unvaccinated (such as children and teenagers), new SARS-CoV-2 variants are emerging and the global incidence is much higher. The circulation of influenza and other respiratory infections were very low over the winter 2020/21¹⁰ due to the measures that were put in place to contain COVID-19 – such infectious diseases may well re-emerge with renewed vigour this winter as restrictions are lifted, mixing increases and the population is more susceptible to these diseases given its limited exposure to these viruses over the last winter.

Last year, deaths and hospitalisations from COVID-19 were high, instances of long COVID were only starting to emerge, and the backlog of care was rising. At present, deaths and hospitalisations from COVID-19 are much lower, we are starting to understand more about the range, severity and duration of long COVID, and the delays in non-COVID-19 care have reached unprecedented levels. In addition, there is growing evidence that the COVID-19 pandemic has indirectly affected the health status of the population at large, ¹¹ including an increase in mental health problems, and a possible epidemic of cognitive and physical decondition amongst older people with frailty that remains unquantified.

Last year, staff in the health and social care sectors were working tirelessly to fight the COVID-19 pandemic and much non-COVID-19 care had to be put on hold. This year, the health and social care workforce is fatigued and is having to continue to provide care for people with COVID-19 while at the same time resuming non-COVID-19 care safely and tackling the long waiting lists that have accumulated.

Therefore, while the challenges that the UK will face this coming autumn and winter are similar in nature to last year, their manifestation is very different. Addressing them will require coordinated effort across government, the health and social care system and the scientific community, who will need to work in tandem with the public, patients and carers to co-produce workable solutions and engagement, as well as clear, understandable and culturally appropriate communication plans to ensure widely adopted, effective interventions.

This report focuses on three challenges that are likely to exacerbate pressures on the health and social care system over the autumn and winter, and sets out a series of options to mitigate their impact. These challenges are:

1. A resurgence of respiratory infectious diseases, including COVID-19, influenza and respiratory syncytial virus (RSV).

- 2. Managing the wider health and wellbeing impacts of the pandemic, including long COVID, mental and physical deconditioning, and delays in diagnosis and disease management.
- 3. Continued disruption to health and social care service delivery, including workforce management, managing the backlog of care and incorporating infection control measures into routine workflow.

These factors need to be considered in the context of winter when:

- Pressures on NHS services are high due to increased incidence of infectious diseases and non-infectious conditions that increase in prevalence or are exacerbated during the winter months, e.g. asthma, chronic obstructive pulmonary disease (COPD), ischaemic heart disease, myocardial infarction and stroke. 12,13,14
- The NHS is typically operating at maximal capacity despite bed capacity rates of over 90% being associated with increased morbidity and mortality, bed occupancy over winter has regularly exceeded 95% in recent years. 15,16 This will be exacerbated by the fact that the NHS is operating with reduced bed capacity due to infection control processes. In addition, social care has been hit by the pandemic, particularly care homes, where reduced bed occupancy has left many providers in financially precarious circumstances.
- Staff across the sectors will have been responding to a prolonged pandemic for over 18 months, many directly affected by COVID-19, compounding issues of staff burnout, turnover and shortages that are likely to be exacerbated by early retirement and recruitment challenges.¹⁷
- As in any winter, availability of NHS staff and facilities (including support facilities such as laboratories) may be reduced due to winter health impacts and winter weather disruption (e.g. snow and flooding).¹⁸
- Adverse winter weather negatively impacts on both physical and mental health, and access to healthcare, particularly in older people and those with disabilities.^{19,20,21,22}

It should be noted that the impact of meteorological and air quality factors (often referred to as 'seasonal variation') on SARS-CoV-2 transmission remain unclear. ²³ Although seasonal climatic patterns (weather) may affect rates of COVID-19, they may not be the primary driver. ²⁴ There is some evidence from laboratory studies that SARS-CoV-2 survives longer under cold, dry and low ultraviolet radiation conditions. ²⁵ However, it is still unclear whether direct meteorological influences on the virus have a meaningful influence on transmission rates under real world conditions. Other relevant drivers include changes in human behaviour, demographics of affected populations and virus mutations. ²⁶ Recent modelling has suggested that SARS-CoV-2 transmission is influenced by seasonal variation. ²⁷ However, while the seasonality of SARS-CoV-2 transmission is comparable in magnitude to the most effective individual behavioural and environmental interventions (e.g. gatherings limited to 10 people or less), it is less than the combined effect of multiple interventions. So, while evidence suggests that warmer climates may slow the spread of SARS-CoV-2, relying on weather changes alone to slow the transmission of COVID-19 is unlikely to be sufficient. ²⁸

Our report focuses on the autumn and winter 2021/22 due to the additional challenges COVID-19 may present over this period. However, we also set out a range of

considerations that will affect the course of the UK epidemic and the country's attempt to transition towards more stable, lower levels of SARS-CoV-2 in the longer term.

3. A resurgence of infectious respiratory diseases, including COVID-19, influenza and respiratory syncytial virus

3.1 A resurgence of COVID-19

At the time of writing (early July 2021), the UK has been experiencing an increase in transmission of SARS-CoV-2. This is due to the emergence of the Delta variant (B.1.617.2), which has now replaced the Alpha variant (B.1.1.7) as the dominant circulating variant (see Annex 4 for an overview of SARS-CoV-2 variants). Since the middle of May 2021 reported cases have increased exponentially consistent with R_t in the range 1.1-1.4.

The current vaccines continue to provide a good level of protection against the Delta variant, particularly following two doses.^{31,32} Combined with the high levels of vaccine uptake across the population, the vaccination programme is reducing both the risks of severe outcomes and the level of onward transmission.

However, vaccines do not provide 100% protection - current estimates suggest approximately 95% protection against hospitalisation but lower levels of protection against infection and symptomatic disease. Turthermore, whilst vaccine roll-out continues, a significant proportion of the population will remain susceptible to infection in the coming weeks because they have either not received the vaccine (notably children) or have only received a single dose that offers lower levels of protection against the Delta variant (35% against symptomatic disease). As restrictions are fully lifted, it is likely that even higher levels of virus than those we are currently experiencing will circulate in the community, and this is expected to result in a third peak of infections (Figure 1).

The scale and timing of this peak remains uncertain as this will depend on the extent to which the full lifting of restrictions returns patterns of contact between people to normal. The degree to which this third peak will put pressure on the health service is also uncertain, but there is a clear risk that services could be stretched over the next two to three months or into the winter period. This would be due not only to the rise in infections, which are likely to result in an increase in hospitalisations, but also due to staff disruptions caused by requirements to self-isolate, etc. While the resulting mortality associated with this wave is expected to be less severe than over winter 2020/21,35 the level of ongoing transmission in those under 50 years old may lead to higher levels of long COVID than observed in the previous two waves. If COVID-19 cases were to rise, or remain elevated, in autumn/winter, this could coincide with a possible peak in influenza and respiratory syncytial virus (RSV) infections, which would put extra pressure on the health service (see sections 3.2.1 and 3.2.2). As natural immunity wanes across the population, it is possible that there could be future smaller waves. As for the coming months, the timing and magnitude of this is uncertain since we do not yet know how long immunity will last.

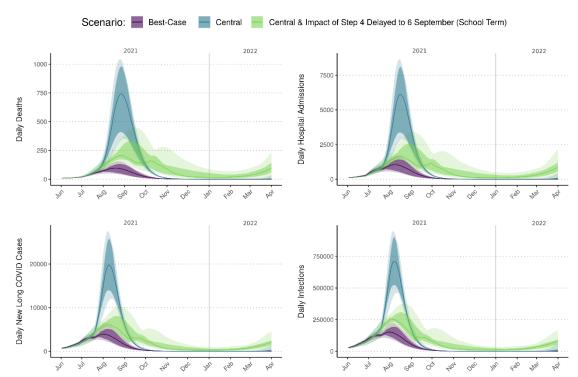


Figure 1: Projected range of possible scenarios for COVID-19 in the UK from June 2021 through to April 2022. The central-case scenarios (blue and green) incorporate current estimates for key epidemiological parameters whilst the best-case scenario (purple) incorporates optimistic assumptions. Two central scenarios are shown reflecting uncertainty in the impact of Step 4 of the roadmap out of lockdown that will occur on 19 July 2021. The 'central' blue scenario assumes an increase of Rt reflecting an increase in contact patterns. The 'central delayed' green scenario assumes that the increase in contact patterns from Step 4 is counteracted by the school summer holidays such that the impact on transmission occurs from early September 2021 when schools reopen. Long COVID incidence shown is based on ONS reports; as these are self-reported data, the scale of this remains highly uncertain. Scenario assumptions are shown in Annex 5. Our reasonable worst-case scenario is shown in Annex 6. All scenarios incorporate current best estimates of vaccine effectiveness.

The emergence and rapid spread of the Delta variant demonstrates that the UK will remain at risk from future variants while SARS-CoV-2 continues to circulate globally. It is not possible to predict the probability of such events nor their timing. However, as demonstrated in our reasonable worst-case scenario (see Annex 6), if such a variant were to emerge later in the year, there remains the potential for a fourth wave of infections occurring early in 2022.

We explore variants of concern in greater detail below, followed by a suite of options to mitigate the impacts of COVID-19.

3.1.1 Variants of concern

3.1.1.1 Drivers of variation

Environments in which variants with a clinically significant change in phenotypic characteristics could arise include settings with high rates of transmission, particularly

where the population has partial immunity.³⁷ Such settings can lead to the selection of variants with a competitive advantage for transmission and/or vaccine escape over existing variants. A number of case studies that have followed immunocompromised people with chronic SARS-CoV-2 infection, in which deep sequencing of samples was undertaken over time to detect genetic variation, have reported that the SARS-CoV-2 genome may evolve within a single host.^{38,39} These changes may follow the administration of specific treatments (e.g. convalescent plasma). It has been speculated that this is one of the circumstances under which important variants may arise.⁴⁰ The SARS-CoV2 virus mutates at a lower rate than many other viruses including influenza, but the more the virus circulates globally, the greater the opportunity it has to change.⁴¹ Fundamentally, limiting the transmission of the virus will be key to preventing the emergence and spread of new variants.

3.1.1.2 Variants of significance

Both the Patient and Carer Reference Group and the public dialogue workshops raised the threat posed by the emergence of variants as a key concern. ⁴² Phenotypic changes in SARS-CoV-2 that could influence our ability to manage and contain the virus are differentially classified by the Centers for Disease Control and Prevention (CDC) ⁴³, World Health Organization (WHO), ⁴⁴ and Public Health England (PHE). ⁴⁵ Factors considered in the assessment of significance are as follows: an increase in transmissibility or detrimental change in COVID-19 epidemiology; an increase in virulence or change in clinical disease presentation; and/or a decrease in effectiveness of public health and social measures or available diagnostics, vaccines, or therapeutics. Here we have chosen to use the PHE definitions.

Variants of concern detected thus far have led to increased virus transmissibility, reduced susceptibility to certain treatments and, for the Alpha variant, more severe illness. 46,47,48 During June 2021, the Delta variant accounted for 94% of cases in the UK, 49 and is responsible for the recent rise in cases. 50

Vaccine effectiveness against symptomatic disease is reduced for the Delta variant and is currently calculated to be 32-38% following one dose and 78-80% following two vaccine doses. ⁵¹ There is also evidence that this variant has been >50% more transmissible than Alpha in the UK between April and June 2021, and may cause more serious disease. ⁵²

This is key evidence that behavioural and environmental interventions, such as limiting close contacts, adequate ventilation and personal protective equipment (PPE), will remain important in preventing infections going forwards and that increased social mixing is likely to be associated with a rise in infection even amongst fully vaccinated individuals. Despite the above limitations, vaccination remains our best tool in combating the Delta variant and it is reassuring that vaccines appear to remain effective in reducing the risk of hospitalisation, with two doses of any vaccine being 94% effective against hospitalisation. The limited available data, even now, on the immunology and risks associated with the Delta and Alpha variants highlight the challenges of collecting evidence at pace to inform decision making. Surveillance measures and cohort studies will continue to be essential in identifying new variants of significance and their impacts as they arise.

3.1.1.3 Detecting clinically significant variants

A challenge in detecting clinically significant variants is that new variants are constantly arising, and the impact of most mutations are relatively poorly understood, particularly outside of the spike protein. It can take weeks or months to establish estimates of transmissibility and/or immunology of new variants after they emerge. This creates a major challenge and we can expect to see many variants emerging that must be managed with an imperfect understanding of their biological meaning. The increasing diversity in combinations of mutations found together is also challenging, as it is difficult to predict the summary impact on biological behaviour of increasingly complex combinations.

3.1.1.4 Immune escape variants

As widespread vaccination programmes remain our best chance of controlling SARS-CoV-2 globally, the potential emergence of vaccine resistant variants is a significant concern for this winter and beyond. A spectrum of mutations is accumulating in the SARS-CoV-2 spike protein gene, which encodes the protein targeted by vaccines. For some variants of concern, *in vitro* studies have demonstrated reduced virus neutralisation by convalescent and post-vaccination sera. Reassuringly however, clinical trial and real-world evidence continues to indicate that vaccines are effective, including against variants that have the most concerning profiles based on experimental evidence and the Delta variant, which is currently dominant in the UK. As mentioned above, current data suggests one vaccine dose is 32-38% effective against symptomatic infection and 69-88% effective against hospitalisation. Two vaccine doses increase this to 78-80% against symptomatic infection and 91-98% against hospitalisation. Importantly, vaccine efficacy in preventing long COVID and long-term consequences of infection remains unknown. Trials of variant vaccines are currently underway, with a view to staying ahead of emerging coronavirus variants.

Evolutionary biologists are postulating how long it might be before a variant of high consequence arises (where there is clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness relative to previously circulating variants). This would have a substantial effect on disease control, but there remains huge uncertainty about the likelihood of this event occurring. Work is currently being undertaken to predict potential driver mutations that may appear in future SARS-CoV-2 variants of concern, which may help inform future public health strategies.

While current vaccines are effective in generating immunity to SARS-CoV-2 variants that have become prevalent thus far, the future emergence of vaccine resistant variants remains a significant concern.⁶¹ This risk suggests adapted versions of currently available vaccines will be needed in the future. **Further large-scale vaccination programmes with modified vaccines are likely to be required as part, of or in addition to, booster vaccination programmes**, given that the longevity of protection provided by vaccines is at present unknown (see section 3.1.2.1). Given the potential interaction between SARS-CoV-2 infection and other respiratory viruses, consideration should be given to programmes of combined influenza and SARS-CoV-2 vaccination (see section 3.1.2.1).⁶²

3.1.1.5 Spread of new variants

Understanding the mechanisms behind why variants are more transmissible is important for determining whether mitigation measures will be effective. For example, NERVTAG assessment suggests higher viral load and/or infectious dose for the Alpha variant, 63 which implies transmission by all routes is easier, and some that may be minor (e.g. airborne) could become more important if there is more virus exhaled or less virus needed to establish an infection.

3.1.1.6 International travel and opening of borders

The opening of borders for travel combined with limited global vaccine availability will facilitate the spread of viral variants. 64,65 While widespread vaccination of those travelling will reduce this risk, it cannot be eliminated and further work is needed to understand the potential role of vaccinated individuals in viral transmission, and impact on severity/risk of hospitalisation, particularly for new variants, such as Delta, which confer a degree of vaccine resistance. 66 Concerns around increasing case numbers and international circulation of new variants are further complicated by the many measures and regulations that then need to be followed by travellers (the need for clear communication on this topic was raised in the public dialogue workshops).⁶⁷ Although travel and tourism are important for the UK and global economy, careful consideration will still be required with regards to combating COVID-19. Evidence has also suggested that international travel played an important part in shaping the early transmission dynamics of the COVID-19 pandemic.⁶⁸ The impact of vaccination and changes to travel rules will need to be carefully monitored by scientists and Governments in all UK nations, particularly as further new variants emerge. Coordination will be needed across the four nations where diverging travel and quarantine rules may allow the introduction and spread of new variants if certain rules are more permissive.

Going forwards, emphasis will need to be placed on mitigating the risks of transmission at every stage of a travel corridor. Consideration will need to be given to requirements for testing at the country of origin and destination, quarantine rules at the destination, and measures to reduce mixing and transmission during travel, factoring in the impact of vaccination status. These will be important considerations ahead of the arrival of international students over the autumn.

The potential for the appearance of new, vaccine-resistant variants and the likelihood of at least some delay in their identification, means that the public should be encouraged to consider behavioural and environmental interventions when travelling to or from countries with high COVID-19 circulation.

3.1.1.7 Global surveillance

Genome sequencing will remain an essential tool in identifying global variants of concern. While there is very strong provision of genome sequencing in the UK supported by the development of the COVID-19 Genomics UK Consortium and public health agencies, many countries have limited or no genome sequencing capabilities or data and do not have clear information on the circulating variants; in particular, whether sequenced isolates were from random or targeted testing. ⁶⁹ Variants detected in many Low- or Middle-Income countries (LMICs) may not be widely sequenced, which also needs to be considered in the context of an increasingly concentrated COVID-19 burden in LMICs (see Figure 2). ⁷⁰ These limited sequencing resources mean that 'blind spots'

exist in many countries.⁷¹ Delays in the identification of new variants of concern means that steps to reduce their spread cannot be taken and enables them to become rapidly disseminated.^{72,73,74} To date, new variants of concern have been associated with rapid increases in case numbers in the affected area, as was seen in Kent, Brazil, South Africa and India. Global monitoring for sudden surges in cases may foretell the identification of a new variant.

Sequencing platforms will need to be adopted globally to enable effective identification and tracking of new variants internationally. The UK has good connectivity between scientists who focus on genomics, genotype to phenotype, immunology, and structural biology. It will be important to regularly review the effectiveness of this connectivity over time and to harness this expertise to benefit global sequencing surveillance systems. The newly announced Centre for Pandemic Preparedness will be essential in spearheading the UK's efforts to bolster global surveillance and genome sequencing. We welcome the recent commitment by G7 countries to boost global surveillance and genomic sequencing, attempting to achieve a level of genomic sequencing of at least 10% of all new positive COVID-19 samples during the pandemic phase and share genomic sequencing information with existing global databases. The UK is currently meeting the 10% target. It is essential this is maintained and that other countries are supported to increase their sequencing capabilities.

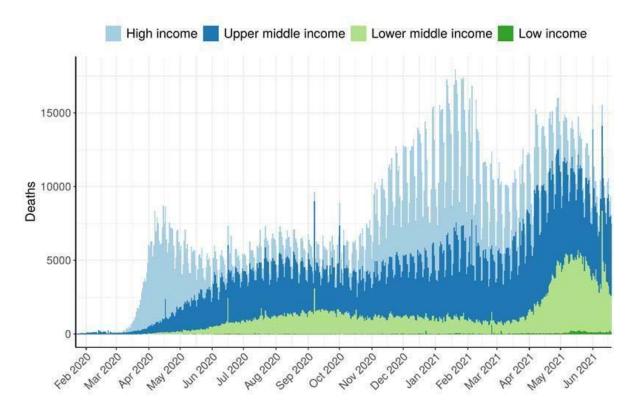


Figure 2: Global reported deaths from COVID-19.⁷⁹ Please visit the website for further details about the methodology and caveats. Copyright © 2020 Imperial College London. MRC Centre for Global Infectious Disease Analysis. All rights reserved.

3.1.2 Mitigating impacts of COVID-19

Mitigating the impacts of COVID-19 and preventing community outbreaks will depend on optimising vaccine coverage and maintaining immunity against the virus; effective use of behavioural and environmental interventions to limit the spread of infection; and testing, tracing and isolating infected individuals, with efficient outbreak investigation and control. Controlling the spread of infection will be particularly important in high-risk environments and vulnerable populations, such as care homes and hospitals (which we discuss in detail in section 5.3), as well as in the wider community (e.g. households, schools, etc.). Effective communication strategies to initiate and sustain behaviour change will underpin the successful implementation of mitigation measures to reduce transmission of SARS-CoV-2 (and other winter viruses).

3.1.2.1 COVID-19 vaccination strategies

A key challenge in the coming months and beyond will be to prevent and control outbreaks of COVID-19. Outbreaks are most likely to occur in unvaccinated populations, or in populations where natural or vaccine-mediated immunity has waned. 80 As discussed in section 3.1.1, the emergence of vaccine-resistant variants is probable, but the extent of resistance is hard to predict. In Chile, there was a rise in infections despite a vaccine coverage of 60%, leading to a lockdown in the capital Santiago in June 2021.81

Clearly, high levels of vaccination need to be combined with behavioural and environmental interventions to limit the spread of infection. Ensuring high uptake of COVID-19 and influenza vaccines was a key concern for the Patient and Carer Reference Group. The benefit of COVID-19 vaccination was also a key discussion topic in the public dialogue workshops. Discussions focussed on vaccine hesitancy, particularly in young people where the benefits of COVID-19 vaccination were considered to be less obvious relative to the risks.

It is important that focussing efforts on COVID-19 vaccination should not interfere with the delivery and production of important non-COVID-19 vaccine programmes, including seasonal influenza (discussed in section 3.2.1.4) and routine child and adolescent immunisations (discussed below).

Unvaccinated adult populations

Overall, the UK population has a high COVID-19 vaccine acceptance rate. 84,85 As of 27 June 2021, 84.4% of people aged 18 and over in the UK had received their first dose (over 44.4 million people), 61.9% their second dose (over 32.5 million people), amounting to over 77 million vaccinations given. 86 Although the UK has one of the largest vaccine uptake rates of any major nation, 87,88 there is regional, 89 ethnic, cultural and socio-economic variation. 90

Recent datasets have shown that deprivation is the most important association with low COVID-19 vaccine uptake, and some cultural and religious groups may be more hesitant than others to accept the COVID-19 vaccination. ⁹¹ Adults living in the most deprived areas of England were three times as likely to report vaccine hesitancy (10%) than adults living in the least deprived areas (3%). ⁹² Lower English language proficiency was associated with lower vaccination rates amongst adults aged 50 years and over. ⁹³ The lowest vaccination rates were for those who do not speak English at all (75.3%) and

those who do not speak English well (75.9%). In comparison, vaccination rates were 92.7% for those whose main language is English.⁹⁴

Recently published UK vaccine uptake data in patients aged over 80 not in a care home (Dec 8 2020-March 17 2021) has shown lower vaccination rates, particularly in those reporting as being from Black backgrounds (68.3%) compared to White British backgrounds (96.2%). 95 Black or Black British adults were much more likely to decline vaccination than White adults: around 1 in 5 (21%) Black or Black British adults reported vaccine hesitancy, the highest compared with all other ethnic groups (28 April to 23 May 2021). 96 Patients with pre-existing medical conditions were equally or more likely to be vaccinated with two exceptions: those with severe mental illness (89.5% vaccinated) and those with learning disability (91.4%). 97

Although positive sentiment towards the vaccine is high and has increased since early December 2020 across all age groups, it is lower among younger than older adults. 98 On 27 June 2021, the NHS announced that it had vaccinated half of all adults in England aged under 30, accounting for more than 4.2 million people aged 18 to 29 years of age. 99 However, the REACT-1 study recently reported that that the increase in prevalence of SARS-CoV-2 during the period 20 May to 7 June 2021 was being driven by younger age groups, with five-fold higher rates of swab-positivity among younger children (ages 5 to 12 years) and young adults (18 to 24 years) compared with those aged 65 years and older, and 2.5-fold higher rates among those below 50 years compared with those 50 years and above. 100 The authors suggested that the expansion of the vaccine programme to those aged 18 years and above should help substantially to reduce the overall growth of the epidemic. 101 To minimise the risk of outbreaks in universities or colleges, as was seen in multiple universities at the start of the 2020/2021 academic year, 102 students should be encouraged to receive two doses of the COVID-19 vaccine before returning to these educational settings in the autumn.

Health and social care workers are at high risk of contracting infection, having severe outcomes and at risk of transmitting the virus to patients and staff. However, there is variation in the percentage of frontline NHS healthcare staff who have been vaccinated against COVID-19 in England. We discuss in section 5.3.3 the importance of maximising vaccination coverage in health and social care workers, including non-clinical and agency staff.

Another group that will warrant further attention is vaccination in pregnant women. A preliminary study did not find any obvious safety signals among pregnant women who received mRNA COVID-19 vaccines in terms of adverse effects or adverse neonatal outcomes. On the other hand, there is evidence of adverse outcomes from contracting COVID-19 in the late stages of pregnancy. In particular, pregnant women from black or ethnic minority groups (or with other risk factors such as hypertension, diabetes or raised BMI), may be at higher risk of complications of COVID-19.

There is mounting acceptance that neutralising antibody in the blood is a surrogate marker for vaccine-induced protection against infection. The protective efficacy of vaccines shows some variation, to but is generally substantial, even against new variants. Vaccines also give substantial protection against viral replication and

therefore both symptomatic and asymptomatic infections. The immune response induced by infection shows considerable durability in most of those infected, and antibody in the airway fluid is boosted by vaccination. Box 1 provides an overview of our understanding of COVID-19 vaccine effectiveness to date.

Box 1: COVID-19 vaccine effectiveness

PHE's Week 26 COVID-19 vaccine surveillance report indicated that: 114

- Vaccine effectiveness against symptomatic disease ranges from ~55-70% after 1 dose, with little evidence of variation by vaccine or age group, and ~65-90% after two doses. Evidence suggests that vaccines have some reduced effectiveness against symptomatic disease with the Delta compared to Alpha variant.
- Vaccine effectiveness against hospitalisation in older adults ranges from ~75-85% after 1 dose of the Pfizer-BioNTech or Oxford-AstraZeneca vaccine. Similar vaccine effectiveness against hospitalisation was seen with the Alpha and Delta variants.
- Data suggests high levels of protection against mortality, with the Pfizer-BioNTech and Oxford-AstraZeneca vaccines ~75-80% effective at preventing death with COVID-19 after a single dose, ~92-98% effective after 2 doses.
- Estimates of effectiveness against infection after 1 dose range from ~55-70% with the Pfizer-BioNTech vaccine, and ~60-70% with the Oxford-AstraZeneca vaccine. Estimates for 2 doses are currently only available for the Pfizer-BioNTech vaccine and indicate effectiveness against infection of ~70-90%.

In addition, vaccines are associated with large reductions in all SARS-CoV-2 infections regardless of symptoms, with protection that is nearly as high as that provided against symptomatic COVID-19. There is increasing evidence that SARS-CoV-2 vaccines can substantially reduce transmission through decreasing the probability of both: 1) a recipient becoming infected, by protecting against both symptomatic and asymptomatic infection; and 2) secondary transmission from an infected vaccine recipient by reducing the duration or degree of infectiousness. Recent evidence from PHE suggests that immunisation with either the Pfizer-BioNTech or Oxford/AstraZeneca COVID-19 vaccines reduces the chance of onward virus transmission by 40-50%.

Given that two doses of the vaccine are required to provide maximum protection, in particular against the Delta variant, ^{118,119,120} **Governments in all UK nations should focus on securing high uptake rates with two doses of COVID-19 vaccine over the summer in all age groups over 18 years of age.** Ensuring clinically vulnerable groups and adults over 50 have received two doses of the vaccine should be the priority, given the increased risk of hospitalisation and deaths in these groups. ¹²¹ Emphasis should also be placed on vaccinating staff or family members who provide close personal care and amongst those living in areas of deprivation and persistent transmission of SARS-CoV-2.

In addition, there should be a particular focus on improving vaccination rates in communities with low vaccination rates (as described above) using methods showing

most promise, including co-design and delivery of approaches with local communities (see below).

Governments in all UK nations should develop specific evidence-based and formally evaluated strategies to enhance vaccine uptake in different communities. Strategies should consider tailored and culturally relevant communications to socially disadvantaged groups (ethnic minorities, homeless, socioeconomically disadvantaged, among others) available in multiple languages; tackling vaccine hesitancy, barriers to accessing the vaccine, and circulating misinformation; engagement and co-production with relevant communities; and use of trusted sources, such as community leaders and health providers (see Box 2). 122 Our Patient and Carer Reference Group highlighted that providing access to and choice of vaccine were important considerations for improving vaccine uptake. The extent of fearmongering over vaccine side-effects was seen as a key factor in deterring people from being vaccinated. They also raised concerns around the alienation of those who cannot be vaccinated, both in terms of people's attitudes and in policy development (e.g. COVID passports).

Box 2: Summary of strategies for interventions to increase vaccination uptake

The following strategies were outlined by Raza M, *et al.*, and offer approaches that clinicians and policymakers can adopt to help people make informed decisions about COVID-19 vaccination: ¹²³

- Offer tailored communication from trusted sources such as community representatives, healthcare providers, and local authorities that is culturally relevant and accessible in multiple languages.
- Improve access to vaccines. This may include flexible delivery models in the community, such as GP practices and outreach programmes with good transportation links.
- Community engagement. Work with community champions, youth ambassadors, faith leaders, and healthcare workers to raise knowledge and awareness on vaccinations; celebrate household members, friends, relatives, and role models being vaccinated; foster an approach of community immunity and helping others; and create locally developed action plans and a continuous, open, and transparent dialogue.
- Training and education of those involved with engagement activities at a local level: use relevant educational materials (e.g. e-Learning modules) in presentations and communication skills training.

The NHS will need to maintain its capability for mass vaccination throughout and beyond this summer, if required alongside the annual autumn influenza vaccination programme (see section 3.2.1.4). It should explore the continued use of non-clinical trained vaccination staff to alleviate pressures on primary care, as well as other initiatives to improve access and uptake (e.g. on-site vaccination centres on university campuses), and be prepared to administer booster doses of SARS-CoV-2 vaccines if levels of protection resulting from prior infection or vaccination

show evidence of decline (e.g. in the vulnerable and those that were first vaccinated – see below).

Outbreak response surge capability should also be available to counter outbreaks in unvaccinated populations, by implementing targeted vaccination strategies and additional behavioural and environmental interventions. Accurate monitoring of coverage and immunological protection will be essential to prepare for and mitigate potentially large outbreaks in poorly covered communities, and to target primary and booster vaccination strategies.

Uncertainty remains regarding possible protection against new SARS-CoV-2 variants. There should be a focus on monitoring for new variants, and coordination across UK Governments, academia and industry in developing and testing new vaccines against known variants of concern and others that might emerge. Some variants of concern can be predicted a few months in advance using modelling and this may help in short-term planning. There is also a need to support global vaccination programmes to control the pandemic and reduce the risk of the emergence of new variants of concern.

Duration of immunity and COVID-19 booster strategies

Neutralising antibody levels have been shown to be highly predictive of immune protection from symptomatic SARS-CoV-2 infection, 125 with variability across the different COVID-19 vaccines. Waning of immunity is likely to impact the risk of infection, transmission and severe disease in different ways, with many unknowns.

Evidence shows that antibody titres in vaccinated individuals peak three to four weeks following vaccination. ¹²⁶ However, there is limited information on duration of immunity post-vaccination, as follow-up periods for vaccinated persons are not yet long enough to draw conclusions on the duration of protection against infection or disease in the long term (the same is true for determining the duration of protection against infection beyond 12 months after natural infection). ¹²⁷ Protection may vary for individuals of different ages, people with underlying comorbidities, people who are immunocompromised and by vaccine product. Studies have shown that chronic infection in patients who are immunocompromised can lead to emergence of escape variants. ^{128,129}

Some vaccine regimens induce higher antibody titres that target the S1 domain of the SARS-CoV-2 spike protein than for natural infection, with serum from vaccinated individuals showing greater neutralisation capacity against homologous SARS-CoV-2 viruses *in vitro*. ¹³⁰ While vaccination has been shown to result in robust T cell responses, and memory and effector function have been demonstrated against multiple viral epitopes, the significance of T cell responses for protection and at population level, independent of memory B cell responses, remains unclear. ^{131,132,133,134} There is also a need to evaluate the durability and cross-reactivity of B cell and T cell responses to variants of concern ¹³⁵ that demonstrate increased transmissibility, severity, and immune escape potential. ^{136,137}

It is thought that protection against outcomes such as infection, transmission risk, or severe disease may wane over time. Indeed, although virus-specific B cell and T cell

responses are evident shortly into the recovery from infection or vaccination, they are prone to wane over time, with decreasing numbers of circulating virus-specific memory T cells, memory B cells, and serum antibodies. Surveys and cohort studies will need to monitor waning immunity, antibody thresholds for protection, neutralisation against current and emerging variants, and how antibody response and waning varies across clinical groups.

Better understanding the duration of immunity following vaccination, and the immunity provided by current vaccines against variants of concern, will be critical to informing a potential COVID-19 booster strategy. We welcome the Joint Committee on Vaccination and Immunisation (JCVI) interim advice that any potential booster programme should begin in September 2021 to maximise protection in those who are most vulnerable to serious COVID-19 ahead of the winter months and that, where possible, it should be delivered alongside the influenza vaccination programme. ¹³⁹ In finalising its advice about a potential COVID-19 booster vaccine programme before September, JCVI will need to confirm:

- When boosters should be administered to offer maximum protection.
- Which populations/age groups should receive a COVID-19 booster vaccine (e.g. prioritising those most likely to have waning immunity, such as the vulnerable and those vaccinated first).
- Whether different types of COVID-19 vaccines can be 'mixed and matched' (heterologous vaccine schedules).
- Whether COVID-19 boosters need to include providing protection against new or multiple variants.
- Whether COVID-19 boosters should be co-administered alongside influenza vaccines (see below).

The COV-BOOST (Comparing COVID-19 Booster Vaccinations) vaccine trial is currently studying the use of seven different COVID-19 vaccines when given as a third dose. 140 This study should provide vital information to inform the possible booster vaccination strategy. A recent study has suggested that a third dose of Oxford-AstraZeneca COVID-19 vaccine, given at least six months after the second, boosted antibody levels, maintained T cell response, and resulted in higher neutralising activity against the Alpha, Beta (B.1.351) and Delta variants. 141,142 Trials are also currently ongoing to investigate mixed (heterologous) vaccine schedules and co-administration of COVID-19 and influenza vaccines. The Com-CoV (Comparing COVID-19 Vaccine Schedule Combinations) trial is exploring the use of different combinations of approved COVID-19 vaccines for the first and second immunisation doses. 143 Initial results suggest that mixing first and second doses of the Oxford-AstraZeneca and Pfizer-BioNTech COVID-19 vaccines yield strong immune responses. 144 The ComFluCOV vaccine study will provide further information on whether COVID-19 and influenza vaccines can be administered at the same time. 145 Novovax is currently testing the immunogenicity and efficacy of a combination quadrivalent seasonal influenza and COVID-19 vaccine, which has shown early success in animal studies. 146

Children and adolescents

Although the risk of severe disease and hospitalisation from COVID-19 are inversely proportional to age, and children and young people remain at low risk of COVID-19

mortality, children and teenagers under 18 represent a significant pool of unvaccinated people, accounting for 21% of the overall population of England and Wales. 147,148,149,150

Infection with SARS-CoV-2 takes a milder acute course in children than in adults. The importance of children in transmitting the virus is not yet clear and difficult to establish due to the large number of asymptomatic cases. ¹⁵¹ The role of children and adolescents in transmission appears to be very similar to adults in household settings, and they play a role in bringing infection into households, particularly when schools are open and other areas of society are in lockdown. ¹⁵² However, an infected student is less likely to transmit the virus within their school than within their household, ¹⁵³ and population-based school studies repeatedly show lower infection rates than in the surrounding community and little evidence of clustering within classes. ^{154,155} Adolescents play a larger role in transmission than younger children. Circulation of the virus in children and adolescents can increase the spread of the virus to more vulnerable groups and the risk of mutations.

Long COVID has been reported to affect children, with a UK Office for National Statistics' (ONS) survey (22 April to 14 December 2020) estimating that 12.9% of UK children aged 2 to 11, and 14.5% of children aged 12 to 16, still have symptoms five weeks after their first infection. 156 Adolescents appear to have a similar risk of post-acute sequelae as adults, 157, 158, 159, 160, 161 although many are self-limiting. It is important to note that studies including control groups (i.e. children who have not had COVID-19) are limited and many of the symptoms of long COVID are also very common in the adolescent population (e.g. fatigue, headache). 162 The degree to which long COVID will have longer term implications for their health and wellbeing remains unclear. There is also uncertainty about whether vaccines prevent or reduce long COVID (for further discussion of long COVID see section 4.2). 163 COVID-19 also has implications for interruptions to children's education, with current COVID-19 regulations stipulating a period of isolation for single or multiple class 'bubbles' following a positive test. This may have longer-term consequences for children's development, educational attainment and careers. 164 The UK Government has recently announced that requiring single or multiple class 'bubbles' to self-isolate after a positive case would end in England over the summer.

Limited data on mRNA COVID-19 vaccines in adolescents have shown that vaccines are highly effective and safe, ¹⁶⁵ although published safety data are limited. There are early reports of rare cases of myocarditis and pericarditis in young males after mRNA vaccines although causality has not been established. ¹⁶⁶ Some countries have or are considering expanding the use of COVID-19 vaccines in adolescents. For example, the United States (US) and France have already done so, by expanding the use of the Pfizer-BioNTech COVID-19 vaccine to adolescents from 12 years of age. ^{167,168} JCVI will need to continue to consider the possibility of vaccinating secondary school-aged children against COVID-19. This will need to consider safety data emerging from other countries, the balance of risks and benefits of both vaccination and natural infection at different ages, ethical issues and other impacts including wider effects on education, transmission and general wellbeing.

In parallel to COVID-19 vaccination, urgent consideration should be given to the impact of the pandemic on routine childhood immunisations, including school-based programmes for children and teenagers.¹⁶⁹ Vaccinations that are routinely delivered in

schools will have been interrupted by school disruptions and are likely to require catchup programmes. The influenza vaccination programme is also delivered through schools to years 1-7. Outbreaks of preventable infectious diseases like meningitis and influenza over the winter would put increased pressure on the healthcare system. Therefore, public health agencies in all UK nations should prioritise routine child/adolescent immunisations in the autumn and catch-up programmes should be implemented as necessary.

3.1.2.2 Continued use of behavioural and environmental interventions

SARS-CoV-2 and other respiratory viruses can be transmitted via four major modes of transmission: direct (physical) contact, indirect contact (fomite), (large) droplets and (fine) aerosols. 171,172 We need to know more about the relative contribution of each mode to the transmission of a particular virus in different settings, and how its variation affects transmissibility and transmission dynamics. While it is likely that droplets and fine aerosols dominate the spread of SARS CoV-2 173,174,175, and this is true for many of the other respiratory viruses, direct physical contact and indirect contact are known to be important mechanisms of spreading for many of these (including rhinovirus). 176

Given the routes of transmission outlined above, behavioural and environmental interventions (also known as 'non-pharmaceutical interventions' or 'NPIs'), such as physical distancing, face coverings, hand hygiene, good ventilation and stay-at-home orders, have proven effective in reducing the spread of SARS-CoV-2 in many contexts. 1777,178,179,180,181,182,183,184 Such interventions are likely to also reduce the transmission of other directly transmitted respiratory infections and therefore mitigate serious disease. 185,186,187,188,189,190 These interventions are largely ignored by the community during most winter virus seasons. If these interventions, including staying at home when ill, continue into the autumn/winter, their use could limit the spread of SARS-CoV-2 as well as other respiratory viral infections such as influenza. 191 There was general support for the continued use of behavioural and environmental interventions to limit the spread of infection at the public dialogue workshops. 192

It should be noted that there is an association between the severity of COVID-19 disease and air pollution, 193, 194, 195, 196 which also affects many other respiratory conditions. Examples include asthma and chronic obstructive pulmonary disease (COPD), which place additional pressure on the health system in the winter. Reducing exposure to air pollution would be beneficial and would contribute to the reduction in respiratory disease burden.

We advise the continued use of some behavioural and environmental interventions, accompanied by effective messaging, over the autumn/winter to decrease the spread of SARS-CoV-2, limit the emergence and spread of new variants, and reduce the likelihood of epidemics of other respiratory diseases like influenza. The approach to using behavioural and environmental interventions will need to focus first on reducing the likelihood that infectious people are interacting with others. As discussed in section 3.1.2.3, continued access to effective testing (including to support attendance at work, education, healthcare and events) and isolation when people are positive are both critical measures. To ensure adherence among those that need to self-isolate, the system must provide effective

support including protection of jobs, income and leave rights as well as practical and emotional support. These actions need to be accompanied by clear and up to date information on symptoms and effective reminders of the actions that people need to take. This should include clear communication around the modes of transmission and guidance for preventing the spread of the disease in households where someone is infected. Practical advice from Governments across all UK nations on how to isolate the infected person, and guidance around ventilation of the house, cleaning, and hand and respiratory hygiene, will be important.

Within workplaces and public buildings, there should be a focus on ventilation and hand and respiratory hygiene as baseline measures that can reduce transmission of SARS-CoV-2 and other viruses without significant restriction on individuals or business activities. Organisational and community guidance, training and financial investment will be needed to ensure infrastructure interventions such as ventilation can be properly implemented - these issues are highlighted in the Royal Academy of Engineering's interim report on infection resilient environments. 197

Consideration should be given to extending existing financial instruments, such as the Adult Social Care Infection Control Fund, to meet the financial needs of care providers with regard to staffing, and to allow additional infection control measures, such as ventilation, to be implemented (see section 5.3). 198

The use of measures such as face coverings, physical distancing and working from home should continue to be implemented in situations where the risk of transmission is high (e.g. crowded indoor spaces, areas with high infection rates, etc.). Such interventions are likely to reduce other respiratory viral infections, such as influenza.

As discussed in further detail in section 3.1.2.4, a comprehensive communication, engagement and funding programme should be developed in the next few months to ensure effective design and implementation of mitigation measures to limit the spread of COVID-19 and other infections prior to winter 2021/22.

All restrictions on social contact are expected to be lifted in England from 19 July 2021 at a time when the number of infections is rising rapidly. Depending on vaccination status, individual and environmental risk factors and people's own view of risk, many people may want to continue to take precautions in environments where the risk of transmission is high, such as indoors, in crowded spaces, and in areas where the levels of circulating virus are high. In addition, many would benefit from advice on how to avoid unnecessarily transmitting the virus where personal actions might put others, who may be more vulnerable, at risk. As restrictions lift, **Governments must provide clear guidance on the environmental and behavioural precautions (such as the use of face coverings, ventilation, physical distancing) that individuals and organisations can take to protect themselves and others, particularly those who are most vulnerable from infection.**

As we see greater variability in COVID-19 transmission and outbreaks at a local level, there needs to be a collaborative partnership between central and local government, with resources available to ensure capability for outbreak investigation and control by local authorities. **Local responses should be co-designed with local communities**

and delivered through local public health teams and primary care. In England, the recently established UK Health Security Agency will need to rapidly establish itself as a high-level trusted and effective health protection body with good connectivity across regional and local public health structures, and the NHS, and with a strong research capability. 199

Clear distinction of the roles and responsibilities between central and local government will allow timely and targeted interventions in response to the rapidly changing challenges of COVID-19. For example, central government has a clear role in the allocation of adequate resources, consistent messaging, monitoring of circulating viruses, vaccination schedules and national behavioural and environmental interventions. However, there should be adequate flexibility to allow local Directors of Public Health to use their extensive local knowledge to coordinate initiatives locally (e.g. vaccinations, test and trace systems, and implementation of local behavioural and environmental interventions) within a national framework. This local flexibility will ensure fast and effective decisions, which are essential to control the pandemic. Similarly, sharing advice and best practice across the four nations will be important.

There are also opportunities to learn from examples of good practice across the UK. For example, the Scottish contact tracing model is delivered by health protection professionals in teams in local NHS Boards with surge capacity provided through the National Contact Tracing Centre operated by NHS National Services Scotland (NSS). Scripts, guidance, digital systems and training resources to support contact tracing are developed centrally through Public Health Scotland, ensuring best use of resource and consistency of practice across Scotland.²⁰⁰ A similar system operates in Wales under Public Health Wales.²⁰¹

3.1.2.3 Test, trace and isolate

Systems for conducting comprehensive infection testing, contact tracing and supporting self-isolation (test, trace and isolate (TTI) system in the UK) are a vital component of epidemic management. ^{202,203} The range of possible scenarios for COVID-19 in winter 2021-22 look different from the previous two winters, primarily due to substantial vaccination during 2021. Furthermore, the proportion of tests turned around within 24 hours, and the proportion of close contacts reached and told to self-isolate, were both over 85% in late May 2021 in England. ²⁰⁴ It should be noted that TTI systems are delivered independently across the four nations and performance may vary. ^{205,206,207}

Nevertheless, many of the concerns around the TTI system in last year's AMS winter report remain, including the need for rapid, accurate testing and tracing that encompasses a high proportion of symptomatic cases, and most urgently the need for effective financial and other support for self-isolation. The possibility remains that the effects of inequalities will be compounded where those least likely to engage with the TTI system (e.g. those in low-paid and precarious employment who are financially unable to self-isolate, from ethnic minority groups, young adults, people with low trust in authority) are also least likely to have been vaccinated.^{208,209,210}

The TTI system needs to be evaluated for value-for-money as it stands, and adjustments made to improve its cost-effectiveness and efficiency both for detecting cases and preventing onward transmission into next year. The

evaluation of TTI requires incorporation of data systems to understand its impact on transmission.

Given the concerns about a potential influenza epidemic (see section 3.2.1), measures against influenza should also be considered for inclusion in the TTI system this winter.

Testing

The best combination of the available multiple testing modalities over the autumn and winter 2021/22 will depend on whether the epidemic is large and continuous, or composed of multiple smaller outbreaks. **As new COVID-19 outbreaks are identified, surge testing will be required.** This testing will often be geographic but targeted to micro-communities seeing enduring high levels of transmission. Local government and other providers will be central to maximizing coverage.

Unless infection rates stay very low, polymerase chain reaction (PCR) testing for symptomatic individuals is likely to be needed this winter to identify cases, provide care and prevent onward transmission. This will be important in hospitals, where testing of admissions should continue as both an important clinical tool, and as a surveillance measure.

A likely resurgence of other respiratory infections (e.g. influenza and RSV - see sections 3.2.1 and 3.2.2)^{211,212} will once again put an additional substantial strain on testing capacity, as seen in the autumn of 2020. **The TTI programmes must prepare for an increased demand for tests as a result of respiratory symptoms.** As advised in our previous report, routine and rapid joint testing for SARS-CoV-2 and influenza (and potentially other respiratory viruses) will be important for surveillance, treatment decisions (including antivirals for influenza), minimising isolation times, and avoiding and reducing rates of transmission. We strongly support multiplex testing; however, if this is not feasible, evidence supports the use of point-of-care testing (POCT) for influenza in hospitals, ²¹³ in primary care settings, ²¹⁴ care homes ²¹⁵ and in community pharmacies. ²¹⁶ Resources should be made available for hospitals, care homes and GP practices to create the infrastructure to upscale and roll out of POCT for SARS-CoV-2 and influenza across the NHS.

Appropriate clinical management could be optimised by distinguishing the cause of influenza-like illness through rapid testing within the TTI system and/or POCT for SARS-CoV-2 and influenza. Multiplex testing may increase participation in testing programmes (particularly for those most at-risk), especially if they enable access to treatments such as oseltamivir for influenza in eligible groups, and any proven early COVID-19 treatments that emerge (see section 3.1.3).²¹⁷

In addition to PCR testing for symptomatic individuals, **routine asymptomatic testing should also be considered where either the rate of susceptible individuals becoming infected or the potential for poor outcomes is particularly high** (e.g. health and social care settings). Wider routine asymptomatic testing, or testing based on common respiratory symptoms may not be either cost-effective, or worth the testing fatigue that may be induced where low prevalence rates lead to more false than true positive results.²¹⁸ **If lateral flow devices (LFD) are used this winter, it will be**

important to consider when their positive predictive value falls too low (i.e. at what level of population infection suppression such tests should be stopped). LFD pilots and full trials need to be subject to rigorous evaluation (including economic evaluation), ²¹⁹ and sufficient to generate actionable findings – including understanding how 'novel' use (e.g. testing to access travel or sports events) will affect wider TTI compliance. All testing strategies will need to be associated with clear cases for use and protocols, and be able to demonstrate their utility for either diagnosis or prevention.

Point of care testing in care homes has depended on a combination of send-off PCR and point-of-care lateral flow tests. However, both POC PCR²²⁰ and automated POC antigen testing have been shown to be feasible and safe in a care home setting.²²¹ **As new technologies emerge, including cheaper POC antigen and PCR tests, and multiplex technologies, it is important that the capability of all healthcare settings to run such technologies safely and effectively is considered, and that the health economic and business cases for their deployment across social care is considered in parallel with healthcare venues.²²²**

Waste water (WW) sampling has the potential to inform estimates of prevalence in realtime, based on quantitative recovery of SARS-CoV-2 RNA from treatment plants. Early work in the UK and elsewhere has illustrated a strong correlation of SARS-CoV-2 RNA in WW with reported cases of COVID-19 and can track the decline in prevalence after March 2020. 223, 224, 225 These studies also indicate challenges in interpretation and the need for further analysis of the effects of water biochemistry and impacts of sewerage dynamics on the outputs generated. WW indirectly samples both symptomatic and asymptomatically infected individuals, thus can provide information about the prevalence of infection and the impact of population interventions. Genomic analysis of WW may indicate the detection of variants as they emerge and spread. 226 WW also has considerable potential for monitoring other pathogens, including influenza and norovirus. 227 Investment to operationalise longitudinal monitoring and incorporate data into routine WW surveillance is likely to be highly cost-effective, especially as more expensive data streams (such as symptomatic community testing and purposive random sampling) are reduced. Waste water surveillance should be strengthened ahead of this winter and continue to be used to identify where infection rates are high, or outbreaks are occurring, so that other types of testing can be implemented.

Contact tracing

Evidence for the benefit of contact tracing as currently performed suggests that its contribution to reducing transmission is limited. Numerous models have suggested that contact tracing provides little benefit over and above asking household members of positive cases to self-isolate (around 75% of all contacts named are household members), and that the speed and comprehensiveness of contact tracing and subsequent testing (if contacts are symptomatic) limits its effectiveness in controlling transmission. 229,230 As behavioural and environmental interventions are relaxed, there are likely to be increased numbers of non-household contacts due to increased social mixing, however the probability of each individual becoming infected is lower, as is the likelihood of contacting them in time - both due to the more transient nature of such contacts.

As general onward contact tracing as currently performed is unlikely to substantially reduce transmission, locally led outbreak investigations and surge testing in outbreak areas are likely to be more efficient ways to control the epidemic – especially if case numbers are low. There is likely to be benefit in providing the infected person and members of their household with clear advice on minimising transmission risk to other household members by physical distancing within or outside the home. ^{231,232,233}

Novel tracking technologies, such as those used in the National Institute for Health Research (NIHR) CONTACT study have the potential to provide useful information that can allow contacts within homes to be tracked, enabling more personalised approaches to risk stratification.²³⁴ UK evidence suggests that contact monitoring apps have been more effective than post-hoc contact elicitation.²³⁵ However, app-use is low in many atrisk populations and may decline over time. Backward contact tracing (i.e. identifying who infected symptomatic cases) has been used successfully in some international settings, and is particularly powerful for viruses like SARS-CoV-2 where a minority of individuals cause the majority of onward infections.^{236,237} Such methods are likely to be most effective in the context of sporadic outbreaks rather than generalized epidemics.

Future efforts should be focussed on evaluating and considering further use of tracing apps and backwards tracing. Local Directors of Public Health may be best placed to encourage and develop community networks where contact tracing is taking place. Given the differences in contact tracing systems across the UK, any changes to current strategies should be developed to maximise their effectiveness in their national context.

Self-isolation

Self-isolation has the greatest capacity to reduce transmission within the TTI system.²³⁸ However, packages of financial and other support for self-isolation have been insufficient to achieve rates needed to reduce transmission, particularly for groups with few material and social resources. As a result, self-isolation by symptomatic individuals has been as low as 50%, and that of contacts even lower.²³⁹ In the absence of comprehensive support (financial, emotional, informational, practical and social), ability to self-isolate will remain low and will continue to be patterned by measures of deprivation and caregiving requirements. Careful evaluation of the benefits of sufficient, timely and targeted support for those required to isolate is needed.²⁴⁰ The effect of reducing onward transmission, uptake among others in the household and community and the impact on the mental health of those isolating should all be considered. Such support will need to include protection of jobs, income and leave rights during isolation – and thus involve engagement with employers, notably those using casual and zero-hours contracts, the Department for Business, Energy and Industrial Strategy and the Treasury.

Test uptake has been lower in deprived areas, and in areas with lower digital literacy.²⁴¹ Fear of income loss from self-isolation has also been a key barrier to testing.^{242,243} Given that crowded households may not be able to follow much of within-home best practice for social distancing, **local action should be taken to support households where people cannot distance** (e.g. by providing other accommodation for some members as is already being offered in some locations).²⁴⁴

Avoiding unnecessary isolation will be essential to support education, the economy, health and wellbeing. Adaptations to current isolation rules may have knock-on benefits for the wider TTI system. These could include reduced requirements for those who have been previously vaccinated with two doses of the COVID-19 vaccine, as recently announced for England by the UK Government, or allowing contacts to take a daily LFD test to avoid isolation. Any such changes should be rigorously evaluated for their acceptability, feasibility and effectiveness in preventing transmission. ^{245,246}

The system of TTI that has operated in UK schools uses LFT followed by PCR confirmation after a positive LFT to identify cases, with subsequent isolation of single or multiple class 'bubbles' of children and young people for 10 days.²⁴⁷ School controls, from improvements in ventilation up to full school closures have been deployed throughout the pandemic and have been broadly effective. ^{248,249,250,251} However, some of these interventions cause considerable harm. School closures are causally related to a range of harms to children and young people's physical and mental health as well as to loss of learning.²⁵² Such testing and isolation systems in schools can lead to considerable school absence at times of high prevalence. 253 Testing and isolation systems in schools in all four UK nations should be evidence-based and balance the benefits of transmission control with the harms of isolating children who are not infected when tested. The UK Government has recently announced that the system of asking 'bubbles' of children to self-isolate after a positive case would cease in England over the summer, which should significantly reduce disruptions to education. The harms of school closures are sufficiently high to mean that schools would only close in future following a careful, evidence-based assessment of the balance of harms and benefits.

3.1.2.4 Communication and behaviour change

Our Patient and Carer Reference Group highlighted the need for community engagement and tailored messaging to guard against the effects of poor communication on adherence to COVID-19 guidelines. The need for clear communication and guidance from government, including around the rationale behind decisions made, also came out strongly in our public dialogue workshops.²⁵⁴

Many people have found the government guidance on physical distancing, isolation and bereavement unclear and contradictory. ^{255,256,257,258} Trust in the UK Government, politicians and the news media declined over 2020 and into 2021, while scientists, doctors, experts, and national health organisations retained higher levels of public trust (this was echoed in our public dialogue workshops). ^{259,260,261262} There has also been a significant increase in the number of people who see the UK Government itself as a source of misleading or false information about COVID-19. ²⁶³ Trust in the government creates prosocial behaviour, ²⁶⁴ so the decline in trust undermines communications and the ability to mobilise public behaviour. Low levels of trust have been linked to vaccine hesitancy. ^{265,266,267}

Inequalities of access to information

Information has not been accessible to some of the most vulnerable groups and health messaging may exclude them. Studies have shown women are engaging less with COVID-19 news, which may be in part due to lack of time with the greater amount of

time that they normally spend on caregiving and household tasks being exacerbated by lockdown, school closures and home working. Those with lower levels of education and lower household income are also less likely to engage with news. The deaf and hard of hearing have been excluded from government briefings in England, though Scotland and Wales briefings have included sign-language interpreters. Disabled people have been largely excluded from the pandemic response and messaging, with many feeling abandoned and forgotten, which has been exacerbated by failures of social care. Studies have also demonstrated linguistic barriers for accessing information about COVID-19 for those who do not speak English.

We also heard through our public dialogue workshops and Patient and Carer Reference Group that news about COVID-19 may be attracting less engagement from the public. 273 Moreover, we heard young people have felt excluded from messaging, which has largely focussed on the elderly, who are at highest risk from the disease. At times, young people have also felt demonised by the media when portrayed as flouting the COVID-19 regulations. They also reported a lack of tailoring of advice and messaging, including the channels of communication through which these are communicated. For example, in our discussions with young adults, we heard that they are more likely to obtain their information through social media platforms rather than through traditional media outlets. An Ofcom survey in March 2021 found that 45% of the 12-15 year olds that they surveyed relied on media and official sources, rather than people they know, for news. 274 Communication with children and adolescents will become particularly important from mid-2021 when they will form the only substantial unvaccinated group within society.

Attention needs to be paid to the content of messages, their source (to ensure credibility and trust), and the social and technological barriers to communication (such as signing, digital exclusion, the breadth of platforms used to access information, and the impact of social inequalities on information access). Certain contexts/events over the autumn and winter may require particular attention in terms of communication - for example, communications to university students (e.g. precautions when returning to campus/home, encouraging vaccine uptake, guidance for socialising and hand/respiratory hygiene), and communications around celebrations, including Eid, Christmas and New Year, among others.

The negative impacts of the pandemic on health (including mortality and health outcomes), education, psychological wellbeing, and financial resources have fallen to a disproportionate extent on lower socio-economic and ethnic minority communities. ^{275, 276} Recognition of the uneven burden associated with lockdown will be important in maintaining the long-term confidence of disadvantaged communities (for example, some ethnic minority communities, travellers, communities characterised by crowded housing or insecure employment, etc.). This will be particularly important as the pandemic may increasingly become localised in disadvantaged communities, for example due to crowded housing and lower levels of vaccine uptake, among others.

There is an urgent need to engage and build trust with communities and groups most at risk of serious and severe outcomes from COVID-19. There is a wide range of experience regarding community engagement across faith groups, prominent community leaders, and NHS staff. Governments in all UK nations should harness this wealth of experience and expertise to develop community-centred,

culturally sensitive COVID-19 communication materials and engage proactively with communities to dispel misconceptions and anxieties (such as those arising around COVID-19 vaccines).²⁷⁷

It is likely that regulations will need to be reimposed from time to time, including over the autumn and winter, be it nationally or locally. Those subject to such local restrictions are likely to be amongst the more disadvantaged. Governments in all UK nations must be as transparent as possible and clearly define the criteria for such reimpositions of regulations. They should also provide extra support to address the additional burden such restrictions will impose on the more disadvantaged. This extra support will better enable such communities to adhere to the restrictions and will provide an important signal that their concerns have been heard and recognised, contributing to the establishment of trust in the authorities. It will also be important to ensure that the eligibility criteria for support is reviewed quickly so as to be able respond to rapidly emerging needs amongst particular sections of the community. This responsiveness may be best achieved if the delivery mechanism is locally based (e.g., in local authorities).

Risk and hazard perception

Even if all formal regulations concerning social contact are suspended, people will need to be aware of how behaviour (their own and others') impacts transmission. When restrictions are in place, there is a sense that the judgement has been made for society by policymakers, guided by expert evidence. As formal restrictions are lifted, the burden of responsibility for identifying hazards and judging risk shifts to fall on the individual. In order to be able to exercise this responsibility well, Governments in all UK nations should provide guidance as to the risks and hazards in everyday environments. Public service communications could help alert people as to what they should look out for as they go about their everyday lives (e.g. poorly ventilated domestic settings/workplaces that may facilitate transmission). Such communication will be important as the absence of formal regulations is likely to encourage the perception that the level of risk is low across all scenarios.

Risk and hazard perception becomes more complicated as social interaction returns to something approaching 'normal'. Interactions with friends and family in domestic settings are likely to be assumed to be safer than interactions with strangers in non-domestic settings. Familiarity and relational closeness likely increase trust, which leads to a lowering of people's guard and riskier behaviour. ^{278,279,280} Governments in all UK nations should develop clear communications alerting people to the risks and hazards in such apparently 'safe' settings with people they are at ease with. Communication concerning such risks should not create fear but rather a practical awareness of how, even in familiar settings, people's physical environment and social interactions may facilitate transmission; it should also recommend acceptable and feasible methods of reducing the risk of transmission²⁸¹.

Messages delivering information on everyday risks should be accompanied by communications that motivate efforts to mitigate transmission. However, the motivation to act on one's knowledge of risk is not enough. The capacity to act on that motivation is key and can be constrained in social situations. For example, it can be difficult to open windows at work if others are feeling the winter cold, or to ask about opening the

windows as a guest in someone's house. Public service communications should raise awareness of such interactional complexities and thereby help facilitate the conversations that need to happen if people are to act on their hazard awareness.

The importance of communications concerning the risks in workplace and domestic settings will increase over the autumn and winter and interactions are increasingly indoors. As mentioned previously, celebrations such as Eid, Christmas, New Year and others will likely require more focused communications on risk perception and mitigation.

Box 3 outlines a series of communication principles that we suggest should be considered to communicate effectively to the public. Figure 3 provides guidance for COVID-19 messaging targeting ethnic minority groups. The importance of clear communication emerged as a key theme from the public dialogue workshops – a summary of the findings relating to communications is provided in the report available on the Academy's website. ²⁸²

Initiating and sustaining behaviour change

Over the next few months, Governments in all UK nations should develop a comprehensive communication and engagement programme to ensure the successful design and implementation of acceptable, feasible and effective mitigation measures to reduce transmission of COVID-19 and other infections prior to winter 2021/22, in the context of the majority of the adult population being vaccinated against COVID-19. This should be co-developed with relevant communities and population sectors - including children, young people, older people, health and social care staff, and representatives from different socio-economic regions and ethnicities - to ensure support for mitigations is appropriate for the target users, community-centred, culturally appropriate and available in relevant languages (Box 1 in our previous report provides further information about co-development of information and guidance). Particular emphasis should be placed on increasing vaccine uptake, adherence with self-isolation requirements, and preventing onward transmission (e.g. in the home) to protect individuals themselves, as well as others. These will require practical support and appropriate messaging.

A century of behavioural science has shown that communicating information to individuals is insufficient to change behaviour.²⁸⁴ To initiate and sustain behaviour change, it is necessary to build upon motivation and create physical and social environments that enable, prompt and support the required behaviours and make them a normative, valued, effortless and habitual way of life. To create these environments will require working intensively with all communities, organisations and sectors of the population to identify barriers and find solutions, as well as evaluating these for their effectiveness in achieving the outcomes intended.

Appropriate messaging content, style and source

- Acknowledge differences amongst ethnic groups no 'one size fits all' approach
- Emphasise ethnicity, culture and faith in messaging content
- Use of authentic messages delivered by community members/influencers/faith leaders from a relevant ethnic group
- Reinforce positive and non judgemental messages, thank communities for their response so far



Vaccine hesitancy

- Approach vaccine related concerns with empathy and humility
- Utilise faith venues as vaccination centres
- Provide targeted messages in vaccine invitations, and at vaccination appointment (e.g. around continued need for mask wearing, hand washing)

Effective and relevant communication mediums

- Train faith leaders to deliver consistent health messages, including reinforcement that faith alone will not protect against health issues
- Make use of local ethnic media outlets, such as radio and television channels
- Utilise accessible social media platforms and school teaching to promote health messages to young people, to support inter-generational transfer of information
- Fund training of community champions and knowledge advocates amongst VCSE and other partner organisations
- Utilise community pharmacies and GP text messaging systems to promote guidance/information

Use of appropriate terminology

- Reduce use of the potentially stigmatising acronym 'BAME', promote alternatives such as the phrase 'ethnic communities'
- Consider interpretations of phrases such as 'social distancing' and the effect/implications for perceived community cohesion

Figure 3: Specific COVID-19 messaging targeting ethnic minority communities. Taken from Ala A, et al. (2021). Specific COVID-19 messaging targeting ethnic minority communities. EClinicalMedicine 35.²⁸⁵ Copyright © 2021 The Authors. Published by Elsevier Ltd, reproduced under creative commons licence CC BY-NC-ND 4.0.

Box 3: Effective communication principles

- Communications should be timely, tailored to the intended audience(s), community-centred, culturally sensitive and available in multiple languages. A one-size-fits-all approach will not be effective.
- Communications must be clear and offer actionable/practicable guidance. Mixed messaging and lack of clear guidance creates uncertainty as to the nature of risk and appropriate mitigations. It also undermines confidence.²⁸⁶
- Communications and policies should be co-produced with the communities that will be affected. Managing a crisis by instructing people to behave in a particular way will likely be less effective and result in resistance by alienating the intended audience. ²⁸⁷ In working with relevant communities, communications should convey information about social norms (i.e. what fellow community members do), which can be particularly influential. ²⁸⁸ Feedback on the effectiveness of communications should be sought from those affected.
- Communications should help to explain why measures are being taken so people feel they are being treated as an equal with insight to the problem and why a certain intervention has been chosen.
- Communications should be respectful of their intended audience. Talk of public 'panic' and irrationality or talk of people being weak-willed is misleading. ^{289,290} Such talk is also likely to be judged as being disrespectful and alienate the intended audience.
- Communications should build, and be built on, trust. This requires communicators to be honest, acknowledge their mistakes and failings, and

- show that they are ready to learn from those mistakes. Communicators should treat their audience as equals and as partners in a dialogue.
- Communications should highlight people's responsibilities to each other. For example, communication on risk should not only focus on individuals' concern for their own health and wellbeing, but also how people's behaviour impacts others' health and wellbeing. This may be especially important as the number of vaccinated people, who feel 'safe' and no longer required to monitor their own behaviour, increases.
- Communications should not blame (sections of) the public for poor outcomes as this would likely alienate the intended audience.
- Communications are likely to be more effective if their source is judged to be someone that the audience can identify with as someone like themselves.²⁹¹
- Advice and guidance must be followed by all regardless of societal position. Failure in this regard undermines trust and credibility and creates a distance between the communicator and the audience.
- Communicators must establish an inclusive sense of community such that all feel they matter and that the communicator has their interests at heart. ²⁹² This requires attention to the diverse nature of the British public and their various concerns.
- Communications should recognise the distinctive needs of those experiencing various forms of social and economic disadvantage and ensure that the support necessary for adherence is provided.²⁹³
- Wherever possible, communications should make constructive behaviours visible, and focus on the majority's adherence to any guidelines rather than a minority's deviation from them.²⁹⁴ Giving high profile to failures in following guidelines can create misleading perceptions (e.g. that the rules are being ignored by large sections of the public), which can in turn impact people's own rule-following behaviour.
- Communications should seek to build people's sense of resilience through creating a strong sense of community and mutual support.^{295,296} Stories of local support groups' successes could feature as models for others, whereas talk of people being weak-willed, unable to cope with restrictions and the danger of 'fatigue' should be avoided.²⁹⁷

3.1.3 Treatments and prophylaxis

3.1.3.1 COVID-19 treatments

COVID-19 treatments will continue to play a crucial role in alleviating the impact of resurgences in infections. Major advances have been made in treatments for those with severe infection requiring hospitalisation²⁹⁸, and the UK has led the way in establishing the evidence-base for the development and repurposing of drugs for prevention and treatment of COVID-19.

The RECOVERY and REMAP-CAP trials are leading examples of adaptive trials that have run at pace, delivering clear outcomes that have changed clinical management. Both trials have enabled existing drugs with established safety profiles to be repurposed (summarised in Table 2 in Annex 7) and, of equal importance, shown that several

proposed treatments are ineffective or possibly even harmful (summarised in Table 3 in Annex 7). In June 2020, the RECOVERY trial identified dexamethasone as the world's first effective treatment for COVID-19. Pexamethasone is now used worldwide as one of the few approved treatments for COVID-19. Since then, there have been positive findings for the use of tocilizumab from the REMAP-CAP and RECOVERY trials. The AGILE-ACCORD platform mirrors these platforms for phase I/II studies, and the PRINCIPLE trial platform is the national urgent public health trial to find treatments for COVID-19 in primary care. The HEAL-COVID trial is another urgent public health trial looking into treatments to improve the longer-term outcomes of patients that were hospitalised with COVID-19.

The COVID-19 Therapeutics Taskforce led by the Department of Health and Social Care (DHSC) was established to coordinate government efforts to ensure research into new treatments continues at pace so that COVID-19 patients in the UK get access to safe and effective treatments as soon as possible. It is supporting a series of clinical trial 'platforms' that are assessing several therapeutic and prophylactic candidates. The therapies for testing in the platform trials are recommended by the UK COVID Therapeutics Advisory Panel (UK-CTAP), which is independent of the Therapeutics Taskforce. 304

3.1.3.2 Development of new antiviral treatments

COVID-19 treatments currently found to reduce mortality in hospitalised patients are primarily immunomodulatory drugs. 305 The exception to this is Regeneron's combination of 2 monoclonal antibodies, which RECOVERY recently confirmed reduces mortality in hospitalised patients who lack an antibody response to SARS-CoV-2 infection. 306,307 It is logical to think that antivirals could be used for both prevention and/or treatment. Remdesivir, whilst showing early promise, failed to show benefit in the largest trial SOLIDARITY, carried out by the WHO. 308 The identification of repurposed or novel compounds that could be used as antiviral agents to prevent the progression of diseases in those who may not have reached a critical stage of illness, or which may have prophylactic functions, remains a major gap. Modelling suggests that the use of antivirals (alongside TTI measures), which decrease the viral load and reduce infectiousness, could be an effective strategy to control local outbreaks of COVID-19. 309

As work involving *de novo* discovery of molecules with activity at viral targets is likely to take several years, a clear strategy to identify potential existing antiviral compounds for testing is needed. The Academy's COVID-19 preclinical drug development database exists to help in this area by supporting collaborations between researchers and mapping ongoing activities to give central bodies oversight. In the long term, the discovery of viral protease inhibitors offers the most likely route to the discovery of new medicines and medicines that can be taken at home and to support their development through clinical trials. The aim is to have at least two effective treatments this year, rolled out to patients as early as the autumn, that the public can take at home following a positive COVID-19 test or exposure to someone with the virus. We support the ambition of the Antivirals Taskforce to identify antiviral drugs and subject them to clinical trials. The timelines are ambitious for making novel drugs available by the end 2021, but ensuring a strong pipeline of effective therapeutics is important.

During periods where the number of people with severe disease is low in the UK, a major challenge will be the availability of patients for enrolment in trials. Under these circumstances, it may be necessary to conduct trials in countries experiencing high infection rates, or in experimental human challenge settings (i.e. where healthy volunteers are infected).³¹⁵

The accelerated development and use of antivirals that are efficacious against SARS-CoV-2 as well as other respiratory viruses could be particularly effective in reducing the burden of respiratory virus-related diseases in future. 316

Initiatives to get treatments for COVID-19 to NHS patients quickly and safely will be important.³¹⁷ They will have a key role to play in ensuring the rapid adoption and deployment of new treatments across health and social care settings once they have proven to be safe and efficacious.

Pre- and post-exposure prophylaxis

One major challenge that remains is pre- and post-exposure prophylaxis. Whilst the vaccine rollout in the UK has been successful, the emergence of the Delta variant has demonstrated that without full immunisation of the population there is a risk of a surge of infection. Moreover, it remains unclear how long immunity will last after different types of vaccine. Non-antibody therapies that can be used as prophylaxis prior to or after exposure would be a major advance and could be used alongside vaccines.

Early in the pandemic, there was use of off-label drugs for prevention, including hydroxychloroquine, which was subsequently shown not to work in prevention in the PRINCIPLE platform. The Emerging evidence suggests that inhaled budesonide may be of some use. International trials have suggested the use of colchicine could be beneficial, but definitive trials are awaited.

The UK is home to the first multicentre cluster RCT platform for evaluating COVID-19 prophylaxis therapies in older people living in care homes. PROTECT-CH is funded by the NIHR and will look at both pre- and post-exposure prophylaxis for COVID-19 in care home populations, starting randomisation in July 2021. Outcomes will focus on hospitalisation and/or mortality from COVID-19. An unrelated study, PROTECT-V, again funded by the NIHR, will consider COVID-19 prophylaxis in multiple at-risk groups.

In July 2020, DHSC established the COVID-19 Prophylaxis Oversight Group to guide development of pre- and post-exposure prophylaxis for SARS-CoV-2 infection. The COVID-19 Prophylaxis Oversight Group made recommendations of prophylactic agents to investigate in the PROTECT-CH and PROTECT-V clinical trials.

The work of the COVID-19 Prophylaxis Oversight Group will be essential to ensure that a data-driven approach is taken to identify drugs that can be used as prophylaxis prior to or after exposure and to ensure national coordination.

3.1.3.3 Clinical trials

Prophylaxis needs to be considered with respect to infrastructure. Whilst RECOVERY has demonstrated the feasibility of large-scale pragmatic adaptive trials during an outbreak, these have been in secondary care. **Similar efforts need to be made in primary care.** PRINCIPLE is the main platform for deployment of trials in primary care, recruiting 5,000 individuals with COVID-19.³²⁴

The UK must maintain strong trials capability in primary and secondary care to make progress on COVID-19 treatment and prophylaxis against severe disease, including participation in trials in countries with a high incidence of disease. Ways to accelerate the early recruitment of patients into trials, such as use of NHS Test and Trace data, should be further explored.

3.1.3.4 Medicines supply

The COVID-19 pandemic has put entire supply chains for medicines manufacture and supply at risk, as is the supply of reagents to research laboratories.³²⁵ Industry-wide shortages of basic materials involved in manufacture will continue to be a major risk over the coming months. The manufacture and supply of drugs need to continue to be modelled in a global context, with forward planning and preparedness for upcoming resurgences in infection and scaling up for potentially effective treatments once clinical trials have been completed.

3.2 A resurgence of other winter diseases, including influenza and RSV

3.2.1 Influenza

3.2.1.1 Increased population susceptibility

The Academy's 'Preparing for a challenging winter 2020/21' report highlighted that the size and severity of the influenza epidemic in winter 2020/21 would be particularly difficult to predict: physical distancing measures implemented around the world might have impacted influenza infections; the actions to reduce COVID-19 transmission in spring 2020 might have diminished exposure to influenza; and it was not clear whether the incidence of influenza infection would continue to be suppressed by physical distancing in winter 2020/21 or may be high because of a mild influenza season in 2019/20. 326

We now know that there were very low levels of influenza activity over winter 2020/21, most likely due to the behavioural and environmental interventions, such as physical distancing measures, that were imposed in the UK and elsewhere in response to the COVID-19 pandemic. 327 Indeed, the routes of influenza transmission are similar to those of COVID-19 transmission, with direct contact and droplet transmission traditionally seen as the main routes, but aerosol transmission is also likely to play an important role. 328,329 Therefore, the same mitigation methods used to reduce COVID-19 transmission also reduce influenza transmission. Influenza is highly infectious but has a lower basic reproduction number (R_0) than COVID-19, 330 especially compared to the more transmissible variants. Behavioural and environmental interventions that are sufficient to reduce the reproduction number (R_1) of COVID-19 below 1 would therefore also be expected to completely prevent influenza epidemics.

Given the very low levels of influenza activity over winter 2020/21 and the mild influenza season in 2019/20,³³¹ it is likely that population immunity to influenza will have diminished. Acquired immunity to influenza wanes over the course of years,³³² with antibodies slowly diminishing and T cell memory responses able to provide a degree of protection (and cross protection) for many years.^{333,334} Therefore, waning of immunity may not have made a large difference to population susceptibility over this time frame.

In the short to medium term, genetic drift and shift of the virus may be more important than waning immunity in determining the degree of protection against influenza in winter 2021/22. The degree of protection is dependent on antibody titres and the match of those antibodies with circulating strains, although a valuable degree of protection persists even when there is a mismatch. There will be a larger number of infants and young children who have never been exposed to influenza, so higher infection levels might be expected in these younger age groups. However, very low levels of influenza over the last two seasons will have led to lower levels of immunity than usually seen, which means a wave of influenza could be problematic.

3.2.1.2 Predicting circulating influenza strains

Vaccines for influenza are typically less effective than vaccines for COVID-19, being approximately 70% effective in healthy adults and 50% effective in the elderly. 336 Immunity conferred by the influenza vaccine is dependent on the degree of match between the vaccine components and the circulating strains, 337 which is updated annually (see PHE's website for an overview of the influenza vaccines that will be offered in 2021/22). 338 In years with mismatch, effectiveness against both infection and severe disease can be markedly reduced, resulting in more severe epidemics. Given the global decrease in influenza circulation, there has been much less information available on which to base predictions about which influenza strains will circulate this winter. As such, there is an increased likelihood that there will be influenza vaccine mismatch this winter, which could result in more infections and disease.

A generalised increase in respiratory infections over the autumn/winter could place enormous pressures on test and trace capacity. Indeed, the symptoms of influenza and other winter respiratory viruses are typically clinically indistinguishable from COVID-19 without a test. Last winter when influenza activity was low, just under 84.5 million COVID-19 tests were carried out under Pillar 2 testing from 1 September 2020 to 31 March 2021, with a peak of over 151,000 tests being carried out in a single day. 339 Demand for community symptomatic testing might be even higher this year given the potential increase in circulating winter respiratory diseases.

3.2.1.3 A possible resurgence of influenza in winter 2021/22

As measures to contain SARS-CoV-2 transmission are eased and mixing increases, influenza may be more common in winter 2021/22. A recent study in the United States³⁴⁰ projected that large future outbreaks of influenza (and RSV - see below) may occur following a period of extended behavioural and environmental interventions. Applying the same modelling to the UK, our reasonable worst-case scenario suggests that an influenza epidemic could be between 1.5 and 2.2 times the

magnitude of a 'normal' year if we fully opened (Figure 4). These outbreaks may reach peak numbers in the winter, increasing the burden to healthcare systems.

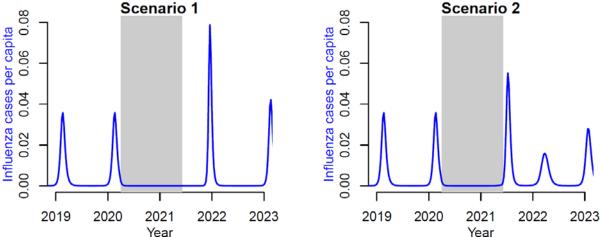


Figure 4: Two potential scenarios for an influenza epidemic in the UK. In Scenario 1, the strain that emerges following relaxation of all behavioural and environmental interventions is assumed to be similar to pre-pandemic years and hence immunity that has built-up in the past remains effective. In this scenario, an influenza epidemic could be ~2.2 times the magnitude of a 'normal' year and occur in winter 2021/22. In Scenario 2, we assume that immunity declines during the period of behavioural and environmental interventions, reflecting the emergence of novel strains. In this scenario, an influenza epidemic could be ~1.5 times the magnitude of a 'normal' year and occur in summer 2021. The summer peak reflects the decreased immunity to novel strains, resulting in transmission of the virus during the summer months, which would not occur in a 'normal' year. The lower magnitude of the peak compared to scenario 1 reflects the behavioural and environmental factors (such as higher temperatures, more time spent outdoors, etc.) that would limit the spread of the virus compared to winter. For both scenarios, we assume that the level of behavioural and environmental interventions in place between March 2020 and June 2021 (grey area) reduced transmission of influenza by 30%, a level that is sufficient to interrupt transmission over this period.

The Flu Watch community cohort study (2006/7-2010/11) shows on average 18% of the unvaccinated England population had serologically confirmed influenza each year, with the highest annual rate being 27% of the unvaccinated population. Approximately three quarters of these serologically confirmed infections were asymptomatic. On average, 4% of the cohort had PCR-confirmed influenza each winter season with the highest annual rate of 9%. Infection rates were typically highest in children and decreased with age. 17% of confirmed infections attended their GP and less than 1% of confirmed cases were admitted to hospital.³⁴¹

In recent years, between approximately 10-30,000 deaths a year have been associated with influenza in England. The winter of 2017/18 was the most recent significant influenza season, with approximately 26,000 deaths associated with influenza in England. Risk of infection generally decreases with increasing age but, much like COVID-19, the risk of severe outcomes increases dramatically with age and to a lesser extent with chronic illness. This means the great majority of hospitalisations and deaths occur in older age groups and those with multiple long-term conditions. Infants can also

develop severe complications of influenza. Based on meta-analysis of studies using serosurveys to estimate the number of infections and national mortality data, the all-age infection fatality risk for COVID-19 is around 0.60% (0.43%–0.77%) but may reach up to 15% in those aged over 60 years. 343,344 This is substantially higher than the infection fatality risk measured for influenza H1N1pdm2009 in Hong Kong, which peaked at <0.2% in those aged 60-74. 345

Although our modelling suggests that a surge in COVID-19 might not occur over the winter period, there is a degree of uncertainty around the timings. We cannot discount the risk that a resurgence of COVID-19 might overlap (at least partially) with outbreaks of other respiratory viruses such as influenza and RSV (see below) over the autumn/winter. Respiratory infections can act synergistically in humans³⁴⁶ and potential interactions between SARS-CoV-2 and other respiratory viruses in relation to disease severity and viral variants is a concern. An initial infection may increase the severity of subsequent infection or can transiently boost innate immunity offering some protection. Early data suggests influenza A leads to an increased susceptibility to SARS-CoV-2 and more severe disease.^{347,348} The wider circulation of other respiratory viruses will apply selection pressures on SARS-CoV-2 and could lead to the emergence of new variants of concern. We therefore advise that actions must be taken to both diminish influenza circulation and mitigate its impacts (see below).

There is also a concern that the large reduction in influenza transmission experienced in recent years may provide an ecological niche for a pandemic influenza strain that is antigenically distinct from previous strains to emerge. Pandemic preparedness plans for future pandemic threats, such as pandemic influenza, should be urgently revised to plan for this possibility.

3.2.1.4 Optimising the UK influenza vaccine strategy

As advised in our last winter report, a priority will be to increase the uptake of the influenza vaccination programme for eligible groups, including high risk groups who are vulnerable to influenza, such as: the elderly and clinically vulnerable; children, who can amplify community spread; and health and social care workers. The influenza vaccination programme for the 2020/21 flu season was extended, with more groups eligible to receive the influenza vaccine than in previous years. Influenza eligibility criteria for winter 2021/22 have yet to be published by PHE. However, given that COVID-19 is likely to be co-circulating with influenza this winter, it will be imperative to protect those at high risk of influenza, who are also those most vulnerable to hospitalisation from COVID-19. As such, public health agencies in all UK nations should consider whether the influenza vaccination programme for this winter should be extended in a similar fashion. As discussed in section 3.1.2.1, JCVI will need to consider whether influenza vaccines could be co-administered alongside COVID-19 boosters.

Provisional data released by PHE suggests an increase in influenza vaccine uptake in GP patients in 2020/21 across all previously eligible groups, ³⁵⁰ including a slight increase in uptake in healthcare workers from 74.3% uptake in 2019/20 to 76.8% uptake in 2020/21. ³⁵¹ There was an 80.9% uptake in the 65+ category and 53% uptake in the clinical risk groups (age 6 months to 65 years).

The overall increase in uptake of influenza vaccination over winter 2020/21 is welcome. **Maximising the uptake of influenza vaccination to close to universal coverage in eligible populations will be crucial for this winter.** Further advice on possible mechanisms to increase coverage in elderly and high-risk populations, children and healthcare workers can be found in our 'Preparing for a challenging winter 2020/21' report (pages 47-49). 352

It should be noted that uptake of influenza vaccination in staff in care home settings was estimated to be at best 25% prior to the pandemic.³⁵³ This is despite research showing that vaccinating care home staff markedly reduces influenza-related hospitalisations and deaths in residents.³⁵⁴ Focussed effort will be needed to maximise the uptake of the influenza vaccine (potentially alongside a booster dose of COVID-19 vaccine - see section 3.1.2.1) in care home staff.

3.2.1.5 Optimising the use of influenza antivirals

As for last winter, we advise that PHE guidance on treatment with neuraminidase inhibitors should be widely implemented, supported by rapid testing, to reduce severe complications of influenza that impact the health service and reduce influenza transmission. PHE recommends treatment with neuraminidase inhibitors, such as oseltamivir, in high-risk community patients within 48 hours of symptom onset (or later at physician discretion); all hospitalised patients irrespective of duration off illness; and recommends consideration of prophylactic use in care homes during outbreaks (irrespective of vaccination status).³⁵⁵

Historically, testing for influenza has been largely confined to secondary care settings and people attending sentinel surveillance practices with influenza-like illness. Testing for influenza in secondary care is important for prevention and control of nosocomial outbreaks and for influenza case management. The lack of widespread community testing has limited the early use of influenza antivirals to prevent hospital admission. Now that community testing of respiratory infections for COVID-19 is common, adding influenza to the tests undertaken could potentially reduce pressure on secondary care (particularly if targeted at older people where antiviral prescription is likely to be most beneficial due to higher risk of admission to hospital).

Distinguishing the cause of influenza-like illness through rapid testing within the TTI system and/or POCT for SARS-CoV-2 and influenza would optimise clinical management, by informing the widespread, effective use of oseltamivir for influenza. Oseltamivir ideally needs to be taken within 48 hours of the onset of influenza symptoms to be effective. The use of antivirals for influenza is low in primary care, but they can reduce recovery time in primary care patients and reduce complications of influenza in high-risk adults in the community. The use of we strongly support multiplex testing; however, if this is not feasible, evidence supports the use of point-of-care testing (POCT) for influenza in hospitals, in primary care settings, care homes and in community pharmacies. Testing must be sufficiently rapid to make an influenza diagnosis within 48 hours of symptom onset for oseltamivir to be clinically useful. Public health agencies across all UK nations should urgently assess optimal joint testing strategies both in hospitals and in the community.

Resources should be made available for hospitals, care homes and GP practices to create the infrastructure to upscale and roll out of POCT for SARS-CoV-2 and influenza across the NHS. In addition to optimising appropriate clinical management, rapid testing would minimise patients of unknown SARS-CoV-2 and influenza status being cohorted together in assessment areas, thereby reducing the risk of nosocomial transmission to patients and staff (see section 5.3).

Since COVID-19 emergence, people with acute respiratory infections have been actively discouraged from attending primary care and there is a much greater reliance on online consultations. This is likely to mean that one of the main pillars of community influenza surveillance (namely sentinel testing in primary care) will be relatively ineffective. Testing a sample of community samples submitted under the TTI programme could therefore be critical to understanding levels of influenza in the community.

3.2.2 Respiratory syncytial virus (RSV)

The recent easing of social contact rules has led to a summer surge of infections that are typically seen in the winter, including RSV, bronchiolitis, parainfluenza and rhinovirus. 366 RSV is a major cause of hospitalisation and mortality in young children, particularly those less than one year old. 367,368,369370 Evidence from Australia 371,372,373 and South Africa 374 suggests an increase in RSV in children in summer following an RSV-free winter in lockdown. Modelling data from the United States, 375 suggests that the loss of population immunity to RSV amongst young children may create a larger susceptible population that is potentially likely to have a larger outbreak this winter.

Our reasonable worst-case scenario modelling similarly suggests that RSV levels could rise rapidly following relaxation of behavioural and environmental interventions, with a peak outbreak in early autumn of between 1.5 and 2 times the magnitude of a 'normal' year. This could result in between a 25% and 65% increase in cases in children under 5 years old, and between 30%-100% increase in the youngest infants (Figure 5). Although our modelling is based on data from England alone, similar patterns would be expected in Wales, Scotland and Northern Ireland.

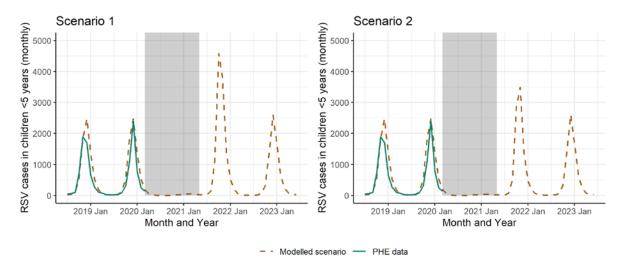


Figure 5: Two potential scenarios for RSV in England. In Scenario 1, we assume that maternal protection decays over the period that behavioural and environmental

interventions are in place due to a lack of exposure. In this scenario, a peak outbreak would be ~2 times the magnitude of a normal year, with a 65% increase in cases in children <5 years, 100% increase in cases in youngest infants and 40% increase in infection across the population. In Scenario 2, we assume no change in pre-existing levels of maternal protection. In this scenario, a peak outbreak would be ~1.5 times the magnitude of a normal year, with a 25% increase in cases in children <5 years, 30% increase in cases in youngest infants and 40% increase in infection across the population. For both scenarios, we assume that the level of behavioural and environmental interventions in place between March 2020 and June 2021 reduced transmission of RSV by 30%, a level that is sufficient to interrupt transmission for most of this period. The model is fitted to data from England (PHE reports from DataMart). Similar patterns would be expected in Wales, Scotland and Northern Ireland.

There is a risk that children's wards and paediatric intensive care units (PICU) may be overwhelmed without appropriate planning to manage a potential large outbreak this winter. In addition to an increase in paediatric cases of RSV, it may also increase in adults. RSV infection in hospitalised adults can result in serious respiratory illness, with complications akin to those caused by influenza. ^{376,377,378} A higher than usual winter peak of RSV activity across children's wards and PICUs may also particularly stress a system with reduced capacity due to physical distancing and will inevitably mean that the PICU system cannot donate capacity to adult intensive care as has happened in previous COVID-19 peaks.

The NHS must develop plans for increased paediatric ICU capacity and for much greater access to the monoclonal antibody pavulizimab to manage this potential large outbreak this winter. The introduction of multiplex testing (at least for SARS-CoV-2, RSV and influenza) will be important for managing febrile children in the coming winter, as well as for vulnerable adults.

Experience from last year could be used to tailor infection control processes specifically for children. The Royal College of Paediatrics and Child Health has developed guidance³⁷⁹ to support the testing for and management of patients with RSV and other infections on admission, which it will continue to update in line with PHE's infection prevention and control (IPC) policies.

A peak in RSV would also put pressure on primary care, which sees the majority of RSV patients, predominantly in the under-fives.³⁸⁰ Primary care, secondary care and 111 will need to work together to prevent large numbers of children and older patients with breathing difficulties from being triaged with the outcome of an emergency ambulance, as many of these patients do not need to be admitted and can be looked after in the community. Face-to-face primary care is best suited to select the most appropriate outcome, which would result in a large extra workload in primary care.

3.2.3 Other winter viruses

3.2.3.1 Respiratory infections

A number of interacting factors occur during the late autumn, winter and early spring months that create additional lung diseases beyond COVID-19.³⁸¹ In addition to influenza and RSV (described above), other common respiratory viruses, such as the common cold

viruses (especially rhinovirus), parainfluenza, adenovirus and metapneumovirus, can cause serious lung disease. This would contribute to the peak of hospital admissions in the colder months, especially in those with pre-existing diseases such as chronic obstructive pulmonary disease (COPD) and other chronic lung diseases. The very young and very old are more vulnerable to serious disease with these viruses, especially RSV and parainfluenza. 383,384

The impact of other respiratory viruses on the clinical state of long COVID is largely unknown but potentially presents a serious problem to those who have previously experienced COVID-19 and its longer-term consequences. Preliminary studies using a range of assessments, including magnetic resonance imaging (MRI), high-resolution computed tomography (HRCT) and single-photon emission computerized tomography (SPECT), indicate that a high proportion of patients with long COVID that were previously hospitalised with COVID-19 have persistently abnormal lung function and may therefore be more susceptible to further lung injury from non-SARS-CoV-2 respiratory viruses. 385,386

It is clear that the healthcare system must plan for a high burden of respiratory diseases this winter. As discussed in section 3.1.2.2, the continued use of some behavioural and environmental interventions by the public over the autumn/winter would help limit the spread of respiratory diseases and alleviate pressures on the healthcare system.

3.2.3.2 Norovirus

Norovirus outbreaks make up around 64% of gastroenteritis outbreaks in care homes and are most common during the winter months, and norovirus outbreaks among care home residents are associated with hospitalisations and deaths. 387 Historical data suggest that norovirus, under normal circumstances, causes approximately 32 outbreaks per 100 care homes per year, which could equate to a third of care home capacity affected by outbreaks, depending on the size of homes affected. 388 Traditional policies around management of norovirus infections in care homes relate to restricting nonessential movement in and out of hospital, quarantine of infected residents within their rooms, close attention to hand hygiene and use of PPE. 389 The competencies developed by care home staff during the pandemic should relate to improved management of norovirus outbreaks when they occur. Technological advances made during the pandemic, including the development of multiplex point of care testing that could be deployed in communities or care homes, has the potential to make norovirus diagnosis more straightforward. It is, however, important that public health agencies and Governments in all UK nations consider and model the likely impact of norovirus outbreaks, and how this might influence care home capacity and patient flow through the NHS during the coming winter months.

4. Managing the wider health and wellbeing impacts of the pandemic

Inequalities in health have been apparent for decades, and while the wider impacts of the COVID-19 pandemic have been experienced by all, vulnerable populations have been more adversely affected.³⁹⁰ Child poverty, food poverty and homelessness have all been exacerbated by the pandemic.³⁹¹ In addition, school closures, job losses and furloughing have all had significant impacts on society, particularly on mothers and single parents.³⁹²

In this section, we explore how the wider health and wellbeing impacts of the pandemic can be managed. We focus on the importance of managing hospitalisations to enable routine care to take place alongside COVID-19 related care, gaining a better understanding of long COVID, and the impact of the pandemic on mental health and wellbeing, as well as on the overall health of the population. We also explore how the pandemic has affected infrastructure capacity across primary, secondary and social care. Supporting people to deal with the wider health, wellbeing and economic impact of the pandemic was a key priority for the Patient and Carer Reference Group and in the public dialogue workshops.³⁹³

4.1 Managing hospitalisations

As described in our previous winter report, every winter results in considerable extra mortality and burden on health and social care resources, with an estimated 50,000 excess deaths reported in England and Wales and 4,800 and 1,500 reported in Scotland and Northern Ireland, respectively, in the winter of 2017/18. 394,395,396,397 Adverse weather also negatively impacts both physical and mental health. The increase in numbers of hospital admissions over the winter period due to infectious diseases could present serious challenges for the NHS, particularly with the limited bed capacity experienced due to current infection prevention and control (IPC) measures (see section 4.4.2.2).

As outlined in section 3.1, there is likely to be a surge in hospital admissions from COVID-19, albeit with considerable uncertainty in magnitude, as this will depend on levels of transmission and the speed of continued vaccine roll-out. Our current projections suggest that a peak of infections and hospitalisations might occur over the summer, but there is uncertainty around the timing of this potential peak. If COVID-19 infection rates and hospitalisations increase this autumn/winter, this could coincide with increased hospital admissions for influenza and respiratory syncytial virus (RSV). As described in section 3.2, hospital admissions for influenza could reach 2.2 times that of a normal year, and 2 times that of a normal year for RSV. Should the waves in hospital admissions for COVID-19, influenza and RSV occur sequentially, there may be less pressure on hospital beds. However, as outlined in section 5.1, this could leave the healthcare workforce fatigued with no respite between epidemics.

Alongside these epidemics will sit the usual winter burden on the healthcare system from non-infectious conditions that increase in prevalence or are exacerbated in the winter months, such as asthma, chronic obstructive pulmonary disease (COPD), ischaemic heart disease and stroke. ³⁹⁹ The health of the general public has also largely declined

over the course of the pandemic, as outlined in section 4.4.1, which will only cause further pressure where capacity in hospitals is already limited. IPC measures will need to be considered as part of any management of hospitalisations and are discussed further in section 5.3. To aid in capacity building last year, the UK government provided funding to access the private sector; similar initiatives may be needed this coming winter. 400

Consideration should also be given to the inequalities associated with hospital admissions. Disparities in hospitalisations between white and ethnic minority populations were reported during both the spring 2020 and winter 2020/21 COVID-19 waves. 401 For some outcomes, disparities have improved during the second wave; for example, an analysis of a population level Office for National Statistics (ONS) dataset found that Black ethnic groups saw no increased risk of death from COVID-19 compared to White populations. 402 However, Pakistani and Bangladeshi groups displayed greater risk. 403 The most recent Public Health England (PHE) and Intensive Care National Audit and Research Centre (ICNARC) data are showing increasing infections and admissions in ethnic minority populations at a younger age, which likely reflect low vaccination rates in these groups. 404,405

As discussed in section 5.2, if we are to avoid pausing routine care, in combination with addressing the backlog, enhanced IPC measures and limited bed capacity, it will be vital to ensure hospitals are adequately prepared and resourced to deal with an increase in hospital admissions over winter. Options might include the use of private sector capacity, or other settings such as surgical hubs, provided that they can be appropriately resourced.

4.2 Understanding and managing long COVID

The level of awareness and understanding of long COVID varied considerably amongst the public participants we engaged with in this project. While it was a major concern for the Patient and Carer Reference Group, the potential health complications associated with long COVID were not as widely recognised in the public dialogue workshops. 406

4.2.1 Defining and understanding long COVID

4.2.1.1 Defining long COVID

Similar to a range of other infections, COVID-19 is associated with a range of post infection syndromes of varying severity and symptoms that are yet to be understood. Long COVID encompasses a wide range of physical and mental health symptoms that persist after acute SARS-CoV-2 infection. 407, 408, 409, 410 There is a limited understanding of long COVID due to the diversity in presentation and severity of symptoms, making it difficult to define. There is also a lack of consensus internationally on the definition of long COVID, including the timeframes related to the persistence of symptoms used (ranging from 4 to 12+ weeks), posing further challenges to research, as findings are not always comparable. While research into long COVID is occurring, **further work is needed to reach a consensus on the definition and clinical diagnostic criteria for long COVID.**

The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners (RCGP) have developed a series of definitions to inform guidance on identifying, assessing and managing the long-term effects of COVID-19. We are aware that the guidance is being kept under review as further evidence emerges. The clinical definitions developed for the initial illness and long COVID at different times are as follows:

- Acute COVID-19: signs and symptoms of COVID-19 for up to 4 weeks.
- Ongoing symptomatic COVID-19: signs and symptoms of COVID-19 from 4 to 12 weeks.
- Post-COVID-19 syndrome: signs and symptoms that develop during or after an
 infection consistent with COVID-19, continue for more than 12 weeks and are not
 explained by an alternative diagnosis.

Long COVID has been reported to include a wide range of conditions, from those seen as less severe, such as loss of smell, to the more severe, which impact on quality of life, such as lung and vascular disease, weakness, chronic fatigue, concentration impairment, neurological and psychological sequelae (including depression and anxiety) and new or worsened disabilities. All, All, All, Long COVID was found in both asymptomatic people and patients that had received hospital treatment including in children, with adolescents at similar risk of post-acute sequalae as adults (however these studies did not include control groups). Similar data is emerging from other countries with different pandemic control restrictions globally. The National Institute for Health Research (NIHR) recently identified four potential subtypes of long COVID:

- 1. After-effects of intensive care including being unable to sit unaided or struggling to speak or swallow. Some patients may also be affected by depression or post-traumatic stress disorder (PTSD).
- 2. Post-viral fatigue, aching muscles and difficulty concentrating.
- 3. Lasting organ damage, including ongoing breathlessness, cough or tachycardia indicative of damage to the lungs or heart. Problems with the liver and skin have also been reported.
- 4. Fluctuating and varying intensity of symptoms.

Data also indicate an increased risk of readmission to hospital following acute COVID-19. 419 This risk was not confined to the elderly and was not uniform across ethnic groups. 420 Over a mean follow-up of 140 days, nearly a third of individuals who were discharged from hospital in the UK after acute COVID-19 were readmitted, and more than one in ten died after discharge, with these events occurring at rates four and eight times greater, respectively, than in the matched control group in the general population. 421 Rates of respiratory disease, diabetes, and cardiovascular disease were also significantly raised in patients with COVID-19. Rate ratios were greater for individuals aged less than 70 than for those aged 70 or older, and in ethnic minority groups compared with the white population. 422

4.2.1.2 Prevalence of long COVID

The ONS estimated on 2 May 2021 that 1 million people in the UK reported experiencing symptoms (ranging from mild e.g. loss of smell or taste, to more severe symptoms such as fatigue and heart palpitations) that persisted for more than four weeks after first suspected infection with SARS-CoV-2. 423 ONS also reported that from 20,000 COVID-19

positive individuals between April 2020 and March 2021, 13.7% continued to experience symptoms for at least 12 weeks.

Recent data from the REACT-2 study estimates that over 2 million people, or in total 6% of those infected in England, have experienced some form of long COVID for 12 weeks or more. 424 While the REACT-2 study found that the prevalence of long COVID increases with age, with a 3.5% increase in likelihood in each decade of life, other studies have identified that long COVID affects previously healthy individuals, without pre-existing conditions, with younger 'working age' adults and especially women at highest risk. 425 In addition, REACT-2 found that people from lower socioeconomic areas, people that were obese or people that smoked were at higher risk, while Asian people were at lower risk. 426 The CONVALESCENCE study recently reported that 17% of middle-aged people who report being infected by SARS-CoV-2 also report some form of long COVID, falling to 7.8% among younger adults. 427 The study found that functionally limiting long COVID for 12 weeks or more affected between 1.2% (age 20), and 4.8% (age 63) of people reporting COVID-19. 428

To inform provision of care and care planning, further studies with control groups are needed to ascertain prevalence and underlying causes of long COVID with more certainty. Efforts to do this have begun. They are yet unpublished, but suggest some similarity between long COVID symptoms and those reported after infection with influenza and community acquired pneumonias. 429 Studies that pre-date the pandemic indicate that reported prevalence of fatigue varies according to case definitions, methods of assessment, and study settings; 430 nevertheless an understanding of post-viral conditions is complicated by the prevalence of some symptoms such as fatigue in the community and in general practice (GP) patients. 431,432 This underpins the need for further research into long COVID, which is highlighted below.

4.2.1.3 Long COVID in children

To date, Multisystem Inflammatory Syndrome in Children (MIS-C) is the primary COVID-19 consequence studied in children. 433434 However, the ONS survey (April to December 2020) revealed that 12.9% of UK children aged 2 to 11, and 14.5% of children aged 12 to 16, have symptoms five weeks after their first infection. 435436 Symptoms like fatigue, muscle and joint pain, headache, insomnia, respiratory problems and palpitations are frequently reported, severe enough to affect daily activities in a high proportion. 437 Studies have also identified immunological differences between children that completely recovered from acute infection and those with long COVID. 438 As discussed in section 3.1.2.1, it is important to note that many of the symptoms of long COVID are also common in the adolescent population (e.g. fatigue, headache). The degree to which long COVID will have longer-term implications for children's health and wellbeing remains unclear.

4.2.1.4 Further research into long COVID is needed

As discussed above, while there are some data on the presentation of syndromes and on the short-term prevalence of long COVID, further research is needed. There is also limited data on the risk factors for developing long COVID, 439 the aetiology underpinning different sequelae, or effective support and therefore the health system requirements. 440 Data is lacking on the impact of vaccination on long COVID and of different variants on the risk of long-term sequelae. 441

There are several research studies investigating long COVID, including the REACT-2 and CONVALESCENCE studies outlined above. Other studies into long COVID include the PHOSP-COVID (exploring long-term health outcomes for patients who have been in hospital with confirmed or suspected COVID-19), the TLC Study (exploring susceptibility and potential therapies), the CLoCK Study (following up in 3,000 children and young people who tested positive for COVID-19), the HEAL-COVID study (comparing different treatments for longer-term outcomes for patients that were hospitalised with COVID-19) and the ISARIC study (following up adults and children in the UK and globally). 442,443,444

Further studies with appropriate control groups are needed to understand the prevalence, range, aetiology, severity and duration of long COVID; inform optimal clinical management for adults and children; and support health service planning and delivery.

4.2.2 Managing long COVID

There is currently no identified evidence on the best treatment and supportive care for long COVID. Emerging evidence indicates a need for multidisciplinary support, targeted to different syndromes and underlying aetiology, including empirical treatment, psychological therapy, physical therapy, rehabilitation and occupational support for adults, children and adolescents.⁴⁴⁵

Specialist 'long COVID' clinics have been set up as a form of administering multidisciplinary support bringing together doctors, nurses, physiotherapists and occupational therapists to offer both physical and psychological assessments and refer patients to the right treatment and rehabilitation services. However, the Patient and Carer Reference Group highlighted that some patients are unable to access these clinics. This has been reinforced by anecdotal reports via support groups. It will be necessary to ensure equitable access to long COVID clinics, including sufficient and comprehensive long COVID assessments, diagnosis, and treatments for all patients, including children and adolescents. These clinics should be delivered in parallel to, rather than at the expense of, routine clinical care, with integrated referral pathways to specialist assessments. The Patient and Carer Reference Group also highlighted the need for equitable employment and educational support for people living with long COVID. Some have drawn comparisons between long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), and highlighted challenges that have been faced by this community in terms of diagnosis and treatment.446,447

As the modelling shows a potential increase in the incidence of long COVID (Figure 1), we can expect an increase in outpatient requirements for imaging, biochemical and functional tests, outpatient review and rehabilitation for pulmonary and non-pulmonary disorders. An increase in patients with complex medical problems may lead to increased hospital admissions for patients with exacerbations of chronic lung and non-pulmonary disease. Increased pressure on existing primary care, post-ICU, rehabilitation, specialist 'long COVID' clinics, chronic fatigue and psychological support services can be expected at a time when capacity and capability of these services are constrained due to IPC measures, pressures to address the backlog of care are mounting, and chronic and acute

referrals delayed or exacerbated due to the pandemic are increasing. These issues are discussed in more detail in sections 4.1 and 5.2.

There is a need for studies into diagnostic assessments, intervention trials, surveillance and monitoring of long COVID to inform robust, evidence based clinical management guidelines and improve long-term COVID-19 outcomes for adults and children. Guidelines should be developed by multi-professional stakeholders, and patients, with mechanisms for regular review and updates as new evidence emerges. Equity in access to robust long COVID diagnosis, assessment and treatment clinics are paramount to improve outcomes for those living with long COVID. Equitable employment and educational support would reduce the risk of long COVID widening health inequalities.

4.3 Mental health

The COVID-19 pandemic has had a significant impact on the mental health of people living in the UK, at least temporarily, both directly through infection and indirectly through the wider social context of living in the pandemic. Improving mental health and wellbeing was a key concern for the Patient and Carer Reference Group and in the public dialogue workshops. 448

COVID-19 can affect the brain, triggering or exacerbating a wide range of neurological and neuropsychiatric disorders. ⁴⁴⁹ It has been found using the electronic health records of over 236,000 patients with COVID-19 that a third developed psychiatric or neurological conditions within six months of infection. ⁴⁵⁰ The COVID-19 Clinical Neuroscience Study (COVID-CNS) is currently investigating the neurological and neuropsychiatric effects of COVID-19 on UK patients, with a view to better understanding risk factors and improving treatment strategies. ⁴⁵¹

Many people have also experienced high levels of stress related to the pandemic, the risk to themselves, and its impact on others. Public health and social measures put in place to control infection, particularly lockdowns, have created an additional set of stressors, including social isolation and financial concerns. The mental health impacts of the COVID-19 pandemic on the general population, vulnerable groups and those in need of support from the social care sector are very likely to persist beyond the duration of the pandemic itself. 453,454

It has been shown that by late April 2020, **mental health in the UK** had deteriorated compared with pre-COVID-19 trends, especially in younger people, women, deprived groups and those with young children, who showed a greater increase in symptoms. ⁴⁵⁵ Similar results have been observed in young people, where increases in anxiety and significant impacts on wellbeing have been observed. ⁴⁵⁶ Evidence also shows a significant decline in maternal mental health during the pandemic. ⁴⁵⁷ However, between April and October 2020, the mental health of most UK adults remained resilient or returned to pre-pandemic levels. ⁴⁵⁸ Similarly, an overall significant decline in mental health symptoms was shown from May-July 2020, following an initial increase during March-April 2020. ⁴⁵⁹

The mental health of **ethnic minority groups** has been disproportionately impacted by COVID-19 with a clear increase in mental health inequalities.⁴⁶⁰ Pre-existing inequalities have exacerbated this (e.g. pre-existing challenges to access services) with men and health workers identifying with ethnic minority groups experiencing the largest increase. ^{461,462} **Local community groups and mental health services should be adequately resourced so that they can work together to facilitate access to service for the more severely affected.**

An increase in mental health problems has been observed among children and adolescents. 463 A 2020 follow-up of England's Mental Health of Children and Young People survey showed an increase in probable mental health problems reported in adults also affected 5-16 year olds in England, with the incidence rising from 10.8% in 2017 to 16% in July 2020 across age, gender, and ethnic groups. 464 Children, young people, and families have been substantially impacted by school closures and other disruptions to daily routines and educational goals. In particular, school closure has been shown to be associated with considerable deterioration of children and young people's health and wellbeing⁴⁶⁵ and impacts vary across ages and socio-economic groups.⁴⁶⁶ Among adolescents, depressive symptoms increased and mental wellbeing worsened significantly during the pandemic.⁴⁶⁷ Increased levels of stress, anxiety, and depression among university students have been linked to worry about their own health and that of their loved ones, difficulty in concentrating, disruptions to sleeping patterns, decreased social interactions, and increased concerns on academic performance. 468 There has been a worrying increase in the number of young people and emerging adults presenting to health services with eating disorders, often requiring urgent or emergency assessment due to their severity. 469

A large number of methodologically poor studies confuse the emerging picture, particularly as convenience samples often fail to reach vulnerable groups, such as those with disabilities, trauma experiences, existing mental health problems, migrant background and low socioeconomic status. ⁴⁷⁰ Furthermore, access to existing datasets, such as the national comorbidity surveys, should be expedited so that we make full use of the data that is currently available. ⁴⁷¹ Continuing to gauge the mental health status of adolescents and young people over time, and better understanding the mental health impacts of the pandemic, will be essential to inform targeted support this winter, and in the longer term.

Despite some studies showing how specific groups of the population have been disproportionately at risk of elevated levels of depression and anxiety during COVID-19, there is still a lack of consistent evidence. This could in part be explained by methodological differences in the measures, sampling strategies used, and the populations studied. There is currently a lack of evidence of a disproportionate increase in mental health problems among older people in the general population, when compared to young adults and adults, despite the larger impact the COVID-19 pandemic has had on this group of the population (higher levels of mortality, higher degree of shielding).

In addition to the impacts of the pandemic, adverse winter weather can negatively affect mental health and may result in an increased mental health burden this winter, 474

particularly if any restrictions on social contact are in place and it becomes more difficult to use outdoor spaces.

There was already a deficit in mental health service provisions in the UK before the pandemic, with long waiting times and insufficient specialist or quality services available. 475 The rise in mental health issues amongst children, young people and adults brought on by the COVID-19 pandemic will need to be closely monitored and managed carefully this winter with a range of clear support options and targeted support for all affected. Substantial expansion of Improving Access to Psychological Therapies (IAPT) programmes and high-quality community mental health services for young and old is urgently needed. Crisis and liaison services will need to be available and promoted all around the country.

4.4 Managing the impact of delayed diagnosis and disruptions to routine care

4.4.1 Health impacts of delayed diagnosis and disruptions to routine care

4.4.1.1 Delays in diagnosis and treatment

The strain the COVID-19 pandemic has placed on the NHS has profoundly disrupted routine care and diagnostic services for other diseases in the UK. The BMA estimates that between April 2020 and March 2021 there were 3.5 million fewer elective procedures and 22.27 million fewer outpatient attendances than 2019/20. Although screening programmes have now resumed, screening was delayed in 2020 to protect people from COVID-19. During the first wave of COVID-19 in the UK, there was an 84% reduction in referrals to the 2-week-wait urgent pathway for suspected cancer cases. It has also been found that the pandemic led to a reduction in the number of people referred, diagnosed and treated for colorectal cancer.

The consequences of delays to diagnosis and the resulting initiation of treatments on health outcomes is yet to be determined. Last year, one study examining the impact of delays in diagnosis caused by the pandemic on cancer survival outcomes in four major tumour types in the UK found substantial increases in the number of avoidable cancer deaths. 480 Delays in diagnosis, which could lead to delays in treatment and worse outcomes, have been observed in other disease areas. For example, a UK-based cohort study has found a significant reduction in diagnosis of type 2 diabetes, with older men from lower socioeconomic backgrounds being the most severely impacted. 481 A study of electronic health records found that there were substantial reductions in primary care contacts for a range of acute physical and mental conditions (including depression, anxiety, diabetes and heart disease) following the introduction of restrictions in March 2020. 482 Although further research is needed to ascertain whether these reductions reflect changes in disease frequency or missed opportunities for care, the study suggested that the conditions examined were sufficiently severe that any unmet need would have substantial ramifications for the people with the conditions as well as healthcare provision. It will be important to understand the full impact of delayed diagnosis on health outcomes across a range of health conditions so that effective mitigation strategies can be designed and implemented.

While the 'stay at home' messaging was successful in limiting the spread of the virus, it has been suggested that it also deterred people from seeking timely access to healthcare and intervention. AB3, AB4 NHS and government messaging in all UK nations should be clear and tailored during future COVID-19 outbreaks and emphasise the importance of seeking, and ways of accessing, care when needed. In addition, appropriate resources should be allocated to protect diagnostic services during future outbreaks.

4.4.1.2 Worsening of chronic conditions and public health

Prior to the pandemic, non-communicable diseases (NCDs) – such as cardiovascular diseases, cancers, chronic respiratory diseases and diabetes – were estimated to cause 89% of deaths in the UK. 485 People living with NCDs require regular care and are therefore particularly affected by disruptions to healthcare services. The pandemic has posed significant challenges to healthcare delivery, as exemplified by the substantial decreases in elective procedures and outpatient attendances between April 2020 and March 2021 compared to 2019/20, as described above. 486 A report into the impact of the COVID-19 pandemic on health services for NCDs published by the World Health Organization in May 2020 highlighted that three-quarters of the countries they surveyed reported a considerable degree of disruption of NCD services, mainly due to cancellations of elective care, lack of transport due to imposed lockdowns, insufficient staff and closure of hospital services. 487

As mentioned previously, the COVID-19 pandemic has affected screening, case identification, and referral systems for cancer, resulting in a substantial decrease in cancer diagnoses. As It also resulted in a substantial reduction in admission to hospital of patients with acute coronary syndrome, which is likely to have resulted in increases in out-of-hospital deaths and long-term complications of myocardial infarction. As study has also found that disruption in rehabilitation services for people with NCDs in various countries has potentially impacted their outcomes and consequently increased the burden of care. In the long term, the disruption to healthcare services is likely to mean an increase in people requiring healthcare services and lead to additional pressures on the NHS.

Obesity and related health problems have been found to be strong and independent determinants of severe COVID-19 disease. ⁴⁹¹ The COVID-19 pandemic may have played a role in increasing obesity, with people spending less time exercising, and increases in unhealthy eating habits under lockdown conditions. Other public health issues exacerbated by the pandemic include substance use disorders (SUDs), where access to the healthcare systems and support groups has been greatly diminished for vulnerable individuals. ⁴⁹² A UK survey on alcohol consumption in patients with alcohol use disorder has found an increase in alcohol consumption during the lockdown, and an increased risk of relapse. ⁴⁹³ Individuals with SUDs have faced heightened vulnerability and susceptibility to COVID-19, and experienced poorer health outcomes. ⁴⁹⁴ As discussed further in section 5.2, **the healthcare system must ensure it retains capacity to attend to, and reduce the backlog of, non-COVID-19 care.**

In addition, the pandemic has led to unequal healthcare disruptions, which if unaddressed, could contribute to the maintenance or widening of existing health inequalities, based on self-reported healthcare disruption (including access to

medication, procedures and appointments). 495 Examples of worsening inequalities around access to health services and adequate care have included women and those living with chronic illnesses experiencing more cancellations, and members of ethnic minority groups living with chronic illness requiring a higher number of care hours. 496

Added to this, we know that COVID-19 has disproportionately impacted disadvantaged groups. A report into the disparities in the risk and outcomes of COVID-19 published by PHE in August 2020 showed that COVID-19 mortality rates were twice as high in the most deprived areas and that socio-economically disadvantaged communities lived in geographic regions where there were outbreaks. 497 It also showed that the risk of dying among those diagnosed with COVID-19 was higher in ethnic minority groups than in White ethnic groups. As highlighted by the COVID-19 Marmot Review, COVID-19 has exposed and amplified existing health inequalities. 498 Public health agencies across all UK nations urgently need to address the wider public health impacts of the COVID-19 pandemic, and improve the UK's resilience ahead of any future outbreaks. In the longer term, Governments of all UK nations must address the wider social determinants of health (environmental, educational, employment, etc.) with a focus on decreasing the health inequalities that have led to the disproportionate impacts of the pandemic. The recently announced reforms to the NHS and public health system in England - including the establishment of the Office for Health Promotion, the UK Health Security Agency and Integrated Care Systems - present an opportunity to systematically reduce inequalities in health related to wider social determinants and access to care.

4.4.1.3 Deconditioning and disruption to physical activity

Deconditioning is the physical, psychological and functional decline that occurs as a result of prolonged inactivity and associated loss of muscle strength. Deconditioning can occur at any age but can occur more rapidly and severely in older adults and those with long-term conditions. Data has shown significant negative impacts of the COVID-19 pandemic on anxiety, motivation and energy, stability and ability to walk, memory, confidence in using public transport, and time spent on everyday activities and with family. These impacts were greater among people with long-term health conditions and those from disadvantaged socioeconomic backgrounds.

Since the onset of the pandemic large disruptions to physical activity, sleep, and time use have been observed with increased co-dependency between the maintenance of lifestyle habits and mental health: larger declines in physical activity were associated with significantly higher rates of depression. ⁵⁰¹ Sport England reports that levels of physical activity have decreased for children and adults, and that some differences in levels of activity between groups have widened as a result of the pandemic. ⁵⁰² It will be essential in the coming months not only to provide clear information on how to stay physically active and mentally healthy during the coming winter, but to facilitate access to the means to follow this advice. An ongoing research priority should be to establish the population prevalence of physical and cognitive deconditioning in the UK population. These data should be used to plan and prioritise reablement and rehabilitation resources to those most in need.

Deconditioning and the resulting loss of muscle (sarcopenia), bone (osteoporosis) and cardiorespiratory fitness will result in a less resilient elderly population more likely to lose their independence and develop long-term conditions, falls and fractures. ^{503,504} We are aware that a forthcoming report by Public Health England models how changes in strength and balance activity levels (informed by data from the Active Lives Survey from Sport England), as a likely consequence of COVID-19 mitigation measures, could lead to deconditioning in older adults (aged 65 and over). The modelling will provide projections on the number of individuals experiencing a fall at least once in a year in the older adult population (aged 65 and over), the potential additional cost in health and social care as a result of the increased number of falls, and potential future scenarios to mitigate these impacts. The report makes recommendations for commissioners and providers to mitigate the impact of deconditioning and to promote strength and balance exercise amongst older adults.

Reaching people at scale will demand a system change approach at every level of a community. For example, in Essex the Prevention and Enablement Model (PEM) is a 12-month 'test and learn' pilot that tests how the health and social care system in Essex can use physical activity to enable independence and improve population health by training carers and care home staff in how to get their residents more active. This is being evaluated and will deliver a whole system approach in getting the most vulnerable and frail adults more active. ⁵⁰⁵

The deconditioning of those already living with mental health difficulties or physical disabilities suggests that this winter, it will be important to ensure that the social care sector is ready to provide both domiciliary care as well residential care (particularly for the elderly). 506,507,508,509

4.4.2 Impact on primary, secondary and social care

There is currently an increased demand for healthcare due to long COVID, the consequences of delayed care, and the reduction in health seeking behaviour for non-COVID-19 conditions earlier in the pandemic (see sections 4.2, 4.4.1 and 5.2). This is combined with decreased capacity to provide services due to existing pressures, infection control and workforce challenges (outlined in sections 5.1 and 5.3, respectively). Several priorities for mitigation were also outlined in the Academy's previous winter report, which should be considered ahead of the coming winter. The services are the control of the section of the

4.4.2.1 Primary care capacity

Primary care deals with around 90% of patient contacts, with over 300 million patient consultations each year, compared to 23 million hospital emergency department visits. ⁵¹² Primary care is also becoming increasingly accessible due to digital platforms, and there has been a substantial increase in the number of appointments being delivered. In May 2021, the BMA estimated that GP appointments had increased by almost 2.8 million (11%) compared to March 2019, and over 4.3 million (18%) compared to March 2020. ⁵¹³ The increase in respiratory infections such as influenza and RSV expected over the coming autumn/winter, as identified above in section 3.2, will only add to the pressures already experienced.

Primary care has delivered over 75% of the COVID-19 mass vaccine rollout alongside routine patient care and community COVID-19 hot clinics (GP-led clinics for people with

COVID-19 symptoms to be seen face-to-face). Primary care is experiencing increased demand due to the sequelae of COVID-19, including long COVID, reduced secondary care and delayed presentation of illness. The increase in remote consultations for secondary care has also led to an increase in investigations in primary care, such as blood tests. The scale of the impacts on primary care may differ by area, as the number of patients per GP in England is 15% higher in the most deprived areas compared with the least deprived. ⁵¹⁴

A recent survey by Pulse revealed that general practitioners (GPs) are working 11-hour days and dealing with an average of 37 patients in a session, more than the 28 patients that is thought to be the safe daily limit in the pandemic. There is a continuous rise in consultations with the latest survey from NHS Digital showing a further increase in 2021 (Figure 6). We expect the pressures on primary care to intensify this autumn/winter, not least due to its ongoing role in the vaccination effort, including the delivery of influenza vaccinations this autumn (possibly in parallel with COVID-19 booster vaccines - see section 3.1.2.1); as more COVID-19 patients are treated in the community (rather than in hospital); as delayed treatment causes worsening of chronic conditions; and with the additional uncertainty of increased respiratory infections.

To safely deliver the anticipated levels of care this winter, the Governments and NHS bodies in all UK nations must ensure that primary care is adequately resourced, particularly as new work is transferred from secondary care. It is essential to allow current resources to remain and an increase may be needed. As discussed previously, the NHS will need to maintain its capability for mass vaccination throughout and beyond this summer and should explore the continued use of vaccination staff that aren't clinically trained to alleviate pressures on primary care. To further reduce pressures, the Governments and NHS bodies in all UK nations should consider additional measures to allow primary care to focus on the delivery of clinical care. Options might include pausing non-emergency non-clinical work, such as Care Quality Commission inspections.

The care in primary care is provided by a wider team of allied health professionals in extended roles, including prescribers from pharmacy, nursing and paramedic backgrounds, and physiotherapists. Community or district nurses provide a vital service to housebound patients. The partnership delivery model is flexible and the response to providing a COVID-19 vaccine shows that given appropriate resources the sector can rapidly respond to need.

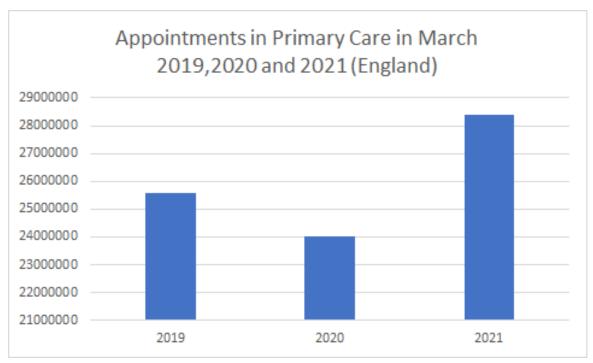


Figure 6: Comparison in the number of primary care appointments in March 2019, 2020 and 2021. 517

4.4.2.2 Secondary care capacity

Bed capacity is a major contributor to the backlog of patient care in hospitals, compounded by IPC measures, with anecdotal reports of elective surgeries being cancelled or postponed due to a lack of beds, despite there being available clinical staff. NHS England has seen a 6.1% reduction in general and acute beds between the last quarter of 2019 and the first quarter of 2021. 518

Prior to the pandemic, the UK had a lower number of beds - at 2.5 acute beds per 1000 people - than many comparator countries with similar health systems, such as France and Germany, with 6 and 8 beds per 1000 people, respectively. In 2018/19, overnight general and acute bed occupancy averaged 90.2%, and regularly exceeded 95% in winter. This lack of capacity has led to frequently cancelled operations and crowding in emergency departments. Challenges in social care provision have put further pressure on the number of beds, as patients wait in acute beds until social care packages or placements are available. 520

The Royal College of Emergency Medicine has calculated that, should admissions match those of the 2019/20 winter period in England, 127,300 hospital beds would be needed to maintain the same bed to admission ratio, representing an additional 5,000 beds in total. However, if a similar number of admissions to the winter of 2017/18 is experienced, the NHS will need just over 7,500 additional beds. 522

Demand is also increasing in critical care, with an average increase of 4% each year. In addition, many ICUs have not been designed to provide a COVID-19 secure environment and the impact of separating COVID-19 patients can result in a 30% drop in capacity in some units. There were a total of 5,446 ICU beds occupied in England in January 2021, an additional 2,023 beds when compared to January 2020. Similar increased

ICU bed occupancy was also reported for Wales and Northern Ireland, while data from Scotland were unavailable. 525

The increase in demand for acute care is driven by an increase in unwell patients requiring admission. While the focus should remain on tackling the backlog of care, this may put additional pressure on emergency departments as they will be unable to admit people to hospital and provide acute treatment in a timely way. This would ultimately lead to hospitals and ambulance services being overwhelmed and should therefore be factored into preparations.

There have been several reports outlining the necessary measures to increase capacity for acute and emergency medicine, including The Royal College of Emergency Medicine's report 'Summer to Recover: winter proofing urgent Emergency Care for 2021'. 526 The report includes recommendations to safely restore the number of acute hospital beds ahead of winter. Increasing the number of beds will need to take into consideration IPC measures (see section 5.3). It must be acknowledged that increasing bed capacity will require extensive workforce planning as outlined in section 5.1. The Faculty of Intensive Care Medicine has outlined requirements for Critical Care staffing, including best practice considerations to build a sustainable workforce. 527 The Intensive Care Society has also set out steps to restore Critical Care services during and after the pandemic. 528

4.4.2.3 Social care capacity

In order to minimise pressures on secondary care, it is vital that social care capacity is available for residents. The Governments and social care providers in all UK nations should prioritise support and protection for care home residents to reduce the pressures on secondary care through admissions, and also ensure they can be discharged safely from hospitals to social care settings.

The care home sector is predominantly made up of small and medium enterprises, many of whom have been left in financially precarious situations as a consequence of the pandemic. Expenditure on Personal Protective Equipment (PPE), environmental modifications, and changes to staffing requirements have been compounded by reduced occupancy because of COVID-19 related deaths and reduced admissions to care homes. It will be important to protect care homes from the financial pressures to ensure they remain open to maximise capacity and therefore reduce pressure on the NHS. The Adult Social Care Infection Control Fund released in instalments over the course of the pandemic has been an important lifeline to many businesses within the sector that remain vulnerable going into next winter. As discussed previously, consideration should be given to extending this fund for sufficient duration to meet the financial needs of care providers with regard to staffing, and extended to allow additional infection control measures, such as ventilation, to be implemented.

5. Continued disruption to health and social care service delivery

5.1 Workforce management

The added demands of COVID-19 on an already-stretched workforce has led to concerns about the impact on the mental health of frontline health and social care staff in terms of burnout, anxiety, depression and post-traumatic stress disorder (PTSD).⁵³² This prolonged period of stress, high illness levels and the lack of many normal coping strategies needs to be addressed to reduce burnout and enhance resilience, particularly as we approach the winter period. It will also be necessary to review health and social care staff retention rates and monitor how many are leaving the sectors. Workforce challenges should be considered alongside infrastructure capacity, as discussed in section 4.4.2.

5.1.1 Health and social care staffing levels

The health and social care sectors have experienced prolonged workforce vacancy rates, with shortages of over 100,000 full-time equivalent (FTE) staff reported by providers across NHS England prior to the pandemic, equating to about 8% of the workforce. More recently, NHS hospitals, mental health services and community providers are reporting a shortage of nearly 84,000 FTE staff, severely affecting key groups such as nurses, midwives and health visitors. Safe General practice (GP) is also reporting a shortage of 2,500 FTE general practitioners (GPs).

Longstanding issues with vacancy rates of around 8% (122,000 FTE staff) across adult social care and high staff turnover have been compounded by the pandemic due to measures such as isolation and regular testing. The impact of recently introduced policies, such as mandatory vaccination for care home workers, are not yet understood but could lead to a further reduction in social care staff. 537

During the early stages of the COVID-19 pandemic, the workforce shortages were partially addressed by re-recruiting retired health and social care staff, including 7,000 former nurses and 11,800 doctors through temporary registration. ⁵³⁸⁵³⁹ Alongside this, clinical staff were redeployed to acute areas to deal with the surge of hospitalisations. However, as the NHS looks to address the backlog of care, this resource will no longer be available for any future surge in hospitalisations. ⁵⁴⁰ It would be reasonable to explore extending temporary registration of professionals to more general work this year to help address the backlog of care and relieve workforce pressures.

The high rates of COVID-19 infection amongst NHS staff led to unprecedented work absences due to sickness, with 1.7 million days' work lost due to COVID-19-related absences between April and September 2020 alone. ⁵⁴¹ In addition to higher rates of infection, health and social care workers experienced the highest prevalence rates of self-reported long COVID, with 3.6% and 3.1% reported respectively in statistics released by the Office for National Statistics (ONS). ⁵⁴² Additional staff absences due to COVID-19 infection, self-isolation and long COVID are likely to occur over the coming summer, autumn and winter (see sections 3.1 and 4.2) and should be factored into workforce planning.

The overall impact of leaving the EU on the health and social care workforce is yet to be determined. However, the number of nurses and midwives from Europe leaving the Nursing and Midwifery Council's register increased from 1,981 in 2015/16 to 2,838 in 2019/20, with the number joining decreasing by 90% over the same timeframe. ⁵⁴³ It is estimated that at least 5,000 more nurses a year will need to be recruited from overseas to fill the shortfall while measures to increase domestic training capacity take effect. ⁵⁴⁴ The Government has committed to recruiting an additional 12,000 nurses from overseas by 2024/25. However, this will not adequately fill the workforce shortages faced this coming winter. ^{545, 546}

Potential measures to optimise the current workforce could include transferring or sharing duties, which allow for the transfer of duties from highly qualified healthcare workers to those with less training and fewer qualifications and the sharing of duties with an equally qualified cadre of healthcare workers, respectively. ⁵⁴⁷ Similarly, upskilling staff to take on a wider range of work could help with workforce pressures.

It will be important to ensure sufficient temporary funding to allow for increased workforce over the summer, autumn and winter, for example through retaining retired staff who volunteered to return to work, rapid recruitment of new staff and accelerated training. This will ideally allow staff to rest and recuperate, ensuring safe and effective patient care over winter. Transferring or sharing duties, and upskilling staff to support clinical care could also play a role in improving staffing levels this winter. In the longer term, the chronic understaffing of the health and social care sectors needs to be addressed, including the expansion of specialist staff groups like ICU, as these workforce issues long precede COVID-19 and have been exacerbated by the pandemic.

5.1.2 Burnout and burnaway

Evidence submitted to the House of Commons Health and Social Care Committee's report recognises that NHS staff are 50% more likely to experience work-related stress compared with the general population. There has been a further requirement of staff to go 'above and beyond', with an estimated 56% of NHS staff working additional unpaid hours on top of their contract. The report recommends that national bodies must continue to monitor the impact of COVID-19 on the NHS and adult social care workforce.

The latest NHS staff survey shows that almost half of NHS staff in England (44%) have reported feeling unwell from work related stress, the highest rate recorded in the past five years. ⁵⁴⁹ For many NHS staff there has been little respite since the beginning of the pandemic, as even when cases of COVID-19 decrease, there is an unprecedented backlog of clinical work. 51% of respondents to the BMA's latest COVID-19 tracker survey reported a worse state of overall health and wellbeing than during the first wave of COVID-19, while 59% reported higher-than-normal levels of exhaustion or fatigue. ⁵⁵⁰ Despite a reduction in face-to-face consultations, the amount of patient contact has not decreased. ⁵⁵¹ The significant changes to working practice, environments, and the marked decrease in face-to-face consultations, particularly in primary care, have created many challenges and caused distress to some. ⁵⁵²

Nursing staff report similar difficulties, with over half of the members who responded to a Royal College of Nursing (RCN) survey in May/June 2020 describing lower morale than pre-pandemic, and nearly 4 in 10 saying staffing levels had worsened, particularly in independent and private sector social care. ⁵⁵³ Further findings from the RCN show that over three quarters report stress levels have increased since the pandemic started, both among their colleagues (87.1%) and themselves (77.2%) while a high percentage (84.1%) stated they were worried about health and safety. ⁵⁵⁴ 75% of social care staff surveyed by the GMB agreed that their work during the pandemic had had a serious negative impact on their mental health. ⁵⁵⁵

Factors contributing to burnout and loss of resilience are identified as chronic excessive workload, a large number of vacancies, a high intensity of work, low pay (particularly in social care), discrimination (particularly against ethnic minority groups) and poor systems and working cultures. ⁵⁵⁶ In addition, unprecedented levels of abuse and aggression from patients towards NHS staff at GP surgeries have been recently reported, with a poll suggesting 75% of GP surgery staff across the UK face daily abuse. ⁵⁵⁷

The impact of these challenges is leading some to consider leaving the profession - when asked if they have changed their career plans for the next year, 26% of doctors said they were more likely to take an early retirement, another 26% said they were more likely to take a career break, and 18% said they were more likely to leave the NHS for another career. Early retirement rates for doctors have increased in recent years, trebling since 2008. A recent survey from the Royal College of Physicians reported that 27% of consultants expect to retire in the next three years - this will place further pressures on the healthcare system.

Mental health illnesses are consistently the most reported reason for sickness absence, accounting for 26% of all sickness absence in December 2020. There is therefore a need for adequate occupational health physicians to give support to health and social care staff affected by the pandemic. There are a range of staff support packages in place across the healthcare services in the UK nations. 162,563,564,565 It will be important to ensure these are adequate to support staff in light of the pandemic.

Given the increases in reported anxiety and low mood, primary care providers are likely to see an increase in patients reporting mental health difficulties, further increasing their workload. For people suffering from more extreme mental health issues, such as PTSD, formal mental health assessment and treatment is likely to be needed. However, the mental health workforce in England remains understaffed, with around 12% of all medical and nursing vacancies in mental health services. ⁵⁶⁶ In addition, compassion fatigue, secondary traumatic stress and vicarious traumatisation have all been recognised as pathways to occupational burnout for mental health professionals, with between 21% and 67% reported to experience burnout at work. ⁵⁶⁷

There will not be a 'one size fits all' solution to the mental health challenges faced by the health and social care workforce, and interventions need to be adapted to different individuals and needs. Although there have been several studies looking at the issue, many lack explicit sample frames and appear to have very low response rates, making the representativeness of their results questionable. Many surveys are cross-sectional,

which, while potentially useful as snapshots, offer little to identify which factors might be predictive of mental health problems, and hence few possible foci for interventions.⁵⁶⁸

Improved research with standardised psychiatric interviews, longitudinal designs, well defined sample frames, and assessment of response rates and bias are required to avoid unnecessarily pathologising of ordinary responses to extraordinary situations, and overlooking those most at risk. As identified in the Health and Social Care Select Committee report, it will be important to improve assessment of staff wellbeing and ensure adequate support for staff mental health.⁵⁶⁹

Fatigue amongst the health and social care workforce will become increasingly likely regardless of when a third COVID-19 wave occurs. With an increase in influenza and respiratory syncytial virus (RSV) infections anticipated over the autumn/winter, a preceding COVID-19 wave in the autumn will leave the workforce challenged. Likewise, should a COVID-19 wave occur over the winter, it will only add to the pressures to care for COVID-19 patients alongside influenza and RSV patients.

Careful workforce planning by NHS bodies across all UK nations for both primary and secondary care is needed in preparation for expected pressures over the coming months, as suggested by our modelling for COVID-19, influenza and RSV (section 3.2). Contingency measures for our COVID-19 reasonable worst-case scenario (Annex 6) should also be considered.

5.1.3 Improving occupational health

While psychological interventions aimed at enhancing resilience might be beneficial, there is a need to tackle the cause of occupational and environmental challenges. Measures include ensuring an adequate workforce, providing a supportive environment for staff, ensuring staff feel valued (e.g. by facilitating them to take annual leave), tackling discrimination, as well as improving access to wellbeing services.

Measures must also be taken to protect the health and social care workforce from COVID-19. It is estimated that between 26 April to 7 June 2020, 10% of all COVID-19 infections were in patient-facing healthcare workers and resident-facing social care worker. ⁵⁷⁰ Seroprevalence studies for COVID-19 antibodies have demonstrated an increased rate of seropositivity in healthcare workers, including non-clinical staff, compared with the general population, with the highest rates in clinical staff involved in direct care of patients with COVID-19. ^{571,572,573} Appropriate infection prevention and control (IPC) measures such as provision of personal protective equipment (PPE) are outlined in further detail in section 5.3.

As mentioned in section 3.1.2.1 of the report, ensuring that strategies are in place to maximise vaccination coverage in health and social care workers for both COVID-19 and influenza, including non-clinical and agency staff, will be vital to improving the occupational health of the workforce. Barriers to vaccination must be eliminated to maximise control of infection and to protect staff and patients.

5.2 Managing the backlog of care

5.2.1 Elective care

The healthcare system must ensure it retains capacity to address and reduce the backlog of non-COVID-19 care (see section 4.4.2). Robust processes should be in place to ensure clinical prioritisation of elective procedures (e.g. regular clinical reviews of waiting lists), and access to treatment should be prioritised by clinical need rather than by length of wait to ensure those most in need of care are prioritised.

As discussed in section 4.4.1, the pausing of most elective outpatient and inpatient activity during the pandemic has led to a backlog in elective care for both inpatients and outpatients, with recent reports of 5.1 million people on waiting lists. ⁵⁷⁴ The health service faces an unprecedented challenge in dealing with the backlog of care while COVID-19 is still a major public health challenge. The demand for both primary care and secondary care, whether urgent or elective, is already putting pressure on the healthcare system. ^{575,576,577,578} Reducing the backlog of care was an important issue for the Patient and Carer Reference Group; interestingly this was not seen as a major issue in our public dialogue workshops with a sense of confidence that the NHS could handle the caseload. ⁵⁷⁹ The measures taken to aid health and social care during the pandemic (e.g. regulatory bodies allowing retired staff to return to work, reduced requirement for appraisal and lighter touch inspection regimes), should remain in place if possible, in addition to efforts to keep COVID-19 levels low nationally.

Attendances to emergency departments in England in March 2021 were 14% higher than in March 2020. There is a similar increase in the proportion of acute admissions. This pressure is exacerbated by IPC measures, including the reduction in inpatient bed capacity. An increase in non-COVID-19 emergency admissions may lead to elective work being cancelled.

The total number of surgical procedures carried out in England and Wales in 2020 was 3,102,674 compared with the predicted number of 4,671,338. This represents a 33.6% reduction in the national volume of surgical activity. There were 763,730 emergency surgical procedures (13.4% reduction) compared with 2,338,944 elective surgical procedures (38.6% reduction). The cumulative number of cancelled or postponed procedures was 1,568,664. It is estimated that this will increase to 2,358,420 up to December 31, 2021. The volume of surgical activity in England and Wales was reduced by 33.6% in 2020, resulting in more than 1.5 million cancelled operations. This deficit will continue to grow in 2021. S83

To address the backlog of care, it is estimated that outpatient clinical activity would need to increase to well above pre-pandemic levels, and remain sustained during any future COVID-19 outbreaks. The BMA has suggested that an increase to 110% of pre-COVID-19 levels could take up to five years to reduce the backlog of elective care in England back down to 2019 levels.⁵⁸⁴ An increase of 13-20% over the most recent comparable pre-COVID-19 month, March 2019, would be needed to tackle the backlog.⁵⁸⁵ Medical outpatient appointments would also require a 14-17% increase in activity. For diagnostic

tests, a 30% increase in endoscopy⁵⁸⁶, and a 15% increase for other diagnostic tests is needed.⁵⁸⁷

The NHS has announced a £160 million initiative to tackle waiting lists and develop a blueprint for elective recovery as early reports show the health service is recovering faster after the winter 2020/21 wave of the COVID-19 pandemic. The 'elective accelerators' will each receive a share of £160 million along with additional support to implement and evaluate innovative ways to increase the number of elective operations they deliver. The £160 million is unlikely to make a large difference in terms of direct care due to the lack of inpatient bed and workforce capacity, which are explored further in sections 4.4.2 and 5.1. Clear and transparent communication by the Governments and NHS bodies in all UK nations is required to inform the public of the challenges that the NHS is facing and the likely impact on care giving, as well as the processes in place to ensure safety while prioritising those most in need.

NHS bodies should explore further measures to help address the backlog of care and rapidly implement novel solutions in order to deal with the expected rise in healthcare provision needed over the autumn/winter. Measures could include maintaining a focus on clinical care, and pausing non-emergency non-clinical work (e.g. Care Quality Commission inspections), the use of private sector capacity or other settings such as surgical hubs, as well as continuing emergency registration of retired healthcare professionals, and increased transferring or sharing of duties, as explored in section 5.1.

5.2.2 Digital consultations

Digital consultations are now well embedded throughout healthcare, and in general offer advantages in both infection control and convenience. Whereas telephone consultations may have been common in some settings (e.g. primary care), video consultations were less so and have rapidly expanded in use during the COVID-19 pandemic to reduce social mixing and reach patients who were isolating. The advantages of video consultations are the ability to have rapid access to a GP without taking time off work and to see those who are isolating or who are less able to leave the house. It is possible to bring relatives and carers onto calls and there is evidence that patients can be more open during a virtual consultation compared to face to face. There have been overall positive reports about remote consultation from clinicians surveyed during the pandemic, although experiences varied depending on their team.

However, there is a lack of evidence on the safety and health outcomes compared to inperson consultations and there is concern that clinicians have not been fully trained to consult with patients virtually. There is an urgent need for more evidence about the efficacy and acceptability of digital consultations. The NHS should work to optimise the balance between remote and in-person consultations to ensure the best outcomes for patients.

In addition to questions over the efficacy of remote consultations, there are concerns around the ability to access healthcare digitally for some groups. For example, older people with cognitive and sensory impairment are large users of health and social care services but are less likely to have access to technologies and may be less able to

engage with them due to their impairments. Similarly, people who are from lower socioeconomic backgrounds or those who do not speak English as a first language may be less able to access and engage with remote consultations.⁵⁹¹

The Patient and Carer Reference Group outlined the need to balance COVID-19 and non-COVID-19 care and voiced concerns over contracting COVID-19 in healthcare settings. The group also expressed the need for different ways of accessing healthcare and expressed concerns over remote consultations leading to poorer health outcomes and exclusion of people unable to access care digitally.

Data and technology should be used to overcome, not exacerbate, inequalities. Greater use of data and new health technologies can come with associated societal concerns about exploitation and possible harms. Gathering appropriate and reliable data will need locally and culturally appropriate systems and solutions alongside equitable and responsible sharing of information. Some technological initiatives, used appropriately and designed well, may also have longer-term benefits for specific groups, such as better data on those with disabilities. Simply gathering more and better data on underrepresented groups is not a solution to inequalities in and of itself, and efforts to implement technological 'quick fixes' may have unpredictable or unwanted outcomes. Further information regarding data considerations can be found in Annex 8.

The Governments and NHS bodies in all UK nations must ensure that appropriate access to care is provided in a way that does not widen the disparities seen during the pandemic in populations such as older people, those from lower socioeconomic areas and ethnic minority populations. Designing flexible services that can enable and prioritise in-person consultations for these groups, even at the height of an outbreak, is essential for the coming winter.

Shorter-term measures have been proposed to mitigate the wider increase in demand. These include novel care delivery methods such as surgical hubs, virtual wards and home assessments, 3D eye scanners, at-home antibiotic kits, 'pre-hab' for patients about to undergo surgery and AI in GP surgeries. 'Super Saturday' clinics – where multi-disciplinary teams come together at the weekend to offer more specialist appointments – will also be trialled. ⁵⁹² While these initiatives may provide an opportunity to introduce innovative service delivery methods, it will be important to build an evidence base and evaluate such initiatives to determine their efficacy, safety, and the most effective way to reduce inequalities.

5.3 Preventing transmission in health and social care systems

The interconnected health and social care systems remain a key high-risk environment for high consequence transmission of SARS-CoV-2, leading to disruption of care due to staff absence and a higher likelihood of severe infection and death among the most vulnerable patients. These systems are also highly connected with communities and as community cases decline, cases within healthcare settings and particularly immunocompromised patients could also become a primary risk for emergence of new variants.

There are still little publicly available surveillance data or analyses of hospital-acquired COVID-19 infections among patients or staff, and we still lack comprehensive data on the death rate in these groups, substantially limiting full understanding of the impact and contribution of healthcare-acquired COVID-19 to the pandemic in the UK, and this restricts our ability to develop evidence-based plans to mitigate this issue.

However, it is estimated that 20-25% of patients hospitalised with COVID-19 had nosocomial infections in the first wave.⁵⁹³ Data showed that 5-10% of patients hospitalised with COVID-19 between November 2020 and March 2021 had symptoms that began ≥7 days after admission,⁵⁹⁴ while an analysis of NHS England data showed over 11,000 cases of hospital-acquired COVID-19 in the first 24 days of January 2021.⁵⁹⁵ A freedom-of-information request indicated that between March 2020 and May 2021, over 32,000 patients were reported with hospital-acquired COVID-19 across 81 trusts, with 27% dying within 28 days.⁵⁹⁶

There were 6,811 outbreaks in 15,476 care homes up to 19 July 2020,⁵⁹⁷ and 29,405 deaths of residents in care homes involving COVID-19 up to 4 June 2021.⁵⁹⁸ Taken together, these incomplete data suggest that healthcare associated COVID-19 infection is a critical issue where we lack data and understanding.

5.3.1 Improving surveillance of nosocomial infection

A key priority is to improve the timeliness, completeness and availability of data on the extent and transmission of healthcare acquired cases of COVID-19. This should include timely data on surveillance, outbreaks, investigations, root-cause analysis and should report infection in both patients and healthcare workers, including where they are affected in the same setting, so that comprehensive mitigations and improvements in respiratory hygiene can be put into place, addressing behaviours, environments and vaccination.

Infection control systems in health and social care should prioritise rapidly controlling outbreaks in hospitals and care homes. This will require a nationwide hospital surveillance system, linked to the social care sector, to track and analyse nosocomial infections, and inform locally led outbreak control approaches.

Strategies to learn from outbreak investigations and share best practice should be implemented, including effective ways of ensuring new understanding or evidence (e.g. for transmission mechanisms or the effectiveness of mitigation) can be collated at a national level to support actions in other hospital trusts.

Data on health and social care associated COVID-19 infections, including analysis of outbreak clusters, should be collected, with transparent and timely reporting on a national level to facilitate effective IPC responses and sharing of best practice. The data should also be reported to regulators as a key quality measure, with senior leadership teams held responsible for strategies to tackle hospital-acquired infection rates.

5.3.2 Infection control in health and social care systems

Infection prevention and control must remain a key priority in hospital and social care. An enhanced evidence base is required to inform strategies for effective IPC and optimised implementation. In improving IPC measures, a proportionate approach must be taken to allow safe visiting of relatives and loved ones in hospitals and care homes. This can be achieved through clear guidance on the appropriate use of testing, behavioural and environmental interventions, and taking account of the vaccination status of visitors, residents and patients. Achieving a proportionate approach will enable family and loved ones to interact and secure the wellbeing of patients and residents.

5.3.2.1 Understanding transmission routes in healthcare settings

There is a lack of robust data on the extent of and risk factors for transmissions in health and social care settings, and there is limited analysis of outbreak clusters. This means that there is limited evidence to understand transmission routes, patient-healthcare worker interactions, the influence of the environment, effective mitigation strategies and how risk factors have changed over the course of the pandemic.

There is little systematically collected, publicly available surveillance data on healthcare-associated COVID-19 infections, and analysis of factors affecting transmission in healthcare is limited to a small number of case and cross-sectional studies, cohort studies and reports from government agencies. A detailed study of over 10,000 staff in the spring 2020 wave identified heterogeneity in risk across hospitals with higher rates among staff working in COVID-19 facing areas, but indicated that those in intensive care were relatively protected, likely by the bundle of PPE. The study also highlighted positive test results were more likely in Black or Asian staff (regardless of role) and in porters and cleaners. During the spring 2020 COVID-19 wave, there were reports of ethnic minority groups receiving inadequate PPE. The NHS needs to ensure full investigation of transmission and outbreaks, prompt and transparent reporting, and publicly available data on rates of hospital-acquired infection so that those factors influencing transmission can be understood and mitigated.

Modelling of outbreak clusters from the spring 2020 wave at one Trust suggests a superspreading pattern where 20% of individuals caused 80% of infections and suggested patients were more likely to be infected by other patients rather than healthcare workers. ⁶⁰³ A recent review of the risk of SARS-CoV-2 acquisition in healthcare workers by the Health Protection Scotland (HPS) Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) group also highlighted the poor quality of evidence relating to the elevated risk of infection in healthcare workers, including incomplete understanding of the relative contribution of transmissions from patients to staff in clinical areas *versus* staff-to-staff in breakrooms, or from non-work settings. ⁶⁰⁴ A summary from the Scientific Pandemic Influenza Group on Modelling (SPI-M) of transmissions in healthcare settings during the spring 2020 wave suggested that nosocomial infections acquired by patients and by healthcare workers were most commonly due to transmissions within rather than between these two groups. ⁶⁰⁵ This suggests that while IPC strategies might be successful in preventing transmissions at the clinical interface between patients and staff, **there is a need to understand and**

differentiate risk of continued infections after the implementation of IPC policies, so that residual transmissions can be prevented. Studies integrating genomic and epidemiological data have the potential to provide additional insights to guide and identify gaps in IPC policies, for example relating to the source and direction of transmission. 606,607,608

Over the course of the pandemic, our understanding of transmission mechanisms has evolved and we now appreciate the increased risk of transmission through inhalation compared to the risk of transmission from the virus on surfaces. This includes emerging evidence for long-range airborne transmission in settings where aerosol generating procedures are not taking place. There remains inconsistency between different sources of guidance on mitigating all routes of transmission in health and social care environments. 609,610,611,612

The limitations of conventional categorisation of respiratory transmission into droplet or aerosol were discussed in a recent SAGE paper, with evidence suggesting that SARS-CoV-2 viral emissions (and possibly other respiratory viruses such as influenza) span the full-size spectrum of respiratory aerosols and droplets; this has implications for the IPC measures that need to be considered. Current IPC guidelines have a focus on behavioural and administrative controls, such as cleaning, hand hygiene, PPE, and testing and separation of patients into pathways depending on SARS-CoV-2 infection risk. Although the most recent guidance recognises the need for IPC to be adapted at a local level based on effective risk assessment, there is still need for a more widespread recognition of the importance of small aerosol transmission, both at close proximity to an infected person and when sharing air in the same area of a healthcare setting.

As more transmissible variants have dominated community transmission over the second wave and into summer 2021, it will be crucial to further evaluate data on transmission within healthcare settings to understand how and where these variants are transmitting, whether the effectiveness of IPC measures has changed over time, and whether there needs to be further changes in response to variants of concern.

5.3.2.2 Enhancing IPC measures

The IPC measures set out in our previous report should be considered to minimise nosocomial COVID-19 infection.⁶¹⁵ We heard from The Royal College of Pathologists that there is a need for clear guidance from the government and a transparent process for the acquisition of appropriate PPE in time for winter.

Examples of IPC measures associated with reductions in probable hospital-acquired COVID-19 have included introduction of universal visor use for patient care, rapid testing for SARS-CoV-2 in emergency departments, and removal of beds to increase bed spacing, along with rapid enhanced staff testing, extended use of PPE, contact tracing, and vaccination. However, there are evidence gaps in the effectiveness and implementation of IPC measures within hospital clinical and non-clinical areas including the proportion of the healthcare estate with effective ventilation, behavioural interactions with PPE, and the impact of technologies such as air cleaning devices. There has also been very little evaluation of individual components of IPC and it is now challenging to know which elements are effective and which elements might be deprioritised in

healthcare or social care settings. Consideration should be given to the need to reduce COVID-19 transmission risk versus the broad challenges to quality of life for those in care homes. Trials into infection control strategies, including technology solutions (carbon dioxide monitoring for ventilation, air cleaning), cleaning approaches, PPE and behavioural interventions, are needed to address these evidence gaps and inform future IPC measures and guidance. These are needed alongside rapid observational data from systematic outbreak investigations to inform ongoing learning within the NHS to mitigate risks of transmission.

Assessments of the quality and effectiveness of infection prevention and control measures should be conducted to identify gaps in capacity and measures to safely care for patients with respiratory infection. In addition, it will be important to strengthen and support the national IPC capacity and the role of Directors of Infection Prevention and Control (DIPC) as they play a vital role both within the hospital and at the interface with other healthcare settings, including residential care, and with the local authority and directors of public health, PHE and its successor organisations.

Data from Public Health England (PHE) suggests that seeding of infection from hospitals into care homes occurred early in 2020 but was largely prevented by infection control and quarantine measures introduced as the pandemic progressed. Alterations to discharge and transfer policies between care settings must remain cognisant of the possibility that seeding could occur again if and when current policies are relaxed, and surveillance should allow for detection of this. Such coordination will be aided by data linkage approaches as discussed in Annex 8.

As discussed in section 3.1.2.2, guidance, training, and financial investment will be needed to ensure interventions can be properly implemented. Consideration should be given to extending existing financial instruments, such as the Adult Social Care Infection Control Fund, for sufficient duration to meet the financial needs of care providers with regard to staffing, and extended to allow additional IPC measures to be implemented.⁶²⁰

As identified in section 3.1.2.3, point of care multiplex testing will be required given the strong possibility of concurrent epidemics (influenza, RSV, and COVID-19) among patients admitted to hospital to allow for patient cohorting and other IPC strategies, as well as effective and appropriate clinical management. Rapid diagnostic tests for influenza, in addition to COVID-19, could also be implemented this winter to inform the use of influenza antivirals.

5.3.2.3 NHS Estate and healthcare infrastructure

Building design may act as a barrier to compliance with IPC guidance and there is a need for more detailed consideration of the role of buildings and the healthcare environment in COVID-19 transmission risk and how this can be managed and improved. This includes evaluating the influence of the environment on the flow and layout of activities and how people interact, including potential COVID-19 free areas or 'green pathways', and the identification of poorly ventilated spaces in clinical and non-clinical areas. Guidance on the importance of the environment also needs to consider primary care settings (e.g. GP practices, dental surgeries and pharmacies), which may not have been

designed with infection control as a consideration, and where actions such as opening windows may conflict with patient privacy and building security concerns. There is a need for a national strategy to evaluate all areas of the healthcare estate and to identify those that will require improvement to optimise infection control. In the short term, all Trusts should optimise use of their estate to mitigate transmission, including identifying spaces that are poorly ventilated and may need immediate improvement or alteration to their use. A more in-depth audit would be beneficial to understand the scale of environmental upgrades that may be required across the NHS estate in the medium to long-term. Evidence generated on the effective control of COVID-19 in hospitals needs to inform the next generation of buildings, and enable renovations of existing spaces to make them respiratory-infection safe.

At the request of the Government Chief Scientific Adviser, the Royal Academy of Engineering is undertaking a project on infection resilient environments. This project is likely to provide further details on improvements that can be made to infrastructure to improve infection control. An interim report of its findings has been published.⁶²³

5.3.3 Vaccination of healthcare workers

Given the possible surge in influenza this autumn/winter, maximising the uptake of influenza vaccination to near universal coverage in eligible populations, including health and social care staff, will be crucial for this winter (see section 3.1.2.1). Priority COVID-19 vaccination of health and social care staff began in December 2020, and results from a large cohort study of hospital-based staff showed that by 5 February 2021 vaccine coverage had reached 89%, with subsequent reductions in symptomatic and asymptomatic infections in the vaccinated group; 624 although these data should be interpreted with caution given the convenience sampling and potential for selection bias within this study. There is a need to collect robust epidemiological data to explore the impact of staff vaccination rates on outbreaks in health and social care.

We note that the Government is planning on enacting new legislation making COVID-19 vaccination a condition of employment for social care workers and that further public consultation is underway to explore making COVID-19 vaccination mandatory for all NHS staff. The impact of this on staff recruitment and retention remains unclear.

Strategies to maximise vaccination coverage for COVID-19 and influenza in health and social care workers, including non-clinical and agency staff and newly recruited staff, require clear communication, addressing misunderstanding or misinformation to target groups who are vaccine hesitant, and ensuring easily accessible opportunities for vaccination, with monitoring of uptake. Throughout the communication processes, it will be important to treat health and social care workers' concerns with respect and engage them in meaningful dialogue. A similar approach to influenza vaccination of health and social care staff is also a priority ahead of the coming winter.

6. Transition towards lower circulation levels of SARS-CoV-2

Eradication of a human infectious disease has only been achieved once - for the smallpox virus in 1980. A combination of a highly effective and stable vaccine, and a clear visual indicator of infection (pustules) that enabled the containment of outbreaks without a need for extensive testing, were key factors in the eradication of smallpox. 626

Some countries, including Australia, Bhutan, China and New Zealand, have to date applied a 'zero-tolerance approach' to COVID-19. In these countries, rapid containment measures, including mass testing, sudden lockdowns and closed borders, have been implemented when outbreaks are detected and have been successful in keeping infection and death rates low. However, there are socio-economic implications of this approach that make it challenging to sustain long-term.

Given the extent of transmission throughout the world, we now have to consider how society might concurrently suppress and live with the virus and reach an 'endemic' state (meaning that the virus will continue to circulate in pockets of the global population for years to come). An example of this is seasonal influenza epidemics, which, as discussed in section 3.2.1, typically account for 10,000 to 20,000 deaths each winter. COVID-19 does, however, have key characteristics that distinguish it from influenza: firstly, it is more transmissible and pathogenic than influenza, which have major implications for the healthcare system should an uncontrolled outbreak occur; and secondly long COVID (see section 4.2) has wider implications for the health and wellbeing of society.

Health and social care capacity, including intensive-care unit capacity, is likely to be an important consideration in determining the levels of hospitalisation and death from COVID-19 that can be endured - particularly if non-COVID care is negatively impacted as a consequence (e.g. delays and cancellations in elective care).

Many other factors are also likely to affect when and whether we reach an endemic state – such as:

- The evolution of the virus and the emergence of new variants of concern.
- The status of COVID-19 epidemics outside the UK.
- The duration of immune responses to infection and vaccination, and how these impact transmission of the virus, as well as the level of vaccination coverage achieved.
- The ability to reduce infection rates, for example through testing, tracing, and isolation, vaccination, new prophylactic treatments, or other behavioural and environmental interventions.
- The ability to reduce the severity of disease and mortality rate through better care and treatments and vaccination.

We consider each of these factors in turn below. Underpinning these factors is the level of risk and mortality that society is prepared to absorb, which raises ethical issues. 632,633 This is likely to vary by country, including across the four nations comprising the UK, and is beyond the scope of this report. There was low awareness of the spread of the pandemic and what a 'normal' level of transmission might be in our public dialogue workshops, suggesting that the public might look to science and the Government for a

signal of when things might return to 'normal'.⁶³⁴ There was discussion of using case or death numbers, but no one had a clear idea of what an acceptable level would be – some were interested in beginning to have this discussion.

6.1 The emergence of new variants of concern

Mutations and combinations of mutations in SARS-CoV-2 variants may lead to one or more changes in the biological behaviour of the virus. Changes that are routinely monitored include an increase in transmissibility or other detrimental change in epidemiology; an increase in virulence or change in clinical disease presentation; escape from immunity derived from natural infection; and/or a decrease in effectiveness of public health or clinical countermeasures.⁶³⁵

As discussed in section 3.1.1, widespread virus circulation and transmission, particularly in populations with partial immunity to SARS-CoV-2, will provide further opportunities for the selection of new variants that have a further step-up in transmissibility and/or immune evasion. Unvaccinated populations, including children and adolescents, present another pool for variants to develop. It is not possible to predict the place of origin, the precise combination of mutations or scale of shift in biology in the next variant of concern. As such, it is key to remain vigilant for new variants, as well as significant genetic changes that arise in existing variants.

Assessment of risk includes information gathering from international news, government reports and research papers; the presence, prevalence and rate of change in prevalence of lineage and variants globally and nationally; genomic epidemiological assessment of clusters; and assessment of variants associated with importation, reinfection and infection post-vaccination. Maintaining sustainable excellence in genome sequencing capabilities in the UK is an essential part of the current pandemic response. There is also a need for long-term planning so that sequencing is immediately available and scalable in the event of a future pandemic.

6.2 Status of COVID-19 epidemics outside the UK

There are likely to be epidemics outside of the UK for the foreseeable future. To date, the response to the pandemic has varied in different countries and includes:

- 1. Countries that have reacted fast and aggressively to suppress transmission (e.g. China, Hong Kong, South Korea, Malaysia, Singapore, Cambodia, Vietnam, Laos, Thailand, Australia, New Zealand). COVID-19 has had a low overall impact in some of these countries, though outbreaks continue to occur with viral variants. There is variability in vaccine supply between these countries, but the biggest challenge is likely to be vaccine uptake/acceptance given the lower perceived risk. 636,637
- 2. Countries that have gone 'in and out' of suppression to varying degrees (e.g. mostly High-Income Countries, such as countries in Europe, Canada, the United States, and the Middle East; Upper Middle-Income Countries in Latin America; South Africa). In these countries, there has been a relatively high burden of COVID-19 disease to date. There has generally been a high supply of

- vaccines in these countries. Most of these countries have the potential to achieve high levels of population immunity this year if vaccine evasion with viral variants does not dominate and vaccine hesitancy can be overcome.⁶³⁸
- 3. Countries in which large and sustained epidemics have exceeded healthcare capacity (e.g. Brazil, Peru, Mexico and other Latin American countries, South Asia, Indonesia, Philippines, Papua New Guinea, Low to Middle Income Countries in the Middle East/Horn of Africa). These countries have experienced varying rates of transmission, but current levels of transmission are generally rising with the emergence of the Delta variant (B.1.617.2). 639 These countries are struggling to balance large epidemics with limited vaccine supply, and are not likely to achieve more than 20% vaccination in 2021. 640
- 4. Countries that appear to have been less affected, for example parts of Africa (with the exception of South Africa, some southern African countries towards the end of 2020, and northern Africa). For reasons that are not fully understood this region appears to have been less affected to date (this may be due in part to limited surveillance and death reporting in these countries, as well as younger populations that are less vulnerable to COVID-19) ⁶⁴¹ although a recent increase in cases is currently occurring in many parts of the continent with the emergence of the Delta variant. Most countries in Africa lack access to vaccines, with current supply both limited and patchy. ⁶⁴²

Global vaccination will be critical if transition to lower levels of infection is to be achieved. In June 2021, G7 countries committed to share at least 870 million doses of COVID-19 vaccines directly, with the aim to deliver at least half by the end of 2021.⁶⁴³ This however is still likely to fall short of global need. Across all countries there are an estimated 258 million essential workers and a further 2.1 billion people in the high-risk groups (defined as over 80, over 60 with at least one underlying health condition or 20-59 with at least two underlying health conditions).⁶⁴⁴ To date, COVAX has distributed over 70 million doses but under the original COVAX objectives, 2 billion doses of vaccines were required worldwide by the end of 2021 with a further 1.8 billion doses targeted to 92 lower income countries by early 2022.⁶⁴⁵ The variable availability and utility of vaccines against viral variants may lead to increased global disparity, which will affect the UK. Travel restrictions will also impact on the risk of importing new variants of concern into the UK.

6.3 The duration of immune responses to infection and vaccination

At present, the duration of immunity following natural infection or vaccination is unknown and will likely vary in different sub-populations, such as the elderly. An update note on immunity to SARS-CoV-2 after natural infection produced by NERVTAG concluded that natural infection with SARS-CoV-2 leads to antibody, B cell, and T cell responses in almost all individuals, which are sustained for over 8 months after infection. At a from other respiratory viruses suggest that a combination of neutralising antibodies produced by long-lived plasma cells, and immunological support from memory B and T cells, can provide long-term protection against severe disease. However, disease-limiting immunity, which provides protection against severe illness but not against infection, is more likely to be maintained long-term, as lower levels of immunity are needed to attenuate severity as opposed to preventing infection.

The duration of immunity will have implications for any long-term vaccination strategy in the UK (and will affect the global requirement for vaccines). There is increasing interest in the role of local (mucosal) immunity and immunoglobulin A (IgA) in providing protection against SARS-CoV-2, as oral and nasal mucosal surfaces serve as primary entry points for the virus. ^{647,648,649} In future, the development of mucosal vaccines may provide an additional means of protection against SARS-CoV-2. ⁶⁵⁰ In addition, immunity against SARS-CoV-2 infection may be diminished by viral evolution and the emergence of variants. ⁶⁵¹ This will have implications for the development of new or modified vaccines, which will influence when and whether we achieve an endemic state.

In the longer term, as high levels of immunity to severe infection build up in the population, COVID-19 may have less severe clinical outcomes. For example, children may build immunity over time, leading to less severe outcomes if infected in adulthood. However, COVID-19 is a new infection in human populations, so long-term adaptation of virus and host remains uncertain.

6.4 The ability to reduce infection rates

Our ability to reduce infection rates will be influenced by our ability to identify and isolate new cases, and to reduce transmission through vaccination, new prophylactic or antiviral treatments, or other behavioural and environmental interventions.

6.4.1 Test, trace and isolate

As discussed in section 3.1.2.3, systems for conducting comprehensive infection testing, contact tracing and supporting self-isolation are a vital component of epidemic management. In order to transition to lower circulation levels of the virus by limiting onward transmission, the need for rapid, accurate testing and tracing that encompasses a high proportion of symptomatic cases, crucially with effective financial and other support for self-isolation, will continue to be required in the medium term. Additional surge testing will also be required to rapidly manage outbreaks where these are identified. In the longer term, wider routine asymptomatic testing using lateral flow devices (LFDs) may not be cost-effective and might result in testing fatigue, especially if low disease prevalence means that such tests lead to more false than true positive results. Requirements for contacts to self-isolate may also be relaxed once high levels of immunity are achieved through vaccination or natural infection, which would significantly reduce societal impacts. Waste water (WW) surveillance could continue to be used to identify where outbreaks are occurring and rapidly manage them to limit onward transmission (see section 3.1.2.3).

6.4.2 COVID-19 vaccines

Modifications to existing vaccines (e.g. for variants of concern/multivalent vaccines against multiple viral strains) are likely to be needed in future. Vaccine design should also be updated to maximise polyclonal immune responses to multiple protective viral epitopes, to lower levels of infection. New vaccine trials may be limited by the reduction in circulating virus and high levels of pre-existing vaccine uptake. The development of Controlled Human Infection Model trials could be a potential safeguard for the development of novel vaccines, though the risks and ethical implications of such trials

will need to be considered. A better understanding of correlates of protection could also speed up the development of new vaccines by enabling surrogate markers of clinical efficacy to be established. To maintain low circulation levels of SARS-CoV-2 in the long-term, regular COVID-19 vaccination programmes may be needed, akin to the annual influenza vaccination programme. Long-term capability for vaccine development and procurement must be part of future resilience planning.

6.4.3 Prophylactic and antiviral treatments

There are currently no proven prophylactic or antiviral treatments, though these would be highly valuable in reaching an endemic state. It is not known whether any will become available in the near term. As described in section 3.1.3, government-led initiatives, including the COVID-19 Therapeutics Taskforce, 653 the Antivirals Taskforce, and the COVID-19 Prophylaxis Oversight Group, 655 should help to coordinate and support the development of new medicines, alongside the UK-COVID Therapeutic Advisory Panel. 656

Emerging results suggest that neutralising monoclonal antibodies may have a role to prevent infections in specific vulnerable groups (e.g. those that are unvaccinated or recently vaccinated).⁶⁵⁷ It will be important for these to be formulated as cocktails to prevent mutational escape to single antibodies.

6.4.4 Behavioural and environmental interventions

As discussed in section 3.1.2.2, behavioural and environmental interventions have played a key role in reducing the levels of SARS-CoV-2 transmission.⁶⁵⁸ The UK roadmap out of lockdown,⁶⁵⁹ a step-by-step plan, has been devised to ease restrictions in England cautiously, analysing data so as not to ease restrictions too quickly. Although there is an expectation that complete lifting of restrictions will occur, in reality this may be difficult, especially in healthcare settings, where some measures will still be required.

We will be likely to need some of the outlined 'safe behaviours' in the longer-term to achieve low levels of endemic transmission. Even as restrictions are lifted, isolation of symptomatic individuals and testing will still be critical (see section 3.1.2.2). Self-isolation of infected people is the most effective means of preventing transmission by reducing the likelihood that those infected are interacting with others. We have already highlighted the need to continue to use measures such as working from home, face coverings and physical distancing, particularly in indoor and crowded situations where risk of transmission is high at times of high level of viral transmission. This may lead to changes to our social norms in the longer term, with a suite of behavioural and environmental interventions (such as wearing face coverings, staying at home when ill, etc.) becoming culturally ingrained and part of the 'new normal'. More permanent changes within the healthcare service will also be required to limit the spread of respiratory infection in patients and staff. This might include the maintenance of more virtual clinics/consultations (see section 5.2.2 for an in-depth discussion) and ongoing COVID-19 testing for patient procedures.

Once the risk of pressures on the healthcare service reduces, legal controls will reduce and leave risk management to individuals, which may further increase inequalities. Some measures are likely to remain across populations (e.g. mask wearing) but it is likely that countries globally will emerge from the last 18 months in different ways.

Globally, the stringency of government-mandated measures has varied substantially between countries during the pandemic, 661 with the most stringent measures generally taken in response to rapidly rising case reports. However, while many countries have relatively few ongoing behavioural and environmental interventions mandated, Google mobility data indicate that behaviour has not yet returned to pre-pandemic levels, suggesting that people are still hesitant to interact as they might have done previously. 662

6.5 The ability to reduce the severity of disease and mortality rate

Reducing the severity of disease and mortality rate through better care, treatments and vaccination (explored above) will also impact on our ability to achieve a manageable state and minimise transmission.

As discussed in section 3.1.3, further research into effective treatments and best clinical practice is required. As for the development of new vaccines, a key challenge in developing effective new treatments as disease severity and burden declines in the UK will be recruiting sufficient numbers of patients for rigorous analysis.

Long COVID could have long-term implications for the health of the population, which in turn would impact on the health and social care system that will have to cope with increasing demand on its services. We have already highlighted the importance of gaining a better understanding of long COVID, determining how to best manage these syndromes, and developing and testing potential treatments. This will include determining whether vaccines and current/future treatments for COVID-19, including antivirals and prophylactics, prevent or ameliorate long COVID.

There are likely to be additional long-term effects of the pandemic on health and wellbeing, which when combined with other inequalities could prolong the 'syndemic' (the interaction of multiple diseases and wider social and environmental factors that enhance the negative effects of disease interaction)⁶⁶³ nature of COVID-19 and its impact on society. These are discussed in detail in the British Academy's report published earlier this year, 'The COVID decade: Understanding the long-term societal impacts of COVID-19'.⁶⁶⁴ The key findings most relevant to this report are summarised in Box 4.

Box 4: Key findings relevant to the health sector from the British Academy's report 'The COVID decade: Understanding the long-term societal impacts of COVID-19¹⁶⁶⁵

The SARS-CoV-2 virus itself will not suddenly disappear. It may continue to mutate in ways that require repeated lockdown measures and regularly updated vaccines, or it may become endemic. There is a risk that the needs of groups impacted by COVID-19 in different ways could be overlooked if societal and medical focus shifts too rapidly away from the virus. The British Academy's report identified nine, significant and interrelated long-term societal impacts of COVID-19. These wider social, economic and cultural effects of the pandemic will cast a long shadow, which will emerge differently

across places; have differential impacts for individuals, communities, regions, and nations; and will play out along different time courses.

The long-term effects may also intersect with other inequalities. For example, a deepening economic crisis resulting from the pandemic and repeated lockdowns may have longer-term negative health impacts for groups already experiencing the effects of structural inequalities. For these reasons, the COVID-19 pandemic is often described as a 'syndemic', characterised by the ways in which social environments, especially conditions of social inequality and injustice, contribute to disease clustering and interaction as well as to vulnerability. 6666

Disasters exacerbate existing inequalities. Without rapid remedial action and allocation of resources that is progressive, inequalities will widen still further. The additional spending pressures, higher need and loss of funding is creating even greater financial pressure on all local authorities and communities, but particularly more deprived ones – which were already facing a funding crisis before the pandemic.

Many people who have suffered more severe health complications from COVID-19 will require varying forms of additional health and social care. This is in addition to the significant direct burden of mortality on the NHS and on society more broadly, as well as the long-term costs of care and loss of productivity for those who have been hospitalised with COVID-19. In addition, the impacts of COVID-19 are exacerbating already perilous conditions in mental health inequalities.

For the health sector in particular, the British Academy's report and others highlight the opportunities presented by integrated reforms to public health and other infrastructure to reduce health inequalities and respond to long-term impacts of COVID-19, such as impacts on mental health and childhood development. There is a need to build resilience within the public health, and health and social care systems to prevent transmission now and for future pandemics and crises. The importance of tackling health inequalities in the long-term recovery from COVID-19 has also been echoed by the COVID-19 Marmot review, which recommends building a public health system that is based on taking action on the social determinants of health and reducing health inequalities.⁶⁶⁷

Annex 1 People's perspective – COVID-19: Preparing for the future

Last year, a group of people came together with the Academy of Medical Sciences as the Patient and Carer Reference Group (PCRG) for a project on forecasting the priorities for a challenging winter 2020-21. This summer, many of us have returned, and been joined by others who bring a wider range of voices with different experiences of the pandemic. This People's perspective has been written by the Patient and Carer Reference Group and does not necessarily represent the position of the Academy of Medical Sciences.

We have, again, worked alongside the Expert Advisory Group to inform their discussions, and been informed by their discussions. We are not representative of the public and are acutely aware that we don't include people whose voices are seldom heard and have been the most impacted by the pandemic, for example those who are homeless, people who don't speak English as a first language and those living with profound physical and mental disability.

In our People's Perspective last year, we wrote a single, strong plea to policymakers:

"We make one simple, heartfelt request. **Involve us now** in preparing for the challenges this winter will present - or create a burden of health problems which may last for decades."

Sadly, that request fell on deaf ears. We have seen no evidence of involvement in service redesign in the NHS. Some funders still undervalue the role of involvement in improving research on COVID or any other topic. As HRA reported, only 20% of COVID research proposals seen by research ethics committees at the beginning of the pandemic involved patients and public. Normally, this would be 80% 668. Government and UKRI must show leadership in this – sadly that has been lacking to date.

Involve us now

While we have additional messages this year, our message from last year remains, **involve us now** while there is time, before winter arrives, and before the burden of enduring health problems created in the last 16 months becomes a torrent that will wash away the NHS.

Work with us, work for all of us

"People who have suffered health, financial and psychological consequences from the last 15 months are dealing with lasting damage to their lives. Without genuine collaboration between government and citizens to mitigate this damage, the future of our society will be badly scarred."

Mandy Rudczenko, Member, PCRG⁶⁶⁹

The need for involvement is greater now than ever before. Involvement has been cast aside when the need is greatest. Decisions with far-reaching consequences are being

made without involvement of those they affect. The right to be involved in decisions affecting people is as ancient as the beginnings of democracy in the United Kingdom. King Edward I, summoning the Model Parliament in 1295 said "what touches all, should be approved by all, and it is also clear that common dangers should be met by measures agreed upon in common." 670

There is no more 'common danger' than a pandemic. While the measures to control it have been approved by Parliament, those most affected are not *in* Parliament, though their needs should be represented by MPs. To make sure local, national, NHS and other public bodies' policies, services, communications and systems work for everyone, they must be developed with involvement from those who will have most difficulty with access and whose need is greatest. They must be implemented, evaluated and refined in the same way.

Services, measures to mitigate infection risk, communications, decisions about our futures should be agreed upon in common with those most affected.

The role of people alongside scientists on SAGE

Those most affected by COVID must be as much a part of national decisions as anyone else. We have thought hard about how to achieve this.

We feel the best option is to have public members involved in SAGE and devolved equivalent group discussions, to ensure the scientific evidence is complemented by the reality of people's experiences. This must not be tokenistic. Public members must make up a substantial portion of the members of SAGE and its subgroups, we suggest an indicative minimum of 25% at any given time.

Public members of SAGE and devolved equivalents should be offered opportunities as part of their role to talk to local communities across the country to find out about the everyday issues each emergency creates. We feel this option is most in line with the principles of co-development, as outlined in Box 1, whereas other options we considered were not (e.g. a separate group to advise SAGE).

Members of the public who can bring voices from communities most affected by emergencies should be included in SAGE, devolved equivalents and their subgroups, at an indicative minimum 25% of membership at any given time, using an approach that fulfils the spirit of co-development, as set out in box 1.

Redress the balance

"The lockdown did save lives, but it cost lives and destroyed them as well."

Kimberlee Cole, Member, PCRG

People in the poorest areas of the UK^{671,672} live shorter, sicker lives than those in the richest, are twice as likely to live with high-impact chronic pain,^{673,674} and more likely to have more than one long-term health condition for more of their life⁶⁷⁵. These problems

were there before the pandemic. They had been there for decades, generations. Then COVID struck.

Between March 2020 and April 2021, the mortality rate from COVID was 175.3 per 100,000 higher in the 10% most deprived places in England than in the least. Similarly, provisional data from Public Health England⁶⁷⁶ show life expectancy fell by similar amounts for both sexes from 2015 to 2018 across all communities. But as the table below shows, there were shocking differences in the drop in life expectancy between 2019 and 2020 for the least and most deprived places.

Life	10% most (0% most deprived 10% least deprived		Change		
expectancy	2019	2020	2019	2020	Most dep	Least dep
Females	78.9	77.3	86.8	85.8	1.6	1
Males	74.3	72.4	83.6	82.6	1.9	1

While these are provisional data which must be treated with caution, the contrast is stark. They illustrate an outrage we cannot tolerate. Accepting a level of mortality from COVID as the price of removing restrictions means accepting that COVID will probably kill more people living in deprivation than people who don't. The same may well be true of other inequalities. To us, that is not levelling up.

Those living in deprivation do not have the financial and other means – the social capital – to adapt to our constantly changing COVID circumstances. These past months have been harder, the impacts greater, and the material and psychological effects more profound, than for those living with the means to adapt and navigate systems successfully.

"We have heard in our discussions about the different ways communities have responded to the pandemic. It was clear that deep, ingrained inequalities, not knowing where to turn or who to trust, poor communications and unwillingness to trust establishment bodies caused problems."

Isaac Samuels, Member, PCRG

National initiatives to address problems such as contact tracing faltered without the onthe-ground knowledge of people, cultures and communities to make things work. For the coming winter, control needs to pass to local areas. Addressing inequalities isn't done by giving everyone the same, national offering, it's done best by those who know who needs most help and what they need.

"When we start to address inequalities and disparities, which can take a significant investment of time, we need to start where the need is greatest, especially in those communities where there is deprivation and lack of opportunities - not just in cities."

Winston Allamby, Member, PCRG

The role of national governments must, from now on, be to provide the budget, support, resources and coordination to enable communities to assist those within their community that need help, starting with those who need it most. Investment now will pay off for decades, by equipping communities to help themselves.

The UK Government and devolved administrations must equip and fund local communities to work together, through local authorities and community groups, to tackle inequalities in their areas.

"What we need now is a handbrake turn in policy, to ensure we are ready for winter and start the process of addressing inequalities for real. We must hand control and management of this pandemic back to communities to manage it in their area, with all the resources national and UK governments can provide behind them."

Colin Wilkinson, Co-Chair, PCRG

The unequal long-term health effects of COVID

Long COVID Support⁶⁷⁷ is monitoring service quality for people with long COVID. The patient stories in that research⁶⁷⁸ are truly shocking. Recent Government and NHS announcements^{679,680} addressing this are welcome, as are guidelines for assessment^{681,682} and management⁶⁸³ of long COVID. However, the route to successful assessment and management – to being listened to and receiving care – is too long and does not exist everywhere, or GPs are unaware of how to refer into it.

For whatever reason, people with long COVID are not getting the care they need. This must change, and quickly.

People with long COVID need coordinated, personalised care. According to the Office for National Statistics⁶⁸⁴, long COVID was most common in a range of groups, including those living in the most deprived areas and those with existing health problems or disabilities. They also showed that long COVID was more common among health and social care workers than those working in other sectors.

Health and social care workers have been at much higher risk of catching COVID, as have many other key workers. For us, the most important reason to make sure that health and social care workers with long COVID get the care they need quickly is that their service to the rest of us – and indeed to our country – demands it. When they are in difficulty, we must help them properly, not with a postcode lottery of uncertain care. Aside from the fact it is the right thing to do, getting health and social care workers fit for work again will help ease staff shortages, a key priority outlined in the expert report.

"All I want to do is to get back to work and help my colleagues deal with this crisis and care for our patients."

Sophie Evans, nurse living with long COVID and Member, PCRG

Everyone living with long COVID deserves better. We need to make sure those in greatest need come first. Local implementation of plans for long COVID care must go hand in hand with planning how to fully and safely restart care for those with long-term conditions needing secondary care support.

"Lack of access to help, support and care has had a profound effect on those living with long-term conditions."

Lynn Laidlaw, Co-chair, PCRG

Some people with pre-existing long-term conditions have had no or little access to vital secondary care support for many months, often worsening their condition. We must ensure this care deficit is addressed alongside providing care for people with long COVID.

Care for people with the long-term effects of COVID must be balanced with addressing the backlog of ongoing care needs for people with pre-existing long-term conditions.

At local level, it appears patients have not been involved in designing changes to services for long-term conditions or initiating services for people with long COVID. There are unacceptable delays for both groups, and those needing surgery or other treatment.

"Before and during the winter, the NHS must make sure people can get seen, and get the treatment they need, much sooner. We can't continue with people waiting so long for care."

Sudhir Shah, Member, PCRG

Long COVID clinics and services, changes to care for people with pre-existing long-term conditions and for those awaiting surgery must be co-developed with those who will use them, demonstrating the approach outlined below.

Box 1: Co-Production Collective approach to Co-production 686

 Being human Valuing diversity of knowledge, experience and perspective Building mutually beneficial relationships based on honesty and trust 	 Being inclusive Removing barriers to participation Recognising people's strengths and supporting their development
 Being transparent Addressing power imbalances and hierarchies Sharing roles and responsibilities 	 Being challenging Continuous reflection, learning and improvement Embracing new ideas and ways of working

The unequal impacts of the COVID crisis on mental health

The COVID pandemic has had a dramatic effect on the nation's mental health, as the Expert Advisory Group's report highlights. In our view, uncertainty and the rate at which facts, policies, regulations and guidelines have changed were key factors in this. We know the effects have been unequal, with those who have pre-existing mental health problems, health and social care workers and those living with difficult circumstances including deprivation, isolation and bereavement during the pandemic most affected.

Urgent action to dramatically increase the availability of co-developed, tailored mental health support is essential to help us through the coming winter. Triage options must be

put in place to ensure people get to the right care quickly. Options must be co-developed with those affected by mental health problems, especially those for whom COVID has overlaid new problems on existing mental health problems.

These options must include significantly higher-profile and better information about how people can care for their own mental health.

Ensuring that IAPT⁶⁸⁷ (open access talking therapies) services have the resources (money, support and training) to meet the dramatic surge in need is essential. It is unacceptable for people to have to wait six months or more to access talking therapies. Community and secondary mental health services will also need additional capacity to respond and meet the needs of those who need them.

Everyone should get the care they need for their mental health quickly, but triage must ensure those in greatest need get the right care first. Open access triage and talking therapies (IAPT) must be expanded to meet the need, as must the community and secondary mental health services that will back them up.

The unequal uptake of vaccinations

"Even with vaccination, we are not free of this virus. We must all be cautious and careful as we move forward and lift more restrictions."

Katherine Barrett, Member, PCRG

One of the most alarming aspects of inequality in the pandemic has been the differential rates of vaccination by the socioeconomic status of communities and people's ethnic origins. Recent data⁶⁹⁸ show 55% of those in the least deprived 10% of communities had received both doses of vaccine, while only 40% of those in the most deprived 10% had. This is a stark and shocking difference. Equally shocking are the differences between groups with different ethnicity, ranging from 95.1% of people of white British ethnicity to 64.8% of people of black or black Caribbean ethnicity aged 50+ having received at least one dose. For those aged 16+, it ranges from 75.6% of white British people to 34.7% of people of Chinese ethnicity. While these inequalities are complex, we do know people respond best to people in their communities – people they trust – giving them messages. Vaccination is the only way for all of us to get out of restrictions.

A rapid, targeted expansion of the COVID-19 Community Champions⁶⁹⁹ programme must be put in place to address local inequalities in vaccine uptake.

An additional issue is the lack of information or clear options for those who, for medical reasons, are unable to have any of the current vaccines. This must be urgently addressed.

These inequalities are symptoms of the underlying, long-standing differences between areas and people in the UK. If 'levelling up' is to be more than words:

Government must help local communities to find their own solutions to inequalities through co-development approaches, with their first priority being to address disparities in the uptake of vaccines, ensuring those in greatest need get help first.

Without urgent action now, we fear the coming winter will make the divides between people and places wider still, making these inequalities even harder to resolve.

Develop better communications and guidance

"Communication is more than just sending a message. It has to be received and understood in the right way too."

Bo Rutter, Member, PCRG

One of our greatest disappointments of the last year has been the communication with the public from Government and NHS organisations. Communications since the first lockdown have been much too unclear.

Having seen the modelling undertaken in this project, we are convinced there is a high probability further restrictions will be needed. As members of the public with a wide range of different experiences of healthcare, we can see that unlocking permanently this summer creates a hostage to fortune.

While we all need hope, it must be realistic hope. We feel very strongly that the effective communication principles in the main report (Box 3) should be the basis for national communications going forward. Communications to those in the clinically extremely vulnerable group need to be shorter. If shielding letters need an easy-read version, they are too complicated. Communications must not be on the basis of 'do as I say, not as I do' – everyone giving these messages must display the highest standards of probity if trust is to be retained.

All agencies must give out consistent messages to ensure the public do not lower their guard against COVID and other winter viruses.

Going forward, communications must be clear, simple, consistent and codesigned with those they address. Clear guidance on what to do and when is essential.

Our key messages

Involve us now

- Services, measures to mitigate infection risk, communications, decisions about our futures should be agreed upon in common with those most affected.
- Members of the public who can bring voices from communities most affected by emergencies should be included in SAGE, devolved equivalents and their subgroups, at an indicative minimum 25% of membership at any given time, using an approach that fulfils the spirit of co-development, as set out in box 1.

Redress the balance

- The UK Government and devolved administrations must equip and fund local communities to work together, through local authorities and community groups, to tackle inequalities in their areas.
- A rapid, targeted expansion of the COVID-19 Community Champions⁶⁹⁰ programme must be put in place to address local inequalities in vaccine uptake.

Develop better communications and guidance

- Going forward, communications must be clear, simple, consistent and codesigned with those they address.
- Clear guidance on what to do and when is essential.

"The members of this reference group, and we are sure, many like us, stand ready to assist."

Winston Allamby Katherine Barrett Kimberlee Cole Sophie Evans Lynn Laidlaw Carol Liddle Nira Malde-Shah Noah Roberts
Mandy Rudczenko
Bo Rutter
Isaac Samuels (they/them)
Sudhir Shah
Colin Wilkinson

Annex 2 Report preparation

This report represents the considered input of the following Expert Advisory Group members. Members participated in a personal capacity, not as representatives of the organisations listed. The report does not necessarily represent the position of the Academy of Medical Sciences or of any of the individuals involved in its development, as listed below.

Expert Advisory Group

Chair

Professor Sir Stephen Holgate CBE FMedSci, Clinical Professor of Immunopharmacology, University of Southampton

Expert Advisory Group members

Dr William Bird MBE, GP, Reading & Chief Executive Officer, Intelligent Health **Dr Adrian Boyle**, VP Policy, Royal College of Emergency Medicine **Professor Chris Butler FMedSci**, Professor of Primary Care, University of Oxford

Professor Stuart Elborn CBE, Faculty Pro-Vice-Chancellor, School of Medicine,

Dentistry and Biomedical Sciences, Queen's University Belfast

Dr Nigel Field, Director, Centre of Molecular Epidemiology and Translational Research, Institute for Global Health, University College London

Professor Tamsin Ford CBE FMedSci, Professor of Child and Adolescent Psychiatry, University of Cambridge

Professor Azra Ghani MBE FMedSci, Chair in Infectious Disease Epidemiology, Imperial College London

Professor Adam Gordon, Professor of the Care Older People, University of Nottingham **Professor Andrew Hayward**, Professor of Infectious Disease Epidemiology and Inclusion Health Research, University College London

Professor David Heymann FMedSci, Professor and Chair, Infectious Disease Epidemiology; Head and Senior Fellow, Centre on Global Health Security, London School of Hygiene and Tropical Medicine

Professor Nick Hopkins, Professor of Psychology, University of Dundee
Professor Dame Anne Johnson DBE PMedSci, Professor of Infectious Disease
Epidemiology, University College London; President, Academy of Medical Sciences
Professor Kamlesh Khunti FMedSci, Professor of Primary Care Diabetes & Vascular
Medicine, University of Leicester

Lynn Laidlaw, Co-Chair, Patient and Carer Reference Group

Professor Ronan Lyons, Clinical Professor of Public Health, Swansea University **Professor Dame Theresa Marteau DBE FMedSci**, Director of Behaviour and Health Research Unit, University of Cambridge

Professor Graham Medley OBE, Professor of Infectious Disease Modelling, London School of Hygiene & Tropical Medicine

Professor Dame Julie Moore DBE, Professor of Healthcare Systems, University of Warwick

Professor Catherine Noakes OBE, Professor of Environmental Engineering for Buildings, University of Leeds

Professor Peter Openshaw FMedSci, Professor of Experimental Medicine, Imperial College London

Professor Sharon Peacock CBE FMedSci, Executive Director and Chair, COVID-19 Genomics UK consortium

Steve Rees, VP, Discovery Biology, Discovery Sciences, R&D, AstraZeneca

Dr Louise Sigfrid, Clinical Research Fellow, Centre for Tropical Medicine and Global Health, University of Oxford

Dr Charlotte Summers, Reader in Intensive Care Medicine and Co-Lead of Perioperative, Acute, Critical Care and Emergency Medicine (PACE) Section, University of Cambridge

Professor Russell Viner, Professor in Adolescent Health, University College London **Professor Sir Simon Wessely FMedSci**, Regius Professor of Psychiatry, King's College London

Colin Wilkinson, Co-Chair, Patient and Carer Reference Group

Professor Lucy Yardley, Professor of Health Psychology, University of Southampton and University of Bristol

Additional expertise (early to mid-career researchers)

We are grateful to the following early and mid-career researchers, who supported the development of the report by working closely with Expert Advisory Group members and the Secretariat.

Dr Shoba Amarnath, Newcastle University Research Fellow, Newcastle University **Dr Heather Bailey**, Lecturer in Infectious Disease Epidemiology, University College London

Dr Gemma Clarke, Marie Curie Senior Research Fellow in Palliative Care, University of Leeds

Dr Mariachiara Di Cesare, Senior Lecturer in Public Health, Middlesex University and Honorary Research Fellow in Population Health, Imperial College London

Dr Upkar Gill, Clinical Lecturer/Medical Research Foundation Early Career Research Fellow and Honorary Consultant Hepatologist, Barts & The London School of Medicine & Dentistry, Queen Mary University of London, UK

Dr Sally Hargreaves, Assistant Professor in Global Health, St George's Hospital University of London

Dr Guy Harling, Wellcome Trust/Royal Society Sir Henry Dale Senior Research Fellow, Institute for Global Health, University College London

Dr Stephen Makin, Senior Clinical Lecturer, Centre for Rural Health, University of Aberdeen

Dr Grace Okoli, Clinical Lecturer, Barts and the London School of Medicine and Dentistry

Dr Ruth Payne, NIHR Academic Clinical Lecturer and Honorary Specialist Registrar Infectious Diseases and Microbiology, University of Sheffield

Dr Reecha Sofat, Clinical Pharmacologist and Senior Clinical Lecturer, University College London

Dr Sarah Tansley, NIHR Academic Clinical Lecturer in Rheumatology, University of Bath and University of Bristol

Dr Yihua Wang, Lecturer in Biomedical Sciences, University of Southampton

Observers

The following representatives from the Government Office for Science acted as observers. They were invited to promote transparency around the study process, but were not involved in the Expert Advisory Group's deliberations nor in the development of its findings or conclusions.

Dr Yoanna Shams, Team Lead Domestic Engagement and Strategy, COVID-19 Response, Government Office for Science

David Busse, COVID-19 Scientific Advisor, Government Office for Science

Patient and Carer Reference Group

We are grateful to the members of the Patient and Carer Reference Group for their insight into the health challenges, opportunities and priorities for this coming winter.

Winston Allamby

Katherine Barrett

Noah Roberts

Kimberlee Cole

Sophie Evans

Lynn Laidlaw, Co-Chair, Patient and Carer Reference Group (also sat on the Expert Advisory Group)

Carol Liddle

Nira Malde-Shah

Mandy Rudczenko

Bo Rutter

Isaac Samuels (they/them)

Sudhir Shah

Colin Wilkinson, Co-Chair, Patient and Carer Reference Group (also sat on the Expert Advisory Group)

Secretariat

Dr Claire Cope (Lead Secretariat), Head of Policy, Academy of Medical Sciences Dr Rachel Quinn, Director of Medical Science Policy, Academy of Medical Sciences George Phillips, Policy Officer, Academy of Medical Sciences Angeliki Yiangou, Policy Manager, Academy of Medical Sciences

We are grateful for the contributions of the Academy's policy interns: **Samuel Usher**, (Medical Research Council-funded PhD student); **Lewis Macdonald** (Medical Research Council-funded PhD student); and **Stephanie Webb** (Wellcome Trust-funded PhD student)

Acknowledgements

We would like to thank the following people for providing informal input to inform the development of the report.

Dr Oliver Watson, Research Associate, Imperial College London, **Dr Alexandra Hogan**, Research Fellow, Imperial College London and **Dr Rachel E Baker** Associate Research Scholar, Princeton University for their invaluable modelling expertise.

Dr Laura Shallcross, Consultant in Public Health Medicine, University College London for her contributions to the infection, protection and control section.

Professor Nishi Chaturvedi, Professor of Clinical Epidemiology (Cardiometabolic Disease), MRC Unit for Lifelong Health & Ageing at UCL, **Dr Ben Goldacre MBE**, Director, The DataLab, **Brian Mackenna**, Specialist Pharmacist Adviser & Medicines Data Clinical Lead, NHS England and NHS Improvement, and the OpenSAFELY Collaborative for sharing their expertise and data.

The Academy of Medical Royal Colleges, the Faculty of Intensive Care Medicine, the Faculty of Pharmaceutical Medicine, the Faculty of Public Health, the Royal College of Paediatrics and Child Health, the Royal College of Pathologists, the Royal College of Pathologists Transfusion Special Advisory Committee, the Royal College of Physicians, the Royal College of Psychiatry, the Genetics Societies (consisting of the Clinical Genetic Society, the British Society for Genomic Medicine and the Joint Committee on Genomics in Medicine), the British Thoracic Society and their members for their perspectives on the challenges for winter 2021/22 and possible mitigation strategies.

The **team at I psos MORI** for their work on the public, patient and carer discussion workshops, with special thanks to all the **public dialogue workshop participants** for sharing their personal experiences and views for this upcoming winter.

Nick Hillier, **Holly Rogers**, **Claire Bithell**, **Naomi Clarke**, **Gaby Richter** and **Melanie Etherton** at the Academy of Medical Sciences for support leading the patient, carer and public engagement, and communications, as well as the **Science Media Centre** for supporting the launch of this report.

We are very grateful to all those who have contributed information to the report and apologise to anyone that we have inadvertently omitted from this list.

Funding

The project was supported by a core grant the Academy received for policy work from the Department for Business, Energy and Industrial Strategy (BEIS), but was carried out independently of Government.

In addition, the public, patient and carer engagement programme was supported by the Health Foundation (grant ID: 2492234), an independent charity committed to bringing

about better health and healthcare for people in the UK, and an award for public and patient engagement from BEIS.

Annex 3 Ipsos MORI summary of findings from the public discussion workshops

The Ipsos MORI report (available from the Academy's website)⁶⁹¹ details the full findings from five workshops carried out by Ipsos MORI between March and June 2021 on behalf of the Academy of Medical Sciences, covering public experiences and perceptions of the pandemic over the winter of 2020/2021 and looking to their expectations around likely experiences during the winter of 2021/2022.

The workshops were conducted with a panel of thirty members of the public drawn from across the UK, including representatives of ethnic minority groups and those who had been told to shield during the COVID-19 lockdown measures. The panel of members of the public included some participants from a similar research project carried out on behalf of the Academy of Medical Sciences in May-June 2020. Young adults (18-24 years old) from the Academy's Planet DIVOC-91 Young Person UK panel also participated in the workshops.

The key findings and reflections on communications derived from this report are included below:

Key findings

Participants' experiences of the pandemic have become increasingly fragmented.

Compared with last year, the groups displayed a wider range of views on factors including government performance, optimism for the coming months and personal well-being. Echoing other research, while many have adapted well to lockdown restrictions and are satisfied overall with how the pandemic has been dealt with, for others this has been a more difficult time and their view of government actions and available support is more critical.

This can also be seen in the sources of information people use to understand the latest news on the pandemic. Most of the group felt fatigued and were not actively seeking out information on the pandemic, while for the younger people group social media was acknowledged as their primary source, despite concerns about the accuracy of the content.

Young people's views of vaccination are driven by different factors to older groups.

Young people tended to view the threat from COVID-19 to their personal health as being negligible and were less likely to be swayed by ideas that getting vaccinated was their 'duty'. This means the risk/benefit calculation they make around vaccination is very different and only a small amount of negative information will move them to become vaccine hesitant. However, as a result these views tended not to be strongly held and may fall away as the vaccination drive is opened to younger people (as was witnessed among the older population).

Across the group most wanted to continue a cautious approach to reopening.

The workshops occurred before the postponement of the June 2021 date for lifting COVID-19 restrictions and there was a high level of apprehension about this date. Many felt that the use of measures including masks and restrictions on foreign travel into the UK were justified across the summer if it helped avoid a spike in cases next winter.

Yet overall there was optimism about this winter.

Many in the groups felt optimistic about the likely path of the pandemic this coming winter. The successful vaccination drive was the key reason for this optimism, but there was also a widespread belief among participants that the UK governments would learn from the mistakes of 2020 (and from best practice abroad) to help contain the disease. Participants were still focussed on COVID-19 when asking this question and were not considering other pressures that might contribute, such as a heavy flu season or NHS overload.

People are looking for distilled, clear information on what is important to them

Most participants had long stopped monitoring the progress of the pandemic and were instead listening for information on when they would be allowed to do particular activities, especially visiting family indoors and travelling abroad. They said they wanted to have the rationale behind decisions made explained and were also keen to understand roadmaps out of the pandemic. This demand for clear communication of long-term plans is a key tension with the nature of scientific and pandemic driven decision-making.

The public are looking to science and the Government for a signal of when things might return to 'normal'.

Low awareness of the spread of the pandemic and what a 'normal' level of transmission might be means the public were unable to say when they thought the pandemic might shift from being a headline threat to the UK to a background disease that does not warrant current social distancing measures. As understanding when things return to normal is among the most important pieces of information the public are looking for, many will likely take an announcement from scientists or the government as the sign that the country has moved from an acute phase of the pandemic to a more chronic stage.

People want to see that the UK Governments are thinking about making provisions to help people deal with the fallout of the pandemic.

For many in the groups the pandemic has heightened attention on the inequalities experienced by different people as well as the unequal impacts on different sectors of the economy. Addressing this is an important factor for many and participants were keen to understand the practicalities of support that is available – for instance on how to make social distancing more accessible for businesses, public sector such as schools and individuals who are in need. Other types of support that were mentioned included financial assistance, greater mental health provision and improved sick pay for those forced to isolate.

Annex 4 SARS-CoV-2 Variants of Concern and Variants of Interest

(taken from https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ on 29 June 2021)

Variants of Concern (VOC)

A SARS-CoV-2 variant that meets the definition of a Variant of Interest (VOI) (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; or
- Increase in virulence or change in clinical disease presentation; or
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines or therapeutics.

WHO label	Pango lineage	GISAID clade/lineag e	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I (V1)	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A	India, Oct-2020	VOI: 4-Apr- 2021 VOC: 11- May-2021

Variants of Interest

A SARS-CoV-2 isolate is a Variant of Interest (VOI) if, compared to a reference isolate, its genome has mutations with established or suspected phenotypic implications, and either:

- Has been identified to cause community transmission/multiple COVID-19 cases/clusters, or has been detected in multiple countries; OR
- Is otherwise assessed to be a VOI by the World Health Organisation (WHO) in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group.

WHO label	Pango lineage	GISAID clade/lineag e	Nextstrain clade	Earliest documented samples	Date of designation
Epsilon	B.1.427/B.1.4 29	GH/452R.V1	21C	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR/484K.V2	20B/S.484K	Brazil, Apr-2020	17-Mar-2021

The Academy of Medical Sciences

Eta	B.1.525	G/484K.V3	21D	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR/1092K.V1	21E	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH/253G.V1	21F	United States of America, Nov-2020	24-Mar-2021
Карра	B.1.617.1	G/452R.V3	21B	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	20D	Peru, Dec-2020	14-Jun-2021

Annex 5 Assumptions underlying COVID-19 modelling

We generated forward scenarios under three sets of assumptions as described in the table below. All scenarios assume best estimates for vaccine effectiveness (from recent Public Health England (PHE) data) against the Delta variant and high vaccine uptake (95% uptake). R_t is assumed to increase from 19 July to 4, 4.75, 5.5 to reflect the uncertainty in impact of Step 4 of the relaxation of measures, as described in the roadmap out of lockdown. 692

Scenario	Best case	Central case	Worst case
Immunity	3-year natural	1-year natural	1-year natural
	immunity; 5-year	immunity, 3-year	immunity, 1-year
	vaccine	vaccine	vaccine
Vaccine impact on	Best PHE estimates	Best PHE estimates	Best PHE estimates
transmission	against Delta	against Delta	against Delta
Immune escape	None	10%	40%
for Delta compared			
to Alpha			
New variants	None	None	September and
			December

Table 1: Assumptions underlying the COVID-19 modelling. The best and central case scenarios are presented in Figure 1. The worst-case scenario is presented in Figure 7 in Annex 6.

Annex 6 Our reasonable worst-case COVID-19 scenario

Given the considerable uncertainty in some key parameters that determine the future UK outlook alongside ongoing circulation of the virus globally, we considered a range of different options for a worst-case scenario. We note that some of the most pessimistic scenarios may be excluded in the coming weeks if there is no rapid increase in hospitalisations and/or deaths.

Details for the assumptions behind these scenarios are shown in Annex 5. In summary, they include:

- More pessimistic assumptions about the durability of natural- and vaccineinduced immunity.
- A more limited impact of vaccines on transmission (reflecting uncertainty in the Delta variant and any new variants of concern).
- Reduced uptake of vaccine boosters in the autumn.
- Scenarios that include the emergence of a new variant of concern in both
 September 2021 and January 2022, with the variants of concern having increased transmissibility but no change in vaccine effectiveness.

As illustrated in Figure 7 below, a wide range of potential scenarios remain plausible under these assumptions with potential for a high number of hospitalisations during the winter months and the potential for ongoing epidemics occurring in 2022. To mitigate against these, it will be critical to ensure vaccine-induced immunity remains high (including through high uptake of the booster vaccine programme) and to ensure that outbreaks of any new variant of concern are rapidly contained.

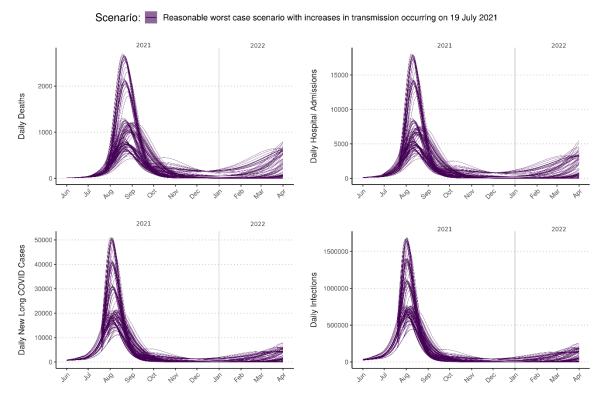


Figure 7: Our reasonable worst-case scenario for a COVID-19 epidemic in the UK. Under our reasonable worst-case scenario, we assume more pessimistic

assumptions about the durability of natural- and vaccine-induced immunity, a more limited impact of vaccines on transmission, reduced uptake of vaccine boosters in the autumn, and the emergence of a new variant of concern in both September 2021 and January 2022, with the variants of concern having increased transmissibility but no change in vaccine effectiveness. See Annex 5 for further details about the assumptions behind these scenarios.

Annex 7 Tables of effective and ineffective COVID-19 treatments

Table 2 summarises the treatments that have been found to be effective in treating COVID-19, as part of the UK clinical trial platforms. Progress has also been made in identifying ineffective treatments, which are summarised in Table 3.

Date	Treatment	Trial	Patient cohort	Further
16 June 2020	NIHR press release: first drug to reduce mortality in hospitalised patients with respiratory complications of COVID-19 found	RECOVERY Dexamethasone results press release	Hospitalised patients requiring oxygen or ventilator support	guidance DHSC press release: world first coronavirus treatment approved for NHS use by government COVID-19 therapeutic alert for corticosteroids NICE prescribing briefing WHO guidance on corticosteroids
7 January 2021	Tocilizumab and sarilumab NIHR press release: arthritis drugs effective in improving survival in sickest COVID- 19 patients	Press release: reduced mortality for sickest COVID- 19 patients	Patients in intensive care	DHSC press release: NHS patients to receive life- saving COVID- 19 treatments that could cut hospital time by 10 days COVID-19 therapeutics alert for IL6 inhibitors
11 February 2021	NIHR press release: RECOVERY trial shows	Tocilizumab results press release	Hospitalised patients who are receiving oxygen and are hypoxic	DHSC press release: thousands more NHS patients to get life-saving

	<u>tocilizumab</u>			COVID-19
	reduces deaths			<u>treatment</u>
	<u>in patients</u>			
	hospitalised			
	with COVID-19			
12 April 2021	Inhaled	PRINCIPLE	COVID-19	COVID-19
	budesonide		patients in the	<u>therapeutic</u>
			community	alert for
	<u>PRINCIPLE</u>		who are 65	<u>inhaled</u>
	press release:		and over or 50	<u>budesonide</u>
	asthma drug		and over with	
	<u>budesonide</u>		an underlying	
	<u>shortens</u>		health	
	recovery time		condition	
	in non-			
	hospitalised			
	patients with			
	COVID-19			

Table 2: Summary of treatments that have been found to be effective in treating COVID-19, as part of the UK clinical trial platforms (taken from: https://www.gov.uk/government/groups/the-covid-19-therapeutics-taskforce [accessed 21 June 2021])

Date	Treatment	Trial	Patient cohort
5 June 2020	Hydroxychloroquine	RECOVERY	Hospitalised patients
		<u>Hydroxychloroquine</u>	
		results press	
		<u>release</u>	
29 June 2020	Lopinavir/ritonavir	RECOVERY	Hospitalised patients
		Lopinavir-ritonavir	
		results press	
		<u>release</u>	
14 December 2020	Azithromycin	RECOVERY	Hospitalised patients
	NHIR press release:	<u>Azithromycin</u>	
	RECOVERY trial	results press	
	shows no clinical	<u>release</u>	
	benefit from		
	azithromycin for		
	hospitalised		
	<u>patients</u>		
22 December 2020	Heparin	REMAP-CAP	Severely ill patients in ICU requiring oxygen support
11 January 2021	Convalescent	REMAP-CAP	Patients in intensive
	plasma		care units

		I	
		Press release:	
	NIHR press release:	international trial of	
	studies find no	SARS-CoV-2	
	evidence of	<u>convalescent</u>	
	<u>convalescent</u>	<u>plasma pauses</u>	
	plasma benefit for	enrollment of	
	hospitalised COVID-	critically ill COVID-	
	19 patients	19 patients	
15 January 2021	Convalescent	RECOVERY+	Hospitalised
	plasma		patients
		<u>Convalescent</u>	
		plasma results	
		press release	
25 January 2021	Azithromycin	PRINCIPLE	Patients aged over
_	-		65 (or over 50 with
	NIHR press release:	PRINCIPLE trial	an underlying
	PRINCIPLE trial	finds antibiotics	health condition) in
	finds no benefit	azithromycin and	the community
	from antibiotics,	doxycycline not	Ţ
	azithromycin and	generally effective	
	doxycycline for	treatments for	
	COVID-19 patients	COVID-19	
25 January 2021	Doxycycline	PRINCIPLE	Patients aged over
J			65 (or over 50 with
	NIHR press release:	PRINCIPLE trial	an underlying
	PRINCIPLE trial	finds antibiotics	health condition) in
	finds no benefit	azithromycin and	the community
	from antibiotics,	doxycycline not	, , , , , ,
	azithromycin and	generally effective	
	doxycycline for	treatments for	
	COVID-19 patients	COVID-19	
5 March 2021	Colchicine	RECOVERY	Hospitalised
			patients
		RECOVERY trial	•
		closes recruitment	
		to colchicine	
		treatment for	
		<u>patients</u>	
		hospitalised with	
		•	
		COVID-19	

Table 3: Summary of treatments that have been found to be ineffective in treating COVID-19, as part of the UK clinical trial platforms (taken from: https://www.gov.uk/government/groups/the-covid-19-therapeutics-taskforce [accessed 21 June 2021])

Annex 8 Data considerations

The COVID-19 pandemic is the first pandemic to be observed in near real time with data playing a major role in developing and testing policy responses. Methods building on existing and new data collection mechanisms have generated rapid insights into health and behaviour.

Results from the CoMIX⁶⁹³ population survey of mixing patterns informed the development of a wide range of mathematical models of infection and likely impact of containment measures, which played a major part in guiding the work of SAGE and the responses of all UK Governments. ^{694,695,696} A range of population surveillance surveys were launched, including the Office for National Statistics (ONS) Coronavirus (COVID-19) Infection Survey (CIS) and REACT studies that have tracked the prevalence of active infection and immunity across the UK. ^{697,698} The ISARIC 4C Coronavirus Clinical Characterisation Consortium rapidly recruited the vast majority of hospitalised patients across the UK, identifying those most at risk of admission or death. ⁶⁹⁹ A host of population surveys have been launched to collect valuable information not routinely collected such as people's experiences and behaviours during various stages of the pandemic (e.g. the Northern Ireland Coronavirus Survey and the COVID-19 Social Study). ^{700,701} Crowdsourcing to provide rapid epidemiological insight into symptoms and experience of non-hospitalised cases came to the fore with the King's College London/Zoe app. ⁷⁰²

During the early phase of the pandemic UK Research and Innovation (UKRI), the National Institute for Health Research (NIHR), charities and devolved government agencies made major investments in levying routine data to respond urgently to the pandemic as is highlighted in the bi-weekly reports from Health Data Research UK (HDRUK) to SAGE. To Strategic investments in a number of trusted research environments (TREs) across the UK provided a huge increase in the breadth, depth, volume and accessibility of routinely collected data, most notably the NHS Digital/BHF centre, ONS, and OpenSafely in England and the EAVEII and Con-COV developments in Scotland and Wales. To 4, 705, 706, 707, 708 Linkage between routine data and research studies has potential to facilitate follow-up as in the RECOVERY trial.

Notable contributions to responding to the pandemic included the identification of highrisk groups for adverse outcomes, ⁷¹⁰ the creation of a risk score to identify those for vaccine prioritisation, ⁷¹¹ first evidence for vaccine effectiveness in the UK, ⁷¹² detailed insight into transmission patterns in households, pupils and school staff, ⁷¹³ and characterisation of symptoms of and risk factors for long COVID. ⁷¹⁴

Alongside innovative use of new and existing technologies there are notable trust and governance issues surrounding the increasing datafication of health as well as the development of public-private health initiatives and data partnerships that have formed in response to the crisis. Recent public engagement about the use of health and care data for research has shown the crucial role of transparency across the whole data cycle as a prerequisite for public benefit. The management of security and privacy concerns are also a challenge in the effective sharing of data generated through interaction with services (e.g. mobility or monetary transaction data), along with the collaborations and

coordination required across academia, the private sector and government departments for this type of work.⁷¹⁷

The collation, analysis and interpretation of complex data require a team science approach with expertise in the strengths and limitations of data sources, such as which groups of people may be under-represented in routine data sources or missing from linked datasets. Privacy-protecting designs in which researchers might access routine data on a subset of individuals, or in aggregate/output format rather than raw values, have potential implications for data checks and the identification of errors by the enduser that need consideration, along with training and capacity-building as these data systems develop. Shared and harmonised definitions and codes for new concepts such as long COVID will be needed to reflect evolving understanding and support research and data sharing.

Any data collection exercise must consider ethnic minority groups. Aggregating the experiences of ethnic minority groups obscures the important differences in experience and health outcomes for these groups during the pandemic. There is a need for better data and more sympathetic and culturally sensitive data collection for these different groups to help make regional, ethnic and social inequalities in health more visible.⁷¹⁸

References

- ¹ Often referred to as 'non-pharmaceutical interventions' or NPIs
- ² 'Hand and respiratory hygiene' includes washing hands and covering the mouth and nose.
- ³ Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21. https://acmedsci.ac.uk/filedownload/51353957
- Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21. https://acmedsci.ac.uk/filedownload/51353957
- The Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21. https://acmedsci.ac.uk/file-download/51353957
- Planet DIVOC-91 (n.d.). https://planetdivoc91.com/
- ⁷ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- The Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21.

https://acmedsci.ac.uk/file-download/51353957

The Green Book (2021). SARS-CoV-2 1 July 2021.

- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/998309/Gr eenbook_chapter_14a_1July2021.pdf
- Public Health England (2021). Surveillance of influenza and other seasonal respiratory viruses in the UK Winter 2020 to 2021.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/995284/S urveillance of influenza and other seasonal respiratory viruses in the UK 2020 to 2021-1.pdf
- ¹¹ Mansfield KE, et al. (2021). Indirect acute effects of the COVID-19 pandemic on physical and mental health in the UK: a population-based study. Lancet Digit. Health, 3, e217-230.
- ¹² Office for National Statistics (2019). Excess winter mortality in England and Wales: 2018 to 2019 (provisional) and 2017 to 2018 (final).
- https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/excesswin termortalityinenglandandwales/latest
- ¹³ National Records of Scotland (2018). Winter Mortality in Scotland 2017/18.
- https://www.nrscotland.gov.uk/files/statistics/winter-mortality/2018/winter-mortality-17-18-pub.pdf
- ¹⁴ Northern Ireland Statistics and Research Agency (2018). Excess Winter Mortality 2017/18.
- https://www.nisra.gov.uk/publications/excess-winter-mortality-201718
- The King's Fund (2020). NHS hospital bed numbers: past, present, future.
- https://www.kingsfund.org.uk/publications/nhs-hospital-bed-numbers [accessed 9 July 2021].

 16 National Institute for Health and Care Excellence (2018). Chapter 39 Bed occupancy. Emergency and acute medical care in over 16s: service delivery and organisation.
- https://www.nice.org.uk/guidance/ng94/evidence/39.bed-occupancy-pdf-172397464704
- The King's Fund (2020). How Covid has magnified some of social care's key problems.
- https://www.kingsfund.org.uk/publications/covid-19-magnified-social-care-problems?gclid=Cj0KCQ jw5uWGBhCTARIsAL70sLJFIGn8oCBt1aIFLvg5xpsqtk84WwNqT66oizjQ0inQKjRG9-Mw6KcaAvywEALw_wcB [accessed 6 July 2021].

 18 NHS Providers (2017). WINTER WARNING - Managing risk in health and care this winter.
- https://nhsproviders.org/media/3215/winter-warning.pdf
- ⁹ Hajat S, Bird W & Haines A (2004). *Cold Weather and GP Consultations for Respiratory Conditions by Elderly* People in 16 Locations in the UK. European Journal of Epidemiology 19(10), 959-968.
- ²⁰ Patterson S (2018). Do hospital admission rates increase in colder winters? A decadal analysis from an eastern county in England. Journal of Public Health **40(2)**, 221-228.

 ²¹ Public Health England (2017). Cold Weather Plan For England; Making the Case: Why long-term strategic
- planning for cold weather is essential to health and wellbeing.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/652568/C old Weather Plan Making the Case 2017.pdf

 22 Hajat S (2017). Health effects of milder winters: a review of evidence from the United Kingdom.
- Environmental Health 16(Suppl 1), 109.
- ²³ McClymont H & Wenbiao H (2021). Weather Variability and COVID-19 Transmission: A Review of Recent Research. International Journal of Environmental Research and Public Health 18(2), 396.
- ²⁴ Smith TP, et al. (2021). Temperature and population density influence SARS-CoV-2 transmission in the absence of nonpharmaceutical interventions. PNAS 118(25), e2019284118.
- ²⁵ World Meteorological Organization (2021). Review on Meteorological and Air Quality Factors Affecting the COVID-19 Pandemic. https://library.wmo.int/doc_num.php?explnum_id=10555
- ²⁶ World Meteorological Organization (2021). Review on Meteorological and Air Quality Factors Affecting the COVID-19 Pandemic. https://library.wmo.int/doc_num.php?explnum_id=10555.
- ²⁷ [pre-print] Gavenčiak T, et al. (2021). Seasonal variation in SARS-CoV-2 transmission in temperate climates. medRxiv. https://www.medrxiv.org/content/10.1101/2021.06.10.21258647v1
- ²⁸ The Centre for Evidence-Based Medicine (2020). *Do weather conditions influence the transmission of the* coronavirus (SARS-CoV-2)? https://www.cebm.net/wp-content/uploads/2020/03/Do-weather-conditionsinfluence-the-transmission-of-the-novel-coronavirus-2019-nCoV .pdf
- Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 17.
- $\underline{\text{https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/997418/V} \\$ ariants_of_Concern_VOC_Technical_Briefing_17.pdf

- ³⁰ UK Government (2021). The R value and growth rate. https://www.gov.uk/guidance/the-r-value-andgrowth-rate [accessed 3rd July 2021].
- Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 17.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/997418/V ariants of Concern VOC Technical Briefing 17.pdf
- ³² Public Health England (2021). COVID-19 vaccine surveillance report: Week 26.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/998411/V accine_surveillance_report_-_week_26.pdf
- ³³ Public Health England (2021). COVID-19 vaccine surveillance report: Week 26.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/998411/V accine surveillance report - week 26.pdf

 34 Public Health England (2021). COVID-19 vaccine surveillance report: Week 26.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/998411/V accine surveillance report - week 26.pdf
- ³⁵ The Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21. https://acmedsci.ac.uk/file-download/51353957
- ³⁶ UK Government (2021). COVID-19 Response Spring 2021 (Summary).
- https://www.gov.uk/government/publications/covid-19-response-spring-2021/covid-19-response-spring-2021summary
- ³⁷ Hanage WP & Russell CA (2021). Partial immunity and SARS-CoV-2 mutations. Science **372**, 354.
- ³⁸ Kemp SA (2021). SARS-CoV-2 evolution during treatment of chronic infection. Nature **592**, 277-282.
- ³⁹ Clark SA (2021). SARS-CoV-2 evolution in an immunocompromised host reveals shared neutralization escape mechanisms. Cell 184, 2605-2617.
- ⁴⁰ Casadevall A, et al. (2021). SARS-CoV-2 variants and convalescent plasma: reality, fallacies, and
- opportunities. The Journal of Clinical Investigation **131(7)**, e148832.

 41 The Royal Society (2020). *The SARS-CoV-2 genome: variation, implication and application.*
- https://royalsociety.org/-/media/policy/projects/set-c/set-c-genome-analysis.pdf

 42 Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- Centers for Disease Control and Prevention (2021). SARS-CoV-2 Variant Classification and Definitions. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html#Interest [accessed 6th July 2021].
- 44 World Health Organization (2021). COVID-19 Weekly Epidemiological Update; 25 February 2021. Special Edition: proposed working definitions of SARS-CoV-2 Variants of Interest and Variants of Concern.
- https://www.who.int/publications/m/item/covid-19-weekly-epidemiological-update

 45 Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 8.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/975742/V ariants_of_Concern_VOC_Technical_Briefing_8_England.pdf

 46 Grint DJ, et al. (2021). Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16
- November to 5 February. Eurosurveillance 26(11):p2100256.
- ⁴⁷ Frampton D, et al. (2021). Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. The Lancet Infectious Diseases.
- ⁴⁸ Davies NG, et al. (2021). Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. Nature 593, 270-274.
- ⁴⁹ GISAID Tracking of Variants. https://www.gisaid.org/hcov19-variants/ [accessed 6 July 2021].
- ⁵⁰ Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 17.
- $\underline{https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/attachment_data/file/997418/Values/system/uploads/sy$ ariants of Concern VOC Technical Briefing 17.pdf
- ⁵¹ Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 17.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/997418/V ariants_of_Concern_VOC_Technical_Briefing_17.pdf
- World Health Organisation (2021). Weekly epidemiological update on COVID-19 6 July 2021. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---6-july-2021 [accessed 9 July 2021]
- ⁵³ [pre-print] Public Health England (2021). Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant. https://khub.net/web/phe-national/public-library/-
- /document library/v2WsRK3ZlEig/view file/479607329? com liferay document library web portlet DLPortle t_INSTANCE_v2WsRK3ZlEig_redirect=https%3A%2F%2Fkhub.net%3A443%2Fweb%2Fphe-national%2Fpubliclibrary%2F-%2Fdocument library%2Fv2WsRK3ZIEig%2Fview%2F479607266
- ⁵⁴ Roy C, et al. (2020). Trends of mutation accumulation across global SARS-CoV-2 genomes: Implications for the evolution of the novel coronavirus. Genomics 112 (6), 5331-5342.
- 55 Gupta RK (2021). Will SARS-CoV-2 variants of concern affect the promise of vaccines? Nature Reviews Immunology 21, 340-341.
- ⁵⁶ Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 17.

- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/997418/V ariants_of_Concern_VOC_Technical_Briefing_17.pdf

 57 Parsons L (2021). AZ doses first participants with COVID-19 variant vaccine. PharmaTimes
- http://www.pharmatimes.com/news/az_doses_first_participants_with_covid-19_variant_vaccine_1372293?MID=edfff707-42a9-4720-9e08-0139959e5c1b&utm_campaign=pt-daily-newsalert&utm medium=email&utm source=pt-daily-newsletter
- ⁸ Centers for Disease Control and Prevention (2021). SARS-CoV-2 Variant Classification and Definitions. https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-info.html#Consequence [accessed 7th July 20211.
- ⁵⁹ Harvey WT, et al. (2021). SARS-CoV-2 variants, spike mutations and immune escape. Nature Reviews Microbiology 19, 409-424.
- ⁶⁰ [pre-print] Maher MC, et al. (2021). Predicting the mutational drivers of future SARS-CoV-2 variants of concern. medRxiv. https://www.medrxiv.org/content/10.1101/2021.06.21.21259286v1.full.pdf
- ⁶¹ Williams TC & Burgers WA (2021). SARS-CoV-2 evolution and vaccines: cause for concern? The Lancet Respiratory Medicine 9(4), 333-335.
- ⁶² Su S, Zezhong L & Jiang S (2021). Double insult: flu bug enhances SARS-CoV-2 infectivity. Cell Research **31**, 491-492.
- ⁶³ New and Emerging Respiratory Virus Threats Advisory Group (2021). Note of growth rate of SARS-CoV-2
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/982503/S 1211_NERVTAG_B.1.1.7_growth_rate.pdf
- ⁶⁴ Hodcroft EB, et al. (2021). Spread of a SARS-CoV-2 variant through Europe in the summer of 2020. Nature. ⁶⁵ Racaniello V (2021). Holiday travel explains spread of a SARS-CoV-2 variant. Virology Blog.
- https://www.virology.ws/2021/06/10/holiday-travel-explains-spread-of-a-sars-cov-2-variant/ [accessed 7th July 2021].
- 66 [pre-print] Bernal JL, et al. (2021). Effectiveness of COVID-19 vaccines against the B.1.617.2 variant. medRxiv https://www.medrxiv.org/content/10.1101/2021.05.22.21257658v1
- ⁶⁷ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- Grépin KA, et al. (2021). Evidence of the effectiveness of travel-related measures during the early phase of the COVID-19 pandemic: a rapid systematic review. BMJ Global Health 6, e004537
- ⁶⁹ World Health Organization (2021). Genomic sequencing of a SARS-CoV-2: A guide to implementation for maximum impact on public health. https://www.jstor.org/stable/resrep30103
- ⁷⁰ Wadman M (2021). Scientists tracking coronavirus variants struggle with global blind spots. Science, 14 $May. \ \underline{www.sciencemag.org/news/2021/05/scientists-tracking-coronavirus-variants-struggle-global-blind-spots}$ ⁷¹ John Hopkins University & Medicine: Coronavirus Resource Center (2021). The Search for COVID-19 Variants. https://coronavirus.jhu.edu/data/variant-data [accessed 7 July 2021].
- ⁷² [pre-print] Dudas G, et al. (2021). Travel-driven emergence and spread of SARS-CoV-2 lineage B.1.620 with multiple VOC-like mutations and deletions in Europe. medRxiv. https://www.medrxiv.org/content/10.1101/2021.05.04.21256637v1
- ³ Mallapaty S (2021). *How a worrisome coronavirus variant spread unnoticed.* Nature, 13 May. https://www.nature.com/articles/d41586-021-01285-4
- ⁷⁴ Wadman M (2021). Scientists tracking coronavirus variants struggle with global blind spots. Science, 14 May. www.sciencemag.org/news/2021/05/scientists-tracking-coronavirus-variants-struggle-global-blind-spots ⁷⁵ UK Government, Department of Health and Social Care (2021). UK and US agree new partnership to fight future pandemics and tackle health inequalities. https://www.gov.uk/government/news/uk-and-us-agree-newpartnership-to-fight-future-pandemics-and-tackle-health-inequalities
- ⁷⁶ G7 (2021). Carbis Bay G7 Summit Communiqué: Our Shared Agenda for Global Action to Build Back Better. https://www.g7uk.org/wp-content/uploads/2021/06/Carbis-Bay-G7-Summit-Communique-PDF-430KB-25pages-3.pdf
- ⁷⁷ Farrar J (2021). A proposal to develop an equitable global pathogen surveillance network in 2021 that can prevent and respond to emerging and endemic infectious diseases at speed and scale. G7.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/990314/Pa thogen_Surveillance_report_to_the_UK_G7_Presidency_2021.pdf
- 78 GISAID. Tracking of Variants. https://www.gisaid.org/hcov19-variants/ [accessed 7 July 2021].
- ⁷⁹ MRC Centre for Global Infectious Disease Analysis. Future scenarios of the healthcare burden of COVID-19 in Low- or Middle- Income Countries. https://mrc-ide.github.io/global-lmic-reports/ [accessed 1 July 2021].
- 80 Centers for Disease Control and Prevention. Science Brief: COVID-19 Vaccines and Vaccination. https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html [accessed 7
- ⁸¹ BBC News (2021). Covid-19 pandemic: Chile capital locks down despite mass vaccination.
- https://www.bbc.co.uk/news/world-latin-america-57436861

 82 Taylor L (2021). Covid-19: Spike in cases in Chile is blamed on people mixing after first vaccine shot. BMJ, 20 April. https://www.bmj.com/content/373/bmj.n1023
- 83 Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- Wouters OJ, et al. (2021). Challenges in ensuring global access to COVID-19 vaccines: production, affordability, and deployment. Lancet, 397, 1023-1034.
- ⁸⁵ Lindholt MF, et al. (2021). Public acceptance of COVID-19 vaccines: cross-national evidence on levels and individual-level predictors using observational data. BMJ Open, 11, e048172.

- ⁸⁶ UK Government. Coronavirus (COVID-19) in the UK. https://coronavirus.data.gov.uk/details/vaccinations [accessed 29 June 2021].
- Our World in Data. Coronavirus (COVID-19) Vaccinations. https://ourworldindata.org/covidvaccinations?country=~GBR [accessed 8 July 2021].

 88 BBC News (2021). Covid-19: Four million in UK get their first vaccine. BBC, 18 January.
- https://www.bbc.co.uk/news/uk-55710758
- England R (2021). England's coronavirus vaccine rollout in maps. BBC News, 6 March.
- https://www.bbc.co.uk/news/uk-england-56293839
- Office for National Statistics (2021). Coronavirus and vaccine hesitancy, Great Britain: 13 January to 7
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandwellbeing/bulletins/cor onavirusandvaccinehesitancygreatbritain/13januaryto7february2021/previous/v1
- Royal Society for Public Health (2021). New poll finds ethnic minority groups less likely to want COVID vaccine. https://www.rsph.org.uk/about-us/news/new-poll-finds-bame-groups-less-likely-to-want-covidvaccine.html
- 92 Office for National Statistics (2021). Coronavirus (COVID-19) latest insights.
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/c oronaviruscovid19/latestinsights#vaccinations [accessed 22 June].
- Office for National Statistics. Coronavirus (COVID-19) latest insights.
- $\underline{https://www.ons.gov.uk/people population and community/health and social care/conditions and diseases/articles/conditions are diseases/articles/conditions/articles/$ oronaviruscovid19/latestinsights#vaccinations [accessed 22 June].

 94 Office for National Statistics (2001)
- Office for National Statistics (2021). Coronavirus and vaccination rates in people aged 50 years and over by socio-demographic characteristic, England: 8 December 2020 to 12 April 2021.
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthinegualities/bulletins/coron avirusandvaccinationratesinpeopleaged70yearsandoverbysociodemographiccharacteristicengland/8december20
- 20to12april2021

 95 [pre-print] Curtis HJ, et al. (2021). Trends and clinical characteristics of COVID-19 vaccine recipients: a federated analysis of 57.9 million patients' primary care records in situ using OpenSAFELY. medRxiv. https://www.medrxiv.org/content/10.1101/2021.01.25.21250356v3
- Office for National Statistics. Coronavirus (COVID-19) latest insights.
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/c oronaviruscovid19/latestinsights#vaccinations [accessed 22 June].
- [pre-print] Curtis HJ, et al. (2021). Trends and clinical characteristics of COVID-19 vaccine recipients: a federated analysis of 57.9 million patients' primary care records in situ using OpenSAFELY. medRxiv. https://www.medrxiv.org/content/10.1101/2021.01.25.21250356v3
- 98 Office for National Statistics. Coronavirus (COVID-19) latest insights.
- $\underline{\text{https://www.ons.gov.uk/people population} and community/health and social care/conditions and diseases/articles/conditions and diseases articles/conditions are diseases. \\$ oronaviruscovid19/latestinsights#vaccinations [accessed 30 June].

 99 NHS (2021). NHS COVID-19 vaccination programme jabs half of adults under 30. NHS News, 27 June.
- https://www.england.nhs.uk/2021/06/nhs-covid-19-vaccination-programme-jabs-half-of-adults-under-30/
- [pre-print] Riley S, et al. (2021). REACT-1 round 12 report: resurgence of SARS-CoV-2 infections in England associated with increased frequency of the Delta variant. medRxiv.
- https://www.medrxiv.org/content/10.1101/2021.06.17.21259103v1.full.pdf
- ¹⁰¹ UK Government. (2021). COVID-19 vaccination: a guide to phase 2 of the programme.
- https://www.gov.uk/government/publications/covid-19-vaccination-guide-for-older-adults/covid-19-vaccination-guide-guid vaccination-a-guide-to-phase-2-of-the-programme [accessed 16 Jun 2021].
- ¹⁰² [pre-print] Enright J, et al. (2021). SARS-CoV-2 infection in UK students: lessons from September-December 2020 and modelling insights for the future student return.
- https://www.newton.ac.uk/files/preprints/ni20004.pdf
- Mutambudzi M, et al. (2021). Occupation and risk of severe COVID-19: prospective cohort study of 120,075 UK Biobank participants. Occupational and Environmental Medicine 78, 307-314.
- BBC (2021). Covid-19: Vaccinated NHS staff numbers vary across England. BBC News, 5 March. https://www.bbc.co.uk/news/health-56291564
- ¹⁰⁵ Shimabukuro TT, et al. (2021). Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. The New England Journal of Medicine 384, 2273-2282.
- ¹⁰⁶ Yang R, et al. (2020). Pregnant women with COVID-19 and risk of adverse birth outcomes and maternalfecal vertical transmission: a population-based cohort study in Wuhan, China. BMC Medicine 18, 330.
- 107 MBRRACE-UK (2020). Saving Lives, Improving Mothers' Care. Rapid report: Learning from SARS-CoV-2 related and associated maternal deaths in the UK. https://www.npeu.ox.ac.uk/assets/downloads/mbrraceuk/reports/MBRRACE-UK_Maternal_Report_2020_v10_FINAL.pdf
- ¹⁰⁸ Khoury DS, et al. (2021). Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nature Medicine, 17 May. https://www.nature.com/articles/s41591-021-01377-8
- [pre-print] Earle KA, et al. (2021). Evidence for antibody as a protective correlate for COVID-19 vaccines. medRxiv. https://www.medrxiv.org/content/10.1101/2021.03.17.20200246v1
- ¹¹⁰ Public Health England (2021). COVID-19 vaccine surveillance report Week 26.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/998411/V accine surveillance report - week 26.pdf

 111 [pre-print] Liu C, et al. (2021). Reduced neutralization of SARS-CoV-2 B.1.617 by vaccine and
- convalescent serum. Cell. https://www.cell.com/cell/pdf/S0092-8674(21)00755-

- 8.pdf? returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867421007558%3F
- showall%3Dtrue

 112 Richterman A, Meyerowitz EA & Cevik M (2021). Indirect Protection by Reducing Transmission: Ending the Pandemic with SARS-CoV-2 Vaccination. Open Forum Infectious Diseases of ab 259.
- ¹¹³ [pre-print] Cagigi A, et al. (2021). Airway antibodies emerge according to COVID-19 severity and wane rapidly but reappear after SARS-CoV-2 vaccination. medRxiv.
- https://www.medrxiv.org/content/10.1101/2020.11.25.20238592v3 114 Public Health England (2021). COVID-19 vaccine surveillance report Week 26.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/998411/V
- accine surveillance report week 26.pdf

 115 Richterman A, Meyerowitz EA & Cevik M (2021). Indirect Protection by Reducing Transmission: Ending the Pandemic with SARS-CoV-2 Vaccination. Open Forum Infectious Diseases ofab259.
- ¹¹⁶ Richterman A, Meyerowitz EA & Cevik M (2021). Indirect Protection by Reducing Transmission: Ending the Pandemic with SARS-CoV-2 Vaccination. Open Forum Infectious Diseases ofab259.
- 117 Harries R, et al. (2021). Impact of vaccination on household transmission of SARS-COV-2 in England.
- $\underline{\text{https:}}//k\text{hub.net/documents/135939561/390853656/Impact+of+vaccination+on+household+transmission+of}$ +SARS-COV-2+in+England.pdf/35bf4bb1-6ade-d3eb-a39e-9c9b25a8122a?t=1619601878136
- [pre-print] Bernal JL, et al. (2021). Effectiveness of COVID-19 vaccines against the B.1.617.2 variant. medRxiv. https://www.medrxiv.org/content/10.1101/2021.05.22.21257658v1
- ¹¹⁹ Sheikh A, et al. (2021). SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission and vaccine effectiveness. Lancet 397, 2461-2462.
- ¹²⁰ [pre-print] Public Health England (2021). Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant. https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZlEig/view_file/479607329?_com_liferay_document_library_web_portlet_DLPortle INSTANCE_v2WsRK3ZIEig_redirect=https%3A%2F%2Fkhub.net%3A443%2Fweb%2Fphe-national%2Fpubliclibrary%2F-%2Fdocument_library%2Fv2WsRK3ZIEig%2Fview%2F479607266
- 121 Williamson EJ et al. (2020). Factors associated with COVID-19-related death using OpenSAFELY. Nature **584**, 430-4.
- 36. https://www.nature.com/articles/s41586-020-2521-4
- Razai MS, et al. (2021). Covid-19 vaccination hesitancy. BMJ 373, n1138.
- ¹²³ Razai MS, et al. (2021), Covid-19 vaccination hesitancy, BMJ **373**, n1138.
- ¹²⁴ [pre-print] Maher MC, et al. (2021). Predicting the mutational drivers of future SARS-CoV-2 variants of concern. medRxiv. https://www.medrxiv.org/content/10.1101/2021.06.21.21259286v1.full.pdf
- ¹²⁵ Khoury DS, et al. (2021). Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nature Medicine, 17 May. https://www.nature.com/articles/s41591-021-<u>01377</u>-8
- ¹²⁶ European Centre for Disease Prevention and Control. Immune responses and immunity to SARS-CoV-2. https://www.ecdc.europa.eu/en/covid-19/latest-evidence/immune-responses [accessed 8 July 2021].
- ²⁷ Grigoryan L & Pulendran B (2020). The immunology of SARS-CoV-2 infections and vaccines. Seminars in Immunology 50, 101422.
- ¹²⁸ Clark SA, et al. (2021). SARS-CoV-2 evolution in an immunocompromised host reveals shared neutralization escape mechanisms. Cell 184(10), 2605-2617.
- ¹²⁹ Kemp SA, et al. (2021). SARS-CoV-2 evolution during treatment of chronic infection. Nature, **592**, 277-282.
- ¹³⁰ Grigoryan L & Pulendran B (2020). The immunology of SARS-CoV-2 infections and vaccines. Seminars in Immunology 50, 101422.
- ¹³¹ Shroti M, et al. (2021). T cell response to SARS-CoV-2 infection in humans: A systematic review. PLoS One, 16(1), e0245532.
- 132 Bertoletti A, Tan AT & Le Bert N (2021). The T-cell response to SARS-CoV-2: kinetic and quantitative aspects and the case for their protective role. Oxford Open Immunology 2, iqab006.
- 133 Reynolds CJ, et al. (2021). Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. Science 372, 1418-1423.
- ¹³⁴ Cromer D, et al. (2021). Prospect for durable immune control of SARS-CoV-2 and prevention of reinfection. Nature Reviews Immunology 21, 395-404.
- ¹³⁵ World Health Organization (2021). COVID-19 Weekly Epidemiological Update; 25 February 2021. Special Edition: proposed working definitions of SARS-CoV-2 Variants of Interest and Variants of Concern. https://www.who.int/publications/m/item/covid-19-weekly-epidemiological-update
- 136 Reynolds CJ, et al. (2021). Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. Science 372, 1418-1423.
- ¹³⁷ Cromer D, et al. (2021). Prospect for durable immune control of SARS-CoV-2 and prevention of reinfection. Nature Reviews Immunology 21, 395-404.
- 138 European Centre for Disease Prevention and Control (2021). Immune responses and immunity to SARS-CoV-2. https://www.ecdc.europa.eu/en/covid-19/latest-evidence/immune-responses [accessed 8 July 2021].
- 139 UK Government, Department of Health & Social Care (2021). JCVI interim advice: potential COVID-19 booster vaccine programme winter 2021 to 2022. https://www.gov.uk/government/publications/jcvi-interimadvice-on-a-potential-coronavirus-covid-19-booster-vaccine-programme-for-winter-2021-to-2022/jcvi-interimadvice-potential-covid-19-booster-vaccine-programme-winter-2021-to-2022#fn:6
- ⁰ COV-Boost: Evaluating COVID-19 vaccine booster (n.d.). <u>https://www.covboost.org.uk/home</u> [accessed 8 July 2021].
- ¹⁴¹ [pre-print] Flaxman A, et al. (2021). Tolerability and Immunogenicity After a Late Second Dose or a Third Dose of ChAdOX1 nCoV-19 (AZD1222). SSRN https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3873839

- ¹⁴² AstraZeneca (2021). *Vaxzevria induced immunity for at least one year following a single dose and strong immune responses following a late second dose or a third dose*. https://www.astrazeneca.com/media-centre/press-releases/2021/vaxzevria-induced-immunity-for-at-least-1-year-following-a-single-dose-and-strong-immune-responses-following-either-a-late-second-dose-or-a-third-dose.html
- ¹⁴³ Com-CoV: Comparing COVID-19 Vaccine Schedule Combinations (n.d.). https://comcovstudy.org.uk/home [accessed 8 July 2021].
- ¹⁴⁴ [pre-print] Liu X, et al. (2021). Safety and Immunogenicity Report from the Com-COV Study a Single-Blind Randomised Non-Inferiority Trial Comparing Heterologous And Homologous Prime-Boost Schedules with An Adenoviral Vectored and mRNA COVID-19 Vaccine. SSRN.

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3874014

- ¹⁴⁵ ComFluCOV Vaccine Study (n.d.). https://comflucov.blogs.bristol.ac.uk/ [accessed 8 July 2021].
- ¹⁴⁶ [pre-print] Massare MJ, et al. (2021). Combination Respiratory Vaccine Containing Recombinant SARS-CoV-2 Spike and Quadrivalent Seasonal Influenza Hemagglutinin Nanoparticles with Matrix-M Adjuvant. bioRxiv https://www.biorxiv.org/content/10.1101/2021.05.05.442782v1
- ¹⁴⁷ Palmer S, Cunniffe N & Donnelly R (2021). *COVID-19 hospitalization rates rise exponentially with age, inversely proportional to thymic T-cell production*. Journal of the Royal Society Interface **18**, 20200982
 ¹⁴⁸ Bhopal SS, *et al.* (2021). *Children and young people remain at low risk of COVID-19 mortality*. The Lancet Child & Adolescent Health **5**, E12-E13.
- ¹⁴⁹ [pre-print] Ward JL, et al. (2021). Risk factors for intensive care admission and death amongst children and young people admitted to hospital with COVID-19 and PIMS-TS in England during the first pandemic year. https://www.medrxiv.org/content/10.1101/2021.07.01.21259785v1
- https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/demographics/agegroups/latest#main-facts-and-figures
- ¹⁵¹ Royal College of Paediatrics and Child Health. *COVID-19 research evidence summaries*. https://www.rcpch.ac.uk/resources/covid-19-research-evidence-summaries [accessed 8 July 2021].
- ¹⁵² [pre-print] House T, et al. (2021). Inferring Risks of Coronavirus Transmission from Community Household Data. arXiv. https://arxiv.org/pdf/2104.04605.pdf
- ¹⁵³ Macartney K, et al. (2020). Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. The Lancet Child & Adolescent Health **4**, 807-816.
- ¹⁵⁴ Ulyte A, et al. (2021). Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school children in the canton in Zurich, Switzerland: prospective cohort study of 55 schools. BMJ, **372**, n616.
- ¹⁵⁵ Ismail SA, et al. (2021). SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England. The Lancet Infectious Diseases **21**, 344-353.
- ¹⁵⁶ Thompson H (2021). *Children with long covid.* New Scientist **249**, 10-11.
- ¹⁵⁷ [pre-print] Osmanov IM, et al. (2021). Risk factors for long covid in previously hospitalised children using ISARIC Global follow-up protocol: A prospective cohort study. European Respiratory Journal. https://erj.ersjournals.com/content/erj/early/2021/06/10/13993003.01341-2021.full.pdf
- ¹⁵⁸ Buonsenso D, et al. (2021). Preliminary evidence on long COVID in children. Acta Paediatrica **110**, 2208-2211.
- ¹⁵⁹ [pre-print] Munblit D, et al. (2021). The risk of overlooking children during the COVID-19 pandemic: Paediatric Long-COVID may be a ticking time bomb. The Lancet Child & Adolescent Health. http://eprints.gla.ac.uk/232679/
- ¹⁶⁰ Say D, et al. (2021). Post-acute COVID-19 outcomes in children with mild and asymptomatic disease. The Lancet Child & Adolescent Health **5**, E22-E23.
- ¹⁶¹ Brackel CLH, et al. (2021). Pediatric long-COVID: An overlooked phenomenon. Pediatr. Pulmonol., 1-8.
- ¹⁶² Viner RM, et al. (2006). Risk factors for persistent fatigue in adolescents: A population-based study. Journal of Adolescent Health **38(2)**, 113-114.
- ¹⁶³ Marshall M (2021). The four most urgent questions about long COVID. Nature **594**, 168-170.
- ¹⁶⁴ Loades ME, et al. (2020). Rapid Systematic Review: The Impact of Social Isolation and Loneliness on the Mental Health of Children and Adolescents in the Context of COVID-19. Journal of the American Academy of Child and Adolescent Psychiatry **59(11)**, 1218-1239.
- ¹⁶⁵ Frenck RW, et al. (2021). Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. The New England Journal of Medicine, 27 May.
- https://www.nejm.org/doi/full/10.1056/NEJMoa2107456
- ¹⁶⁶ Centers for Disease Control and Prevention. Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults.
- https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html [accessed 9 July 2021].

 167 US Food & Drug Administration (2021). Coronavirus (COVID-19) Update: FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Adolescents in Another Important Action in Fight Against Pandemic. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-
- biontech-covid-19-vaccine-emergency-use [accessed 9 July 2021].

 168 Ministère des Solidarité et de la Santé (2021). Covid vaccination in France: as of June 14, 2021, more than 44,800,000 injections have been performed. https://solidarites-sante.gouv.fr/actualites/presse/communiques-
- de-presse/article/vaccination-contre-la-covid-en-france-au-14-juin-2021-plus-de-44-800-000 [accessed 9 July 2021].
- ¹⁶⁹ UK Government. Routine childhood immunisation schedule.
- https://www.gov.uk/government/publications/routine-childhood-immunisation-schedule [accessed 9 July 2021].

- ¹⁷⁰ Vaccinations delivered in school include the human papillomavirus (HPV) vaccine, MenACWY vaccine that provides protection against meningitis and blood poisoning, and Td/IPV vaccine that provides protection against tetanus, diphtheria and polio.
- ¹⁷¹ World Health Organization. Coronavirus disease (COVID-19): How is it transmitted?
- https://www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-how-is-it-transmitted [accessed 9 July 2021].
- Leung NHL (2021). Transmissibility and transmission of respiratory viruses. Nature Reviews Microbiology 19, pages 528-545.
- World Health Organization. Coronavirus disease (COVID-19): How is it transmitted?
- https://www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-how-is-it-transmitted [accessed 9 July 2021].
- ¹⁷⁴ Scientific Advisory Group for Emergencies (2021). Masks for healthcare workers to mitigate airborne transmission of SARS-CoV-2.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/979441/S 1169 Facemasks for health care workers.pdf
- ¹⁷⁵ Greenhalgh T, et al. (2021). Ten scientific reasons in support of airborne transmission of SARS-CoV-2. Lancet 397, 1603-1605.
- ¹⁷⁶ Leung NHL (2021). *Transmissibility and transmission of respiratory viruses*. Nature Reviews Microbiology 19, pages 528-545.
- Leung NHL, et al. (2020). Respiratory virus shedding in exhaled breath and efficacy of face masks. Nature Medicine 26(5), 676-680.
- ¹⁷⁸ Jefferson T, et al. (2011). Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Systematic Reviews 7, CD006207.
- ¹⁷⁹ Pei S, Kandula S & Shaman J (2020). Differential effects of intervention timing on COVID-19 spread in the United States. Science Advances 6(49), eabd6370.
- ¹⁸⁰ Tian H, et al. (2020). An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China. Science 368, 638-642.
- ¹⁸¹ Lai S, et al. (2020). Effect of non-pharmaceutical interventions to contain COVID-19 in China. Nature **585**, 410-413.
- ¹⁸² Chinnazi M, et al. (2020). The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. Science 368, 395-400.
- ¹⁸³ Hsiang S, et al. (2020). The effect of large-scale anti-contagion policies on the COVID-19 pandemic. Nature **584**, 262-267.
- ¹⁸⁴ Noakes CJ, et al. (2006). Modelling the transmission of airborne infections in enclosed spaces. Epidemiology and Infection 134(5), 1082-1091.
- ¹⁸⁵ Leung NHL, et al. (2020). Respiratory virus shedding in exhaled breath and efficacy of face masks. Nature Medicine 26(5), 676-680.
- ¹⁸⁶ Jefferson T, et al. (2009). Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. BMJ **339**, b3675.

 187 Hayward AC, et al. (2020). Public activities preceding the onset of acute respiratory infection syndromes in
- adults in England implications for the use of social distancing to control pandemic respiratory infections. Wellcome Open Research 5, 54.
- ¹⁸⁸ Cowling BJ, et al. (2020). Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. Lancet Public Health 5(5), E279-E288.
- ¹⁸⁹ Parry MF, et al. (2020). Precipitous Fall in Common Respiratory Viral Infections During COVID-19. Open Forum Infectious Diseases 7(11), ofaa511.
- ¹⁹⁰ Noakes CJ, et al. (2006). Modelling the transmission of airborne infections in enclosed spaces. Epidemiology and Infection 134(5), 1082-109.
- 191 Parry MF, et al. (2020). Precipitous Fall in Common Respiratory Viral Infections During COVID-19. Open Forum Infectious Diseases 7(11), ofaa511.
- 192 Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- ¹⁹³ Copat C, et al. (2020). The role of air pollution (PM and NO2) in COVID-19 spread and lethality: A
- systematic review. Environmental Research **191**, 110129.

 194 Agarwal N, et al. (2021). Indoor air quality improvement in COVID-19 pandemic: Review. Sustain Cities Society 70, 102942.
- ¹⁹⁵ Nor NSM, et al. (2021). Particulate matter (PM2.5) as a potential SARS-CoV-2 carrier. Scientific Reports **11(1)**, 2508.
- ¹⁹⁶ Harvard T.H. Chan School of Public Health. Coronavirus and Air Pollution. https://www.hsph.harvard.edu/cchange/subtopics/coronavirus-and-pollution/ [accessed 9 July 2021].
- 197 Royal Academy of Engineering (2021). Infection resilient environments.
- https://www.raeng.org.uk/infection-resilient-environments
- ¹⁹⁸ UK Government. About the Adult Social Care Infection Control Fund.
- https://www.gov.uk/government/publications/adult-social-care-infection-control-fund/about-the-adult-socialcare-infection-control-fund [accessed 9 July 2021].
- ⁹⁹ Academy of Medical Sciences (2021). Academy of Medical Sciences response to the Department for Health and Social Care 'Transforming public health' consultation. https://acmedsci.ac.uk/file-download/66394796 ²⁰⁰ Scottish Government (2021). Coronavirus (COVID-19) - testing strategy: update - March 2021.
- https://www.gov.scot/publications/scotlands-testing-strategy-update-march-2021/ [accessed 9 July 2021].
- ²⁰¹ Public Health Wales. Test, trace, protect: coronavirus. https://phw.nhs.wales/topics/latest-information-onnovel-coronavirus-covid-19/guidance-accordion/test-trace-protect-coronavirus/ [accessed 9 July 2021].

- ²⁰² National Audit Office (2021). The government's approach to test and trace in England interim report. https://www.nao.org.uk/wp-content/uploads/2020/12/The-governments-approach-to-test-and-trace-in-
- England-interim-report.pdf

 203 National Audit Office (2021). Test and trace in England progress report. https://www.nao.org.uk/wpcontent/uploads/2021/06/Test-and-trace-in-England-progress-update.pdf
- ²⁰⁴ UK Government, Department of Health and Social Care (2021). Weekly statistics for NHS Test and Trace (England): 27 May to 2 June 2021.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/992580/Te st_and_Trace_Week53.pdf

 205 Welsh Government (2021). Test Trace Protect. https://gov.wales/test-trace-protect [accessed 9 July 2021].

²⁰⁶ NHS Scotland. Test and Protect: Help stop the spread of coronavirus (COVID-19). https://www.nhsinform.scot/campaigns/test-and-protect [accessed 9 July 2021]

- ²⁰⁷ HSC Public Health Agency. Test and tracing for COVID-19. https://www.publichealth.hscni.net/covid-19coronavirus/testing-and-tracing-covid-19 [accessed 9 July 2021]
- Razai MS, et al. (2021). Covid-19 vaccination hesitancy among ethnic minority groups. BMJ, 372, n513.
- ²⁰⁹ [pre-print] Nafilyan V, et al. (2021). Sociodemographic inequality in COVID-19 vaccination coverage amongst elderly adults in England: a national linked data study. medRxiv.

https://www.medrxiv.org/content/10.1101/2021.05.13.21257146v1

- [pre-print] Curtis HJ, et al. (2021). Trends and clinical characteristics of COVID-19 vaccine recipients: a federated analysis of 57.9 million patients' primary care records in situ using OpenSAFELY. medRxiv. https://www.medrxiv.org/content/10.1101/2021.01.25.21250356v3
- Baker RE, et al. (2020). The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. PNAS, 117(48), 30547-30553.
- ²¹² Foley DA, et al. (2021). The Interseasonal Resurgence of Respiratory Syncytial Virus in Australian Children Following the Reduction of Coronavirus Disease 2019 - Related Public Health Measures. Clinical Infectious Diseases ciaa1906.
- ²¹³ Brendish NJ, et al. (2017). Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. The Lancet Respiratory Medicine 5(5), 401-411.
- ²¹⁴ de Lusignan S, et al. (2019). Feasibility of point-of-care testing for influenza within a national primary care sentinel surveillance network in England: protocol for a mixed methods study. JMIR Research Protocols 8(11), e14186.
- ²¹⁵ Buckle P, et al. (2021). COVID-19 point-of-care testing in care homes: what are the lessons for policy and
- practice? Age and Ageing afab101.

 216 Klepser DG, et al. (2003). Evaluation of a community pharmacy-based influenza and group A streptococcal pharyngitis disease management program using polymerase chain reaction point-of-care testing. Journal of the American Pharmacists Association 59(6), 872-879.
- ²¹⁷ National Institute for Health and Care Excellence (2009). Amantadine, oseltamivir and zanamir for the treatment of influenza. https://www.nice.org.uk/guidance/ta168/resources/amantadine-oseltamivir-andzanamivir-for-the-treatment-of-influenza-pdf-82598381928133

 ²¹⁸ Du Z, et al. (2021). Comparative cost-effectiveness of SARS-CoV-2 testing strategies in the USA: a
- modelling study. Lancet Public Health, 6(13), E184-E191.
- ²¹⁹ Gill M & Gray M (2021). Mass testing for covid-19 in the UK. BMJ **371**, m4436.
- ²²⁰ Micocci M, et al. (2021). Is point-of-care testing feasible and safe in care homes in England? An exploratory usability and accuracy evaluation of a point-of-care polymerase chain reaction test for SARS-CoV-2. Age and Ageing afab072.
- ²²¹ [pre-print] Micocci M, et al. (2021). Point of Care Testing using rapid automated Antigen Testing for SARS-CoV-2 in Care Homes - an exploratory safety, usability and diagnostic agreement evaluation. medRxiv. https://www.medrxiv.org/content/10.1101/2021.04.22.21255948v2
- Buckle P, et al. (2021). COVID-19 point-of-care testing in care homes: what are the lessons for policy and practice? Age and Ageing afab101.
- ²³ Hillary LS, et al. (2021). Monitoring SARS-CoV-2 in municipal wastewater to evaluate the success of lockdown measures for controlling COVID-19 in the UK. Water Research 200, 117214.
- ²²⁴ [pre-print] Fitzgerald SF, et al. (2021). COVID-19 mass testing: harnessing the power of wastewater epidemiology. medRxiv 2021.05.24.21257703; doi: https://doi.org/10.1101/2021.05.24.21257703

 225 Medema G, et al. (2020). Presence of SARS-Coronavirus-2 in sewage. Environmental Science & Technology Letters 7(7), 511-516.
- ²²⁶ Martin J, et al. (2020). Tracking SARS-CoV-2 in Sewage: Evidence of Changes in Virus Variant Predominance during COVID-19 Pandemic. Viruses 12(10), 1144.
- ²²⁷ Sims N & Kasprzyk-Hordern B (2020). Future perspectives of wastewater-based epidemiology: Monitoring infectious disease spread and resistance to the community level. Environment International 139, 105689.
- ²²⁸ UK Government, Department of Health and Social Care (2021). The Rum Model Technical Annex: Assessing the impact of test, trace and isolate parameters on COVID-19 transmission in an October-like environment. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/960110/R UM_model_technical_annex_final__100221.pdf
- ²²⁹ Kucharski AJ, et al. (2020). Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study. The Lancet Infectious Diseases 20(10), 1151-1160.
- ²³⁰ Gill M & Gray M (2021). Mass testing for covid-19 in the UK. BMJ **371**, m4436.
- ²³¹ Galow L, et al. (2021). Lower household transmission rates of SARS-CoV-2 from children compared to adults. Journal of Infection 83(1), e34-e36.

- ²³² Little P, et al. (2020). Reducing risks from coronavirus transmission in the home the role of viral load. BMJ 369, m1728.
- [pre-print] Denford S, et al. (2020). Preventing within household transmission of COVID-19: Is the provision of accommodation feasible and acceptable? medRxiv.
- https://www.medrxiv.org/content/10.1101/2020.08.20.20176529v2
- ²³⁴ NHS Health Research Authority. *CONtact TrAcing in Care homes using digital Technology (CONTACT)*. https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/researchsummaries/contact-tracing-in-care-homes-using-digital-technology-contact/
- Wymant C, et al. (2021). The epidemiological impact of the NHS COVID-19 app. Nature 594, 408-412.
- ²³⁶ Endo A, et al. (2020). Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. Wellcome Open Research 5:67.
- ²³⁷ Endo A, et al. (2021). Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks. Wellcome Open Research 5:67.
- ²³⁸ UK Government, Department of Health and Social Care (2021). The Rúm Model Technical Annex: Assessing the impact of test, trace and isolate parameters on COVID-19 transmission in an October-like environment. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/960110/R UM model technical annex final 100221.pdf
- ²³⁹ Smith LE, et al. (2021). Adherence to the test, trace, and isolate system in the UK: results from 37 nationally representative surveys. BMJ 372, n608.
- ²⁴⁰ Patel J, Fernandes G & Sridhar D (2021). How can we improve self-isolation and quarantine for covid-19?
- ²⁴¹ UK Government, Department of Health and Social Care (2021). Liverpool COVID-19 community testing pilot: interim evaluation report summary. https://www.gov.uk/government/publications/liverpool-covid-19community-testing-pilot-interim-evaluation-report-summary/liverpool-covid-19-community-testing-pilotinterim-evaluation-report-summary#main-findings
- ²⁴² UK Government, Department of Health and Social Care (2021). Liverpool COVID-19 community testing pilot: interim evaluation report summary. https://www.gov.uk/government/publications/liverpool-covid-19community-testing-pilot-interim-evaluation-report-summary/liverpool-covid-19-community-testing-pilotinterim-evaluation-report-summary#main-findings
- Reed S, et al. (2021). Tackling Covid-19: A case for better financial support to self-isolate. Nuffield Trust, 14 May. https://www.nuffieldtrust.org.uk/files/2021-05/tackling-covid-19-6.pdf
- ²⁴⁴ Burford R (2021). Newham residents with Covid living overcrowded households to be put in hotels so they can isolate alone. Evening Standard, 3 February. https://www.standard.co.uk/news/london/newham-residentshotel-bill-paid-isolate-covid-b918446.html
- Martin AF, et al. (2021). Engagement with daily testing of self-isolating in contacts of confirmed cases of SARS-CoV-2. BMC Public Health 21, 1067.
- ²⁴⁶ [pre-print] Love N, et al. (2021). The acceptability of testing contacts of confirmed COVID-19 cases using serial, self-administered lateral flow devices as an alternative to self-isolation. medRxiv. https://www.medrxiv.org/content/10.1101/2021.03.23.21254168v1
- ²⁴⁷ Department for Education (2021). Schools COVID-19 operational guidance (applies until Step 4). $\underline{https://www.gov.uk/government/publications/actions-for-schools-during-the-coronavirus-outbreak/schools-during-the-coronavi$ coronavirus-covid-19-operational-quidance [accessed 9 July 2021].
- ²⁴⁸ [pre-print] House T, et al. (2021). Inferring risks of coronavirus transmission from community household data. arXiv. https://arxiv.org/pdf/2104.04605.pdf
- ²⁴⁹ Macartney K, et al. (2020). Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. The Lancet Child and Adolescent Health 4(11), 807-816.
- ²⁵⁰ Ismail SA, et al. (2021). SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England. Lancet Infectious Diseases 21, 344-353. ²⁵¹ Ulyte A, et al. (2021). Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school children in the canton in Zurich, Switzerland: prospective cohort study of 55 schools. BMJ 372, n616.
- ²⁵² [pre-print] Viner RM, et al. (2021). Impacts of school closures on physical and mental health of children and young people: a systematic review. medRxiv.
- https://www.medrxiv.org/content/10.1101/2021.02.10.21251526v1.full.pdf
- ²⁵³ UK Government (2021). Week 26 2021: Attendance in education and early years settings during the coronavirus (COVID-19) outbreak. https://explore-education-statistics.service.gov.uk/findstatistics/attendance-in-education-and-early-years-settings-during-the-coronavirus-covid-19-outbreak [accessed 1 July 2021].
- ²⁵⁴ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- Williams SN, et al. (2020). Public perceptions and experiences of social distancing and social isolation during the COVID-19 pandemic: a UK-based focus group study. BMJ Open, 10(7), e039334.
- ²⁵⁶ Denford S, et al. (2020). Understanding patterns of adherence ro COVID-19 mitigation measures: A qualitative interview study. Journal of Public Health.
 ²⁵⁷ Ipsos Mori and King's College London. *Life under lockdown: coronavirus in the UK.*
- https://www.kcl.ac.uk/policy-institute/assets/coronavirus-in-the-uk.pdf
- ²⁵⁸ The British Academy (2021). The COVID decade: understanding the long-term societal impacts of covid-19. https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf
- The British Academy (2021). The COVID decade: understanding the long-term societal impacts of covid-19. https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf

- ²⁶⁰ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- ²⁶¹ Nielson RK, et al. (2020). Communications in the Coronavirus Crisis: Lessons for the Second Wave. Reuters Institute/University of Oxford, 27th October. https://reutersinstitute.politics.ox.ac.uk/communicationscoronavirus-crisis-lessons-second-wave
- ²⁶² Castell S, Clemence M & Kamvar R (2020). Covid-19 winter preparedness: An online dialogue project for the Academy of Medical Sciences. Ipsos MORI, July 2020. https://acmedsci.ac.uk/file-download/28843909 ²⁶³ Fletcher R, Kalogeropoulos A & Nielsen RK (2021). Trust in UK government and news media COVID-19 information down, concerns over misinformation from government and politicians up. Reuters Institute, 1st June. https://reutersinstitute.politics.ox.ac.uk/trust-uk-government-and-news-media-covid-19-informationdown-concerns-over-misinformation
- [pre-print] Han Q, et al. (2021). Trust in government and its associations with health behaviour and prosocial behaviour during the COVID-19 pandemic. psyArXiv https://psyarxiv.com/p5qns/
- ²⁶⁵ [pre-print] Jennings W, et al. (2021). Lack of trust and social media echo chamber predict COVID-19 vaccine hesitancy. medRxiv https://www.medrxiv.org/content/10.1101/2021.01.26.21250246v1
- ²⁶⁶ [pre-print] Paul E, Steptoe A & Fancourt D (2020). Anti-Vaccine Attitudes and Risk Factors for Not Agreeing to Vaccination Against COVID-19 Amongst 32,361 UK Adults: Implications for Public Health Communications. SSRN https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3716874
- [pre-print] Lalot F, et al. (2021). Distrustful complacency and the COVID-19 vaccine: How concern and political trust interact to affect vaccine hesitancy. PsyArXiv https://psyarxiv.com/y9amb/
 ²⁶⁸ Nielson RK, et al. (2020). Communications in the Coronavirus Crisis: Lessons for the Second Wave. Reuters
- Institute/University of Oxford, 27th October. https://reutersinstitute.politics.ox.ac.uk/communicationscoronavirus-crisis-lessons-second-wave
- ²⁶⁹ Fletcher R, et al. (2020). Information inequality in the UK coronavirus communications crisis. Reuters Institute, 23rd July. https://reutersinstitute.politics.ox.ac.uk/information-inequality-uk-coronavirus-
- communications-crisis
 270 [pre-print] Shakespeare T, et al. (2021). Disabled People in Britain and the Impact of the COVID-19 Pandemic. Preprints https://www.preprints.org/manuscript/202101.0563/v1
- [pre-print] Shakespeare T, et al. (2021). Disabled People in Britain and the Impact of the COVID-19 Pandemic. Preprints https://www.preprints.org/manuscript/202101.0563/v1
- ²⁷² Knights F, et al. (2021). Impact of COVID-19 on migrants' access to primary care and implications for vaccine roll-out. British Journal of General Practice.
- ²⁷³ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- ²⁷⁴ Ofcom (2021). Covid-19 news and information: consumption and attitudes Children's News Consumption Survey: Covid-19 March 2021 key findings. https://www.ofcom.org.uk/research-and-data/tv-radio-and-ondemand/news-media/coronavirus-news-consumption-attitudes-behaviour [accessed 12 July 2021]. ²⁷⁵ Whitehead M, et al. (2021). Poverty, health and covid-19. BMJ, **372**, n376.
- ²⁷⁶ Mishra V, et al. (2021). Health Inequalities During COVID-19 and Their Effects on Morbidity and Mortality. J. Healthc. Leadersh., 13, 19-26.
- ²⁷⁷ Ala A, et al. (2021). Specific COVID-19 messaging targeting ethnic minority communities. Eclinical Medicine, **35**, 100862.
- ²⁷⁸ Cruwys T, et al. (2020). A social identity perspective on COVID-19: Health risk is affected by shared group membership. British Journal of Social Psychology, 59(3), 584-593.
- ²⁷⁹ Hult Khazaie D & Khan S (2019). Shared social identification in mass gatherings lowers health risk perceptions via lowered disgust. British Journal of Social Psychology, 59(4), 839-856.
- ²⁸⁰ Reicher SD, et al. (2016). Core disgust is attenuated by ingroup relations. PNAS, 113(10), 2631-2635. ²⁸¹ Little P, et al. (2020). Reducing risks from coronavirus transmission in the home—the role of viral load. BMJ, **369**, 1728.
- ²⁸² Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- ⁸³ Academy of Medical Sciences (2020). *Preparing for a Challenging Winter.*
- https://acmedsci.ac.uk/policy/policy-projects/coronavirus-preparing-for-challenges-this-winter
- Hagger MS, et al. (2020). The Handbook of Behavior Change. Cambridge Handbooks in Psychology.
- ²⁸⁵ Ala A, et al. (2021). Specific COVID-19 messaging targeting ethnic minority communities. EClinicalMedicine, **35**, 100862.
- ²⁸⁶ Elcheroth G & Drury J (2020). *Collective resilience in times of crisis: Lessons from the literature for socially* effective responses to the pandemic. British Journal of Social Psychology, **59**, 703-713.
- ²⁸⁷ Haslam SA, et al. (2021). Identity Leadership in a Crisis: A 5R Framework for Learning from Responses to COVID-19. Social Issues and Policy Review, 15, 35-83.
- ²⁸⁸ Prentice D & Paluck EL (2020). Engineering social change using social norms: Lessons from the study of collective action. Current Opinion in Psychology, **35**, 138-142. ²⁸⁹ Reicher SD, Drury J & Stott C (2020). *The two psychologies and Coronavirus*. The Psychologist.
- https://thepsychologist.bps.org.uk/two-psychologies-and-coronavirus [accessed 12 July 2021]. Reicher SD, Drury J & Stott C (2020). *The truth about panic*. The Psychologist.
- https://thepsychologist.bps.org.uk/two-psychologies-and-coronavirus.
- https://thepsychologist.bps.org.uk/truth-about-panic [accessed 12 July 2021].
- ²⁹¹ Elcheroth G & Drury J (2020). Collective resilience in times of crisis: Lessons from the literature for socially effective responses to the pandemic. British Journal of Social Psychology, 59, 703-713.
- ²⁹² Haslam SA, et al. (2021). Identity Leadership in a Crisis: A 5R Framework for Learning from Responses to COVID-19. Social Issues and Policy Review, 15, 35-83.

```
<sup>293</sup> Templeton A (2020). Inequalities and identity processes in crises: Recommendations for facilitating safe
response to the COVID-19 pandemic. British Journal of Social Psychology, 59, 674-685.

<sup>294</sup> Elcheroth G & Drury J (2020). Collective resilience in times of crisis: Lessons from the literature for socially
effective responses to the pandemic. British Journal of Social Psychology, 59, 703-713.
Drury J, et al. (2021). Public behaviour in response to the COVID-19 pandemic: understanding the role of
group processes. BJOpen 7, e11, 1–6.
  <sup>6</sup> Templeton A, et al. (2020). Inequalities and identity processes in crises: Recommendations for facilitating
safe response to the COVID-19 pandemic. British Journal of Social Psychology, 59, 674-685.
<sup>297</sup> Reicher SD, Drury J & Stott C (2020). The two psychologies and Coronavirus. The Psychologist.
<sup>298</sup> Gallagher J. (2021). Coronavirus cure: What progress are we making on treatments? BBC News.
https://www.bbc.co.uk/news/health-52354520 [accessed 9 July 2021].
<sup>299</sup> UK Government (2021). The COVID-19 Therapeutics Taskforce.
https://www.gov.uk/government/groups/the-covid-19-therapeutics-taskforce [accessed 9 July 2021]
<sup>300</sup> Griffiths G, et al. (2020). AGILE-ACCORD: A Randomized, Multicentre, Seamless, Adaptive Phase I/II
Platform Study to Determine the Optimal Dose, Safety and Efficacy of Multiple Candidate Agents for the
Treatment of COVID-19: A structured summary of a study protocol for a randomised platform trial. Trials, 21,
<sup>301</sup> The PRINCIPLE Trial (n.d.). <a href="https://www.phc.ox.ac.uk/research/covid-19/projects/principle-trial">https://www.phc.ox.ac.uk/research/covid-19/projects/principle-trial</a> [accessed 9]
July 2021].
<sup>302</sup> HEAL-COVID (n.d.). <a href="https://www.heal-covid.net/">https://www.heal-covid.net/</a> [accessed 9 July 2021].
<sup>303</sup> UK Government (2021). The COVID-19 Therapeutics Taskforce.
https://www.gov.uk/government/groups/the-covid-19-therapeutics-taskforce [accessed 9 July 2021].
304 UK Research and Innovation (2021). Outcomes of the UK COVID-19 Therapeutics Advisory Panel (UK-
CTAP).
https://www.ukri.org/about-us/policies-standards-and-data/data-collection/uk-covid-19-therapeutics-advisory-
panel/ [accessed 9 July 2021].
<sup>305</sup> Alijotas-Reig J, et al. (2020). Immunomodulatory therapy for the management of severe COVID-19. Beyond
the anti-viral therapy: A comprehensive review. Autoimmun Rev, 19(7) 102569.
<sup>306</sup> [pre-print] Horby PW, et al. (2021). Casirivimab and imdevimab in patients admitted to hospital with
COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial.
https://www.medrxiv.org/content/10.1101/2021.06.15.21258542v1
   [pre-print] Weinreich DM, et al. (2021). REGEN-COV Antibody Cocktail Clinical Outcomes Study in Covid-
19 Outpatients. medRxiv https://www.medrxiv.org/content/10.1101/2021.05.19.21257469v2
308 WHO Solidarity Trial Consortium (2021). Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity
Trial Results. New England Journal of Medicine, 384, 497-511.
<sup>309</sup> Torneri A, et al. (2020). A prospect on the use of antiviral drugs to control local outbreaks of COVID-19.
BMC Med., 18, 191.
310 The Academy of Medical Sciences. COVID-19 preclinical drug development database.
https://covidpipeline.acmedsci.ac.uk/ [accessed 11th July 2021].
<sup>311</sup> Pfizer (2021). Pfizer initiates phase 1 study of novel oral antiviral therapeutic agent against SARS-CoV-2.
23rd March. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-initiates-phase-1-study-
novel-oral-antiviral
<sup>312</sup> Erlanson DA (2020). Many small steps towards a COVID-19 drug. Nature Communications, 11, 5048.
<sup>313</sup> Iketani S (2021). Lead compounds for the development of SARS-CoV-2 3CL protease inhibitors. Nature
Communications, 12, 2016.
<sup>314</sup> UK Government, Department of Health and Social Care (2021). Government launches COVID-19 Antivirals
Taskforce to roll out innovative home treatments this autumn. 20th April.
https://www.gov.uk/government/news/government-launches-covid-19-antivirals-taskforce-to-roll-out-
innovative-home-treatments-this-autumn
   The Academy of Medical Sciences (2018). Controlled Human Infection Model Studies.
https://acmedsci.ac.uk/file-download/55062331
   Synairgen PLC (n.d.). COVID-19. https://www.synairgen.com/covid-19/ [accessed 11th July 2021].
317 National Institute for Health and Care Excellence (n.d.). Research to access pathway for investigational
drugs for COVID-19 (RAPID C-19). https://www.nice.org.uk/covid-19/rapid-c19 [accessed 11th July 2021].
Nuffield Department of Primary Care Health Sciences (n.d.). The PRINCIPLE Trial.
https://www.phc.ox.ac.uk/research/covid-19/projects/principle-trial [accessed 11th July 2021].
<sup>319</sup> Ramakrishnan S, et al. (2021). Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2,
open-label, randomised controlled trial. Lancet Respiratory Medicine, 9(7), 763-772.
<sup>320</sup> Tardif JC, et al. (2021). Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase
3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial. Lancet Respiratory Medicine.
<sup>321</sup> University of Nottingham (n.d.). Prophylactic Therapy in Care Homes Trial (PROTECT-CH).
https://www.protect-trial.net/ [accessed 11th July 2021].
322 LifeArc (n.d.). PROTECT-V: A basket trial of prophylactic interventions in multiple at-risk patient groups.
https://www.lifearc.org/funding/covid-19-funding/protect-v/ [accessed 11th July 2021].
323 National Institute for Health Research (2021). COVID-19 Prophylaxis Oversight Group - terms of reference.
4th January. https://www.nihr.ac.uk/documents/covid-19-prophylaxis-oversight-group-terms-of-
```

³²⁴ Nuffield Department of Primary Care Health Sciences (n.d.). *The PRINCIPLE Trial*. https://www.phc.ox.ac.uk/research/covid-19/projects/principle-trial [accessed 11th July 2021].

reference/26508

325 Williams S (2021). Supply Shortages Hit Life Science Labs Hard. The Scientist, 21st April. https://www.the-scientist.com/news-opinion/supply-shortages-hit-life-science-labs-hard-68695

- ³²⁶ Academy of Medical Sciences (2020). *Preparing for a Challenging Winter.*
- https://acmedsci.ac.uk/policy/policy-projects/coronavirus-preparing-for-challenges-this-winter [accessed July 8 2021].
- ³²⁷ Public Health England (2021). *National flu and COVID-19 surveillance reports*.
- https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports [accessed 9 July 2021].
- ³²⁸ Cowling BJ (2013). *Aerosol transmission is an important mode of influenza A virus spread.* Nature Communications, **4**, 1935.
- ³²⁹ Tellier R (2006). *Review of Aerosol Transmission of Influenza A Virus*. Emer Infect Dis, **12(11)**, **1657-1662**.
- ³³⁰ Biggerstaff M (2014). Estimates of the reproduction number for seasonal, pandemic, and zoonotic influenza: a systematic review of the literature. BMC Infectious Diseases. **14:480.**
- ³³¹ Public Health England (2020). Surveillance of influenza and other respiratory viruses in the UK: Winter 2019 to 2020. https://www.england.nhs.uk/south/wp-
- content/uploads/sites/6/2020/08/Surveillance Influenza and other respiratory viruses in the UK 2019 to 2020_FINAL.pdf
- ³³² Kucharski AJ, et al. (2018). *Timescales of influenza A/H3N2 antibody dynamics*. PLoS Biology, **16(8)**, r2004974.
- ³³³ Hayward A, *et al.* (2014). *Natural T Cell–mediated Protection against Seasonal and Pandemic Influenza*. Results of the Flu Watch Cohort Study. American Journal of Respiratory and Critical Care Medicine, **191(12)**. ³³⁴ Sridhar S, *et al.* (2013). *Cellular immune correlates of protection against symptomatic pandemic influenza*. Nature Medicine, **19**, 1305-1312.
- ³³⁵ Tricco AC, et al. (2013). Comparing influenza vaccine efficacy against mismatched and matched strains: a systematic review and meta-analysis. BMC Medicine, **11**, 153.
- ³³⁶ Cochrane (2018). Featured Review: Three updated Cochrane Reviews assessing the effectiveness of influenza vaccines.
- $\underline{\text{https://www.cochrane.org/news/featured-review-three-updated-cochrane-reviews-assessing-effectiveness-influenza-vaccines}$
- ³³⁷ Tricco AC, et al. (2013). Comparing influenza vaccine efficacy against mismatched and matched strains: a systematic review and meta-analysis. BMC Medicine, **11**, 153.
- ³³⁸ Public Health England (2021). Annual flu programme. https://www.gov.uk/government/collections/annual-flu-programme#2021-to-2022-flu-season [accessed 9 July 2021].
- ³³⁹ UK Government (2021). *Testing in the UK.* https://coronavirus.data.gov.uk/details/testing [accessed 9 July].
- ³⁴⁰ Baker RE, et al. (2020). The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. PNAS **117 (48)**, 30547-30553.
- ³⁴¹ Hayward A, et al. (2014). Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. The Lancet Respiratory Medicine, **2(6)**, 445-454.
- ³⁴² Public Health England (2019). Surveillance of influenza and other respiratory viruses in the UK Winter 2018 to 2019.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/839350/S_urveillance_of_influenza_and_other_respiratory_viruses_in_the_UK_2018_to_2019-FINAL.pdf
- ³⁴³ Meyerowitz-Katz G & Merone L (2020). *A systematic review and meta-analysis of published research data on COVID-19 infection fatality rates.* International Journal of Infectious Diseases, **101**, 138-148.
- ³⁴⁴ Meyerowitz-Katz G & Merone L (2020). *A systematic review and meta-analysis of published research data on COVID-19 infection fatality rates.* International Journal of Infectious Diseases, **101**, 138-148.
- ³⁴⁵ Wong JY, *et al.* (2013). *Infection Fatality Risk of the Pandemic A(H1N1)2009 Virus in Hong Kong.* American Journal of Epidemiology, **177(8)**, 834-840.
- ³⁴⁶ Troy NM & Bosco A (2016). *Respiratory viral infections and host responses; insights from genomics.* Respiratory Research, **17**, 156.
- ³⁴⁷ Bai L, et al. (2021). Coinfection with influenza A virus enhances SARS-CoV-2 infectivity. Cell Research 31, 395-403
- ³⁴⁸ Su S, et al. (2021). Double insult: flu bug enhances SARS-CoV-2 infectivity. Cell Research, **31**, 491–492.
- ³⁴⁹ Public Health England (2021). *Annual flu programme*. https://www.gov.uk/government/collections/annual-flu-programme#2021-to-2022-flu-season [accessed 9 July 2021].
- ³⁵⁰ Public Health England (2021). Seasonal flu vaccine uptake in GP patients: monthly data, 2020 to 2021. https://www.gov.uk/government/statistics/seasonal-flu-vaccine-uptake-in-gp-patients-monthly-data-2020-to-2021 [accessed 9 July].
- 351 Public Health England (2021). Seasonal flu vaccine uptake in GP patients: monthly data, 2020 to 2021. https://www.gov.uk/government/statistics/seasonal-flu-vaccine-uptake-in-gp-patients-monthly-data-2020-to-2021 [accessed 9 July].
- 352 Academy of Medical Sciences (2020). Preparing for a Challenging Winter.
- https://acmedsci.ac.uk/policy/policy-projects/coronavirus-preparing-for-challenges-this-winter
- 353 The Science and Technology Committee (2018). Flu vaccination programme in England.
- https://publications.parliament.uk/pa/cm201719/cmselect/cmsctech/853/85306.htm#_idTextAnchor030
- ³⁵⁴ Hayward A, *et al.* (2006). Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. BMJ, **333**, 1241. ³⁵⁵ Public Health England (2019). PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/833572/PHE guidance antivirals influenza 201920.pdf

- ³⁵⁶ Public Health England (2019). Sources of UK flu data: influenza surveillance in the UK. https://www.gov.uk/guidance/sources-of-uk-flu-data-influenza-surveillance-in-the-uk
- Muthuri SG, et al. (2014). Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection; a meta-analysis of individual participant data. The Lancet Respiratory Medicine 2(5), 395-404.
- 358 Adriaenssens N, et al. (2011). European Surveillance of Antimicrobial Consumption (ESAC): systemic antiviral use in Europe. The Journal of Antimicrobial Chemotherapy, 66(8), 1897-1905.
- ³⁵⁹ Butler CC, et al. (2020). Oseltamivir plus usual care versus usual care for influenza-like illness in primary care: an open-label, pragmatic, randomised controlled trial. The Lancet, 395(10217), 42-52.
- ³⁶⁰ Ison MG, et al. (2018). Phase 3 trial of baloxavir marboxil in high-risk influenza patients (CAPSTONE2 study). Open Forum Infectious Diseases 5(1), S764-S765.
- ³⁶¹ Brendish NJ, et al. (2017). Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. The Lancet Respiratory Medicine 5(5), 401-411.
- ³⁶² Brendish NJ, et al. (2019). Impact of point-of-care testing for respiratory viruses on antibiotic use in adults with exacerbation of airways disease. The Journal of Infection, 79(4), 357-362.
- ³⁶³ Buckle P, et al. (2021). COVID-19 point-of-care testing in care homes: what are the lessons for policy and practice? Age Ageing, **12**.

 364 de Lusignan S, et al. (2019). Feasibility of point-of-care testing for influenza within a national primary care
- sentinel surveillance network in England: protocol for a mixed methods study. Journal of Medical Internet Research Protocols 8(11), e14186.
- ³⁶⁵ Klepser DG, et al. (2003). Evaluation of a community pharmacy-based influenza and group A streptococcal pharyngitis disease management program using polymerase chain reaction point-of-care testing. Journal of the American Pharmacists Association 59(6), 872-879.
- ³⁶⁶ Campbell D (2021). A&E units in UK report rapid rise in children's infections. The Guardian.
- https://www.thequardian.com/society/2021/jun/25/ae-units-in-uk-report-rapid-rise-in-childrens-infections [accessed 9 July 2021].
- ³⁶⁷ National Institute for Health and Care Excellence (n.d). Influenza: Description of condition.
- https://bnf.nice.org.uk/treatment-summary/influenza.html. [accessed 9 July 2021].
- Geoghegan S, et al. (2017). Mortality due to Respiratory Syncytial Virus Burden and Risk Factors. American Journal of Respiratory Critical Care Medicine, 195(1), 96–103.
- ³⁶⁹ Public Health England (2019). Guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza. Version 10.0, September 2019.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/833572/P HE_guidance_antivirals_influenza_201920.pdf [accessed 9 July 2021].
- ³⁷⁰ Reeves RM, et al. (2019). Burden of hospital admissions caused by respiratory syncytial virus (RSV) in infants in England: A data linkage modelling study. Journal of Infection, 78(6), 468-475.
- ³⁷¹ Foley DA, et al. (2021). The Interseasonal Resurgence of Respiratory Syncytial Virus in Australian Children Following the Reduction of Coronavirus Disease 2019-Related Public Health Measures. Clinical Infectious Diseases.
- ³⁷² Sullivan SG, et al. (2020). Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. Eurosurveillance, 25(47).
- ³⁷³ Britton PN, et al. (2020). COVID-19 public health measures and respiratory syncytial virus. The Lancet Child Adolescent Health, 4(11), e42-43.
- ³⁷⁴ National Institute for Communicable diseases (2020). Increase In Respiratory Syncytial Virus (Rsv) Cases 2020. https://www.nicd.ac.za/increase-in-respiratory-syncytial-virus-rsv-cases-2020/ [accessed 9 July 2021].
- ³⁷⁵ Baker RE, et al. (2020). The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. Europe PMC, 117(48), 30547-30553.
- ³⁷⁶ Atamna A, et al. (2021). Morbidity and mortality of respiratory syncytial virus infection in hospitalized adults: Comparison with seasonal influenza. International Journal of Infectious Diseases, 103, 489-493. ³⁷⁷ Falsey AR & Walsh EE (2005). Respiratory syncytial virus infection in elderly adults. Drugs Aging, **22(7)**, 577-87.
- ³⁷⁸ Centers for Disease Control and Prevention (2017). Older adults are at high risk for severe RSV infection. https://www.cdc.gov/rsv/factsheet-older-adults.pdf [accessed 9 July 2021].
- ³⁷⁹ Royal College of Paediatrics and Child Health (2021). National guidance for the management of children with bronchiolitis and lower respiratory tract infections during COVID-19.
- https://www.rcpch.ac.uk/resources/national-guidance-management-children-bronchiolitis-during-covid-19 [accessed 9 July 2021].
- ³⁸⁰ Jansen A, *et al.* (2008). *Rate-difference method proved satisfactory in estimating the influenza burden in* primary care visits. Journal of clinical epidemiology, **61(8)**, 803-812.

 381 Moriyama M, et al. (2020). Seasonality of Respiratory Viral Infections. Annual Review of Virology, **7(1)**, 83-
- ³⁸²Lee N, et al. (2021). Burden of noninfluenza respiratory viral infections in adults admitted to hospital: analysis of a multiyear Canadian surveillance cohort from 2 centres. CMAJ, 193(13), e439-446.
- ³⁸³ Zhu G, et al. (2021). Epidemiological characteristics of four common respiratory viral infections in children. Virol J, 18(1), 10.
- ³⁸⁴ Aronen M, et al. (2019). Respiratory tract virus infections in the elderly with pneumonia. BMC Geriatrics, 19(1), 111.
- ³⁸⁵ Gonzalez J, et al. (2021). Pulmonary Function and Radiologic Features in Survivors of Critical COVID-19: A 3-Month Prospective Cohort. Chest, 160(1), 187-198.

- ³⁸⁶ Wu X, et al. (2021). 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study. The Lancet Respiratory Medicine, 9(7), 747–754.
- ³⁸⁷ Inns T, et al. (2020). What proportion of care home outbreaks are caused by norovirus? An analysis of viral causes of gastroenteritis outbreaks in care homes, North East England, 2016-2018. BMC Infectious Diseases,
- ³⁸⁸ Inns T, et al. (2019) Estimating the burden of care home gastroenteritis outbreaks in England, 2014–2016. BMC Infect Dis, 19, 12.
- ³⁸⁹ Chen Y, et al. (2017). Norovirus Disease in Older Adults Living in Long-Term Care Facilities: Strategies for Management. Current Geriatrics Reports. 6, 26-33.
- ³⁹⁰ The Health Foundation (2021). Emerging evidence on health inequalities and COVID-19: March 2021. https://www.health.org.uk/news-and-comment/blogs/emerging-evidence-on-health-inequalities-and-covid-19-
- Whitehead M, et al. (2021). Poverty, health and covid-19. BMJ 372, 367.
- ³⁹² The British Academy (2021). The COVID Decade: understanding the long-term societal impacts of COVID-19. https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf
- ³⁹³ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-the-
- future-public-dialogue

 394 Office for National Statistics (2019). Excess winter mortality in England and Wales: 2018 to 2019 (provisional) and 2017 to 2018.
- https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/excesswin termortalityinenglandandwales/2018to2019provisionaland2017to2018final#: ~: text=1.-%20, Main %20 points, and %20 2017 %20 to %20 2018 %20 winters. [accessed 9 July 2021].
- ³⁹⁵ Pebody RG, et al. (2018). Significant Spike in Excess Mortality in England in Winter 2014/15 Influenza the Likely Culprit. Epidemiology and Infection 146(9), 1106-1113.
- ³⁹⁶ National Records of Scotland (2018) Winter Mortality in Scotland 2017/18.
- https://www.nrscotland.gov.uk/files/statistics/winter-mortality/2018/winter-mortality-17-18-pub.pdf
- ³⁹⁷ Northern Ireland Statistics and Research Agency (2018). Excess Winter Mortality 2017/18.
- https://www.nisra.gov.uk/publications/excess-winter-mortality-20171818
- For a review, see Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21. https://acmedsci.ac.uk/file-download/51353957
- ³⁹⁹ Public Health England (2017). Cold Weather Plan For England Making the Case: Why long-term strategic planning for cold weather is essential to health and wellbeing. Public Health England.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/652568/C old_Weather_Plan_Making_the_Case_2017.pdf
- 400 The Financial Times (2020). Private hospitals to be paid £1bn to ease NHS waiting lists.
- https://www.ft.com/content/3aab4ef6-6f2b-4726-87aa-40071ad80544 [accessed 9 July 2021].
- ⁰¹ Rohini M, et al. (2021). Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform. The Lancet, 397(10286), 1711-1724.
- ⁴⁰² Nafilyan V, et al. (2021). Ethnic differences in COVID-19 mortality during the first two waves of the Coronavirus Pandemic: a nationwide cohort study of 29 million adults in England. European Journal of Epidemiology.
- ⁴⁰³ Nafilyan V, et al. (2021). Ethnic differences in COVID-19 mortality during the first two waves of the Coronavirus Pandemic: a nationwide cohort study of 29 million adults in England. European Journal of Epidemiology.
- ⁴⁰⁴ Public Health England (2021). SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 14.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/991343/V ariants of Concern VOC Technical Briefing 14.pdf [accessed 9 July].
- ⁴⁰⁵ ICNARC (2021). ICNARC report on COVID-19 in critical care: England, Wales and Northern Ireland 26 March 2021.
- 406 Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- ⁴⁰⁷ Nalbandian A, et al. (2021). Post-acute COVID-19 syndrome. Nature Medicine 27, 601-615.
- ⁴⁰⁸ National Institute for Health Research (2021). *Living with Covid19 Second review.*
- https://evidence.nihr.ac.uk/themedreview/living-with-covid19-second-review/
- [pre-print] Michelin M, et al. (2021). Characterising long term Covid-19: a living systematic review. https://www.medrxiv.org/content/10.1101/2020.12.08.20246025v1
- [pre-print] Osmanov I, et al. (2021). Risk factors for long covid in previously hospitalised children using the ISARIC Global follow-up protocol: A prospective cohort study. European Respiratory Journal 58(1).
- ⁴¹¹ [pre-print] Sigfrid L, et al. (2021). Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. https://www.medrxiv.org/content/10.1101/2021.03.18.21253888v3

 12 National Institute for Health Research (2021). Living with Covid19 – Second review.
- https://evidence.nihr.ac.uk/themedreview/living-with-covid19-second-review/
- [pre-print] Michelin M, et al. (2021). Characterising long term Covid-19: a living systematic review. https://www.medrxiv.org/content/10.1101/2020.12.08.20246025v1
- [pre-print] Osmanov I, et al. (2021). Risk factors for long covid in previously hospitalised children using the ISARIC Global follow-up protocol: A prospective cohort study. European Respiratory Journal 58(1). https://www.medrxiv.org/content/10.1101/2021.04.26.21256110v1

- ⁴¹⁵ Office for National Statistics (2021). Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021.
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/ prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021 [accessed 9 July 2021].

 ⁴¹⁶ Blomberg B, et al. (2021). Long COVID in a prospective cohort of home-isolated patients. Nature medicine.
- https://doi.org/10.1038/s41591-021-01433-3
- Buonsense D, et al. (2021). Preliminary evidence on Long COVID in children. Acta Paediatrica 110(7), 2208-2211.
- ⁴¹⁸ National Institute for Health Research (2020). Living with Covid19.

https://evidence.nihr.ac.uk/themedreview/living-with-covid19/

- Donnelly J, et al. (2021). Readmission and Death After Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System. JAMA, 325(3), 304-306.
- ⁴²⁰ UCL (2021). Nearly a third of Covid-19 patients readmitted within 140 days.
- https://www.ucl.ac.uk/news/2021/apr/nearly-third-covid-19-hospital-patients-readmitted-within-140-days [accessed 9 July 2021].

 421 Ayoubkhani D, et al. (2021). Post-covid syndrome in individuals admitted to hospital with covid-19:
- retrospective cohort study. BMJ 372, n693.
- ⁴²² Ayoubkhani D, et al. (2021). Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. BMJ 372, n693.
- 423 Office for National Statistics (2021). Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 4 June 2021.
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/ prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/4june2021 [accessed 9 July 2021]
- [pre-print] Whitaker M, et al. (2021). Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508 707 people. Imperial College London. https://spiral.imperial.ac.uk/handle/10044/1/89844.
- ⁴²⁵ [pre-print] Sigfrid L, et al. (2021). Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. https://www.medrxiv.org/content/10.1101/2021.03.18.21253888v3
- [pre-print] Whitaker M, et al. (2021). Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508 707 people. Imperial College London. https://spiral.imperial.ac.uk/handle/10044/1/89844.
- ⁴²⁷ [pre-print] Thompson E, et al. (2021). Risk factors for long COVID: analyses of 10 longitudinal studies and electronic health records in the UK.

https://www.medrxiv.org/content/10.1101/2021.06.24.21259277v1

- [pre-print] Thompson E, et al. (2021). Risk factors for long COVID: analyses of 10 longitudinal studies and electronic health records in the UK.
- https://www.medrxiv.org/content/10.1101/2021.06.24.21259277v1
- [pre-print] Thompson E, et al. (2021). Risk factors for long COVID: analyses of 10 longitudinal studies and electronic health records in the UK.

https://www.medrxiv.org/content/10.1101/2021.06.24.21259277v1

- Walters SJ, Stern C & Stephenson M (2019). Fatigue and measurement of fatigue: a scoping review protocol. JBI Database of Systematic Reviews and Implementation Reports 17(3), 261-266.
- ^x³¹ Pawlikowska T, *et al.* (1994). *A population based study of fatigue and psychological distress.* BMJ **308**, 743-
- ⁴³² Gallagher AM, et al. (2004). Incidence of fatigue symptoms and diagnoses presenting in UK primary care from 1990 to 2001. Journal of the Royal Society of Medicine 97(12), 571-575.
- ⁴³³ Ahmed M, et al. (2020). Multisystem inflammatory syndrome in children: A systematic review. The Lancet
- ⁴³⁴ Tang Y et al. (2021). Multisystem inflammatory syndrome in children during the coronavirus disease 2019 (COVID-19) pandemic: a systematic review of published case studies. Translational Pediatrics 10(1), 121-135.
- The survey defined 'any symptom' as any occurance of the following symptoms, starting at or within 5 weeks of infection: fatigue, cough, headache, loss of taste, loss of smell, myalgia, sore throat, fever, shortness of breath, nausea/vomiting, diarrhoea, abdominal pain.
- ⁴³⁶ Thompson H (2021). Children with long covid. New Scientist **249**, 10-11.
- 437 Munblit D, et al. (2021). Legacy of COVID-19 infection in children: long-COVID will have a lifelong health/economic impact. Archives of Disease in Childhood.
- ⁴³⁸ [pre-print] Di Sante G, et al. (2021). Immune profile of children with post-acute sequelae of SARS-CoV-2 infection (Long Covid). medRxiv 2021.05.07.21256539. https://doi.org/10.1101/2021.05.07.21256539
- ⁴³⁹ [pre-print] The OpenSAFELY Collaborative (2021). Rates of serious clinical outcomes in survivors of hospitalisation with COVID-19: a descriptive cohort study within the OpenSAFELY platform. https://www.medrxiv.org/content/10.1101/2021.01.22.21250304v3
- ⁴⁰ Phillips S & Williams MA. (2021). *Confronting Our Next National Health Disaster Long-Haul Covid. The New* England Journal of Medicine.
- ⁴⁴¹ Marshall M (2021). The four most urgent questions about long COVID. Nature.
- https://www.nature.com/articles/d41586-021-01511-z [accessed 9 July 2021].
- National Institute for Health Research (2021). £18.5 million awarded to new research projects to understand and treat long COVID.
- https://www.nihr.ac.uk/news/185-million-awarded-to-new-research-projects-to-understand-and-treat-longcovid/26895 [accessed 9 July 2021].

⁴⁴³ [pre-print] PHOSP-COVID Collaborative Group (2021). Physical, cognitive and mental health impacts of COVID-19 following hospitalisation – a multi-centre prospective cohort study.

https://www.medrxiv.org/content/10.1101/2021.03.22.21254057v2

- International Severe Acute Respiratory and Emerging Infection Consortium (2021). ISARIC study. https://isaric.org/ [accessed 9 July 2021].
- 445 Norton A, et al. (2021). Long COVID: tackling a multifaceted condition requires a multidisciplinary approach. Lancet Infectious Diseases 21(5), 601-602.
- ⁴⁴⁶ Wong TL & Weitzer DJ (2021). Long COVID and Myalgic Encephalomyelitis/Chronic Fatique Syndrome (ME/CFS)-A Systemic Review and Comparison of Clinical Presentation and Symptomatology. Medicina 57(5),
- ⁴⁴⁷ Phillips S & Williams MA (2021). Confronting Our Next National Health Disaster Long-Haul Covid. The New England Journal of Medicine. https://www.nejm.org/doi/full/10.1056/NEJMp2109285
- ⁴⁴⁸ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue [accessed 9 July 2021].
- Varatharaj A, et al. (2020). Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. The Lancet. Psychiatry. 7(10), 875-882.
- ⁴⁵⁰ Taquet M, et al. (2021). 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. The Lancet. Psychiatry. **8(5)**, 416–427. University of Liverpool (2021). *COVID-19 Clinical Neuroscience Study*.
- https://www.liverpool.ac.uk/neurosciences-research-unit/research/covid-cns-study/ [accessed 6 July 2021]. ⁴⁵² Pierce M, et al. (2020). Mental health before and during the COVID-19 pandemic: a longitudinal probability
- sample survey of the UK population. The Lancet Psychiatry 7(10), 883-892. ⁴⁵³ The British Academy (2021). The COVID decade: understanding the long-term societal impacts of covid-19. https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf
- ⁴⁵⁴ Xiong J, et al. (2020). Impact of COVID-19 pandemic on mental health in the general population: A
- systematic review. Journal of Affective Disorders **277**, 55–64.

 455 Kwong A, et al. (2021). Mental health before and during the COVID-19 pandemic in two longitudinal UK population cohorts. The British Journal of Psychiatry 218(6), 334-343.
- Kwong A, et al. (2021). Mental health before and during the COVID-19 pandemic in two longitudinal UK population cohorts. The British Journal of Psychiatry **218(6)**, 334-343.

 457 Centre for Mental Health (2021). *Maternal mental health during a pandemic.*
- https://www.centreformentalhealth.org.uk/sites/default/files/publication/download/CentreforMH_MaternalMHPa
- ndemic FullReport 0.pdf

 458 Pierce M, et al. (2021). Mental health responses to the COVID-19 pandemic: a latent class trajectory analysis using longitudinal UK data. The Lancet Psychiatry 8(7), 610-619.
- ⁴⁵⁹ [Pre-print] Robinson E, et al. (2021). A systematic review and meta-analysis of longitudinal cohort studies comparing mental health before versus during the COVID-19 pandemic. medRxiv. https://www.medrxiv.org/content/medrxiv/early/2021/03/08/2021.03.04.21252921.full.pdf
- ⁴⁶⁰ Smith K, Bhui K, Cipriani A (2020). COVID-19, mental health and ethnic minorities. Evidence-Based Mental Health 23(3), 89-90.
- ⁴⁶¹ Hanna K, et al. (2021). Emotional and Mental Wellbeing Following COVID-19 Public Health Measures on People Living With Dementia and Carers. Journal of Geriatric Psychiatry and Neurology 25, 891988721996816. ⁴⁶² Proto E, Quintana-Domeque C (2021). COVID-19 and mental health deterioration by ethnicity and gender in the UK. PLoS One 16(1), e0244419.
- ⁴⁶³ Newlove-Delgado T, et al. (2021). Mental Health of Children and Young People group. Child mental health in England before and during the COVID-19 lockdown. The Lancet Psychiatry 8(5), 353-354.
- ⁴⁶⁴ Vizard T, et al. (2020). Mental Health of Children and Young People in England 2020, Wave 1 follow-up to the 2017 survey. https://files.digital.nhs.uk/AF/AECD6B/mhcyp_2020_rep_v2.pdf
- [Pre-print] Viner RM, et al. (2021). Impacts of school closures on physical and mental health of children and young people: a systematic review. medRxiv.
- https://www.medrxiv.org/content/10.1101/2021.02.10.21251526v1
- 466 Ford T, John A, Gunnell D (2021). Mental health of children and young people during pandemic. BMJ 372, n614.
- ⁴⁶⁷ Thorisdottir IE, et al. (2021). Depressive symptoms, mental wellbeing, and substance use among adolescents before and during the COVID-19 pandemic in Iceland: a longitudinal, population-based study. The Lancet Psychiatry
- ⁴⁶⁸ Son C, et al. (2020). Effects of COVID-19 on College Students' Mental Health in the United States: Interview Survey Study. Journal of Medical Internet Research 22(9), e21279.
- 469 Proto E, Quintana-Domeque C (2021). COVID-19 and mental health deterioration by ethnicity and gender in the UK. PLoS One 16(1), e0244419.
- ⁴⁷⁰ Pierce M, et al. (2020). Says who? The significance of sampling in mental health surveys during COVID-19. The Lancet Psychiatry 7(7), 567–568.
- ⁴⁷¹ Ford T, et al. (2021). The challenges and opportunities of mental health data sharing in the UK. The Lancet Digital Health 3(6), e333-e336.
- ⁴⁷²Polanczyk GV, et al. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. Journal of Child Psychology and Psychiatry, and Allied Disciplines 56(3), 345-365.
- ⁴⁷³ Vahia IV, Jeste DV, Reynolds CF (2020). Older Adults and the Mental Health Effects of COVID-19. Journal of the American Medical Association 324(22), 2253-2254.

people?. Aging (Albany NY) 12(10), 9959-9981.

```
<sup>474</sup> National Health Service (2018). Seasonal affective disorder (SAD).
https://www.nhs.uk/conditions/seasonal-affective-disorder-sad [accessed on 7 July 2021].
   <sup>5</sup> NHS Benchmarking (2019). Mental Health (Inpatient/CMHT) project.
https://www.nhsbenchmarking.nhs.uk/news/2019-mental-health-inpatientcmht-project-results-published
[accessed on 7 July 2021].
<sup>476</sup> British Medical Association (2021). Pressure points in the NHS. https://www.bma.org.uk/advice-and-
support/nhs-delivery-and-workforce/pressures/pressure-points-in-the-nhs [accessed 7 July 2021].
   <sup>7</sup> Cancer research UK (2021). Cancer screening and coronavirus. https://www.cancerresearchuk.org/about-
cancer/cancer-in-general/coronavirus/cancer-screening [accessed on 7 July 2021]

478 Sud A, et al. (2020). Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19
pandemic on cancer survival in the UK: a modelling study. The Lancet Oncology 21(8), 1035–1044.

Additional on the detection and management of colorectal pandemic on the detection and management of the colorectal pandemic on the detection and management of the colorectal pandemic on the detection and management of the colorectal pandemic on the detection and the colorectal pandemic on the detection and the colorectal pandemic on t
cancer in England: a population-based study. The Lancet Gastroenterology & Hepatology 6(3), 199-208.
<sup>480</sup> Maringe C, et al. (2020). The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis
in England, UK: a national, population-based, modelling study. The Lancet Oncology 21(8), 1023-1034.
<sup>481</sup> Carr MJ, et al. (2021). Impact of COVID-19 on diagnoses, monitoring, and mortality in people with type 2
diabetes in the UK. The Lancet Diabetes & Endocrinology 9(7), 413-415.
<sup>482</sup> Mansfield KE, et al. (2021). Indirect acute effects of the COVID-19 pandemic on physical and mental health
in the UK: a population-based study. The Lancet Digital Health 3(4), e217-e230.
483 BBC News (2020). https://www.bbc.co.uk/news/health-52417599 [accessed 8 July 2021].
<sup>484</sup> Ipsos MORI (2021). 2021 GP Patient Survey Results. https://gp-patient.co.uk/surveysandreports
World Health Organization (2014). Non-communicable Diseases (NCD) Country Profiles.
http://www.who.int/nmh/countries/gbr_en.pdf.
British Medical Association (2021). Pressure points in the NHS. https://www.bma.org.uk/advice-and-
support/nhs-delivery-and-workforce/pressures/pressure-points-in-the-nhs [accessed 8 July 2021].

487 WHO (2020) The impact of the Carried 102 minutes in the
     WHO (2020). The impact of the Covid-19 pandemic on noncommunicable disease resources and services:
results of a rapid assessment. https://www.who.int/publications/i/item/9789240010291 [accessed 8 July
<sup>488</sup> Jones D, et al. (2020). Impact of the COVID-19 pandemic on the symptomatic diagnosis of cancer: the view
from primary care. The Lancet Oncology 21(6), 748-750.
<sup>489</sup> Mafham MM, et al. (2020). COVID-19 pandemic and admission rates for and management of acute coronary
syndromes in England. The Lancet 396(10248), 381–389.

490 Negrini S, et al. (2020). Up to 2.2 million people experiencing disability suffer collateral damage each day of
COVID-19 lockdown in Europe. European Journal of Physical and Rehabilitation Medicine 56(3), 361-365.
<sup>491</sup> Stefan N, Birkenfeld AL, Schulze MB. (2021). Global pandemics interconnected - obesity, impaired metabolic
health and COVID-19. Nature Reviews Endocrinology 17(3), 135-149.
<sup>492</sup> Wei Y, Shah R (2020). Substance Use Disorder in the COVID-19 Pandemic: A Systematic Review of
Vulnerabilities and Complications. Pharmaceuticals (Basel, Switzerland) 13(7).
<sup>493</sup> Kim JU, et al. (2020). Effect of COVID-19 lockdown on alcohol consumption in patients with pre-existing
alcohol use disorder. The Lancet Gastroenterology & Hepatology 5(10), 886-887
<sup>494</sup> Wei Y, Shah R (2020). Substance Use Disorder in the COVID-19 Pandemic: A Systematic Review of
Vulnerabilities and Complications. Pharmaceuticals (Basel, Switzerland) 13(7)
<sup>495</sup> [pre-print] Maddock J, et al. (2021). Inequalities in healthcare disruptions during the Covid-19 pandemic:
Evidence from 12 UK population-based longitudinal studies. medRxiv.
https://www.medrxiv.org/content/10.1101/2021.06.08.21258546v1
   <sup>6</sup> Topriceanu CC, et al. (2021). Evaluating access to health and care services during lockdown by the COVID-
19 survey in five UK national longitudinal studies. BMJ Open 11(3), e045813.
<sup>497</sup> Public Health England (2020). Disparities in the risk and outcomes of COVID-19.
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/892085/di
sparities_review.pdf. [accessed 8 July 2021].
<sup>498</sup> The Health Foundation (2020). Build back fairer: the COVID-19 marmot review.
https://www.health.org.uk/sites/default/files/upload/publications/2020/Build-back-fairer-the-COVID-19-
Marmot-review.pdf [accessed 8 July 2021].
     [pre-print]. Di Lorito C, et al. (2020). Deconditioning in people living with dementia during the COVID-19
pandemic: findings from the Promoting Activity, Independence and Stability in Early Dementia (PrAISED)
process evaluation. medRxiv.
https://www.medrxiv.org/content/medrxiv/early/2020/11/17/2020.11.16.20231100.full.pdf
     AGE UK (2020). The impact of Covid-19 to date on older people's mental and physical health.
https://www.ageuk.org.uk/globalassets/age-uk/documents/reports-and-publications/reports-and-
briefings/health--wellbeing/the-impact-of-covid-19-on-older-people_age-uk.pdf [accessed 8 July 2021].

501 Giuntella O, et al. (2021). Lifestyle and mental health disruptions during COVID-19. Proceedings of the
National Academy of Sciences of the United States of America 118(9).
<sup>502</sup> Sport England (2021). Active Lives Adult Survey November 2019/2020 report. https://sportengland-
production-files.s3.eu-west-2.amazonaws.com/s3fs-public/2021-
04/Active%20Lives%20Adult%20November%202019-
20%20Report.pdf?VersionId=OjWdwCLnI3dNgDwp3X4ukcODJIDVG7Kd [accessed 8 July 2021]. 503 Cunningham C & O'Sullivan R (2020). Why physical activity matters for older adults in a time of pandemic.
European Review of Aging and Physical Activity 17(1), 1-4.
<sup>504</sup> Mueller AL, McNamara MS & Sinclair DA (2020). Why does COVID-19 disproportionately affect older
```

```
<sup>505</sup> Active Essex Local Delivery Pilot (2020). Prevention and Enablement Model.
https://www.activeessex.org/local-delivery-pilot/our-bigger-projects/pem/ [accessed 8th July 2021].
  <sup>6</sup> Hamada K & Fan X (2020). The impact of COVID-19 on individuals living with serious mental illness.
Schizophrenia Research 222, 3-5.
<sup>507</sup> Steptoe A & Di Gessa G (2021). Mental health and social interactions of older people with physical
disabilities in England during the COVID-19 pandemic: a longitudinal cohort study. The Lancet Public Health
6(6), e365–e373.
<sup>508</sup> Hanna K, et al. (2021). Emotional and Mental Wellbeing Following COVID-19 Public Health Measures on
People Living With Dementia and Carers. Journal of Geriatric Psychiatry and Neurology. 891988721996816.
De Biase S, et al. (2020). The COVID-19 rehabilitation pandemic. Age and Ageing 49(5), 696-700.
<sup>510</sup> The Health Foundation (2020). Health care usage during COVID-19. https://www.health.org.uk/health-care-
<u>usage-during-covid-19.</u> [accessed 8 July 2021].

511 Academy of Medical Sciences (2020). Preparing for a Challenging Winter.
https://acmedsci.ac.uk/policy/policy-projects/coronavirus-preparing-for-challenges-this-winter
  NHS England (2017). Next Steps on the Five Year Forward View: Primary Care.
https://www.england.nhs.uk/five-year-forward-view/next-steps-on-the-nhs-five-year-forward-view/primary-
care/#:~:text=General%20practice%20provides%20over%20300,practice%20than%20on%20hospital%20out
patients [accessed 8 July 2021].
513 British Medical Association (2021). Pressures in General Practice. https://www.bma.org.uk/advice-and-
support/nhs-delivery-and-workforce/pressures/pressures-in-general-practice [accessed on 8 July 2021]. The Health Foundation (2019). A worrying cycle of pressure for GPs in deprived areas.
https://www.health.org.uk/news-and-comment/blogs/a-worrying-cycle-of-pressure-for-gps-in-deprived-areas
[accessed on 8th July 2021].

515 Pulse Today (2021). One million more GP appointments taking place than before pandemic.
https://www.pulsetoday.co.uk/news/workload/one-million-more-gp-appointments-taking-place-per-week-
than-before-pandemic/ [accessed 8 July 2021].
516 NHS Digital (2021). Appointments in General Practice - April 2021. https://digital.nhs.uk/data-and-
information/publications/statistical/appointments-in-general-practice/april-2021 [accessed 8 July 2021].
<sup>517</sup> NHS Digital (2021). Appointments in General Practise - April 2021. https://digital.nhs.uk/data-and-
information/publications/statistical/appointments-in-general-practice/april-2021. [accessed 8 July 2021].
 The Nuffield Trust (2021). Hospital Bed Occupancy. https://www.nuffieldtrust.org.uk/resource/hospital-bed-
occupancy [accessed 8 July 2021].

519 The Kings Fund (2020). NHS hospital bed numbers. https://www.kingsfund.org.uk/publications/nhs-
hospital-bed-numbers [accessed on 8 July 2021].

520 NHS England (n.d.). Statistics: Delayed Transfers of Care. https://www.england.nhs.uk/statistics/statistical-
work-areas/delayed-transfers-of-care/ [accessed 8 July 2021].
   Royal College of Emergency Medicine (2021). RCEM exploins: Hospital Beds.
https://www.rcem.ac.uk/docs/Policy/210628 RCEM briefing on hospital beds.pdf [accessed 8 July 2021].
 Royal College of Emergency Medicine (2021). RCEM exploins: Hospital Beds.
https://www.rcem.ac.uk/docs/Policy/210628_RCEM_briefing_on_hospital_beds.pdf [accessed 8 July 2021]. Faculty of Intensive Care Medicine (2021). Critical Staffing.
https://www.ficm.ac.uk/sites/default/files/critical_staffing_1_-
a best practice framework for safe and effective critical care staffing.pdf [accessed 8 July 2021].

524 Intensive Care Society (2021). Recovery and Restitution of Critical Care in Covid-19.
https://www.ics.ac.uk/ICS/ICS/News_Statements/Recovery_and_Restitution_of_intensive_care.aspx [accessed
8 July 2021].
<sup>525</sup> Intensive Care Society (2021). Recovery and Restitution of Critical Care in Covid-19.
https://www.ics.ac.uk/ICS/ICS/News Statements/Recovery and Restitution of intensive care.aspx [accessed
<sup>526</sup> Royal College of Emergency Medicine (2021). Summer to Recover.
https://www.rcem.ac.uk/docs/Policy/Summer%20to%20Recover.pdf [accessed 8 July 2021].
   Faculty of Intensive care Medicine (2021). Critical Staffing.
https://ficm.ac.uk/sites/default/files/critical_staffing_1 -
a best_practice_framework_for_safe_and_effective_critical_care_staffing.pdf [accessed 8 July 2021].

528 Intensive Care Society (2021) Recovery and Restitution of Critical Care in Covid-19.
https://www.ics.ac.uk/ICS/ICS/News_Statements/Recovery_and_Restitution_of_intensive_care.aspx [accessed
8 July 2021].
<sup>529</sup> Competition and Markets Authority (2017). Care Homes Market Study. https://www.gov.uk/cma-
cases/care-homes-market-study [accessed 8 July 2021].
   The Nuffield trust (2021). Beyond Covid wave two: what now for care homes?
https://www.nuffieldtrust.org.uk/news-item/beyond-covid-19-wave-two-what-now-for-care-homes [accessed 8
<sup>531</sup> Department of Health and Social Care (2021). Adult Social Care Infection Control Fund -round 2: guidance.
https://www.gov.uk/government/publications/adult-social-care-infection-control-fund-round-2/adult-social-
care-infection-control-fund-round-2-guidance [accessed 8 July 2021].

532 The British Academy (2021). The COVID Decade: understanding the long-term societal impacts of Covid-19.
https://www.thebritishacademy.ac.uk/publications/covid-decade-understanding-the-long-term-societal-
impacts-of-covid-19/
533 UK Parliament: House of Commons Library (2020). The Health and Social Care Workforce Gap.
```

https://commonslibrary.parliament.uk/the-health-and-social-care-workforce-gap/ [accessed 9 July 2021].

```
<sup>534</sup> The King's Fund (2021). NHS Workforce: Our Position.
```

https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed on 9 July 2021].

535 The Kingle Fund (2021). All City 1.5

⁵ The King's Fund (2021). NHS Workforce: Our Position.

https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed on 9 July 2021].

The King's Fund (2021). NHS Workforce: Our Position.

https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed on 9 July 2021].

The King's Fund (2020). How Covid-19 has magnified some of social care's key problems.

https://www.kingsfund.org.uk/publications/covid-19-magnified-social-care-

Mw6KcaAvywEALw wcB [accessed 9th July 2021]

Nursing Times (2020). More than 7,000 ex nurses answer Covid-19 call to return to service.

https://www.nursingtimes.net/news/coronavirus/more-than-7000-ex-nurses-answer-covid-19-call-to-returnto-service-27-03-2020/ [accessed 9 July 2021].

539 General Medical Council (2020). COVID-19 – GMC grants temporary registration to 11,800 doctors

.https://www.gmc-uk.org/news/news-archive/coronavirus---gmc-grants-temporary-registration-to-11800doctors [accessed 8 July 2021].

¹⁴⁰ Sykes A & Pandit M (2021). Experiences, challenges and lessons learnt in medical staff redeployment during response to COVID-19. BMJ Leader 5, 98-101.

⁵⁴¹ Appleby J (2021). NHS sickness absence during the covid-19 pandemic. BMJ **372**, n471.

⁵⁴² Office of National Statistics (2021). Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021.

https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/ prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021 [accessed 8th July

⁵⁴³ The King's Fund (2021). NHS Workforce: Our Position.

https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed on 9 July 2021].

⁵⁴⁴ The King's Fund (2021). NHS Workforce: Our Position.

https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed on 9 July 2021].

⁴⁵ The King's Fund (2019). What have the parties pledged on health and care?

https://www.kingsfund.org.uk/publications/parties-pledges-health-care-2019#international-recruitment [accessed 9th July 2021]

546 The King's Fund (2021). NHS Workforce: Our Position.

https://www.kingsfund.org.uk/projects/positions/nhs-workforce [accessed on 9 July 2021].

⁵⁴⁷ Centers for Disease Control and Prevention (2020). Sharing and Shifting Tasks to Maintain Essential Healthcare During COVID-19 in Low Resource, non-US settings. https://www.cdc.gov/coronavirus/2019ncov/global-covid-19/task-sharing.html [accessed 9 July 2021].

¹⁸ House of Commons: Health and Social Care Committee (2021). Workforce burnout and resilience in the NHS and social care. https://committees.parliament.uk/publications/6158/documents/68766/default/ [accessed 9 July 2021].

⁵⁴⁹ O'Dowd A (2021). NHS staff's stress levels rose last year as covid pandemic took its toll. BMJ **372**, n703 ⁵⁵⁰ British Medical Association (2021). COVID-19 Tracker Survey. https://www.bma.org.uk/media/3810/bmacovid-tracker-survey-february-2021.pdf [accessed 9 July 2021].

551 House of Commons: Health and Social Care Committee (2021). Workforce burnout and resilience in the NHS and social care. https://committees.parliament.uk/publications/6158/documents/68766/default/ [accessed 9 July 2021].

⁵⁵² NHS Scotland Deanery (2021). COVID-19 Wellbeing Study. https://www.scotlanddeanery.nhs.scot/yourdevelopment/scottish-medical-education-research-consortium-smerc/research/covid-19-wellbeing-study/ [accessed 9 July 2021].

553 Royal College of Nursing (2020). Building a Better Future for Nursing: RCN members have their say. https://www.rcn.org.uk/professional-development/publications/rcn-builliding-a-better-future-covid-pub-009366

Royal College of Nursing (March 2021). Submission to the NHS Pay Review Body: 2021/22 Pay Round. https://www.rcn.org.uk/professional-development/publications/rcn-submission-pay-review-body-2021-2022uk-pub-009601 [accessed 9 July 2021].

555 GMB Union (2021). Social Care GMB Survey.

https://www.gmb.org.uk/sites/default/files/social_care_gmbsurvey_23032021.pdf [accessed 9 July 2021].

¹⁵⁶ House of Commons: Health and Social Care Committee (2021). Workforce burnout and resilience in the NHS and social care. https://committees.parliament.uk/publications/6158/documents/68766/default/ [accessed 9 July 2021].

⁵⁵⁷ Peel House Medical Practise (2021). *Institute of General Practice Managers (IGPM) – campaign to end abuse* of General Practice staff.

https://peelhouse.gpsurgery.net/institute-of-general-practice-managers-igpm-campaign-to-end-abuse-ofgeneral-practice-staff/ [accessed 9 July 2021].

British Medical Association (2021). Rest, recover, restore: Getting UK health services back on track. https://www.bma.org.uk/media/3932/bma-getting-nhs-back-on-track-covid-report-march-2021.pdf [accessed 9 July 2021].

⁵⁵⁹ Moberly T (2021). Doctors' early retirement has trebled since 2008. BMJ **373**, n1594

⁵⁶⁰ Royal College of Physicians (2021). COVID-19 and the workforce: a desire for flexible working to become the norm. https://www.rcplondon.ac.uk/projects/outputs/covid-19-and-workforce-desire-flexible-workingbecome-norm [accessed 9 July 2021].

- ⁵⁶¹ NHS Digital (2021). NHS Sickness Absence Rates NHS Sickness October 2020 to December 2020, Provisional Statistics. https://digital.nhs.uk/data-and-information/publications/statistical/nhs-sickness-absence-rates/october-2020-to-december-2020-provisional-statistics [accessed 9 July 2021].
- <u>absence-rates/october-2020-to-december-2020-provisional-statistics</u> [accessed 9 July 2021].

 562 NHS England: Support Offers. https://www.england.nhs.uk/supporting-our-nhs-people/wellbeing-support-options/support-offers/ [accessed 9 July 2021].
- ⁵⁶³ Welsh Government (2020). *Mental health services: coronavirus*. https://gov.wales/mental-health-services-coronavirus [accessed 9 July 2021].
- ⁵⁶⁴ NHS Scotland (n.d.). Support for NHS and social care workforce in Scotland.
- https://www.practitionerhealth.nhs.uk/accessing-the-service-in-scotland [accessed 12 July 2021].

 565 The Public Health Agency (n.d.). Staff health and wellbeing. https://www.publichealth.hscni.net/covid-19-
- ⁵⁶⁵ The Public Health Agency (n.d.). Staff health and wellbeing. https://www.publichealth.hscni.net/covid-19-coronavirus/guidance-hsc-staff-healthcare-workers-and-care-providers/staff-health-and [accessed 12 July 2021].
- ⁵⁶⁶ British Medical Association (2020). *Measuring progress: Commitments to support and expand the mental health workforce in England*. https://www.bma.org.uk/media/2405/bma-measuring-progress-of-commitments-for-mental-health-workforce-jan-2020.pdf [accessed 9 July 2021].
- ⁵⁶⁷ Morse G, et al. (2011). Burnout in Mental Health Services: A Review of the Problem and Its Remediation. Administration and Policy in Mental Health and Mental Health Services Research **39**, 341–352.
- ⁵⁶⁸ Lamb D, *et al.* (2020). Mixed signals about the mental health of the NHS workforce. The Lancet Psychiatry. **7(12)**, 1009–1011.
- ⁵⁶⁹ House of Commons: Health and Social Care Committee. *Workforce burnout and resilience in the NHS and social care*. https://committees.parliament.uk/publications/6158/documents/68766/default/ [accessed 9th July 2021].
- ⁵⁷⁰ Royal Society DELVE Initiative (2020). Scoping Report on Hospital and Health Care Acquisition of COVID-19 and its Control. https://rs-delve.github.io/reports/2020/07/06/nosocomial-scoping-report.html [accessed 9 July 2021].
- ⁵⁷¹ Grant JJ, et al. (2021). Seroprevalence of SARS-CoV-2 antibodies in healthcare workers at a London NHS Trust. Infection Control and Hospital Epidemiology **42(2)**, 212–214.
- ⁵⁷² [pre-print] Abo-Leyah H, et al. (2020). Seroprevalence of SARS-COV-2 Antibodies in Scottish Healthcare Workers. medRxiv https://www.medrxiv.org/content/10.1101/2020.10.02.20205641v1
- ⁵⁷³ National Health Executive (2020). Ethnicity, seniority impacts Covid-19 antibody prevalence among NHS staff.
- https://www.nationalhealthexecutive.com/articles/ethnicity-seniority-nhs-covid-antibody-prevalence [accessed 9 July 2021].
- ⁵⁷⁴ NHS Providers (2021). Ethnicity, seniority impacts Covid-19 antibody prevalence among NHS staff. https://nhsproviders.org/news-blogs/news/trusts-grappling-with-challenges-on-multiple-fronts-as-survey-reveals-revealing-lists-covid-19-and-winter-pressures [accessed 9 July 2021].
- ⁵⁷⁵ The British Medical Association (2021). *Pressure points in the NHS*. https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/pressures/pressure-points-in-the-nhs
- 576 The British Medical Association (2021). *Pressures in general practice*. https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/pressures/pressures-in-general-practice
- ⁵⁷⁷ Bodkin H (2021). *A&E departments under pressure as non-Covid patients flood back*. The Telegraph, 4 April. https://www.telegraph.co.uk/news/2021/04/04/ae-departments-pressure-non-covid-patients-flood-back/[accessed 13 July 2021].
- ⁵⁷⁸ Campbell A (2021). *A&E units in UK report rapid rise in children's infections*. The Guardian, 25 June. https://www.theguardian.com/society/2021/jun/25/ae-units-in-uk-report-rapid-rise-in-childrens-infections [accessed 13 July 2021].
- ⁵⁷⁹ Ipsos MORI (2021). *Winter 2021/22 under COVID-19*. https://acmedsci.ac.uk/covid-19-preparing-for-the-future-public-dialogue [accessed 9 July 2021].
- 580 NHS England (2021). A&E Attendances and Emergency Admissions March 2021 Statistical Commentary. https://www.england.nhs.uk/statistics/wp-content/uploads/sites/2/2021/04/Statistical-commentary-March-2021-jf8hj.pdf [accessed 9 July 2021].
- ⁵⁸¹ The Nuffield Trust (2021). NHS performance summary: February-March 2021.
- https://www.nuffieldtrust.org.uk/news-item/nhs-performance-summary-february-march-2021#treatment-and-diagnostic-test-activity-and-waiting-times [accessed 9 July 2021].
- ⁵⁸² Dobbs TD (2021). Surgical activity in England and Wales during the COVID-19 pandemic: a nationwide observational cohort study. British Journal of Anaesthesia.
- ⁵⁸³ Dobbs TD (2021). *Surgical activity in England and Wales during the COVID-19 pandemic: a nationwide observational cohort study.* British Journal of Anaesthesia.
- ⁵⁸⁴ British Medical Association (2021). *Rest, recover, restore: Getting UK health services back on track.* https://www.bma.org.uk/media/3910/nhs-staff-recover-report-final.pdf [accessed 9 July 2021].
- ⁵⁸⁵ The Health Foundation, Gardiner T & Frazer C (2021). *Longer waits, missing patients and catching up; How is elective care in England coping with the continuing impact of COVID-19?* https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-comment/charts-and-infographics/how-is-elective-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-covid-19">https://www.health.org.uk/news-and-care-coping-with-the-continuing-impact-of-c
- ⁵⁸⁶ Rutter MD, et al. (2021). Impact of the COVID-19 pandemic on UK endoscopic activity and cancer detection: a National Endoscopy Database Analysis. Gut **70**, 537-543.
- ⁵⁸⁷ The Nuffield Trust (2021). *Diagnostic test waiting times*.
- https://www.nuffieldtrust.org.uk/resource/diagnostic-test-waiting-times [accessed 9 July 2021].
- 588 NHS England (2021). NHS's £160 million 'accelerator sites' to tackle waiting lists.
- https://www.england.nhs.uk/2021/05/nhss-160-million-accelerator-sites-to-tackle-waiting-lists/

- ⁵⁸⁹ Greenhalgh T, et al. Virtual online consultations: advantages and limitations (VOCAL) study. BMJ Open **6(1)**, e009388. ⁵⁹⁰ Bhardwaj A, et al. (2021). Survey of CAMHS clinicians about their experience of remote consultation: brief
- report. BJPsych open. 7(1), e34.
- Parker RF, et al. (2021). Inequalities in general practice remote consultations: a systematic review. BJGP Open 5(3).
- NHS England (2021). NHS's £160 million 'accelerator sites' to tackle waiting lists.

https://www.england.nhs.uk/2021/05/nhss-160-million-accelerator-sites-to-tackle-waiting-lists/

SAGE paper. Contributions of nosocomial infections to the first wave.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961210/S 1056 Contribution of nosocomial infections to the first wave.pdf
594 SAGE paper. Dynamic CO-CIN report to SAGE and NERVTAG (Recent cases).

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/974733/S 1173_CO-CIN_Dynamic_Report.pdf

⁵⁹⁵ Discombe M (2021). Over 450 people a day caught covid in hospitals in January. HSJ.

https://www.hsj.co.uk/coronavirus/over-450-people-a-day-caught-covid-in-hospitals-duringjanuary/7029404.article

⁵⁹⁶ Oliver D (2021). Deaths from hospital acquired covid are everyone's problem. BMJ **373**, 1492.

⁵⁹⁷ Public Health England (2020). *Outbreaks in care homes in England*.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/903085/C OVID19_Care_Homes_22_July.pdf [accessed 9 July 2021].

⁵⁹⁸ Office for National Statistics (2021). Deaths registered weekly in England and Wales, provisional: week endina 28 May 2021.

https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsreg isteredweeklyinenglandandwalesprovisional/weekending28may2021 [accessed 9 July 2021].

Abbas M, et al. (2021). Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to protect both patients and healthcare workers. Antimicrobial resistance and infection control 10, 7. https://aricjournal.biomedcentral.com/articles/10.1186/s13756-020-00875-7

600 Eyre DW, et al. (2020). Differential occupational risks to healthcare workers from SARS-CoV-2 observed during a prospective observational study. Elife 9, e60675.

Royal College of Nursing (2020). Second Personal Protective Equipment Survey of UK Nursing Staff Report: Use and availability of PPE during the COVID-19 pandemic. https://www.rcn.org.uk/-/media/royal-college-ofnursing/documents/publications/2020/may/009-269.pdf?la=en

⁶⁰² British Medical Association (2020). BAME doctors hit worse by lack of PPE. https://www.bma.org.uk/newsand-opinion/bame-doctors-hit-worse-by-lack-of-ppe

⁶⁰³ [pre-print] Illingworth C et al. (2021). Superspreaders drive the largest outbreaks of hospital onset COVID-19 infection. OSF Preprints https://osf.io/wmkn3/

⁶⁰⁴ ARHAI Scotland (2021). Rapid review of the literature – Risk of SARS-CoV-2 acquisition in healthcare workers. https://hpspubsrepo.blob.core.windows.net/hps-website/nss/3162/documents/1_covid-19-rapidreview-sars-cov-2-acquisition-hcw.pdf

605 SAGE paper (n.d.). Masks for healthcare workers to mitigate airborne transmission of SARS-CoV-2.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/979441/S 1169 Facemasks for health care workers.pdf

606 Meredith L, et al. (2020). Rapid implementation of SARS-CoV-2 sequencing to investigate cases of healthcare associated COVID-19: a prospective genomic surveillance study. The Lancet Infectious Diseases 20 (11), P1263-1271.

607 Lucey M, et al. (2021). Whole-genome Sequencing to Track Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Transmission in Nosocomial Outbreaks. Clinical Infectious Diseases 72 (11),

⁶⁰⁸ Li KK, et al. (2021). Genetic epidemiology of SARS-CoV-2 transmission in renal dialysis units – A high risk community-hospital interface. Journal of Infection 83(1), 96-103.

609 NHS (2021). Guidance and standard operating procedures - General practice in the context of coronavirus (COVID-19). https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C1288-COVID-19-SOP-GP-practice-v4.3 May-2021.pdf
610 Public Health England (2021). COVID-19: epidemiology, virology and clinical features.

https://www.gov.uk/government/publications/wuhan-novel-coronavirus-background-information/wuhan-novelcoronavirus-epidemiology-virology-and-clinical-features

611 Public Health England (2021). COVID-19: Guidance for maintaining services within health and care settings - Infection prevention and control recommendations (Version 1.2).

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/990923/2 0210602 Infection Prevention and Control Guidance for maintaining services with H and C settings

pdf
612 Scottish Dental Clinical Effectiveness Programme. Resources for COVID-19.

https://www.sdcep.org.uk/ [accessed 12 July 2021].
613 SAGE paper (2021). Masks for healthcare workers to mitigate airborne transmission of SARS-CoV-2. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/979441/S

1169 Facemasks for health care workers.pdf
614 Public Health England (2021). COVID-19: Guidance for maintaining services within health and care settings - Infection prevention and control recommendations (Version 1.2).

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/990923/2

0210602 Infection Prevention and Control Guidance for maintaining services with H and C settings 1

pdf
615 Academy of Medical Sciences (2020). Preparing for a challenging winter 2020/21.

https://acmedsci.ac.uk/file-download/51353957

- ¹¹⁶ SAGE paper (2021). Masks for healthcare workers to mitigate airborne transmission of SARS-CoV-2. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/979441/S 1169 Facemasks for health care workers.pdf
 617 Ford M (2021). Covid-19 vaccines to be made mandatory for all care home staff in England. Nursing Times,
- June 16. https://www.nursingtimes.net/news/social-care/covid-19-vaccines-to-be-made-mandatory-for-allcare-home-staff-in-england-16-06-2021/ [accessed 12 July 2021]
- SAGE paper (2021). Masks for healthcare workers to mitigate airborne transmission of SARS-CoV-2. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/979441/S
- 1169_Facemasks_for_health_care_workers.pdf
 619 Public Health England (2021). A data linkage approach to assessing the contribution of hospital-associated SARS-CoV-2 infection to care home outbreaks in England, 30 January to 12 October 2020.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/997553/D ata linkage approach to assessing the contribution of hospital-associated SARS-CoV-

- <u>2 infection to care home outbreaks in England.pdf</u>
 ⁶²⁰ UK Government (2021). *Adult social care given over £250 million extra to continue coronavirus (COVID-19)* protections. https://www.gov.uk/government/news/adult-social-care-given-over-250-million-extra-tocontinue-coronavirus-covid-19-protections [accessed 12 July 2021]
 621 Healthcare Safety Investigation Branch (2020). COVID-19 transmission in hospitals: management of the
- risk a prospective safety investigation. https://www.hsib.org.uk/documents/258/hsib-summary-report-covid-
- 19-transmission-hospitals.pdf
 622 Healthcare Safety Investigation Branch (2020). COVID-19 transmission in hospitals: management of the risk - a prospective safety investigation. https://www.hsib.org.uk/documents/258/hsib-summary-report-covid-19-transmission-hospitals.pdf
- 623 Royal Academy of Engineering (2021). Infection resilient environments.

https://www.raeng.org.uk/infection-resilient-environments

- Hall VJ, et al. (2021). COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. The Lancet **397(10286)**, 1725-1735.
- ⁶²⁵ Wise J (2021). Covid-19: Is the UK heading towards mandatory vaccination of healthcare workers? BMJ
- ⁶²⁶ Henderson DA (2011). The eradication of smallpox An overview of the past, present, and future. Vaccine
- ⁶²⁷ Phillips N (2021). The coronavirus is here to stay here's what that means. Nature.

https://www.nature.com/articles/d41586-021-00396-2 [accessed 9 July 2021].

- Public Health England (2021). Surveillance of influenza and other seasonal respiratory viruses in the UK
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/995284/S urveillance of influenza and other seasonal respiratory viruses in the UK 2020 to 2021-1.pdf [accessed 9 July 2021]
- ⁶²⁹ Flerlage T, et al. (2021). Influenza virus and SARS-CoV-2: pathogenesis and host responses in the respiratory tract. Nature Reviews Microbiology, 19, 425-441.
- ⁶³⁰ Office for National Statistics (2021). Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: April 1 2021.
- https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/ prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021#duration-of-reportedsymptoms-following-confirmed-coronavirus-covid-19-infection [accessed 12 July 2021].
- 631 [pre-print] Whitaker M, et al. (2021). Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508 707 people. Imperial College London.
- https://spiral.imperial.ac.uk/bitstream/10044/1/89844/9/REACT_long_covid_paper_final.pdf
- Mallapaty S (2021). How many COVID deaths are acceptable in a post-pandemic world? Nature.

https://www.nature.com/articles/d41586-021-01220-7 [accessed 9 July 2021].

- Archard D (2021). An acceptable level of deaths? Nuffield Council on Bioethics, July 9.
- https://www.nuffieldbioethics.org/blog/an-acceptable-level-of-deaths [accessed 12 July 2021].
- 634 Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- Garry FR (2021). Mutations arising in SARS-CoV-2 spike on sustained human-to-human transmission and human-to-animal passage. Virological. https://virological.org/t/mutations-arising-in-sars-cov-2-spike-onsustained-human-to-human-transmission-and-human-to-animal-passage/578 [accessed 9 July 2021]. 636 Sallam M (2021). COVID-19 Vaccine Hesitancy Worldwide: A Concise Systematic Review of Vaccine
- Acceptance Rates. Vaccines (Basel) 9(2), 160.
- 637 Lee CH & Sibley CG (2020). Attitudes toward vaccinations are becoming more polarized in New Zealand: Findings from a longitudinal survey. EClinicalMedicine 23, 100387.
- 638 UK Government (2021). Coronavirus (COVID-19) in the UK Vaccinations in the United Kingdom. https://coronavirus.data.gov.uk/details/vaccinations [accessed 9 July 2021].
- Our world in data (2021). Total confirmed COVID-19 cases. https://ourworldindata.org/grapher/covidcases-income [accessed 9 July 2021].

- ⁶⁴⁰ Litewka SG & Heitman E (202). Latin American healthcare systems in times of pandemic. Wiley online library
- ⁶⁴¹ Soy A (2020). Coronavirus in Africa: Five reasons why Covid-19 has been less deadly than elsewhere. BBC. https://www.bbc.co.uk/news/world-africa-54418613 [accessed 9 July 2021].
- ⁴² David Pilling & Anna Gross (2021). There are no vaccines: Covid fears rise in Africa as inoculations stall. Financial Times. https://www.ft.com/content/418d7904-9e7b-47a6-b18a-a0606bf11170 [accessed 9 July
- ⁶⁴³ G7 (2021). Carbis Bay G7 Summit Communiqué: Our Shared Agenda for Global Action to Build Back Better. https://www.g7uk.org/wp-content/uploads/2021/06/Carbis-Bay-G7-Summit-Communique-PDF-430KB-25pages-3.pdf
- ⁴⁴ Wang W et al. (2020). Global, regional, and national estimates of target population sizes for covid-19 vaccination: descriptive study. BMJ 371, 4707.
- ⁶⁴⁵ World Health Organisation (2021). COVAX Joint Statement: Call to action to equip COVAX to deliver 2 billion doses in 2021. https://www.who.int/news/item/27-05-2021-covax-joint-statement-call-to-action-to-equipcovax-to-deliver-2-billion-doses-in-2021 [accessed 12 July 2021].

 646 Openshaw P, et al. (2021). NERVTAG Update note on immunity to SARS-CoV-2 after natural infection.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/992944/S 1255 NERVTAG - Immunity following natural infection.pdf [accessed 9 July].
 647 Sterlin D, et al. (2021). IgA dominates the early neutralizing antibody response to SARS-CoV-2. Science
- Translational Medicine 13(577).
- 648 Russell MW, et al. (2020). Mucosal Immunity in COVID-19: A Neglected but Critical Aspect of SARS-CoV-2 Infection. Frontiers in Immunology.
- https://www.frontiersin.org/articles/10.3389/fimmu.2020.611337/full [accessed 9 July 2021].
- Mudgal R, et al. (2020). Prospects for mucosal vaccine: shutting the door on SARS-CoV-2. Human Vaccines and Immunotherapeutics 16(12), 2921-2931.
- 650 Mudgal R, et al. (2020). Prospects for mucosal vaccine: shutting the door on SARS-CoV-2. Human Vaccines and Immunotherapeutics 16(12), 2921-2931.
- 651 Openshaw P, et al. (2021). NERVTAG Update note on immunity to SARS-CoV-2 after natural infection. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/992944/S 1255 NERVTAG - Immunity following natural infection.pdf [accessed 9 July 2021].
 652 Academy of Medical Sciences (2018). Controlled human infection model studies.

- https://acmedsci.ac.uk/file-download/55062331
 653 UK Government (2021). *The COVID-19 Therapeutics Taskforce*.
- https://www.gov.uk/government/groups/the-covid-19-therapeutics-taskforce [accessed 9 July 2021].
- 654 UK Government (2021). Government launches COVID-19 Antivirals Taskforce to roll out innovative home treatments this autumn. https://www.gov.uk/government/news/government-launches-covid-19-antiviralstaskforce-to-roll-out-innovative-home-treatments-this-autumn [accessed 9 July 2021]
- ⁵⁵ National Institute for Health Research (2021). COVID-19 Prophylaxis Oversight Group.
- https://www.nihr.ac.uk/documents/covid-19-prophylaxis-oversight-group-terms-of-reference/26508 656 UK Research and Innovation (2021). Outcomes of the UK COVID-19 Therapeutics Advisory Panel (UK-CTAP).
- https://www.ukri.org/about-us/policies-standards-and-data/data-collection/uk-covid-19-therapeutics-advisorypanel/ [accessed 9 July 2021].
- ⁵⁷ Taylor PC, *et al.* (2021). *Neutralizing monoclonal antibodies for treatment of COVID-19*. Nature Reviews Immunology 21, 382-393.
- ⁶⁵⁸ Michie S, et al. (2020). Behavioural, environmental, social, and systems interventions against covid-19. BMJ, 370, 2982.
- 659 UK Government (2021). COVID-19 Response Spring 2021.
- https://www.gov.uk/government/publications/covid-19-response-spring-2021/covid-19-response-spring-2021summary [accessed 9 July 2021].
- 660 Medley GF & Vassall A (2017). When an emerging disease becomes endemic. Science 357(6347), 156-
- 661 University of Oxford (n.d.). Oxford COVID-19 Government Response Tracker. OxCGRT [accessed 9 July 20211.
- ⁶⁶² Google (n.d). COVID-19 Community Mobility Reports. https://www.google.com/covid19/mobility/ [accessed 9 July 2021].
- ⁶⁶³ Singer M, et al. (2017). Syndemics and the biosocial conception of health. The Lancet 389(10072) 941-
- 664 The British Academy (2021). The COVID decade: understanding the long-term societal impacts of covid-19. https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf
- 665 Singer M, et al. (2017). Syndemics and the biosocial conception of health. The Lancet 389(10072), 941-
- 666 Singer M, et al. (2017). Syndemics and the biosocial conception of health. The Lancet 389(10072), 941-
- ⁶⁶⁷ Marmot M, et al. (2020). Build back fairer: the COVID-19 Marmot Review.
- https://www.health.org.uk/sites/default/files/upload/publications/2020/Build-back-fairer-the-COVID-19-Marmot-review.pdf
- https://www.hra.nhs.uk/about-us/news-updates/involving-public-covid-19-research-guest-blog-bec-hanleyand-maryrose-tarpey/
- ⁶⁶⁹ Patient and Carer Reference Group (for this project)

- 670 https://www.britannica.com/topic/Model-Parliament (the original is in Latin, so translations vary)
- https://data.oecd.org/inequality/income-inequality.htm
- https://data.oecd.org/inequality/poverty-gap.htm#indicator-chart
- https://jech.bmj.com/content/53/10/603.short
- https://www.versusarthritis.org/media/23782/chronic-pain-report-june2021-print-friendly.pdf
- https://richmondgroupofcharities.org.uk/sites/default/files/multimorbidity -
- <u>understanding_the_challenge.pdf</u>

 676 https://analytics.phe.gov.uk/apps/covid-19-indirect-effects/#
- https://www.longcovid.org/
- 678 https://www.longcovid.org/impact/long-covid-clinic-survey-may-analysis
- 679 https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/06/C1312-long-covid-plan-
- https://www.england.nhs.uk/2020/12/long-covid-patients-to-get-help-at-more-than-60-clinics/
- https://www.nice.org.uk/guidance/ng188/chapter/2-Assessing-people-with-new-or-ongoing-symptomsafter-acute-COVID-19
- 682 https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/11/C1248-national-quidancepost-covid-syndrome-assessment-clinics-v2.pdf
- 683 https://www.nice.org.uk/guidance/ng188

https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/ prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1july2021

- https://www.coproductioncollective.co.uk/
- Reproduced with kind permission of the Co-production Collective:

https://www.coproductioncollective.co.uk/what-is-co-production/our-approach

- 687 Improving Access to Psychological Therapies https://www.nhs.uk/mental-health/talking-therapiesmedicine-treatments/talking-therapies-and-counselling/nhs-talking-therapies/
- 688 https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-vaccinations/
- https://www.gov.uk/government/news/community-champions-to-give-covid-19-vaccine-advice-and-boosttake-up
- 690 https://www.gov.uk/government/news/community-champions-to-give-covid-19-vaccine-advice-and-boosttake-up
- ⁶⁹¹ Ipsos MORI (2021). Winter 2021/22 under COVID-19. https://acmedsci.ac.uk/covid-19-preparing-for-thefuture-public-dialogue
- 692 UK Government (2021). COVID-19 Response Spring 2021 (Summary).

https://www.gov.uk/government/publications/covid-19-response-spring-2021/covid-19-response-spring-2021summary [accessed 9 July 2021].

- ³ Munday JD, et al. (2021). CoMix Age structured contact matrices for 9 key periods of the COVID-19 epidemic in England. Zenodo.
- 694 UK Government (2021). Scientific Pandemic Influenza Group on Modelling (SPI-M).

https://www.gov.uk/government/groups/scientific-pandemic-influenza-subgroup-on-modelling [accessed 9 July 20211.

- ⁶⁹⁵ Welsh Government (2021). Technical Advisory Group: policy modelling update 25 June 2021
- https://gov.wales/sites/default/files/publications/2021-07/technical-advisory-group-policy-modelling-update-25-june-2021.pdf
- ⁶⁹⁶ Jarvis CI, et al. (2021). The impact of local and national restrictions in response to COVID-19 on social contacts in England: a longitudinal natural experiment. BMC Medicine 19, 52.
- 697 Ward H, et al. (2021). Prevalence of antibody positivity to SARS-CoV-2 following the first peak of infection in England: Serial cross-sectional studies of 365,000 adults. The Lancet Regional Health - Europe 4, 100098. ⁶⁹⁸ Office for National Statistics (2021). COVID-19 Infection Survey.
- https://www.ons.gov.uk/surveys/informationforhouseholdsandindividuals/householdandindividualsurveys/covid 19infectionsurvey [accessed 9 July 2021].
- Knight SR, et al. (2020) Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ 370, m3339.
- ⁷⁰⁰ UCL COVID-19 Social Study. *Understanding the psychological and social impact of the pandemic.*
- https://www.covidsocialstudy.org/ [accessed 9 July 2021].

 701 Northern Ireland Statistics and Research Agency (2021). NISRA Coronavirus (COVID-19) Opinion Survey. https://www.nisra.gov.uk/publications/nisra-coronavirus-covid-19-opinion-survey [accessed 9 July 2021].
- Menni C, et al. (2020). Real-time tracking of self-reported symptoms to predict potential COVID-19. Nature Medicine 26, 1037-1040.
- 703 HDRUK (2021). COVID-19 Health Data Research. https://www.hdruk.ac.uk/wp-
- content/uploads/2021/06/2021-06-08-Health-Data-Research-UK-SAGE-report.pdf [accessed 9 July 2021].
 704 Wood A, et al. (2021). Linked electronic health records for research on a nationwide cohort of more than 54 million people in England: data resource. BMJ 373, 826.
- 705 Office for National Statistics (2021). More information on data sources related to coronavirus (COVID-19). https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/m oreinformationondatasourcesrelatedtocoronaviruscovid 19/2020-12-11 [accessed 9 July 2021].
- ⁷⁰⁶ Mathur R, et al. (2021). Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform. The Lancet, 397, 1711-1724.

- ⁷⁰⁷ Simpson SR, et al. (2020). Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II): protocol for an observational study using linked Scottish national data. BMJ Open **10**, 6. ⁷⁰⁸ Lyons J, et al. (2020) Understanding and responding to COVID-19 in Wales: protocol for a privacy-
- protecting data platform for enhanced epidemiology and evaluation of interventions. BMJ Open 10, 10. ⁰⁹ University of Oxford (2021). RECOVERY. https://www.recoverytrial.net/ [accessed 9 July 2021].
- ⁷¹⁰ Knight SR, et al. (2020) Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ 370,
- ⁷¹¹ Clift AK, et al. (2020). Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 371, m3731.
- ⁷¹² Torjesen I (2021). Covid-19: First doses of vaccines in Scotland led to a substantial fall in hospital admissions. BMJ 372, n523.
- ⁷¹³ Thompson DA, et al. (2021). Staff-pupil SARS-CoV-2 infection pathways in schools in Wales: a populationlevel linked data approach. BMJ Paediatrics Open 5, e001049.
- 714 Sudre CH, et al. (2021) Attributes and predictors of long COVID. Nature Medicine 27, 626–631.
- ⁷¹⁵ The British Academy (2021). *The COVID decade: understanding the long-term societal impacts of covid-19.* https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf
- UK Government (2021). Putting Good into Practice: A public dialogue on making public benefit assessments when using health and care data.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/977737/P GIP Report FINAL 1304.pdf
 717 The Royal Society (2020). Data Readiness: Lessons from an Emergency. https://rs-
- <u>delve.github.io/reports/2020/11/24/data-readiness-lessons-from-an-emergency.html</u> [accessed 9 July 2021]. ⁷¹⁸ The British Academy (2021). The COVID decade: understanding the long-term societal impacts of covid-19. https://www.thebritishacademy.ac.uk/documents/3238/COVID-decade-understanding-long-term-societalimpacts-COVID-19.pdf [accessed 7 July 2021].



Academy of Medical Sciences 41 Portland Place London, W1B 1QH +44(0)20 3141 3200



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