Northern Ireland Assembly

Research and Information Service Briefing Paper

Paper No. 22/20 19th May 2020 NIAR 126-2020

Dr Janice Thompson

‘Exit’ From COVID-19 ‘Lockdown’: Health-Related Issues

This paper has been produced to support the COVID-19 Ad Hoc Committee and the Health Committee with their scrutiny of the pandemic response.

It discusses a number of factors relating to the spread of infectious disease to be borne in mind when considering measures to control the virus going forward. This includes the impact of infectious dose, viral load and asymptomatic cases and the relationship between the ‘lockdown’ and the ‘R’ number of the virus.

It goes on to review a range of health-related measures and actions related to easing the ‘lockdown’. Some are shorter-term (for example the test, track and trace approach) and others are longer term (such as a vaccine development). These include: ‘Test, Track and Trace’; antibody testing and immunity; new treatments and vaccine development; wearing of masks; continued social distancing and ‘shielding’ of the most vulnerable.

Contents

1. Context – Easing out of 'Lockdown' 3

1.1 Northern Ireland - Current Regulations 3

1.2 Moving Forward 4

2. Infectious Disease Factors 5

2.1 Infectious Dose, Viral Load and Symptomless Cases 5

2.2 The Link between 'Lockdown' and the 'R' Number 7

3. Test, Track and Trace in the UK 8

3.1 Background to Test, Track and Trace 8

3.2 Diagnostic Testing, Surveillance Testing and Antibody Testing 9

3.3 Tracking and Contact Tracing 12

4. Wearing Face Coverings or Masks 14

5. Social Distancing (the two metre guidance) and Additional Advice to Vulnerable People 16

5.1 The Two Metre Guidance 16

5.2 Vulnerable People 18

6. New Treatments 19

6.1 Overview 19

6.2 The Solidarity Trial 21

6.3 The RECOVERY Trial - Randomised Evaluation of COV-id19 thERapY 22

6.4 PRINCIPLE Trial (UK) - Platform Randomised trial of INterventions against COVID-19 In older PeopLE 22

6.5 Other Selected Treatment Trials 23

7. Development of a Vaccine 24

7.1 How Does a Vaccine Work? 24

7.2 Progress of Vaccine Development to SARS-CoV-2 25

8. Conclusion 28

1. Context – Easing out of 'Lockdown'

The UK government recently published 'Our Plan to Rebuild' setting out a three-phase strategy for gradually lifting the current restrictions in England.[1] The devolved governments of Northern Ireland (NI)[2], Scotland[3] and Wales[4] have each published their own plans, which are generally of a more cautious nature.

The devolved regions rejected the UK government's new "stay alert" message in favour of retaining 'stay at home' and also largely decided against setting projected dates for easing restrictions. The NI plan ('Pathway to Recovery') broadly aligns with those for Scotland and Wales.[5] The government of the Republic of Ireland has also published a five stage roadmap for reopening society and business in a phased manner, at three week intervals from 18th May 2020.[6] This paper will not go into detail on the plans of all the jurisdictions but the main points for the NI Executive's five stage approach is now summarised.

1.1 Northern Ireland - Current Regulations

On 28th March 2020, the NI Executive agreed regulations that introduced restrictions to slow the spread of coronavirus, including the closure of certain businesses and prohibiting anyone from leaving their house except for very limited reasons. The Regulations also banned gatherings of more than two people from outside the same household. The lockdown has essentially been extended to the 28th May 2020. The **original reasons** to leave home during lockdown are as listed below but there are now a number of relaxations to these as described later in section 2.1:[7]

- The need to work, or deliver voluntary or community services, where that cannot be done at home;
- Go to a shop for food or a chemist for medication;
- Carry out basic necessities such as taking our animals to the vet;
- Take exercise either alone or with others who live in the same household;
- Get medical assistance;
- Help a vulnerable person that we are caring for, or to provide emergency assistance;
- Donate blood;

[1] Our plan to rebuild: The UK Government's COVID-19 recovery strategy, HM Government, 11th May, 2020, https://www.gov.uk/government/publications/our-plan-to-rebuild-the-uk-governments-covid-19-recovery-strategy
[2] Executive Approach to Decision-Making, NI Executive, 12th May 2020, https://www.executiveoffice-ni.gov.uk/publications/coronavirus-executive-approach-decision-making
[3] Coronavirus (COVID-19): framework for decision making, Scottish Government, https://www.gov.scot/publications/coronavirus-covid-19-framework-decision-making/
[4] Traffic light system to ease Wales out of lockdown, Welsh Government, 15th May 2020, https://media.service.gov.wales/media-library/traffic-light-system-for-wales
[5] Carroll, R. (2020), Northern Ireland reveals five-stage lockdown exit plan, The Guardian, 12th May 2020, https://www.theguardian.com/politics/2020/may/12/northern-ireland-cautious-lockdown-exit-plan-five-stage-road-map

[6] Government publishes roadmap to ease COVID-19 restrictions and reopen Ireland's economy and society, Department of the Taoiseach and Department of Health, Republic of Ireland, 1st May 2020, https://www.gov.ie/en/news/58bc8b-taoiseach-announces-roadmap-for-reopening-society-and-business-and-u/?referrer=/roadmap/
[7] Executive Approach to Decision-Making, NI Executive, 12th May 2020, paragraphs 1.7-1.8, https://www.executiveoffice-ni.gov.uk/publications/coronavirus-executive-approach-decision-making

- Attend a funeral of a close family member or someone that we live with;
- Fulfil a legal obligation;
- Access critical public services; and
- Move house if absolutely necessary.

1.2 Moving Forward

The NI Executive has adopted principles (aligning closely with the World Health Organisation (WHO) guidance) to be applied when considering whether a specific restriction or requirement should be retained, withdrawn or modified:[8]

- **Controlling transmission** - the key metric is the reproduction number 'R'. A restriction or requirement should only be relaxed when there is a reasonable prospect of maintaining 'R' at or below 1;

- **Protecting healthcare capacity** - the healthcare system should have sufficient capacity to treat COVID-19 patients while phasing in the reintroduction of usual services. The system should not be allowed to be overwhelmed by a second or subsequent wave of the pandemic;

- **Necessity** - in accordance with the Regulations, a specific restriction or requirement should be retained only as long as it is considered necessary to prevent, protect against, control, or provide a public health response to the incidence or spread of the virus;

- **Proportionality** - the detrimental impacts on health, society and the economy that can reasonably be attributed to the restriction or requirement should be tolerated only as long as the risks associated with withdrawal or modification are assessed to be more severe; and

- **Reliance on evidence** - Proposals for change or for the retention of a restriction or requirement should be informed by the best available evidence and analysis.

The NI Executive has set out a series of five steps, called the 'Pathway to Recovery', (with no timeframe to allow for flexibility depending on scientific and medical advice) in different areas to show the path it will follow in relaxing the restrictions. Steps will not necessarily apply at the same time in different sectors – e.g. 'Step 1' for work, may apply at a different time than 'Step 1' for retail, reflecting the complexities in each environment. The aspects covered are work, retail, education, travel, family and community, sport, cultural and leisure activities.

For each of the five steps, the NI Executive have provided examples of the measures, which could be taken. As all of the areas are interlinked, it intends to adopt one overall approach to them, rather than treating them as a series of individual decisions. It will

[8] Executive Approach to Decision-Making, NI Executive, 12th May 2020, paragraph 2.6, https://www.executiveoffice-ni.gov.uk/publications/coronavirus-executive-approach-decision-making

be necessary to allow time between each step of relaxations to monitor the impact on the spread of the virus and on the health system, so the Regulations will continue to be reviewed within every three-week period.

As part of 'Step 1' garden centres and recycling centres in NI reopened (with appropriate social distancing measures in place) from Monday 18th May 2020. In addition, the Department of Agriculture, Environment and Rural Affairs reopened 91 fishing facilities to anglers on that date. The carparks will not be opened so anglers must stay local. In addition, in a compassionate move, marriage ceremonies where a person is terminally ill will also now be allowed.[9]

From 20th May 2020, other 'Step 1' measures are allowing groups of four to six people who do not share a household to meet outdoors only while maintaining physical distancing, churches allowed to open for private prayer and hold drive-through services and some sports such as golf and tennis start with appropriate distancing and hygiene measures in place.[10]

In 'Step 2', further non-food retailers will be able to open, as will some libraries and open-air museums. By 'Step 3' school will expand provision to accommodate a number of priority cohorts on a part time basis with a blended learning approach involving a combination of in-school and remote learning. In 'Step 4' hairdressers, fitness studios and tattoo parlours will reopen and schools will open for all children on a part-time basis, blending in-school and remote learning. It will not be until 'Step 5' that cafes, restaurants and pubs will be able to open.[11]

2. Infectious Disease Factors

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the 2019 novel coronavirus disease pandemic. This section looks briefly at a range of factors that influence how fast and effectively SARS-CoV-2 spreads in the population. These factors will have an increasing impact on case numbers and spread of the virus going forward as NI starts to ease out of lockdown.

2.1 Infectious Dose, Viral Load and Symptomless Cases

The average number of viral particles needed to establish an infection in an individual is known as the **infectious dose**. Given how rapidly SARS-CoV-2 has spread, its infectious dose is likely to be relatively low – in the region of a few hundred or thousand particles. **Viral load** relates to the number of viral particles being carried by an infected

[9] Coronavirus: First moves to ease NI lockdown can start next week, BBC News, 14th May 2020, https://www.bbc.co.uk/news/uk-northern-ireland-52666472
[10] Coronavirus: NI Executive agrees to lift more lockdown measures, 18th May 2020, https://www.bbc.co.uk/news/uk-northern-ireland-52711301
[11] Carroll, R. (2020), Northern Ireland reveals five-stage lockdown exit plan, The Guardian, 12th May 2020, https://www.theguardian.com/politics/2020/may/12/northern-ireland-cautious-lockdown-exit-plan-five-stage-road-map

individual and shed into their environment. If an individual has a high viral load, they are more likely to infect other people.[12]

It is known that the virus can also be asymptomatic, causing no noticeable illness in some people. Such cases were first recognised in China in January 2020. The Centre for Evidence-based Medicine (University of Oxford) attempted to answer the question "what is the proportion of people with SARS-COV-2 who are asymptomatic?" The authors reviewed 21 published reports and found that there is not yet a[13]:

> *single reliable study to determine the number of asymptomatics. It is likely we will only learn the true extent once population based antibody testing is undertaken.*

Their review indicated that:

- Published studies have shown a very wide range in terms of percentage of asymptomatic cases testing positive (5% to 80%);
- Symptom-based screening will likely miss many cases;
- Some asymptomatic cases will go on to become symptomatic over the next week ("pre-symptomatics"); and
- Children and young adults can be asymptomatic.

Further information on two of the studies is now discussed.

Research published in March 2020 analysed the course of the epidemic in 375 Chinese cities between 10th January and 23rd January - when containment measures were imposed. The study concluded that 86 per cent of cases were either asymptomatic or had very mild symptoms.[14] These people were estimated to be only 55 per cent as contagious as those with more noticeable symptoms but the study found that they were the source of 79 per cent of further infections, due to there being more of the cases, and the higher likelihood that they were 'out and about' before the restrictions came in.

A project in Italy also found symptomless cases. When all 3,000 residents of the town of Vò were tested[15] in early March 2020, 60 per cent of the people who tested positive were found to have no symptoms. This mass testing allowed the quarantining of people before they showed signs of infection and stopped further spread. At the time the first symptomatic case was diagnosed, about 3% of the population of Vò had already been infected – yet most of them were completely asymptomatic.[16]

---

[12] Geddes, L. (2020), Does a high viral load or infectious dose make covid-19 worse? *New Scientist*, 27th March 2020, https://www.newscientist.com/article/2238819-does-a-high-viral-load-or-infectious-dose-make-covid-19-worse/

[13] Jefferson, T et. Al. (2020), COVID-19: What proportion are asymptomatic? CEBM, University of Oxford, 6th April 2020, https://www.cebm.net/covid-19/covid-19-what-proportion-are-asymptomatic/

[14] Lawton, G. (2020), You could be spreading the coronavirus without realising you've got it, New Scientist, 24th March 2020, https://www.newscientist.com/article/2238473-you-could-be-spreading-the-coronavirus-without-realising-youve-got-it/

[15] A number of rounds of testing were carried out.

[16] Crisanti, A. and Cassone, A. (2020), In one Italian town, we showed mass testing could eradicate the coronavirus, The Guardian, 20th March 2020, https://www.theguardian.com/commentisfree/2020/mar/20/eradicated-coronavirus-mass-testing-covid-19-italy-vo

At present in the UK, the combined impacts of likely low 'infectious dose' for SARS-CoV-2, the unknown number of asymptomatic cases and unknown 'viral load' that symptomatic and asymptomatic cases are 'shedding', means the public health measures around social distancing, hand-washing, face-coverings etc. are going to continue to be very important as NI eases out of lockdown.

2.2 The Link between 'Lockdown' and the 'R' Number

The lockdown has been deemed an essential public health measure by the UK government for containing the spread of SARS-CoV-2. However, it has come at the cost of huge social and economic disruption. A recent NI Assembly RaISe publication reviewed the lockdown and related public health measures across the UK and selected countries.[17] If all the measures were 'lifted' all at once, then another substantial outbreak is thought to be inevitable as the virus is still circulating and known to be very contagious. Monitoring what is known as the 'R' number of the virus is seen as crucial in planning and monitoring easing of the lockdown.

The 'R' number can refer to either the basic reproduction number, known as R 'nought' or R 'zero' (R_0), or the effective reproduction number (R_e or R_t). R_0 describes how many people each infected person will infect on average at the start of a disease outbreak, assuming there is no pre-existing immunity in the population. The progression of the disease is then measured by the effective reproduction number, R_e (sometimes called R_t or just R). This represents the number of people in a population who can be infected by an individual at any specific time after the initial onset of the disease. Further information on the 'R' number and its limitations can be found in a recent RaISe blog article.[18]

Before lockdown across the UK, the 'R' number being used for planning was three i.e. one infected person passed it onto at least three others on average. Initial estimates of the outbreak in Wuhan, China, suggested an R_0 of 2.2–2.7. However, the calculations from a more recent study show that the median R_0 value could be as high as 5.7.[19]

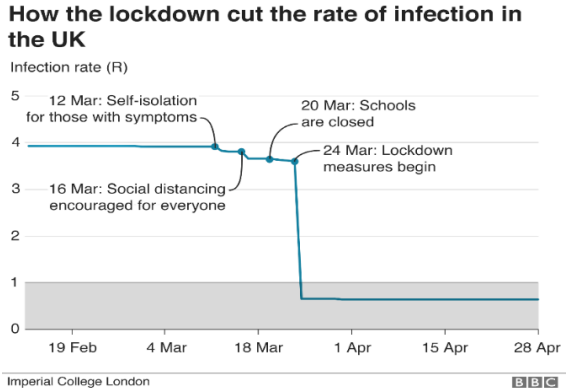
The goal of lockdown has been to cut infections by around 70% to force the 'R' below one (the point at which the outbreak starts to decline). The UK government believes that has now been achieved. The following infographic (prepared by Imperial College

[17] Thompson, J. and McMurray, M. (2020), COVID-19, Background, Public Health Measures and Testing for SARS-CoV-2, 1st April 2020, Paper 13/20, NIAR 14-2020, http://www.niassembly.gov.uk/globalassets/documents/raise/publications/2017-2022/2020/health/1320.pdf

[18] Barry, R. (2020), Ten reasons to be cautious about using R to support decision-making during the COVID-19 pandemic, 19th May 2020, https://www.assemblyresearchmatters.org/2020/05/19/ten-reasons-to-be-cautious-about-using-r-to-support-decision-making-during-the-covid-19-pandemic/

[19] Sanche, S. et. al. (2020), High Contagiousness and Rapid Spread of Severe Acute Respiratory Syndrome Coronavirus 2, *Emerging Infectious Diseases*, 26(7), July 2020 – Early Release Article, *Disclaimer: Early release articles are not considered as final versions. Any changes will be reflected in the online version in the month the article is officially released,* https://wwwnc.cdc.gov/eid/article/26/7/20-0282_article

London) taken from the BBC Website shows how the 'lockdown' cut the Reproduction number or rate of infection to below one:[20]



However, at present it is only just below one in parts of the UK, which means there is not room for the government to make a huge number of changes immediately. Following changes to lockdown it will take at least two to three weeks for the new value of 'R' to become apparent with confidence, although it may be possible to estimate the effect of changes more rapidly through modelling.[21]

3. Test, Track and Trace in the UK

3.1 Background to Test, Track and Trace

The WHO has consistently called for extensive testing of all suspected cases so that confirmed cases are promptly isolated and receive care, and their close contacts are rapidly identified so that they can also self-isolate/be quarantined and monitored.[2]

A recent NI Assembly RaISe briefing paper (NIAR 125-2020) entitled 'COVID-19: Testing for SARS-CoV-2 in the UK; and the Use of Testing and Contact Tracing in Selected Countries', highlighted the importance of both timely testing and contact tracing (manual tracing and ICT developments) to drive suppression of transmission of the virus. It also reviewed the approaches taken to testing, contact tracing and related measures in NI, other jurisdictions of the UK and a number of selected countries.[22]

This section updates Section 5 of that RaISe paper on the progress of the 'test, track and trace' plans in the UK and specific NI information in that regard. The UK strategy's three interconnected aims going forward are:

[20] Gallagher, J. (2020), Coronavirus lockdown: When will it end and how?, BBC News, Health, https://www.bbc.co.uk/news/health-52183295

[21] Coronavirus: Executive Approach to Decision-Making, NI Executive, 12th May, 2020, paragraph 1.6, https://www.executiveoffice-ni.gov.uk/sites/default/files/publications/execoffice/execuitveour-approach-to-decision-making.pdf

[22] Thompson, Dr. J. and McMurray, S. (2020), COVID-19: Testing for SARS-CoV-2 in the UK; and the Use of Testing and Contact Tracing in Selected Countries', 4th May, 2020, RaISe, NI Assembly Paper 18/20, NIAR 125-2020, http://www.niassembly.gov.uk/globalassets/documents/raise/publications/2017-2022/2020/health/1820.pdf

- Test people to uncover the virus;
- Track how and where the virus is spreading; and
- Trace people who may be infected.

3.2 Diagnostic Testing, Surveillance Testing and Antibody Testing

3.2.1 Diagnostic Testing

The methods for **diagnostic testing** for SARS-CoV-2 and antibody testing were described in Section 2.2 of the recent RaISe paper NIAR 125-2020.[23] The methods and places of testing under the UK government's strategy remains unchanged from what is described in that paper, however the list of those eligible for testing has been widened to now cover all those aged 5 and over (with symptoms).[24] Testing is currently available in NI by methods and places as also described in that previous paper for:

- All healthcare and other defined 'key workers' who are self-isolating due to symptoms or because a member of their household has symptoms;
- Residents and staff in any care home identified as having a potential outbreak or cluster of infection;
- Patients/residents being transferred into a care home from any setting, whether that be from hospital, supported living or directly from their own home;
- Patients who are admitted to hospital for emergency or elective care; and
- Patients being discharged from acute hospital care to a care home.

The UK government met its target of 100,000 tests a day by the end of April - but this figure included testing kits sent out by post. Actual daily tests had dropped back to around 80,000[25] but have now increased again to over 100,000 per day. The number of tests does not equate to the numbers of patients tested, as more than one test per patient can be needed to double check an inconclusive result or recheck a negative test.

In NI, as of 15th May 2020, a total of 45,241 tests (4317 positive for SARS-CoV-2) had been completed for 37,221 individuals.[26]

[23] Thompson, Dr. J. and McMurray, S. (2020), COVID-19: Testing for SARS-CoV-2 in the UK; and the Use of Testing and9Contact Tracing in Selected Countries', 4th May, 2020, RaISe, NI Assembly Paper 18/20, NIAR 125-2020, http://www.niassembly.gov.uk/globalassets/documents/raise/publications/2017-2022/2020/health/1820.pdf

[24] Coronavirus: Five and overs in UK now eligible for test, BBC News, 18th May 2020, https://www.bbc.co.uk/news/uk-52713127

[25] Coronavirus: What is the UK's test, track and trace strategy? BBC News, 14th May 2020, https://www.bbc.co.uk/news/health-52475688

[26] COVID-19 Testing Overview, Department of Health NI, 15th May 2020, https://app.powerbi.com/view?r=eyJrIjoiZGYxNjYzNmUtOTlmZS00ODAxLWE1YTEtMjA0NjZhMzlmN2JmIiwidCI6IjljOWEzMGRlLWQ4ZDctNGFhNC05NjAwLTRiZTc2MjVmZjZjNSIsImMiOjh9

3.2.2 Surveillance Testing

Section 4.7 of RaISe paper NIAR 125-2020[27] described the range of 'surveillance testing' being carried out across England by the:

- Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) working with Public Health England (PHE) to monitor the number of suspected COVID-19 cases in the community;
- Public Health England (PHE) GP in-hours system (and separate 'Out-of-Hours' system) monitors the daily number of GP consultations where patients presented with a range of respiratory symptoms; and
- RCGP 'Swabbing Scheme', which sees around 200 GP practices taking swabs from patients or asking patients to swab themselves.

That paper also highlighted enhanced community surveillance for the virus in Scotland and in NI. In NI, this is based on:

- GPs utilising the established 'Influenza GP Spotter Surveillance System' - testing a sample of patients with respiratory symptoms that do not require referral to hospital or to a COVID centre; and
- Emergency Departments - testing a sample of patients who attend an ED with mild to moderate respiratory symptoms, and who following assessment do not require admission to hospital.

The UK government also commenced a population-based study on 23rd April 2020 in order to help track the current extent of transmission and infection in the UK. The aim is to contact 20,000 households in England and request a nose and throat swab test. They will be asked to take further tests every week for the first five weeks, then every month for a year. In addition, adults in 1,000 of the households will also be asked to provide a blood sample to help establish what proportion of the population has developed antibodies. It is hoped the study will eventually be extended to include up to 300,000 participants within the next 12 months.[28]

The first pilot survey covered 10,000 households in England, working with the University of Oxford, IQVIA and UK Biocentre Milton Keynes to collect and analyse the samples. All individuals aged two years and over in sampled households were invited to provide samples for testing. This means approximately 25,000 people are involved in the pilot study. Following completion of the pilot survey, it is intended to expand the

[27] Thompson, Dr. J. and McMurray, S. (2020), COVID-19: Testing for SARS-CoV-2 in the UK; and the Use of Testing and Contact Tracing in Selected Countries', 4th May, 2020, RaISe, NI Assembly Paper 18/20, NIAR 125-2020, http://www.niassembly.gov.uk/globalassets/documents/raise/publications/2017-2022/2020/health/1820.pdf

[28] Gregory, A. (2020), New government study aims to test 300,000 for coronavirus and track immunity levels in UK population, The Independent, 23rd April 2020, https://www.independent.co.uk/news/health/coronavirus-test-immunity-antibodies-government-study-covid-19-matt-hancock-ons-a9479416.html

size of the sample over the next 12 months and aim to cover people across all four UK nations. The initial results of the pilot are as follows[29]:

- At any given time between 27th April and 10th May 2020, it is estimated that an average of 0.27% of the community population in England had COVID-19 (95% confidence interval: 0.17% to 0.41%);
- It is estimated that an average of 148,000 people in England had COVID-19 during this time (95% confidence interval: 94,000 to 222,000); and
- Out of the 10,705 participants' swab tests included in the analysis, 33 individuals in 30 households tested positive for COVID-19.

3.2.3 Antibody Testing

An accurate antibody test has long been seen as key to helping the UK exit lockdown. Such a test is a 'serological test' and works by testing a person's blood for coronavirus antibodies to see if they have already had the virus and therefore may have gained some immunity to it.[30]

The development of immunity to a virus through natural infection is a multi-step process that typically takes place over 1-2 weeks. The body responds immediately with a 'non-specific response' in which a range of white blood cells slow the progress of virus and may even prevent it from causing symptoms. This is followed by an 'adaptive response' - the body makes antibodies (proteins called 'immunoglobulins') that specifically bind to the virus and also 'T-cells' that recognise and eliminate other cells infected with the virus. This is called 'cellular immunity'. This combined adaptive response may clear the virus from the body, and if the response is strong enough, may prevent progression to severe illness or re-infection by the same virus.[31]

Recent progress in this area has been rapid, with media reports on 4th May 2020 stating that a first coronavirus antibody test could soon be approved by PHE as government scientists were evaluating the accuracy of a test made by Roche (cleared for use by the US Food and Drug Administration on 2nd May 2020).[32] The specificity and accuracy of this test is **now approved** by PHE[33]:

> *This is a very positive development, because such a highly specific antibody test is a very reliable marker of past infection. This in turn may*

[29] Coronavirus (COVID-19) Infection Survey pilot: England, 14 May 2020, Office for National Statistics, https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveypilot/england14may2020

[30] How do coronavirus home antibody tests work, and how do I get one? 17th May 2020, The Telegraph, https://www.telegraph.co.uk/news/2020/05/17/antibody-test-coronavirus-uk-covid-19-buy-home/

[31] "Immunity passports" in the context of COVID-19, The World Health Organisation, 24th April, 2020, https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19

[32] Thompson, Dr. J. and McMurray, S. (2020), COVID-19: Testing for SARS-CoV-2 in the UK; and the Use of Testing and Contact Tracing in Selected Countries', 4th May, 2020, RaISe, NI Assembly Paper 18/20, NIAR 125-2020, http://www.niassembly.gov.uk/globalassets/documents/raise/publications/2017-2022/2020/health/1820.pdf

[33] Bodkin, H. (2020), Exclusive: First coronavirus antibody test given approval by Public Health England, The Telegraph, https://www.telegraph.co.uk/news/2020/05/13/exclusive-first-coronavirus-antibody-test-given-approval-public/

> *indicate some immunity to future infection, although the extent to which the presence of antibodies indicates immunity remains unclear.*

The PHE has also now approved another antibody test, made by US company Abbott Laboratories.[34]

It has been suggested that the detection of antibodies to the virus that causes COVID-19, could serve as the basis for an "immunity passport" or "risk-free certificate" that would enable individuals to travel or to return to work assuming that they are protected against re-infection. However, how long immunity lasts is not yet clear.[35] According to the WHO, there is yet no evidence that people who have recovered from COVID-19 and have antibodies are protected from a second infection.[36]

Mount Sinai[37] researchers have reviewed the huge amount of immunology research coming out about the coronavirus. They concluded that studies of SARS-CoV-2's proteins and genetics suggest that the virus seems likely to induce a long-term immune response similar to that of other coronaviruses. Research on SARS 1 and MERS suggests that some level of antibody immunity persists for at least two or three years, starting high and gradually waning as time goes by.[38]

A recent publication highlighted that such 'immunity passports' are currently impractical given current gaps in knowledge and technical limitations, but also pose equitable and legal concerns as they:[39]

> *would impose an artificial restriction on who can and cannot participate in social, civic, and economic activities and might create a perverse incentive for individuals to seek out infection, especially people who are unable to afford a period of workforce exclusion, compounding existing gender, race, ethnicity, and nationality inequities.*

3.3 Tracking and Contact Tracing

In terms of tracking how and where the virus in moving, RaISe paper NIAR 125-2020 described the UK government's plans for its 'centralised' contact-tracing app (currently in second phase trials on the Isle of Wight), designed by NHSX. The goal of the app is to alert people who may have been exposed to the virus so they can take action to protect themselves, their families, friends and the health service, but will only

[34] Hodgson, C. and Cookson, C. (2020) Abbott joins Roche in winning UK approval for virus antibody test, Financial Times, 15th May 2020, https://www.ft.com/content/14b69e2b-c55b-48e0-8c66-2232f2e857df
[35] Pappas, S. (2020), After recovering from COVID-19, are you immune? 11th May 2020, Live Science, https://www.livescience.com/covid-19-immunity.html
[36] "Immunity passports" in the context of COVID-19, The World Health Organisation, 24th April, 2020, https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19
[37] Mount Sinai - one of the US's largest and most respected hospitals, acclaimed internationally for excellence in clinical care, https://www.mountsinai.org/locations/mount-sinai
[38] Pappas, S. (2020), After recovering from COVID-19, are you immune? 11th May 2020, Live Science, https://www.livescience.com/covid-19-immunity.html
[39] Phelan, A. L. (2020), COVID-19 immunity passports and vaccination certificates: scientific, equitable, and legal challenges, 4th May 2020, The Lancet, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31034-5/fulltext

be successful if a large proportion of the population installs it and follow the advice it provides.

The app uses Bluetooth technology to register when people come into close contact with each other. It relies on users to flag when they develop symptoms, and then uses a central database to alert others with whom they have come into contact that they are at risk of infection so that they can then self-isolate and get tested if necessary.[40]

In an update, the Prime Minister's official spokesperson has stated that[41]:

> *Well over half the population [on the Isle of Wight] have downloaded the app. We said the pilot would last for three weeks or so, and that remains the case. As issues have been coming up, we are ironing those out. The current intention is to go from the Isle of Wight to nationwide rollout.*

RaISe paper NIAR125-2020 discussed the alternative 'decentralised' app (with no central database involved) being developed by Google and Apple. Recent media reporting noted technical hitches with the NHSX app emerging and that the NHS was now evaluating the possibility of switching its contact-tracing system to that of Apple and Google.[42]

It will be for each devolved administration to determine if they will use the NHSX app as a central part of their contact-tracing plans. In Scotland, the First Minister, Nicola Sturgeon, recently expressed caution around the use of the app and said that it will be available in Scotland, but the country will not be "building a whole system around it". She intends that the Scottish NHS will rely on specialist contract tracers who will directly inform a patient's contacts.[43] The First Minister for Wales, Mark Drakeford, has stated that Wales was looking at utilising the technology to see whether they can make use of it in Wales.[44]

An additional consideration for NI is that fact that residents in NI and the Republic of Ireland (RoI) may need to download two contact tracing apps in order to travel across the border. The RoI has opted to work with Google and Apple's 'decentralised app and experts have warned that this system will be impossible to make compatible with the UK's app.[45]

[40] Murphy, S. et. al. (2020), NHS preparing to roll out Covid-19 contact-tracing app by end of May, The Guardian, 15th May, 2020, https://www.theguardian.com/world/2020/may/15/nhs-preparing-to-roll-out-covid-19-contract-tracing-app-by-end-of-may

[41] Murphy, S. et. al. (2020), NHS preparing to roll out Covid-19 contact-tracing app by end of May, The Guardian, 15th May, 2020, https://www.theguardian.com/world/2020/may/15/nhs-preparing-to-roll-out-covid-19-contract-tracing-app-by-end-of-may

[42] Field, M. (2020), Northern Irish residents may be forced to download two contact-tracing apps, Stormont admits, The Telegraph, 10th May, 2020, https://www.telegraph.co.uk/technology/2020/05/10/northern-irish-residents-may-forced-download-two-contact-tracing/

[43] Dixon, H. (2020), Scotland will not recommend NHS coronavirus tracing app until 'confident that it works', The Telegraph, 5th May, 2020, https://www.telegraph.co.uk/news/2020/05/05/scotland-will-not-recommend-nhs-coronavirus-tracing-app-confident/

[44] Smith, M. (2020), What we know about Wales' plans to use the coronavirus contact tracing app, WalesOnline, News, 4th May 2020, https://www.walesonline.co.uk/news/health/contact-tracing-app-coronavirus-wales-18197438

[45] Field, M. (2020), Northern Irish residents may be forced to download two contact-tracing apps, Stormont admits, The Telegraph, 10th May 2020, https://www.telegraph.co.uk/technology/2020/05/10/northern-irish-residents-may-forced-download-two-contact-tracing/

On top of privacy concerns about the app, experts also cautioned that as many as 10 million people in the UK risk being 'locked out' of using the app because of the "digital divide". The Commons culture, media and sport committee heard that almost 2 million households do not have internet access and that a further 7 million may have used the net, but only have very basic skills and may not know how to use an app.[46]

To complement the contact tracing app, the UK government is planning to use trained teams to find people who have coronavirus symptoms, working with the Army to make thousands of calls a day to track the spread of COVID-19.[47] The UK government had set a target of recruiting 18,000 contact tracers by the middle of May 2020. Contact tracing in the UK had ended in early March 2020 as the strategy moved from 'containment' to 'delay' of the virus, but the health secretary, Matt Hancock, has said recently that "large scale" tracing will now be a key strategy going forward as the country relaxes its lockdown measures. He has recently faced criticism for only advertising the posts for an initial three months - seemingly running contrary to the advice of health experts, who predict the staff will be needed for up to 18 months to assist in controlling the spread of the virus.[48]

4. Wearing Face Coverings or Masks

The debate has been ongoing around whether wearing a face covering or mask protects the public (either the wearer and/or others around them) against contracting SARS-CoV-2.

There is little dispute that clinically-approved masks, including respirators and surgical face masks, help reduce the spread of the new coronavirus in healthcare settings. However, the advice for the public varies by country. For many countries in Asia, wearing a mask in public spaces has been the norm since the outbreak of the new coronavirus and over the last couple of months, various European cities and countries have also begun to enforce the use of face masks in community settings.[49]

The WHO currently says medical masks should be reserved for healthcare workers and only two groups of people should wear protective masks, those who are[50]:

- Sick and showing symptoms; and
- Caring for people suspected to have coronavirus.

[46] Murphy, S. et. al. (2020), NHS preparing to roll out Covid-19 contact-tracing app by end of May, The Guardian, 15th May, 2020, https://www.theguardian.com/world/2020/may/15/nhs-preparing-to-roll-out-covid-19-contract-tracing-app-by-end-of-may

[47] Chowdhury, H. et. al. (2020), NHS contact tracing app: how does it work and when can you download it? 17th May, 2020, https://www.telegraph.co.uk/technology/2020/05/17/nhs-contact-tracing-cornavirus-app-download-uk-covid/

[48] Southworth, S. and Malnick, E. (2020), Contact tracers only being hired by Government for initial three months, 16th May 2020, The Telegraph, https://www.telegraph.co.uk/news/2020/05/16/contact-tracers-hired-government-initial-three-months/

[49] Lewis, K (2020), Do face masks protect against the new coronavirus? FullFact, 9th April 2020, https://fullfact.org/health/coronavirus-public-wearing-masks/

[50] Roberts, M. (2020), Coronavirus: Who should wear a face mask or face covering? BBC News, 12th May 2020, https://www.bbc.co.uk/news/health-51205344

It does not generally recommend masks for the public because:

- They can be contaminated by other people's coughs and sneezes, or when putting them on or removing them;
- Frequent hand-washing and social distancing are more effective; and
- They might offer a false sense of security.

The evidence suggests that some people are contagious before showing any symptoms and some infected people never show symptoms, so the key benefit from mask/face coverings seems to be that it is not that they stop people catching the virus, but that they might help to stop people spreading it. As the virus is commonly transmitted via exhaled droplets, this means that mask wearing for people who appear healthy can help to stop transmission of the new coronavirus virus to other people.[51]

Recent research in Singapore was conducted to test the effectiveness of masks in reducing the spread of respiratory droplets. Using laser beams and a high-speed, high-sensitivity camera to "see" the tiny droplets which are produced when a subject coughed, it could be seen that when a mask is properly worn, little or no droplets were released into the atmosphere. The scientists concluded[52]:

- When people cough or sneeze without wearing a mask, the droplets they produce can travel 2-3m away. If these droplets land on someone else's face, or a surface which is touched by someone else, it may make that person ill;
- Heavier, larger droplets drop to the ground while the smaller droplets appear to drift in the air;
- When any type of mask is properly worn over the nose and mouth, **most if not all droplets are blocked from getting out** into the air or landing on someone else;
- Wearing a mask is therefore important, as it serves as a **mechanical barrier** to the dispersion of droplets.

While the team did not investigate the effectiveness of different types of masks, Associate Professor Loh stated:

> *A simple cloth mask is effective in curbing the spread of droplets from inside-out. That is, it protects those around the person coughing.*

Across the UK, there is differing advice for the four jurisdictions about wearing masks/face coverings. People in England are now advised to wear face coverings in some enclosed spaces - on public transport and in some shops and also in other enclosed spaces where 'social distancing' is not always possible, where they' come

[51] Lewis, K (2020), Do face masks protect against the new coronavirus? FullFact, 9th April 2020, https://fullfact.org/health/coronavirus-public-wearing-masks/

[52] The science behind why masks help prevent COVID-19 spread, Government of Singapore, 20th April 2020, https://www.gov.sg/article/the-science-behind-why-masks-help-prevent-covid-19-spread

into contact with others that they do not normally meet. The advice is that 'face coverings' should be worn and **not surgical masks or respirators** which should be left for healthcare staff and other workers who need them. People do not need to wear face coverings where they are[53]:

- Outdoors or while exercising;
- In schools;
- In workplaces such as offices and shops;
- Children under two or primary aged children who cannot use them without assistance; and
- People who have problems breathing while wearing a face covering.

The Scottish government recommends people wear 'face coverings' when in shops and on public transport. People in NI have been told to consider wearing face coverings if they are in places where they cannot 'social distance'. In Wales, face coverings have not yet been recommended for the public.[54]

The UK government has published advice on staying safe outside the home, including how to wear and make a cloth face covering[55]:

- A cloth face covering should cover the mouth and nose while allowing comfortable breathing;
- It can be as simple as a scarf or bandana that ties behind the head;
- Wash hands or use hand sanitiser before putting it on and after taking it off and after use; and
- Avoid touching the eyes, nose, or mouth at all times and store used face coverings in a plastic bag until there is an opportunity to wash them.

5. Social Distancing (the two metre guidance) and Additional Advice to Vulnerable People

5.1 The Two Metre Guidance

Within all the UK jurisdictions' plans to ease lockdown the two-metre social distancing guidance remains and members of the public are advised to continue staying at least two metres apart from people outside their own household. Although shops, workplaces, schools etc. have and will be implementing many other safety and hygiene measures, the social distancing will remain a continuing key measure as lockdown is

[53] Roberts, M. (2020), Coronavirus: Who should wear a face mask or face covering? BBC News, 12th May 2020, https://www.bbc.co.uk/news/health-51205344

[54] Roberts, M. (2020), Coronavirus: Who should wear a face mask or face covering? BBC News, 12th May 2020, https://www.bbc.co.uk/news/health-51205344

[55] Staying safe outside your home, UK Government Guidance, 11th May 2020, https://www.gov.uk/government/publications/staying-safe-outside-your-home/staying-safe-outside-your-home

eased. The UK government's document acknowledges that the science behind it is complex and it is based on PHE's best understanding of how coronavirus spreads:[56]

> *The risk of infection increases the closer you are to another person with the virus and the amount of time you spend in close contact: you are very unlikely to be infected if you walk past another person in the street…..the key thing is to not to be too close to people for more than a short amount of time, as much as you can.*

The two-metre recommendation can be traced back to research conducted in the 1930's when scientists established that droplets of liquid released by coughs or sneezes will either evaporate quickly in the air or be dragged by gravity down to the ground. It was concluded that the majority of those droplets, would land within one to two metres. Therefore, the greatest risks come from having the virus coughed at you from close range or from touching a surface that someone coughed onto and then touching your face.[57]

However, not all scientists feel that two-metres is enough, citing as an example the case of widespread transmission in a choir practice in Washington (US) raising the question of whether SARS-CoV-2 can be spread via tiny aerosols, which can stay suspended in air for long periods. If that is the case, particles could potentially travel up to eight metres before drying out.[58]

Other research has shown that even large droplets expelled with extreme force (as when coughing or sneezing), or carried by the wind can travel farther than 6 feet before falling to the ground or on to a surface. The following quote demonstrates how complex the issue is[59]:

> *When you breathe out or cough, you release bits of watery mucus from inside your body in a wide array of sizes…..All of these are droplets. The smallest droplets are commonly described as aerosols…..any of these bits of mucus may be laced with viral pathogens…when the water component of droplets dries up in the air, the remaining bits of floating virus are called "droplet nuclei," which are even lighter and more apt to travel long distances. Aside from size, other factors, such as local humidity and any drafts of air, will also affect how far a droplet flies.*

It should, however, be borne in mind that much research on airborne transmission of viruses is focused on medical settings, meaning it is less clear how even the most

[56] Our plan to rebuild: The UK Government's COVID-19 recovery strategy, HM Government, 11th May, 2020, https://www.gov.uk/government/publications/our-plan-to-rebuild-the-uk-governments-covid-19-recovery-strategy
[57] Shukman, D. (2020), Social distancing and coronavirus: The science behind the two-metre rule, BBC News, 3rd May 2020, https://www.bbc.co.uk/news/science-environment-52522460
[58] Letzter, R. (2020), Is 6 feet enough space for social distancing? Live Science, 31st March 2020, https://www.livescience.com/coronavirus-six-feet-enough-social-distancing.html
[59] Khamsi, R. (2020), They Say Coronavirus Isn't Airborne—but It's Definitely Borne By Air, Wired, https://www.wired.com/story/they-say-coronavirus-isnt-airborne-but-its-definitely-borne-by-air/

common viruses, never mind this novel coronavirus, might pass from person to person under everyday circumstances.[60]

5.2 Vulnerable People

Across the UK, there are certain groups of people for whom the general social distancing public health guidance is not sufficient. The government guidance to date has mentioned three categories of vulnerable people (clinically extremely vulnerable, clinically vulnerable and vulnerable). In its recently published 'Our Plan to Rebuild' for lifting the current restrictions in England, Annex B lists the advice going forward for each group and is reproduced in the table below.[61]

Group	Explanation	Current and continuing guidance	Government support
Clinically extremely vulnerable people (all people in this cohort will have received communication from the NHS)	People defined on medical grounds a clinically extremely vulnerable, meaning they are at the greatest risk of severe illness. This group includes solid organ transplant recipients, people receiving chemotherapy, renal dialysis patients and others.	Follow shielding guidance by staying at home at all times and avoiding all non-essential face-to-face contact. This guidance is in place until end June.	Support available from the National Shielding Programme, which includes food supplies (through food boxes and priority supermarket deliveries), pharmacy deliveries and care. Support is available via the NHS Volunteer Responders app.
Clinically vulnerable people	People considered to be at higher risk of severe illness from COVID-19. Clinically vulnerable people include the following: people aged 70 or older, people with liver disease, people with diabetes, pregnant women and others.	Stay at home as much as possible. If you do go out, take particular care to minimise contact with others outside your household.	Range of support available while measures in place, including by local authorities and through voluntary and community groups. Support is available via the NHS Volunteer Responders app.
Vulnerable people (non-clinical)	There are a range of people who can be classified as 'vulnerable' due to non-clinical factors, such as children at risk of violence or with special education needs, victims of domestic abuse, rough sleepers and others.	People in this group will need to follow general guidance except where they are also clinically vulnerable or clinically extremely vulnerable, where they should follow guidance as set out above.	For those who need it, a range of support and guidance across public services and the benefits system, including by central and local government and the voluntary and community sector.

In NI, advice was issued to vulnerable and extremely vulnerable people at the start of lockdown to apply for 12 weeks. The guidance for these groups remains available on the NI Direct website and reflects the UK government advice from PHE, for example as regards 'shielding' for the clinically vulnerable and extremely vulnerable.[62] The Health Minister Robin Swann stated on 18th May 2020 that guidance on shielding for people at

[60] Khamsi, R. (2020), They Say Coronavirus Isn't Airborne—but It's Definitely Borne By Air, Wired, https://www.wired.com/story/they-say-coronavirus-isnt-airborne-but-its-definitely-borne-by-air/
[61] Our plan to rebuild: The UK Government's COVID-19 recovery strategy, HM Government, 11th May, 2020, https://www.gov.uk/government/publications/our-plan-to-rebuild-the-uk-governments-covid-19-recovery-strategy
[62] Coronavirus, Vulnerable People, NI Direct, https://www.nidirect.gov.uk/information-and-services/coronavirus-covid-19/vulnerable-people

potentially higher risk from Covid-19 is being actively reviewed and will be updated ahead of the end of the initial 12-week shielding period.[63]

With regard to getting COVID-19, people over the age of 70 are considered vulnerable, even if they do not have an underlying health condition. Those under 70 who have a range of chronic health conditions and those who are pregnant are considered vulnerable. People considered to be at the highest clinical risk have received letters from their GP or hospital care team to inform them they should:

- Stay at home at all times; and
- Avoid all face-to-face contact for a period of at least 12 weeks.

This is known as 'shielding' and it reflects the guidance from PHE. People who fall into the **highest clinical risk** group include:

- Recipients of solid organ transplants;
- People with specific cancers;
- People with severe respiratory conditions including all cystic fibrosis, severe asthma and severe COPD;
- People with rare diseases and inborn errors of metabolism that significantly increase the risk of infections (such as SCID, homozygous sickle cell);
- People on immunosuppression therapies sufficient to significantly increase risk of infection;
- Women who are pregnant with significant heart disease, congenital or acquired; and
- People who have had a 'splenectomy' (spleen removed).

GPs and hospital clinicians providing care to people in these groups have also reviewed their patient lists to help make sure all patients in this highest risk group are identified and contacted.[64]

6. New Treatments

6.1 Overview

Researchers across the world are moving potential therapeutics to treat COVID-19 into clinical trials at a very rapid pace. The primary aim is to investigate drugs originally derived for other diseases and looking to repurpose approved drugs that have worked against similar coronaviruses, or are hypothesised to address SARS-CoV-2 based on their mechanism of action.

[63] Shielding will last no longer than necessary – Minister, Department of Health NI, News, 18th May 2020, https://www.health-ni.gov.uk/news/shielding-will-last-no-longer-necessary-minister

[64] Coronavirus, Vulnerable People, NI Direct, https://www.nidirect.gov.uk/information-and-services/coronavirus-covid-19/vulnerable-people

Currently there are just two antiviral therapeutics (drugs) that have been approved in their respective countries to treat COVID-19: Avigan (Favilavir) in China and Italy, and Veklury (Remdesivir) in Japan.[65]

In the US, the National Institutes of Health has partnered with a number of biopharmaceutical companies to accelerate development of drug and vaccine candidates. In Europe, the European Medicines Agency is building procedures for accelerated drug and vaccine development.[66]

Several large trials are examining potential therapeutic options, including the WHO SOLIDARITY trial[67] and the worldwide 'RECOVERY' trial.[68] In the UK, the PRINCIPLE trial is investigating drug treatments particularly for older patients.

There are a number of COVID-19 Drug Trial Tracker web publications describing the progress of research into drug candidates. The Regulatory Affairs Professional Society (RAPS)[69] tracker highlights the current frontline and novel drug candidates in trials as follows[70]:

- **Remdesivir** (Antiviral) - Developer: Gilead Sciences - Original use: treatment for Ebola and Marburg virus infections;
- **Hydroxychloroquine (Plaquenil) and chloroquine (Aralen) -** Developer: Sanofi (Plaquenil and Aralen); Mylan, Teva, Novartis, Bayer, Rising Pharmaceuticals (generics) - Approved US Indications: *Hydroxychloroquine* is used to treat acute attacks of malaria as well as for suppressive treatment. *Chloroquine* is indicated to treat uncomplicated malaria and for prophylaxis of malaria. It is also used to treat rheumatoid arthritis and systemic lupus erythematosus;
- **Favilavir** (Antiviral) - Developer: Fujifilm Toyama Chemical (as Avigan) and Zhejiang Hisun Pharmaceutical - Approved Indication: approved in China and Italy to treat COVID-19;
- **Lopinavir-ritonavir** (Kaletra) (HIV protease inhibitor) - Developer: AbbVie - Approved US Indication: Lopinavir-ritonavir is used in combination with other antiretrovirals to treat HIV-1 infection;
- **Therapy: Convalescent plasma (Immunoglobulin)** - Researchers are testing to see if convalescent plasma could be used as passive immunotherapy.

[65] Craven, J. (2020), COVID-19 therapeutics tracker, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker
[66] Craven, J. (2020), COVID-19 therapeutics tracker, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker
[67] Craven, J. (2020), COVID-19 therapeutics tracker, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker
[68] RECOVERY trial, https://www.recoverytrial.net/news/update
[69] The Regulatory Affairs Professionals Society (RAPS) is the largest global organisation of and for those involved with the regulation of healthcare and related products
[70] Craven, J. (2020), COVID-19 therapeutics tracker, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker

RAPS is also tracking the progress of other novel treatments, for example:[71]

- **EIDD-2801** (broad-spectrum antiviral) - Developer: Drug Innovation Ventures at Emory (DRIVE);
- **Mavrilimumab** (Monoclonal antibody) - Developer: Kiniksa Pharmaceuticals; and
- **CD24Fc** (Recombinant fusion protein) - Developer: OncoImmune.

6.2 The Solidarity Trial

The 'Solidarity Trial' is an international clinical trial launched by the WHO and partners. The following information is summarised from the WHO website.[72]

Adults with COVID-19 admitted to participant hospitals (in over 100 countries), who provide consent, can join the trial to compare four treatment options against 'standard care'. It is hoped that one single randomised trial will overcome the risk of multiple small trials not generating the evidence needed to determine the relative effectiveness of potential treatments. The trial aims to discover whether any of the options slow disease progression or improve survival. Other drugs may be added based on emerging evidence. The following treatment options are included in the trial:

- **Remdesivir** – this antiviral was previously tested as an Ebola treatment and generated promising results in animal studies for Middle East Respiratory Syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS);
- **Lopinavir/Ritonavir –** antiviral drug combination - a licensed treatment for HIV - this combination may be effective against COVID-19;
- **Lopinavir/Ritonavir plus Interferon beta-1a** – the latter is used to treat multiple sclerosis; and
- **Chloroquine or Hydroxychloroquine** - are very closely related drugs and used to treat malaria and rheumatology conditions respectively.

The WHO recently stated[73]:

> *We do have potentially positive data coming out but we need to see more data to be 100% confident that we can say this treatment over that one.*

[71] Craven, J. (2020), COVID-19 therapeutics tracker, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-therapeutics-tracker

[72] "Solidarity" clinical trial for COVID-19 treatments, WHO, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

[73] Farge, E. (2020) WHO sees 'potentially positive data' in treating coronavirus, Reuters World News, 12th May 2020, https://uk.reuters.com/article/uk-health-coronavirus-who/who-sees-potentially-positive-data-on-covid-19-treatments-idUKKBN22O1HL?feedType=RSS&feedName=worldNews&rpc=69

6.3 The RECOVERY Trial - Randomised Evaluation of COV-id19 thERapY

The RECOVERY trial has been described as the world's largest randomised clinical trial of potential coronavirus treatments and it was rolled out across the UK in early April 2020.[74] As already stated, a range of potential treatments across the world have been suggested for COVID-19. The RECOVERY Trial will begin by testing some of these suggested treatments, of which a number are common to the SOLIDARITY trial[75]:

- Lopinavir-Ritonavir (commonly used to treat HIV);
- Low-dose Dexamethasone (a type of steroid, which is used in a range of conditions typically to reduce inflammation);
- Hydroxychloroquine (related to an anti-malarial drug);
- Azithromycin (a commonly used antibiotic); and
- Tocilizumab (an anti-inflammatory treatment given by injection).

In the UK, the trial is being conducted in over 130 NHS hospitals. The UK is testing Lopinavir-Ritonavir; Dexamethasone and Hydroxychloroquine and it is designed so that further medicines can be added to the study within days.[76]

6.4 PRINCIPLE Trial (UK) - Platform Randomised trial of INterventions against COVID-19 In older PeopLE

The PRINCIPLE trial, by the Primary Care Clinical Trials Unit of the University of Oxford's Nuffield Department of Primary Care Health, aims to find treatments for COVID-19 specifically for older people. It is recruiting at least 3000 participants through its website and through GP practices across the UK.[77]

A person can take part if they have symptoms of COVID-19 (for fewer than 15 days) and are aged 65, or are aged 50 to 64 with at least one of the following conditions - weakened immune system due to a serious illness or medication (e.g. chemotherapy); heart disease or high blood pressure; asthma or lung disease, diabetes not treated with insulin; liver disease; stroke or neurological problem.[78] In the first phase, the trial is evaluating whether a seven-day course of hydroxychloroquine can reduce the severity of symptoms in vulnerable groups and help avoid hospital admission. The antibiotic azithromycin will also be added to the trial.[79]

[74] The RECOVERY Trial, https://www.recoverytrial.net/news/update
[75] The RECOVERY Trial, https://www.recoverytrial.net/
[76] The RECOVEREY Trial, 6th April 2020, https://www.recoverytrial.net/news/update
[77] The PRINCIPLE Trial, https://www.phctrials.ox.ac.uk/principle-trial/resources-for-recruiting-practices
[78] Principle Participant Information Leaflet, https://www.phctrials.ox.ac.uk/principle-trial/resources-for-recruiting-practices
[79] PRINCIPLE trial rolled out across UK homes and communities, Primary Care Clinical Trials Unit, 12th May 2020, https://www.phctrials.ox.ac.uk/news/principle-trial-rolled-out-across-uk-homes-and-communities

6.5 Other Selected Treatment Trials

6.5.1 RECOVERY-RS (Respiratory Support) Trial

The RECOVERY-RS (Respiratory Support) Trial in the UK is being co-ordinated by the University of Warwick and will compare three different ways of providing respiratory support to patients. All three methods are currently in use in clinical practice and patients in the trial will receive one of these, chosen at random:[80]

- High Flow Nasal Oxygen (HFNO);
- Continuous Positive Airway Pressure (CPAP); and
- Normal care involving regular oxygen therapy.

Around 4000 patients will be included in the study from 60+ hospital sites. It will look at which treatment is more effective in relation to survival of patients and the need for intubation (tube inserted in to patient's throat to help them breathe). There is currently little evidence to support HFNO or CPAP compared to standard care.[81]

6.5.2 Novel Therapies

Scientists are also looking at other ways to target the virus or treat the complications of COVID-19 and a number of these novel therapies were listed in section 6.1. A range of these is discussed below:[82]

- Monoclonal antibodies - these drugs trigger the immune system to attack the virus. The US company 'Vir Biotechnology'[83] has isolated antibodies from patients who survived SARS and the company is working with Chinese firm 'WuXi Biologic's' to test them as a treatment for COVID-19. 'AbCellera Biologics Inc.' (Canada) has isolated 500 unique antibodies from a person who recovered from COVID-19 and is set to start testing them as a treatment;[84]

- Blood plasma transfers - the Food and Drug Administration in the US has announced 'Trusted Source' - a process for medical facilities to conduct trials on an experimental treatment that uses blood plasma from people who have recovered from COVID-19. The theory is that the plasma contains antibodies that will attack this particular coronavirus. In late March 2020, the 'New York Blood Center' began collecting plasma from people who have recovered from COVID-19;

- Stem cells - US-based Athersys Inc.[85] released preliminary data last year showing that its stem cell treatment could potentially benefit people with acute

[80] RECOVERY- RS Trial, https://warwick.ac.uk/fac/sci/med/research/ctu/trials/recovery-rs/
[81] RECOVERY - Respiratory Support, Ventilation Strategies in COVID-19; CPAP, High-flow, and standard care, National Institute for Health Research, https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282338
[82] Radcliffe, S. (2020), Here's Exactly Where We Are with Vaccines and Treatments for COVID-19, Healthline, https://www.healthline.com/health-news/heres-exactly-where-were-at-with-vaccines-and-treatments-for-covid-19
[83] www.vir.bio
[84] www.abcellera.com
[85] Athersys Inc., international biotechnology company that is focused in the field of regenerative medicine, https://www.athersys.com/our-company/overview/default.aspx

respiratory distress syndrome (ARDS). Australian company 'Mesoblast' tested its stem cell product in a small group of people with COVID-19 with positive results;[86] and

- Immune suppressants - in some people with COVID-19, the immune system goes into overdrive, releasing large amounts of small proteins called cytokines. Scientists think this "cytokine storm" may be the reason certain people develop ARDS. Several immune suppressants are being trialled to see whether the drugs can quell the cytokine storm and reduce the severity of ARDS. The FDA in the US has also approved a device to filter cytokines out of the blood of patients.[87]

7. Development of a Vaccine

7.1 How Does a Vaccine Work?

A vaccine works by training the human immune system to recognise and combat pathogens, either viruses or bacteria. To do this, certain molecules (antigens) from the pathogen must be introduced into the body to trigger an immune response. By injecting these antigens into the body, the immune system can learn to recognise them as 'hostile invaders', produce antibodies, and remember them for the future. If the bacteria or virus reappears, the immune system will recognise the antigens immediately and attack aggressively before the pathogen can cause sickness.[88]

Vaccines work both on an individual level and at a population level. Once enough people are immunised, opportunities for an outbreak of disease become so low even people who are not or cannot be immunised benefit. Essentially, a bacteria or virus simply will not have enough eligible hosts to establish a foothold and will eventually die out entirely. This phenomenon is called 'herd immunity' or 'community immunity'.

In some cases, natural immunity — meaning actually catching a disease, becoming ill and producing natural antibodies - can result in a stronger immunity to the disease than a vaccination. However, it is known that the dangers of this approach far outweigh the relative benefits and this has clearly been shown in the current pandemic.[89]

[86] Mesoblast, https://www.mesoblast.com/

[87] Radcliffe, S. (2020), Here's Exactly Where We Are with Vaccines and Treatments for COVID-19, Healthline, https://www.healthline.com/health-news/heres-exactly-where-were-at-with-vaccines-and-treatments-for-covid-19

[88] How Vaccines Work, Public Health, Health Guides, CDC US, https://www.publichealth.org/public-awareness/understanding-vaccines/vaccines-work/

[89] Vaccine Myths Debunked, How Vaccines Work, Public Health, Health Guides, CDC US, https://www.publichealth.org/public-awareness/understanding-vaccines/vaccine-myths-debunked/

7.2 Progress of Vaccine Development to SARS-CoV-2

A vaccine for SARS-CoV-2 is likely to be the most effective public health tool and long-term solution to ending the coronavirus pandemic. Experts estimate that a fast-tracked development process could speed a vaccine to market in approximately 12-18 months.

To guide the efforts of vaccine developers, the WHO has drawn up 'Global Target Product Profiles' (TPPs) for COVID-19 outlining the minimum and desired attributes of vaccines. The TPPs cover two types: vaccines for the long-term protection of people at higher risk of COVID-19 (such as healthcare workers) and vaccines for use in response to outbreaks with rapid onset of immunity.[90]

There are a number of different types of vaccines in development, falling into three broad categories: traditional killed/inactivated-virus vaccines, protein-based vaccines (use a modified cold virus to deliver the protein that activates the immune response) and gene-based vaccines (contain a gene or part of a gene from the virus). Trials of any vaccine are carried out in a number of phases:[91]

- Phase 1 - test for safety and proof-of-concept. Researchers give a small number of human volunteers the vaccine. Then they look for medical problems and see if it induces some sort of immune response;
- Phase 2 - researchers give the vaccine to hundreds of volunteers to determine the optimal vaccine composition, dose and vaccination schedule; and
- Phase 3 trials - involve thousands of volunteers and provide data on how good the vaccine is at preventing infection. These large trials will also uncover rarer side effects or health issues that may not show up in the smaller trials.

The biggest hurdle for vaccine development once it passes phase 3 trials is the manufacture and distribution at scale.[92]

7.2.1 International Developments

One of the key organisations in this regard is the Coalition for Epidemic Preparedness Innovations (CEPI)[93], a global partnership between public, private, philanthropic, and civil society organisations. It was set up in response to the Ebola outbreak in West Africa in 2014 to 2016. CEPI's mission is to respond to epidemics by providing the

[90] The 4 critical elements of WHO global R&D efforts in detail, WHO, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-trial-accelerating-a-safe-and-effective-covid-19-vaccine

[91] Garcia-Ojeda, M. E. (2020), What needs to go right to get a coronavirus vaccine in 12-18 months, The Conversation, 8th May 2020, https://theconversation.com/what-needs-to-go-right-to-get-a-coronavirus-vaccine-in-12-18-months-136816

[92] Coronavirus vaccine 'may never be found' - latest news on UK trials, The Telegraph, Global Health Security Team, 12th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/covid-coronavirus-vaccine-trials-latest-uk/

[93] CEPI, https://cepi.net/about/whoweare/

money to researchers to develop vaccines. The UK has committed £250 million aid to CEPI.[94]

CEPI is already developing at least eight potential vaccines for COVID-19. For example, it recently announced that it will invest up to an additional US $384 million to accelerate the development and manufacture of Novavax Inc's. vaccine candidate. CEPI's investment in Novavax will fund preclinical studies, phase 1 and phase 2 clinical trials. A phase 1 clinical trial will begin this month in Australia, followed by phase 2 clinical trials in multiple countries.[95]

In America, the US government has committed $1 billion (£800m) to vaccine development with Johnson & Johnson. Human trials on its vaccine candidate have already started in the US after it bypassed standard animal testing in an accelerated process.[96]

There are a number of 'COVID-19 Vaccine Tracker' publications describing COVID-19 vaccine candidates around the world currently in Phase 1 to 3 trials, as well as major candidates in pre-clinical stages of development and research. The most recent list of those in Phase 1 to 3 trials are summarised below from the RAPS tracker:[97]

Phase 2/3 Trials - Vaccine Candidates:

- **Bacillus Calmette-Guerin (BCG) live-attenuated vaccine** - the University of Melbourne and Murdoch Children's Research Institute (Australia); the Radboud University Medical Center (The Netherlands); and the Faustman Lab at Massachusetts General Hospital (MGH) (United States) are all currently recruiting volunteers for trials;
- **mRNA-1273 -** Moderna is the Massachusetts-based biotech company behind mRNA-1273, a vaccine candidate developed using prior studies of related coronaviruses, such as SARS and MERS. The company has progressed mRNA-1273 to Phase 2 and is finalising the protocol for a Phase 3 trial, for early summer 2020;
- **No name announced -** Beijing Institute of Biological Products/Wuhan Institute of Biological Products; the China National Pharmaceutical Group (Sinopharm) - developing an inactivated COVID-19 vaccine candidate. On 30th April, Sinopharm told 'China Daily' the vaccine had received approval from the National Medical Products Administration and had reached Phase 2 status.

[94] Coronavirus vaccine 'may never be found' - latest news on UK trials, The Telegraph, Global Health Security Team, 12th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/covid-coronavirus-vaccine-trials-latest-uk/
[95] CEPI extends collaboration with Novavax to advance development and manufacture of COVID-19 vaccine, CEPI, 11th May 2020, https://cepi.net/news_cepi/cepi-extends-collaboration-with-novavax-to-advance-development-and-manufacture-of-covid-19-vaccine/
[96] Coronavirus vaccine 'may never be found' - latest news on UK trials, The Telegraph, Global Health Security Team, 12th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/covid-coronavirus-vaccine-trials-latest-uk/
[97] Craven, J. (2020), COVID-19 vaccine tracker, Regulatory Focus, 7th May 2020, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker

Phase 1/2 Trials – Vaccine Candidates:

- **Ad5-nCoV -** CanSino Biologics (China) has developed a recombinant novel coronavirus vaccine that incorporates the adenovirus type 5 vector (Ad5). The preliminary safety data from the Phase 1 trial has allowed the company to plan to initiate a Phase 2 trial;
- **ChAdOx1 -** the University of Oxford is developing a chimpanzee adenovirus vaccine vector called ChAdOx1 - on 24 April, investigators said they had begun human testing in around 1,100 people;
- **INO-4800 -** Inovio Pharmaceuticals are developing a DNA vaccine that is in line with other DNA vaccines the company is developing, such as for the MERS coronavirus. On 16th April, Inovio and The International Vaccine Institute (IVI) announced they are working with the Korea National Institute of Health (KNIH) to conduct a Phase 1/2 clinical trial in South Korea. Interim results expected in late June;
- **BNT162 -** Pfizer and BioNTech have announced an agreement to collaborate on developing four vaccine candidates originally developed by BioNTech. On 22nd April, the Paul-Ehrlich-Institut in Germany approved BNT162 for a Phase 1/2 trial. Human trials in two US locations began on 5th May; and
- **Formalin-inactivated and alum-adjuvanted candidate vaccine for COVID-19 -** Sinovac - released details on 17th April of its Phase 1 randomised controlled trial and said that participants had received their first doses.

7.2.2 Specific UK Developments

On April 17th 2020, the UK government launched a Vaccine Taskforce designed to "rapidly develop a coronavirus vaccine", as well as scale up manufacturing so it can be quickly produced and delivered in mass quantities. It is led by Sir Patrick Vallance (Chief Scientific Adviser) and Professor Jonathan van Tam (Deputy Chief Medical Officer), and members include AstraZeneca and the Wellcome Trust.[98]

The government initially earmarked £14 million for 21 coronavirus research projects, including the work at the University of Oxford and Imperial College London outlined below. On April 21st, a further £44.5 million was announced:[99]

- University of Oxford - On April 23rd 2020, a potential vaccine - ChAdOx1 (see section 7.2.1 above) - began human trials. A clinical trial involving up to 510 healthy volunteers between the ages of 18 and 55 is under way in Oxford and

[98] Coronavirus vaccine 'may never be found' - latest news on UK trials, The Telegraph, Global Health Security Team, 12th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/covid-coronavirus-vaccine-trials-latest-uk/

[99] Coronavirus vaccine 'may never be found' - latest news on UK trials, The Telegraph, Global Health Security Team, 12th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/covid-coronavirus-vaccine-trials-latest-uk/

Southampton, with three further sites likely to be added. It is hoped that 'signals' about whether it works could emerge by mid-June; and

- Imperial College London - Researchers have developed a candidate vaccine which, when injected, will deliver the genetic instructions to muscle cells to make the SARS-CoV-2 spike surface protein. This protein should then provoke an immune response. Clinical trials are expected to begin in June 2020.

The UK government has also announced a new partnership between Oxford University and Astra Zeneca, which aims to ensure that a successful vaccine could be manufactured at scale and rapidly rolled out.

7.2.3 Challenge Trials

As described in section 7.2.1, phase 2 and 3 trials of vaccines are typically tested using large groups of people whose infection rates with a disease are compared with a separate group of unvaccinated controls. However, waiting for enough people to be exposed to an illness can take months and require thousands of participants.

Challenge trials sidestep this problem - they are vaccine trials in which 100 or so volunteers could be intentionally infected with COVID-19 allowing efficacy of the trial vaccine they have been given to be established within weeks.

The WHO has released new guidance on how the approach could be ethically justified despite the potential dangers for participants i.e. for COVID-19, a safe dose of the virus has not yet been established and there are no failsafe treatments if things go wrong. It lists eight criteria that would need to be met for the approach to be ethically justified, including restricting participation to healthy people aged 18-30 and fully informed consent. A safe dose for COVID-19 would need to be established – enough to cause illness, but not severe illness.[100]

8. Conclusion

The decision to enter the unprecedented lockdown across the UK might well have been easier than working out how to 'exit'.

The UK has made progress in controlling the pandemic since it entered lockdown on 23rd March 2020. However, as the four jurisdictions move out of lockdown at varying speeds, it is of concern that a thorough system of testing, tracing, and isolating is not yet in place and it has been stated that the safe isolation of cases is an omission from that plans. There is anecdotal evidence of household transmissions arising from failed isolation in high-density living households, particularly intergenerational living and vulnerable household members are also present. Lack of secure and adequate

[100] Devlin, H. (2020), WHO conditionally backs Covid-19 vaccine trials that infect people, The Guardian, 8th May 2020, https://www.theguardian.com/science/2020/may/08/who-conditionally-backs-covid-19-vaccine-trials-that-infect-people

provision of high-quality PPE and high rates of transmissions in care homes, hospitals, and households have also been highlighted as continuing issues.[101]

Research from the London School of Hygiene and Tropical Medicine and the Alan Turing Institute strongly suggests there is a "high degree of individual-level variation" in the transmission of COVID-19. By applying a mathematical model to reported outbreaks of the disease outside China, they estimated that 80 per cent of all secondary transmissions were caused by a small fraction (around 10 percent) of infected individuals. Therefore, a small number of so-called 'superspreading events' appear to be responsible for the majority of coronavirus cases.[102] This does raise the prospect of controlling transmission of the virus if those 'events' can be reliably pinned down with robust use of 'test, track and trace'.

In terms of new treatments, while a lot of the research focus is on developing drug treatments for COVID-19, research and trials into improvements in how doctors care for patients using existing technology are also crucial.

With regard to vaccine development, Sir Patrick Vallance – the UK's chief scientific adviser has moved to temper public expectations, saying:

> *All new vaccines that come into development are long shots. Only some end up successful. Coronavirus will be no different and presents new challenges. This will take time.*[103]

The WHO emergencies director, Dr Mike Ryan, has recently warned against trying to predict when the virus would disappear:[104]

> *It is important to put this on the table: this virus may become just another endemic virus in our communities, and this virus may never go away….HIV has not gone away - but we have come to terms with the virus.*

On a positive note, Dr Ryan highlighted that there are currently more than 100 potential vaccines in development for SARS-CoV-2, but cautioned that there are other viruses, such as measles, for which there are vaccines, that still have not been eliminated.

In an alternative view, Professor Karol Sikora (former WHO Director), an oncologist and chief medical officer at Rutherford Health, has stated that:[105]

---

[101] Cheng, K.K. and Gong, W. (2020), Covid-19: How can we safely exit lockdown?, The BMJ Opinion, 11th May 2020, https://blogs.bmj.com/bmj/2020/05/11/covid-19-how-can-we-safely-exit-lockdown/

[102] Nuki, P. (2020), 'Superspreader' events may be responsible for 80 percent or more of all coronavirus cases, The Telegraph, 18th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/superspreader-events-may-responsible-80-percent-coronavirus/?li_source=LI&li_medium=liftigniter-rhr

[103] Coronavirus vaccine 'may never be found' - latest news on UK trials, The Telegraph, Global Health Security Team, 12th May 2020, https://www.telegraph.co.uk/global-health/science-and-disease/covid-coronavirus-vaccine-trials-latest-uk/

[104] Coronavirus may never go away, World Health Organization warns, BBC News, 14th May 2020, https://www.bbc.co.uk/news/world-52643682

[105] Southworth, P. (2020), Coronavirus could 'burn out naturally' so vaccine not needed, former WHO director claims, The Telegraph, 17th May 2020, https://www.telegraph.co.uk/news/2020/05/16/coronavirus-could-burn-naturally-vaccine-not-needed-former-director/

There is a real chance that the virus will burn out naturally before any vaccine is developed…. We are seeing a roughly similar pattern everywhere….We need to keep slowing the virus, but it could be petering out by itself.