Witness Name: Professor Sir Gregor Smith
Statement No.: 2
Exhibits: GS3
Dated: 23 February 2024

UK COVID-19 INQUIRY

MODULE 3

WITNESS STATEMENT BY THE CHIEF MEDICAL OFFICER FOR SCOTLAND

This statement is one of a suite provided for Module 3 of the UK Covid Inquiry by the Scottish Government and these should be considered collectively. In relation to the issues raised by the Rule 9 request dated 24 August 2023 served on the Scottish Government, in connection with Module 3, the Chief Medical Officer for Scotland will say as follows:

Overview of CMO Directorate (CMOD)

1. Professor Sir Gregor Smith is the current Chief Medical Officer (CMO) for Scotland. He is a General Practitioner (GP) and former medical director for primary care in NHS Lanarkshire and began working for the Scottish Government as a medical adviser in primary care in 2012. As medical adviser, he was part of the negotiating team for the Scottish GP contract, subsequently leading the development of a new quality framework for general practice in Scotland.

2. Professor Smith was appointed interim CMO in April 2020, and CMO in December 2020.

3. The previous CMO was Catherine Calderwood, who held the position from February 2015 to April 2020.

4. The CMO Directorate (CMOD) is led by the CMO, which seeks to achieve the best health and care outcomes for people by working with Scottish Ministers and stakeholders to protect and improve public health, and to oversee the effectiveness of healthcare services in Scotland.

5. The CMOD is responsible for:

- Providing policy advice to Scottish Ministers on healthcare and publichealth;
- Leading medical and public health professionals to improve the mental and physical wellbeing of people in Scotland;
- Providing clinical advice on professional standards and guidelines;
- Investing in research, particularly related to the NHS; and
- Encouraging young people to take up jobs in the medical and public health sector.

6. The CMOD is part of the Director General Health and Social Care family of Directorates which is headed up by Caroline Lamb, who was appointed Chief Executive NHS and Director General Health and Social Care in January2021.

7. The role of the CMO, and their team, is as independent clinical advisers to government. The way the role of CMO is set up has the effect that it sits slightly separately to the rest of government. As a clinician and as a scientist, the CMO's first duty is a professional and ethical one, to the regulatory body, which is the General Medical Council (GMC). To remain as a medical doctor, the CMO cannot breach good medical practice which provides the CMO with their independence. In addition, an important part of the role of CMO is to be able to use judgement and experience to be able to communicate effectively and fully, so that commitment to professional and ethical requirements as defined by the GMC is not breached.

8. In Scotland, where a decision requires to be taken by Scottish Ministers that may, or is likely to, impact on the health of members of the public, it is embedded in Scottish Government processes that clinical advisers are involved at an early stage. These processes ensure clinical views are sought (verbally and/or in writing) and attendance requested at decision-making meetings, such as the Scottish Government Resilience Room (SGoRR) or Cabinet.

9. The role, function, responsibilities and accountability of the CMO, the Deputy Chief Medical Officers (DCMO) and CMOD during the relevant period in relation to the response of the Scottish healthcare system to the Covid-19 pandemic is set out in the following paragraphs.

10. Expert medical and scientific advice was sought, carefully considered and acted upon by Scottish Ministers throughout the relevant period covered by this statement (1 March 2020 to 28 June 2022). The CMO attended Cabinet throughout this period when requested to do so and gave a verbal update of the epidemiology of the pandemic. The CMO sought to explain and 'translate' clinical and scientific advice to enable Scottish Ministers to understand it and make their decisions. The dates of the CMO's attendance at Cabinet throughout the relevant period are provided [GS3/001-INQ000398889].

11. When presenting complex expert, medical and scientific evidence, data and statistical modelling, the CMO would first look to understand the degree of scientific confidence in that information so that they may advise Scottish Ministers accordingly.

12. There were occasions, particularly in the early stages of the pandemic, where data and/or evidence did not have a consensus of scientific agreement, given that this was a novel virus. However, whenever any data was available, it was shared across the UK via the Scientific Advisory Group for Emergencies (SAGE) and other scientific advisory groups for analysis and discussion. This included epidemiology and research data. There were no instances where requests from CMOD for access to data, information or expertise were declined, withheld or unavoidably delayed.

13. To formulate advice to Ministers, the CMOD seeks to identify trusted sources of evidence (for example published, peer reviewed journals) on which to base its advice. In a novel situation, such trusted sources of evidence may be absent. In that case, CMOD can look to data from our own country, but can evaluate information that has been shared globally from other countries, based on their experiences. The overarching principle, as a clinical adviser to Scottish Ministers is, first and foremost, whether the evidence under consideration is of sufficient quality for the purposes of decision making. There are three broad categories for assessing the quality of evidence: low, medium, and high confidence. One of the functions of SAGE and other advisory committees is to consider sources of evidence and their quality.

14. Throughout the Covid-19 pandemic, the four CMOs of Scotland, England, Wales and Northern Ireland enjoyed exceptionally good and productive professional relationships.

15. There was and still is excellent co-operation between the CMO's office and clinical advisers, the Chief Scientific Adviser (CSA), the Chief Nursing Officer (CNO), the National Clinical Director (NCD) and the Chief Scientist Officer Health (CSO Health). The relevant period saw a collegiate form of working which existed across all four nations. There were regular meetings between the UK CMOs, often taking place daily some weeks. A further UK wide group meeting involved not only CMOs, but other senior clinicians and scientific advisers. This was the Quint Senior Clinicians Group meeting and attendees included (but were not limited to) the four UK CMOs, the medical director NHS England, DCMOs from the four nations, the four CNOs, and representatives from the UK public health agencies. This group met twice weekly during the first 6 months of the pandemic at least and weekly thereafter. The evidence presented at these meetings was discussed and carefully considered and where relevant would be used to formulate advice for clinical/medical colleagues, Scottish Government policy officials and Scottish Ministers. Further details can be obtained from the office of the CMO for England as they were responsible for the co-ordination and administration of these meetings.

16. In respect of international co-operation, the current CMO had some informal contact with the World Health Organization (WHO), though in the main this contact was co-ordinated through the CMO in England. There were also evidence meetings with Centers for Disease Control and Prevention (CDC) in the USA and the Israeli Health Ministry. These virtual meetings usually took place at least monthly or more frequently if required, particularly in the post vaccination phase where amongst other things, evidence regarding the effectiveness of the vaccine was shared, such as the latest intelligence on variants and viral properties. There was direct contact with colleagues in Denmark in connection with the concern around the virus within the mink population and indirect contact via the UK CMO's group with South African clinicians.

17. SAGE and bodies such as New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) are part of the critical function of how evidence is received

and considered. SAGE tries to identify what evidence is needed, whether it exists, and if so, where it can be obtained.

18. The current CMO attended Scottish Government resilience (SGoRR) meetings whenever requested to do so, depending on the issues being discussed and the need for clinical advice. As far as the current CMO can recall, they attended the majority of SGoRR meetings, missing very few. It has not been possible to find an accurate attendance list for the meetings as this was not captured in the notes from the Resilience Team. The CMO calendar may not also be entirely accurate (e.g. a meeting may have been in the diary, but the CMO may have not been able to attend at the last minute due to urgent matters elsewhere. If CMO was unable to attend due to a clash of meetings, then a DCMO would attend on their behalf, so someone from the CMOD was present.

19. The CMO was (and continues to be) routinely informed when SAGE is being convened, but attendance at the meetings may be taken up by other senior clinicians, depending on their availability or the issues being discussed.

20. Details of the role of CMO in respect to public health incidents can be found in the Management of public health incidents: guidance on the roles and responsibilities of NHS led incident management teams (2020) (MPHI), provided [GS3/002- INQ000130954]. During the first wave of Covid-19 and preceding the first lockdown Scottish Government assumed leadership as set out in the MPHI. Health Protection Scotland (HPS), subsequently Public Health Scotland (PHS) provide advice to the CMO either directly or through the National Incident Management Team (NIMT). The role of the NIMT was to coordinate intelligence from health protection teams across the country, address requests for specific advice or identify issues, and where appropriate offer assessment and advice to the CMO for consideration by Scottish Government.

21. CMOD's role in relation to operation decision-making within the NHS in Scotland was one of providing clinical advice to Scottish Ministers and Scottish Government policy officials if requested to do so but was not the operational decision maker.

Understanding Covid-19

22. Understanding of the transmissibility, infection, mutation, reinfection, the nature of the virus including its severity and the measures available to limit it spread and how this understanding developed over the course of the pandemic can be found in the Technical Report on the Covid-19 Pandemic in the UK of the four UK CMOs, provided [GS3/003– **INQ000203933**].

23. Four broad reflections run through the Technical Report. The first is that there were multiple strands of scientific work from different disciplines needed, and these had to be integrated at considerable speed. The UK started with a strong science and research base and even with this and swinging most of the medical scientific and research effort over to COVID-19, accumulating evidence for policy was incremental, with initially wide confidence intervals and uncertainty. Evidence will continue to accumulate as time goes on, and new evidence will no doubt come to light that enables a better understanding of some of the issues we discuss here.

24. The second is that, unsurprisingly, the UK was relatively effective and rapid in responding in areas in which we already had strengths and substantial capacity, including in biomedicine, which could be adapted and built on. For example, UK strengths in phase 3 clinical trials allowed very rapid progress in assessing clinical effectiveness of pharmaceutical interventions; the relatively small relevant diagnostics industry meant scale up of diagnostic tests was slower and was a significant limitation on the initial response.

25. The third is that science and medicine are international and pandemics cross borders. Much of what we learned was from scientists, public health experts and clinicians in other countries. The experience of each country in the Covid-19 pandemic, facing the same pathogen, is different, and all had different scientific strengths. It would however have been unwise to have relied entirely on the scientific capacity of others and the UK provided a significant contribution to the global scientific output as well as insights specific to the UK experience.

26. Fourth and finally, the engagement of policymakers and the public in the scientific insights, with their ability to have a clear, deep, and sometimes sudden understanding of a complicated problem was profound and critical to the response. People rightly wanted to understand why specific interventions, actions or treatments were being recommended and the underlying rationale and

evidence for each. Often the most difficult part of medical and scientific communication is explaining uncertainty or evolving science in a transparent way without it leading to paralysis in decision making. Our experience of this was almost entirely positive. Just as people in a one-to-one clinical encounter want to understand the logic, risks, benefits and uncertainties of a course of action, the same was true at national levels in this pandemic.

27. This statement draws extensively from the Technical Report on the Covid-19 Pandemic in the UK (published on 1 December 2022) by the UK CMOs (England, Scotland, Wales and Northern Ireland), the Government Chief Scientific Adviser (GCSA), the NHS National Medical Director and the relevant DCMOs, with additional contributions from many distinguished scientists.

28. The Technical Report contains information that is likely to be of significant assistance to the Inquiry. This and other witness statements produced on behalf of the CMOD should be read in conjunction with the Technical Report.

29. The Technical Report has considerably more detail on many of the key issues considered in this statement including references and examples of some key documents and public advice to government Ministers from the joint UK CMOs. Paragraphs 32-37, 40-72, 81-90, 93, 95, 102, 115-133, 142-159, 162-174, 186-198 and 216-223 of this statement reproduce information from the Technical Report and supplement this with further insights provided by the current CMO where relevant.

30. Expert opinions were forthcoming from a variety of sources, not only from members of scientific groups. The current CMO read articles and evidence pieces and often approached the authors of such literature directly. Early in the pandemic response, much of this information came from weekly commissioned literature reviews that were led by Dr Muge Cevik, Clinical Academic, University of St Andrews. As EAVE II began to develop data later in the response, there were prolific high quality evidence papers shared from this team by Professor Sir Aziz Sheikh. These are examples only from the wide range of contributions given to clinical advisers and do not represent the entirety of the large response.

Modes of transmission, including asymptomatic, presymptomatic, airborne and surface

31. It was established early in the pandemic by scientists that the likely principal route of transmission for Covid-19 was respiratory, although secondary routes including faeco-oral were not excluded. From early in the pandemic, three components have been considered potentially important for Covid-19: fomite, droplet and aerosol spread. However, global scientific consensus on the relative importance of these different transmission routes, and the potential role of other routes, shifted as new evidence emerged, and evidence has been continually reviewed as new variants of SARS-CoV-2 have become established. The relevant paper, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, published 24 January 2020, is provided: [GS3/004-INQ000408060].

32. There were important complexities in understanding transmission routes. First, transmission depends on multiple factors including:

- Pathogen dynamics, such as viral load;
- Environmental factors, such as temperature and ventilation;
- Host-related factors, such as behavioural adaptation, immunity and contact patterns; and
- Wider contextual factors, such as prevalence of the disease.

33. The relevant papers, Visualising SARS-CoV-2 transmission routes and mitigations, published 1 December 2021, and Factors contributing to risk of SARS-CoV2 transmission associated with various settings, 26 November 2020, are provided: [GS3/005- INQ000212016], [GS3/006- INQ000224425].

34. Second, some routes of transmission were easier to measure than others. It was relatively rapidly identified that close contacts were at elevated risk and from that it was inferred that close range droplet transmission was likely to be important. It was less easy to identify the most likely pathway in those with more distant exposure (where respiratory particles will have been diluted by distance) as a contact event was often harder to identify.

35. Third, there was a need to balance the level of infection risk from a given transmission route with the frequency and likelihood of exposure to this in day-

to-day activities. For example, aerosol transmission across a room may present a low risk from any single exposure, but the ability of one infectious person to expose multiple people at the same time, means it could present a higher population level risk in some settings than for close direct contact with an infectious person.

36. Finally, given the challenges inherent in attempting to determine the relative impacts of different routes of transmission, it was important to retain an open mind, as understanding evolved over the course of the pandemic. It was also important to ensure that absence of evidence was not interpreted as evidence of absence, and that important transmission routes to which there were potential countermeasures were not ignored.

37. Initially, knowledge of other coronaviruses (SARS-CoV-1 and MERS-CoV) was used to develop broad estimates of the expected kinetics of viral shedding of SARS-Cov-2, but this needed to be supplemented with pathogen-specific evidence. SARS-CoV-2 viral load and detection of infectious virus in the respiratory tract are the two key parameters for estimating infectiousness. As shedding of infectious virus is required for onward transmission, understanding viral shedding characteristics is relevant for public health interventions.

38. Epidemiological studies of transmission chains provided the earliest estimates of infectious periods. Studies of clusters and chains of transmission, and early models of transmission dynamics, were used to infer the infectious period.

39. After 3 to 4 months of the first data collection being made available internationally, initial estimates of the infectious period, informed by longitudinal data on viral shedding, were available. Longitudinal data is collected through a series of repeated observations of the same subjects over some extended time frame and is useful for measuring change. Longitudinal data effectively follows the same sample over time, which differs fundamentally from cross-sectional data because it follows the same subjects over some time, while cross-sectional data samples different subjects (whether individuals, households, countries, or regions) at each point in time. The first viral culture results from the UK became available in April 2020. At this time, absolute numbers of data points and persons investigated remained small.

40. By mid 2020, accumulating data on viral dynamics (as measured by RT-PCR) had demonstrated a peak in viral load at the onset of symptoms, followed by a gradual decline in viral load. Viral culture data suggested that cultivable virus levels were correlated with PCR values and time after symptom onset, and that viable virus could be isolated from pre-symptomatic cases, providing support for infectiousness of pre-symptomatic cases. Longitudinal or cross-sectional sampling and culture showed that beyond 14 days the majority of infected people shed virus at amounts lower than could be cultured, suggesting they were no longer infectious.

41. By the end of 2020 there was a robust understanding of viral dynamics over time. Further data emerged to suggest a strong relationship between Ct values and ability to recover viable virus. Throughout 2021, comparisons of viral kinetics across people infected with different variants were undertaken, as well as across vaccinated and unvaccinated individuals.

The infectiousness of the disease

42. At the onset of the Covid-19 pandemic, when information on SARS-CoV-2 itself was limited, initial risk assessments and hypothesis generation for research drew upon what was already known about similar pathogens. Fortunately, identification and initial characterisation of the causative virus came swiftly, as detailed in the Technical Report. This early virological information fed into risk assessments about the nature of the virus and its risk to the population, when and whether it would be imported into the UK, as well as supporting the development of a diagnostic molecular test.

43. Following the first official reports of pneumonia of unknown origin in Wuhan, China, at the end of December 2019, very early information about the pathogen came from China and other countries that experienced early imported cases. Within days, the causative pathogen was identified as a beta coronavirus, and was subsequently named as SARS-CoV-2. Chinese scientists rapidly performed laboratory-based characterisation (virus culture, electron microscopy) and sequencing (unbiased meta-genomic techniques) of the pathogen from clinical samples.

44. The first genomic sequence was generated on 3 January 2020 and publicly released on 10 January 2020. Within weeks, the virus receptor was identified as ACE2, with TMPRSS2 also flagged as important for viral entry.

45. Early on, phylogenetic analysis of available genomes and epidemiological studies of early cases gave signals that the virus had recently emerged, and consideration was given to the possible origin. Local expertise and access to high-end technology in China enabled rapid identification and characterisation of SARS-CoV-2. In the earliest stages, knowledge and expert opinion was reliant on accessible international data. Channels to access this rapidly such as the Global Initiative on Sharing Avian Influenza Data (GISAID) were key.

46. Comparison of genome sequences with other known human pathogens demonstrated that SARS-CoV-1 was the closest related human pathogen, with around 80% genomic similarity to SARS-CoV-2. It was known that SARS-CoV-1 caused severe human infections and used the same ACE2 receptor. Other related human pathogens were also drawn upon for scientific insight, including:

- MERS-CoV, which showed around 50% genomic similarity but did not use ACE2;
- NL63, an endemic coronavirus that used ACE2;
- Other endemic coronaviruses: OC43, 229E and HKU1; and
- Influenza, as a pandemic respiratory virus.

47. As data about SARS-CoV-2 accumulated with time, it became apparent that SARS-CoV-2 was different from SARS-CoV-1 in several aspects, such as in its pre-symptomatic infectiousness, levels of asymptomatic or subclinical infections, and routes of transmission.

48. In the early stages of the pandemic, before robust data on SARS-CoV-2 itself became available, prior experience and knowledge about related pathogens guided early understanding and public health actions, for example by:

- Facilitating prioritisation of potential therapeutics that had already shown in vitro or clinical activity against human and zoonotic coronaviruses; and

- Signalling the potential for reinfections due to prior observations of waning immunity to seasonal coronaviruses.

49. There was a review of data on the persistence of SARS-CoV-2 on surfaces, other household materials and in airborne droplets, and how long it remains in an infectious form. Assessments are supplemented by associated recommendations. The paper was discussed at SAGE meeting 8 on 18 February 2020.

50. Prior knowledge also fed into early estimates of the incubation period, which was known to be longer for coronaviruses than influenza. Reviewing existing data on the environmental persistence of coronaviruses informed early policy thinking on decontamination.

51. In characterising the pathogen from early clinical material, relationships between public health agencies and laboratory networks were key in prioritising distribution of virus isolate (to those with established biocontainment facilities) and planning further investigations. On a global level, academic laboratories with technical expertise collaborated with those running approved biocontainment facilities in other organisations to set up and lead work on virus characterisation, such as sequencing, in vitro studies and animal models. This supported assay development and furthered our knowledge of the virus. Clinical studies, in particular use of established protocols via the UK's International Severe Acute Respiratory Infection Consortium (ISARIC) Clinical Characterisation Protocol and, later, human challenge studies also delivered important data about the virus and the disease it caused.

52. As the virus reached the UK, early recognition and detection of cases was important in supporting further research into SARS-CoV-2. As detailed within the Technical Report, after the first case was detected in the UK in late January 2020, the virus was cultured and sequenced within days and shared with academic partners, enabling early virological work and feeding into wider research to develop our understanding of the pathogen. This wider research included potential pharmaceutical interventions, the duration of protective immunity to this pathogen and likelihood of reinfection, and the nature of severe and long-term disease. Gauging the potential impact of Covid-19, and the appropriate response

to take, relied heavily on understanding both the severity of acute disease and its possible longer-term sequelae.

The mortality rate amongst those infected with the disease

53. Mortality rates were difficult to define in the initial stages of this pandemic, as was the case for H1N1 influenza and SARS-CoV-1, but for slightly different reasons. For SARS-CoV-1 in 2003, initial case fatality rate (CFR) figures underestimated severity due to early estimates missing delayed deaths, though statistical methods were developed to provide a more robust estimate of severity in similar situations which were useful in this pandemic. For H1N1 influenza in 2009, initial CFR estimates were about 500 times higher than the later agreed infection fatality rate (IFR) of 0.001% to 0.002% due to initially measuring only symptomatic or confirmed cases and missing milder and asymptomatic ones.

54. For SARS-CoV-2 too, there were varying estimates of CFRs in the early stages. In the UK, before widespread surveillance was set up, initial estimates of the CFR came from dividing numbers of reported deaths by the estimated number of cases in Wuhan, China at a given time. These estimates were greatly improved by Chinese Centres for Disease Control (CCDC) data: for example, in mid-February 2020, the CCDC weekly bulletin provided a CFR estimate of 2.3% from 72,314 cases identified using either PCR testing (63%) or clinical diagnosis (37%). Of this group 1.3% were thought asymptomatic. Of the PCR confirmed cases, 81% were classified as mild (which included non-pneumonia or mild pneumonia) and 19% were described as severe or worse (which was classified as dyspnoea, low oxygen saturations and/or greater than 50% lung infiltrates on imaging). The CFR for those with severe disease was high at 49% and increased substantially with age (though the age distribution of this cohort was relatively young compared to the UK, with 68.8% of patients under 60). Another early study incorporated a wider range of cases from PCR testing for international travellers arriving to China, alongside cases and deaths in Wuhan, and reported a CFR of 1.4% for symptomatic Covid-19 cases. It was initially difficult to interpret such studies for a UK context, in part because denominators and numerators varied and in part because their source populations differed from the UK in several important ways (such as age distribution). The relevant paper, *Review of data on persistence of SARS-CoV-2 in the environment and potential infection risk*, published 14 February 2020, is provided: [GS3/007- INQ000074898].

55. Population-wide surveillance (positive tests, syndromic surveillance) linked to outcomes (hospitalisation, deaths) provided high quality data for the routine calculation of CFRs by providing a robust denominator. In the UK this was initially done using serology (the scientific study or diagnostic examination of blood serum especially with regard to the response of the immune system to pathogens or introduced substances), which was difficult to interpret due to waning antibody levels, and after late spring 2020 by large scale surveillance studies such as the Office for National Statistics (ONS) Covid-19 Infection Survey (CIS), Real-time Assessment of Community Transmission (REACT) and Early Assessment of Vaccine and anti-viral Effectiveness 2 (EAVE-2), and in cohorts such as SIREN (healthcare workers) and Vivaldi (care homes).

56. The calculation of an accurate IFR required serological testing of a representative random sample of the population, and establishing a regular serological survey allowed the estimation of the severity of disease on a regular basis. However, this took time to set up and for results to indicate severity more clearly, CFR was available much more quickly. Early establishment of data storage and linkage systems was important for the timely calculation of these statistics. Securely sharing data with academic groups facilitated rapid analysis.

57. Investigations of large outbreaks of Covid-19, like previous experience with H1N1 influenza, also supported CFR and IFR estimates early on, as well as giving signals on the proportion of asymptomatic infections. An outbreak on the cruise ship Diamond Princess in February 2020 provided early data on outcomes for 3,711 passengers and crew and gave a CFR of 2.6% and an IFR of 1.3%, likely due to testing across the ship picking up asymptomatic cases. Studies of Wuhan residents outlining the likely delay distribution between onset and death were critical in estimating both CFRs and, as testing and surveillance expanded, IFRs. Other opportunities for screening were passengers on flights from affected areas. However, these figures needed to be interpreted in context, and could not readily be applied to different population groups with different demographic characteristics.

58. It was not until late Spring 2020, when many countries were experiencing high transmission, and testing was being ramped up alongside surveillance studies,

that a shift from CFR to IFR occurred and estimates converged towards an overall IFR of around 1%.

59. The presence of asymptomatic cases and transmission for Covid-19 was particularly problematic in early mortality rate estimates, and this had not been the case for the closely related SARS-CoV-1 (for which peak infectiousness matched peak clinical symptoms). Many early studies missed asymptomatic cases in the absence of widespread testing and community surveillance, and in the UK in February to April 2020 several cases due to Covid-19 occurred in the community without confirmatory testing. This was likely the reason behind higher early CFR estimates: collated data in England from 31 January to 22 April 2020, for example, recorded 99,137 cases with 16,271 deaths, a crude mortality ratio of 16.4%. Around the same time, adjusting for age and using serological data alongside case data gave an IFR of 1.6% for the UK. The source of this data is the UK Security Agency Surveillance data, 23 April 2020, and Estimates of the severity of coronavirus disease 2019: a model-based analysis, 20 March 2020, both of which are provided: [GS3/008- INQ000411152], [GS3/009-INQ000236303].

60. Global comparisons proved difficult as hospitalisation criteria, testing availability and case definitions varied over time and across different health jurisdictions. Mortality itself varied significantly from country to country, likely due to different age structures of populations as well as differences in a range of other risk factors such as obesity, levels of social deprivation and important comorbidities. As stated in Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy, published 23 March 2023, a study in Italy, where 37.6% of cases were aged 70 years or older, gave an estimated CFR of 7.3% up to 15 March 2020, compared to a much lower CFR in a Chinese study where just 11.9% of cases were over 70, provided: [GS3/010-INQ000411158]. Understanding of how these complex and interacting demographic factors influenced severe disease evolved throughout the pandemic and underscored the importance of continual evaluation of variation in severity.

The rate of severe illness in infected people

61. Healthcare data was needed to understand disease severity across different demographic groups and the likely resultant pressures on the healthcare system.

General acute hospital admissions and admissions to intensive care for Covid-19 were important in understanding rates of severe disease from the outset. Early in the pandemic in England, the first data set that provided insight into hospitalisations was the Covid-19 Hospitalisation in England Surveillance System CHESS (later, renamed Severe Acute Respiratory Infections (SARI). This was an aggregate and line list data set, providing detail on general admissions and high dependency unit (HDU) or intensive care unit (ICU) admissions. It was sourced from sentinel sites and other participating trusts. The sentinel trusts were not a representative sample of hospital admissions within England and therefore inferences that were drawn had limitations. This data was biased towards critical care admissions, which made it unrepresentative of clinical pathways and severity.

62. Testing to identify cases had multiple applications throughout this pandemic, supporting clinical management, infection prevention and control (especially in health and care settings), contact tracing, surveillance, and to understand transmission force, transmission routes and severe disease rates. Testing was especially important because the symptoms of Covid-19 were often non-specific, minimal or absent. It was therefore an early priority in the UK and globally, to develop diagnostic tests for the SARS-CoV-2 virus.

63. Mortality was not the only measure of severity; admissions to hospital and ICU with Covid-19 were also important metrics in this pandemic – particularly to help plan healthcare delivery. Understanding delays between infection and severe disease was also crucial in estimating the correct denominator and likely rates of severe disease at any given point. As noted in the Technical Report, a delay from infection to death was around four weeks but with wide variation.

64. Initial clinician impressions from the first cases can give early signals but can be misleading. Many of the early patients seen in the UK with Covid-19 were returning travellers from Europe, the majority of whom were young and fit patients with greater rates of mild disease than the wider population. Within about two weeks the disease had spread more widely in the population and hospitals were faced with large numbers of older patients with severe disease and high mortality.

65. As case rates rose, determining wider population levels of morbidity was complex. Although routine statistics on hospitalisations within the UK were available from early on, a need to prioritise tests during times of limited testing capacity meant that it was difficult to estimate the proportion of cases likely to require hospital admission or ICU care. Early, large-scale testing within the population is of course the best way to gauge severity more accurately, but this is not always feasible, especially when tests need to be developed, or are limited in supply and need to be prioritised to high-risk settings.

Whether any specific pre-existing health conditions increased the likelihood of becoming severely ill with Covid-19 and whether age, sex and/or ethnicity affected the likelihood of becoming severely ill with Covid-19 infection

66. Infectious disease epidemics and pandemics usually expose and exacerbate existing disparities in society, such as those associated with deprivation, ethnicity, sex, age and sexuality. The pandemic had some less predictable disparities in health outcomes such as the striking age gradient in risk, and the risk of severe disease for people living with obesity.

67. By February 2020 there was evidence of increased risk of hospital admission for older adults, men and those with certain underlying health conditions. The relevant report, ICNARC report on COVID-19 in critical care, published 27 March 2020, is provided: [GS3/011- INQ000191305]. The regular publication of intensive care data also supported a rapidly growing understanding of ethnic disparities in the UK: in the first wave, statistics highlighted high rates of hospitalisations among patients of black and Asian ethnic groups compared to white ethnic groups, as shown in the report CNARC report on COVID-19 in critical care, published 10 April 2020, provided: [GS3/012- INQ000191308]. However, ethnic disparities were often confounded by deprivation and living in areas with high prevalence of the disease. As the pandemic went on, patterns of risk for both infection and severe disease changed as the epicentre shifted to areas with different ethnic makeup and as vaccines were rolled out with differing levels of uptake across different communities.

68. As highlighted in the Technical Report, testing data also supported understanding of disparities: Covid-19 laboratory reporting forms included age and sex from the outset, and ethnicity information was then added by linking laboratory surveillance data with Hospital Episode Statistics data sets.

69. Public engagement exercises were used throughout the pandemic to understand the experiences and drivers of observed disparities in Covid-19 health outcomes. For example, an in-depth public engagement exercise with representatives of key affected groups alongside a rapid literature review and qualitative analysis culminated in the publication of a report in June 2020: Understanding the Impact of Covid-19 and Minority Ethnic (BAME) Communities, provided [GS3/013-INQ000176354], which produced a series of recommendations on how to better understand and mitigate the impact of the pandemic on ethnic minority groups, summarised below:

- Mandate ethnicity data collection and recording as part of routine NHS and social care data collection systems, including the collection of ethnicity data at death certification and ensure this data is readily available to local health and social care partners;
- Support community participatory research in which researchers and community stakeholders engage equally to understand the full range of determinants of Covid-19 in BAME communities;
- Improve access, experiences and outcomes of NHS, local government and integrated care systems commissioned services by BAME communities;
- Accelerate the development of occupational risk assessment tools that can be employed in a variety of settings and used to reduce the risk of employee's exposure to and acquisition of Covid-19;
- Fund, develop and implement culturally competent Covid-19 education and prevention campaigns to rebuild trust and update with clinical services and prepare communities to take advantage of interventions, such as contact tracing and antibody testing;
- Accelerate efforts to target culturally competent health promotion and disease prevention programmes for non-communicable diseases; and
- Ensure that Covid-19 recovery strategies actively reduce inequalities caused by the wider determinants of health to create long term sustainable change.

Fully funded, sustained and meaningful approaches to tackling ethnic inequalities must be prioritised.

70. Alongside this, weekly calls between the CMO's office and Directors of Public Health helped highlight emerging issues in their communities.

71. Co-morbidities such as diabetes, severe asthma and obesity were identified as risk factors for poor outcomes and were more prevalent in more deprived and in some ethnic minority groups. Linked primary care records of over 17 million adults with over 10,000 deaths between February and December 2020 found that while comorbidity did explain some of the different death rates by ethnicity, people from black and South Asian ethnic groups were both more likely to test positive and more likely to die from Covid-19 during the first wave compared with people from white ethnic groups after adjustment for deprivation, age, sex and comorbidity. Analysis of the second wave found that while differences in testing positive and higher death rates among South Asian ethnic groups remained, they were far less stark for black ethnic groups.

72. Disentangling the principal drivers was often complex because of the overlapping nature of many of the risk factors. For example, some South Asian populations might have higher probability of being in contact professions such as taxi driving or care work, higher rates of diabetes, more multigenerational households and being in an area of enduring transmission such as in the North-West England. Some populations may use care and testing differently or face barriers in their access. Working out which was a risk factor, and which was a confounding factor was inevitably complex and some residual confounding was likely.

The risks of infection for pregnant women and to foetal health

73. Scottish Government maternity professional advisers and policy leads had daily contact on a range of issues, with weekly and sometimes twice weekly meetings with internal colleagues and external stakeholders from Health Boards, professional bodies and networks. The current CMO was not involved personally but relevant advice was provided from these meetings either directly or via discussion at Professional Advisory Group or the Clinical Cell. The wider work of CMOD is detailed below.

74. Additionally, new or repurposed working groups on key policy areas were utilised, with the objective of assessing pregnancy risk.

75. CMOD and policy teams worked with several organisations on research studies and to produce guidance documents and advice. These organisations are:

- Public Health Scotland (including Scottish Intensive Care Society Audit Group);
- Royal College of Obstetricians & Gynaecologists (RCOG);
- Royal College of Midwives (RCM);
- MBRRACE-UK: Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK;
- Sands - Saving babies' lives. Supporting bereaved families;
- Bliss Scotland - Bliss Scotland is part of Bliss, the UK's leading charity for babies born premature or sick and is registered with the Scottish Charity Regulator (OSCR);
- Fertility Network UK; and
- National Bereavement Care Pathway.

76. The Covid-19 Pregnancy in Scotland (COPS) study revealed that women with Covid-19 towards the end of their pregnancy are at higher risk of birth-related complications, while vaccination poses no increased risk. The COPS study is a partnership between PHS and The University of Edinburgh. Statistics provided by the COPS study are shared on Public Health Scotland's website.

77. The COPS study, supported by Sands, looks at how Covid-19 infections and vaccinations affect pregnant women in Scotland. The study found that all women who get Covid-19 close to their due date are more likely to have problems during birth than those who might get it earlier on in pregnancy. It also showed that for women who caught Covid-19 during later pregnancy, those who are not vaccinated are more likely to have a preterm birth or lose their baby, than women who are vaccinated.

78. The COPS study provides clear evidence that there are no additional risks to mothers and babies from being vaccinated against Covid-19, and that vaccination is the best way to protect babies from the effects of Covid-19.

79. COPS provides population-based information for the whole of Scotland on the incidence of, and outcomes following, Covid-19 infection in pregnancy.

The possibility of re-infection

80. As a novel infection, understanding the duration of immunity and risk of reinfection over time for Covid-19 was important to enable individuals, scientists, and policymakers to determine who was protected against infection and for how long, to predict the likely duration of impact of any vaccines, and to inform epidemic modelling. Knowledge of the duration of passive immunity from antibodies was also important for understanding the potential role of antibody drugs. In April 2020, SAGE was discussing the possibility of reinfection, with information inferred from generic understanding of viral and host immune systemdynamics. The earliest case reports came from overseas and even by Jan 2021, the BMJ was reporting that anticipated evidence of reinfection, due to postulated waning immunity, would begin to reveal itself.

81. Extrapolation from biologically similar or evolutionarily related pathogens provided the earliest clues to whether reinfection was likely, and after what interval. Immunity to SARS-CoV-1 and MERS-CoV was thought to wane over time, and there was evidence of confirmed reinfections with seasonal human coronaviruses. This meant that from an early stage there was an assumption that reinfections with SARS-CoV-2 were possible. It was possible to explore the impact of reinfection through mathematical models, monitor early case reports for evidence of proven reinfection and design studies to investigate reinfection rates. There was also a reasonable assumption that the virus would mutate over time which in turn could impact reinfection risk.

82. As detailed in the Technical Report, by early 2020, data emerged indicating that many individuals infected with SARS-CoV-2 displayed an antibody response between ten to 14 days after symptom onset. Data showed that in mild cases, antibodies took longer to appear or were low or undetectable during the timescale of completed studies. Data was gathered through observational studies with serial sampling on small numbers of participants, however, a lack of available validated assays to measure antibody or cell-mediated immunity in early 2020 hampered early attempts to characterise the immune response soon

after the emergence of the pathogen. Around this time, data from animal models signalled that the presence of antibody protected against reinfection when challenged with SARS-CoV-2.

83. Antibodies did not, however, inevitably mean protection from infection (nor did lack of antibodies preclude it due to other immunological mechanisms such as T-cell mediated immunity), so there was a need for further longitudinal studies to examine reinfection risk. The Vivaldi (care homes) and SIREN (healthcare workers) cohort studies were key to developing understanding of infection, transmission and immunity. Key examples of published reports from the SIREN studies are provided: [GS3/014-INQ000223820], [GS3/015-INQ000398897], [GS3/016-INQ000348250], [GS3/017-INQ000398899], [GS3/018-INQ000212138], [GS3/019-INQ000398900]. These studies were initiated in the first half of 2020 and adapted to provide up-to-date information on issues as they emerged, through adjustment of protocols to include questions on vaccine effectiveness and variant characteristics. SIREN, for example, recruited its first participant in June 2020, investigated its first reinfection in September 2020, produced an initial reinfection analysis in December 2020, and published its first vaccine effectiveness analysis in January 2021.

84. The first published case reports of SARS-CoV-2 reinfection confirmed by whole genome sequencing also emerged in mid-2020. Several other reports of reinfection emerged at this time, though many did not have sufficient data to distinguish between persistent primary infection and reinfection. The corroboration of early reports of reinfections with SARS-CoV-2 was complicated due to restricted access to testing during the time of primary infections. During the 'first wave', the great majority of infected persons did not have access to PCR testing, and viral isolates were not regularly obtained for sequencing. At this point, reliable information on the proportion of people likely to experience reinfection, the timeline of reinfection, and the characteristics that make reinfection more or less likely was still missing.

85. As time since the first infections with SARS-CoV-2 elapsed, the length of time over which the immune response was characterised increased. By the end of 2020, antibodies, in particular neutralising antibodies, were shown to be a useful correlate of protection against SARS-CoV-2, through a combination of animal studies, outbreak studies and cohort studies. Nevertheless, the concentration of

antibodies that correlated with protection was not yet established. The antibody response following natural infection was shown to persist for at least three to six months, and the cellular immune response for over five months, though seroprevalence studies in the UK showed a decline in the presence of antibody positivity and confirmed reports of reinfection began to emerge, suggesting a waning in protection over time. Evidence from longitudinal observational and cohort studies emerged to suggest that people who had experienced asymptomatic or mild SARS-CoV-2 infection could experience waning immunity over three to five months.

86. Data collection in longitudinal cohort studies included the demographic characteristics of participants, routine samples (systematic testing for the identification of the pathogen and its antibodies, with genetic sequencing of the pathogen where applicable), and routine collection of information on symptoms and exposures. Once established, these longitudinal cohort studies were cross-purpose sources of information, providing insight not only into reinfection risk, but also the duration of the protective effect of vaccination following rollout, and the prevalence and incidence of infections in defined populations. Healthcare workers were a useful target population as they were essential for the functioning of the health system, could provide insight into the effectiveness of personal protective equipment, assist in the understanding of nosocomial transmission, and facilitated the establishment of cohort studies at pace.

87. Numerical estimates of the protective effect of baseline antibodies to SARS-CoV-2 against symptomatic reinfection, asymptomatic reinfection, or all infections combined (over a period of 3 to 5 months) also became available. The end of 2020 also brought the first clinical trial data demonstrating that SARS-CoV-2 vaccines could provide a high level of protection against disease, however, the duration of immunity provided remained unknown.

88. By mid-2021, descriptions of viral loads (as measured by cycle threshold (Ct) values) in reinfected individuals were available. Cultivable virus had also been isolated from reinfected individuals, demonstrating that reinfections presented a risk of onward transmission. Throughout the first half of 2021, understanding of the duration of the immune response to SARS-CoV-2 improved. Antibody was found to be detectable in saliva for at least eight months following infection, and in blood for at least nine months, as set out in NERVTAG - Update note on

immunity to SARS-CoV-2 after natural infection, 27 May 2021, provided: [GS3/020-INQ000411161]. The presence of antibody was shown to be associated with a protective effect against infection over at least seven to ten months, with a lower effect in those aged over 65. The cell-mediated immune response to SARS-CoV-2 was shown to be detectable up to eight months after infection. Characterisation of neutralising antibody titres over time since either infection or vaccination or both (through longitudinal serological sampling) continued throughout 2022.

89. In March 2021, early evidence showed that the risk of reinfection with the Alpha variant was comparable to the risk of reinfection with the wild type, though these findings were confounded by the shorter time from primary infection in the case of the alpha variant. National surveillance data was used to monitor reinfections, including with newly emerging variants, and showed evidence of increased reinfections at the emergence of the delta and omicron variants.

Any increased risks to workers in healthcare settings

90. Certain occupational groups such as factory workers, healthcare workers, emergency service workers, social care workers and high contact professions, such as taxi drivers or security professionals, were shown to carry a heightened risk of exposure to infection. The relevant study, Deprivation and exposure to public activities during the COVID-19 pandemic in England and Wales, 12 October 2021, is provided: [GS3/021-INQ000411162].

91. However, there was a need to consider local circumstances when assessing the evidence. For example, early data from China suggested a limited role for healthcare settings in driving transmission, but this was in the context of important differences between these settings in China and the UK, including the imposition of different mitigation measures against aerosol transmission.

92. CMOD did not have any direct involvement in relation to the development of Covid-19 antigen tests for workers in healthcare settings.

The emergence of variants, and whether variants differed in their infectiousness, presentation or severity of symptoms

93. Over time, new variants arose that led to different clinical outcomes. Detecting these differences was challenging, as it required linking large scale genomic data with hospitalisation and mortality rates. Greater severity of symptoms was seen with one of the first variants (Alpha), although a subsequent group of variants (Omicron) was found to have had reduced hospitalisations and deaths per case, though due to higher transmissibility and therefore high case rates, still resulted in large numbers of hospitalisations. Changes in pathogenicity were difficult to measure and it was not possible to assume a shift towards less severe outcomes as the virus evolved. Levels of immunity (both natural and vaccine-derived) were an important confounding factor in determining the intrinsic severity of new variants, as were changing demographic factors (such as the age group predominantly infected) across different waves.

Post-Covid-19 Condition (Long Covid)

94. Strategic decisions relating to the healthcare provisions and treatment to Long Covid were made by Scottish Ministers. The CMO was amongst the advisers who attended meetings with policy officials where advice was discussed, agreed and submitted to Scottish Ministers. Officials from across Scottish Government provided a breadth of submissions and advice across a wide range of key areas to Scottish Ministers. CMO and CMOD provided professional clinical advice to officials alongside opinion when requested to do so but were not (and are not) the policy or strategy lead. CMO/CMOD, in collaboration with other senior clinicians from other UK nations, commissioned the joint development of guidance on Long Covid by NICE, RCGP and SIGN. CMOD do not hold the clinical advice or guidance provided, these will be with the relevant policy teams located in other HSCD Directorates.

95. By the summer of 2021, it was becoming apparent that many patients had ongoing symptoms after recovery which persisted for longer than three months. One prospective study of 431 individuals testing positive for Covid-19 in Switzerland, published in July 2021, found that six to eight months after infection 55% of the cohort reported ongoing fatigue, 25% had some degree of breathlessness, and 26% fulfilled criteria for depression. The relevant study, Burden of post-COVID-19 syndrome and implications for healthcare service planning: A population-based cohort study, 22 July 2021, is provided: [GS3/022- INQ000381217]. Since that time, the range of chronic symptoms recorded for cases of Covid-19 has

expanded greatly. A diagnostic definition of the condition has been made as post-Covid-19 syndrome by the National Institute for Clinical Excellence (NICE), more commonly referred to as 'Lond Covid' by sufferers and clinicians, although it is likely to represent several overlapping syndromes.

96. In September 2021, SIGN published a decision support toolkit on managing the long-term effects of COVID-19 (also known as 'Long Covid'). The guideline was developed by the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners (RCGP). It provided advice on how to care for people who had signs and symptoms that developed during or after an infection consistent with Covid-19, continued for more than 4 weeks and could not be explained by an alternative diagnosis. As part of CMOD the Scottish Government's Clinical Guidance Cell and the Professional Advisory Group (PAG) were consulted during the development of the guideline. NICE said that the comments were invaluable in helping to develop and refine the guideline. CMOD's comments and advice included but were not limited to the following:

- Draft guideline (which contains recommendations, rationales, giving a summary of how recommendations were formed, and research recommendations);
- Equality Impact Assessment (which shows how the guideline has been assessed for its likely impact on equality groups);
- Lists of included and excluded studies (which formed the evidence reviewed); and
- Evidence tables (which gives fuller details of the evidence used.

97. All stakeholder comments received during the consultation were published, as was the response from NICE, and both are provided [GS3/023-INQ000398877], [GS3/024-INQ000398878].

98. The toolkit, produced and published by National Institute for Health and Care Excellence (NICE) & the Scottish Intercollegiate Guidelines Network (SIGN) provides clinicians with a single, integrated point of access to key information from SIGN guideline 161 on managing the long-term effects of Covid-19 and the Scottish Government's accompanying Implementation Support Note. Available

via both a web-based platform and a mobile app, the toolkit presents current evidence and helpful recommendations on assessment, investigations and referral, planning care, management and follow up for people experiencing long-term effects of Covid-19, as well as case definitions and associated clinical codes for different stages of individuals' experiences of symptoms.

99. The toolkit is for use by health and care practitioners of all disciplines in all settings involved in the assessment and management of people experiencing long-term symptoms of acute Covid-19. The methods and search strategies used were published and are provided [GS3/025-INQ000398880], [GS3/026-INQ000398882].

100. The final guideline was published on the NICE website on 18 December 2020, provided [GS3/027-INQ000365766], along with an Equality Impact Assessment to support the guideline, provided [GS3/028-INQ000398905].

101. The exact number who have experienced longer-term symptoms after Covid-19 is likely substantial but remains unclear, as does the aetiology of the syndrome, including whether it was one or (perhaps more likely) several different overlapping syndromes. In July 2022 the ONS CIS estimated that 1.4 million people in the UK were experiencing Long Covid symptoms that adversely affected their day-to-day activities in the four weeks ending 4 June 2022.

102. Most children had very minimal medium and long-term health impacts from Covid-19, but rarely some children developed a multisystem inflammatory condition termed paediatric inflammatory multisystem syndrome (PIMS-TS) temporally associated with SARS-CoV-2, or multisystem inflammatory syndrome (in children) (MIS-C). The true incidence of PIMS-TS was unclear, as many Covid-19 infections in children went undiagnosed. One study from the US (Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2, published 10 June 2021) estimated 316 cases per ten Covid-19 infections in persons under 21 years old, provided: [GS3/029-INQ000411164]. The relationship between the syndrome and Covid-19 infection was about two-thirds of presentations being associated with seroconversion to SARS-CoV-2, and about one-third testing positive for SARS-CoV-2 on admission. In some cases, the association was suspected because of close contacts with

a confirmed case but without seroconversion or positive viral PCR. Most cases presented between two to four weeks after Covid-19 infection was documented. 70% of cases required ICU admission, though mortality was relatively low at 1.1%. Some children also experienced Long Covid but at a much lower rate than adults.

103. Long Covid likely includes a combination of conditions including organ damage by severe or milder Covid-19 infections, perhaps disease caused by persisting infection, persistent clotting and more traditional post-viral syndromes. Research into the causes, pathophysiology and management of this disorder is ongoing, with recognition and understanding improving over time.

104. It is important to note for future pandemic preparedness that there may be longer-term consequences of an infection affecting a large percentage of the population, and that adequate surveillance mechanisms should be in place to capture the epidemiology of the condition accurately to allow adequate planning of healthcare resources in the longer term.

Healthcare provision and treatment for Covid-19

105. Strategic decisions relating to the healthcare provisions and treatment to Covid-19 were made by Scottish Ministers. The CMO was amongst the advisers who attended meetings with policy officials where advice was discussed, agreed and submitted to Scottish Ministers. Officials from across the Scottish Government provided a breadth of submissions and advice across a wide range of key areas to Scottish Ministers. CMO and CMOD provided professional clinical advice to officials alongside opinion when requested to do so but were not (and are not) the policy or strategy lead. CMOD do not hold the clinical advice or guidance provided, these will be with the relevant policy teams. This is supported by an established process and email instruction which states the following: “Responsibility for filing key documents and communications on the record, including those sent to CMO Mailbox and Gregor Smith, rests with relevant policy and operational areas within Directorates. The CMO Private Office does not keep

official records of such e-mails or attachments". This same email instruction applied to CMOD and DCMOs.

106. In the first two months of the pandemic, when only a small number of known Covid-19 cases had entered the UK, health services adopted existing high consequence infectious disease (HCID) protocols to prevent any transmission risk within healthcare settings, delivering support to a small number of cases in highly specialised settings. The aim was to prevent any spread from known cases while optimising care for the patients involved.

107. Clinical management in HCID units was based on existing knowledge of broadly similar diseases, as well as emerging evidence from outbreaks and case reports across the world.

108. For clinical management, initially the sharing of contemporary best practice by clinicians and scientists from countries hit early in the pandemic (including China, Singapore and Italy) allowed the early management of people with Covid-19 in the UK to be based on some prior knowledge.

109. Examples where clinical practice changed early in the first three to six months of the pandemic and in advance of formal trials include:

- The recognition of the high rates of pulmonary embolism and substantial use of empiric prophylactic and therapeutic doses of anticoagulants;
- A systematic approach to the use of high flow oxygen therapy (including the continuous positive airway pressure (CPAP) approach) based on oxygen levels;
- The regular adoption of proning in intensive care units (ICUs);
- A move away from mechanical ventilation; and
- The identification of several distinct Covid-19 related syndromes.

110. As cases began to rise rapidly following widespread seeding in the community, (leading to the first wave), health services saw a surge in needs across the population as high volumes of Covid-19 patients presented to healthcare settings. At this point it was necessary to simultaneously:

- Manage rising demand alongside existing health needs;
- Reduce transmission risk within healthcare settings; and
- Rapidly scale up clinical care for a cohort of patients with a variety of care requirements, including for intensive care.

111. At this point, the disease was still relatively new and evidence on appropriate clinical care still emerging. As the wave progressed, clinicians rapidly developed and shared best practice, including on the importance of proning, anticoagulation and effective use of high-flow oxygen guided by pulse oximetry.

112. Following the first wave, formal evidence based on studies and then trials of effective pharmaceutical interventions began to emerge and this was implemented rapidly and effectively. So, too, did approaches to Infection Prevention and Control (IPC) and the balance of transmission risk with the impact of highly specified IPC guidance on service delivery. The broader management of healthcare services also adjusted, and routine and non-urgent care was then expanded alongside continuing support for Covid-19 patients.

113. At the same time, an improved understanding of Covid-19 and shared developments in clinical practice, alongside available therapeutics, helped manage the second wave in clinical settings. It is the considered and professional opinion of the four CMOs that the impact of the second wave on non-Covid-19 was smaller, despite the larger numbers of cases, because of this adaptation.

114. As the pandemic and subsequent waves progressed and the seroprevalence of the population rose through a combination of vaccine rollout and infection-derived immunity, rates of severe disease reduced, and clinicians became increasingly familiar with management of Covid-19 as part of regular practice. They increasingly saw patients with Covid-19 in healthcare settings with, rather than due to, the disease. Being able to distinguish between the two was important not only for clinical management but also national surveillance of severe disease, and it was difficult to achieve in a timely way.

115. There was an initial need to rapidly identify existing drugs that could be safely and effectively repurposed. Hundreds of candidate therapeutics were proposed in the first

days and weeks of the pandemic, and prioritisation was necessary to maximise use of limited resources and ensure adequately powered clinical trials that delivered fast results. Initially, NERVTAG, a committee advising the CMO and the Department of Health and Social Care (DHSC), carried out an assessment of potentially viable existing pharmaceuticals that could be repurposed.

116. As the pandemic progressed, focus shifted from repurposed disease-modifying therapeutics (largely with impact on the immune system) to specific antiviral treatments and prophylaxis such as monoclonal antibodies against the virus and directly acting antiviral drugs. These were not available earlier in the pandemic.

117. While Covid-19 is primarily a respiratory disease in most patients, in the early weeks of the pandemic there was increasing recognition that severe Covid-19 is a complex multisystem disease, involving immunological, coagulation, renal and cardiovascular systems. Severe disease requiring ICU admission might therefore present with respiratory failure alone, or with multi-organ impairment/failure, each adding to the burden on ICUs.

118. The exaggerated immunological response observed was characterised by hyperproduction of proinflammatory cytokines in the most severely affected patients, typically in the second week of their illness. This was closely associated with capillary leak syndrome, disseminated intravascular coagulation, acute respiratory distress syndrome (ARDS), and multi-organ failure, ultimately leading to death in the most severe cases.

119. Despite initial understandable concern based on experience with SARS-CoV- 1 and MERS-CoV that broadly acting immunosuppressant drugs might impair immune responses, dexamethasone was extensively trialled in hospitalised patients during the first wave as part of the RECOVERY trial. Less than six months after the first UK case, based on trial evidence, dexamethasone was approved for immediate widespread use in hospitalised patients with requirement for supplemental oxygen, substantially reducing morbidity and mortality in second and subsequent waves of the pandemic.

120. A further component to the multisystem disease observed by clinicians early in the pandemic was the increased incidence of acute kidney injury among patients hospitalised with Covid-19, which had also been reported in Wuhan. This association was particularly pronounced in the first wave, where more than 25% of patients admitted to critical care required renal replacement therapy (RRT), with very high mortality (80%).

121. In the first wave, in many ICUs it was the availability of RRT (machines and disposables) rather than ventilators that was most challenging in terms of equipment provision. Improved understanding of the disease and less restrictive fluid management strategies likely contributed to this becoming less of a challenge as the pandemic waves progressed.

122. The acute inflammatory state seen in Covid-19 probably led to the increased risk of thromboembolic events that was a feature of severe Covid-19, and, to a lesser extent, bleeding. This presented as both micro and macro thrombotic phenomena, with up to a third of patients admitted to ICU experiencing thromboembolic events.

123. Enhanced thromboprophylaxis was rapidly introduced for patients identified as being at risk. However, even with heparin prophylaxis as standard, pulmonary thromboembolism was identified in about one-quarter of Covid-19 patients admitted to ICU, with deep vein thrombosis also observed in one-quarter of patients with pulmonary thromboembolism.

124. Cardiovascular compromise was a further challenge of the multisystem disease seen in severe Covid-19 with cardiomyopathy, myocarditis and arrythmias all contributing to advanced cardiovascular support being required for one in three patients requiring mechanical ventilation.

125. By the end of the first wave, the management of hospitalised patients had evolved significantly. Seriously unwell patients were often trialled on non-invasive rather than invasive ventilation, hypovolaemia was avoided, enhanced thromboprophylaxis provided as standard for at risk patients, and many were randomised to receive dexamethasone.

126. By the start of the second wave, dexamethasone was in widespread use. As the pandemic progressed in the second and third waves, evidence from other clinical trials mounted, filling in gaps that could not be met by observational studies and clinical networks.

127. As a result of these trials, many patients who were hospitalised during the third wave were also treated with more targeted drugs including directly acting antivirals and monoclonal antibodies which further improved clinical outcomes, albeit with a smaller, more incremental effect. It was important that in the UK use of unproven medicines outside the setting of a clinical trial was effectively minimised.

128. Acute hypoxemic respiratory failure was almost universally seen in severely unwell patients with Covid-19, with senior clinicians describing "a lifetime of acute respiratory distress syndrome patients in 2 years".

129. At the start of the first wave, there was an emphasis on early intubation for the sickest patients, with differential ventilator management practices based on different presumed phenotypes. However, international experiences in Lombardy and China reported high mortality in patients requiring invasive mechanical ventilation and highlighted the potential risk that ICU capacity might be exceeded.

130. In addition to increasing national ICU capacity approximately 3-fold, consideration of non-invasive respiratory support strategies such as CPAP and high-flow nasal oxygen (HFNO) was therefore central to reducing the need for tracheal intubation and invasive ventilation, both to reduce pressures on ICUs and as a potential strategy to reduce mortality.

131. High rates of failure are reported when treating other viral or bacterial pneumonias with non-invasive ventilation, leading to concern that similarly high failure rates might be observed in patients with Covid-19, with treatment delaying intubation and mechanical ventilation (rather than preventing it) and exacerbating lung injury. Over time, however, the approach of delaying intubation for a trial of non-invasive ventilation became a routine part of practice in many centres with general success.

132. A key component of respiratory support soon became the widespread use of prone positioning of mechanically ventilated patients, a strategy which already had an established evidence base for non-Covid-19 ARDS in ventilated patients.

133. Informed by this pre-Covid-19 evidence base, anecdotal reports of improved oxygenation and ventilation in Covid-19 patients and later, formalised guidance, the approach was also extended to include conscious non-ventilated patients. In some ICUs, the volume of patients requiring this management led to the development of 'proning teams' of redeployed staff to reduce workload on ICU staff, standardise the process and maintain patient safety.

Expanding ICU and acute bed capacity and equipment

134. It was evident from global experience that the pandemic coronavirus in circulation led to severe acute respiratory disease. A major focus early in the pandemic was on expanding ICU capacity (staff, space, systems and equipment) both within the existing health estate and beyond. This included repurposing operating theatres and later taking over other general wards to drive up critical care space, alongside efforts to expand the workforce and equipment. Work was jointly commissioned by Health and Social Care Directors, to ensure capacity and capability was enhanced through a Short Life Working Group that reported to the Chief Operating Officer (COO) NHS Scotland and which had extensive clinical input from Scottish Government clinical advisers and NHS clinicians.

135. This required both an increase in provision of devices to deliver this therapy and a review of hospital sites to ensure oxygen supplies were not exhausted in the face of unprecedented demands. Some hospitals found existing piped oxygen capacity insufficient. Hospital estates teams played an important role in reviewing the capacity of oxygen supplies, hardware and maintaining safe delivery.

136. In the first wave, in many ICUs it was the availability of RRT (machines and disposables) rather than ventilators that was most challenging in terms of equipment provision.

137. Supply of renal replacement machines and disposables was also a key issue for many units across the country. So too were consumables, such as anaesthetic drugs and renal consumables.

138. National and regional teams supported local health services to pool equipment in mutual aid systems. They also supported the scaling up of production and procuring equipment at pace, an important process in the context of high global demand for equipment supporting Covid-19 clinical care. Repurposing equipment to different service areas was important to meet demand but had to be balanced with the risks of healthcare professionals using unfamiliar equipment.

Infection prevention and control

139. Strategic decisions relating to the provision of IPC were made by Scottish Ministers. The CMO was amongst the advisers who attended meetings with policy officials where advice was discussed, agreed and submitted to Scottish Ministers. Policy officials provided a breadth of submissions and advice across a wide range of key areas, including IPC to Scottish Ministers. The CMOD provided professional clinical advice to policy officials alongside opinion if requested but was not (and is not) the policy or advisory lead for IPC. CMOD do not hold the clinical advice or guidance provided, these will be with the relevant IPC policy teams.

140. Following the first wave, formal evidence based on studies and then trials of effective pharmaceutical interventions began to emerge and was implemented rapidly and effectively. So, too, did approaches to IPC and the balance of transmission risk with the impact of highly specified IPC guidance on service delivery.

141. There has been a continual evolution of practise during this pandemic: in clinical management, managing surges in demand alongside competing healthcare priorities, and in IPC practices.

142. IPC is a vital patient safety consideration across health and social care interactions. Its importance has been especially evident through the Covid-19 pandemic, with an increased focus on IPC practice not just in health and social

care, but across the breadth of community settings (schools, prisons and places of detention).

143. The IPC guidance for Covid-19 was developed by a specialist cell of practitioners on behalf of the four UK nations. This supported consistency in practice and a shared understanding of the scientific evidence across the UK. CMOD is not part of the specialist cell. This guidance is issued jointly by the DHSC, Public Health Wales (PHW), Public Health Agency (PHA) Northern Ireland, NHS National Services Scotland, UK Health Security Agency (UKHSA) and NHS England as official guidance. The guidance is published on their behalf by UKHSA.

144. The aims of the Covid-19 IPC guidance were to reduce the transmission of SARS-CoV-2 in health and care settings, protecting patients, staff and visitors, while supporting the safe delivery of health and care services.

145. This guidance was produced in the context of an evolving evidence base, with clinical practice adapting in response to emerging health needs, which required the following considerations to be considered:

- Emerging evidence on transmission risks for SARS-CoV-2, which initially was often based on rapid assessments of real-world scenarios and inevitably featured variations in methodology and outcomes;
- International recommendations regarding best practice in IPC. These built on the established evidence base for IPC practices derived from the WHO. IPC guidance in the UK was initially based on amended DHSC UK pandemic flu guidance but was adapted throughout the pandemic in accordance with emerging evidence, expert recommendations (such as from SAGE and subgroups) and changes in the epidemiology of SARS-CoV-2;
- The evolving healthcare situation in the UK. The Covid-19 IPC guidance developed over the course of the pandemic to reflect these changes, moving from initially focusing on managing Covid-19 patients during the first wave to balancing this with supporting the safe restoration of NHS services from mid-2020 onwards, such as through establishment of risk-based clinical pathways;
- Ensuring that guidance was consistent with established IPC practice and easily understood by staff and implementable in all health and care settings; and

- The impact of IPC guidance on workforce morale, to support and reassure clinicians who were responding to a novel virus and were concerned for the safety of their patients, colleagues, families and themselves.

146. These are complex issues with inherent tensions between them due to a range of different stakeholders each with their own views and self-interest priorities, as outlined for each of the points above. At a national level, strong relationships between organisations across the UK ensured that these tensions were discussed and consensus, evidence-based IPC practice was reflected in the UK Covid-19 IPC guidance. This collaboration brought broad consistency of approach across the four national health and care systems.

147. Collaboration and co-operation with external stakeholders, such as the Academy of Medical Royal Colleges (AoMRC), the Health and Safety Executive and ventilation experts, added additional expertise (and credence) to the Covid-19 IPC guidance and over time contributed to increased certainty and standardisation of approach across the system. There was, however, never complete consensus across all professional groups.

148. Continual evidence reviews were undertaken by the UK public health bodies to identify changes in the evidence base for IPC interventions and reflected in updated guidance, to provide assurance to all stakeholders that the full range of evidence was being assessed.

149. Creating a systematic and consolidated way of communicating this knowledge from the four UK health systems' specialist IPC advice to all frontline workforces was vital, and not always easy. This was done via regular webinars with directors of nursing and directors of IPC in providers, as well as specific communications materials to support implementation of IPC measures. Again, four-nation alignment on this was important.

150. Many of the IPC measures recommended across the NHS for Covid-19 were known and established IPC practices:

- Standard infection control precautions (SICPs); and
- Transmission-based precautions (TBPs).

151. The Covid-19 IPC guidance, as well as outlining when and where SICPs and TBPs should be used, contained several specific measures for Covid-19 universal masking for source control, Covid-19 specific patient pathways and physical and social distancing within healthcare settings. There was also an added emphasis on the use of a hierarchy of controls approach, which encompasses a risk assessment of the effectiveness of potential interventions in individual contexts including consideration of the environment, the patient and the healthcare practitioner.

152. Together these approaches brought together three critical system components: clinical care for patients, IPC, and assessment and management of risks. In addition, the Personal Protective Equipment (PPE) Innovation and Sustainability group and NHS bodies collaborated to develop an educational programme on the safe use of non-sterile gloves, appropriate respiratory protective equipment (RPE) fit testing, and the assessment of novel PPE.

153. The IPC guidelines were initially informed by experience and evidence of responding to the risks posed by other pathogens, including respiratory infectious diseases (notably, influenza). There is good evidence regarding the effectiveness of SICPs and TBPs to prevent and control the transmission of known pathogens if applied correctly.

154. The Covid-19 IPC guidance built on this evidence base and added specific measures based on the evidence of the transmission and impact of SARS-CoV-2, such as universal masking in healthcare settings and patient cohorting.

155. Covid-19 IPC measures were implemented while the epidemiology of the pandemic was changing (for example, emergence of variants of concern, the introduction and effect of population-level public health mitigations, and the availability of licensed vaccines and therapeutics).

156. There was continual adaptation of measures in response to epidemiology and wider measures in place and use of the hierarchy of controls approach to risk assessment across different settings and services.

157. It is widely accepted that it is very difficult to assess the effectiveness of individual IPC interventions in this context, due to the multi-interventional nature of IPC practice and widespread community transmission during the pandemic response. However, evidence suggests that the application of the established IPC practices was effective in markedly reducing the transmission of SARS-CoV-2 in healthcare settings across the UK.

158. The evidence (anecdotal and published) also suggests that the effectiveness of IPC practice in preventing transmission was related to their optimised application in the healthcare environment.

159. Universal masking (source control) with face coverings or surgical masks (type II or IIR) to prevent the transmission of SARS-CoV-2 and other respiratory infectious agents was implemented in healthcare settings from 15 June 2020. There is evidence to suggest that this intervention was effective in reducing transmission of Covid-19 in the healthcare environment, though importantly as part of the hierarchy of controls and considering possible associated risks if not properly managed. The relevant studies, Front lines of the COVID-19 pandemic: what is the effectiveness of using personal protective equipment in health service environments? – a systematic review, 8 June 2020, Efficacy of face masks against respiratory infectious diseases: a systematic review and network analysis of randomized-controlled trials, 13 September 2021 and Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis, 17 November 2021, are provided: [GS3/030-INQ000411165], [GS3/031-INQ000411166], [GS3/032- INQ000218210].

Personal Protective Equipment

160. Strategic decisions relating to the provision of PPE were made by Scottish Ministers. The CMO was amongst the advisers who attended meetings with policy officials where advice was discussed, agreed and submitted to Scottish Ministers. The CMOD provided professional clinical advice to policy officials alongside opinion if requested but was not (and is not) the policy or strategy lead

for PPE. CMOD do not hold the clinical advice or guidance provided, these will be with the relevant PPE policy teams.

161. As is widely acknowledged, pharmaceutical interventions (PIs) were not available in the early stages of the pandemic and so the focus was on non-pharmaceutical interventions (NPIs) initially. These focused primarily on reducing ingress and transmission of SARS-CoV-2 in healthcare settings to reduce the frequency and size of outbreaks.

162. In the first 2 months of the pandemic, when only a small number of known Covid-19 cases had entered the UK, health services adopted existing HCID protocols to prevent any transmission risk within healthcare settings, delivering support to a small number of cases in highly specialised settings. The aim was to prevent any spread of known cases while optimising care for the patients involved.

163. Clinical management in HCID units was based on existing knowledge of broadly similar diseases, as well as emerging evidence from outbreaks and case reports across the world.

164. As cases began to rapidly rise following widespread seeding of cases in the community leading to the first wave, health services saw a surge in needs across the population as high volumes of Covid-19 patients were presented to healthcare settings.

165. As previously mentioned in this statement under IPC, the PPE Innovation and Sustainability group and NHS bodies collaborated to develop an educational programme on the safe use of non-sterile gloves, appropriate respiratory protective equipment (RPE) fit testing, and the assessment of novel PPE.

166. Clinicians were understandably concerned that IPC practices and resources should not only protect them from becoming infected at work and subsequently lead to the risk of infecting their patients, but also be appropriately tailored to the levels of risk in different settings and for different activities.

167. Especially in the early stages of the pandemic there was widespread concern in some informal groupings of clinicians and formal groups such as the British Medical Association (BMA) that IPC measures being recommended were

insufficient, based in part on a concern it was being driven by supply constraints rather than science. There were also vigorous debates about what constituted an aerosol generating procedure (AGP) requiring higher levels of IPC. The current CMO does not recall the exact detail of how they became informed in each case, some may have been formalised in communications, others were reported verbally during engagement. The key aspect is that expert advice in relation to this came from the UK IPC cell and senior clinicians such as the CNOs, who were generally responsible for this area of professional practice, and CMOs received this advice from this group.

168. The evidence base for IPC measures to mitigate the risks from Covid-19 continued to develop and evolve as understanding of the pathogen increased. In this context of evolving evidence, and particularly at the outset of the pandemic, some clinicians or groups of clinicians advocated for approaches based on an interpretation of latest evidence (for example, in relation to issues such as routes of transmission and the use of RPE).

169. Recommendations in IPC guidance was always made using the best available evidence. However, undeveloped supply chains meant that PPE supplies came under widespread pressure due to increased demand and required prolonged use and in some cases re-use of PPE.

170. It was important that UK Covid-19 IPC guidance remained consistent with WHO recommendations and that the UK-wide Covid-19 guidance and principles had consistency of strategic approach across the four national health and care systems.

171. Collaboration and co-operation between IPC policy and operational leads and external stakeholders, such as the Health and Safety Executive, ventilation engineers and clinical experts, added additional expertise (and independence) to the IPC Covid-19 guidance and thus contributed to increased certainty and standardisation of approach across the system.

172. While there was cross-UK variation in terms of governance, all UK countries had a shared view that there needed to be clear communication, understanding of responsibilities, and ownership of IPC and health protection guidance and its implementation across IPC and health protection stakeholders.

173. The complexity and rapidity of asks falling on clinicians and healthcare settings means that interpreting IPC guidance at speed was difficult and as a result IPC guidance was at risk of being inconsistently applied across different settings. CMOD are unaware of any specific details where this risk materialised. The remit for IPC lays elsewhere so further opinion on this is best sought from the CNO Directorate or PHS in their returns.

174. Appropriate strategic and educational support was key, not only at a local level but also from regional and national IPC teams, both of which were strengthened in terms of resource during this period. Fit testing for staff was also an important way to ensure that everyone was aware of relevant RPE requirements and had the appropriate PPE to protect them in different scenarios.

175. On 1 and 2 April 2020 letters were sent jointly from the CMO and CNO to Chief Executives and Chief Officers, provided [GS3/033-INQ000276939] and [GS3/034-INQ000259889]. The first letter made recipients aware of the imminent publication of revised PPE guidance, which would mean some changes to the PPE which health and social workers in Scotland were advised to wear. The second provided further details and rational for these changes, primarily the widespread transmission of the virus within the community and the need to protect those who were most vulnerable to the virus in a variety of settings.

176. On 9 April 2020 there was a UK Senior Clinicians meeting where PPE was discussed for Gowns and coveralls. A readout from that call is provided [GS3/035-INQ000343631].

177. There were advisory groups such as the National PPE Clinical Oversight Group (NCPG) which was chaired by NHS Scotland. The aim of the NCPG was to provide clinical leadership and advice on a PPE demand and allocation approach, to ensure supply, distribution and optimum use of PPE best meets the need of Health and Care Workers (HCW) across Scotland.

178. NCPG commissioned the PPE Clinical Advisory Panel (CAP) to provide clinical insight to support the purchasing of PPE, within an agreed process to review,

evaluate and reach consensus on safe and effective PPE products. They considered clinical use of different types of PPE.

179. On 26 May 2020 the CNO sent a letter to NHS Board Chief Executives providing clarity on the Scottish Government's policy regarding the reuse of single-use personal protective equipment (PPE). CMOD had been involved in discussions to agree that Scottish Government was clear that single-use PPE must not be reused and should be disposed of after use into the correct waste stream. The letter is provided [GS3/036-INQ000398868].

180. On the 20 January 2021 CMO along with Caroline Lamb (Director General Health & Social Care and Chief Executive NHS Scotland) wrote to Jill Vickerman, National Director (Scotland) of the BMA regarding a letter the Chair of the BMA, Dr Chaand Nagpaul, had written to Public Health England on the issue of concerns doctors have raised around feeling inadequately protected by current PPE, provided [GS3/037-INQ000398869].

181. In late November 2021 there was correspondence with the Cabinet office national PPE cell Medical Director to try to achieve approval and release of the Alpha Solway transparent face masks to be used in clinical environments. The development of these transparent masks was important as they significantly aided communication between healthcare staff and individuals who relied on lip reading or facial expression to communicate, such as those with hearing impaired or mental health conditions. A briefing from NHS National Services Scotland (NSS) further detailing this is provided [GS3/038-INQ000411151].

182. In relation to advice provided by the CMOD on testing the adequacy or standard of PPE that was out-of-date or without a CE mark, despite non-CE-Marked PPE being allowed during the pandemic, it had to be assessed by the Health and Safety Executive (HSE) and NSS.

183. The EU introduced an easement whereby PPE could be eased by HSE rather than having to be CE marked – it still had to meet CE standards but was assessed in a different manner to keep up the flow of PPE to the country. This was then extended in UK nations, with the PPE Unit working to create a Scottish Statutory Instrument (SSI) for this purpose under the Coronavirus Act 2020. The Policy Note that accompanied the SSI is provided [GS3/039-INQ000398871].

184. Finally, in relation to PPE in general, a system was put in place whereby if NHS staff were aware of any specific issues, they could email the Scottish Government and officials would then look in to this further and liaise with the relevant single points of contact at NHS Boards to find a solution. This work was managed and co-ordinated by the Scottish Government PPE Division on a day-to-day business, so not requiring comment or advice from CMOD unless specifically asked to do so, such as that outlined above. The current CMO is unable to recall any other instances where they were asked to provide specific advice or comment on that work.

Testing for healthcare workers

185. Strategic decisions relating to the provision of testing for healthcare workers were made by Ministers. The CMO was amongst the advisers who attended meetings with policy officials where advice was discussed, agreed and submitted to Scottish Ministers. Policy officials provided submissions and advice across a wide range of key areas, including testing to Scottish Ministers. The CMOD provided professional clinical advice to policy officials alongside opinion if requested but was not (and is not) the policy or strategy lead for testing. CMOD do not hold the clinical advice or guidance provided, these will be with the testing policy teams.

186. Throughout the pandemic, the capacity and effectiveness of laboratory processing, delivery and distribution routes, global demand and supply of materials continually changed. Testing strategies were continually adapted in response, and as the epidemiology changed and wider pandemic strategies also adjusted (for example, where routine testing enabled strategies supporting the labour market).

187. Testing strategies also evolved as new technologies became available and as evidence emerged on the potential needs, use cases and population responses to different testing options – such as self-testing, as opposed to that undertaken by a health professional or in clinical settings only, or accessibility of public testing centres. What was available and what tests were used for changed over the course of the pandemic.

188. To expand capacity, reduce risk of supply failure and to service anticipated use cases, a wide selection of diagnostic technologies was supported into development and evaluation in this pandemic. At the inception of testing, several technologies were explored as it was unclear how effective, scalable or reliable each was. Broadly, there were three methods:

- Molecular, to detect viral ribonucleic acid (RNA);
- Antigen, to detect viral proteins; and
- Serology, to detect host antibodies.

189. There were other important antigen tests besides lateral flow devices (LFDs), such as microfluidic immunofluorescence assay point-of-care antigen tests using nasal and nasopharyngeal swab samples which were used for rapid admissions testing in clinical settings.

190. As the first few hundred cases reached the UK, testing of symptomatic patients was central to refining the clinical case definition, confirming clinical diagnoses, and conducting epidemiological studies to understand the speed and extent of the transmission to inform public health control measures.

191. Diagnostic polymerase chain reaction (PCR) tests, processed by existing lab infrastructure, were primarily used in hospitals for case finding and early outbreak management, to prevent incursions of SARS-CoV-2 into healthcare settings, and for infection prevention and control in clinical settings.

192. The early diagnostic test (as is the case for many viruses) was molecular reverse transcription polymerase chain reaction, (RT-PCR), though development of serological assays was also a major strand from an early stage, and later commercially developed antigen tests were also deployed at scale.

193. RT-PCR tests for SARS-CoV-2 were developed early in the pandemic in the UK, with tests available in small numbers from January 2020. RT-PCR tests did not easily distinguish between whole viable virus and viral fragments, and so repeat PCR tests were not advised within 90 days of infection.

194. For widespread deployment of asymptomatic testing, LFDs enabled rapid point-of-care or self-test for current infection and when people are likely most

infectious, with results appearing on the device in 10 to 30 minutes. LFDs did not require sophisticated laboratory infrastructure or skilled personnel and therefore provided decentralised testing.

195. Typically, with current methods, the development of specific molecular diagnostics for any new emerging viral pathogen requires knowledge of the virus genomic sequence. Once the target sequence is known, sensitivity and specificity of PCR-based or nucleic acid amplification test (NAAT) based diagnostics is typically greater than 95% and 99%, respectively.

196. Very early in the pandemic Chinese scientists performed genomic sequencing of SARS-CoV-2 and shared the full sequence globally via a public database. It was important to have the entire viral sequence for SARS-CoV-2 because different regions of the viral genome could be used for different purposes for diagnostic detection.

197. Whole genome sequencing also enabled identification of genetic similarity with other coronaviruses, particularly SARS-CoV-1, for which diagnostic expertise and clinical materials existed in several public health laboratories across the world, including the UK. This facilitated rapid development of a diagnostic assay through international collaboration between public health laboratories. SARS-CoV-1 clinical samples were used as control material during the early development of an RT-PCR assay.

198. RT-PCR was a core technology in the UK's testing system and has provided most of the molecular symptomatic diagnostic testing to date. It was also used for asymptomatic testing with weekly PCR tests supplemented by further LFD testing as part of the care home staff testing regime until March 2022.

199. In relation to the involvement of the CMOD on the development of Covid-19 antigen tests for workers in healthcare settings, the LumiraDx rapid tests were raised in August 2020. The Cabinet Secretary for Heath and Sport requested CMOD advice on a briefing that was submitted regarding the rapid tests. The briefing and CMOD's advice in response are provided [GS3/040-INQ000245172], [GS3/041-INQ000398884]. The CMOD advised that claims of the LumiraDX test's high sensitivity and specificity were a significant advantage over other rapid tests but that this required validation, as acknowledged in the

contract model. Once the results had been appropriately validated then the necessity for a confirmatory PCR test could be better judged. The LumiraDX test kit could have a role in environments where accessing testing was challenging or a rapid assessment was needed.

200. There was an issue with these tests in September 2020 as validation exercises had revealed that the tests were not considered suitable for use in an emergency admissions or care home environments. The submission is provided [GS3/042-INQ000241679].

201. There was various other correspondence and briefings that CMO was part of or issued on the emerging testing strategy, particularly in March 2020 when it was clear that Scotland's testing capacity would require significant expansion, at pace. On 18 March 2020 Scottish Ministers were advised to agree to a proposed initial testing and monitoring approach to increase testing capacity and to support a surveillance testing model though the sentinel system or a suitable alternative, provided [GS3/043-INQ000471220]. On 23 March 2020 CMO advised the First Minister and Cabinet Secretary for Health and Sport on a proposed approach to testing Covid-19 to allow key workers to return to work, provided [GS3/044-INQ000398886]. Guidance was subsequently circulated from the CMO to Health Boards on 24 March providing testing prioritisation advice, provided [GS3/045-INQ000398888]. On 29 March 2020 CMO updated Scottish Ministers on the work undertaken to support the increase in testing capacity and seeking agreement that officials should continue to develop a Scottish Covid-19 Testing Strategy, and to the creation of a Scottish Testing Oversight group to oversee the Strategy, provided [GS3/046-INQ000316272].

Shielding and at-risk individuals

202. Scottish Ministers were first approached to give authorisation to the broad approach to protecting those considered most vulnerable from Covid-19 in our society by officials, based on clinical advice from the CMO, on 21 March 2020, three weeks after the first confirmed case of Covid-19 in Scotland, provided [GS3/047-INQ000261358].

203. The four UK CMOs jointly identified certain health conditions which could, based on risk from respiratory illnesses such as flu, mean someone was potentially at

higher risk of negative outcomes if they contracted Covid-19. There was no divergence across the UK with respect to this identification. The initial six groups were as follows:

- Group 1: Solid organ transplant recipients;
- Group 2: People with specific cancers;
- Group 3: People with severe respiratory conditions including all cystic fibrosis, severe asthma and severe COPD;
- Group 4: People with rare diseases and inborn errors of metabolism that significantly increase the risk of infections (such as SCID, homozygous sickle cell);
- Group 5: People on immunosuppression therapies sufficient to significantly increase risk of infection; and
- Group 6: People who are pregnant with significant congenital heart disease.

204. On 26 March 2020, the CMO wrote to Nursing and Medical Directors for NHS Scotland Boards advising of the highest risk groups and asking for hospital clinicians and GPs to identify patients within these six groupings who may not have been identified through the national identification process, provided [GS3/048-INQ000351885]. Clinicians could also, based on their clinical judgement, add people to the Shielding/Highest Risk list if they were clinically at the highest risk from Covid-19 but were not included in the initial six group set by the four CMOs. If someone thought that they were in the highest risk group but had not received a letter, the central list was updated to ensure people could be supported to shield.

205. The initial crisis response Shielding Programme was a major exercise which ran from 26 March to 1 August 2020 involving collaboration among a range of stakeholders. Identifying the criteria for the Shielding List was based on expert clinical opinion provided by the Clinical Advisory Group for Scotland, chaired by Dr John Harden, Deputy National Clinical Director.

206. The programme aimed to provide individuals with guidance to help minimise interaction between them and others and ultimately to reduce the risk of infection, severe illness and death. The programme sought to provide individuals with the

necessary support to enable them to follow the Shielding guidance, including, for example, priority access to online supermarket delivery slots.

207. The Shielding List, which later became known as the Highest Risk List as our policy moved away from the strict self-isolation of the first few weeks of the pandemic, was a list of people identified as having those health conditions through their medical records or by their GP or clinician, as outlined above. In total, approximately 185,000 people were on Scotland's Shielding List at any given time.

208. By early May 2020 the Shielding policy team was aware of the negative impact that self-isolation was having on quality of life, as well as the mental and physical health of people advised to shield. Around this time, the threat of Covid-19 continued to be significant. However, it was anticipated that extending shielding beyond 18 June 2020, particularly with no end date, would increase the anxiety of individuals and their families as it could signal that shielding would need to continue until such time as a vaccine for Covid-19 became available. The Shielding policy team was aware that any easing of restrictions for family and household members could make it harder for people who were shielding to protect themselves, and the added complexity/nuances of change could make it harder to comply with shielding advice.

209. Between the period of 19 June 2020 and 31 July 2020, it was clear that substantial work was first needed to foster the conditions in communities which could support personal choice. This highlighted the need to extend the shielding period beyond the initial twelve weeks, i.e. which had been due to end on 18 June.

210. The CMOD endorsed that position, and the team recommended a transition period to Ministers until 31 July 2020, with the significant caveat that this depended on the community infection rates continuing to improve and so could be delayed if necessary. A transition phase from 19 June until end of July was recommended, during which:

- Levels of community infection and the impact of lifting lockdown restrictions for the public would be monitored before any changes were recommended forthe shielding population;

- People would be asked to continue to shield, with a gradual increase in the day-to-day activities they were advised to consider, starting with access to outdoor exercise;
- Further support mechanisms were developed and put in place to allow people to make informed decisions, based on their individual clinical risk and their local environmental risk; and
- Support with food and employment continued to be in place for those who needed or chose it.

211. This was agreed by Ministers and the announcement was made on 8 June, when a CMO's letter was issued [GS3/049-INQ000470010]. A paper, called Shielding - A way forward for Scotland was published on 8 June 2020 [GS3/050-INQ000480821]. Shielding was 'paused' on 1 August 2020.

212. As we approached the 'pause' in the Shielding programme on 1 August 2020, the Shielding policy area became an established Division within the Population Health Directorate.

213. Policy in relation to people at highest risk from Covid-19 moved away from the concept of strict shielding from this point and over the course of the pandemic, given:

- The harms we knew prolonged strict self-isolation could cause, particularly in terms of mental health and physical deterioration;
- The roll-out of an effective vaccination programme which prioritised those at highest risk;
- The emergence of evidence relating to the course and impacts of the virus, and the risks to certain groups; and
- The development of new treatments to decrease the risk of severe illness and fatality.

214. The Division responsible for policy in relation to people at highest risk continued working to support this group until, and beyond, the ending of the Highest Risk List on 31 May 2022.

215. For more details on the involvement of the CMOD in the development of policy and guidance for 'at risk' individuals in Scotland, identified as being on the Shielding/Highest Risk list, please refer to the Module 3 DG Health and Social Care corporate statement, submitted in draft to the Inquiry 10 November 2023.

Clinical trials

216. In the first three months as Covid-19 moved from being a localised disease in China to a pandemic, basic epidemiological and clinical data were urgently needed to inform public health and clinical advice.

217. Studies on virology and immunology were important to inform an understanding of the clinical picture and potential interventions. Early establishment of sample collections was important.

218. Observational clinical studies were also needed both to inform early policy and clinical practice. Recognising this, several important clinical and cohort studies were conceived or launched in these early months. These included:

- The International Severe Acute Respiratory and emerging Infection Consortium's (ISARIC) Covid-19 Clinical Information Network (CO-CIN) study of patients from across the UK with severe disease;
- The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study of healthcare workers; and
- The Vivaldi study in care homes.

219. The Vivaldi and SIREN studies were key to developing understanding of infection, transmission and immunity. These studies were initiated in the first half of 2020 and adapted to provide up-to-date information on issues as they emerged, through adjustment of protocols to include questions on vaccine effectiveness and variant characteristics. SIREN, for example, recruited its first participant in June 2020, investigated its first reinfection in September 2020, produced an initial reinfection analysis in December 2020, and published its first vaccine effectiveness analysis in January 2021.

220. The clinical trials infrastructure in the UK and the rapid enrolment of patients into trials even at the height of the pandemic provided essential evidence that improved clinical care in the UK and globally. From March 2020 to March 2021, the National Institute for Health and Care Research (NIHR) Clinical Research Network supported recruitment of over one million patients from across the UK into urgent public health studies.

221. Following the first wave, formal evidence based on studies and then trials of effective pharmaceutical interventions began to emerge and was implemented rapidly and effectively. So, too, did approaches to IPC and the balance of transmission risk with the impact of highly specified IPC guidance on service delivery.

222. Research from early case studies to wider network intelligence such as through CO-CIN, to large clinical trials has been critical. Emerging evidence has informed guidance and clinical practice, alongside shared expertise as clinicians developed and shared new ways to treat and support patients with Covid-19 through local groups and clinical networks.

223. As major observational studies like SARS-CoV2 immunity and reinfection evaluation (SIREN) and the Covid-19 Clinical Information Network (CO-CIN) and then therapeutic trials including the Randomised Evaluation of Covid-19 study (RECOVERY) started to publish, change in clinical practice was increasingly and rightly driven by formal scientific methodologies and outcomes.

224. CMOD's involvement in general would involve monitoring of the major observational studies like SIREN and CO-CIN or therapeutic trials such as RECOVERY as well as how learning from such studies and trials could inform clinical practice in the treatment of Covid-19 in Scotland.

Other matters within the scope of Module 3

225. In relation to the response of the healthcare system in Scotland to the Covid-19 pandemic and the extent to which the CMOD was involved in providing advice; there was a huge volume of requests for clinical advice from across Scottish Government to the Directorate particularly to the CMO and the DCMOs.

226. These requests were typically via telephone calls, within meetings or questions posed in emails and/or to review policy documents and Ministerial submissions between 1 March 2020 and 28 June 2022 ("the relevant period").

227. Further information on advice can be found in the Module 3 DG Health and Social Care corporate statement, submitted in draft to the Inquiry 10 November 2023, and included:

- The clinical criteria or treatment protocols relating to the escalation of care for patients severely or critically ill with Covid-19;
- The establishment of temporary Covid-19 hospitals;
- The use of private hospitals to increase the capacity of the healthcare system in Scotland;
- Increasing staffing levels and critical care capacity within the healthcare system;
- Allocation of staff and resources within the healthcare system;
- Clinical criteria for discharge of patients from hospital;
- Increased use of technology in primary care, e.g. remote patient consultations;
- Suspending non-urgent elective surgery and diagnostic screening programs;
- Maintaining healthcare and treatment for patients with non-Covid conditions;
- Such the establishment of risk-based clinical pathways; and
- Palliative care.

228. With respect to the establishment of temporary Covid-19 hospitals, the NHS Louisa Jordan Governance Board was set up in April 2020. The board was chaired by Fiona McQueen who was the CNO, Scottish Government at that time. The CMOD did not give any direct advice regarding the establishment of the hospital. Further information on the NHS Louisa Jordan Hosptial will be provided in later Module 3 statements by the Scottish Government.

229. During the "stay at home" messaging periods of the Covid-19 pandemic, there was anecdotal evidence from NHS teams that urgent suspicion of cancer referrals was falling and some data suggesting reduced presentations at emergency departments for chest pain/myocardial infarction (heart attack).

230. As this came to light, the current CMO made several direct appeals at lunchtime media briefings for people to still come forward to emergency departments with worrying symptoms. This same message went out via social media posts and other comms released at the time as Scottish Government was very proactive in this area. The former and current CMO provided a strong clinical voice at the media briefings, alongside other clinicians. The former and current CMO answered questions from the media, providing an accessible clinical response for the journalists and public audience.

Regulatory issues

231. The CMOD does not grant professional registration for retired and trainee doctors and nurses in Scotland during the pandemic. This was (and still is) a matter for the regulatory body, the General Medical Council (GMC) and the Nursing and Midwifery Council who are the nursing and midwifery regulator for England, Wales, Scotland and Northern Ireland.

232. CMOD did have general discussions with the GMC at the time to support their efforts in recruiting retired and trainee doctors and nurses to increase the number of registered healthcare practitioners in Scotland during the pandemic.

233. A letter was sent from Professor Graham Ellis (DCMO) to retired doctors on the emergency register. This letter was approved by CMO and is provided [GS3/051-INQ000398873].

234. CMOD did not provide advice and was not directly involved in the decision to pause routine inspections of healthcare settings by Healthcare Improvement Scotland (HIS). This was under the direction of the CNO, however CMO was supportive of the principle.

Impact and Inequalities

235. With respect to the impact of the Covid-19 pandemic on the mental health and well-being of those working in the healthcare system this is covered in detail within the Module 3 DG Health and Social Care draft corporate statement, to which CMO has contributed.

236. There were several Directorates that contributed to the delivery of this policy for health and social care, including but not limited to, the Directorate for Health Workforce and the Directorate for Mental Health and Wellbeing.

237. This pandemic, in common with many others, reflected and in many cases exacerbated existing inequalities. Understanding how the combination of existing inequalities and pathogen specific vulnerabilities affect individuals across the population was essential to inform the policy and public health responses.

238. There was also a major potential for NPIs to create or exacerbate inequalities and have widespread impacts across society in health, economic and social terms. Decisions on whether and how to implement such wide-ranging interventions go well beyond health and rightly sit with elected Scottish Ministers on behalf of society.

239. Throughout the pandemic, as part of the Four Harms process and the Scottish Government's Framework for Decision Making, CMOD considered how the advice, policies or guidance to which it contributed might impact upon groups such as disabled people, older people, people in "at risk" groups, members of ethnic minority communities, people from disadvantaged socio-economic backgrounds, and/or people with existing health inequalities.

240. Further details of this consideration can be found in the Scottish Government's Framework for Decision Making, published in April 2020, provided [GS3/052-INQ000369689]. This document enunciated Scottish Government's principles and approach to managing the pandemic.

241. A key part of the approach described in the Framework for Decision Making was to marshal the many and various harms of the pandemic into four categories:

- Harm 1: direct Covid-19 harm;
- Harm 2: other health harm caused by the pandemic;
- Harm 3: societal harm; and
- Harm 4: economic harm.

242. The CMOD (via CMO and DCMO) was a contributor to the development of and subsequent participation in, the Four Harms process.

Future risks, reviews, reports and lessons learned exercises

243. As well as the Technical Report on the Covid-19 pandemic in the UK, CMOD is aware of the following reports which are relevant to the issues in the outline of scope for Module 3:

- The Interim Report from the Standing Committee on Pandemic Preparedness (SCOPP), provided [GS3/053-INQ000103004];
- Audit Scotland: NHS in Scotland 2020, provided [GS3/054-INQ000182702]; and
- Scotland's Wellbeing: The Impact of Covid-19 provided [GS3/055-INQ000369725].

244. These documents each contain a summary of the conclusions and recommendations of the reviews, including reflections on the response of the healthcare system in Scotland to the Covid-19 pandemic and what changes if any should be made to relevant systems and processes.

245. Implementation of any changes are carefully considered and implemented if appropriate. Plans of the CMOD relating to the response of the healthcare system in Scotland to any future pandemic will be reviewed and actioned as appropriate; these will be based on the findings and recommendations from the SCOPP and from both the UK and Scottish Covid-19 Inquiries.

246. CMOD has not produced or commissioned reports relating to any of the issues in the Provisional Outline of Scope for Module 3 since March 2020.

Statement of Truth

I believe that the facts stated in this witness statement are true. I understand that proceedings may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief of its truth.

Signed: Personal Data

Dated: 21 February 2024