Witness Name: Malcolm (Calum) Semple
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COVID-19 INQUIRY – MODULE 2

First Witness Statement of Professor Malcolm (Calum) Gracie Semple (OBE)

1: I, **PROFESSOR MALCOLM (CALUM) GRACIE SEMPLE**, of **Irrelevant & Sensitive** **Irrelevant & Sensitive** will say as follows:

2: Introduction

2.1. I make this statement pursuant to the COVID-19 Inquiry's Module 2 Rule 9 request of 31 March 2023 ('**The Rule 9**').

2.2. I previously submitted a response to the Inquiry's Rule 9 Questionnaire of 2 September 2022 (**'The Rule 9 Questionnaire Response'**).

2.3. The matters I set out within this statement are within my own knowledge save for where I state otherwise. Where I refer to facts not within my own knowledge, I will provide the source for those facts. The contents of this statement are true to the best of my knowledge and belief.

2.4. I participated in the Scientific Advisory Group for Emergencies (**'SAGE'**) as an external and independent expert from March 2020 to February 2022. My role as a SAGE participant was to provide evidence and analysis of limited evidence to government advisors (specifically the Chief Scientific Advisor (**'GCSA'**) and in turn the Chief Medical Officer (**'CMO'**)) who then relayed this advice to policy makers. As a rule, SAGE participants do not provide any opinion on policy arising or not arising from that advice. To do so would compromise our ability to provide dispassionate analysis of the

evidence that we bring and consider as a group to SAGE and jeopardise the opportunity to bring advice to policy makers in the future.

2.5. In addition to this, the substance of the considerations taken by policy makers when making policy decisions, and the nature of those decisions, are not within the ambit of my knowledge. Accordingly, I have indicated throughout this statement where I consider that I am not in a position to comment on certain matters as they involve policy matters or considerations and decisions taken by policy makers.

3: Professional Background and expertise

3.1. I am a medical doctor and clinical researcher, with expertise in managing severe respiratory viral diseases and conducting clinical research in response to outbreaks. My current positions are Professor of Child Health and Outbreak Medicine at the Irrelevant & Sensitive and Consultant Respiratory Paediatrician at Irrelevant & Sensitive Irrelevant & Sensitive

3.2. I have studied severe virus disease outbreaks since 1989 in the fields of diagnostics, clinical characterization, and clinical trials. I have led studies on COVID-19, Monkeypox, Ebola (in acute Ebola Virus disease and survivors), Influenza, and Bronchiolitis, at times being field-based in austere circumstances. I participated in many meetings of SAGE for the COVID-19 response, and I am a member of the New Emerging Respiratory Viral Threats Advisory Group (**'NERVTAG'**).

3.3. I am a former member of the World Health Organisation Scientific Technical Advisory Committee for Ebola Emergencies (**'STAC-EE'**) (2014-2016) and the UK Pandemic Influenza Group (2008-11).

3.4. I was jointly appointed Senior Clinical Lecturer in Child Health at Irrelevant & Sensitive I&S with tenure and Honorary Consultant Respiratory Physician at I&S I&S in 2006. In 2008 I was seconded to work on pandemic influenza preparedness with the UK Government, a timely appointment, as I supported the CMO and the Department of Health's policy response when Swine Flu emerged in 2009.

3.5. I co-founded the International Severe Acute Respiratory and emerging Infections Consortium (**'ISARIC'**) in 2012. ISARIC protocols and case report forms were used in Guinea and Sierra Leone to enable the rapid action research public health response in the 2014-2016 Ebola outbreak, in Wuhan in 2019-2020, and multiple outbreaks

(some with pandemic potential) in the interval between. 'Action research' is the generation of knowledge during an event that informs the response to the event. ISARIC has collated and analysed global data on COVID-19, and I am the Chief Investigator for ISARIC's Comprehensive Clinical Characterisation Consortium in the UK (**'ISARIC4C'**). ISARIC4C members are mostly clinician-scientists, and this includes several public health agency staff.

3.6. In 2016 my team and I were awarded the Queen's Ebola Medal for Service in West Africa in response to the Ebola outbreak (2014-2016) and in 2019 I and a colleague received a Commonwealth Association Award for our subsequent work with Ebola survivors in Sierra Leone. I was appointed Officer of the Order of the British Empire in the Queen's Birthday Honours 2020 for my role in the COVID-19 response.

3.7. Medical research involving humans is conducted according to protocols. Protocols are the tools we use to make discoveries and generate knowledge. To be ethical and lawful, protocols are subject to external scrutiny in the UK by Research Ethics Committees and the Health Research Authority. ISARIC's Clinical Characterisation Protocol (**'CCP'**) is one of the key tools of our global consortium. Research Protocols can be revised over time subject to regulatory approval.

3.8. Prior to September 2022, the UK approved version of the Clinical Characterisation Protocol ('**CCP-UK'**) allowed investigators to gather detailed clinical information (data) and human material (samples) from people affected by pathogens of public health interest. Since the 15th of September 2022, the protocol allows us to gather data and samples from people exposed to pathogens, chemicals, toxins, or potentially harmful energy sources of public health interest. The protocol is publicly available along with its associated documents **(MCS/01 - [INQ000231463])** .

4: COVID-19 Clinical Information Network (CO-CIN)

4.1. As mentioned in paragraph 2.5, I have been a member of ISARIC since its inception in 2012. As the consortium's name indicates, it is a global collaboration comprising at present 59 member networks with a presence in 137 countries. ISARIC'S CCP-UK was activated in 2020 for disease caused by the novel Coronavirus 2019 **('COVID-19'**). In response to the Coronavirus pandemic threat, over 300 NHS Hospital Trusts across the UK rapidly agreed to work with ISARIC4C using the CCP-UK to gather clinical information (data). Henceforth this network of hospitals was known as the Coronavirus Clinical Information Network (**'CO-CIN'**). The CO-CIN dynamic reports

and commissioned papers were produced by ISARIC4C for SAGE using data collected from the CO-CIN hospitals.

4.2. In 2012, ISARIC, with the World Health Organization (**'WHO'**), developed the ISARIC CCP. This is a study protocol designed to characterise an outbreak of a novel disease in great clinical, biological, and genetic detail, in time to inform clinical management and health policy during the outbreak of that disease and to save lives. I was one of several authors of the protocol. The protocol has been developed and refined over subsequent years. The generic protocol has ethical approval from the WHO. Country specific versions of the protocol have relevant ethical and regulatory approval **(MCS/02 [INQ000231462])]** . The protocol was first activated for MERS-CoV in 2013 and has been adapted and implemented in multiple outbreaks since, including Ebolavirus disease, Zika, yellow fever, tick-borne encephalitis, Lassa fever, Mpox, SARS-CoV-2 ('COVID-19'), severe acute hepatitis in children and severe enterovirus disease in neonates. I am Chief Investigator for the protocol in the UK. That is, I have ultimate professional responsibility for the study activities and am accountable to the study sponsor by contract for my conduct in regard to the activities described by the protocol. The protocol enables the collection of routine clinical information from hospital records (age, biological sex, ethnicity, pre-existing medical conditions, usual medication, vital signs on admission, new drug treatments in hospital, respiratory support required, complications experienced during admission, and status at day 28 of admission- i.e. discharged alive with/without new care needs, still receiving care in hospital, or deceased) and permits sampling of human material. This means the data collated can be analysed in a timely manner and the human material can be split and shared with research groups greatly accelerating discovery. The protocol is internationally harmonised, allowing global collation and analysis of data, again accelerating discovery.

4.3. Professor Dame Sally Davies (CMO for England from 2010 to 2019 and GCSA at the Department of Health, England from 2004 to 2016) required all acute NHS trusts in England (then around 120 trusts, each with one or more acute hospitals) to approve ISARIC's CCP-UK in 2013 when MERS and an emerging pathogenic avian influenza were considered a potential risk to public health. Dame Sally showed great foresight. Her action meant that a protocol was in place and approved "on the shelf and oven-ready" for use in the event of the emergence of a novel disease with pandemic potential. A portfolio of other pandemic protocols was commissioned and supported by

the National Institute for Health Research (**'NIHR'**). These "Pandemic Portfolio" studies were developed by other investigators, and the ISARIC/WHO protocol was listed among these as the 'ISARIC/WHO Severe Acute Respiratory Infection Biological Sampling Study' **(MCS/03 [INQ000231424])** , **(MCS/04 [INQ000231457])** . The other studies included drug trials (steroids & antivirals), the development of community and hospital triage tools and their evaluation, and observational studies of maternal & perinatal outcomes. With the exception of ISARIC's CCP-UK study, which was not commissioned by NIHR, but was adopted by NIHR, this portfolio was given funds for development, test activation, hibernation, and additional ring-fenced funds and priority support plans kept ready for activation for a future disease X pandemic. Widely known as the "Pandemic Portfolio", each study in the portfolio was given special status for priority support in the event of an outbreak **(MCS/05 [INQ000231514])** . Professor Colin Simpson and the other Chief Investigators of the Pandemic Portfolio described the studies in 2019 **(MCS/06 [INQ000146462])** and their activation in 2020 in response to COVID-19 **(MCS/07 [INQ000231453])]**. The development and maintenance of a portfolio of research studies in readiness for a future outbreak of disease of public health interest or a pandemic has to be one of the most important and successful pandemic preparedness measures taken by past policy makers. I wish to emphasize that it is my opinion that a similar portfolio of Pandemic Action Research Studies should be developed without delay, as at present the status of the portfolio is uncertain. The pandemic portfolio studies enabled actionable knowledge to be generated right from the start of the outbreak in the UK. This knowledge informed health policy and clinical management in the UK and many other countries, and this saved lives.

4.4. ISARIC's global CCP was developed by ISARIC Investigators in our own time. The ISARIC project was global and ambitious, and while we had some charitable funding to maintain the consortium office and pay for a consortium members meeting, we were not able to attract substantial funding for the UK study from UK funders. In 2015 Dr Gail Carson (the original Chief Investigator) and I had a pre-application enquiry meeting arranged with a Medical Research Council ('**MRC**') programme Manager in London. This was to discuss a potential application for a £50,000 grant to be spent over 5 years to maintain the CCP-UK in readiness for activation. The meeting was cancelled while we were both on separate trains to London, but we insisted on being seen. My recollection of the explanation for cancelling the meeting was that they did not consider there was a need for our proposed study in a future digitally connected

NHS. Not to be put off, Dr Gail Carson, Dr Jake Dunning, Dr Kenneth Baillie (now Professor), I and others continued to develop and maintain the protocol. Later we were able to source £5,000 of funding from each of the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections and the NIHR Health Protection Research Unit in Respiratory Infection. We never secured substantive funding until commissioned by the CMO via NIHR and by UK Research and Innovation **('UKRI')** via MRC for our work on COVID-19.

4.5. The ISARIC CCP-UK has been activated on several occasions, mostly at centres experienced in the care of patients with high-consequence infectious diseases, but not exclusively **(MCS/02 [INQ000231462])]** . This means that prior to February 2020 the NIHR's comprehensive research network based in NHS hospitals comprising research active doctors, research nurses, research administrators and research managers were at least vaguely familiar with the protocol and in some cases had hands-on involvement in using the protocol.

4.6. The pandemic potential of what was then known as Wuhan Flu was recognised by ISARIC members when onward transmission by humans was reported in districts outside of Wuhan in early January 2020 and then to neighbouring countries. ISARIC members in the UK had internal discussions in January 2020 that included colleagues in Public Health England (**'PHE'**), which included the challenges of handling clinical material for research purposes where the pathogen was classified as a High Consequence Infectious disease.

4.7. On the 17th of January 2020, there was a telephone discussion between me, Professor Sir Peter Horby (Chair of ISARIC's Global Consortium, and Chair of NERVTAG) and Dr Gail Carson (Director of Network Development for ISARIC and Vice Chair of the WHO's Global Outbreak Alert and Response Network (**'GOARN'**)). We considered the capacity of ISARIC investigators in the UK and abroad to activate the ISARIC WHO CCP in readiness for a likely pandemic of Wuhan Flu. We agreed that Peter would contact the CMO, Professor Sir Chris Whitty, and the Deputy Chief Medical Officer (**'DCMO'**), Professor Jonathan Van Tam, to recommend activating ISARIC's Clinical CCP-UK, noting that I was Chief Investigator. Professor Whitty agreed to activation, and I took the process forward **(MCS/08 [INQ000231446])** , (**MCS/09 [INQ000231416])** . In this act, we can evidence that in the UK Clinician Scientists and Public Health leaders were on the front foot to use science as a countermeasure to COVID-19.

4.8. Professor Jonathan Van Tam called me in the next day or so to ask if I could establish a CO-CIN of hospitals across the UK to provide a timely understanding of the disease and its impact on health and health services. I was able to agree to his request, offering the CCP-UK as an "oven-ready" solution **(MCS/02 [INQ000231462])** . I have since read "DCMO has established a system, CO-CIN, to catalogue data from cases of COVID-19." in minute 2 of SAGE meeting 11 on the 27th of February 2020 **(MCS/10 [INQ000075777])** , evidencing this action and flagging to SAGE that analysis of clinical data would soon be available.

4.9. Recognising the likely scale of the work involved, I identified the need to federate responsibility for parts of the protocol. I was fortunate to have as named collaborators on the protocol Professor J Kenneth Baillie of the Roslin Institute, University of Edinburgh and Professor Peter JM Openshaw of the National Heart & Lung Institute at Imperial College London. Professor Baillie was keen to lead on human genomic susceptibly and inflammatory response and Professor Openshaw on immunological response, allowing me to focus on the collation and analysis of the clinical information. So, in addition to my responsibility for the general conduct of the study and regulatory matters, I took responsibility for the collation, analysis, and presentation of the clinical data from CO-CIN, Professor Baillie led on genomics and Professor Openshaw led on mucosal immunology. Later we would further federate responsibility for virology, cellular and humoral immunology, microbiome, and follow-up studies to other investigators and other consortia such as the UK Coronavirus Immunology Consortium **('UK-CIC'**, Professor Paul Moss) and Post-hospitalisation COVID-19 study ('**PHOSP-COVID'**, Prof. Chris Brightling). On the 31st of January 2020 ISARIC CCP-UK recruited the first cases admitted to hospital in the UK. I have seen that it was noted in SAGE meeting 18 on the 23rd of March 2020 that the work of collating COVID-19 Clinical Information from the network (**CO-CIN**) of NHS hospitals had started **(MCS/11 INQ000052717** . Most of ISARIC Investigators' work in the UK was self-directed, with a broad interest in characterising the people severely affected by COVID-19, then understanding the pathophysiology, immunopathology and host-genetic features in people with severe disease. From ISARIC's inception in 2012, we had aimed to anticipate future health policy needs. Most of our work was not done in response to GCSA, CMO or SAGE commissions.

4.10. As the magnitude of our activity grew with the exponential increase of the pandemic, so our scientific power (statistical ability to make discoveries with confidence due to

the larger number of people being recruited and their greater number of samples being collected) to make discoveries quickly exceeded our capacity, and so we federated responsibility to other research groups and invited them to collaborate. From the earliest stage of our work, we shared samples and data with UK national public health agencies **('PHE'** and later '**UKHSA', 'PHS' & 'PHW')**, the agency with responsibility for making international standards (National Institute for Biological Standards and Controls, **'NIBSC'** and the UK Medicines and Healthcare products Regulatory Agency **'MHRA'**), those developing and validating Covid tests and the Oxford Vaccine Group. After some negotiation, we shared data with the European Centre for Disease Prevention and Control (**'ECDC'**) and WHO.

4.11. NIBSC developed five International Standards using material from our protocol [NIBSC products 20-118, 20-136, 20-268, 21-234 and 21-338]. These are: COVID-19 convalescent plasma panel, 30th April 2020 **(MCS/12 [INQ000231422])** ; First WHO International Standard for anti-SARS-CoV-2, 17th December 2020 **(MCS/13 [INQ000231420])** ; First WHO International Reference Panel for anti-SARS-CoV-2, 17th December 2020 (**MCS/14 [INQ000231419**]) ; Working reagent for anti-SARS-CoV-2 immunoglobulin and First WHO International Standard for antibodies to SARS-CoV-2 variants of concern (**MCS/15 [INQ000231417**]) and (**MCS/16 INQ000231418])** . These early International Standards were used to validate COVID-19 tests **(MCS/17 [INQ000231487])** and characterise the immunological properties of the Oxford ChAdOx1 nCoV-19 vaccine **(MCS/18 [INQ000231521]).**

4.12. Data collated from the 120 hospitals in England, and soon the 306 hospitals in the UK that comprised the CO-CIN, was analysed in near real time, initially every 30 minutes, and the output of this analysis was provided on a secure website, in effect an on-line dashboard. The content could be printed or saved as a "pdf" file to provide a dynamic snapshot for tabling in a bundle of committee papers. However, in most SAGE and NERVTAG meetings, where there was time, the live website would be viewed as this gave up to date information. A further snapshot would be made of the analysis as viewed by the group, by way of a pdf, and this would usually be preserved as a factual record of the committee papers. Examples of the Dynamic CO-CIN reports can be found in the GOV.UK 'Collection of Scientific evidence supporting the government response to coronavirus: Evidence considered by the Scientific Advisory Group for Emergencies' (**MCS/19 [INQ000236609**]) .

4.13. A draft Dynamic CO-CIN report was shared with Professor Jonathan Van Tam on the 10th of March 2020, reporting on the first 61 patients recruited **(MCS/20 [INQ000231476])**. Following review by Professor Van Tam, format revisions were made, and additional analyses were added. The first formal Dynamic CO-CIN report was sent on the 13th of March 2020 to Professor Van Tam, reporting on 101 patients, along with news that the report could be provided as a secure online dashboard for near real-time viewing **(MCS/21 [**INQ000151581**])**. The GCSA, Professor Patrick Vallance, provided feedback on the 14th of March 2020. Professor Van Tam asked me to present the CO-CIN analysis to SAGE on Tuesday the 17th of March 2020 in London and I came down and stood-by to attend, but I was not called, so I returned to Liverpool. I gather several other outbreak-related events took precedence, so the meeting planned for the 17th of March had been moved to the 18th of March 2020, but I was not called to attend. By the 22nd of March 2020, Professor Van Tam had reviewed the online live version of the Dynamic CO-CIN report. He asked me to add detail regarding levels of support needed by people admitted to intensive care, which was done by Professor Ewen Harrison's team at the Usher Institute at the University of Edinburgh over the next day. By the 24th of March 2020, access to the revised Dynamic CO-CIN report by a secure web-based online dashboard had (in addition to the CMO's office) been provided to SPI-M members. I was invited to present the Dynamic CO-CIN data report to SAGE meeting 19 on the 26th of March 2020 **(MCS/22 [INQ000119706])** by video conference and shared a pdf snapshot of the Dynamic CO-CIN report on 1464 patients from 22:00hr the night before (**MCS/23 [INQ000231480])**, though I see an earlier version reporting on 1383 patients from 16:00hr is in the collection **(MCS/22 [INQ000119706])**.

4.14. The Dynamic CO-CIN report formats evolved over time to meet the needs of SAGE and NERVTAG, though the general layout was fairly consistent. The snapshot pdfs of these reports are available at the collection of scientific evidence supporting the government response to coronavirus hosted by GOV.UK **(MCS/19 [INQ000236609])** , **(MCS/18 [INQ000231521**]) . Earlier reports began with an Executive Summary text in lay language. There followed a section describing hospital admissions with COVID-19 by sex over time, and in later reports, we provided graphics for outcomes grouped by sex and stratified by age both in total for the current wave and for those admitted >=14 days and <=28 days, the latter interval selected to give a window of information about the most recent hospital admissions along with their outcomes.

4.15. The next section described admissions on a map of the UK with circles of size relating to the number of admissions. This gives some geographic understanding of where the disease is, and as importantly, tells the reader how widely representative the data in the report is for people in hospitals across the UK.

4.16. Next, there is a section that describes the symptoms and signs (complaints described and features found) among those people admitted to hospitals for management of COVID-19, and those who acquired COVID-19 in hospital, and besides this their co-morbidities (current other diseases known at admission). Together these features are vitally important to describe and understand a new disease. Firstly, they allow us to sense check the "case definition" in current use. The case definition is the collection of features used by public health agencies to determine the incidence and prevalence of COVID-19, and indeed it was good enough during the early phase of the first pandemic wave, though not later as the virus changed. Secondly, the clinical details we collate identify those people most at risk of admission to hospital, and among those, the people most at risk of needing the highest levels of care, and the people most at risk of dying. This is key for forward planning. A lesson learned from similar work on characterising people admitted to hospital with Swine Flu in 2009/10 was that while it may appear obvious there will be considerable overlap in common features of people between these groups, there are often features that distinguish some people as being at particular risk of one particular outcome but not another, (such as the particularly high risk of admission but not death for people with asthma during Swine Flu 2009-10). Third, it is important to identify extremely high-risk individuals so as to best tailor their care in hospital. Later in the outbreak, when multiple novel medical interventions had been discovered, and vaccines rolled out, we found using this protocol and CO-CIN data, groups of people who remained at the very highest risk of severe COVID-19. (**MCS/24** **[INQ000231535])**.

4.17. In April 2020 a section was added to the Dynamic CO-CIN report describing the proportion of patients over time who experienced COVID-19 symptom onset after admission to hospital. This is described variously as; hospital-onset COVID-19, hospital-acquired COVID-19 or nosocomial COVID-19. The median (middlemost) period between exposure and symptom onset is called the "Incubation Period". The incubation period is usually a good surrogate for the onset of infectiousness, but this assumption was later found not to be true for COVID-19.

4.18. The median incubation period was believed to be 5.2 days at the start of the pandemic based on observational data pre-printed (**MCS/25** **[INQ000231421])** and only marginally revised to 5.1 days in the peer-reviewed published paper (**MCS/26** **[INQ000231425])**, but this was later found to be an overestimate.

4.19. The human challenge study (**MCS/27** **[INQ000231441**]) involved deliberately exposing 36 healthy volunteers with SARS-CoV-2, closely monitoring their health, and testing samples from their throats and noses for infectious virus. This was, by necessity, a small study, so the confidence in the results is moderate. The seed virus for this research was provided by ISARIC's CCP-UK study so I am familiar with the findings. 18 of the volunteers became infected. 16 (89% or around 9/10) experienced symptoms 2 to 4 days after exposure, much quicker than the median 5-day incubation period previously estimated from observational studies, meaning that the incubation period was shorter than previously assumed. 2 remained symptom-free despite being infected and infectious. Importantly, Killingley found the median time after exposure to detection of the virus (the pre-infectious period or latent period) in the throat was 1.67 days and from the nose was 2.4 days. This means that not only was the original estimate of the median incubation period too long but also the assumption that the onset of infectiousness coincided with the onset of symptoms was wrong. A substantial proportion of people are infectious before exhibiting symptoms. Based on virus detection, the infectious period began 2 days after exposure. Working backwards, in people with symptoms, 9 out of 10 were infected sometime in the period 2 to 4 days before symptom onset. I did not know this in April 2020, though I read later that a good report on the "Temporal dynamics in viral shedding and transmissibility of COVID-19" had been made in Nature Medicine on the 15th of April 2020 (**MCS/28** **[INQ000231538])** . Subsequent dominant variants of SARS-CoV-2 were recognised to have shorted incubation periods than the ancestral (Wuhan) strain **(** **MCS/29** **[INQ000231524])**.

4.20. I was asked by SAGE to provide four graphs on the Dynamic CO-CIN reports showing the proportion of people with COVID-19 symptom onset occurring after hospital admission, where admission to symptom onset was >= 2 days, >=5 days, >=7 days and >=14 days. These four graphs were requested because of the uncertainty of the incubation period during the early weeks of the pandemic response. With the benefit of the human challenge study, we can now report with greater confidence that the two graphical analyses using the onset of symptoms >= 2 days and >=5 days after

admission give a better dynamic estimate of the proportion of nosocomial cases over time.

4.21. 9 out of 10 people, who developed symptoms of COVID-19 four or more days after their admission to hospital for another reason, were infected in hospital. That is to say with regret, we can be confident that they had COVID-19 as a result of exposure to SARS-CoV-2 in the hospital setting. If we accept that acquiring COVID-19 is bad for a person, catching it in hospital is often worse for that person than if they caught COVID-19 in the community. While hospital patients may receive treatment quicker than those diagnosed in the community, they tend to be more vulnerable to poor and fatal outcomes, as they were already sickened by another disease when they caught the virus.

4.22. Two sections relating to patient use of hospital resources follow. A section labelled 'Patient Flow' described the patients' locations by ward and respiratory support by days from admission. Another section was labelled 'Oxygen requirement'. It was not a good label, as the section was rapidly developed to describe much more than just oxygen requirement, but we kept the label for consistency. This section describes the placement of patients on their first day of admission as one of two categories, either a general ward ('ward') or high dependency unit / intensive care unit ('**HDU/ICU**') and their placement on any subsequent day, followed by their maximum treatment need and outcome. Despite Oxygen gas ('**O_2**') probably being the most commonly used drug in hospitals, the recording of routine low flow (<6L/min) oxygen administration typically by nasal cannula is often not made in patient medical notes and is typically not considered as needing to be prescribed. So, interpretation of the Patient Flow graphic requires caution, as many patients appear to not need oxygen when in reality, they are receiving low-flow oxygen, but this is not recorded well. The administration of high-flow oxygen involves specialist equipment and so is usually recorded accurately. Two modes of ventilation are captured: non-invasive and invasive. Non-invasive ventilation involves the use of pressure (which may be varied) in addition to additional oxygen by way of a tight-fitting nasal mask, face mask, or fitted hood. This allows the patient some autonomy and ability to move, by remaining free of the sedative and anaesthetic drugs required for invasive ventilation. Invasive ventilation involves placing a tube within the patients' trachea (the tube from the back of the throat that leads to the lungs) and then supporting breathing by additional cyclical pressure and additional oxygen. Because a tube is placed into the trachea, where the normal reaction is to cough, and touches

the back of the throat where the natural reaction is to gag, sedative and anaesthetic drugs need to be given to people who receive invasive ventilation. This reduces their autonomy, and ability to move, and vastly increases their care resource needs, including the need for one-to-one or two-to-one nursing and dedicated use of a mechanical ventilator. I understand that this section and the data that derived the graphic was particularly useful in the first months of the UK outbreak for the four National Health Services (NHS England, NHS Scotland, HSC Northern Ireland and NHS Wales), in that it described the type and magnitude of care needs that would be needed in the coming weeks, and then at the start of each subsequent wave of infection caused by a new variant, the previous assumptions could be checked, and next plans refined.

4.23. Further graphics follow that show use of resources by age. These illustrate that different resources were favoured by clinicians for use in different age groups. For example in the Dynamic CO-CIN report to SAGE and NERVTAG (all cases) – 17th December 2020 (**MCS/30** **[INQ000231469])** it can be seen that over the course of the first two waves of the outbreak in the UK fewer elderly people were admitted to critical care units (ICU/HDU) and fewer were supported by invasive mechanical ventilation than were represented by the population in hospital (page 11 of 22 figure 10 upper left panel and lower right panel) with the commoner age range for being admitted to ICU/HDU and receiving invasive ventilation being around 60 to 65 years. The commoner age for receiving high-flow oxygen is between 80 and 90 years (figure 10 upper right panel), and the commoner age for non-invasive ventilation is between 60 and 80 years (figure 10 lower left panel). I understand that in many circumstances there are good reasons for this allocation of care. For example, a frail elderly person may not tolerate invasive mechanical ventilation which causes physiological stress and in addition, the predictable loss of muscle bulk and physical deconditioning associated with days of immobility during invasive mechanical ventilation, would condemn that person to loss of any residual independence and most likely lead to death on the ventilator. However, in some cases one wonders if due to resource constraints (such as ICU capacity), decisions were sometimes made based on patients' age to place a limit on the escalation of care, and this could be explored with experts in adult intensive care and their representative professional societies.

4.24. Lastly, data was presented in graphic format to show the length (duration) of admission in people grouped by outcome (those discharged alive or those who died) and stratified

by age. I understand this information was very useful in understanding current resource use in near-real-time and planning subsequent needs.

4.25. Thereafter, at nearly all SAGE and NERVTAG meetings, at the start of the meeting during the situation report, I would present the Dynamic CO-CIN report by video conference, screen-sharing the online dashboard and bringing to the attention of the group, particular features of interest and then take questions on the data. The details of these SAGE meetings and minutes, and links to the documents, were provided in my first Rule 9 questionnaire response and are listed in an Excel spreadsheet (**MCS/31** **[INQ000231437])**.

4.26. The collection of data for CO-CIN was well resourced in terms of money provided by the Department for Health and Social Care (**'DHSC'**) to the University of Liverpool and the Department of Health of Scotland to the University of Edinburgh to pay for NHS research costs. We were rapidly commissioned and originally funded to analyse 1000 cases in a first wave and a further 1000 in a subsequent second wave if there was one, over a six-month period (**MCS/32** **[INQ000231427])**. Instead, we operated over two years and analysed over 303,000 cases. It is not surprising that my cost model and my staffing assumptions in the original proposal were inadequate, given my team did 151 times more work than first expected. DHSC England and Department for Health Scotland asked me to continue the work of CO-CIN and did permit remodelling of the staff profile with additional analytical and administrative support subject to contract variations. Contract variations take time. This meant that academic resources worked "in-trust at-risk" often for months beyond the contract whilst the variations to contracts were agreed. This was uncomfortable for me and our institutions, but I cannot see how it could be done better under the circumstances of the period and I have no criticism to make. Other studies on the pandemic preparedness study portfolio had, as part of their award contract, access to funds triggered by pandemic activity. ISARIC's CCP-UK did not, as it had no pre-pandemic enabling award contract with a UK funder such as NIHR or UKRI MRC pre-award funding.

4.27. ISARIC's CO-CIN activity had to be rapidly commissioned by the CMO's office through the NIHR. This was done at pace. However, the question as to why ISARIC's protocol was not funded in preparedness is important to address. In October 2015 Dr Gail Carson and I visited one of the UK medical research funders in their London headquarters to seek preliminary advice on funding before formal application. My recollection of that short meeting was that we were told that they did not consider there

was a need for our proposed study in a future digitally connected NHS. In 2023 we still do not have a digitally connected NHS. We are still missing the digital-data equivalents of telephone exchanges that should connect all hospitals, GPs, walk-in centres, out-of-hours facilities, dentists, and national immunisation databases, to name but the core of NHS activities. As such, the UK's ability to collate and analyse information at scale, and in a timely manner for the benefit of public health or individual protection, remains limited. During the COVID-19 outbreak, our group relied on manual data entry from all but 1 of 306 NHS trusts. The one site that worked hard to provide digital upload could not, for technical reasons, provide key clinical information (such as vital signs, oxygen saturations and oxygen use at admission), and was not able to transmit key demographic, clinical information and outcome data from their digital records in time to contribute to our analysis. In a best-case scenario, it will take weeks to approve and then connect a new digital pipework that allows data to flow.

4.28. CO-CIN was uniquely placed to collate, analyse and share both raw data and our interpretation of the data. In the first few months of the outbreak in the UK, CO-CIN was vital, providing data and analysis to Cabinet Office, SAGE, SPI-M, NERVTAG, and the four national public health agencies. My understanding is that CO-CIN was the only detailed source of clinical data on people admitted to hospital (age, sex, and ethnicity), their health needs and resource use, and their outcomes for wave one. For the first few hundred cases, we collated data on nearly all cases, about two thirds of all cases in wave one. By the end of wave two we estimated we represented one third of all admissions, so were confident that our data were representative. That is to say, the analysis could be used to generalise on COVID-19 activity in hospitals. During the third wave non-COVID-19 research and medical school activities had restarted. This reduced the size of the pool of research nurses and medical students available to collect the information from patient notes, so we purposely moved to enrol every tenth patient at sites where research resources were limited. Nonetheless, due to the number of cases that continued to be admitted, we remained reasonably confident that our data was generalisable but had to take greater care with our statistical analysis. On occasion, this meant delays in producing analysis due to the need to collate sufficient cases to provide acceptable statistical power and avoid false discovery.

4.29. All research studies have limitations, and it is important to understand how these might affect an analysis. We did not collect data on the inpatients that were not enrolled, or people managed in community settings, such as usual domestic residences and older

people's care homes. We are unable to comment on community risk factors that drive or protect from hospital admission (such as vaccination) except by inference from expected representation at admission and self-reported health conditions at admission, (the problems in linking to community health care data and vaccination are discussed below). A large amount of data was missing in the early growth phase of wave 1 and we suggest there are two main reasons for this. Firstly, enrolment occurred in the nonlinear growth phase of the outbreak when outcomes for recent admissions (the majority) were not yet reported. Secondly, the research network was dealing with unprecedented numbers of patients at a time when many were seconded to clinical practice or were themselves off sick. It is possible that the sickest patients were enrolled in our study. We thought this could partly explain the early high mortality rates we observed in hospitals, but others have confirmed our findings. Some of the sickest patients in the study had the longest lengths of hospital stay. If the sickest patients were enrolled, this could bias our analysis of resource use.

4.30. Access to national datasets was very delayed despite support from SAGE and BEIS. We got access to NHS Secondary Uses Service (**'SUS'**) in February 2022. We only got access to the National Immunisation Management System on a single occasion in June 2021. Despite proper requests with SAGE support, we were not able to get access to Primary Care (General Practitioner and Community Care) records from the main electronic health record providers, Egton Medical Information systems **('EMIS')**, The Phoenix Partnership **('TPP')**, NHS Datastore, Pillar One and Pillar Two COVID-19 testing, and National Cancer Registration and Analysis Service.

4.31. This problem of access to primary care data for linkage to CO-CIN data was not unique to the ISARIC CCP-UK. I lead another pandemic-prioritised urgent public health research study ('**FLU-CATs**') that was designed to validate an NHS Community Assessment Tool for triage during the early phase of a pandemic (**MCS/33 [INQ000231548]).** The study was set to run rapidly over a few weeks, in time for the tool to be ready for use in 'surge', where healthcare seeking behaviour exceeds healthcare capacity. The case of need is obvious and so the FLU-CAT study was well funded and supported by the NIHR. We maintained seasonal activations to keep the engine running. That study depended wholly on unfettered access to anonymous primary care data. Despite prior agreements, Research Ethics Committee **('REC')** and Health Research Authority **('HRA')** approval, and specific approval under section 251 of the National Health service Act 2006 **('The NHS Act 2006')** and regulation 5 of the

Health Service (Control of Patient Information) **('COPI')** Regulations 2002 that predated the COVID-19 pandemic, TPP, a major provider of electronic health records (**'eHRs'**) determined that the Secretary of State's COPI notice did not apply to them as data processors. This was an irrelevant decision as we already had a prepositioned project- specific approval under section 251 of the NHS Act 2006 and regulation 5 of the COPI Regulations. TPP later declared that in any case, they were not in a position to support our research project due to other pressures. EMIS, the other major provider of eHRs, had also agreed to support that project and they co-developed the national GP consultation template for COVID-19 with us during early 2020, so our relationship with them appeared strong. But EMIS experienced competing pressures to retool their solutions for a variety of purposes and later withdrew from providing data directly to all research teams. Instead, EMIS provided data to NHS-Digital in what would become the General Practice Dataset of Planning and Research, but its implementation was significantly delayed, and it did not cover the full dataset we required. OpenSAFELY is a highly secure, transparent, open-source software platform for analysis of electronic health records data derived from primary care. It got access to the EMIS data on the 13th of June 2023, so our work in validating a community-based triage tool has only just begun and will be of no value to managing COVID-19, and have no impact.

4.32. A matter of interest to the CO-CIN work was to establish a robust denominator of hospital admissions against which to reference our data. That is an independent value for all hospitalisations ideally stratified by age and sex. We requested the all-England COVID-19 hospitalisation data from three different "front doors" to the NHS COVID-19 datastore and none provided the data, including Health Data Research UK **('HDRUK')**, the UK's National Institute for Data Science that was established to convene access to UK Health Data. Limited access to summary UK Hospitalisation data, which we linked to community testing data, was provided through an unrelated NIHR research project in July 2021 after a 7-month delay. Equivalent data were available to us in near real-time from one regional integrated data system, Cheshire and Merseyside's Combined Intelligence for Public Health Action (**'CIPHA'**)(**MCS/34** **[INQ000231523])**. A national federation of regional data platforms like this could accelerate policy-shaping intelligence in urgent public health situations.

4.33. A lesson learnt from the pandemic is that there are great advantages in establishing regional data platforms where health (community, hospital and public health), social care and civic administrative data can be housed and linked and used for multi-agency

intelligence production in a trusted data analytic environment. Such data platforms or hubs are designed to serve local needs and are locally governed providing confidence in their purpose, hence federated. These regional power stations of data can be linked with care to provide a 'national grid' of health and social data.

4.34. An agile and effective example of a regional integrated data and intelligence platform is CIPHA **(MCS/34 [INQ000231523])**. Prior to 2020, and under the leadership of Professor Iain Buchan of the University of Liverpool, Cheshire and Merseyside was planning CIPHA across NHS, local government, and University partners. CIPHA is a population health management platform for work across health and social care. This platform was rapidly commissioned in the first three months of 2020 to help the health and care system manage the Coronavirus crisis, later including local test and vaccination data, ultimately driving Merseyside to an early recovery, and allowing the safe opening of our cultural economy **(MCS/35 [INQ000231491])**,(**MCS/36 [INQ000231500]).** ISARIC was able to link CO-CIN data with CIPHA data in under two weeks.

4.35. The SUS is the single, comprehensive repository for healthcare data in England which enables a range of reporting and analyses to support the NHS in the delivery of healthcare services. Access to SUS data was only achieved in February 2022, one month before the collection of data for CO-CIN closed.

4.36. Our application to access the National Cancer Registry data commenced in August 2020 and at present we have still not had access to the data. The vaccine rollout began on the 8th of December 2020, and despite direction from the UK GCSA in SAGE, ISARIC's CO-CIN team only got "backdoor" access to National Immunisation Management system data on a single occasion in June 2021.

4.37. The OpenSAFELY initiative led by Professor Ben Goldacre has been a positive development and allows access to some retrospective data needed by ISARIC's CO-CIN for follow-up work. As I mentioned at paragraph 3.31, OpenSAFELY is a highly secure, transparent, open-source software platform for analysis of electronic health records data derived from primary care. It is a partnership between NHS England, the University of Oxford, the London School of Hygiene and Tropical Medicine, TPP and EMIS, but it is in its infancy. The reality is that during the key period of the first two years of the pandemic, despite our and others' best efforts, ISARIC's CO-CIN work was not linked to primary care data. This limited our ability to understand the importance of prior community prescribing and underlying health issues (co-

morbidities) on the severity of COVID-19. This deficit also added greatly to the burden of work for the 2648 nurses and medical students who were our army of data collectors.

4.38. When data was collated from the CO-CIN, it was made available immediately for external analysis by modellers in SPI-M and public health agencies via a secure application programming interface (**'API'**). SPI-M and public health analysts had direct access to the raw uncleaned data from CO-CIN, and produced their own reports to SAGE, NERVTAG and SPI-M using this data and several academic publications (**MCS/37 [INQ000231526])**, (**MCS/38 [INQ000231544])**, (**MCS/39 [INQ000212082])**, (**MCS/40 [INQ000231423])**, (**MCS/41 [INQ000231498])**. Bespoke analysis conducted by the ISARIC Investigators, their collaborators, members of SPI-M and public health agencies were submitted for reading at SAGE and NERVTAG. Not all submitted papers were tabled for reading due to time constraints and new events taking precedence. These papers which were not read were put into a repository as "papers of interest". However, it was my experience that members of SAGE were encouraged by Sir Patrick Vallance to raise key figures or points of note that they felt were critical to the knowledge of SAGE and direct the committee members to all reports, even when not formally tabled for reading. Sometimes this would lead to further discussion such that a paper that was originally destined as a paper of interest would be read in full.

4.39. As I have previously indicated at paragraphs 1.4 and 1.5, I am not in a position to comment on how CO-CIN's findings were used to inform policies and interventions.

5: Inequalities

5.1. It is a mistake to say that the infectious diseases which cause pandemics do not discriminate. They do, and they typically discriminate against extremes of age, specifically by sex, and greatly by ethnicity and deprivation. Those working in the field of public health, or who have an interest in the medical management of outbreaks, understand that inequality plays an important role in increasing risk of infection, risk of adverse outcome and risk of adverse social impact. The case report form that was prepositioned by ISARIC for global use just prior to the COVID-19 pandemic and was used in January 2020 for the first COVID-19 cases in the UK and Wuhan, collected anonymised routine clinical demographic data that included age, sex and self-reported ethnicity.

5.2. ISARIC's protocols and case report forms are harmonised to allow rapid collation around the world and direct comparison between countries. For this reason, ISARIC chose to use an internationally applicable scheme for ethnic classification, with people's ethnicity characterised as East Asian, South Asian, West Asian, Black, White, Arab, Latin American, Aboriginal/First Nations and Other (**MCS/42 [INQ000231486])**. For analysis in the UK, based on the distribution of UK patients by ethnicity and by nation, the collective ethnicities were collapsed further into South Asian, East Asian, Black, Other Ethnic Minority (all of West Asian, Arab, Latin American, Aboriginal/First Nations, and Other) and White. CO-CIN reports included counts of hospital admissions by ethnicity from the 1st of April 2020 (**MCS/43 [INQ000231481])**. The paper "CO-CIN: Ethnicity and outcomes from COVID-19 in UK hospital patients using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study" (**MCS/44 [INQ000231470])** was tabled for SAGE meeting 39 on the 28th of May 2020 **(MCS/45 [INQ000119951])**, but was not able to be considered due to pressures of time, so is not mentioned in the minutes of that meeting. My recollection is that it was mentioned at meeting 38 (**MCS/46 [INQ000075421])** that the next SAGE meeting would have time to focus on ethnicity. In this, our first paper devoted to the topic, we investigated ethnic variations in the risks of critical care admission, invasive mechanical ventilation (IMV), and in-hospital mortality, among UK hospitalised patients with COVID-19 **(MCS/43 [INQ000231481])** . This was an important and very early paper on this topic. We found that ethnic minorities in hospitals with COVID-19 were more likely to be admitted to critical care and receive invasive mechanical ventilation than white patients, despite similar disease severity on admission and duration of symptoms. South Asian patients were at greater risk of dying, at least partly due to higher rates of pre-existing diabetes. That paper included the following advice: "South Asian people are over-represented in frontline key worker occupations, and policies should consider shielding advice regarding at-risk patients." **(MCS/43 [INQ000231481**]) . The paper's major finding (a 20% increase in the chance of death among hospitalised COVID-19 patients of South-Asian background after adjusting for other risk factors including age, gender, comorbidities, and available markers of social deprivation) was discussed in SAGE meeting 40 on the 4th of June 2020 (minute 23) **(MCS/47 [INQ000120526])** and we were asked to continue to explore this issue. This paper was submitted to the Lancet, a peer-reviewed medical journal, for rapid publication but not accepted **(MCS/48 [INQ000231509**]) due to one adverse review that took a political position on our findings. The reviewer claimed (falsely) that we were

supporting biological determinism (a discredited racist belief that human behaviour is directly controlled by an individual's genes or some component of their physiology, generally at the expense of the role of society and environment) without addressing the validity of our analysis. In fact, we took no such belief-based or belief-biased view, only presenting observed data and explaining that despite our best efforts to control for known confounders (e.g., age, sex, multiple deprivations, and known co-morbidities), we could not explain the disproportionate poor outcome in some ethnic groups. In response, we bolstered our analysis with more data and published six papers in other journals that included ethnicity in the analysis, and which attributed much but not all of the excessive poor outcome to excessive pre-existing multi-morbidity in some ethnic groups (**MCS/48 [INQ000231509])**, (**MCS/49 [INQ000231537])**, (**MCS/50 [INQ000231528])**, (**MCS/51 [INQ000231539])**], (**MCS/52 [INQ000231460])**, **(MCS/53 [INQ000231515])** , (**MCS/54 [INQ000231488])**. Over subsequent waves, we were able to observe subtle differences in the magnitude of risk and at times the order of ethnic groups most at risk of severe disease, but these subtle changes, while interesting, did not in my opinion and that of SAGE dictate a need to change advice to policymakers beyond that already given, except to reinforce those elevated risks persisted for some ethnic groups.

5.3. Extremes of age present a risk to people through several mechanisms. The immune system of an infant is naïve and if born prematurely does not benefit from the placental transfer of antibodies that occurs in the latter weeks of pregnancy. Infants' small airways present a particular challenge when infected. Serious illness in infants is often recognised late in the disease process. The immune system in elderly people is less agile and older people are more likely to have multiple underlying medical conditions. That combined with social isolation puts the frail elderly at particular risk. From the 1st of April 2020 **(MCS/43 [INQ000231481])** , Dynamic CO-CIN reports included a multivariable logistic regression analysis for death (adjusted odds ratio plot) which uses real data to illustrate the relative impact one risk has in comparison to all other risks. The accuracy of this analysis improves with more data. Even from the early Dynamic CO-CIN report of the 1st of April 2020 **(MCS/43 [INQ000231481])** , the increased risk associated with age and male sex is observable.

5.4. It might surprise people to hear that biological sex has an impact on the risk of severe disease. Even in infancy, male infants are more at risk than female infants of having severe respiratory viral disease that needs supplemental oxygen or mechanical

ventilation (**MCS/55** **[INQ000231529])**. Thus, data on sex were collated by ISARIC from the CO-CIN network, and the stark impact of male sex on poor outcome was quickly described in our early reports to SAGE and NERVTAG.

5.5. We did not record postcode at the start of the UK outbreak as postcode is a personal identifier, for which regulatory approval and consent would be required for collection, and at activation in January 2020 our study relied upon collection of routine anonymised health data without consent. In any case, postcodes being such a strong personal identifier, when collected alongside confidential health information would likely be a hindrance to gaining consent. From the 23rd of April 2020, following Research Ethics Committee approval and changes in the regulatory framework enabled by the COPI 3(4) Notice, we were able to collect limited personal identifiers without consent including date of birth, postcode, NHS number in England and Wales and CHI number in Scotland. We did not collect Northern Ireland Health and Care numbers. Collection of this personal information was vital to allow understanding of multiple deprivations at local community level, and later in the pandemic would allow linkage to other health data sets such as immunisation records. Data on deprivation derived from postcode was included in the CO-CIN paper "Ethnicity and outcomes from COVID-19 in UK hospital patients using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study" **(MCS/44 [INQ000231470])** tabled for SAGE meeting 39 on the 28th of May 2020 **(MCS/45 [INQ000119951])** .

5.6. ISARIC's case report forms (they evolved during the pandemic) did not gather information on self-declared disability status but did gather extensive detail on co-morbidity (underlying medical problems) and frailty (**MCS/56** **[INQ000231454])**. As such disability as a status did not feature in CO-CIN reports, but co-morbidity did, including in our dynamic analysis that explored risk of death. Regarding protected characteristics, CO-CIN data by design did not include data on self-declared gender, sexual orientation, marriage or civil partnership, or religious belief. ISARIC's CCP (**MCS/02** **[INQ000231462])** was a research study whose primary aim was to characterise emerging infectious disease. All data points collected had to be justified to the NHS Research Ethics Committee on a reductionist basis and take into consideration any risk of disclosure leading to harm and breach of duty of confidentiality.

5.7. The role of inequalities, particularly those associated with age, sex, ethnicity, deprivation, and multi-morbidity, was well known to SAGE. Evidence on these topics was presented by ISARIC to SAGE at meeting 39 on the 28th of May 2020 **(MCS/45 [INQ000119951])** and meeting 40 on the 4th of June 2020 **(MCS/57 [INQ000142134]),** (**MCS/58 [INQ000231456]),** **(MCS/50 [INQ000231528]).** Other groups presented papers on ethnicity, and these are references in the minutes of these two SAGE meetings and are available to interested parties in the collection. There are extensive minutes on the subject made in SAGE meeting 40, including six actions (**MCS/47 [INQ000120526]).** An ethnicity sub-group was later established. I am therefore sure that inequalities were identified and considered by ISARIC using CO-CIN data and by SAGE. I am not able to comment on the considerations of policy makers nor those of the core political or administrative decision makers with regard to the COVID-19 response.

5.8. With regards to understanding what impact the evidence produced by CO-CIN and others on the topic of inequalities had on the policy response to COVID-19, including Non-Pharmaceutical Interventions, I am not in a position to comment on the considerations of policy makers nor those of the core political or administrative decision makers.

6: Children

6.1. The work of ISARIC's CO-CIN was all hospital based. It did not include the study of transmission in the community, where nearly all children acquired or transmitted COVID-19, so I am not able to comment on transmission by children. Our group did take great interest in the impact of COVID-19 on children admitted to hospital.

6.2. We characterised COVID-19 disease in children (those under 19 years old) in the early stages of the pandemic and were invited to support colleagues in China in doing the same. In the UK we illustrated the numbers of children admitted to hospital in proportion to other ages in the demographic sections of all CO-CIN reports and in rapidly published peer reviewed publications **(MCS/59 [INQ000231492]), (MCS/60 [INQ000221983]),** **(MCS/61 [INQ000231543])** , **(MCS/62 [INQ000231522]).**

6.3. This data was useful to many as it illustrated that children comprised less than 1 in 100 COVID-19 admissions (651 children out of 69,519 people between 17th January and 3rd July 2020), though around 1 in five of these admitted children needed critical care

(high dependency and intensive care). One in five children were admitted "with COVID-19" rather than "for COVID-19" (**MCS/62** INQ000231522]) Mercifully, death of children is a rare event in any case, and we showed that death in children admitted with COVID-19 was a rare event in wave one, compared to death due to COVID-19 in adults in the same period.

6.4. We described the clinical characteristics of children and young people admitted to hospital with COVID-19 in the United Kingdom and how these differed from the features of COVID-19 in adults (**MCS/61** **[INQ000231543])** . Most important, children (people aged less than 19 years) were much less likely to be admitted to hospital than adults, comprising 0.9% (651 children from a total of 69 516 people) of the CO-CIN cohort enrolled between 17th January and 3rd July 2020. Next their outcomes were in general much better than adults. In Dr Swann's report 1% (6 from a total of 651 children) of the children had died, 89% (557 from a total of 627 children) had been discharged alive, and 10% (62 from a total of 627 children) were still in hospital. In comparison, adult fatality in the CO-CIN cohort was 26%.

6.5. Children's symptoms at presentation were different to adults. Children's symptoms clustered in three distinct groups: a) headache, myalgia, sore throat, vomiting, abdominal pain, diarrhoea, fatigue and rash b) cough, fever, shortness of breath, lower chest wall indrawing, runny nose and wheeze, and c) seizures and confusion. In comparison, symptoms in adults clustered in two groups, a homogenous collection of: a) headache, chest pain, diarrhoea, vomiting, abdominal pain, cough, wheeze, shortness of breath, fever, and fatigue and b) seizures and confusion.

6.6. We did identify that around 1 in 10 children admitted to hospital with COVID-19 had a novel Multisystem Inflammatory Syndrome temporally associated with COVID-19 ('**MIS-C**') as defined by the WHO (**MCS/61** **[INQ000231543])** , **MCS/63** **[INQ000231438]**). These children suffered a severe systemic mucocutaneous-enteric cluster of symptoms, including fever, conjunctivitis, oral mucositis and ulceration, shock, myocardial dysfunction, coagulopathy, diarrhoea, vomiting, and abdominal pain. Some of these children required the highest levels of care. While most children admitted to hospital with COVID-19 avoided the need for critical care, children with MIS-C were five times more likely to be admitted to critical care (73% v 15%).

6.7. We later compared the differences in disease in children admitted to hospital between first, second and third pandemic waves and presented this to SAGE meeting 95 on the 9th of September 2021 **MCS/64** **[INQ000220188])**, and again for the third wave

(Omicron) to SAGE meeting 102 on the 6th of January 2022 **(MCS/65 [INQ000231468])** and SAGE 103 on the 13th of January 2023 **(MCS/66 [INQ000231475])** so as to understand the impact of Omicron on children. The comparison between wave 1 and wave 2 was later peer-reviewed and published **(MCS/62 [INQ000231522])**. These analyses were important because of anecdotal reports from other countries that children and young people ('**CYP**') were being more severely affected in subsequent waves of the pandemic. Our key findings were: around 1 in 5 children admitted to hospital had asymptomatic/incidental SARS-CoV-2 infection, that is to say they were admitted for another reason and were found to be infected with the virus, and not admitted because of COVID-19 (the disease cause by the virus). Patients in wave 2 were significantly older (median age 6.5 years) than wave 1 (median age 4.0 years). Fever was more common in wave 1, otherwise presenting symptoms and comorbidities were similar across waves. There was no change in the proportion of CYP admitted to critical care between wave 1 and wave 2. MIS-C remained responsible for a large proportion of critical care admissions, invasive and non-invasive ventilatory support, inotrope and intravenous corticosteroid use in CYP without comorbidities. We repeated the comparison using data for wave 3, though the scope of this analysis was limited as we only enrolled one-in-ten cases and CO-CIN closed to enrolment on the 28th of February 2022. There were proportionally more infants (<1 year) in data for the 4 weeks (14th December 2021 to 12th January 2022) compared with prior periods (42.2% vs 30.8% previously). A greater number of hospital admissions from the most deprived socioeconomic groups was seen in the most recent 4 weeks (43.5% vs 32.6% previously), with no strong difference in the distribution of socioeconomic status across age groups. No other strong signal of a change in patient characteristics, severity, or management was seen.

6.8. We have studied the sequelae of COVID-19. Our group collaborated with others to describe the risk factors for post-COVID-19 syndrome (aka long COVID) in previously hospitalised children **(MCS/67 [INQ000231432])**. Median (and Inter Quartile Range) follow-up time since hospital admission was 268 (233–284) days (i.e. around 9 months). The prevalence of the symptoms present at the time of discharge declined over time. At the time of the follow-up interview, parents of 25% of children reported at least one persistent symptom, with fatigue in 11%, insomnia in 5%, disturbed smell in 5% and headache in 4% being the most common. Older age, pre-existing allergies, excessive weight and obesity were risk factors for persisting symptoms in children.

6.9. We continue to study the sequelae of COVID-19 in children and collaborate with the Long Covid in Children and Young People (**'The CLoCk Study'**), led by Professor Terence Stephenson **(MCS/68 [INQ000231546])**.

6.10. The activity of ISARIC's CO-CIN did not extend to opining on Non-Pharmaceutical Interventions. As I previously indicated in paragraphs 1.4 and 1.5 I am not in a position to comment on how policies and the Covid-19 response, including Non-Pharmaceutical Interventions, were informed by our work on COVID-19 in children.

7: Nosocomial (Hospital Acquired) Infections

7.1. I was not a member of SAGE until meeting 19 on the 26th of March 2020, and at the time did not presume that I would become a regular attendee. The minutes from previous meetings were not made available to me until they were published publicly. On reading the minutes from the Precautionary SAGE meeting held on the 22nd of January 2020 **(MCS/69 [INQ000106047])**, it is clear from line 19 of the minutes, that the risk of SARS-CoV-2 transmission within healthcare settings with subsequent development of COVID-19 was suspected. There were precedents for this with the documented transmission in hospitals of the Middle East Respiratory Syndrome (**'MERS'**) coronavirus in Saudi Arabia and South Korea, causing hospital outbreaks. Acquiring an infection while being treated in a hospital for another reason is known as nosocomial infection. Nosocomial infection can be devastating for a patient, already weakened by their original illness. It is also a shameful event for attendant healthcare professionals to witness, offending their principle *primum non nocere,* that is "first, do no harm" {Hippocrates, Of the Epidemics circa. 400 BCE) **(MCS/70 [INQ000231534])**.

7.2. The presence of nosocomial (within hospital) transmission is first noted in minute 6 of SAGE meeting 14 on the 10th of March 2020 **(MCS/71 [INQ000109125])**. It is not clear what the source of this clinical information was, or what the size of the problem of nosocomial infection was. The draft CO-CIN report that I provided to Professor Jonathan Van Tam on the 10th of March 2020 **(MCS/20 [INQ000231476])** included 61 recruited hospital in-patients but did not provide analysis for nosocomial infection as I was not aware of the problem at that time or SAGE's interest in it. In any case, at that time there would have been too few cases in CO-CIN to allow analysis. An action from SAGE meeting 14 was to establish the COVID-19 Hospitalisation in England Surveillance System **('CHESS')** that would report daily **(MCS/72 [INQ000119666])**.

This reporting system included date of admission and date of symptom onset, so would have the capability to identify nosocomial infection, where date of admission preceded the date of symptom onset by a period greater than the incubation period. CO-CIN had been doing this since the first patient enrolled on the 31st of January 2020, so had a head start on data acquisition, but as I will say, we had not developed the analysis on the 10th of March 2020.

7.3. On the 16th of March 2020 at SAGE 16, in the situation update section, minute 6 records "London has the greatest proportion of the UK outbreak. It is possible that London has both community and nosocomial transmission (such as in hospitals)" **(MCS/73 [INQ000075664])**

7.4. On the 18th of March 2020 at SAGE 17, in minute 29, nosocomial transmission is noted as possibly contributing to hotspots of spread in the Derby, Nottingham and Leicester areas, however, the size of the problem and source of this information is not clear **(MCS/74 [INQ000075778])**.

7.5. On the 23rd of March 2020 at SAGE 18, in the situation update section, minute 10 notes evidence of nosocomial clusters of transmissions based on genome sequencing **(MCS/11 [INQ000213096])**.

7.6. I attended SAGE 19 for the first time on the 26th of March 2020 and heard that among urgent priorities for providing data and analysis to SAGE to inform policy advice were "nosocomial transmission, risk markers for severe disease and severity scoring for COVID-19", noted in minutes 2 and 7 **(MCS/75 [INQ000119726])**. These were matters that ISARIC's CO-CIN was able to address, and I took this challenge back to my group for development. Minute 40 notes that the agenda for a SAGE meeting planned for the 31st of March 2020 would include nosocomial transmission **(MCS/76 [INQ000221758])**.

7.7. SAGE next met on the 29th of March 2020 (SAGE 20) but did not discuss nosocomial transmission. That meeting identified a need for information on patients' age (minute 3 and 16) and duration of admission to intensive care units (minute 4) **(MCS/76 [INQ000221758])**, a matter which ISARIC's CO-CIN could and would address in future Dynamic CO-CIN reports, but that the Intensive Care National Audit and Research Centre (**'ICNARC'**) led by Professor Kathy Rowan was best placed to address and already had in hand. After discussing with Professor Jonathan Van Tam, I passed the request to Professor Rowan and introduced her to Professor Van Tam. In the

meantime, the Dynamic CO-CIN added analysis on the duration of admission to intensive care units stratified by patients' age.

7.8. At 09:30 on the morning of the 31st of March 2020, the Dynamic CO-CIN dashboard included 3354 participants, and our first attempt at analysis of nosocomial cases over time showed a steep and sustained rise of the proportion of these cases, beginning around the 10th of March from when we had recruited 61 cases. After our analysts, led by Professor Ewen Harrison and Dr Annemarie Docherty at the University of Edinburgh, conducted additional checks, I alerted Professor Van Tam by WhatsApp **(MCS/77 [INQ000231443])** and Email **(MCS/78 [INQ000231444])** to raise his urgent attention to the matter and he responded rapidly. Following discussion by email with Professor Van Tam, I understood he discussed the issue with the CMO and then came back to me with a revised commission. We agreed to provide a graphical analysis describing the rolling 7-day average of the proportion of enrolled participants with COVID-19 symptoms with onset occurring 14 days after admission. This 14-day cut was a highly conservative threshold for nosocomial infection given the median incubation at that time was believed to be 5 days and also would not include the many cases discharged before 14 days. The provision of that analysis could not be made in the next few hours in time for SAGE meeting 21 due to be held that afternoon. My recollection is that Professor Van Tam asked if SPI-M could "check my homework" using the API access that they had to the raw data. I understand that SPI-M members from the University of Lancaster, University College London and the London School of Hygiene and Tropical Medicine agreed with our early analysis and realised opportunities to make other use of the CO-CIN data. This led to ongoing collaboration and the production of several reports and publications discussed later in my statement.

7.9. Nosocomial transmission was the main topic of discussion planned for SAGE meeting 21 on the afternoon of the 31st of March 2020 **(MCS/79 [INQ000119727])**. A paper was presented by Professor Stephen Powis, Medical Director NHS England and NHS Improvement, with the purpose of providing an overview of possible nosocomial transmission of coronavirus, outlining potential research options and implications for the management of findings **(MCS/80 [INQ000231467])**. The paper states that "Anecdotal/indirect evidence indicating possible nosocomial transmission of COVID-19' includes increasing staff absence rates (e.g., London Ambulance Service, workforce reports demonstrating 25% of staff in London off sick/in isolation) and the rapid increase in hospitalised cases overall".

7.10. I presented orally that CO-CIN had data indicating an increasing proportion of nosocomial cases among overall cases (minute 11) **(MCS/79 [INQ000119727])** .

7.11. An action from that meeting was for the "NHS to urgently create and chair a nosocomial infection sub-group, with DCMO support, involving modelling, genomics, clinical expertise and engineering: the sub-group needs to consider the role of healthcare workers in nosocomial spread, the risk to care homes and solutions for reducing nosocomial spread" **(MCS/79 [INQ000119727])** .

7.12. My group's graphical analysis (referred to in paragraph 6.8) describing the proportion of people in hospitals who acquired COVID-19 in hospital (nosocomial infection) was included in a Dynamic CO-CIN report circulated to SAGE members in preparation for SAGE Meeting 22 on the 2nd of April 2020 **(MCS/81 [INQ000120503])** , **(MCS/44 [INQ000231470])** . The report included data from 4639 patients. The data shows that using the extremely conservative definition of symptom onset 14 or more days after admission, the proportion of people in hospitals who acquired COVID-19 in hospital as of the 1st of April 2020 was exceeding 10% and on a steeply rising trajectory. Minute 7 of the situation update states "CO-CIN data is signalling nosocomial infection more strongly than previously. SAGE will discuss this in detail at its next meeting following output from the specialist sub-group."

7.13. Minute 5 of SAGE Meeting 22 on the 2nd of April 2020 notes "A nosocomial transmission sub-group will be co-chaired by the National Infection Service and the NHS nursing director, with a secretariat from the NHS. It will meet twice weekly starting immediately." **(MCS/81 [INQ000120503])**

7.14. Based on this record of the CO-CIN report being read at SAGE meeting 22, and the actions recorded, I am confident that the magnitude of nosocomial infection in hospitals was recognised by Government Advisors and would have been available to policymakers who read SAGE minutes on or shortly after the 2nd of April 2020 **(MCS/81 [INQ000120503])** . With hindsight and learning from the human challenge study (described earlier in paragraph 3.19), I am sure the size of the problem of nosocomial infection was larger than we first estimated.

7.15. The risk of nosocomial infection described by CO-CIN applied to the acquisition of COVID-19 in hospitals where it could be expected that great care is taken by staff to reduce such infection. Infection Prevention and Control (**'IPC'**) precautions, including handwashing, proper use of disposable personal protective equipment and the

engineered hospital environment are all intended to reduce such risks. The hospitals in the CO-CIN included general and specialist hospitals, some community-based intensive nursing care units (mostly in Wales) and some residential mental health units including secure units. Therefore, I will say that the risk of nosocomial infection identified by ISARIC's CO-CIN are generalisable to other settings such as community nursing homes, where if anything the risk is likely to be higher.

7.16. All subsequent Dynamic CO-CIN reports included rolling analyses of the proportion of nosocomial infections in the hospital inpatient population at the 306 NHS Trusts participating in the study. Reports from the 13th of April 2020 **(MCS/82 [INQ000151750])** read in SAGE 25 on the 14th of April 2020 **(MCS/83 [INQ000120505])** provided four graphs illustrating the proportion of people in hospitals whose COVID-19 symptoms began 2 or more, 5 or more, 7 or more and 14 or more days after admission. This was done because of early uncertainty over the true median incubation period, and because all patients discharged after a given cut-off would not be included in the analysis, leading to an underestimation of the magnitude of the problem. We know now that the graphs illustrating the proportion of people in hospitals whose COVID-19 symptoms began 2 or more and 5 or more days after admission give a better estimate of the problem. This new and more appropriate analysis including 12,332 patients shows that the proportion of nosocomial infection in the first two weeks of April 2020 was around 20%, that is one in five patients in hospitals with COVID-19 acquired their infection in these hospitals.

7.17. ISARIC provided access to the CO-CIN line list of raw data to SPI-M members to allow further analyses and this supported a rolling report considered by SPI-M and its nosocomial infection sub-group, which described the proportion of nosocomial infection at hospital level, laid out in a way that allowed inexplicable variation to be identified. Two key early papers were "Modelling the daily rate of nosocomial infections in UK hospitals using CO-CIN data" by Jonathan Read (Lancaster University) and Sebastian Funk (LSHTM) 2020-04-09 **(MCS/84 [INQ000231428])** and "Investigating nosocomial infections using CO-CIN COVID-19 patient data – version 4" by Jonathan Read (Lancaster University) and Sebastian Funk (LSHTM) 2020-04-30 **(MCS/85 [INQ000231430])** . These papers provided summary analyses for the proportion of nosocomial cases by NHS Region, and NHS Hospital Trust, and provided these in a coded form, ranked to order to allow comparisons. Later papers included "Estimates of nosocomial and community transmission COVID-19 in England" Abbott S et al 2020-

05-03 **(MCS/86 [INQ000231570])** and an "Update from the Nosocomial Modelling Team" 2020-05-04 **(MCS/87 [INQ000231571)]**

7.18. After review of the first of these analyses from 2020-04-09 ("Modelling the daily rate of nosocomial infections in UK Hospitals using CO-CIN data" **(MCS/84 [INQ000231428])** by NERVTAG and Professor Van Tam, the report along with the "key list" which gave the code aligned to the name of each hospital was offered to NHS England via Ruth May, the Chief Nursing Officer (**'CNO'**) to enable targeted learning from exemplars of good practice in infection prevention and control and focus on hospital trusts where improvement was indicated. However, there was an unfortunate misunderstanding within the CNO's Office as to the representative nature of the data and report. A letter from Ruth May dated the 29th of April 2020 **(MCS/88 [INQ000068984])** states (wrongly) "due to small sample numbers at trust level, we have had to conclude that the research does not provide individual trusts with sufficient data to make informed decisions on next steps." At that time CO-CIN data included 1 of every 3 hospital cases, and nearly all hospitals in England, making it highly representative and probably the biggest study of nosocomial infection ever conducted. I followed up with a video meeting with the CNO's advisors but did not feel that they were receptive to making use of the data as offered.

7.19. In response, Read and Funk for SPI-M rapidly provided an updated analysis ("Investigating nosocomial infections using CO-CIN COVID-19 patient data – version 4" 2020-04-30) **(MCS/85 [INQ000231430])** and the matter was discussed at SAGE 30 on the 30th of April 2020 (Minute 10) **(MCS/89 [INQ000075781])** and shared with NHS England. My recollection on reading the minutes in preparing this statement is that the action points from SAGE 30 for the "Nosocomial Working Group to ensure all relevant SPI-M modelling on hospital-borne infections is incorporated into its analysis" referred to the discussion in SAGE that NHS England should attend without further delay to the hospital trust level analysis of CO-CIN data by Read and Funk as endorsed by SPI-M. I do not know if the trust level analysis of variation in nosocomial infection was shared by NHS England with NHS Trusts or used by NHS England to understand good and bad practices. If comparative practices in infection prevention and control were not explored, then an early opportunity to improve care and save lives was missed.

7.20. The Nosocomial Working Group (a SAGE Sub-Group) continued to benefit from CO-CIN and SPI-M modelling. The SPI-M paper by Abbot et al "Estimates of nosocomial

and community transmission of COVID-19 in England" 2020-05-03 **(MCS/86 [INQ000231570])** used a 5-day incubation period to identify regional changes in the reproduction number, rate of spread, and doubling time during the course of the COVID-19 outbreak in nosocomial and community populations.

7.21. A report titled "Update from the SPI-M Nosocomial Modelling team" (2020-05-04) **(MCS/87 [INQ000231571)]** using CO-CIN data indicated that the proportion of nosocomial cases across all Trusts combined was 13% (95%CI 10.0,16.7) for week of symptom onset commencing 27 April 2020 (page 2). Three other important findings were reported in this update from SPI-M. I describe them below.

7.22. First, at a hospital level, new nosocomial infections each week are much more strongly associated with new nosocomial infections the previous week than they are with new community-acquired cases the previous week. This suggests either that nosocomial infections lead to much more secondary transmission or that there are confounding factors leading to this association (e.g. active infection amongst Health Care Workers). Or both may be important.

7.23. Second, while there is considerable variation between hospitals in rates of infections, overall rates of infection are not consistent with self-sustained patient-to-patient transmission in most cases.

7.24. Third, most self-reported infection prevention control measures analysed are associated with reduced rates of nosocomial infection, and in some cases these associations are strong and consistent with the infection prevention control measures having a large beneficial impact.

7.25. My interpretation of these three key findings is that infectious Health Care Workers were an important source of nosocomial infection, and that adherence to best infection prevention control practice was highly effective in preventing nosocomial infection. This increases my confidence in asserting that focusing on understanding trust level variation in nosocomial infection rates, as provided by SPI-M working with CO-CIN, would have saved lives.

7.26. A "Consensus Statement on COVID-19" (3rd June 2020) produced by the SPI-M-O group **(MCS/90 [INQ000231439])** read at SAGE 40 **(MCS/47 [INQ000120526])** on the 4th of June 2020 indicated that, "as of the 1st of May, 30% of positive tests in hospital were linked to hospital acquired infection, including those up to the fourth generation of transmission following discharge".

7.27. Dr Jonathan Read presented "Nosocomial infection trends using CO-CIN COVID-19 patient data" by region and care provision type in the second wave (Winter 2020) in a paper presented to SPI-M **(MCS/91 [INQ000231436])**. He identified that proportions of nosocomial infection were rising, that long term residential facilities had higher rates than acute care trusts and that there was no clear relationship between levels experienced by a trust in wave 1 compared to early wave 2. To my eye, most trusts had reduced nosocomial infection proportions from wave 1 to wave 2, signalling lessons learnt with improved infection prevention control. However, there was not a strong one-way relationship and many trusts showed higher proportions of nosocomial infection in wave 2 compared with wave 1, indicating deterioration in standards of infection prevention control in many hospitals.

8: Onwards transmission from hospitals - amplification into the community.

8.1. SPI-M members took the nosocomial work forward and estimated that the amplification of COVID-19 in hospitals spilt over on discharge, leading to the onward amplification of cases in the community of around 1% **(MCS/92 [INQ000231451]), (MCS/39 [INQ000212082]])**. However, that work was based on the wrongly observed incubation period of 5 days from exposure to disease onset and assumed that the incubation period was the same as the period from infection to infectiousness. Had their calculation used the correct 2-day period from infection to infectiousness, their calculations would show that the transmission from hospitals and onward amplification of COVID-19 into the community was greater than reported.

8.2. Academic investigators and Clinicians Scientists are always keen to publish their findings in peer-reviewed journals. Grant income and published papers are sadly the hard metrics of our success. It is hard to show lives saved through our efforts. The Inquiry may be interested to know that had the academic investigators acted contrary to the interest of transparency and not shared their reports on nosocomial infection using the COVID-1 Collection of Scientific Evidence **(MCS/19 [INQ000236609])**, then there would have been an inordinate delay in theses analyses being published. Using the traditional model of academic publication, our report "Hospital-acquired SARS-CoV-2 infection in the UK's first COVID-19 pandemic wave" **(MCS/93 [INQ000231485])** was eventually published in Lancet on the 21st of August 2021, 20 months after the start of the event, when nosocomial infection and transmission in care-homes was old news.

9: Relationships with Government, SAGE and other Groups

9.1. ISARIC's CO-CIN project became a feature from SAGE meeting 19 on the 26th of March 2020 and I would typically report any new information of note within the Situation Update. My attendance coincided with the start of video conference software being used to host SAGE meetings, which suited the presentation of the most up-to-date Dynamic CO-CIN reports, using screen-sharing with me providing my direct access to the dashboard server.

9.2. SAGE was attended by personnel from SPI-M, PHE and the NHS so they were able to see opportunities and potential analysis within scope of this timely CO-CIN data. Some analysis was best conducted by ISARIC investigators familiar with the limitations of the data. In other situations, particularly with regard to hospital resource use, it was better for ISARIC data managers to provide SPI-M, NHS and PHE staff with direct API access. API access enabled external users to analyse patient level data using their own tools. ISARIC carefully controlled API access.

9.3. For the most part, I think we (SPI-M, NHS and Public Health agencies) did work effectively together.

9.4. SPI-M and ISARIC's CO-CIN groups were particularly effective in working together to understand the magnitude and locality of nosocomial infection, and rapidly co-produced outputs that were shared in SAGE, NERVTAG, SPI-M, the Hospital Onset COVID-19 Infection Sub-Group (**'HOCI-SG'**) and the Ethnicity Subgroup. Many of these outputs were published (albeit much later) in academic journals and are now cited as exemplars of public health action research in Government policies and WHO guidance.

9.5. I believe we worked well with the National Health Services of the four nations, but this is harder to evidence. I received feedback from Professor Van Tam that NHS England found CO-CIN data on the use of oxygen, ventilators, and critical care beds extremely useful **(MCS/94 [INQ000231426])**. I have already indicated at paragraph 6.18 that there was frustration shared by my group and colleagues on SPI-M with the reluctance of some clinical colleagues in NHS England to accept the value of regional and trust level data on nosocomial infection.

9.6. It was clear to me where evidence from ISARIC's CO-CIN featured in SAGE advice as the minutes were very well curated. There was no reason that CO-CIN's data should

inform advice at every meeting. Often, I would report that trends had not changed, or that features were stable.

9.7. One of our early Dynamic CO-CIN reports, using data collected up to the 25th of March 2020, identified that the commonly used triage and early warning tool, the National Early Warning Score ('**NEWS**') **(MCS/23 [INQ000231480])**, **(MCS/95 [INQ000231512])** was not suitable to predict death or deterioration in COVID-19 patients **(MCS/75 [INQ000119726])**. Minute 14 of SAGE Meeting 22 on the 2nd of April 2020 notes "CO-CIN data suggests that obesity, lung disease, heart disease and neurological disease are important risk markers for COVID-19. Conventional risk scores do not seem helpful." **(MCS/81 [INQ000120503])**

9.8. Without being commissioned to do so, ISARIC Investigators using CO-CIN data, developed new clinical tools that allowed: a) people most at risk of poor outcomes (death and deterioration) to be identified early in the clinical course of their illness so as to focus care to improve their outcome and b) identify people at low risk of poor outcomes who can safely be managed in the community **(MCS/96 [INQ000231507])**, **(MCS/97 [INQ000231502])**, **(MCS/98 [INQ000203595])**. The ISARIC4C Mortality Score assesses the presence of six clinical features and two laboratory values, and gives a value of 0, +1, or +2 if these are abnormal. The values are simply added up to give a score out of 21. The score is read against a look-up table which gives the risk of death as a percentage. The ISARIC 4C Mortality Score has been validated in 15 countries and has been adopted into commercial clinical management software. The ISARIC4C Mortality Score is used by health professionals in many countries. The 4C Deterioration Score is similar but uses more variables. Despite advances in the treatment and management of adults hospitalised with COVID-19, prospective validation shows the ISARIC4C Mortality and Deterioration scores can continue to inform clinical decision making.

9.9. As I said earlier, I am highly confident that the CMO and GCSA, their deputies and the team at GO-Science appreciated the value of CO-CIN data. We provided early evidence that helped understand the nature of COVID-19 from the start of the UK outbreak, the magnitude and locations of nosocomial infection, disease in different age groups, and contributed to resource planning (for example planning the priority age bands for vaccine rollout). I am highly confident that the CMO and GCSA both have the communication skills and wherewithal to support their advice to policy makers by relying on the evidence SAGE members provided, such that policy makers would be

left in no doubt what advice was been offered, and what confidence these advisors had in their evidence.

9.10. It was less clear to me and other members of SAGE how advice was received and acted on by policy makers, or put another way, where advice had impact and where it landed within Government. The GCSA and CMO did, on many occasions, express gratitude to the committee at the start of meetings where a particular piece of work or advice had been particularly valuable. Often no feedback was given, and we did not press for feedback as we appreciated that policy makers must consider many factors in addition to the science advice in coming to decisions and developing policy. Often the battle rhythm of SAGE demanded we focus on the matters of the day.

9.11. In addition to the clinical data activity, the structured method of biological sampling of human material for research purposes, paired with the clinical data, led to early discoveries about the nature of COVID-19, supported the Oxford Vaccine's development **(MCS/18 [INQ000231521])** **(MCS/41 [INQ000231498])** , enabled covid test development **(MCS/99 [INQ000231520])** and evaluation **(MCS/18 [INQ000231521])** , **(MCS/37 [INQ000231526])** **(MCS/100 [INQ000231513])** in the UK, provided the first five WHO International standards for global use **(MCS/12 [INQ000231422])** , **(MCS/13 [INQ000231420])** , **(MCS/14 [INQ000231419]) (MCS/15 [INQ000231417]) (MCS/16 [INQ000231418]),** enabled the Human Challenge study **(MCS/27 [INQ000231441])**, and by understanding the genetic susceptibilities of people with severe COVID-19, contributed to the discovery of novel therapeutics **(MCS/101 [INQ000203594])**.

9.12. Other work that the CO-CIN data enabled included provision of the first post-trial evidence of vaccine efficacy **(MCS/102 [INQ000220192])**, definition of the highest risk clinical sub-groups for COVID-19 Neutralising Monoclonal Antibodies (**'nMABs'**) and Antivirals Access **(MCS/69 [INQ000106047]).** , and monitoring of adoption of clinical guidance **(MCS/69 [INQ000106047])** , **(MCS/103 [INQ000231477])**

10: CO-CIN and Commissioning

10.1. CO-CIN was commissioned by the CMO with a limited scope of activity and expectations **(MCS/32 [INQ000231427])** . The initial expectations of the project were: to describe approximately 1000 cases in any first wave - expected imminently / Spring 2020 and to describe the next 1000 cases in any second wave, likely Winter 2020/21. ISARIC Investigators committed to produce summary reports on alternate weeks

addressing and analysing the clinical characteristics of COVID-19 patients by outbreak wave, identifying risk factors for infection and disease severity. This was to include data such as age, pregnancy, obesity, co-morbidities, ethnicity, prior medications, laboratory features, and then the likely value of triage, the predictive value of early warning tools, and the effectiveness of public measures. We rather overdelivered, producing near real-time dynamic CO-CIN reports, and numerous bespoke analyses mentioned above. The value of the reports and data generated from CO-CIN led to the continuation of our work until the end of February 2022, when over 300,0000 cases had been characterised over two years.

10.2. ISARIC Investigators working on CO-CIN were not otherwise commissioned centrally or by any other government department, agency or by any other of the UK nations' government departments. Rather, while attending SAGE and NERVTAG and appearing on a 'Zoom' screen beside other independent experts and government departments' advisors, matters would arise where the GCSA, CMO, other members or I would suggest that one or more groups could work together on a particular topic such as understanding the magnitude and importance of; nosocomial infection, ethnicity, disease in children, or steroids being adopted as a Covid therapy **(MCS/104 [INQ000128574])**

10.3. There was no need for a formal mechanism to commission such ad hoc work. Typically, when a matter of interest was identified for exploration, relevant teams would set to work immediately after the SAGE meeting. Groups of academics, public health teams and government advisors would typically work late every day, and through the weekends, to draft a paper in time for the next SAGE or sub-group meeting. There was no financial compensation for this activity. Were there a need for a formal process for such commissions with prior costing and approvals for budgets, I very much doubt that any useful work would have been done in time to save lives. So, on reflection, I would say that this was an efficient process.

10.4. I will say that there was sufficient academic freedom to operate effectively within this system. In any exploration of the CO-CIN data, our scope of academic inquiry was not limited, as the data that we had collated from UK hospitals and held was "ours to use" within the limits of the Clinical Characterisation Protocol as approved by the Health Research Authority.

10.5. I have no doubt that sometimes the results of our analysis will have been uncomfortable for policy makers and others to read, for example our several reports

detailing with very high proportions of nosocomial infection in many hospitals in wave 1 and wave 2, but I never saw any external interference in the scope of our activity. The situation may have been quite different had there been a formal commissioning process where planned activity, milestones and outputs would need to be negotiated and scrutinised by various government departments with differing interests or priorities that differed from SAGE, CMO or GCSA.

10.6. The Institute for Government (**'IFG'**) found that "decision-making at the centre of government was too often chaotic and ministers failed to clearly communicate their priorities to science advisers" **(MCS/105 [INQ000075385])** . Without additional context, it is hard for me to comment, but I will say that if the science advisers referred to are the CMO and GCSA, then I was never party to such communications. If the science advisers referred to are SAGE and NERVTAG members, then the IFG's understanding of the respective roles and processes for seeking advice from SAGE and NERVTAG differs from mine. I would not expect decision makers to have any special understanding of the role and work of ISARIC's CO-CIN beyond understanding that a competent group existed whose role was to understand the nature of COVID-19 in people admitted to hospitals from the perspective of a patient's health needs and resource use. I was never aware of SAGE being asked to provide policy strategy. SAGE was a scientific advisory group that used evidence where it was available, and scientific principles where evidence was lacking. Advice was usually caveated with descriptive "bounds of confidence". I understand that it is the view of the IFG that "in the initial months, ministers put too much weight on SAGE - relying on it to fill the gap in government strategy and decision-making that was not its role to fill." I understand their view, as it may well have appeared to external observers that there were times where there appeared to be gaps in government strategy, but I do not know if there were gaps in strategy as I was not party to government strategy development. I disagree strongly with the IFG's view that the government relied on SAGE to fill gaps in strategy or indeed to provide any strategy. I never saw public health strategy or other policy discussed at any of the 80 SAGE meetings that I participated in. IFG conflates the issue of apparent gaps in strategy by inferring that SAGE filled these gaps which it did not. I am certain that government did not rely on SAGE to fill any gaps, if there were gaps. It was never SAGE's role to fill that space, nor did SAGE ever seek to do so.

10.7. I believe that the Inquiry understands that SAGE provided advice to the government on the basis of consensus among its attendees, and that the GCSA and CMO were the interlocutors with policymakers. I agree that GCSA and CMO were the interlocutors with policy and decision makers. I disagree with the notion that SAGE provided advice to the government on the basis of consensus among its attendees, because this is a gross oversimplification. For a start, this view does not credit the GCSA and CMO with their success in the difficult task of representing the spectrum of advice offered by different SAGE members, secondly there is nuance associated with options of advice and likely impacts predicted were certain courses of advice followed. Science at the edge of knowledge rarely has one known right answer, more there are a few probable right answers and several probably wrong answers. While in some matters there was consensus as the science pointed towards a particular outcome, requiring a particular decision to be made, in many matters there was lack of evidence and little prior relevant knowledge, leading to uncertainty, not consensus.

10.8. I am confident that the GCSA and CMO were skilled in science communication and representing "the art of scientific uncertainty" to policymakers. Through their medical training and years of clinical practice, both have had specialist training in communication skills, including breaking bad news, and after decades of experience in practising this skill in the field of medicine, science and health policy, they have honed the skill to masterly status. Communication requires dialogue and if there was any difficulty or delay in dialogue between ministers and their advisors, one might ask if some ministers had sufficient scientific literacy to engage meaningfully in such dialogue.

11: Complications of Covid and Long-term sequelae arising from Covid

11.1. Complications are medical problems that arise during the course of an illness, for example a reduction in kidney function, heart damage or liver damage. These can be caused directly by the disease process or indirectly by necessary treatments. Complications are often temporary but may have long-term consequences. Most people admitted to hospital survived COVID-19, particularly younger people. It is important to know what happens to people who survive.

11.2. ISARIC Investigators are interested in the outcomes of severe emerging infections such as COVID-19. This is because survivors of severe emerging infection often have new health needs, and only through understanding these health needs can resources

be established. An example is our seminal work describing Post Ebola Syndrome in Sierra Leone **(MCS/106 [INQ000231431])**, **(MCS/107 [INQ000231465])**. Because we are hospital-based investigators, using hospital resources to inform our research, we focus on those complications where hospital-based patient interaction provides information about in-patient care and outpatient follow-up.

11.3. We described outcomes for severe emerging infections such as MERS and COVID-19, 28 days after admission in three broad terms: Discharged alive, Hospitalisation and Death. If a period longer than 28 days is used, there is a greater delay in reporting key features of a new disease to policymakers. An example of how that data can be used is when ISARIC Investigators were asked by CMO to provide a report describing 28-day outcomes for wave 2 to inform vaccine policy and public health messaging. The data and figures from that report were used by the CMO in slide 5 of the National Covid Briefing from No 10 on the 3rd of February 2021 **(MCS/108 [INQ000231449])**. The CMO's use of the data and figures is at 5min 57seconds of the briefing **(MCS/109 [INQ000231569])**. The report was read at SAGE 79 on the 4th of February 2021 **(MCS/110 [INQ000231447])**. We maintained a webpage for this outcome data **(MCS/111 [INQ000231474])**. We also described complications that occurred at any time during the hospital episode. We have recently sought permission from the Health Research Authority and Research Ethics Committee for a protocol change that extends our scope to events of Public Health Interest with the freedom to operate in community settings. Using data from CO-CIN, we have produced several reports detailing the complications of COVID-19 and we shared a report focusing on complications with SAGE 79 on the 4th of February 2021 **(MCS/112 [INQ000231450])**, **(MCS/113 INQ000092855**. This report was published after peer review in the Lancet **(MCS/114 [INQ000231433])**.

11.4. Many of these COVID-19 complications can be considered long-term injuries and will have long-term, sometimes life-limiting impacts on COVID-19 survivors. There may be some overlap between the complications we have described, and the various problems described by others and known as Long-Covid (or post-covid syndrome), but it is important that the Inquiry understand that ISAIRC Investigators do not make any claim that the complications of COVID-19 that we describe are all the same as Long-Covid.

11.5. We reported in **(MCS/114 [INQ000231433])** that 49.7% of people had at least one complication from their acute COVID-19. Kidney complications were most common (24.3%). Lung complications were next most common (18.4%), followed by heart

complications (12.3%), then liver (10.8%). At the end of their hospital stay, in those who survived, (26.6%) had a worse ability to look after themselves. This was highest in people who had a complication that affected the brain or nerves (four times more likely). Those with complications were nearly twice as likely to die and seven times more likely to require intensive care when compared to people without complications. Complications were most common in those over 50 years old (51.3%) but were also very common in younger people too (38.9%). Even in the youngest age group (19 to 29-year-olds), 27% of these younger adults had a complication during their time in hospital.

11.6. Complications affect a large proportion of people admitted to hospital with COVID-19. Unlike death, complications affect nearly all age groups and those who were previously healthy. My recollection of advice given at SAGE 79 on the 4th of February 2021 **(MCS/113 INQ000092855** regarding the complications of COVID-19 and Long Covid matches that were recorded in minutes numbered 9-11 and 43-52. A paper from ISARIC Investigators was read **(MCS/114 [INQ000231433])** . A paper from the Welsh Government Technical Advisory Group **(MCS/115 [INQ000231448])** and two papers from the Office of National Statistics ('**ONS**') **(MCS/116 [INQ000086986])** and **(MCS/117 [INQ000231445])** were also read. The nature of complications and Long Covid were discussed. SAGE advised "*Longitudinal studies, that include both people who have been hospitalised and those who have not, will be required to better understand these issues*" (minute 52). The subsequent commissioning of the Post Hospital COVID (**'PHOSP-COVID'**) consortium (detailed below) is evidence that SAGE advice was heeded. This research action led to better understanding of the long-term complications of COVID-19 and Long Covid.

11.7. ISARIC Investigators produced several other reports regarding the complications of COVID-19 (**MCS/53 [INQ000231515]), (MCS/118 [INQ000231459]), (MCS/54 [INQ000231488])** , **(MCS/60 - [INQ000221983]), (MCS/119 [INQ000231497]), (MCS/120 [INQ000231496]), (MCS/121 [INQ000231510]), (MCS/122 [INQ000231489])** , **(MCS/49 [INQ000231537]), (MCS/51 [INQ000231539]), (MCS/123 [INQ000231501]), (MCS/124 [INQ000231499]), (MCS/125 [INQ000231516]), (MCS/126 [INQ000231484]), (MCS/127 [INQ000231504]).** We were interested in the reports of Post Covid Syndrome but did not have capacity to lead on long-term follow-up studies that were necessary to do justice to understanding this problem. Instead, we collaborated with Prof Chris Brightling who established the

UK wide consortium Post Hospital COVID (PHOSP-COVID) consortium. In a data-secure process, ISARIC Investigators shared clinical data about people admitted to hospital for management of COVID-19 with PHOSP-COVID Investigators to enable these important Long Covid Studies. Reports on Long Covid were provided by the PHOSP-COVID Investigators and have subsequently been published after peer review **(MCS/128 [INQ000231494])**. The Inquiry could approach Professor Brightling for these should it wish.

12: Public Health Messaging and Communications

12.1. I am not qualified to comment on government communication of policies related to public health as the art or science of policy communication is not within the ambit of my knowledge and expertise. Therefore, what follows is purely my opinion on the matter. Many media formats were used to communicate scientific understanding with the public. Where this was done by Government Official Advisors (GCSA, CSAs, CMO, and DCMOs) and at times by external independent government advisors (such as SAGE participants, and members of NERVTAG, JCVI, myself included), then on the whole, I felt this was done with care and attention to detail, with nuance, and caveated with the levels of confidence we had in the evidence.

12.2. I am less comfortable with how some key government policy and decision makers, claimed that they were "following the science" when they announced changes in their policy and decisions to the public. As indicated above, I am not qualified to comment with any authority on the art or science of policy communication. I appreciate that politicians often rely on the "soundbite" to convey messages to the public. It is my opinion, however, that ministers should not have relied so readily on the phrase "we are following the science" when announcing their policy decisions.

12.3. Relying on the phrase, 'we are following the science' in the media caused two big problems, the first of which is reflected in the IFG view, which I have heard in many fora, that "in the initial months, ministers put too much weight on SAGE - relying on it to fill the gap in government strategy and decision-making that was not its role to fill" **(MCS/105 [INQ000075385])** . I believe the public, parts of the broadcast and print media, and IFG were wrong to make this conclusion, but I can appreciate how they came to that conclusion. I will expand on this in the next paragraph.

12.4. SAGE was not a strategy or decision-making body. Until now, SAGE attendees have not discussed SAGE business outside of the committee. I never heard a SAGE

member or chair say, "Wouldn't it be a good idea if we did…". I think it would have been much better if ministers had said "We have listened to the science and having considered that among other matters, we have decided to do…" I appreciated that it is inconvenient for ministers to add this nuance in front of a camera, but there was a most unfortunate side-effect caused by the omission of this nuance. The frequent habit of ministers tagging *their* public announcements of *their* decisions with "we are following the science" flagged that ministers were simply following the scientists, and logically that meant that scientists were leading the ministers. Nothing could have been further from the truth, as scientists were not leading on policy or strategy.

12.5. The second big problem caused by ministers saying they were "following the science" arose when they were not following the science. The independent and external attendees of SAGE and NERVTAG were experienced in the etiquette of working in Government Advisory committees, so as a rule, did not discuss their business outside of committees. At times this meant we sat on our hands and bit our tongues when policy decisions were announced, claiming to follow the science, often with elaborations that had never been discussed in committee. I believe we generally accepted that this was the nature of our role, and some political embellishment was to be expected. These were usually minor transgressions, but a few were egregious.

12.6. An example of this is when plans to ease lockdown restrictions including opening schools and allowing a rule of six for non-household members to meet, from Monday the 31st of May 2020 were announced in a press conference on the 28th of May 2020 **(MCS/129 [INQ000231505])**, and the details in this briefing were at odds with advice in the two most recent SAGE meetings. In SAGE 38 on the 21st of May 2020 **(MCS/44 [INQ000231470])** , R was predicted to rise steeply with planned further easing in behavioural and social interventions (minute 4), the impact of previous changes of non-pharmaceutical intervention policy had not been assessed (minute 12) and multiple simultaneous changes to restrictions had the possibility of large, unintended, negative consequences (minute 20). In SAGE 39 on the 28th of May 2020 **(MCS/45 [INQ000119951])** , concern around ongoing high incidence of infection (10,000 cases per day) in the UK was noted (minute 1 and 11) despite R being estimated to be just below 1 in all four nations (minute 6), and nosocomial infections remaining a significant concern (minute 9). Minute 33 noted that "SAGE participants reaffirmed their recent advice that numbers of COVID-19 cases remain high (around 10,000 cases per day with wide confidence intervals); that R is 0.7 to 0.9 and could be very close to 1 in

places across the UK; and that there is very limited room for manoeuvre especially before a test, trace and isolate system is up and running effectively. It is not yet possible to assess the effect of the first set of changes which were made on easing restrictions to lockdown." The rule of six was never discussed in SAGE, so does not appear in any SAGE minute. Despite this advice ministers pressed ahead with easing restrictions, which was their constitutional right, but persisted in claiming to be following the science, the Prime Minister specifically citing SAGE in his statement on the 28th of May, when this was not the case. This led to a schism between government and their independent advisors. As a result, five of the independent experts who regularly attended SAGE broke etiquette and publicly voiced their concerns. This coincided with the Barnard Castle event. I think that together, these events are likely to have undermined public confidence in public health measures to mitigate the effects of the pandemic, contrary to the best interests of the public.

12.7. The IFG observed that the government's communication of risk was *'confusing…ministers have switched back and forth between alarm and reassurance, while failing to drive home key messages, such as the risk of gathering in indoor and poorly ventilated settings'* **(MCS/105 [INQ000075385])** . I broadly agree with this observation and have explained my opinions on the government's communication of some public health policies in the preceding paragraphs. I am also of the view that the provision of the Eat Out to Help Out Scheme and the details of how that scheme operated were confusing for the public, as they contradicted earlier public health advice. However as I have indicated in paragraphs 11.1 and 11.2, I am not an expert in policy communication and these are my personal opinions on these matters. The scheme ran on 13 days, these being the Mondays, Tuesday and Wednesdays from the 3rd to the 31st of August 2020. My understanding was that the scheme was one of several measures intended to support the hospitality sector following the end of the first lockdown by encouraging people to eat out by way of a subsidy for meals and non-alcoholic drinks. I think it was also intended that people would then regain confidence in going out and using the hospitality sector in general. The scheme did not apply to food that could be ordered from participating restaurants for eating at home, so did not offer a safer option for those who wished to limit social mixing but still enjoy the diversity of dining from a restaurant. The scheme was popular and led to increased social mixing and COVID-19 cases quickly began to rise. A paper from the Royal Society's DELVE Initiative found areas with higher take-up saw both a notable increase in new COVID-19 infection clusters within a week of the scheme starting and a deceleration in

infections within two weeks of the program ending **(MCS/130) [INQ000228093])**. The scheme closed on the 31st of August and new restrictions were introduced on the 14th of September. The Government messaging on risk of "catching COVID-19" flipped over these six weeks from "don't eat out - don't mix", to "eat out but stay in your bubble" and then to "don't eat out but meet up with five of your mates". It is my opinion based on observation of these policy U-turns and their associated communications, that these policy changes and associated communications, together undermined public confidence in evidence-based public health advice, specifically about the risks of people gathering in poorly ventilated buildings, and public transportation.

13: Lessons Learned

13.1. ISARIC's Clinical Characterisation Protocol UK allows the rapid collation and analysis of data and clinical material from people affected by exposures of public health interest for action research. The COVID Clinical Information Network (CO-CIN) of 306 NHS Trusts provided the clinical data for this program of research. CO-CIN was not a stand-alone study, it was a tier of activity within ISARIC's Clinical Characterisation Protocol in the UK (CCP-UK), with interdependence between these tiers. The CCP-UK was one of the UK research activities that placed the UK as a leader in the Health Science response to COVID-19.

13.2. The CCP-UK was hospital-based so did not contribute to generating knowledge about community transmission of the virus, but it did make a significant contribution to understanding the amplification of infection in hospitals (nosocomial infection) and how this contributed to additional transmission of infection in the community. Our data also enabled an NIHR-funded research study led by Prof Heather Loveday, that evaluated the implementation of pandemic preparedness plans during COVID-19 at the interface with infection prevention and control services in acute and community care.

13.3. ISARIC's work using CO-CIN data was vital to understanding the nature of severe (i.e. hospitalised) COVID-19 in the UK and was generalisable to understanding COVID-19 in developed countries across the world. We provided the first very large, generally representative prospective (unbiased) report of this novel disease outside of China, which described the disease in people of all ages. The first report appeared in pre-print (i.e. unreviewed) in **medRxiv** on the 28th of April 2020 **(MCS/131) [INQ000151856])**, and soon after in open-access form after peer review in the British Medical Journal **('BMJ')** on 22nd May 2020 **(MCS/60) [INQ000221983])**, allowing for the widest

dissemination. UK health planners and policymakers benefited from first sight and direct access to the raw data behind this report from the 10th of March 2020. This one report and its related data has informed multiple health policies, including those of the WHO, UK Government and The National Institute for Health and Care Excellence ('**NICE**'). It was relied upon to inform vaccine prioritisation and has been cited by over 3000 other publications. Based on these metrics it is possibly the most impactful work of my career.

13.4. Our report with focus on children admitted to hospital with SARS-CoV-2 infection was published in pre-print (**medRxiv** 17th July 2020) **(MCS/132 [INQ000231527])**, and open access from the BMJ was given on the 27th of August 2020) **(MCS/61 [INQ000231543])**. Again, UK health planners and policymakers benefited from first sight and direct access to the raw data behind this report from the 10th of March 2020. This report and related data informed our understanding of the much lower risk of severe COVID-19 in children and young people, and is also cited in multiple health policies, including that of the WHO, UK Government, Scotland and Sweden. It has been cited by over 600 other publications.

13.5. We repeated our characterisation of how COVID-19 affected people over subsequent waves with different variants, and how presentation of the disease changed particularly in CYP **(MCS/64 [INQ000220188])** . This paper was presented to SAGE and passed to JCVI to inform vaccination policy in the UK. It was also published after peer review **(MCS/61 [INQ000231543])** . This paper reassured us that the alpha variant did not lead to more severe disease, contrary to many other reports that did not use sound scientific technique. At least 20% of CYP admitted to hospital had asymptomatic incidental SARS-CoV-2 infection (i.e. one in five CYP was admitted *with* the virus and *not because* of the virus).

13.6. The extensive work we did to understand the impact of COVID-19 on those with existing inequities has been described earlier in my statement.

13.7. Reflecting on the impact of just the first two of our over one hundred outputs, I can say with confidence that ISARIC's CCP-UK programme is key to future preparedness, as is ISARIC's global activity.

13.8. It is a mistake to think that ISARIC's programme of work in this pandemic prepares or protects the UK for a future pandemic. We are not producing a playbook for future reference as a panacea for the next pandemic. ISARIC's CCP-UK provided a

mechanism for the rapid understanding of a novel disease of public health interest. CO-CIN provides an estate of hospitals ready to provide biological samples and clinical information should a pandemic break out.

13.9. If ISARIC's CCP-UK were to be maintained with adequate funding and continued to have priority access to all NHS Hospitals, so as to provide a future Clinical Information Network (the CIN), then I would say that the programme as a whole would contribute positively to the UK response to a future pandemic. It may surprise the Inquiry to hear that ISARIC Investigators in the UK have not yet secured long-term funding to maintain the CCP-UK programme. The Urgent Public Health Status conferred on the portfolio of pandemic preparedness studies since 2014 has been rescinded to allow recovery of non-COVID research. I gather the portfolio of Urgent Public Health Research studies is under review by the NIHR. I would welcome an open competitive tender from UKRI or NIHR to maintain the CCP-UK for five years in readiness for future local outbreaks of public health interest and to keep the engine warm for a future pandemic event.

13.10. ISARIC's CCP-UK does not have a remit to work on endemic respiratory disease. We focus on research that understands high consequence communicable diseases and other risks to public health. This is compliant with the sharing of personal information under Regulation 3 of the COPI regulations, which is key to the nature of our partnership work in actin research which bridges academia, the public health agencies and national health services.

13.11. ISARIC's CCP-UK has been activated three more times for outbreaks of public health interest since being activated for COVID-19 in January 2020. We activated on the 1st April 2022 to investigate an outbreak in Children of Acute Severe Hepatitis of Unknown Origin (**'CASHUO'**) in Europe and America. Using the programme infrastructure that had been enhanced during COVID-19, and in close collaboration with UKHSA and Public Health Scotland, we were able to identify the cause of the outbreak within 100 days and share this knowledge widely **(MCS/133 [INQ000231511])**, **(MCS/134 [INQ000231503])**. We also activated in response to the outbreak of Mpox on the 1st of May 2022 to facilitate research efforts by others (the **'MOSAIC'** and **'PLATINUM'** studies).

14: SAGE and its Subgroups; structure and function

14.1. I cannot comment on how effective SAGE and its subgroups were in informing decision-making as this was a ministerial responsibility. But to the point of their

effectiveness in providing advice based on evidence and expert opinion – I consider that SAGE and its sub-groups were agile appropriately responsive, and gave expert advice based on the best analysis of available data. The GCSA and CMO were able to convene expertise at short notice without the hindrance of formal commissioning and appointment committees. I have provided as evidence, numerous examples of analysis that were provided by ISARIC4C based on the CO-CIN data in a timely manner to SAGE, which were all available for policymakers, and later withstood independent peer review, resulting in publication in high-impact journals, and subsequent citation in several public health agencies' policies.

14.2. The IFG states that "as an ad hoc committee, SAGE was not designed for the semi-permanent role it has had during the Covid crisis." **(MCS/105 [INQ000075385])**. It is not in my nature to share opinions, being more inclined to rely on data to inform my statements. However, I would ask first, "What evidence the IFG has to support their view?" Next, I will state that when SAGE was convened, the nature of the new disease, how it would affect society beyond healthcare, and the duration of the outbreak were all unknown, and could not have been predicted with confidence. That is why studies such as ISARIC's CCP-UK were so important. I do not know how SAGE was originally designed. I did observe changes in participants and the opening of sub-groups and task and finish work groups as challenges arose. I observed SAGE adapting to change and challenge. Lastly, I would point out that many countries said in international fora that they wished that they had a SAGE. It is my opinion that SAGE worked well. A cadre of ex-SAGE could be maintained for future events, and I think this is being done, but there will always be a need for new experts to cover novel events as they occur.

Experiences as a participant in SAGE

14.3. I wish to add some context to the conditions that I and other regular non-governmental SAGE attendees experienced whilst contributing to the COVID-19 response. It was an honour to be considered sufficiently expert in my field to be asked to present evidence to SAGE and more so to be asked to return on many occasions to make further contributions on behalf of ISARIC Investigators. I considered attending SAGE to be a privilege, and with this, there came great responsibility to ensure that our evidence was presented with care. I took personal responsibility for our analysis of CO-CIN data and vouched for it to be as accurate as it could be, that our interpretation of meaning was cautious and caveated by a statement of confidence and included relevant limitations. SAGE attendees were robust in challenging any analysis. In any analysis, to over-

interpret or fail to identify limitations would demonstrate a lack of scientific rigour in the presenter. If bad science was allowed to inform policy, this would cost lives.

14.4. Non-governmental SAGE attendees were not remunerated for their contributions, though at some point, a scheme was established to compensate universities for the loss of teaching time. I and my team often worked irregular hours, long days and over weekends to provide topic reports in time for SAGE, NERVTAG and sub-group meetings. These meetings could be called at short notice. I often worked through family holidays.

14.5. My and my family's experience of the public's perception of SAGE's role did not reflect the devotion and sacrifice we as a family made to the COVID-19 response. I am experienced in working in hostile environments and have trained in the basics of personal security. It is not unusual to experience targeted harassment when working abroad on a high-profile research project or a politically sensitive outbreak of infectious disease. I did not expect targeted harassment of my family and threats to our personal security because I contributed to the COVID-19 response in our own countries.

14.6. In addition to many instances of anonymous threats of physical harm and deliberate harmful misinformation made on social media, there were multiple instances of serious abuse in the 'real world'. Examples include two vexatious complaints to the General Medical Council ('**GMC**'), "poison-pen" letters and a "suspicious package" containing white powder (it was garlic powder) sent to me at my place of employment, I&S I&S I also received emails threatening "Nuremberg Justice", details of where I live alongside false information (presumably to attract secondary protest, threats, or harm) were posted on various internet bulletin boards, I was "called-out" when walking my dogs, and on one occasion one of my children was harassed in her classroom by a teacher who was upset by the government's policy and blamed me.

14.7. I received good support in relation to my and my family's security from the SAGE Secretariat, security services and local police. For a few weeks, I had a police officer accompany me when I gave lectures and attended meetings that were open to the public. I am aware that other government and non-governmental SAGE advisors experienced similar and greater levels of serious abuse. Dealing with this persistent serious abuse was tough at times, and for reasons of security, we did not share details of these threats, except with immediate family and work colleagues on a need-to-know basis. My immediate family, colleagues on SAGE and work colleagues were a source of strength and solace.

The UK's science-policy advisory mechanisms

14.8. On the topic of the UK's science-policy advisory mechanisms, and whether they should be re-evaluated, my view is that the term re-evaluation suggests that some evaluation has already occurred. I am not aware that an evidence-based approach has evaluated the SAGE activations or other science-policy advisory mechanisms that our various elected Governments have for emergencies. I would welcome an evidence-based evaluation of SAGE's advice for COVID-19 if done alongside the advice of past SAGEs for other emergencies as I expect that common themes for knowledge acquisition and public protection will emerge. It was a process such as this that ISARIC used to develop its core studies for outbreaks and pandemics and these core studies positioned ISARIC to generate knowledge in time to save lives.

14.9. It is my opinion that Scientists and Policymakers would work better together if the Policymakers, their Special Advisors, and Civil Servants included people with a greater diversity of thought by being drawn from a wider pool of backgrounds that included people with some experience in science, technology, engineering, mathematics, and medicine. It has been my experience that most of our Policymakers and many of their Special Advisors have well-developed excellence in the skills of analysis of literature and the art of communication. This is probably because of their work in developing policy and legislation, requiring skills that lean more on qualifications in the humanities. In government, dialogue discourse and debate, often supported by the agreement of a majority, provide the levels of confidence in a course of action. In such a setting, challenging an agreed policy or changing one's mind on an agreed course of action is anathema and can be seen as disloyal. I think this culture pervades government departments and at times the civil service. Policy people are less familiar with the language of science and the behaviour of Scientists. Scientists qualify our analysis with terms such as "confidence bounds" and "levels of certainty". We abhor debate based on eminence and unsupported opinion, and favour debate of evidence based on data. Good Scientists change their minds when the data contradicts a previous understanding. Good Scientists respect flexibility in the mind, when that change is based on evidence. Likewise, Scientists and Clinicians would work better with Policymakers were more Scientists and Clinicians willing to step into policy teams, even if only on a part-time basis for short secondments to projects. I learned a great deal about how evidence can be translated into policy and policy into practice when I

was seconded from my clinical academic role to the role of a Senior Medical Advisor in the Department of Health's Pandemic Influenza Planning group in 2008-10.

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.

Name: Professor Malcolm (Calum) Gracie Semple

Signed: Personal Data

Dated: 31st August 2023