Witness Name: Professor Nishi Chaturvedi
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COVID-19 INQUIRY – MODULE 2

First Witness Statement of Professor Nishi Chaturvedi

I, **PROFESSOR NISHI CHATURVEDI**, of the Faculty of Population Health Sciences at University College London, 170 Tottenham Court Road, London, W1T 7HA will say as follows:

1: Introduction

1.1. I make this statement pursuant to the Covid-19 Inquiry's Module 2 Rule 9 Request of 4 May 2023 (**'The Rule 9'**).

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

1.3. 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 a source for those facts. The contents of this statement are true to the best of my knowledge and belief.

2: Professional Background and Expertise

2.1. I am a professor of clinical epidemiology. I obtained my first degree in medicine at London University in 1985. I then completed specialist training in general medicine, public health, and epidemiology.

2.2. I was appointed to a Chair in the National Heart and Lung Institute at Imperial College London in 2000, and then to the Institute of Cardiovascular Sciences at University College London (**'UCL'**) in 2014. My research career includes leadership

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of international observational cohort studies and clinical trials in understanding and mitigating the complications of diabetes. I lead the Southall and Brent Revisited (**'SABRE'**) study of a tri-ethnic cohort, which was designed to examine ethnic differences in the risks and consequences of cardiometabolic disease.

2.3. I was appointed Director of the Medical Research Council (**'MRC'**) Unit for Lifelong Health and Ageing at UCL in 2017.

2.4. In 2020, I was asked to lead the Longitudinal Health and Wellbeing Covid-19 National Core Study (**'LH&W NCS'**). The National Core Studies (**'NCS'**) were established by the Government Chief Scientific Advisor (**'GCSA'**), Sir Patrick Vallance, in October 2020 to bring together Covid-19 research in key domains, synthesise, and report findings as requested, and identify research gaps and ways of addressing these. There are six Core Studies. They cover the following topics: epidemiology and surveillance, clinical trials and infrastructure, transmission and environment, immunity, longitudinal health and wellbeing (the LH&W NCS, led by me) and data and connectivity.

2.5. I wish to be as helpful as I can to the Inquiry to further the important work that they are undertaking. However, there are limits to my knowledge. This is due to certain matters not being within the realm of my knowledge and expertise, not having direct knowledge of some of the events and matters that occurred during the pandemic and the fact that I did not keep a personal diary or any contemporaneous notes or records of events throughout the pandemic. I also had to maintain my usual day job of running an MRC Unit as well as responding to the pandemic, so had little time to maintain notes or attend all meetings to which I was invited. Covid-19, and Long-Covid, as diseases, are not my area of expertise. Both the LH&W NCS and the associated CONVALESCENCE Long-Covid study (**'The CONVALESCENCE study'**) arose from my standing in the field of epidemiology and track record in leading consortia. Accordingly, I have indicated throughout this statement where I consider that I am not able to comment on certain matters as they are beyond the scope of my knowledge and expertise.

2.6. It is not the role of SAGE participants to provide views on policy matters or decisions. Accordingly, I am not able to comment on these issues within this witness statement, nor am I able to comment on how the data provided through the LH&W NCS was used to inform policy decisions.

3: Involvement in SAGE and other groups

3.1. I participated in two SAGE meetings in my capacity as lead of the LH&W NCS. I participated in SAGE meeting 82 on 25 February 2021 and SAGE 94 on 22 July 2021 **[NC/01 – INQ000120602; NC/02 – INQ000092856]**.

3.2. I also attended two of Lord Bethell's Long-Covid Ministerial Roundtable meetings on 13 October 2020 and 23 September 2021 **[NC/03 – INQ000250173; NC/04 – INQ000250174]**. I received some invitations to the Long-Covid National Taskforce meetings, co-ordinated by the National Health Service England ('**NHSE**') and NHS Improvement ('**NHSI**'), but I did not attend any of these meetings due to time constraints. I attended 4 meetings of the Chief Medical Officer's ('**CMO**') Long-Covid working group **[NC/05– INQ000251614; NC/06 – INQ000251615; NC/07 – INQ000251616; NC/08 – INQ000251617]**.

4: Long-Covid

4.5. The study of Long-Covid, or other long-term sequalae arising from Covid-19 as a disease, is not my area of expertise, and I did not specifically follow the identification and progression of the disease during the initial stages of the pandemic, being more focussed on the NCS when I was invited to participate in this.

4.6. I cannot pinpoint exactly when I became aware of the risk of long-term sequalae arising from Covid-19. As I mention above at paragraph 2.5, I did not keep a personal diary or contemporaneous notes or records of events during the pandemic. I do recall that I was aware of publications reporting subclinical cardiac damage in response to Covid-19 infection, detected by cardiac magnetic resonance imaging ('**MRI**'), in July 2020 **[NC/09 – INQ000250175]**. In parallel, as a member of the National Institute of Health Research/UK Research and Innovation ('**NIHR/UKRI**') panel on rapid research response funding, I was aware of a NIHR/UKRI call wishing to understand the neuropsychiatric consequences of Covid-19, including mental health, cognition, and post-traumatic stress disorder ('**PTSD**') in May 2020. In addition to this, in August 2020, although our LH&W NCS was not formally in existence, the GCSA notified me of the creation of the Long-Covid ministerial (Bethell) group **[NC/10 – INQ000250176]**. So, although I cannot pinpoint an exact date, from the above recollections I can say that I certainly must have at least been aware of the risk of long-term sequalae arising from Covid-19 by mid- 2020.

4.7. I cannot recall when the risk of long-term sequalae from Covid-19 was first identified in the United Kingdom. The science around infection is not within my area of expertise, so I was essentially an informed observer of the pandemic until I became formally involved in it through the NCS in the summer of 2020. As I mentioned at paragraph 2.5, I did not keep a personal diary or contemporaneous notes of events throughout the pandemic, so I am not able to comment on when and how UK-wide knowledge around long-term sequalae from Covid-19 evolved.

4.8. I cannot comment on the international understanding of long-term sequalae arising from Covid-19 as I did not conduct a formal, scientific review of this topic at any point during or after the pandemic. In addition to this, the vast body of scientific evidence around this topic was rapidly evolving during the pandemic, so published scientific analyses were not readily available as they took time to be developed and published. One could only rely on social media and pre-print uploads to MedRxiv (a pre-print service enabling the research community to view findings online as authors developed and submitted their manuscripts) raising awareness of new discoveries. Furthermore, my job, at the time, was focused on the LH&W NCS.

4.9. I am not able to comment on when and how SAGE responded to the developing recognition of the risk of long-term sequalae from Covid-19. As I mentioned at paragraph 3.1, my involvement with SAGE was limited, having only participated in two meetings in 2021, which focussed on the NCS **[NC/01– INQ000120602; NC/02 – INQ000092856]**.

4.10. As I mentioned at paragraph 4.3, the science around infection is not my area of expertise. I am aware of the experience we had of Severe Acute Respiratory Syndrome (**'SARS'**) and Middle East Respiratory Syndrome Coronavirus (**'MERS'**) around a decade or so ago. These were Coronaviruses which did have long-term sequalae of the same nature that we are seeing with Covid-19, so in that sense it was reasonable to hypothesise that there would be a risk of long-term sequalae from Covid-19, as a Coronavirus, and this was a foreseeable consequence of the disease. However, my position on this is purely speculative as infectious disease epidemiology is not my area of expertise.

4.11. I am not able to comment on how the risk of long-term sequalae altered or impacted upon the approach taken by SAGE in its provision of advice to core decision-makers. My involvement in SAGE was limited and I did not attend my first meeting until

February 2021 **[NC/01– INQ000120602]**. In addition to this I was not aware of the previous thinking on the subject matter by SAGE.

4.12. I am aware that providers of general practice ('**GPs'**) IT systems created a series of codes for Long-Covid that GPs could use. These electronic health records (**'EHRs'**) can then be used for analysis. Separately, the Zoe app, which was used to study the symptoms of Covid-19 and track the spread of the virus, asks people to self-register and report symptoms on the app. This captured symptoms of Long-Covid. Finally, the Office for National Statistics ('**ONS**'), as part of the epidemiology and surveillance national core study, sent out regular surveys to samples of the general population, while the LH&W NCS distributed questionnaires to participants in previously established population cohorts, both to capture symptoms of Long-Covid. All these mechanisms have their inadequacies. Uptake of Long-Covid codes in primary care was low in the initial stages of the pandemic **[NC/11 – INQ000250177]**. Further, this relies on patients consulting with their GP, and the GP choosing to assign a Long-Covid diagnosis to their symptoms. In contrast, while the Zoe app does not require a GP diagnosis, it relies on volunteers, and so does not capture characteristics of the entire population. Questionnaires to the general population and cohort participants may suffer from non-response bias (i.e., people who are unwell, possibly with Long-Covid are less able to complete questionnaires). So, neither platform is perfect. However, it is hard to envisage a cost-effective unbiased solution. Triangulation of findings across these admittedly imperfect data resources may be of value, in that consistent results across different platforms are potentially more likely to be valid.

5: Longitudinal Health and Wellbeing National Core Study (LH&W NCS)

5.5. In July 2020 I was approached by the GCSA by telephone, to establish the LH&W NCS. The LH&W NCS was part of a family of NCS described at paragraph 2.4, that were created by the GCSA to coordinate Covid-19 research, essential to our understanding of the SARS-CoV-2 pandemic, and to respond to government needs for information. As I have described at paragraph 2.4, apart from the LH&W NCS, other NCS covered topics such as immunity, surveillance, transmission and the environment, clinical trials, data and connectivity and vaccination. An Oversight Group, chaired by the GCSA, coordinated, and provided recommendations for the activities of each of the NCS and advised on leadership. Membership of the Oversight Group included the CMO, senior academic advisors, representation from

the devolved nations, research funding bodies, and independent international members. The Oversight Group responded to requests from the government and made decisions on the direction of the NCS, considering the progression of the epidemic. Funding was agreed with the government in October 2020 and provided to the LH&W NCS via UKRI.

5.6. As part of the LH&W NCS, I brought together leaders of major longitudinal population studies ('**LPS**') in the UK. These studies have recruited large numbers of volunteers from the general population for health-related research and have measured an array of health and sociodemographic characteristics, with repeat measures at intervals for many years. This is a unique resource to understand the health impacts of Covid-19 infection, as we had significant information on the health of these participants before the pandemic. Additionally, I approached leaders in the analysis of national EHR, including the recently established OpenSAFELY platform. EHR have the advantage of full national coverage, with detailed data on medication and outcomes, but lack the in-depth health measures on all participants, regardless of health status, which is available in the LPS. Addressing research questions across these complementary platforms allows us to harness the strengths of each, and provides validation if findings are replicated across different studies and platforms.

5.7. We assembled a group of researchers and associated analysts experienced in the use of EHR platforms (i.e., OpenSAFELY or the British Heart Foundation CVD-COVID-UK platform), as well as lead investigators of key population cohorts and associated analysts. We created teams around the various key themes such as healthcare disruption and mental health. The group discussed what the priority analyses were, which were then put forward to the executive group and then to our Scientific Advisory Board ('**SAB**') for ratification. The analysts then would write a statistical analysis plan for each of these key questions, which would be circulated, reviewed, and agreed. After this process, they would conduct the analysis, and come back together with findings, which again would be discussed and put together in publications which would be sent to the various groups that wanted them.

5.8. I was appointed as the lead of the LH&W NCS by the GCSA. The oversight group that the GCSA chaired, had been meeting for some time before I was approached for this position. The Chief Executive of the MRC, who at the time was Fiona Watt, was a part of the oversight group, and she was asked by the GCSA to recommend candidates to lead the LH&W NCS. I believe, but I am not certain that, she

recommended me for the role. The GCSA subsequently approached me. I am not able to provide information on why I was put forward as a candidate. However, my experience as a leader of two population cohorts, my leadership of an MRC funded research unit, my collaboration with groups using electronic health records for research, my standing in the field and my track record in co-ordinating previous research consortia may all have contributed to my selection for the role. My role as lead of the LH&W NCS was to provide strategic overview and co-ordination, as well as being the first point of contact for external partners to come into the program.

5.9. An Executive Group was established within the LH&W NCS, consisting of representatives from the research team and funders to identify research domains and key questions, responding to the evolving pandemic and requests for information. The LPS had programme management support, and a communications officer. I also invited Professor Jonathan Sterne from Bristol University, who was also a member of the research team, to co-lead the LH&W NCS. This enabled the sharing of strategic and reporting responsibilities. We reported to the SAB, chaired by Dame Anne Johnson, who was also a member of the Oversight Board. We presented plans of our work to the SAB for review and revision and sought their advice in terms of ensuring our work was best aligned to policy needs. The co-leads of the LH&W NCS (myself and Professor Sterne), alongside Dame Anne, reported progress back to the Oversight Board. Additionally, after external review in October 2021, Professor Sterne and I also reported to the UKRI NCS Programme Board. **[NC/12 – INQ000250178]** lists the membership of the LH&W NCS Executive Board and the Scientific Advisory Board.

5.10. The aim of the LH&W NCS was to investigate the medium and long-term health, social and economic impacts of the Covid-19 pandemic to inform policy. The objectives were to:

a. Establish a centralised, responsive resource linking data assets from a diverse range of LPS with health, social and environmental records, with harmonised governance for processing and research interrogation. This is what eventually became the UK Longitudinal Linkage Collaboration ('**UK LLC**').

b. Establish a cadre of highly skilled big data scientists.

c. Create processes, such as a regular meeting format, shared research question database, and shared workspace to ensure co-ordination across and between LPS and EHR analysis.

5.11. To achieve this, a multidisciplinary team of over one hundred scientists from leading UK institutions, as described in sections 5.2 and 5.3, was formed with pooled and aligned complementary resources and skill sets. New infrastructure/national EHR platforms were created, and we brought together LPS at an unprecedented scale. Additionally, we harnessed the power of newly created national EHR platforms, such as OpenSAFELY and the NHS Digital Trusted Research Environment ('**TRE**'), established by the British Heart Foundation Data CVD-COVID-UK.

5.12. The LH&W NCS team also trained a new generation of data scientists, both from within the collaborating institutions, and secondees across the country, in the use of unique, complex, and highly informative datasets. Early career researchers were given the opportunity to lead the research and gain valuable experience working in a large collaboration.

5.13. Public involvement and engagement throughout have ensured that all work is informed by the experiential knowledge that is held by people who have been directly or indirectly affected by Covid-19 and Long-Covid. This has maximised the potential benefits of the work to people who have been impacted and the wider society.

5.14. The team work collectively across several areas:

a) Uptake, safety and effectiveness of ***vaccination and treatment***; Impact of the pandemic on ***healthcare disruption***.

b) ***Mental health*** as both a determinant and consequence of infection and of the wider pandemic.

c) Inter-relations between ***society and health***, including education, employment, and financial security.

d) ***Serology*** and its association with infection and vaccination.

e) ***The Risks and consequences of Covid-19 infection***: This became the CONVALESCENCE Study (upon gaining new competitive research funds from a joint NIHR/MRC call).

Types of data analysed by the LH&W NCS

5.15. The LH&W NCS united, for the first time, twelve highly characterised key population-representative LPS and four population-level linked EHR. To provide robust evidence that can inform policy we created a framework to facilitate triangulating analyses in EHR and LPS. Collectively this UK-wide consortium is a representative resource **[NC/13 – INQ000250179]**. These different types of datasets are described below:

5.16. **EHR:** National entire population EHRs provide an impressive breadth of coverage, as virtually the whole population is registered with a GP. They capture all individuals presenting to health professionals, with linked prescribing, consulting, referral, and outcome data. However, linked EHRs miss those not presenting to services and do not systematically capture all symptoms, such as fatigue, and subclinical mental health distress, which are required for a full impact evaluation. Results from this consortium also show that Long-Covid is poorly measured in primary care **[NC/11 – INQ000250177]**.

5.17. **LPS (n=200,000):** In this study, 12 LPS joined forces so that we had detailed information on a total of 200,000 people from both before and during the pandemic. LPS studies recruit volunteers from a defined sampling frame (e.g., all births in a certain timeframe, all those between certain ages living in a geographical area), measuring key characteristics, including health measures at recruitment, and returning periodically to repeat measures. In this way, we can understand the association between exposures (e.g., smoking), and disease (e.g., heart disease, cancer). A key advantage of the LPS during the pandemic was that significant pre-pandemic health data were available, so that we could distinguish between the health impacts of Covid-19 from general health status that existed pre-pandemic. A collaborative of 12 LPS was created, enhanced by questionnaire and serological measures, and linked to both health and administrative data. Though representing a smaller sub-population than national EHR systems, LPS provide a rich depth of pre-pandemic health and socioeconomic data, collected at multiple time points, dating back to 1946. The LPS span the UK, representing participants from wide socio-economic and demographic backgrounds and importantly capture individuals that do not present to health professionals.

5.18. **New data collection**: Questionnaires completed by LPS participants throughout the pandemic collected information on Covid-19 signs and symptoms, the effect of lockdown on physical and mental health and overall wellbeing, neighbourhood

issues, domestic violence, alcohol use, healthcare, thoughts on the lockdown and new connections made during the pandemic. In parallel to the questionnaires, serial antibody testing results have also been collected on a subsample of 33,000 people drawn from the 200,000 plus participants in the LPS **[NC/13 – INQ000250179]**.

5.19. **Data harmonization**: The team has harmonized data from diverse sources and increased statistical power to answer policy-relevant questions.

5.20. **UK LLC:** As part of the LH&W NCS, the UK LLC has established a new national TRE for longitudinal research. For the first time, a considerable proportion of the interdisciplinary UK longitudinal community have committed to a new-way-of-working based on a centralised TRE -The UK LLC. The UK LLC is now acting as a 'pathfinder' TRE for the UK. Work using the UK LLC includes an exploration of the disruption of healthcare provision because of pandemic mitigation measures. The UK LLC has allowed linkage of individual reports of experience of disrupted healthcare to health outcomes in the EHRs of the same individuals across several large cohort studies, enabling the identification of the risks associated with disrupted care **[NC/14 – INQ000250180]**. It has also enabled individual level quantification of Long-Covid GP coding which shows a striking discrepancy between Long-Covid, as perceived and reported by participants in LPS, and evidence recorded in their EHRs **[NC/15 – INQ000250181]**. This could reflect substantial unmet clinical need, in keeping with patient reports of difficulties accessing healthcare and sub-optimal recognition of, and response to, their illness when they do.

5.21. **Open Science:** The team have embraced modern open approaches to data science, sharing statistical code used for analysis openly to the whole community, as the bedrock of deep technical collaboration; working closely with research software engineers alongside traditional domain experts with research knowledge; and moving away from "manual labour" on datasets towards "reproducible analytic pathways", with well tested and re-executable code, in line with best practice in data science. They have also developed new methods for preserving patients' privacy which allowed an unprecedented scale of data access - using 58 million patients' full GP records in research for the first time ever and earning active and positive support from privacy campaigners who have previously blocked access on this scale by other means.

Findings of the LH& W NCS

5.22. I am not able to discuss how the findings of the LH&W NCS were used to inform political decision making. This is because 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. However, I describe the findings of the LH&W NCS below:

5.23. Mental Health: The pandemic had immediate and long-term effects on people's mental health, and the extent of these effects has varied from person to person. Our research showed that people with pre-existing poor mental health experienced greater adverse effects of the pandemic, including healthcare and economic disruptions **[NC/16 – INQ000250182]**. We also showed that mental health deteriorated during the initial stages of the pandemic, with severity varying by demographics and mental and physical health history **[NC/17 – INQ000250183]**. This mental health decline did not recover when lockdown was lifted **[NC/17 – INQ000250183]**. We also provide some of the first evidence from population based longitudinal studies on the mental health aspects of mild and moderate Covid-19 infection **[NC/18 – INQ000250184]**. This research demonstrates the importance of using longitudinal studies and other population-based data to understand the mental health impacts of the pandemic, rather than relying on convenience samples, which are participants who are selected at random as they are the easiest for the researcher to access.

5.24. **Society and Health:** We investigated the impact of furlough and home working on mental and physical health behaviors during the pandemic **[NC/19– INQ000250185] [NC/20 – INQ000250186; NC/21 – INQ000250187; NC/22 – INQ000250191]**. We found that furlough had a protective effect on psychological distress and loneliness, compared to those who lost their jobs **[NC/21 – INQ000250187]** and **[NC/23 – INQ000250194; NC/24 – INQ000250188]**. There was no clear evidence of an association between home working and mental wellbeing **[NC/25 – INQ000250189]**. Long-Covid can lead to worse subjective financial wellbeing, new benefit claims, and decreased household income **[NC/26 – INQ000250190]**, which suggests that extending employment protection and financial support to people with Long-Covid may be necessary.

5.25. **Healthcare Disruption:** Using a three nations (England, Scotland, and Wales) EHR approach we showed that hospital care for non-Covid diseases fell substantially, with reductions persisting for at least six months. The most deprived and minority ethnic

groups were impacted more severely **[NC/27 – INQ000250195]**. LPS data showed that females, ethnic minority groups and those in a more disadvantaged social class were more likely to report healthcare disruptions **[NC/28 – INQ000250196]**. In linked LPS-EHR data, more than 1 in 3 people (35%) reported that they experienced some form of disrupted access to healthcare during the Covid-19 pandemic. People who experienced disrupted access to healthcare were more likely to have experienced avoidable or potentially preventable hospitalisations. Disrupted access to appointments (e.g., visiting their GP or an outpatient department) and procedures (e.g., surgery, cancer treatment) were key pathways for explaining increased risk of avoidable hospitalisations **[NC/14 – INQ000250180]**. Action is needed to remedy these inequalities, and efforts to ensure continuity of care during pandemic-related disruptions may need to be more clearly targeted to those most in need of care.

5.26. **Serology:** The Serology team has been studying SARS-CoV-2 antibody levels in the LPS to assess immune responses following natural infection or vaccination. We found that individuals with the lowest 20% of anti-Spike antibody levels had a 3-fold greater risk of SARS-CoV-2 infection compared to the top 20%. Individuals at increased risk of Covid-19 complications had consistently greater odds of having low antibody levels. We found that third vaccination increased absolute antibody levels for almost all individuals and reduced relative disparities compared with earlier vaccinations, demonstrating the value of triple vaccination **[NC/29 – INQ000250197]**. The LPS are also playing a key role in the NCS Immunity programme, where cohorts are charting the immune response to infection in the real world, longitudinally and in great detail.

5.27. **Vaccination:** Our early Covid mortality risk stratification work was a critical part of creating the prioritisation groups, responding to the UK Joint Committee on Vaccination and Immunisation ('**JCVI**') on requests for data **[NC/30 – INQ000250198]**. Our work in LPS, describing participants views on whether they would accept vaccination or not **[NC/31 – INQ000250199]**, was reflected in actual uptake by subgroup in analyses performed in OpenSAFELY **[NC/32 – INQ000250200; NC/33 – INQ000250201]**. This demonstrated hesitancy in key ethnic subgroups **[NC/34 – INQ000250202]** which informed policies to improve uptake. We also informed on the comparative effectiveness of initial vaccines **[NC/35 – INQ000250203]** and **[NC/36 – INQ000250204]**, how that effectiveness has changed over time **[NC/37 – INQ000250205]**, the effects of dosing intervals on vaccine

efficacy **[NC/38 – INQ000250206; NC/39 – INQ000250207]** and the effectiveness of booster vaccination **[NC/40 – INQ000250208]**.

5.28. **Treatment:** We reported on which patient groups were being given new Covid-19 treatments, finding large regional variation, with particularly low administration in socioeconomically deprived areas and care homes **[NC/41 – INQ000250209]**. We then described the real-world effectiveness of these treatments, initially comparing two of the first used treatments, molnupiravir and sotrovimab **[NC/42 – INQ000250210]**. We have demonstrated that data about roll out of new treatments can be rapidly linked to primary care and other data, to monitor drug coverage and effects in near-real time and produce unbiased estimates of drug effectiveness. This data has been used to inform the National Institute for Health and Care Excellence (**'NICE'**) and NHSE prescribing guidance and World Health Organisation (**'WHO'**) as part of their review of the recent guidance.

5.29. **Long- Covid:** Our work showed that diagnostic codes for Long-Covid to be used in primary care computer records, essential for researchers in identifying cases, were poorly and inconsistently used, and this, in tandem with difficulty and hesitancy in obtaining a primary care consultation, meant that Long-Covid was greatly under-reported in routine health care records **[NC/11– INQ000250177]**. Further work on Long-Covid is reported under the details of the CONVALESCENCE study.

5.30. To date the team have provided policy makers with information via presentations, SAGE reports and briefing notes on:

a) Long-Covid burden of disease, risk factors, and the definition and long-term outcomes **[NC/43 – INQ000250211]**.

b) Long-Covid GP coding differences **[NC/43 – INQ000250211]**: The reporting of low levels of GP Long-Covid coding led to an enhanced NHS service specification.

c) The significance of pre-pandemic mental health on health care disruptions **[NC/44 – INQ000250212]**.

d) How government initiatives such as the furlough scheme have affected health and wellbeing **[NC/45 – INQ000250213]**.

e) Inequalities in healthcare disruption **[NC/46 – INQ000250214]**.

f) Explanations for differential vaccine uptake **[NC/47 – INQ000250215]**.

g) Vaccination prioritisation, delivery, and measurement of safety and effectiveness.

h) Rates of vascular complications following vaccination **[NC/43 – INQ000250211]**.

i) The importance of the booster vaccination **[NC/48 – INQ000250216 ; NC/24 – INQ000250188].**

j) Using a three-nation approach we have quantified the extent of healthcare disruption. This is the largest study (over 74 million person-years- i.e., a multiplication of the number of people involved times the number of years each person provided follow up data) investigating the impact of Covid-19 disruption and associated lockdown measures on hospital admissions **[NC/27 – INQ000250195]**.

5.31. During lockdown, the team identified instances of inappropriate switching of blood thinners that resulted in a national alert to GPs **[NC/49 – INQ000250217]**.

5.32. Increased risk of cardiovascular complications (including blood clots) **[NC/43 – INQ000250211 ; NC/50 – INQ000250218]** (**and further unpublished work**), diabetes **[NC/51– INQ000251933]** and mental health complications up to a year after Covid-19 infection.

5.33. Treatment work has shown that data regarding the roll out of new treatments can be rapidly linked to primary care and other data, to monitor drug coverage and effects in near-real time and produce unbiased estimates of drug effectiveness. This work informed NHSE prescribing guidance. It also shows the possibility of better use of linked data to conduct or emulate low-cost, rapid Randomised Control Trial's ('**RCT's**')– particularly when drug effectiveness is likely to be changing rapidly, as at present.

6: The CONVALESCENCE study

6.5. The CONVALESCENCE study is a cross-institution, multidisciplinary collaboration of biomedical, social and data scientists, spanning cohorts, EHRs, quantitative and qualitative analysts, detailed clinical investigations, and policy groups such as NICE. The approach is similar to that described for the LH&W NCS, namely analysis of existing LPS data, enhanced by questionnaire data collection during the pandemic, and national linked EHR. Additionally, people with Long-Covid, and people without,

were recruited from our portfolio of LPS to attend a central London clinic for detailed examination which included non-invasive imaging of the heart, brain, lungs, liver and kidneys, tests of exercise capacity, cognition, and assessment of mental health. Qualitative interviews were undertaken with a separate group of LPS participants reporting Long-Covid, and healthcare providers.

6.6. There is limited evidence, of varying quality, of the long-term effects of previous pandemics on physical health, for example cardiovascular disease. I was aware of publications reporting subclinical cardiac damage in response to Covid-19 infection, detected by MRI in July 2020 **[NC/09– INQ000250175]**. In parallel, as member of the NIHR/UKRI panel on rapid research response funding, I was aware of a call wishing to understand the neuropsychiatric consequences of Covid-19, including mental health, cognition, and PTSD in May 2020.

6.7. As stated above, I was made aware of an NIHR and UKRI call on the topic of long-term sequalae arising from Covid-19 by the MRC, who were funders of the NCS. We were invited to an advisory group on that call, recognising that we may well be applicants to the call. The NCS seemed very well placed to address key aspects of the call, and after a discussion with the executive group we decided to submit an application for the call. In February 2021, our consortium, including all those involved in the LH&W NCS, and additional members, to inform a detailed phenotyping sub study of LPS participants willing to come forward to a London clinic for in-depth examinations including MRI of brain and heart, exercise testing and deployment of wearable devices, was awarded competitive research funds from a joint call by NIHR and UKRI to study Long-Covid **[NC/52 – INQ000250220]**. This became known as the CONVALESCENCE study described above in paragraph 6.1. The governance of the CONVALESCENCE study was wrapped into that of the LH&W NCS.

6.8. The CONVALESCENCE study aims to answer the following questions:

a) How can we best define Long-Covid?

b) What are its risk factors and mechanistic pathways?

c) What are the consequences for physical and mental health, and for work, education, and social and familial relations?

d) Can we enhance Long-Covid's diagnosis and management through GP records?

6.9. CONVALESCENCE research has improved diagnostic precision for research and informed strategies for care provision by being directly reported to:

a) Policymakers: via SAGE reports **[NC/43 – INQ000250211]** meetings and a Cabinet Office Teach-in session **[NC/53 – INQ000250221; NC/54 – INQ000250222]**.

b) The NHS: via NHSEI presentations.

c) NICE: to provide evidence for living guidelines.

6.10. The work of the CONVALESCENCE study included the following findings on definition, risk factors, healthcare access issues and long-term outcomes in relation to Long-Covid:

6.11. **Long-Covid definition**: Data from 42,000 people pooled from nine different LPS showed that symptoms for Long-Covid included fatigue, shortness of breath, muscle pain or aches, difficulty concentrating and chest tightness. Two distinct symptom patterns were found, representing high and low symptom burden. The identified patterns among individuals with Covid-19 more than twelve weeks ago were strongly associated with self-reported length of time unable to function as normal due to symptoms **[NC/55 – INQ000250223]**.

6.12. Long-Covid risk: Triangulation of ten LPS and EHR (OpenSAFELY) data showed that risk factors for Long-Covid were consistent and included increasing age, female sex, white ethnicity, poor pre-pandemic general and mental health, being overweight/ having obesity, and asthma **[NC/56 – INQ000250224; NC/35 – INQ000250203; NC/36 – INQ000250204]**. Consistent findings across analysis of different datasets to address the same question, known as 'triangulation,' provides greater assurance that findings are valid.

6.13. Health care access issues: We found that GP coding for Long-Covid in primary care computer records was low, inconsistent and is significantly below other estimates of Long-Covid prevalence. Codes for describing Long-Covid in primary care were created in late 2020. OpenSAFELY described the early use of those codes and identified generally low use of the codes compared to survey-based estimates, as well as substantial geographic variation, and different levels of coding depending on the EHR software that practices used. We subsequently had substantial discussion with NICE about how our findings might impact their subsequent revision of Long-Covid guidance (for example, by prompting GPs to consider a diagnosis of

Long-Covid in those consulting with fatigue). We also shared the results with EHR software providers to discuss how their software might affect recording of these details. Since our initial publication, we have continued to monitor recording of Long-Covid and have seen gradual increases in recording over time **[NC/11– INQ000250177]**.

6.14. The NICE group suggested including a prompt within GP records, asking practitioners to consider the possibility of Long-Covid when they typed in fatigue as a patient symptom. This suggestion did not materialise due to the fact that suppliers of the computer IT systems for primary care improved the way that GPs could access the Long-Covid codes in primary care computer records. Therefore, we ultimately did not end up conducting substantial research on the diagnosis and management of Long-Covid.

6.15. In addition, forty qualitative interviews were conducted by the team with people with Long-Covid, alongside twelve interviews with healthcare professionals providing Long-Covid support in Bradford, as part of a UK wide CONVALESCENCE Qualitative Longitudinal Study. Those living with Long-Covid had significant difficulty in accessing healthcare services for Long-Covid support. The team categorised the healthcare access experiences of participants into five main types: 1) being unable to access primary care 2) accessing primary care but receiving (perceived) inadequate support 3) extreme persistence in trying to access healthcare 4) accessing alternatives to mainstream healthcare 5) positive experiences. There was a severe lack of access to specialist Long-Covid services. Ethnic minority participants faced a further barrier of mistrust and fear of services, deterring them from accessing support. Healthcare professionals discussed systemic barriers to delivering services. This work has been passed onto the NHSE/I Long-Covid Taskforce **[NC/57 – INQ000250225]**. This work is not yet published.

6.16. Long-Covid outcomes: Using EHR data, the team showed an increased risk of cardiovascular complications (including blood clots) **[NC/50 – INQ000250218]** and **[NC/34 – INQ000250202]**, diabetes **[NC/51 – INQ000251933] (unpublished)** and mental health complications up to a year after Covid-19 infection. Using LPS data we saw that Long-Covid can lead to worse mental health **[NC/18 – INQ000250184]** and subjective financial wellbeing, new benefit claims, and decreased household income, which suggests extending employment protection and financial support to people with Long-Covid may be necessary **[NC/26 – INQ000250190]**.

6.17. Deep phenotyping and remote assessment using wearable devices and smartphones have been employed in LPS participants to identify subclinical damage or dysfunction in people experiencing Long-Covid. The data collection phase has now ended, and we have begun data analysis. No findings are available yet. We expect initial findings to be ready during quarter 4 of 2023.

Research platforms used by the CONVALESCENCE study and LH&W NCS

6.18. OpenSAFELY, hosted by the Bennett Institute for Applied Data Science at the University of Oxford (whose lead is Ben Goldacre), was established in the initial stages of the pandemic and provides a secure platform for analysis of English national EHRs, specifically linking primary care, hospital and Covid-19 testing data. The core research team across Oxford (led by Professor Ben Goldacre) and the London School of Hygiene and Tropical Medicine ('**LSHTM'),** (led by Liam Smeeth, and then Laurie Tomlinson) rapidly addressed key questions on risk factors for Covid-19 infection, its consequences, vaccine uptake and the impact of the pandemic on healthcare utilisation. The approach used was that adopted by the LH&W NCS, (i.e., that priority research questions were agreed by the LH&W executive, ratified by the SAB and the Oversight Board). Analysts from these institutions were assigned to the work, and tasked with developing an analysis protocol, to be shared with the wider group. All code developed for analysis is shared, and analysis performed in the secure OpenSAFELY environment to preserve patient anonymity. The OpenSAFELY team onboarded new researchers from other institutions participating in the LH&W NCS, notably Bristol, to extend capacity. This platform has been hugely valuable to the LH&W NCS, and to policy understanding as a whole in response to the pandemic. Examples include demonstration of inequalities in obtaining Covid-19 vaccination **[NC/41 – INQ000250209]**, impacts of Covid-19 treatments **[NC/42 – INQ000250210]**, and risk factors for Long-Covid (the latter in alliance with the LPS analysis) **[NC/56 – INQ000250224]**. Analyses were also performed to identify those at high risk of Covid-19 infection and its sequelae, specifically some groups targeted for shielding such as those living in care homes **[NC/58 – INQ000250226]** or severe learning disabilities **[NC/59 – INQ000250227]**.

6.19. Some months later, the British Heart Foundation (**'BHF'**) CVD-Covid UK was established by Health Data Research UK ('**HDRUK'**), led by Cathie Sudlow (also a member of the LH&W SAB). This also provides access to linked national primary and secondary healthcare records, with a focus on cardiovascular disease research in

association with Covid-19. This platform was used by the Bristol team in understanding the effect of Covid-19 infection on cardiovascular outcomes **[NC/43 – INQ000250211]**. This platform is less widely used by the LH&W NCS as it has limited primary care data, compared to the OpenSAFELY platform.

6.20. Both platforms are limited for research on the syndrome of Long-Covid. Researchers rely on patients coming forward to GPs to articulate their symptoms, the GPs arriving at a diagnosis of Long-Covid, and the ready availability of Long-Covid codes from system suppliers for GPs to use. In contrast, we sent questionnaires to our LPS participants directly, interrogating the presence of Long-Covid symptoms. In a comparison of LPS reports with EHR data in OpenSAFELY, it is clear that there is significant under-reporting of Long-Covid in primary care **[NC/56 – INQ000250224]**.

6.21. We invested in the UK LLC part of the portfolio of activity of the LH&W NCS. This enabled and streamlined linkage of LPS data to their EHRs. Previously, each LPS would have to negotiate such linkage separately, a time consuming and costly activity. Such linkage allows us to study associations between, for example, Long-Covid and receipt of health care, and health outcomes, in a way not possible with the EHR resource alone (due to under-reporting of Long-Covid in primary care, and to missing health data variables pre-pandemic). Establishing the UK LLC was a lengthy process, due to the various approvals needed and is only now beginning to produce outputs **[NC/14 – INQ000250180; NC/15 – INQ000250181]**.

6.22. The UK LLC has been successful in obtaining competitive funds from UKRI to consolidate and extend their work, as a unique and valuable service to multiple LPS. Generally, though there are limited funds from funding bodies such as UKRI and NIHR to support infrastructures, such as the UK LLC, OpenSAFELY and the BHF CVD-Covid-UK initiative. To my knowledge, OpenSAFELY is currently still seeking funds for continuation. All these platforms were created at the beginning of the pandemic, and to an extent they relied on the NCS funding to develop, which has now ended. They are therefore reliant on finding competitive research funds to continue. However, the research landscape revolves around answering questions rather than funding infrastructure. These platforms have therefore struggled, and will continue to struggle, to source funds as there is no real scheme for them to apply to. This lack of funding options has resulted in the platforms being under threat going forward. The platforms are also dependent upon permissions for use from service providers, such as EMIS and TPP, which provide systems used by primary care, and

NHSE, which is the gateway to secondary care linkage. These providers juggle competing priorities and also require significant funding to provide data.

6.23. At the inception of the LH&W NCS, we liaised with the Post-Hospitalisation Covid-19 study (**'PHOSP study'**) investigators, at first to ensure we had access to PHOSP findings that could inform our work, and, after the award of the CONVALESCENCE study, to align data capture and analytic protocols to measure target organ damage as a result of Covid-19 infection. This allows us to compare the effect of largely community managed Covid-19 infection in convalescence on target organ damage, with PHOSP-Covid, which recruited only from hospital treated cases, thus allowing us to understand the spectrum of consequences based on severity of disease. Meetings with PHOSP investigators have been frequent on an as needed basis to ensure alignment and dialogue. Professor Sterne attended twenty-nine meetings of the CMO Long-Covid working group to represent the LH&W NCS (including convalescence work) **[NC/06 – INQ000251615; NC/07 – INQ000251616; NC/05 – INQ000251614; NC/60 – INQ000251618; NC/61 – INQ000251619; NC/62– INQ000251620; NC/63 – INQ000251621; NC/64 – INQ000251622; NC/65 – INQ000251623; NC/66 – INQ000251624; NC/67 – INQ000251625; NC/68 – INQ000251626; NC/69 – INQ000251627; NC/70 – INQ000251628; NC/71 – INQ000251629; NC/72 – INQ000251630; NC/73 – INQ000251631; NC/74 – INQ000251632; NC/75 – INQ000251633; NC/76 – INQ000251634; NC/77 – INQ000251635; NC/78 – INQ000251636; NC/79 – INQ000251637; NC/80 – INQ000251638; NC/81 – INQ000251639; NC/82 – INQ000251640; NC/83 – INQ000251641; NC/84 – INQ000251642; NC/85 – INQ000251643**. I attach a schedule confirming the dates on which he attended meetings **[NC/86 – INQ000251644]**. As indicated at paragraph 3.2, I attended two of Lord Bethell's Long-Covid Ministerial Roundtable meetings on 13 October 2020 and 23 September 2021. I do not recall making any contribution at these meetings and I do not recall what was discussed at the meetings. Other members of the LH&W NCS also attended these meetings as well as the NHSE/NHSI Long-Covid National Taskforce meetings. However, they did not attend these meetings on behalf of the LH&W NCS. Professor Claire Steves of Kings College London attended on behalf of the Zoe App, Ben Goldacre, of Oxford University, represented OpenSAFELY and Dr Felix Greaves represented NICE. I asked them to inform the LH&W NCS if there was anything of value for us that arose during these meetings, and this would be raised at our Executive Group. In the Executive Group, we discussed any information that was

useful to NCS from all of the various other meetings our members attended, not solely the NHSE/NHSI Long-Covid National Taskforce meetings.

6.24. I am not aware of the existence of the Long-Covid Oversight board, nor can I recall the NCS interacting with them. Therefore, I am not able to provide any comment on the group.

6.21 Furthermore, I am not able to comment on whether the data sharing between the NCS, the PHOSP study, the CMO Long-Covid working group and the NHSE/NHSI Long-Covid National Taskforce was adequate. The groups in question were three very distinct groups, each of which had a different relationship with the NCS. I had informal ad hoc discussions with the PHOSP study group as and when issues arose and we did stay connected, however there was no formal meetings between NCS and PHOSP. Regarding the CMO Long-Covid working group, my co-lead Professor Jonathan Stern attended their meetings on a regular basis, therefore information sharing with them was as good as it possibly could be. As mentioned above at paragraph 6.19, members of the LH&W NCS, such as Ben Goldacre and Claire Steves, did frequently attend the NHSE/NHSI Long-Covid National Taskforce meetings and present to the group. However, they attended in their capacity as leaders of the OpenSAFELY project and the Zoe app respectively, as opposed to representatives of the LH&W NCS. However, given that they were also part of the LH&W NCS they would also have been able to bring forward any information they thought was relevant from the NCS to the NHSE/NHSI Long-Covid National Task Force. However, without completing a thorough review of the minutes, I do not think I can comment on the full extent of the sharing of information. As explained above, I do not know what the Long-Covid Oversight Board is and therefore I am not able to discuss whether the information sharing between this group and the NCS was adequate.

7: SAGE

7.1. From my recollection, I was asked to attend the eighty-second meeting of SAGE on 25 February 2021 by the SAGE secretariat to hear evidence from the International Severe Acute Respiratory and Emerging Infection Consortium (‘**ISARIC**’) study on their findings on Long-Covid **[NC/01 – INQ000120602]**. It was suggested that I would have some useful inputs into the findings being presented by them. ISARIC is a study of people hospitalised with Covid-19 infection. They reported on rates of recovery from Covid-19 infection, reports of persistent symptoms, clustering of symptoms and

at-risk groups. It was noted that hospitalised cases represent the most severe end of the infection spectrum, and that the majority of Covid-19 cases are managed in the community. With access to largely community-based cases through our LPS resource, we could provide complementary information to ISARIC. We attended to hear what ISARIC had to say, to absorb this information and to share that we had complementary information on people who were not hospitalised from our longitudinal population studies and the EHRs. My involvement in the meeting was very brief and included a very high-level overview of the work we were conducting at the NCS and the CONVALESCENCE study. I did not provide substantial input to this meeting other than the overview, and there was a further discussion regarding workforce. I am not aware of any actions that followed from the meeting.

7.2. We also shared findings on risks of Long-Covid, risk predictors, and clustering to the CMO Long-Covid working group, the CMO and the Oversight Board as they emerged.

7.3. The findings were also included in a paper we co-authored titled 'Short Report on Long Covid' for the ninety-fourth meeting of SAGE on 22 July 2021 **[NC/02 – INQ000092856; NC/43 – INQ000250211]**. The report is very detailed and highlighted many areas of uncertainty. We also noted that the NCS PROTECT study, as part of the work of the Transmission and Environment NCS led by Professor Andrew Curran, would be the best source of data on occupation and infection.

7.4. After the SAGE meeting I attended on 25 February 2021, a member of the SAGE Secretariat asked me to prepare the 'Short Report on Long Covid' mentioned above at paragraph 7.3 **[NC/01 – INQ000120602] [NC/43 – INQ000250211]**. This was prepared in collaboration with other members of the CMO Long-Covid working group, which includes the Office of National Statistics (**'ONS'**), the Real-Time Assessment of Community Transmission (**'REACT'**) study and the PHOSP study. I was invited to the ninety-fourth SAGE meeting on 22 July to present and discuss the report **[NC/02 – INQ000092856] [NC/43 – INQ000250211]**. The report was well received, with the GCSA noting that it was the most comprehensive review to date on the topic, and he requested that we share it with his European Chief Scientific Advisor counterparts, which we agreed to. The SAGE Secretariat subsequently asked us to put together an update of the report, which we did. However, the updated report was never presented to SAGE, for reasons I am not aware of.

7.5. My limited and late association with SAGE makes it impossible for me to know how SAGE responded to the emergence of Long-Covid, and I am not aware of how the 'Short Report on Long Covid' was used by SAGE to inform their advice **[NC/43 – INQ000250211]**.

7.6. There is interest in whether groups like the LH&W NCS were involved in the assessment of how emergency response measures such as non-pharmaceutical interventions ('**NPIs**') would impact upon those likely to be at risk of developing long-term sequalae arising from Covid-19. While we did pull together some patchy information on at risk groups, I cannot recall the LH&W NCS or CONVALESCENCE study producing any kind of formal report on at risk groups and NPIs. What we did do, was look at who was at a high risk of developing infection and long-term consequences from Covid-19. We did not, as indicated above, consider at risk people in the context of NPIs. So, we did not for example, delve into issues such as whether shielding worked for some groups and not for others.

8: Lessons Learned

8.1. The LH&W NCS was established from scratch in response to the pandemic. We have been successful in creating a national network of research analysts, versed in Open Science methods of protocol publication and code sharing, collaboration across LPS and EHR, access to high level domain specific expertise in data science and clinical specialties, and newly established platforms such as the UK LLC, OpenSAFELY and the BHF-CVD-Covid-UK initiative. However, this did mean we lost valuable time at pandemic inception in terms of delivering research in a timely fashion for policy makers. My view is that these platforms should have been created long before the pandemic. Instead, we had to create them from scratch when the pandemic broke out, and therefore familiarise ourselves with some very new systems that had not been used or tested before, which inevitably experienced technical glitches. This was occurring at a time when we urgently needed them and was therefore not optimal as it slowed down our ability to respond. Although the data from GPs was already there, we had to establish linkages between primary care and the new testing infrastructures that were in place so that we could find out who had been tested for Covid, who had tested positive and link this with their health records. All of this had to be newly established, and we needed to check that it worked before we could commence any analysis. If these systems had already been in place before the start

of the pandemic, and our staff had been using them for years beforehand, we would have been able to produce outputs much faster.

8.2. It would be a loss if both this network, collaborative way of working, and critical platforms could not be continued. Currently though, the platforms described are seeking continued funding piecemeal, in a research funding landscape which is not designed to support infrastructure platforms for the good of research, and there is no obvious way of maintaining the research network and ways of working in preparation for subsequent crises. I have outlined the funding issues faced by the relevant platforms at paragraph 6.18.

8.3. During the pandemic, the Government Office for Science acted as a bridge to policy makers in the Cabinet Office and other departments, as well as a series of new groups that were created in response to the pandemic. We were often struggling to navigate our way through these different groups, so it was helpful to have a direct line to the CMO and GCSA in relation to responding to and informing policy.

8.4. The LPS did respond in a co-ordinated fashion to capture questionnaire data on Long-Covid on our participants, that we would not have obtained any other way.

8.5. I am not able to comment on how any lessons learned during the pandemic would have affected the advice and briefings given to core decision-makers, as the pandemic was an ever-evolving situation where lessons were continually being learned, and are still being learned, so it is impossible to say how they affected advice at the time. Furthermore, I was not directly involved in providing advice to the core-decision makers, so I cannot comment on this.

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 Nishi Chaturvedi

Signed: Personal Data

Dated: 24.8.2023

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