UK COVID-19 Inquiry: Module 2 - Rule 9 Request to Professor Ruth Keogh - Reference: M2/SAGE/01/RXK

1. A brief overview of your qualifications, career history, professional expertise and major publications.

I am a Professor of Biostatistics and Epidemiology at the London School of Hygiene & Tropical Medicine. I am currently funded by a UK Research and Innovation Future Leaders Fellowship.

My qualifications are:

- 2007: DPhil in Medical Statistics, University of Oxford
- 2003: MSc Applied Statistics, University of Oxford
- 2002: BSc Mathematics and Statistics (1st Class Hons), University of Edinburgh

My career history is as follows:

- 2012-present: London School of Hygiene & Tropical Medicine, Department of Medical Statistics, Faculty of Epidemiology and Population Health. Professor - 2019-present; Associate Professor (formerly Senior Lecturer) – 2015-2019; Lecturer – 2012-2015.
- 2008-2012: University of Cambridge, Department of Public Health and Primary Care and MRC Biostatistics Unit. Research Associate/Investigator Statistician.
- 2006-2007: University of Oxford, Cancer Epidemiology Unit. Research Assistant.

My research focuses on the development and application of statistical methodology for analysis of observational data, such as that arising from cohort studies, disease registries and electronic health records. I have published research on causal inference methods, prediction methods, methods for survival analysis and analysis of case-control studies, and methods for handling missing data and measurement error. I have also worked in a number of areas of application, most notably in cystic fibrosis, but also in cancer, tuberculosis, as well as Covid-19. Some key publications illustrating my expertise in the above-mentioned areas are listed below (excluding any papers relating to Covid-19 research).

- Newsome SJ, Daniel RM, Carr SB, Bilton D, KEOGH RH; Using Negative Control Outcomes and Difference-in-Differences Analysis to Estimate Treatment Effects in an Entirely Treated Cohort: The Effect of Ivacaftor in Cystic Fibrosis. American Journal of Epidemiology (2021) 191 (3), 505-515 10.1093/aje/kwab263.
- KEOGH RH, Shaw PA, Gustafson P, Carroll RJ, Deffner V, Dodd KW, Kuechenhoff H, Tooze JA, Wallace MP, Kipnis V, Freedman LS; STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 1-Basic theory and simple methods of adjustment. Statistics in Medicine (2020) 39 (16), 2197-2231
- TANNER KT, SHARPLES LD, Daniel RM, KEOGH RH; Dynamic survival prediction combining landmarking with a machine learning ensemble: Methodology and empirical comparison. Journal of the Royal Statistical Society Series A: Statistics in Society (2020) 184 (1), 3-30 10.1111/rssa.12611.
- KEOGH RH, Seaman SR, Barrett JK, Taylor-Robinson D, Szczesniak R; Dynamic Prediction of Survival in Cystic Fibrosis: A Landmarking Analysis Using UK Patient Registry Data. Epidemiology (2018) 30 (1), 29-37 10.1097/EDE.0000000000000920.
- KEOGH RH, Morris TP; Multiple imputation in Cox regression when there are time-varying effects of covariates. Statistics in Medicine (2018) 37 (25), 3661-3678 10.1002/sim.7842.
- Paige E, Barrett J, Stevens D, KEOGH RH, Sweeting MJ, Nazareth I, Petersen I, Wood AM; Landmark Models for Optimizing the Use of Repeated Measurements of Risk Factors in

Electronic Health Records to Predict Future Disease Risk. *American Journal of Epidemiology* (2018) *187* (7), 1530-1538 10.1093/aje/kwy018.

- MANGTANI P, NGUIPDOP-DJOMO P, KEOGH RH, Sterne JAC, Abubakar I, SMITH PG, FINE PEM, VYNNYCKY E, Watson JM, Elliman D, Lipman M, RODRIGUES LC; The duration of protection of school-aged BCG vaccination in England: a population-based case-control study. *International Journal of Epidemiology* (2017) *47* (1), 193-201 10.1093/ije/dyx141.
- Abrahão R, KEOGH RH, Lichtensztajn DY, Marcos-Gragera R, Medeiros BC, COLEMAN MP, Ribeiro RC, Keegan THM; Predictors of early death and survival among children, adolescents and young adults with acute myeloid leukaemia in California, 1988-2011: a population-based study. *British Journal of Haematology* (2016) *173* (2), 292-302 10.1111/bjh.13944.

2. A list of the groups (i.e. SAGE and/or any of its sub-groups) in which you have been a participant, and the relevant time periods.

I attended two SPI-M meetings (22 April 2020, 13 January 2021). I was a member of a NERVTAG risk stratification subgroup (led by Prof Hippisley-Cox, University of Oxford) from May 2020 to around July 2021.

3. An overview of your involvement with those groups between January 2020 and February 2022, including:

a. When and how you came to be a participant;

- SPI-M: Around the end of March 2020, I joined my colleague Prof Karla Diaz-Ordaz in analysing data coming from the ISARIC group (CO-Cin) in order to investigate case fatality rates, and length of stay in hospital or ICU. Our involvement was via a connection with Prof John Edmunds (LSHTM).
- NERVTAG risk stratification subgroup: On 15th May 2020 I was invited by Prof Peter Horby to contribute to this subgroup. This arose from my involvement in the analysis of the CO-Cin data. The first meeting took place on 18th May 2020.

b. The number of meetings you attended, and your contributions to those meetings;

- SPI-M: At a meeting on 22 April, I contributed to presentation of results about risk of death and hospitalisation by age groups, and length of stay in ICU and hospitalisation, based on analysis of the CO-Cin data.
- SPI-M: On 1st May 2020 I sent further results from analysis of the Co-Cin data to the SPI-M secretariat. These were on cumulative incidence of death by week of hospital admission, and this was again work done in collaboration with Prof Diaz-Ordaz. I believe I did not attend the meeting at which the papers were discussed.
- SPI-M: At the meeting on 13 January 2020 I contributed to the presentation of LSHTM's findings on the increased risk of death associated with the Alpha variant when compared with wild type (the original strain). My role was to respond to any technical questions about the statistical models used by the LSHTM team.
- NERVTAG risk stratification subgroup: I attended approximately weekly meetings from 18 May 2020 to July 2020, then less frequent meetings as updated models were developed. I contributed to the discussion of methods that were appropriate to the risk prediction task, including around the handling of competing risks, handling of missing data, and prediction model building, and later about interpretation of results.

c. Your role in providing research, information and advice.

- SPI-M, April/May 2020: I performed statistical analysis to produce estimates of risk of death and hospitalisation, and estimates of length of stay in ICU and hospital using CO-Cin data.
- SPI-M: In December 2020 and January 2021, I provided statistical advice on methodology, analysis and oversight, but did not have access to the data. I contributed to the interpretation of results and the writing of two published papers.

- NERVTAG risk stratification subgroup: I contributed advise on the handling of competing risks, handling of missing data, and prediction model building, and later about interpretation of results. I contributed to the writing of the protocol and the published papers. The NERVTAG risk stratification subgroup resulted in the development of the QCOVID risk model.

4. A summary of any documents to which you contributed for the purpose of advising SAGE and/or its related subgroups on the Covid-19 pandemic. Please include links to those documents where possible.

- I contributed to estimating length of stay in hospital and ICU using the CO-Cin data, and these estimates were used in the late April 2020 models that LSHTM presented at SPI-M meetings. These models went on to inform consensus statements https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/926900/S0345_SPI-M-O_Planning_scenarios_and_current_estimates_of_severity_and_length_of_stay.pdf
- During the January 2021 Alpha variant wave, I contributed to the statistical analyses finding evidence of an increased risk in mortality associated with the alpha variant (compared to wild type). The findings were summarised and presented by NERVTAG to SAGE https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961037/NERVTAG_note_on_B.1.1.7_severity_for_SAGE_77__1_.pdf
- NERVTAG risk stratification subgroup: this resulted in the tool https://digital.nhs.uk/coronavirus/risk-assessment and https://qcovid.org/. I did not have direct involvement in the development of the web-based tool. I contributed to the statistical approach that resulted in the tool, as outlined above, and resulting in the papers listed below.

5. A summary of any articles you have written, interviews and/or evidence you have given regarding the work of the above-mentioned groups and/or the UK's response to the Covid-19 pandemic. Please include links to those documents where possible.

A list of published manuscripts relating to Covid-19 research, on which I am an author:

- Horne EMF, Hulme WJ, KEOGH RH, Palmer TM, WILLIAMSON EJ, PARKER EPK, Green A, Walker V, Walker AJ, Curtis H, Fisher L, MacKenna B, Croker R, Hopcroft L, Park RY, Massey J, Morley J, Mehrkar A, Bacon S, Evans D, Inglesby P, Morton CE, Hickman G, Davy S, Ward T, Dillingham I, GOLDACRE B, Hernán MA, Sterne JAC; Waning effectiveness of BNT162b2 and ChAdOx1 covid-19 vaccines over six months since second dose: OpenSAFELY cohort study using linked electronic health records. *British Medical Journal* (2022) *378*, e071249 10.1136/bmj-2022-071249.
- OpenSAFELY Collaborative, WILLIAMSON EJ, TAZARE J, BHASKARAN K, MCDONALD HI, Walker AJ, Tomlinson L, WING K, Bacon S, Bates C, Curtis HJ, FORBES HJ, Minassian C, Morton CE, Nightingale E, Mehrkar A, Evans D, Nicholson BD, LEON DA, Inglesby P, MacKenna B, Davies NG, DeVito NJ, Drysdale H, Cockburn J, Hulme WJ, Morley J, Douglas I, RENTSCH CT, Mathur R, WONG A, SCHULTZE A, Croker R, Parry J, Hester F, Harper S, GRIEVE R, Harrison DA, Steyerberg EW, EGGO RM, DIAZ-ORDAZ K, KEOGH R, EVANS SJW, SMEETH L, GOLDACRE B; Comparison of methods for predicting COVID-19-related death in the general population using the OpenSAFELY platform. *Diagnostic and Prognostic Research* (2022) *6* (1), 6 10.1186/s41512-022-00120-2.
- Clift AK, Coupland CAC, KEOGH RH, Hemingway H, Hippisley-Cox J; COVID-19 Mortality Risk in Down Syndrome: Results From a Cohort Study of 8 Million Adults. *Annals of Internal Medicine* (2021) *174* (4), 572-+ 10.7326/M20-4986.
- DAVIES NG, ABBOTT S, BARNARD RC, JARVIS CI, KUCHARSKI AJ, MUNDAY JD, PEARSON CAB, RUSSELL TW, TULLY DC, Washburne AD, Wenseleers T, Gimma A, WAITES W, WONG KLM,

VAN ZANDVOORT K, Silverman JD, CMMID COVID-19 Working Group, COVID-19 Genomics UK (COG-UK) Consortium, DIAZ-ORDAZ K, KEOGH R, EGGO RM, FUNK S, JIT M, ATKINS KE, EDMUNDS WJ; Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science* (2021) *372* (6538), 149-+ 10.1126/science.abg3055.

- DAVIES NG, JARVIS CI, CMMID COVID-19 Working Group, EDMUNDS WJ, JEWELL NP, DIAZ-ORDAZ K, KEOGH RH; Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. *Nature* (2021) *593* (7858), 270-274 10.1038/s41586-021-03426-1.
- Docherty AB, Mulholland RH, Lone NI, Cheyne CP, De Angelis D, DIAZ-ORDAZ K, Donegan C, Drake TM, Dunning J, FUNK S, García-Fiñana M, Girvan M, Hardwick HE, Harrison J, Ho A, Hughes DM, KEOGH RH, Kirwan PD, Leeming G, Nguyen Van-Tam JS, Pius R, Russell CD, Spencer RG, Tom BD, Turtle L, Openshaw PJ, Baillie JK, Harrison EM, Semple MG; Changes in in-hospital mortality in the first wave of COVID-19: a multicentre prospective observational cohort study using the WHO Clinical Characterisation Protocol UK. *The Lancet. Respiratory Medicine* (2021) *9* (7), 773-785 10.1016/S2213-2600(21)00175-2.
- Hippisley-Cox J, Coupland CA, Mehta N, KEOGH RH, DIAZ-ORDAZ K, Khunti K, Lyons RA, Kee F, Sheikh A, Rahman S, Valabhji J, Harrison EM, Sellen P, Haq N, Semple MG, Johnson PWM, Hayward A, Nguyen-Van-Tam JS; Risk prediction of covid-19 related death and hospital admission in adults after covid-19 vaccination: national prospective cohort study. *British Medical Journal* (2021) *374*, n2244 10.1136/bmj.n2244.
- LECLERC QJ, FULLER NM, KEOGH RH, DIAZ-ORDAZ K, Sekula R, Semple MG, ISARIC4C Investigators, CMMID COVID-19 Working Group, ATKINS KE, PROCTER SR, KNIGHT GM; Importance of patient bed pathways and length of stay differences in predicting COVID-19 hospital bed occupancy in England. *BMC Health Services Research* (2021) *21* (1), 566 10.1186/s12913-021-06509-x.
- Clift AK, Coupland CAC, KEOGH RH, DIAZ-ORDAZ K, WILLIAMSON E, Harrison EM, Hayward A, Hemingway H, Horby P, Mehta N, Benger J, Khunti K, Spiegelhalter D, Sheikh A, Valabhji J, Lyons RA, Robson J, Semple MG, Kee F, Johnson P, Jebb S, Williams T, Hippisley-Cox J; Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *British Medical Journal* (2020) *371*, m3731-m3731 10.1136/bmj.m3731.
- WILLIAMSON EJ, TAZARE J, BHASKARAN K, Walker AJ, MCDONALD HI, TOMLINSON L, Bacon S, Bates C, Curtis HJ, FORBES H, MINASSIAN C, Morton CE, NIGHTINGALE E, Mehrkar A, Evans D, Nicholson BD, LEON D, Inglesby P, MacKenna B, Cockburn J, DAVIES NG, Hulme W, Morley J, DOUGLAS IJ, RENTSCH CT, MATHUR R, WONG A, SCHULTZE A, Croker R, Parry J, Hester F, Harper S, Perera R, GRIEVE R, Harrison D, Steyerberg E, EGGO RM, DIAZ-ORDAZ K, KEOGH R, EVANS SJW, SMEETH L, GOLDACRE B; Study protocol: Comparison of different risk prediction modelling approaches for COVID-19 related death using the OpenSAFELY platform. *Wellcome Open Research* (2020) *5*, 243-243 10.12688/wellcomeopenres.16353.1.

6. Your views as to whether the work of the above-mentioned groups in responding to the Covid-19 pandemic (or the UK's response more generally) succeeded in its aims. This may include, but is not limited to, your views on:

a. The composition of the groups and/or their diversity of expertise;

I don't know the full composition of SPI-M or whether it represented diverse expertise. As I only attended two meetings, I did not form an impression. The NERVTAG risk stratification subgroup appeared to include experts with a wide range of expertise and from a range of institutions and other bodies.

b. The way in which the groups were commissioned to work on the relevant issues;

I don't know the processes by which the groups were commissioned.

c. The resources and support that were available;
For the results I was involved in presenting for SPI-M, I was given access to a dataset quite quickly in March/April 2020 and this arose via a more senior person at LSHTM. I did not form an impression of the resources and support available to the group in general. The NERVTAG subgroup made use of existing data resources to develop the risk stratification tool. There was administrative support in the organisation of the virtual meetings.

d. The advice given and/or recommendations that were made;
I was not part of any SAGE meetings, so did not contribute or witness any advice or recommendation. The NERVTAG subgroup developed a risk stratification tool, and discussions in the meetings I was involved in primarily concerned the statistical analysis and subsequent interpretatioon. My opinion is that the resulting risk stratification tool addressed the specified aims.

e. The extent to which the groups worked effectively together;
For SPI-M, my understanding was that each university group worked to produce their own results/models, which were then considered collectively. As I only attended two meetings, I did not form an impression. The NERVTAG subgroup developed the protocol for the risk stratification tool in a collaborative way. The data analyses were performed by a few individuals with access to the data, but results were discussed in the wider group.

f. The extent to which applicable structures and policies were utilised and/or complied with and their effectiveness.
I was not sufficiently involved to have any views on this.

7. Your views as to any lessons that can be learned from the UK's response to the Covid-19 pandemic, in particular relating to the work of the above-mentioned groups. Please describe any changes that have already been made, and set out any recommendations for further changes that you think the Inquiry should consider making.
I was not sufficiently involved to have any views on this.

8. A brief description of documentation relating to these matters that you hold (including soft copy material held electronically). Please retain all such material. I am not asking for you to provide us with this material at this stage, but I may request that you do so in due course.
I have computer code that we used to perform analyses of the CO-Cin data described above. I have electronic copies of reports on results from these analyses, which we provided for consideration at SPI-M meetings in April/May 2020. I have access to email exchanges relating to my contributions to SPI-M and the NERVTAG risk stratification subgroup.