Statement on Covid-19 antibody testing, issued on 14th April 2020

Royal Statistical Society Covid-19 Task Force

The Royal Statistical Society (RSS) welcomes the publication last week by the Medicines & Healthcare products Regulatory Authority (MHRA) of the specification criteria that MHRA expects to be met by an acceptable point-of-care test in blood for determination of Immunoglobulin-G (IgG) antibodies to coronavirus-2. The criteria include clinical sensitivity, clinical specificity (both greater than 98%, but minimum sample sizes to determine this are not pre-specified) and analytical specificity to ensure against interferents, notably cross-reactivity with other coronaviruses.

The RSS Covid-19 Task Force reminds MHRA and others that antibody tests which meet lesser criteria on clinical sensitivity and specificity can still be acceptable for use in the context of a powerful suite of population surveillance studies, because estimates can be corrected for the marketed surveillance test's performance in terms of sensitivity and specificity (Reiczigel et al, 2010; Diggle, 2011). Cross-reactivity may be trickier to resolve.

There are historical precedents. Surveillance studies for HIV and Hepatitis C Virus (HCV) antibodies were undertaken by testing saliva samples at a time when only a test in blood was accepted for making personal diagnoses.

The RSS Task Force presses the case for there to be a suite of well-designed, powerful, co-ordinated and geographically representative surveillance studies that engage men, women, children (around 12 years of age when Human Papilloma Virus vaccine is offered universally; younger for seasonal flu vaccine); antenatal women (mainly 16-44 years); repeat blood donors (18-59 years); healthcare workers (18-69 years); vulnerable adults and persons aged 70+ years (in the high-risk group for seasonal flu vaccine). Building population surveillance studies as part of already established cohorts and groups under surveillance delivers practical solutions. Co-ordination (e.g. common protocols, consistent definitions, brief self-completion questionnaire etc.) is crucial to allow studies to be combined for application to large populations. Ensuring overlapping age-groups, as between repeat blood donors, healthcare workers and antenatal women, is also important. In addition, the potential to obtain repeat blood samples, such as from repeat blood donors, antenatal women and healthcare workers, is necessary to establish the persistence of antibodies.

The extent of asymptomatic transmission is a particular dilemma in COVID-19 as is the wide spectrum of illness from mild to critical. For these reasons, at least some surveillance studies need to be able to link a brief self-completed questionnaire to the participant's blood sample so that participants can be asked who – definitely /probably /possibly - had COVID-19 or considered they were unlikely to have been infected. A symptom checklist can be completed by those who thought they had been infected. Repeat blood donors should have time to do this; and healthcare workers are likely to want to do this. Ideally, there should be sufficient co-ordination that the same brief questionnaire can be adopted across surveillance-strata.

Concern about a lack of persistent antibodies following mild disease was heightened last week after a report from China (Wu et al, 2020). There is a need for well-designed studies to bring forth clear UK evidence on this important topic and too much pessimism should not be engendered by the results of this study alone.

Diggle, P.J. (2011). Estimating prevalence using an imperfect test. *Epidemiology Research International*, Article ID 608719. doi:10.1155/2011/608719.

 Reiczegel, J., Foldi, J. and Ozsvari, L. (2010). Exact confidence limits for prevalence of a disease with an imperfect diagnostic test. *Epidemiology and Infection*, **138**, 1674–1678

Wu, F et al (2020) Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered 2 patient cohort and their implications. medRxiv preprint doi: https://doi.org/10.1101/2020.03.30.20047365.