Public Health England

Protecting and improving the nation's health

Serological Surveillance: Summary report 2

28 April 2020

Background

Control of COVID-19 requires the ability to detect asymptomatic and mild infections, that would not present to healthcare and would otherwise remain undetected through existing surveillance systems. This is important to determine the true number of infections within the general population to understand transmission, to inform control measures such as social distancing and school closures and to provide a denominator for the estimation of severity measures such as infection fatality and infection hospitalisation ratios.

A number of serological collections have been established by PHE to provide an age-stratified geographically representative sample across England over time. These have been derived from a number of sources and have been supplemented by samples from : healthy blood donors, supplied by the NHS Blood and Transplant (NHS BT), instigated by the Wellcome Trust, and paediatric patients seen at Great Ormond Street Hospital (GOSH), 6).
Approximately 1000 samples per week are being provided by NHSBT from different geographic regions, and 100 samples per week are being collected from GOSH patients residing in London and the South East.

The results from the testing of NHSBT and GOSH samples undertaken to date, are summarised in this report. Samples from other sources continue to be being collected and analysed and will be presented in subsequent reports. All results presented in this summary report are based on samples using the commercial Euroimmun IgG ELISA.

Results

Baseline Testing

Initial testing of 175 RCGP samples from 2019 and just over 100 SEU samples from the January 2020 baseline were tested with the EuroImmun assay. A higher proportion of the SEU samples were positive, around 3% (3/111), compared to only 1/175 of the RCGP samples. Children were disproportionally represented in the January SEU sample, and it is notable that the three positives were in toddlers aged 2-4 years. Analysis of quantitative index values (ratio of test result to cut-off) suggests that background levels are higher in young children, so these three positives may represent some non-specific cross reactivity. The baseline levels in RCGP and January SEU samples suggest a combined false positive rate of ~ 1.4%, but this may depend on age.

Seroprevalence estimates

Seroprevalence estimates are based on adult samples from NHSBT (n= 4683) and paediatric samples obtained from GOSH (n=284).

The NHSBT results include two sets of data from London collected two weeks apart (weeks 13-14 (n=799), and weeks 15-16 (n=1080)), data collected from the Midlands (week 14, n=937), and most recently from the North-East region (week 16, n=994) and North-West region (week 16, n=881).

Given that results in young infants likely reflect maternal antibodies, these were excluded from the analysis this week, giving a total of 284 samples of children aged 1 – 19 years, including 190 from late March and 94 from early April.

To explore the potential impact of assay sensitivity and specificity on prevalence outputs, we analysed used a Bayesian model assuming a sensitivity 10 days post onset of symptoms of 44/69 (64%) and specificity from baseline and manufacturer data of 777/786 (98.9%).

Table 1 summarises the main results by collection and chronological order of sampling. Given that blood donors are unable to donate blood for 2 weeks after recovery from any acute illness, the symptomatic prevalence in NHSBT samples corresponds to that of at least 2-3 weeks prior to collection.

Table 1: Summary of the Prevalence Estimates by Collection and Chronological order of Sampling, using the Euroimmun Assay

Region and collection	Date range	Week of collection	#pos	#ind	#neg	Total	% pos (95% CI)
GOSH							
London & SE	6-31 Mar	Week 11-14	16	8	166	190	8.4% (4.9% – 13.3%)
London & SE	1-6 Apr	Week 14	7	4	82	94	7.4% (3.0% - 14.8%)
NHSBT							
London	26-27 Mar	Week 13-14	24	12	755	791	3.0% (2.0% -4.5%)
Midlands	2-3 Apr	Week 14	26	13	898	937	2.8% (1.8% -4.0%)
London	9-13 Apr	Weeks 15-16	107	15	958	1080	9.9% (8.2% -11.8%)
North East	15-17 Apr	Week 16	45	12	937	994	4.5% (3.3 – 6.0%)
North West	15-17Apr	Week 16	50	12	819	881	5.7% (4.2% - 7.4%)

Comment

A sizeable increase in prevalence in the NHSBT samples was observed in London between samples taken in late March and those taken two weeks later (difference in prevalence: 6.9% (95% CI: 4.7% to 9.0%).

The point prevalence found in London in week 15-16 was close to 10%. This prevalence may well be higher when taking into account the sensitivity and specificity of the assay. For example, using current data of sensitivity and specific our adjusted prevalence is 14% (95%CrI 10.3 - 19.1). The

adjusted prevalence needs to be interpreted with caution, as prevalence may be closer to the crude prevalence once more data is obtained on the performance of the EuroImmun assay.

Given the timing of the immune response and because blood donors are excluded from donating bloods in the two weeks following an acute illness, the prevalence in London samples collected in mid-April likely reflect estimates of transmission almost one month prior to that. The difference in prevalence between weeks 14 and 16 in London need to be interpreted with caution, as it may reflect a combination of recent transmission and the antibody dynamics in the weeks following infection. More testing on convalescent sera is required to better disentangle those effects.

The lower prevalence in the samples from the Midlands, North East and North West regions is consistent with data from other surveillance systems. The prevalence in the Midlands in week 14 was similar to that in London in weeks 13-14. At this low prevalence, it is likely that a high proportion of positives will be false positives, and so caution should be used in interpreting any demographics generated. The prevalence in North East and North West regions in weeks 16 is well above baseline, higher than in London and the Midlands in week 14, but not as high as seen in London in week 16, which is consistent with the surveillance trends reported for England. Further sets of samples from the Midlands and London in the coming week(s) would help better understand the transmission dynamics following the lockdown.

No such increase has been observed in the GOSH samples among 1 – 19y olds in London. Whilst initial analysis indicated a higher point prevalence and similar increase (report 21/04/20), when samples from infants were excluded these changes disappeared. These samples were excluded given the potential for any positives in neonates to reflect maternal antibodies. As these samples come from a highly specialised hospital, it would be sensible to explore other paediatric samples urgently which are more representative of the paediatric population and have more robust estimates to inform public health strategies.

Recommendations

1. PHE continues to collect samples for assay evaluation including later convalescent samples from cases and additional sample sets to better establish specificity, including among paediatric age groups.

2. PHE continues to investigate alternative commercial assays. Results generated using the EuroImmun assay should be used with caution for modelling until more information is available on the test characteristics or a more accurate assay is available.

3. Additional evaluation on the existing convalescent panel with other PHE assays under development continues, and will be used to retest some of the above samples sets (or equivalents) to confirm the initial findings.

4. Attempts to source more representative samples from young children should continue. Testing of precious low volume samples (such as those from children) should proceed with caution, ideally using the most accurate assays.

5. If collections need to be prioritised, collecting a third batch of NHSBT samples from London donors in the coming two weeks would be more informative than obtaining single snapshots from new areas, as the change in prevalence over 3 time points would enable, in concert with other surveillance data, to better understand both transmission and antibody dynamics.

6. PHE continue to work with other groups in the NHS and academia to increase the pool of information on the range of assays available to select the best choice of tests for current and future sero-epidemiology studies.

PHE surveillance cell 28/04/2020