

Antibody Testing for COVID-19: An Open-Labelled, Pan-European Prevalence Study in Front-Line Essential Workers; UK and Ireland Reporting

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Abstract

To estimate the prior SARS-CoV-2 exposure rate in Accord Healthcare employees and compare this to regional and national statistics, as well as to monitor the impact of the infection rate when all employees return to the office. This may provide reassurance and support to many organisations and the economy when return to work is implemented ubiquitously.

Keywords: COVID-19; Anti-body; Key workers; Epidemiology; Immunity

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Introduction

The COVID-19 pandemic has resulted in major disruptions to business activity and changed the way people work; many governments and employers have mandated working-from-home (WFH) wherever possible. In the UK, a limited number of essential key workers have continued to attend their usual workplace throughout the pandemic (e.g. healthcare workers, carers, manufacturing, pharmaceuticals sites, etc.). The UK government had initially published a COVID-19 recovery strategy aiming for “significant normality” by Christmas; however the resurgent of the virus and likelihood of a third wave means the government had to prepare for different scenarios. The aim is now to return towards normality after Spring 2021. It is likely that COVID-19 will continue into 2021 until majority of the population are vaccinated [1]. Temperature checks face mask and social distancing rules are likely to remain when employees return to the office. However, considerable uncertainty still remains with regards to the impact on the infection rate when business activity returns to normality.

Testing for acute SARS-CoV-2 infection is undertaken through nasal and throat swabs with rt-PCR for the detection of this novel virus. However, another approach for the detection of acute and previous infection relies on the detection of IgG or IgM antibodies in blood either assessed through laboratory ELISA techniques or using lateral flow serology kits. The latter is a relatively expedient and inexpensive way of assessing for the presence of antibodies, though widespread adoption has been hampered by availability and concerns relating to sensitivity or specificity [2,3].

There have been a number of studies that have assessed acute infection rates at certain time points. However, there are relatively few studies assessing the prevalence or previous exposure of COVID-19 infection across a variety of local populations. A UK government sponsored study shows that the overall population weighted prevalence among blood donors in England was 6.7% (unadjusted; 95% CI 6.1%-7.3%) or 7.1% (after adjustment for the accuracy of the Euroimmun assay; 95% CrI 6.5%-7.8%) for the period 8th June - 6th July 2020 (weeks 24-28) [4].

We know little about the prevalence of COVID-19 within organisations, and the impact on the infection rate when employees return to work. Accord Healthcare has undertaken a study to estimate the prevalence of prior SARS-CoV-2 exposure

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amongst its employees and compare it to national and regional statistics, as well as to monitor the impact on the infection rate when the working from home restriction is relaxed. Accord Healthcare has employees across different geographical locations in the EU, with individuals travelling to the pharmaceutical factories to continue medicine production (essential workers) during the pandemic as well as others working from home. This manuscript reports the initial results from the UK and Ireland employee population.

Research Methodology

All eligible (permanent employees of Accord Healthcare and subsidiary companies, Astron, and Lambda) in the UK and Ireland working across a variety of departments and locations (e.g. office, factory, field, or home based) were invited to have an antibody test using lateral flow serology for SARS-CoV-2 throughout June and July 2020. The decision to participate was entirely voluntary. Eligible participants were asked to complete a questionnaire regarding normal place of work, place of work during the pandemic, any previous COVID-19 related symptoms, previous tests, etc. Employees with haemophilia or currently taking anti-coagulants were asked to seek medical approval before their participation.

The primary endpoint is the proportion of positive and negative cases, presented as negative (no exposure), recent exposure (IgM positive and IgG positive), or previous exposure (IgM negative and IgG positive). Recent positive cases will also undergo an antigen test to determine if they are viral shedding. Secondary endpoints include comparisons against national statistics, comparison against regional statistics, sub-group analysis (age, gender, ethnicity), impact of a relaxed lock-down on the infection rate, and proportion of positive antigen tests. Exploratory endpoints include duration of antibody presence in the body to provide additional data with regards to possible re-infection (data being assembled and results to be provided in a later edition).

All data were blinded by the assessors and remained anonymous.

Tests were conducted by Occupational Health practitioners. This study was approved by an Accord Ethics Committee.

Lateral Flow Serology testing

We elected to use the Healgen lateral flow COVID-19 serology testing cartridges. The illustration of the test kit is shown in **Figure 1** and management of positive/negative results explained in **Figure 2**. The Healgen lateral flow serology assay has been tested previously using convalescent sera in individuals confirmed to have had COVID-19 infection from rt-PCR swabs and also with pre-pandemic sera as negative infections. The study revealed a 100% sensitivity provided the test is undertaken 14 days or more after symptoms and a 96% specificity [5,6]. These data support the use of this kit for rapid assessment of subjects' antibody status in the community.

A positive result for IgG suggests an infection likely took place at least 10 days prior to the test being taken [6,7]. IgM antibodies are generated as the first antibody response to infection and rise from about the fifth day post-contamination and persist only for a short period of time [6,8].

Results

A large majority of all UK and Ireland employees (80.5%; n=1,018) volunteered to participate in the study. The main reason for non-participation was transport (unable to get to the site to do the test, i.e., no access to a personal mode of transportation). The results showed 2.5% (n=25) of the employees tested positive for COVID-19 (defined as showing either IgG and/or IgM antibodies). This is considerably lower than the government published weighted prevalence among blood donors of 6.7% (95% CI 6.1% -7.3%) in England (unadjusted) for the period 8th June- 6th July 2020 (weeks 24 - 28) [4].

Of the 25 individuals testing positive, 17 (1.7%) individuals presented with only IgG antibodies detection, indicating prior exposure to SARS-COV-2 and 8 individuals (0.8%) showed a more

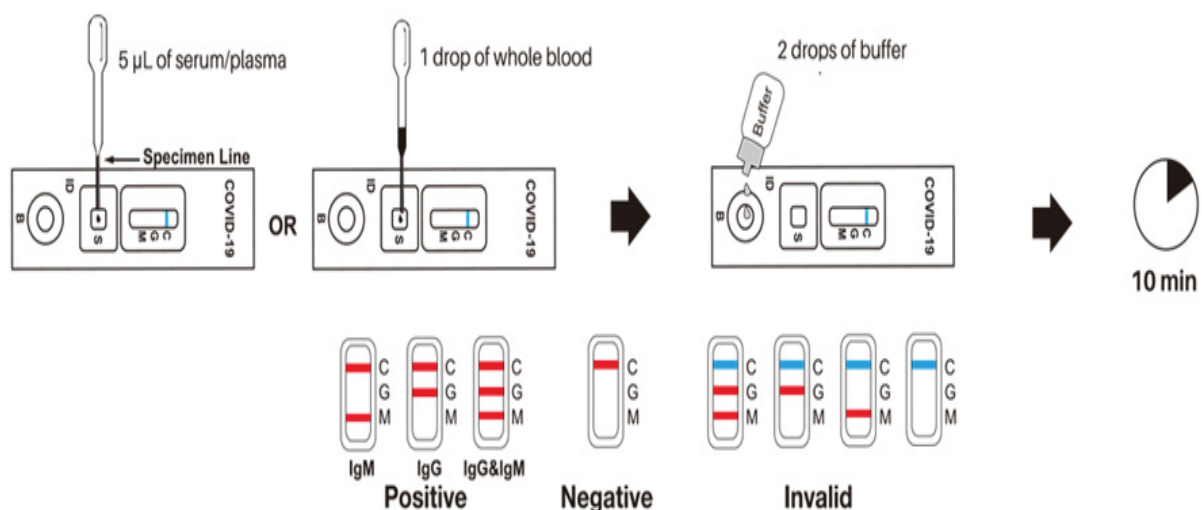


Figure 1 Illustration (taken from <https://www.healgen.com/if-respiratory-covid-19>) to show how the Healgen testing kit works.

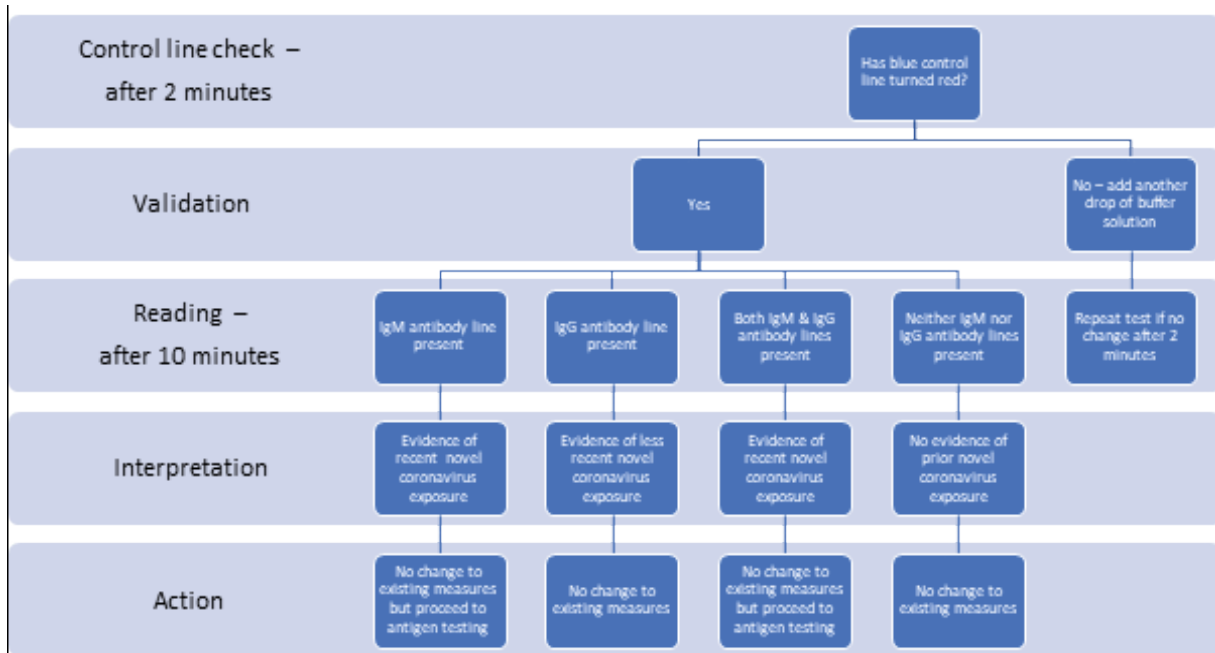


Figure 2 Process flow diagram for the operating mode of the antibody testing and management of the results.

recent exposure to SARS-CoV-2 with IgM and IgG antibodies positive detection. No subjects presented with lone IgM detection and none of the tests presented were invalid. Individuals that had a more recent exposure were also asked to have a subsequent antigen test to assess whether they were viral shedding. There were no cases of individuals testing positive at the subsequent antigen test.

Results of secondary endpoints have been summarised in **Table 1**, showing a higher prevalence rate in higher age groups and the Asian/Black minority groups. This is in-line with national data [9,10]. Interestingly, employee's working from home at the time of the pandemic had a slightly higher prevalence of SARS-Cov-2 compared to those working in the factories (3.3% versus 2.2%).

Discussion

At the turn of the 19th century, the US was gripped by a yellow fever epidemic. City lockdowns and interruption of business activity was common. However, there evolved the term 'acclimation', whereby those having survived yellow fever had an advantage in terms of employment and education [11]. Reports reveal that individuals deliberately contracted the illness to achieve acclimation enabling them to gain employment and training from businesses that actively sought immune individuals [12]. A similar scenario may play out with COVID-19 infection. Travel to certain countries may require a "COVID-19 passport" (evidence of confirmed COVID-19 prior exposure or vaccination), with travel and life insurance has also been affected by the pandemic [13]. Consequently, there may be some advantage in demonstrating prior infection through antibody testing.

To our knowledge, this study is believed to be the first to assess prevalence of COVID-19 and antibody status within a commercial

organisation. Antibody testing of COVID-19 has been advocated as offering the potential to support control strategies to minimise spread of the disease but may also offer confidence to both staff and clients in terms of potential immunity. Whilst uncertainty persists regarding the clinical implications of positive and negative serology in relation to long-term immunity, there has been limited confirmed reports yet of re-infections [14,15]. In this study, Accord Healthcare acknowledged that the positive outcome in the detection of either IgM and/or IgG was not an indicator of gained immunity against SARS-CoV-2 virus and COVID-19 as there is currently not sufficient evidence to establish such correlation and whether individuals are protected from potential reinfection.

There are a number of analytical techniques available for the diagnosis of COVID-19; ranging from laboratory testing kits to point-of-care tests. We employed lateral flow serology tests within this study as the test is inexpensive, does not rely on laboratory/scientists to analyse results, provides a quick turnaround with results within 15-minutes, and requires a non-invasive procedure (finger-prick) with very little training. Consequently, it is ideal for assessing a large cohort. However, the disadvantage of lateral flow tests is that they are relatively new and evidence for its specificity and sensitivity still accumulating. As a result, the Medicines and Healthcare products Regulatory Agency (MHRA) has mandated that companies utilising this technology undertake appropriate independent evaluation of their equipment in at least 200 subjects [16]. We elected to use the Orientgene (Orientgene own Healgen) lateral flow serology equipment based on the published independent evaluation of the technology revealing 100% sensitivity and 96% specificity. This was also supported by unpublished Welsh data revealing 94% sensitivity and 99.5% specificity. These data strongly support the applicability of this test in wider populations to determine past infection. This is

Table 1 Prevalence of COVID-19 in Accord Healthcare employee population.

Variables		Total Tested	Prevalence Rate (n)
England (antibody test)			6.7% (6.1%- 7.3%)
Accord HC overall		1018	2.5%(25)
Accord HC IgM+IgG antibody		1018	0.8% (8)
Accord HC IgM antibody only		1018	0% (0)
Accord HC IgG antibody only		1018	1.7% (17)
Accord HC	WFH (All locations)	243	3.3% (8)
	New Castle (Factory based)	308	3.6% (11)
	Devon (Factory based)	438	0.7% (3)
	Harrow (Laboratory based)	29	10.3% (3)
	Ireland	TBC	TBC
Accord HC	Working onsite	775	2.2% (17)
	WFH	243	3.3% (8)
Accord HC	Male	670	2.5% (17)
	Female	345	2.3% (8)
Accord HC	White	910	1.8% (16)
	Asian	86	9.3% (8)
	Black	9	11.1% (1)
	Other	5	0% (0)
Accord HC	18-25 years	83	0% (0)
	25-39 years	347	2% (7)
	40-49 years	261	3.4% (9)
	50-59 years	247	3.2% (8)
	Over 60	73	1.4% (1)

AC: Accord Healthcare

particularly important for staff protection with a resurgent virus, as these data endorse the approaches to infection control and prevention delivered by the organisation.

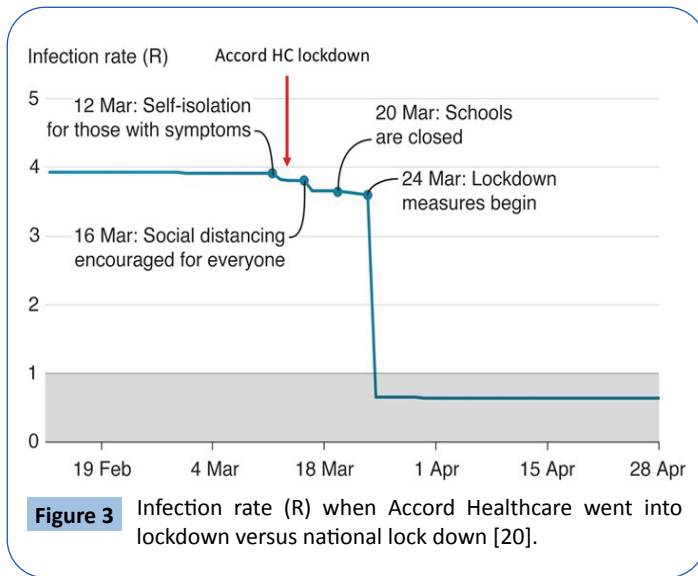
The results of this study revealed that of key workers working within the pharmaceutical sector, only 25 subjects (2.5%) had positive serology suggesting prior infection with SARS-CoV-2 virus. Certainly, our data is lower than prevalence data published amongst key workers within the NHS including HCPs and cleaning staff; the UK government reports prevalence rates of 6.7% (95% CI 6.1% -7.3%) in England. Yet, we do note regional differences; in the London region, the prevalence of positive serology to prior COVID-19 infection has been reported as 10.7%, which is similar to the 10.3% noted in the Harrow branch, a suburb of London [4]. Prevalence estimates also vary across the country over time with the highest prevalence estimates being in London with 15.7%. However, our low prevalence rates endorse the strategy of staff protection that was employed and delivered by the organisation.

Whilst there were no differences between the variables such as gender, site, working from home etc. there was a significant difference between positive serology and ethnicity. This is an interesting observation with a significantly higher prevalence of prior COVID-19 infection amongst Black and Asian (BAME) employees versus Caucasian employees. Whilst higher morbidity and mortality has been reported in studies of COVID-19 amongst BAME subjects, we are unaware of data revealing a higher rate of infection per se than Caucasian subjects. [17].

One explanation for the observed lower rates of infection within

Accord Healthcare employee population could be due to the early action from the Management at Accord to initiate a working from home scheme for all non-essential employees much earlier than the official lock down date, when the infection rate (R) was the highest. **Figure 3** illustrates the chronological implementation of government responses to the emerging pandemic. Similarly, factory-based employees and delivery drivers were given early guidance with regards to the 2-metre social distancing requirement and were provided with effective Personal Protective Environment (PPE) for all staff including those working from home, and a structured operational policy and procedure in relation to COVID-19 infection and testing.

Another possible explanation for the low prevalence amongst staff is that some did not generate a sufficient antibody response to COVID-19 infection. Moreover, these tests could also not have measured any cellular responses which may show an increased importance in the fight against this novel disease. A recent Swedish study revealed positive serology through antibody detection in roughly 10% of the Swedish population despite governmental strategy avoiding lockdown and a move towards developing herd immunity within the population [18,19]. This low rate of antibodies and relatively high mortality in comparison to its Scandinavian neighbours is worrying. Yet the study went further to explore T cell immunity finding that a further 20% demonstrated T cell immunity suggesting a much higher rate of prior infection and potential immunity. Such T cell immunity without the generation of antibodies may also have some role to play in the observed lower prevalence of positive serology in our study.



Although the number of individuals infected is low, it remains the largest study in a corporate industry. The low rates of infection demonstrate that it is possible to suppress spread of infection by implementing effective measures early. We believe this study will provide reassurance and confidence to implement changes within organisations. This study only presents results for the prevalence rates in the UK and Ireland; subsequent data is currently being collected to determine whether antibodies remain for positive individuals after 6-months and will be subject to another publication alongside data from other participating European offices of Accord Healthcare, as well as repeated tests for all employees when working from home is relaxed.

Whilst a positive antibody test is not an indicator of gained immunity against SARS-CoV-2 virus and COVID-19, the presence of antibodies often suggests some degree of immunity in other cases of viral infections assuming no significant viral mutations [20-22]. The evidence to establish a correlation between antibodies against SARS-CoV-2 and immunity from re-infection is yet to be determined. However, to-date there are over 77-million worldwide confirmed COVID-19 confirmed cases and no confirmed

reports of a re-infection [23]. However, asymptomatic individuals may express a weaker immune response to SARS-CoV-2 infection and the reduction in IgG and neutralizing antibody levels in the early convalescent phase may have implications for immunity strategy and serological surveys [24].

The limitations to this study were that we only looked at staff within a pharmaceutical organisation who received early and specific advice regarding prevention of infection. Consequently, it would be difficult to draw conclusions regarding prior infection for the wider population. Secondly, antibody production to SARS-CoV-2 does appear to decline with time so the actual figures of positive serology may indeed be an underestimate of prior infection [8,24]. Another potential confounding factor is that the study enrolled volunteers to have serology testing. 80% of staff participated in the study. These individuals may be more inquisitive to know their antibody status based on asymptomatic or pauci-symptomatic disease. Hence these would be less likely to be positive for antibodies to SARS-CoV-2. Conversely, some of the 20% of staff that did not participate may have been those that had confirmed COVID-19 infection through government testing. We did not explore this within the study. Finally, there may be a small number of individuals that could have tested positive following earlier exposure to SARS-CoV-2 at the peak (March/April 2020), however antibody levels may have been undetectable at the time this study was completed.

Conclusion

In summary, this study reveals a low rate of positive serology to SARS-CoV-2 found using lateral flow serology amongst a large cohort of essential staff working for a pharmaceutical company. The study reveals that an early preventative and concerted strategy including earlier than mandated working from home, adequate PPE and social isolation is effective for the prevention of infection amongst key workers during the pandemic. It also suggests that the simple implementation of lateral flow serology tests with wide adoption could be considered for future repeated campaigns while waiting for therapeutic solutions and vaccine herd immunity.

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