Testing to contain the second wave threat

By Gordon Woo for

COVID-19 Actuaries Response Group – Learn. Share. Educate. Influence.

Summary

In early February, when there were less than two hundred confirmed COVID-19 cases outside mainland China, each country formulated its own national strategy for dealing with the emerging coronavirus. The most successful strategies, which have minimised loss of life, contained the first wave through a rigorous regime of testing, contact tracing and quarantining, in addition to social distancing measures.

Strategies relying on self-isolation of infected people have failed because of widespread asymptomatic transmission. Mass testing is a prerequisite for breaking the invisible chains of asymptomatic transmission which inflate the reproduction number.

UK antigen testing capacity, manifestly deficient in the spring, should be up to South Korean levels by the autumn, thanks to newly authorised Roche and Abbott tests. These testing developments provide pharmaceutical grounds for UK optimism that the reproduction number, R, can be maintained below the epidemic threshold, and that a potential second wave threat of COVID-19 infection can be contained.

Introduction

With a population of 52 million, only a few million less than England, South Korea (SK) has successfully managed to contain COVID-19 and suppress associated mortality down to only a few hundred deaths – less than 1% of UK confirmed deaths. Starting from a huge cluster of super-spreader cases, SK registered a thousand cases in late February, at a time when the number in UK was just thirteen. But by mid-March, when UK registered a thousand cases, containment had ceased to be UK government policy[1].

SK was able to leverage an efficient testing network which was developed in the aftermath of a severe 2015 MERS outbreak, which caused an economic loss of $8.5 billion. Unlike SK, UK never had the mass testing capacity needed to contain the first wave of COVID-19. Prestigious academic labs like the Francis Crick Institute revived the spirit of Dunkirk in combatting the coronavirus, but more than 30,000 UK citizens have been lost in the first wave.

However, with the number of infections being forced down through stringent lockdown measures, UK has the opportunity in the autumn to contain the second coronavirus wave using mass testing technology. In testing capacity, the whole world will be far better prepared for a second wave than for the first. In particular, SK has the capacity to produce millions of test kits per week, most of which can be exported because the daily number of infections in SK is now extremely low. On 16 March, the WHO director-general had a simple message for all countries: *test, test, test*. Six months later, test technology mass production, and further bioscience innovation, will allow this simple message to be actioned all over the world.

Testing to reduce asymptomatic transmission

If a person has any of the symptoms of COVID-19, e.g. fever, dry cough, etc.., even though there may be doubt over coronavirus infection, the person can take steps to self-isolate and quarantine themselves, and their household. However, if an infected person is asymptomatic, that person may be completely unaware of spreading the infection. The first well documented asymptomatic case travelled from Wuhan to visit her family outside Hubei province, and unwittingly infected them.[2]

[1] COVID-19: government announces moving out of containment phase and into delay. Gov.UK press release 12 March.
[2] Bai Y., Yao L., Wei T. (2020) Presumed asymptomatic carrier transmission of Covid-19. JAMA, 323(14): 1406-1407.

Asymptomatic transmission is a major challenge in suppressing COVID-19. The scale of the problem was highlighted in a study undertaken in the small town of Vò in northern Italy, which was locked down for 14 days after a resident died on 21 February. From mass testing of the population, it was found that about 40% of confirmed infections were asymptomatic. This study involved the Imperial College COVID response team[1].

Whilst there is substantial variability in the degree and extent of asymptomatic transmission, what is clear is that lack of testing of those without symptoms has contributed to the high UK death toll. The discharge of untested hospital patients back into care homes freed hospital beds, but this was a high-risk policy. Testing of care home residents and staff has shown that many residents were asymptomatic. Indeed, asymptomatic transmission has been described as the Achilles' heel of current strategies to control COVID-19[2]. The testing of UK care homes has become a priority with the increased availability of UK testing resources.

Outside care homes and hospitals, there is an urgent need to ramp up the capacity to test far more people who have no symptoms. This could break invisible chains of community transmission and reduce the reproduction number, R. Selecting asymptomatic people for testing could be based on hunting down the coronavirus through contact tracing. Social networks and contact tracing apps will help identify specific sets of people, many of whom may well be asymptomatic, who have been in close proximity to confirmed infected cases, and therefore should be tested, and quarantined if tested positive. Speed of testing and contact tracing are crucial for containing the second wave threat. Enhancements in the speed, reliability and mass production scale of testing technology can elevate the UK's preparedness for a second wave to be closer to that attained by SK in March.

Minimal testing requirements

A key national metric for diligence in hunting COVID-19 infections is the amount of resources spent in finding a case[3]. Countries which conducted mass testing in the early stages of an outbreak have been able to contain COVID-19. At the end of April, the top country in this respect was Vietnam[4], with just a few hundred cases in a population of 96 million. It used its own WHO-approved test kits to perform almost a thousand tests to find each of these. Taiwan was second with almost 150 tests to find each case, and New Zealand third with about 125. Australia, which has about a hundred deaths from within a population of 25 million, was fourth with about 80 tests. One of the many gains from widespread testing is early identification of infection, which can lead to timely health care support and hospitalisation, and better prospects for recovery.

SK was fifth with about sixty tests per confirmed case at the end of April. Unlike the top ranked four countries, SK had an explosive localised outbreak of COVID-19, centred in a very large close-knit church community, where fewer tests within a mass testing programme were required to find cases.

By comparison, the number of tests per confirmed UK and US case has been an order of magnitude lower, reflecting the very limited amount of testing before the lockdowns in these countries. Both are urgently ramping up their testing capacity and will be much better prepared to contain a second wave of infection.

Any country aspiring to be as successful as SK at finding asymptomatic cases, will need to perform as many tests per confirmed case as SK. If there are around 4,000 new UK confirmed cases per day (the figure on 10 May when the 'Stay Alert' messaging was introduced, mooted as a high ambient UK level of infection), this would require about 250,000 tests per day. This should be understood as a minimum number to contain the asymptomatic spread of COVID-19, not some arbitrary aspirational figure floated by the Prime Minister.

If 250,000 tests per day can be achieved over the summer, and contact tracing is implemented effectively, UK should be in a good position to contain a second wave of infection in the autumn. UK is already following SK's

[1] Lavezzo E., Crisanti A., Ferguson N.M. et al. (2020) Suppression of COVID-19 outbreak in the municipality of Vo, Italy. MedRxiv
[2] Gandhi M., Yokoe M.D., Havlir D.V. (2020) Asymptomatic transmission, the Achilles' heel of current strategies to control COVID-19. NEJM, doi: 10.1056/NEJMe2009758.
[3] Ourworldindata.org/grapher/number-of-covid-19-tests-per-confirmed-case
[4] Kingler-Vidra R. et al. (2020) State capacity and COVID-19 testing. www.kcl.ac.uk

precedent of introducing drive-through screening stations, which allow for the early detection and swift quarantining of infected persons.

South Korean testing technology

SK was able to move very rapidly with testing in February because of its biotech industry preparedness. Most South Korean diagnostic kits use the standard polymerase chain reaction (PCR) detection method. Kogene Biotech had the first test kit approved by the Korean Ministry of Food and Drug Safety as early as 4 February. A second test from Seegene was cleared on 12 February. Soon afterwards, when a spike in cases occurred in Daegu city, it was possible to test 10,000 church members, and show that 40% were infected[1]. Had no tests been approved by mid-February, packed church services may have continued, seeding further nationwide infection. A stark comparison can be made with Italy, which also had a major outbreak in February, but which lacked the testing capacity of SK.

For SK, WHO has explicitly listed the approved testing products and manufacturers. By mid-March, apart from Kogene Biotech and Seegene, three further test kit manufacturers were approved: Solgent and SD Biosensor (27 February); and BioSewoom (5 March). SolGent has a plan to build a US manufacturing site, and has been registered with the US Federal Emergency Management Agency (FEMA) as a supplier to the US strategic stockpile. SD Biosensor is also a supplier to FEMA.

Other South Korean biotech firms are marketing high performance tests. iONEBIO claims 99.9% accuracy for its test kits, which can provide results within 20 minutes[2]. Each kit equipment contains 288 individual tests, all of which can be completed in one hour. Throughput of tests through a laboratory can thus be accelerated, increasing overall testing productivity. The entrepreneurial initiatives by South Korean biotech companies are taking place against a background of falling local demand for testing, due to the successful domestic suppression of the coronavirus. The highly competitive nature of the global testing market is a boon to those nations which urgently need to increase testing to suppress COVID-19 infection.

UK testing capacity

At the outset of the COVID-19 crisis, UK had an innovative, but rather small diagnostics industry. Viewing the crisis as an opportunity for technological advancement, the UK government has issued a call to British life science companies to turn their resources to creating and rolling out mass testing. As a start, the largest ever UK network of diagnostic testing facilities has been formed by three Lighthouse labs in Milton Keynes, Alderley Park, and Glasgow.

Unlike the remarkable Nightingale hospitals, the expansion of UK mass testing cannot be achieved within weeks, and international collaboration is essential. A public/private partnership between Public Health England (PHE) and Roche Diagnostics uses Roche's high throughput PCR machines. UK roll-out of the Roche PCR test is coordinated by PHE in partnership with NHS.

There is also an important collaboration with Thermo Fisher Scientific, which is a US company based in Waltham, Massachusetts. Its COVID-19 PCR testing kit was approved on 21 March for diagnostic use throughout Europe[3]. The kit supports the goal of mass testing. It can be used by clinical and public health laboratories to evaluate up to 382 patient specimens in under two hours. Thermo Fisher can supply 100,000 tests per day, using its 26 UK labs and 5,000 staff. Rather than importing testing kits, Thermo Fisher is planning to manufacture these kits for local supply.

A reliable antibody test to tell if someone already has been infected has been sadly unavailable so far; rapid home finger-prick tests have been wildly inaccurate. A reliable serology test that requires lab processing has been developed by Roche Diagnostics. Perfect sensitivity in detecting antibodies to SARS-CoV-2 is claimed and

[1] How Korea trounced U.S. in race to test people for coronavirus. Special report: UK.reuters.com, 18 March
[2] www.covid19korea.com
[3] www.thermofisher.com/uk/en/home/clinical

99.8% specificity, i.e. only 1-in-500 false positives. Elecsys has received FDA emergency use authorisation[1] and approval from PHE. Hundreds of thousands of Elecsys tests per week will be provided to UK[2]. A phased UK roll-out is planned, with front-line workers prioritised.

PHE has also approved in mid-May the SARS-CoV-2 immunoglobulin (IgG) test developed by Abbott Laboratories, which has the capacity to provide 5 million tests per month for UK[3]. The Abbott test is also being made commercially available for home use, with the blood sample being sent for lab analysis. Mass antibody testing over the summer will provide key information for estimating R and for making changes in the COVID-19 traffic light system to contain a potential second wave of infection.

Rapid detection technology

If only there were a reliable detection technology which could determine rapidly (within around 30 seconds) whether a person has the coronavirus. If such a technology existed, screening for SARS-CoV-2 would be like screening for terrorist explosives. It could be deployed at airports, surgeries, entertainment venues – and even important office buildings.

The Groningen ViroTact company is at an advanced stage in developing such a practical test, based on its proprietary smart molecule technology[4]. Contingent on regulatory approval, this could be available after the summer to combat a second wave of COVID-19. The CoviTact disruptive technology is based on detecting the presence of an essential protease encoded for SARS-CoV-2. (A protease is an enzyme that breaks the peptide bonds of proteins, and is associated with fluorescence.) The CoviTact proprietary quenched substrate, on which the enzyme acts, is added to a sample of saliva of an individual being tested. Infrared light is released in the presence of the viral protease, which is received by a portable detector.

CoviTact is highly specific to SARS-CoV-2, and is sensitive enough to detect very low levels of pathogens. However, it is unclear if this quick and affordable test is sensitive enough to detect most asymptomatic infection. But as with security searches for explosives, some error tolerance might be acceptable to enable entertainment venues to operate with a reasonable audience capacity.

Another rapid detection technology, which was originally developed to study single living cancer cells, is based on aptamers explicitly synthesised for SARS-CoV-2. An aptamer is a short single-stranded DNA or RNA molecule that can bind to a specific target. This technology is under development at Pinpoint Science's labs in Berkeley, California[5]. A nasal or throat swab is taken from the individual being tested, and using nanosensor technology, a viral agent may be found. The nanosensor-based assay is claimed to be able to accurately detect the coronavirus in both symptomatic and asymptomatic cases, and distinguish it from other pathogens. Clinical testing is planned for August in California, with a provisional milestone set in September for FDA approval.

If neither of these rapid technologies succeeds, there is a slower point-of-care test for SARS-CoV-2 under development by the Intelligent Fingerprinting company, in conjunction with Imperial College. Developed for illegal drugs testing, the screening diagnostics can detect picogram amounts of chemicals in the sweat collected from fingerprints[6]. Testing takes ten minutes, but delivers on-site results without the need for lab processing. In situations where no regular testing would ordinarily be done and social distancing is unrealistic, as in many workplaces, this technology might potentially be deployable.

[1] www.roche.com/media/releases
[2] www.med-technews.com
[3] www.medscape.com
[4] www.dedactdiagnostics.com/virotact
[5] www.pinpointscience.com/covid-19-test
[6] www.intelligentfingerprinting.com