A miscarriage of diagnosis

PCR testing for COVID aims to detect individuals who have a high likelihood of being infectious.

False positive test results have more than one cause in PCR testing and productive conversations about them require these categories to be distinguished.

The **operational false positive rate** refers to the rate of error across the whole process. This will vary day to day so the rate should be measured as a tendency to a mean not taken as the minimum. Each laboratory will have its own operational false positive rate and this can vary over time depending on the factors below.

1. Profiling Errors

Who is being tested has a significant bearing on the false positive rate. Any positive pregnancy test from, say, testing children in a reception class at primary school must be a false positive. Likewise testing asymptomatic people for COVID is much more likely to produce false positive results than testing symptomatic patients.

As it happens, some subpopulations within communities can have a higher baseline false positive rate for unknown reasons. This is a frequent problem we see, for example, in breast and cervical cancer screening in young women. Indeed, this is why those screening programmes do not screen young women. For COVID a similar unexpected level of false positives was seen in the summer with people in their [C1] 20s. When this subpopulation with a high false positive rate was discovered, they were targeted for more testing. We now know they were false positive results because the evidence from spring across the world proves that *genuine* COVID outbreaks spread rapidly between age groups. This did not happen throughout August which proves that the “outbreak” amongst young people was a pseudo-epidemic made up of false positives.

It is important to target testing to people who have symptoms that provide a high clinical suspicion of the disease you are testing for. This targeting of a subpopulation because they have a high false positive rate is bad profiling. The more people in this subpopulation that you target the higher the false positive rate will be driven for testing as a whole.

2. Mistaken Identity

The likely underlying cause of the false positives in young people was mistaken identity. When testing for RNA (the viral equivalent of DNA used for replication) the test should be able to distinguish between sequences that are unique to COVID and sequences seen on other viruses or even in human DNA. However, no test is perfect.

Human DNA **has been mistaken** for a different coronavirus when doing PCR testing. The human genome comprises three billion letters of code. While none of it may be an exact match for what the PCR test should be detecting, a near match could result in errors in a proportion of the tests. This type of mistaken identity could lead to particular subpopulations being targeted for testing creating profiling errors.

A 2003 outbreak of SARS1 **in a care home in British Columbia**, turned out to be a common cold causing coronavirus. Coronaviruses are a family of viruses and, although the spike protein of the COVID virus is unique, the rest of the virus has many similar features to other common colds. These similarities can cause mistakes in PCR testing. Because coronaviruses are seasonal, this type of mistaken identity can cause a seasonal variation in the false positive rate.

3. Contamination of the chain of evidence

There is a chain of evidence from the sample being taken, through delivery to the laboratory, checking in of samples and then opening and working on them. Contamination can happen at any stage. This contamination may come from the individuals carrying out the work or from other patients’ samples once in the laboratory.

Claims that PPE would be effective at preventing contamination from swab takers etc is like claiming that wearing chain mail would prevent you getting sandy on a beach. A delivery driver who is post-infective and shedding RNA could contaminate the containers the samples are transported in. Whoever opens those containers could then transfer the RNA to the contents. If the same gloves are worn when opening numerous patient sample pots then the possibility for contamination between samples will be high. Many readers may have seen the disturbing images of an undercover Dispatches reporter showing how some samples have been handled when they arrive at a lab.

Contamination is an issue largely because of the nature of the test rather than sloppy handling. Having turned the RNA into DNA, the second step in testing is to multiply the DNA by one billion to a trillion times. That means that even with highly competent sample handling the risk of contamination will remain because only the tiniest fragment of contaminant RNA can create a false positive test result. Reducing the number of times the DNA is multiplied reduces the chance of these errors but not to zero.

4. Equipment Errors

The testing equipment itself will have a low and fairly constant false positive rate. This is of the least significance but has had the most effort put into understanding it. It is possible to calculate based on retesting samples with different test kits. There seems to be a general misunderstanding that this is the only cause of false positive error and that because it is a low value there is no false positive problem.

5. Burden of Proof

As well as choosing a reasonable cycle threshold to reduce contamination errors other variations in the criteria used to determine positivity will lead to differences in the false positive rate. It is standard practice to test for three genes belonging to the COVID virus. However, if positive is defined as the presence of a single gene rather than all three then the false positive rate will be higher.

For example, the REACT study at Imperial carried out calibration between PCR tests in commercial laboratories and the same samples tested in Public Health England laboratories. They found 57% false positive rate in May. To minimise this error they used a different criteria to the commercial laboratories. Instead of reporting on one gene at any threshold they chose to define as positive the presence of one gene below a cycle threshold of 37 or the presence of two genes.

The Operational False Positive rate is made up of five types of false positive error: **Profiling errors; mistaken identity; contamination errors; equipment errors and differences in the burden of proof.** Changes in who is targeted; seasonal infections and laboratory quality standards can lead to changes in the false positive rate over time. The five types of false positive will vary between laboratories so investigations as to the rate at one laboratory can not be extrapolated to another, and each has its own interaction with underlying community prevalence rates, so that the overall epidemiological false positive rate will vary by place, time and testing strategy.

clarecraigfrcpath November 28, 2020 Uncategorized 11 Comments

Links to other publications on COVID

Talk Radio interview

Lockdown Sceptics

When is COVID not COVID?

Flu Like Illness

The Spectator

Our testing regime is dangerously flawed – here's how to fix it

COVID-19 and the false positive trap

clarecraigfrcpath October 25, 2020 Uncategorized 1 Comment

Characteristics of Patients on ITU

Admissions to ITU will be biased by circumstances in spring vs September. For example, in spring only the sickest and younger patients were given an ITU because of fear of more patients coming in the next few days. In September, the threshold for admission is likely lower for patients who are at higher risk e.g. high BMI, male, Asian or Black ethnicity.

Despite this bias the proportion of patients who were of black ethnicity in spring was 16% compared to only 7% in September.

The length of stay is much closer to the background rate for ITU admissions. Again there may be a bias with patients being kept longer because COVID patients in spring could deteriorate suddenly and unexpectedly.

The data on age, ethnicity etc is hard to interpret without knowing the control distribution for average ITU admissions.

Characteristics	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
% died in critical care	45	11.6 (but 50% still in critical care at end of study)	13
Median stay on ITU of survivors (days)	14	5	2.4
Median stay on ITU of non-survivors (days)	10	5	2.3
% with CPR prior to admission to ITU	4.0	1.4	6.1

AGE	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
Median age	62.6	61	60.5
% 16-29 yrs	2.0	4.0	TBC
% 30-39 yrs	5.0	6.4	TBC
% 40-49 yrs	9.0	14.8	TBC
% 50-59 yrs	22.0	22.0	TBC
% 60-69 yrs	30.5	27.2	TBC
% 70-79 yrs	23.5	20.4	TBC
% 80+ yrs	8.0	5.4	TBC

SEX	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
% male	70.5	69.5	55.7

ETHNICITY	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
% White	52.0	65.3	TBC
% Asian	18.0	21.8	TBC
% Black	16.0	6.9	TBC
% Mixed and Other	7.0	6.0	TBC

BMI	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
Median BMI	28.6	Not reported	TBC
% BMI <25	21.9	21.1	TBC
% BMI 25-30	38.8	31.8	TBC
% BMI 30-40	32.1	36.9	TBC
% BMI >40	7.1	11.2	TBC

CO-MORBIDITY	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
% with serious co-morbidities	9.0	11.7	19.2
DEPENDENCY			
% independent	81.8	88.7	75.8
% some assistance	17.7	11.2	23.0
% total dependence	0.5	0.1	1.2

SEVERITY	First 200 COVID ITU patients	COVID ITU patients since Sept 1st	Non-COVID ITU patients 2018-2019
% on ventilation	69.4	24.5	38.7
Oxygenation (Ratio of arterial oxygen to inspired oxygen)			
% Severe	38.7	48.7	TBC
% Moderate	49.5	39.6	TBC
% Mild	11.8	11.8	TBC
APACHE II score (ITU mortality prediction score from 0-70 with higher worse)			
Median score	16	13	15.2

clarecraigfrcpath **October 12, 2020** **Identifying true COVID**
Age, **autumn**, **Ethnicity**, **ITU**, **Obesity**, **Severity**, **summer** **1 Comment**

Have you got COVIDITIS?

Juliet might have been right about the rose smelling just sweet by another name but what we name things is critical. A rose by any other name is a mislabelled rose. What we label as COVID is critical to tackling the problems we face.

What is COVID? The case definitions that were set out at the beginning of the epidemic, **but vary slightly by country,** are excellent definitions for an epidemic. They remain excellent definitions for any area with exponential spread of infection. What is excellent about these definitions is that they aim and succeed to capture every possible case. This is essential to stop spread.

However, once disease falls to low levels in the community these definitions are harmful. By labelling every patient with a positive laboratory test as COVID we have caused immense harm. By mass testing a healthy population over the summer we have incorrectly labelled a huge number of individuals. The **SAGE estimate** of the false positive rate is 1% my own estimates are **slightly lower**. We have now tested for COVID nearly 20 million times. The SAGE estimate would mean we have had 200,000 false positives out of 350,000 total positives. **There is increasing evidence that these were indeed false positives.**

How false positives cause harm:

1. Life / world changing political decisions based on false data.
2. COVID looks increasingly benign. The current death rate of hospital admissions labelled as having COVID is only 1.5%. This is the background death rate for all hospital admissions. COVID had a 6% death rate.
3. By labelling patients without classic symptoms as having COVID, we have all accepted the idea that the symptoms can vary hugely. Unpicking this mess to really understand which symptoms matter will be incredibly difficult. Does asymptomatic COVID really exist even?
4. Test and Trace have been spread thin and have been chasing non-cases. Over summer there were over 500 false positive results a day. Their contacts were then reached and tested. 1% of them will have tested positive too. This can create the illusion of spread.
5. New and better tests may be dismissed as lacking in sensitivity because they fail to recognise all these false positive cases.
6. Without addressing the false positive issue we will have a constant stream of cases and be unable to return to normal.

In areas with high prevalence and active spread the definition needs to capture every possible case. In areas where prevalence is low continuing with that approach will include numerous non-cases. The problem that WHO and the USA in particular are facing is that they need different definitions for different areas.

So let's try having new labels for different scenarios. The key factor is that the definitions will need to be situation specific. Case definitions and testing strategy go hand in hand (I will write about that next). The percentages in these definitions are highly dependent on a sensible testing strategy.

My proposal is to have a three tier naming system with COVID; COVIDOID and COVIDITIS being separate categories.

In an area with true exponential spread defined by more than 6% of test results coming back positive:

COVID will be defined as any patient with **any one** of the below:

1. Fever
2. Cough
3. Sudden loss of smell
4. COVID skin rash
5. A single positive PCR test

When characteristic skin rashes were first documented there was no way of tracking them to see if they were significant. If there is an as yet unidentified symptom that appears to be attributed to COVID that has not yet been confirmed as such we still need a label. Anyone with this symptom and none of the above will be labelled COVIDOID (oid being latin for kinda like).

In an area with moderate disease prevalence defined by 2-9% of PCR test results coming back positive.

COVID will be defined as any patient with **any two** of the below:

1. Fever or Cough
2. Loss of or change to sense of smell
3. COVID skin rash
4. A single positive PCR test

Patients with only one of the above will be labelled COVIDOID.

In an area with low disease prevalence defined by fewer than 2% of PCR test results coming back positive. Any positive PCR results will be assumed to be false positives and not reported unless proven otherwise.

COVID will be defined by any patient with one of the below:

1. Positive viral culture
2. Ground glass changes on CT

These changes are highly specific and that it what is needed at times of low prevalence.

PCR testing could still be used to screen the nursing home and vulnerable hospital population (e.g. over 70) in order to protect them. However, a positive PCR result alone will not be enough. Confirmation using the above criteria would be needed to reach a diagnosis. Anyone with sudden loss of smell will be tested by PCR and a positive result would be diagnostic.

That leaves the following situations in the low prevalence area:

1. Cough or fever
2. Skin rash
3. Sore throat
4. Knowing someone with one of the above and thinking you've caught it.

Anyone who believes they have COVID in that situation just has COVIDITIS.

clarecraigfrcpath **September 13, 2020** **Uncategorized** **2 Comments**

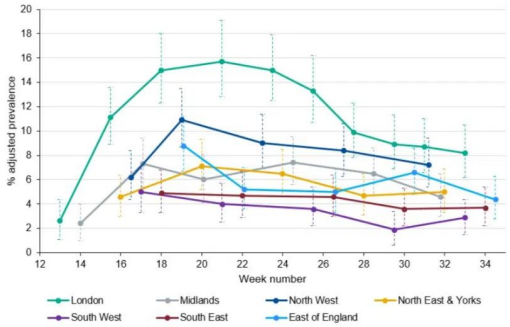
Evidence for and against false positive COVID 'cases' in July and August

For False positives:

I am working full time on gathering evidence that we have had a significant false positive issue. Listed is the current evidence. This is a live post that I will add to as I get more information in:

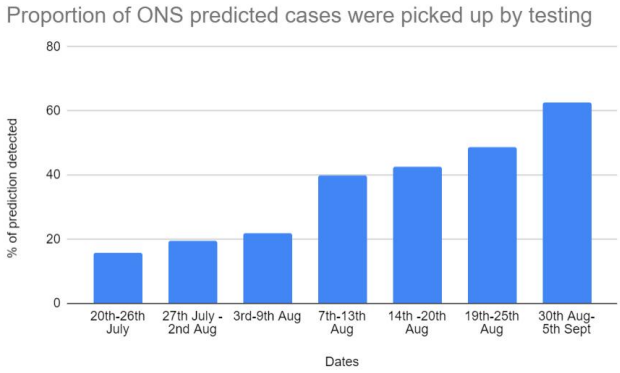
1. Characteristics of patients diagnosed with COVID
   - March April 60% were over 60yrs old. July August only 11% were over 60yrs.
   - March April 2% were under 20yrs old. Jul August it was 19%.
   - March April 60% men. July August 50%.
   - Ethnicity data TBC
2. Characteristics of disease behaviour of hospital admissions
   - March April death rate was 6%. July August death rate 1.5% = background rate for all hospital admissions.
   - Length of stay TBC
   - % admitted to ITU TBC
   - % with oxygen saturations below 95% at any point TBC
   - % with ground glass changes on chest CT TBC
3. Random sampling of general population
   - 95% of households in ONS survey had only one case since June
4. Antibody levels in the population
   - Since June, percentage of population with antibodies to COVID has fallen away. The last rise seen was seen in the Midlands at the beginning of June.

Figure 40: Overall SARS-CoV-2 antibody seroprevalence (%) in blood donors by PHE centres, using Euroimmun test adjusted for sensitivity (83.0%) and specificity (99.3%) and 95% confidence intervals (dashed lines)



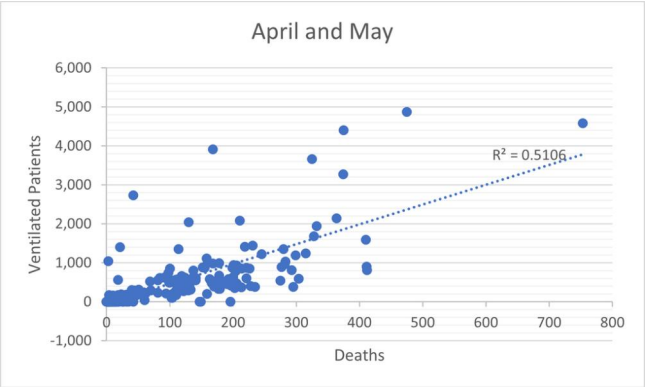
5. Lack of **antibody** production in cohorts diagnosed with PCR testing

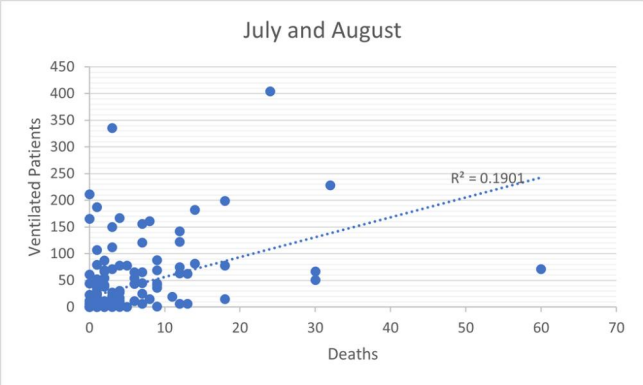
6. Increasing proportion of ONS predicted total cases are being detected by testing. It looks like we'll be detecting more cases than are predicted in a month's time.



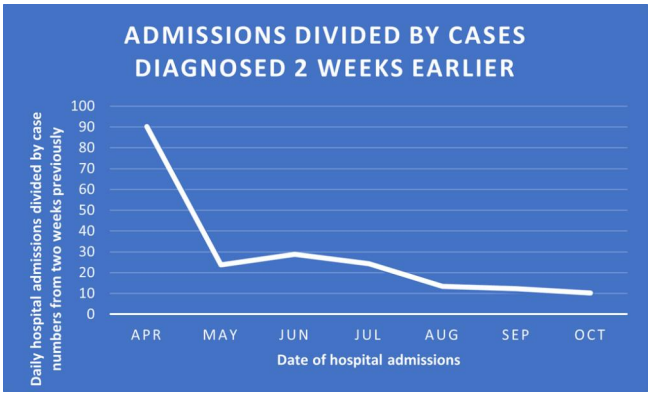
7. Deciding what caused and contributed to death involves piecing together evidence and drawing reasonable conclusions. Despite 'evidence' of COVID it was left off one third of summer death certificates in alleged COVID deaths. **https://www.cebm.net/covid-19/death-certificate-data-covid-19-as-the-underlying-cause-of-death/**

8. Data on patients in ITU and deaths per hospital trust showed a tight correlation in spring that was lost since.





9. Ratio of hospital admissions to cases from two weeks earlier would imply CFR of 0.15% unless diluted by false positive results



Against false positives

ICNARC has carried out an audit of the characteristics of patients on ITU with a COVID diagnosis. They characteristics are similar for patients admitted in Sept and those admitted up to 31st August. To draw definite conclusions we need to compare March, April and May admissions with July onwards.

https://t.co/qcohHhMyZ8?amp=1

Table 1. Patient characteristics: demographics

Demographics	Patients with confirmed COVID-19	
	Admitted from 1 Sep (N=856)	Admitted up to 31 Aug (N=10,894)
Age at admission (years) [N=856]		
Mean (SD)	59.0 (14.6)	58.8 (12.7)
Median (IQR)	61 (49, 70)	60 (51, 68)
Sex, n (%) [N=855]		
Female	261 (30.5)	3259 (29.9)
Male	594 (69.5)	7629 (70.1)
Ethnicity, n (%) [N=781]		
White	510 (65.3)	6919 (66.1)
Mixed	6 (0.8)	191 (1.8)
Asian	170 (21.8)	1669 (15.9)
Black	54 (6.9)	1003 (9.6)
Other	41 (5.2)	692 (6.6)
Index of Multiple Deprivation (IMD) quintile *, n (%) [N=838]		
1 (least deprived)	89 (10.6)	1541 (14.3)
2	93 (11.1)	1728 (16.1)
3	123 (14.7)	2073 (19.3)
4	210 (25.1)	2603 (24.2)
5 (most deprived)	323 (38.5)	2794 (26.0)
Body mass index *, n (%) [N=726]		
<18.5	3 (0.4)	79 (0.8)
18.5-<25	143 (19.7)	2639 (25.5)
25-<30	231 (31.8)	3554 (34.3)
30-<40	268 (36.9)	3252 (31.4)
≥40	81 (11.2)	826 (8.0)

* Please see Definitions on page 17.

clarecraigfrcpath September 12, 2020 Uncategorized 4 Comments

When is COVID-19 not COVID-19?

Here's my first formal publication on this:

> **When is COVID-19 not COVID-19?**

clarecraigfrcpath September 11, 2020 Uncategorized Leave a comment

Why are we seeing an increase in cases?

When we break a recent record for the number of COVID cases we have dramatic headlines. On 7th Sept there were 2,048 new cases in the UK with 2,988 the day before up from around 1,500-1,900 in the preceding days. This has created a spike over and above the already upward trend. (I believe the upward trend that preceded it to be due to the increasing number of cases being tested as set out **here**).

There are four possible explanations for the increase:

1. There are now significant numbers of true positive cases appearing in addition to the background false positives. The outbreaks in the North West are real and if they have taken another leap this will feed through to national data.
2. The numbers being tested increased and the percentage testing positive remained similar. These numbers are yet to be published for these two days.
3. Testing laboratories had a bad couple of days with higher than usual false positive rates.
4. When Pillar 3 or 4 antibody testing returns a positive result these values are added to the totals. It is not described whether this is done on a daily basis or in batches but this would artificially inflate the data.

The spike has been seen in England and the other nations, while showing an increase, appear to be following the general trend due to more testing. This supports the first hypothesis. If the rate of positivity in patients from the North West has reached 5% of those tested we would expect to see 2,800 cases a day assuming the rest of the country still had only false positives. That is one possible explanation for the rise. This would be a massive jump for that region and suggest the beginning of exponential growth.

Another explanation would be a spike in 20-29 year olds returning from holidays and this spike could be spread out more generally across the country. However, without knowing the ages of those tested it is impossible to interpret the significance of a higher rate in any one age group.

Aside from these two sources of infection, there is another possible explanation. Looking at data from testing since the end of June, when laboratories have had a higher false positive rate it tends to take a few days before it reverts to the mean. A significant part of the uptick could be due to false positives. This would be exacerbated if the number of tests carried out on 6th and 7th of September was record breaking. For example, if there were 200,000 tests with a false positive rate of 1.2% that would imply a rate in the North West of 2.5%. If we either increased the testing to 250,000 tests or had a false positive rate at 1.4% then the spike is compatible with there being no excess of cases in the North West.

Even when the data showing the number of tests carried out is published, there will still be ambiguity over the contribution of the above factors to the rise.

The numbers of false positive results are high and the daily fluctuations mean that on a national level it is worth being sceptical of spikes during the summer months. Earlier in the summer there were similar fluctuations but the total numbers were smaller so the differences were less noticeable. Look out for the regional data to see genuine reasons for concern. When COVID returns it is likely to be regional to start with.

clarecraigfrcpath September 8, 2020 Uncategorized 7 Comments

Variation in the false positive rate

There are numerous factors that can contribute to a false positive result. We understand some more than others. Error can creep in right from the moment the swab is opened until it passes quality control checks in the lab. Examples we

understand include other RNA being present from a different source and cross contamination. Each source of error may be tiny but there are enough of them that they add up to a significant number.

Contaminant viral RNA can be found because of viruses which many of us carry around obliviously (3). Symptomatic patients may have a cross reaction with another coronavirus which has been reported with SARS 1 (2). Contaminant human DNA from the X chromosome has produced false positive results for other coronavirus PCR testing (4). (Interestingly, women seem far more likely than men to have tested positive. It would be good to see how this has changed over time). A common cause of false positive rates in the real world is cross contamination. However, there is no suggestion of incompetence. For the kinds of false positive rates that we are getting there is clearly minimal risk of this happening but the risk cannot be reduced to zero.

Through experimentation we can label a particular test with a percentage of false positive results that can be expected. This is a constant so long as all the variables are constant. However, that does not happen in real life. There will be day to day variation but the mean over a longer time period will be the same.

Similarly, the number will be a constant for a specific population but could be different for another population. For example, a symptomatic population is more likely to carry RNA from other viruses that could cross react than an asymptomatic one.

For the above reasons, the Pillar 4, random testing of the public, can be expected to be lowest and seems to be around 0.05%. The Pillar 2 testing of patients in the community will include many symptomatic cases and the false positive rate for this testing seems to have settled around 0.8%. The rate for patients and staff in hospitals will include a smaller proportion of symptomatic patients and the false positive rate falls between the two at 0.4%. Each of these figures has a range and the overall day to day variation seems to be between 0.2% and 1.5% overall. Patients testing antibody positive in Pillar 3 tand 4 testing are reported in the Pillar 1 and 2 data. Without being able to see the raw data for PCR testing alone these estimates of false positive rates may be inflated. Having said that the numbers being identified by Pillar 3 and 4 are relatively low.

It has been suggested that the discrepancy is largely due to Pillar 4 testing being subject to additional scrutiny. Specifically, requiring more than one positive result before reporting as positive. I have not found any evidence that that is the case but this would be one way of improving on the false positive rates. It will not get it to zero though as sometimes the reason for the false positive will be constant for both samples.

Between April and June the PIllar 4 results showed a constant ratio of symptomatic to asymptomatic patients which was used to claim that these must all be true positive cases (1). However, nothing is perfect. If the ratio of symptomatic patients to asymptomatic patients is the same for true positives and false positives then there will be no difference. The positive results from Pillar 4 show a certain amount of noise over time until June, whereupon the level is absolutely constant. This is a good indication that a false positive rate has been reached. Assuming a false positive rate of absolutely zero is not credible.

Extrapolating from the range above, when testing 200,000 patients the false positive results could be anywhere from 400 to 3000 a day. On 19th August we had probably reported 60,000 false positive results out of a total of 324,000 tests. By the beginning of December, when seasonal coronaviruses rear their heads, we could have amassed an extra 170,000 or more false positive cases.

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2. https://pubmed.ncbi.nlm.nih.gov/26077969/
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2095096/
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clarecraigfrcpath September 8, 2020 Uncategorized 2 Comments

Waiting for Zero

For all the people carefully counting COVID deaths and cases there may be an expectation that the number we are aiming for is zero. This is a mistake. There will always be a proportion of cases tested who will be given a false positive test result when they do not have COVID.

What does zero look like?

Thankfully for COVID testing the false positive rate is less than 1%. But it is not zero. It will be impossible for us to ever reach zero. No more COVID will mean we only have cases and deaths that can be attributed to false positive test results.

I do not think we have reached zero COVID. The outbreaks in Leicester and Oldham were genuine. The prediction by the government SAGE advisors of a best-case scenario of zero deaths this winter is as absurd as their worst-case scenario of 80,000 deaths. However, understanding what the data will look like when COVID is gone is critical to prevent it causing prolonged unnecessary damage and to allow us seasonal freedoms.

What is the false positive rate?

There are two ways to find out what the false positive rate of a test is. One is to run the test on cases where there is certainty about the diagnosis and figure out how many results are wrong. This can give a false impression of the rate of false-positives because the experimenters usually remove all ambiguous or complicated scenarios to enable that certainty, but the ambiguous and complicated cases exist in real life. The other method is to use it in the real world and compare testing in different laboratories and over time.

Our real-world testing has resulted in a summer where the hospital positive rate has flatlined at 0.4%. For two full months there have been day to day fluctuations but that has been the figure it keeps returning to. Incidentally this is the figure the government is using to estimate false positive results (1). Having 99.6% of your results not being false positives is a phenomenal result. Testing rarely gets better than this.

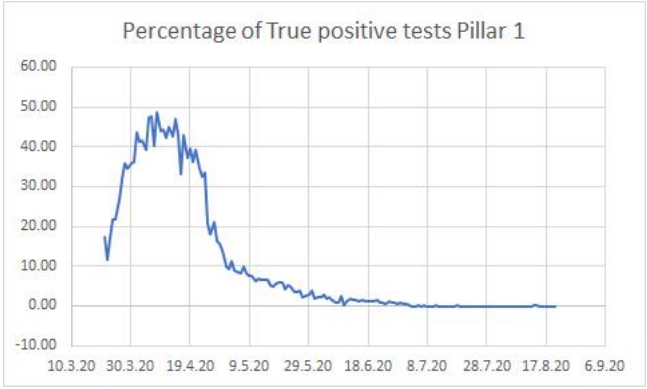

Figure 1: Percentage of cases as a proportion of tests processed minus the 0.4% false positive tests

When COVID is zero, how many false positive cases should we be expecting?

On an average month there are 1,400,000 admissions to hospital. Tragically that figure was only 900,000 in June. Data has not yet been published for July and August. Although the trend was upwards for the purposes of this prediction a conservative 900,000 will be assumed (2).

For that period, all admissions to hospital were tested for COVID. That is 30,000 tests a day of which 120 a day will give a false positive.

Some of these patients will die with this false positive COVID result (they die because whatever brought them into hospital kills them, not COVID, which they don't have). In a normal year, across all patients admitted to hospital, the average risk of dying is 1.7% (3). So, I will assume that 1.7% of our false-positive die each week. This would account for 14 deaths a week falsely labelled as COVID deaths. With admission levels back to normal at 1,400 a month then we can expect 22 deaths a week. It will be impossible for deaths to fall below that level.

That is the level that deaths in hospitals have reached at the end of August.

How can we tell they are not genuine COVID deaths?

In April, the chance of someone dying having been admitted to hospital with COVID was 6%. By June that had fallen to 1.5%. This was attributed to changes in treatment and some of that drop may well be due to improved treatment. However, as soon as the rate of death reached the background death rate for general hospital admissions we have to be suspicious about how many of these patients actually had COVID.

If these cases were false positives then there would be other signals in the data. For example, cases would be randomly dispersed through the population with only one per household rather than clustering. Since the beginning of June, the ONS Infection Survey pilot (the pillar 4 testing of randomly selected households), has found 95% of the positive cases have been the only case in their household (4). This compares with the ONS estimate of an average of 1.6 cases per

household in May (4). (This is worth emphasising – either the large majority of these positive cases in the survey are false-positive, as I am arguing – or Coronavirus is so hard to catch from people in your household that only 5% of the time does this happen.)

In addition, the age distribution would shift. Cases during the epidemic were disproportionately seen among older people, in fact 60% were over 60 yrs old. Of the cases we are seeing now only 11% are in the over 60s. This means they are slightly under represented but this may be a reflection of their willingness to be tested compared with younger people and it would help to know the age of those tested for comparison. In contrast, only 2% of cases were seen in the under 20s during the epidemic and this is now up to 19%, much closer to the 24% that would be seen if positive tests were distributed entirely randomly through the population (5). The age distribution of COVID deaths has been the same as the usual mortality data throughout.

During the pandemic men accounted for 60% of deaths. An increasing proportion of false positive results would push that figure nearer to 50%. Throughout June and July that figure has been 50% (6).

Until the beginning of June, asymptomatic cases accounted for less than 1% of reported cases. By August that figure had reached 72% (7). This may be in part due to the criteria for testing at the beginning but false positives are likely to play a significant role here.

Finally, a tight relationship of the time from diagnosis to death would become broader as cases moved from true positives to false positives. I have not been able to find data on this. However, there is evidence of the diagnosis and deaths becoming uncoupled. Public Health England were counting all deaths after a diagnosis regardless of the time frame. When they moved to only counting those that had occurred within 28 days of diagnosis, over 5000 deaths were no longer counted and these deaths were almost all from patients who had died in the summer (8).

Testing the hypothesis

The trends in the data above may not be enough to convince everyone that the explanation is testing of false positives rather than a change in the biology of the virus. The following work could test the hypothesis:

1. Using information of the age distribution of people tested to give a probability of a positive test for each age group over time. If the probability tends to the same number for every age group then that would be indicative of reaching a false positive rate. (Incidentally, this may show an age below which there have been no true positive cases).
2. For laboratories that have reached a positivity rate of below 2% use viral culture of those that are PCR positive to give an indication of the true positive rate. No positive cultures will be possible if they are false positive cases.
3. A cohort of patients with a positive PCR test should have CT lung scans to demonstrate ground glass or other radiological changes in those that are true positives. It has been shown that, even in pre-symptomatic patients, ground glass changes are seen in 77-93% on CT scan (9-11). Ground glass opacities are a very specific finding which would not be seen in false positive cases.
4. Post Mortem examination of a cohort of patients who have died with a label of COVID. True positive cases will show hyaline membranes in the lungs and/or interstitial lymphocytic infiltrate (94%) and positive PCR can be demonstrated up to 28 days after death (12).

Predictions for this winter

Coronaviruses are seasonal and that season begins in December running through to May or June. Between now and then we will see occasional small outbreaks like Leicester and Oldham but the numbers (largely false positives) will remain stable elsewhere. This means the R value will remain at 1. As the number of people being tested continues to increase to reach the 250,000 a day target, the number of cases will increase in line with this. This will cause a slight increase in the R value. As the numbers attending hospital returns to normal, there will be a rise in false positive deaths causing unwarranted concern. However, the numbers will not breach 1.7% of admissions. The R value will suddenly pick up in December simply because this is a seasonal infection and real cases will start to appear. Admissions will increase in December and before Christmas there will be speculation as to why the death rate from COVID has rocketed back up to somewhere near 4% or higher. An early family Christmas in November might be worth planning ahead for.

EDIT 13/09/2020 I have started a **live blog** listing evidence as it comes in to demonstrate that these were false positive results.

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