# Expert Report on COVID testing

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## 1. Introductory summary

1.1. COVID-19 (hereinafter "COVID") is an acute respiratory infection caused by the virus SARS-CoV-2 (Severe Acute Respiratory Syndrome-Coronavirus-2). There are a number of tests to diagnose COVID, but PCR testing is the one used to determine case numbers. It is our opinion that there are many issues with PCR testing which leads to inflation of the case numbers:

1.1.1. issues with the strategy for testing, including the definition of a case;[1]

1.1.2. emphasizing speed and volume of testing over quality;

1.1.3. choosing to prioritize finding every possible case over ensuring the PCR positive results are definite cases.

1.2. Regarding the way testing has been carried out there are issues with:

1.2.1. PCR as a diagnostic test in general;

1.2.2. this specific PCR test;

1.2.3. the fact that the results are being interpreted to label as cases numerous people who are not infectious;

1.2.4. lack of quality controls;

1.2.5. total absence of confirmatory testing.

1.3. False positive pseudo-epidemics have previously been caused by PCR testing. This is where the illusion of an epidemic occurs due to erroneous test results. When these events have occurred in the past those involved have fully believed they were in a fully fledged epidemic. Even in retrospect, with plenty of evidence that they had been mistaken, it can be difficult to persuade those who believed it at the time, that they were wrong. It is our opinion that there are large numbers of false positive results leading to an exaggerated number of cases and deaths, with both categories including individuals falsely labelled as having COVID.

1.4. Asymptomatic positives have been misinterpreted because of this testing strategy. There is minimal to no evidence that people who are asymptomatic, but have tested positive, can spread disease. It is our opinion that, aside from presymptomatic spread,

asymptomatic transmission is insignificant, if it exists at all, and policy should not be based on studies, largely using modelled data, that have massively exaggerated this risk.

1.5. The inflation of COVID case numbers and the misinterpretation of the significance of a positive test in an asymptomatic individual together have led to disastrous policy decisions.

## 2. What is COVID and what causes it?

2.1. COVID is a disease caused by infection with the virus SARS-CoV-2. A virus is an infectious agent, but unlike bacteria, it is incapable of replication outside of a cell. Viruses are made up of replicative material contained in a protein shell. The replicative material can be DNA or a different nucleic acid, RNA. Human cells work by converting DNA into RNA and then into functional proteins. The protein shell includes proteins that can bind to the surface of human cells and allow the virus to enter the cell. Once inside the cell, the virus hijacks that replicative apparatus, and its RNA will be made into proteins. These proteins form the viral particles that will enable viral spread. The viral material is replicated repeatedly creating numerous viral particles and ultimately these virus particles are released to infect other cells and to be exhaled and infect others.

2.2. A novel virus will spread in an epidemic fashion in a susceptible population. However, after passing once through the population, the population will reach levels of immunity that impact on viral spread. This immunity is comprised of the population's prior immunity, together with those who developed a new immune response to the novel virus. After passing once through the population, the virus will become endemic. That means epidemic spread is no longer a concern. However, a susceptible population remains and, as with all respiratory viruses, localized outbreaks will be seen each winter. A seasonal pattern develops with peak contagion mid-winter which is due to seasonal depression of the immune system rather than increased virulence of the virus, which remains the same. The virus cannot spread in an epidemic way so interventions are of no benefit. Every winter, people succumb to respiratory viruses, including occasional young, previously healthy, individuals. However, no intervention has ever been shown to have any effect at all on these seasonal deaths from endemic viruses.

2.3. By April 2021, there had been 400 deaths per million people worldwide. However, Canada had had 636 deaths per million. Canada accounts for 0.5% of the World's population but has had 0.8% of the world's COVID cases and 0.8% of the world's COVID deaths.[2]

2.4. The risk of someone dying if they catch COVID is age dependent, with more than 90% survival even in the oldest age bracket. The Infection Fatality Rate (IFR) is the percentage of those who catch it who will die from it (table 1).[3] The risk of dying is also heavily dependent on prior health status, with most deaths occurring in people with existing comorbidities (figure 1).

2.5. The infection fatality rate is dependent on many factors and varies from country to country depending on the age of their population. Global estimates of infection fatality rates are much lower than estimated in table 1. After collating the sum of the evidence on IFR, Prof Ioannidis, Professor of Medicine and Epidemiology at Stanford University estimated a global IFR of 0.15% (i.e. 99.85% would survive overall).[4] He estimated that the IFR in America and Europe was 0.2% for people living outside of institutions in the community, and 0.3-0.4% overall.

| Age group | Infection fatality rate (% of cases that will die) | Numbers dying per case |
|---|---|---|
| 0-9 | 0.002% | 2 in 100,000 |
| 10-19 | 0.007% | 7 in 100,000 |
| 20-29 | 0.031% | 31 in 100,000 |
| 30-39 | 0.084% | 84 in 100,000 |
| 40-49 | 0.161% | 161 in 100,000 |
| 50-59 | 0.595% | 6 in 1000 |
| 60-69 | 1.93% | 19 in 1000 |
| 70-79 | 4.28% | 43 in 1000 |
| 80+ | 7.80% | 78 in 1000 |
| OVERALL | 2.8% | 28 in 1000 |

**Table 1: Percentage of those who catch COVID who will die (IFR) by age from.**[3]

**Chance of Surviving Covid-19 by Age and Sex**

| | FEMALE | | MALE | |
|---|---|---|---|---|
| Age | No Underlying Conditions | One or Greater Underlying Conditions | No Underlying Conditions | One or Greater Underlying Conditions |
| 0-9 | 99.99996 | 99.9639 | 99.99996 | 99.9603 |
| 10-19 | 99.99996 | 99.9639 | 99.99996 | 99.9603 |
| 20-29 | 99.9998 | 99.9466 | 99.9997 | 99.9037 |
| 30-39 | 99.9991 | 99.8636 | 99.9986 | 99.79 |
| 40-49 | 99.998 | 99.8153 | 99.9965 | 99.6943 |
| 50-59 | 99.9888 | 99.3647 | 99.9815 | 99.2135 |
| 60-69 | 99.9562 | 98.7605 | 99.8895 | 97.9992 |
| 70-79 | 99.8251 | 97.6094 | 99.5245 | 95.6517 |
| 80+ | 98.9087 | 92.8152 | 96.3318 | 79.9154 |

"Predicted COVID-19 Fatality Artes Based on Age, Sex, Comorbidities, and Health System Capacity" Stockholm University, June 2020

**Figure 1: Chance of surviving COVID infection based on age, sex and co-morbidities.**[5]

## 3. What COVID tests are available?

There is no test which can 100% accurately diagnose COVID. Using a single test to define a disease will lead to errors in diagnosis. All tests are subject to error. Confirmatory testing, alongside clinical judgement on the basis of symptoms and circumstances, are the ways to reach an accurate diagnosis.

### 3.1. PCR testing

The most common test in use for COVID is a RT-PCR test (real time PCR test aka qPCR) for the virus SARS-CoV-2. This test cannot diagnose the disease on its own and has been misused. A nasopharyngeal swab or sputum is used to collect viral material and this is sent to a laboratory for testing. A PCR test is designed to identify DNA sequences. SARS-CoV-2 is an RNA virus. RNA is a similar molecule to DNA, based on nuclei acids, and certain viruses use it as their replicative material. The RNA is first converted to DNA so the test can be carried out. Technical details are set out in section 10.

### 3.2. Antigen testing (Also known as Lateral Flow tests)

These tests are capable of identifying the viral protein shell or fragments of it. They use the same technology as pregnancy testing. A nasal or nasopharyngeal swab is taken, the swab is squeezed into a liquid and this is dropped onto the testing strip.

### 3.3. Antibody testing

Antibodies are produced by the immune system in response to infection and these can be tested for with a blood sample. Antibodies that will only be present in active or recent infection (IgM antibodies) and antibodies that will remain present over a longer time course (IgG antibodies) can be tested separately.

### 3.4. Viral culture

Swab samples can be taken and used to try and infect cells that are growing in culture in a laboratory. Viable virus will invade, replicate and then successfully burst open these cells.

### 3.5. Whole genome sequencing

Every letter of the genetic sequence present in a sample can be read with whole genome sequencing. This is only possible for DNA samples so RNA would have to be converted to DNA first. The resulting sequences of billions of letters are compared with databases of known human, bacterial and viral sequences to try to allocate each strand of DNA to a category and decide whether there is sufficient, specific SARS-CoV-2 RNA (converted to DNA) present to make a diagnosis.

## 4. Advantages and Disadvantages of different tests

### 4.1. PCR testing

**Advantages**:

Numerous genetics and microbiology laboratories carry out PCR testing every day to diagnose genetic conditions, cancer risk and cancer mutations relevant to treatment and infectious diseases. The global polymerase chain reaction market size was valued at USD 4.5 billion in 2019[6] and has grown significantly in 2020. It is usually a reliable test that allows detection of specific nucleic acid sequences. The test itself is readily adapted to testing something new.

**Disadvantages**:

Although it is good at correctly identifying genetic material from a virus, it does not detect whole virus. It is therefore not a good test for infectivity. COVID patients are infectious for 7-8 days,[7] but the person infected can test positive with PCR when they are no longer infectious. People who have had COVID can test positive with PCR results for 80 days[8] or more, even when they are no longer infected or contagious. This is because after the infection, when no viable virus capable of infecting others is being produced, there will remain debris of the viral genetic sequence that cells will continue to reproduce. Patients who are immune and never have symptoms can test positive. PCR testing also has a propensity to false positive results creating pseudo-epidemics in the absence of real disease. PCR tests have to be transported to a laboratory for processing and results take 24-48 hours.

## 4.2. Antigen testing

**Advantages**:

Results of antigen testing take only 30 minutes. Because they detect viral particles they identify actively infective patients and do not detect those who have passed beyond the infectious phase. The lack of labour and transportation required makes these a cheap option.

**Disadvantages**:

These tests have been criticized for missing genuine cases. However, this conclusion can only be reached by assuming that PCR results never overcall. They do miss a small proportion of cases and have a low false positive rate too (as does any test).

## 4.3. Antibody testing

**Advantages**:

The manufacturers designed these tests using pre-COVID blood donor samples as a negative control. They therefore are a good way of testing who has developed a new immune response to COVID, and do not demonstrate who had prior immunity to COVID. A positive test demonstrates that the patient has developed immunity as a result of a genuine COVID infection, and was not immune prior to COVID's arrival.

**Disadvantages**:

Although they are a good test from 7-10 days after symptom onset in severe disease, it takes longer for the immune response to develop in mild and moderate cases so these are not useful for distinguishing current infections.

4.4. **Viral Culture**

**Advantages**:

Viral Culture is the gold standard test, that is, it is considered the most accurate testthat other tests should be compared to it in order to determine their accuracy. Only viable virus capable of infection will be detected using this test.

**Disadvantages**:

Testing is expensive and requires skilled laboratory staff with laboratories that reach the optimum biosafety standards.

4.5. **Whole genome sequencing**

**Advantages**:

By reading every letter of the sequence,[9] it is hard for a different virus to mimic and result in a false positive.

**Disadvantages**:

Whole genome sequencing has only been used in clinical medicine recently and, thus far, has been used to add qualitative information where a diagnosis is already known. It has never been used as a diagnostic test before and has not been stress tested to understand the risks of it going wrong or results being misinterpreted. It is expensive. Only samples with a good quality and quantity of DNA can be tested.

## 5. Diagnosing Infectiousness

5.1. A meaningful test would identify infectious individuals.

5.2. A person infected with SARS-CoV-2 is infectious from a maximum of 2 days prior to symptom onset to 7-8 days[7] afterwards (figure 2).

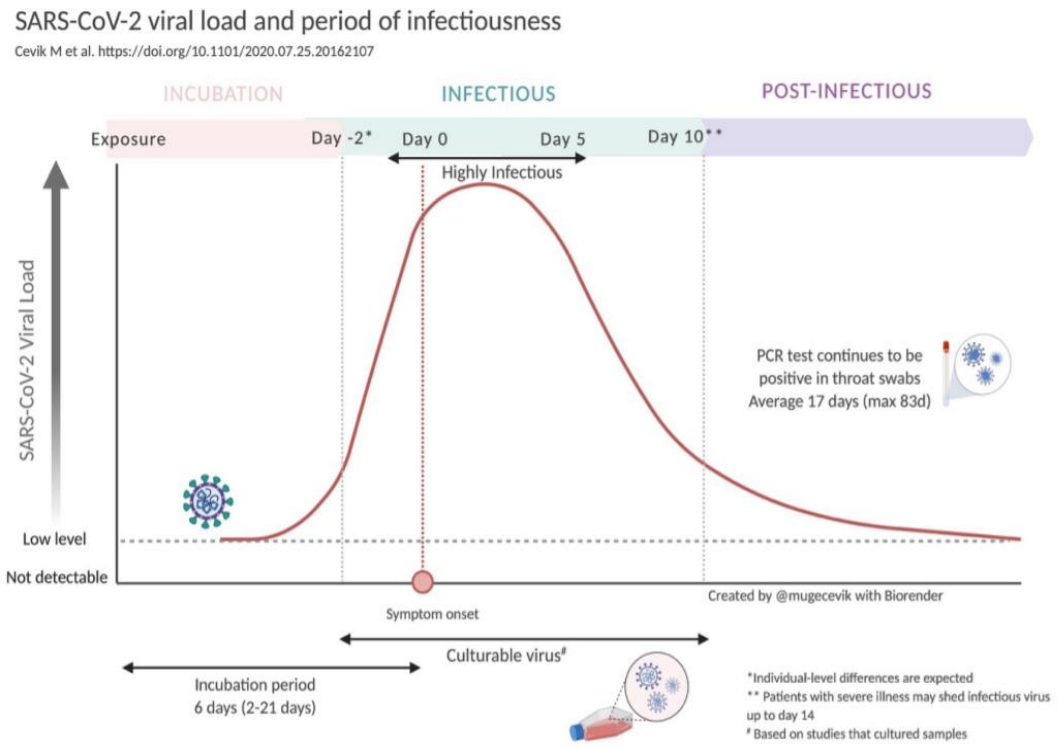



**Figure 2: Diagram from UK Government[10] showing the maximum period where viable virus can be cultured and the shorter period where there has been evidence of transmissibility.**

5.3. It is critical that testing can accurately identify infectious cases as failing to do so risks exposing non-infected patients to infected ones in hospital, as well as giving an erroneous impression of the extent of an outbreak.

5.4. The right testing strategy will depend on what question is being asked. If asking whether an individual patient had COVID recently, then a PCR test that may be positive even after the infective period, can be of use.

5.5. However, for population assessment, when trying to control spread of an infectious disease, the question being asked is whether the patient is currently in their infective window and therefore capable of transmitting disease. Testing being used in order to identify infectious people should be measured against this standard, and not the standard described above suitable for diagnosing an individual.

5.6. After an infection, viral debris can remain for some time. The patient is no longer contagious. In fact, the RNA present is not sufficient to make an intact viral particle. However, RNA continues to be present and can be shed onto a swab resulting in a positive test. The average time patients continue to shed RNA for is 17 days after symptoms onset[11] (or between 15 and 20 days). There are reports of shedding continuing for up to 83 days in the upper respiratory tract on occasion[8].

5.7. The CDC estimate in section 5.6 is based on assessment of all research on the topic. However, there are outliers within the research. For example, van Kampen et al found that <5% were still viral culture positive after 15.2 days.[12] (see section 12.12 figure 14) and Bullard et al found no viable virus after 8 days.[13]

5.8. We concur with the CDC when they stated:[14]

> "*Thus, for persons recovered from SARS-CoV-2 infection, a positive PCR without new symptoms during the 90 days after illness onset more likely represents persistent shedding of viral RNA than reinfection.*"

5.9. The two references above indicate that someone who has had a COVID infection can continue to test positive for up to a quarter of a year.[8,14] This phenomenon is well recognised. According to the UK government guidance,[15]

> *"Immunocompetent staff, patients and residents who have tested positive for SARS-CoV-2 by PCR should be exempt from routine re-testing by PCR or LFD antigen tests (for example, repeated whole setting screening or screening prior to hospital discharge) within a period of 90 days from their initial illness onset or test (if asymptomatic) unless they develop new COVID-19 symptoms."*

This is to avoid unnecessary self-isolation of healthy individuals who would need to withdraw from work.

5.10. If testing the population randomly, the vast majority of PCR positive results would be in the post infectious phase (see figure 3)[11]. The exact proportion will depend on how testing is carried out. Specifically, it matters how long after symptom onset people are tested and how often.

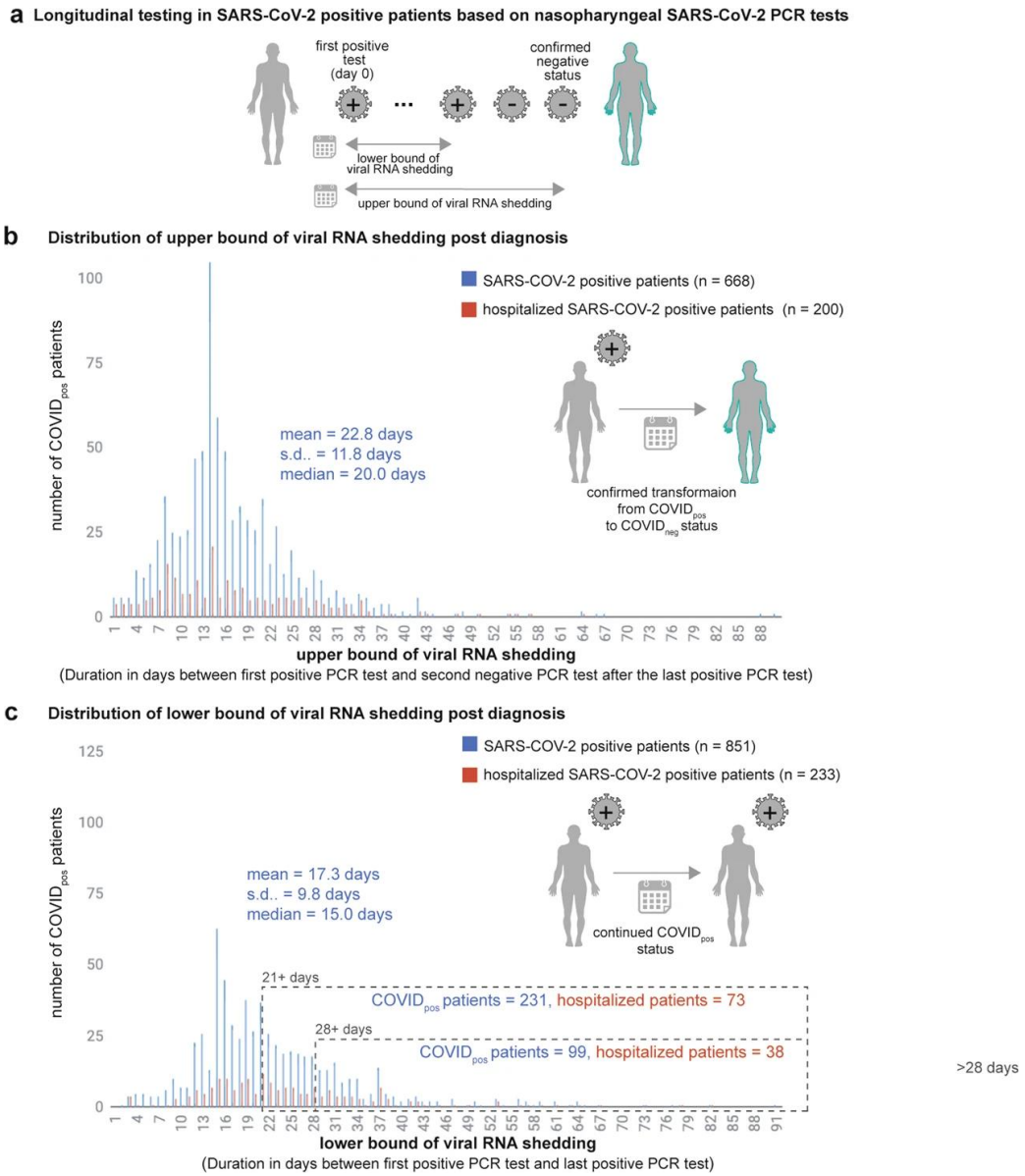



**Figure 3: Diagram[11] showing how long in days patients continued to be PCR positive after their first PCR positive test. b shows the time interval from the first positive test to the first negative test. c shows the time interval from the first positive test to the last positive test.**

5.11. Given that there is no evidence of infectivity 10 days after symptom onset, post infectious positive test results are meaningless in terms of diagnosis of disease and containment of infectious individuals.[14]

5.12. It is our professional opinion that:

5.12.1. PCR tests are poor at indicating whether a patient is currently infectious. Antigen testing is a good indicator of whether a patient is currently infectious (see section 20).[16]

5.12.2. Post infectious positive results are one cause of false positive results, but there are many other causes (see section 13).

5.12.3. Post infectious and other false positive results have resulted in confusion over what it means to test positive and be asymptomatic (see section 18).

## 6. Case definition for diagnosis

6.1. A disease by definition requires symptoms. Asymptomatic disease is an oxymoron.[17] The Miriam Webster dictionary definition of a disease is

> *"a condition of the living animal or plant body or of one of its parts that impairs normal functioning and is typically manifested by distinguishing signs and symptoms."*[18]

Confusion can arise because in infectious disease people who do not yet have disease can be about to develop it because they are presymptomatic and may be capable of spreading it.

6.2. Of all the scientific publications since 1965 that contain the words "asymptomatic"; "respiratory" and "virus", 58% were published in 2020 and 2021. Of the earlier studies, many defined asymptomatic disease based on PCR results (figure 4).[19]

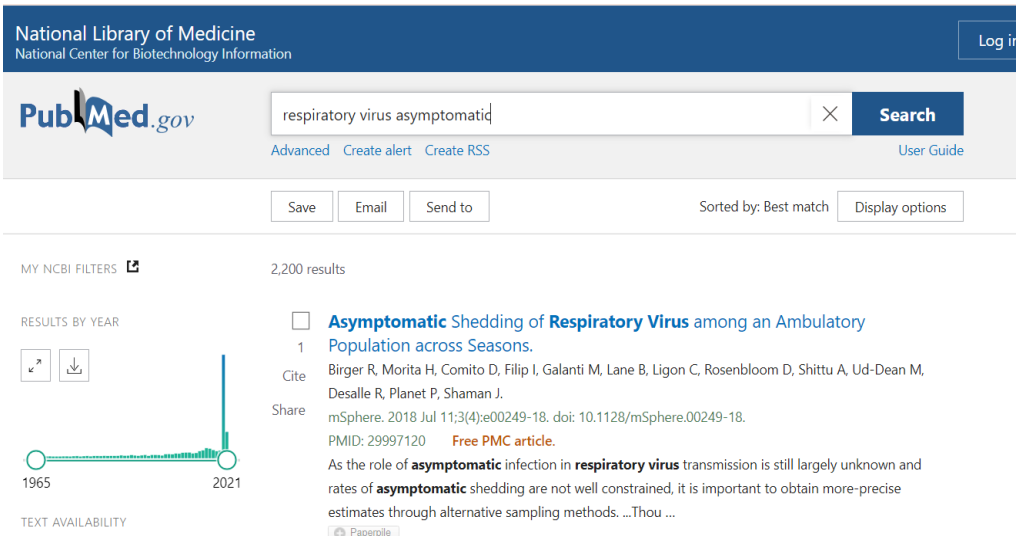



**Figure 4: National Library of Medicine search results for "respiratory virus asymptomatic".**[19]

6.3. Testing is designed and calibrated based on its ability to differentiate people with symptoms and disease from those without.[20] In the absence of symptoms, it is not possible to calibrate a test. The exception to this is for pre-symptomatic disease, where, given time, symptoms appear.

6.4. A diagnosis of disease always starts with a symptomatic patient or a patient at risk of having a presymptomatic illness. Testing is then carried out to confirm the diagnosis. Using testing to define disease leads to overdiagnosis and overtreatment.

6.5. When trying to diagnose a disease before symptoms have started, e.g. cancer screening, then a screening test is carried out on asymptomatic people. However, a positive screening test is not a diagnosis of disease. 95% of women called back after a breast cancer mammogram had a false positive result.[21] In these circumstances disease is diagnosed only after confirmatory testing.

6.6. COVID is the first disease that has been defined by testing. This is not a scientifically sound approach as, by definition, it denies testing errors. As the balance in the diagnostic decision shifts from symptoms to testing, overdiagnosis increases. [22] A person testing positive has become the definition of a 'case'. A useful definition would identify people who had disease and were sick or else people who were infectious and a danger to others. A positive PCR result is not a measure of either of these two useful classifications.[23] [16]

6.7. Instead of finding characteristic symptoms and confirming with a test, people with a positive test were studied to see what symptoms they had. Some had no symptoms and never developed symptoms. Consequently, the list of possible symptoms became extensive and the concept of an 'asymptomatic disease' (as opposed to presymptomatic) was formed.[24] The Canadian authorities list 18 different symptoms[25], involving every bodily system except the urinary tract and have different regional definitions for presenting symptoms[26]:

> "*Each province and territory has its own list of clinical presentation and these can be found on provincial and territorial health ministry websites."*

6.8. With regard to infectious diseases, there are four situations in which someone can test positive but be asymptomatic:

6.8.1. Presymptomatic infection i.e. the incubation period after infection before symptoms begin. The incubation period lasts on average 5 days and spread is possible in the two days prior to symptom onset.[10]

6.8.2. Immune individual. Immunity does not stop viral entry into the respiratory tract. An immune individual remains oblivious to the infection as their immune system handles the infection preventing viral replication. Evidence of spread of other diseases from immune individuals does not exist. The evidence that these individuals are a source of infectious spread of COVID is lacking (see section 18).

6.8.3. A post infectious individual. For hepatitis, poliomyelitis and Salmonella Typhus, a post infectious individual can become asymptomatic and continue to be infectious e.g. Typhoid Mary. For COVID such post infectious individuals are unable to spread disease (see section 5).

6.8.4. A test error resulting in a false positive test result.

6.9. As testing numbers increased, more testing of asymptomatic people was possible and, therefore, the importance of symptoms as part of the case definition was diluted.

6.10. From the outset of the pandemic, countries were under pressure to promptly publish daily figures. Centralized reporting and publishing of results meant that input from the treating doctor could not be considered before cases were declared.

6.11. The media and even the public health bodies have conflated the meaning of the number of “positive tests”, “cases” and “infections”. Only active infections, during the infective window are of practical importance. These represent a small proportion of the numbers reported. Inflated numbers are reported without thought about their meaning in terms of risk of infecting others.

6.12. In March 2020, the Canadian Government used a symptom based case definition with testing being used for confirmation.[27] At the time, testing was restricted in number and only used for suspicious cases. This meant that symptoms were a key eligibility criteria for getting tested, and so were an indirect criteria in PCR positive individuals. The criteria in March 2020 were:

> ***Probable***
>
> *A person:*
>
> *with fever (over 38 degrees Celsius) and/or new onset of (or exacerbation of chronic) cough*
>
> *AND*
>
> *who meets the 2019-nCoV exposure criteria*
>
> *AND*
>
> *in whom laboratory diagnosis of 2019-nCoV is inconclusive, not available, or negative (if specimen quality or timing is suspect) or in whom the laboratory test for 2019-nCoV was positive but not confirmed by the National Microbiology Laboratory (NML)*
>
> ***Confirmed***
>
> *A person with laboratory confirmation of infection with 2019-nCoV which consists of positive real-time PCR on at least two specific genomic targets or a single positive target with sequencing AND confirmed by NML by nucleic acid testing.*

6.13. The current Canadian Government definition of a case is[26]:

*"**Probable case***

*A person who:*

*1. Has symptoms compatible with COVID-19*

***and***

*Had a high-risk exposure with a confirmed COVID-19 case (i.e. close contact)* ***or*** *was exposed to a known cluster or outbreak of COVID-19*

***and***

*Has not had a laboratory-based NAAT* (PCR) *assay for SARS-CoV-2 completed* ***or*** *the result is inconclusive*

***or***

*Had SARS-CoV-2 antibodies detected in a single serum, plasma, or whole blood sample using a validated laboratory-based serological assay for SARS-CoV-2 collected within 4 weeks of symptom onset*

***or***

*2. Had a POC* (point of care) *NAAT* (PCR) ***or*** *POC antigen test for SARS-CoV-2 completed and the result is preliminary (presumptive) positive*

***or***

*3. Had a validated POC antigen test for SARS-CoV-2 completed and the result is positive*

***Confirmed case***

*A person with confirmation of infection with SARS-CoV-2 documented by:*

*The detection of at least 1 specific gene target by a validated laboratory-based nucleic acid amplification test (NAAT) assay (e.g. real-time PCR or nucleic acid sequencing) performed at a community, hospital, or reference laboratory (the National Microbiology Laboratory or a provincial public health laboratory)*

***or***

*The detection of at least 1 specific gene target by a validated point-of-care (POC) NAAT that has been deemed acceptable to provide a final result (i.e. does not require confirmatory testing)*

***or***

*Seroconversion or diagnostic rise (at least 4-fold or greater from baseline) in viral specific antibody titre in serum or plasma using a validated laboratory-based serological assay for SARS-CoV-2"*

***Deceased case***

*A probable or confirmed COVID-19 case whose death resulted from a clinically compatible illness, unless there is a clear alternative cause of death identified (e.g., trauma, poisoning, drug overdose).*

*A Medical Officer of Health, relevant public health authority, or coroner may use their discretion when determining if a death was due to COVID-19, and their judgement will supersede the above-mentioned criteria.*

*A death due to COVID-19 may be attributed when COVID-19 is the cause of death or is a contributing factor.*

6.14. The Quebec case definition (translated from French):[28]

**Confirmed Case**:

Detection of SARS-CoV-2 nucleic acids

**Death**: Compatible clinical manifestations observed before death
AND
detection of SARS-CoV-2 nucleic acids

**Case confirmed by epidemiological link**:

Clinical symptoms compatible with COVID-19
AND
high risk exposure with a laboratory-confirmed case during its contagious period,
AND
no other apparent cause

**Death**: Compatible clinical manifestations observed prior to death

AND

High-risk exposure with a laboratory-confirmed case during its period of infectivity, and no other apparent cause

**Probable case**:

1. Presence of multisystem inflammatory syndrome in 19 years and younger

OR

Presence of severe respiratory illness in a person hospitalized and on oxygen therapy

WHO

Has a negative NNAT [PCR] for SARS-CoV-2 following the onset of multisystemic inflammatory syndrome or severe respiratory illness;

AND

Has a prior history of clinical manifestations compatible with COVID-19 to document the onset of illness;

AND

Had serology that met pre-established criteria

2. Has a positive antigen test for SARS-CoV-2

WHO

Has clinical manifestations compatible with COVID-19

OR

Has had close contact with a COVID-19 case

OR

Has been exposed to an outbreak setting

AND

Does not meet the criteria for a confirmed case.

**Clinical Case**:

Clinical symptom consistent with COVID-19 with no other apparent cause.

6.15. The use of PCR, by the Canadian Government and the Quebec Ministry of Health and Social Services to define a case, means the case definition does not meet the WHO requirement of considering signs, symptoms and contacts before making a diagnosis.[29]

6.16. The definition of an outbreak is very wide. Anyone attending a large institution would be at high risk of being included in this definition if they tested positive, as only one other person must test positive to declare an outbreak. An outbreak is defined as[26]:

> "*Two or more confirmed cases of COVID-19 epidemiologically linked to a specific setting and/or location*."

6.17. The definition of a probable case means that any two individuals who are contacts and test positive will by definition be cases, even in the absence of symptoms. When carrying out mass testing in large groups e.g. work places and schools, this is a poor definition as the risk of two false positive test results will be significant when testing a large population.

6.18. In Quebec, anyone with a pneumonia can be counted as a clinical case of COVID in the absence of any other evidence of COVID.[28]

6.19. The definition of a COVID death includes not only deaths directly caused by COVID but also any deaths where COVID was a contributing factor. Deaths from influenza were not defined in the same way and were attributed to the underlying cause even where influenza contributed to death.[30] Defining deaths in this way will lead to concerning numbers when making comparisons with death data from previous years.

6.20. If there are more than two patients with positive test results in a hospital setting then the hospital will by definition be an "outbreak". Anyone dying, untested, in such a hospital of respiratory disease can be classed as a COVID death.

6.21. In Quebec, anyone dying of a respiratory illness requiring oxygen could be classed as a COVID death if they have antibodies to SARS-CoV-2.[28] The antibodies present may have developed from an infection at some other point since March 2020.

## 7. Testing strategy in a pandemic

7.1. The Canadian Pandemic flu plan defines a pandemic as a disease resulting in more severe disease than seasonal influenza, with deaths in the young and healthy:[31]

> *"Whatever the pandemic impact, the epidemiological picture is expected to be significantly different from that of seasonal influenza, in that* ***relatively more severe disease and mortality will occur in the young and in persons without underlying health conditions*** *compared to seasonal influenza.*
>
> *There are important concepts to consider when planning and implementing public health measures. The measures should be used in combination to provide "multi-layered protection", as the effectiveness of each measure on its own may be limited. Actions should be tailored to the anticipated pandemic impact and the local situation, supporting the principles of flexibility and proportionality. Some measures, like hand hygiene and respiratory etiquette, are applicable in all pandemics. Other measures (e.g., proactive school closures and travel restrictions) might be used only in moderate- to high-impact situations, as they can be associated with significant societal and economic costs.*
>
> *A risk management approach will help weigh the potential advantages of particular interventions against their disadvantages and unintended consequences. Decisions about which measures to deploy also raise fundamental ethical challenges. For example, when considering restrictive measures, it is important to balance respect for autonomy against protection of overall population health. In such situations, the principles of proportionality, reciprocity and flexibility are involved, with a view to safeguarding individual freedom to the extent possible while promoting protection against the health and societal consequences of influenza infection.*
>
> *While aggressive measures (e.g., widespread antiviral use and restriction of movement) to attempt to contain or slow an emerging pandemic in its earliest stages were previously considered possible on the basis of modeling, experience from the 2009 pandemic has resulted in general agreement that such attempts are impractical, if not impossible."*

7.2. All tests strike a balance between false positive results and false negative results.

7.2.1. Diagnostic testing is never a black and white situation. There is always a grey area and it matters how that is dealt with. A line must be drawn that determines what test results will be called positive and what will be called negative. There is therefore a binary choice either:

7.2.1.1. Sensitive testing: diagnose every possible case accepting that there will be overcalling of cases that are not real (false positives) or

7.2.1.2. Specific testing: diagnose only definite cases accepting that there will be undercalling of cases that are real (false negatives).

7.2.2. Neither scenario is ideal, but there are ways to test that will minimize problems. It is also possible to measure these errors so that there is a full understanding of the risk of incorrect diagnosis.

7.2.3. There is always a tradeoff between false negatives and false positives. Actions taken to reduce false negative results will result in an increase in false positive results.

7.2.4. False negative test results have been the focus of testing strategy. However, a false negative result is unlikely to result in a misdiagnosis, as the patient will still develop the symptoms characteristic of the disease.

7.2.5. False positive results have the potential to exaggerate the cases and give the impression of a crisis resulting in public health decisions that have a far greater negative impact on the population. We agree with this list of wide ranging negative impacts of false positive results published by Surkova et al:[32]

***Panel:*** **Potential consequences of false-positive COVID-19 swab test results**

**Individual perspective**

*Health-related*

- For swab tests taken for screening purposes before elective procedures or surgeries: unnecessary treatment cancellation or postponement
- For swab tests taken for screening purposes during urgent hospital admissions: potential exposure to infection following a wrong pathway in hospital settings as an in-patient

*Financial*

- Financial losses related to self-isolation, income losses, and cancelled travel, among other factors

*Psychological*

- Psychological damage due to misdiagnosis or fear of infecting others, isolation, or stigmatisation

**Global perspective**

*Financial*

- Misspent funding (often originating from taxpayers) and human resources for test and trace
- Unnecessary testing
- Funding replacements in the workplace
- Various business losses

*Epidemiological and diagnostic performance*

- Overestimating COVID-19 incidence and the extent of asymptomatic infection
- Misleading diagnostic performance, potentially leading to mistaken purchasing or investment decisions if a new test shows high performance by identification of negative reference samples as positive (ie, is it a false positive or does the test show higher sensitivity than the other comparator tests used to establish the negativity of the test sample?)

*Societal*

- Misdirection of policies regarding lockdowns and school closures
- Increased depression and domestic violence (eg, due to lockdown, isolation, and loss of earnings after a positive test).

**Figure 5: List of impacts and harm caused by false positive results.**[32]

## 7.3. The impact of false positive results depends on the prevalence of disease

7.3.1. Testing with an over sensitive test leads to false positive test results. False positive results occur as a percentage of all tests done.[33] A false positive rate of 1% means that 1% of tests done will be positive in the absence of disease. If there was no virus at all, then a 1% false positive rate would lead to 10 positives for every 1000 tests. All 10 of these positive results would be false positive results. Although 1% of the tests would return a false positive, the percentage of the positive results that were false positive would be 100%. 99% of the results were negative and correct.

7.3.2. When there is plenty of virus around, there will be high numbers of true positive results. To take an extreme example, let's say 1 in 5 people tested have the disease. With a low

false positive rate, of say 1%, then for 100 tests, 1 will be false positive and, 20 will be true positive. The remaining 79 results would be negative. Therefore, of all the positive test results, only 5% would be false positive.

7.3.3. However, as the number of true positives fall and the proportion of tests done rises, these ratios can change dramatically.[34] For example, if only 1 in 100 of those tested is a true positive. Out of 100 tests, 1% will be false positive and a further 1% would be true positive. Therefore, of the positive results, only 50% of them will be true positives.

7.3.4. If testing is increased this effect is amplified. Say the 100 tests in the previous example were those carried out on people in hospital who the doctors thought had the disease. This would mean that the proportion that would be true positives would be high. If instead you tested every hospital patient, the hospital staff, all care home residents and staff, people wanting to visit care homes and anyone in the community with common cold symptoms, then the proportion of true positives would fall. In the first example, the ratio of true positives to false positives would be high, In the second example, false positive results are likely to far exceed true positive results.

7.3.5. Let's say we test 10,000 people. We do this by testing people who individually are much less likely to have disease than patients in the hospital that the doctor thought had disease. The one person that would have been tested positive, if we had focused testing in hospitals, still tests positive. We also see, say, 5 further true positive tests from all the extra people tested who individually were less likely to have disease. That would mean that the 6 out of 10,000 tests would be true positive, a 0.06% true positive rate. However, the 1% of tests testing false positive will result in 100 false positive test results. Therefore, even at a very low false positive rate of 1% of the tests done, it is easy to end up with 94% of positive test results being false positive results (see figure 6).

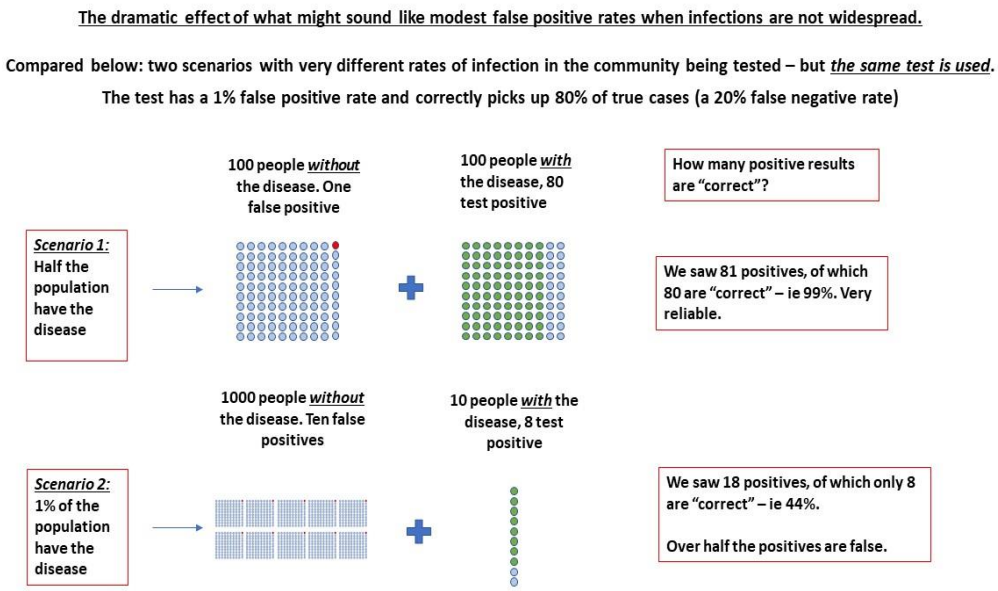



**Figure 6**: **Low percentage false positive rates (per test carried out) can result in a high proportion of positive test results being false positive results. A test with a low false positive result of 1% will result in 44% of positive results being false positives when testing for an uncommon condition with large testing volumes. The examples given can be extended further as the more testing the greater the proportion of false positive tests.**

7.3.6. A false positive rate would lead to more false positive results. For example, a false positive rate of 5% would lead to 500 false positive results per 10,000 tests.

7.3.7. False positive results are a known risk of PCR testing. The WHO states[35] that they use PCR for influenza surveillance, despite the inherent issues with erroneous results:

*"The role of RT-PCR in influenza surveillance and diagnostics: Despite inherent issues such as false positives (caused by contamination, the non-specific hydrolysis of primers or reduced primer specificity due to virus evolution) and false negatives (caused by factors such as poor sample quality, inefficient nucleic acid extraction, the presence of reaction inhibitors or primer mismatch due to virus evolution) RT-PCR is the established basis of both influenza virological surveillance and diagnostic activities in a broad range of settings."*

7.3.8. We concur with the WHO when they stated,[35] in regard to PCR testing for influenza testing:

*"Challenges encountered include the low sensitivity of some real-time RT-PCR kits, and distinguishing unsubtypable influenza A viruses from false positive results. Issues of under- or over-sensitivity are inherent challenges in RT-PCR testing and may be one area in which WHO and WHOCC advice to laboratories could usefully be strengthened."*

7.3.9. More testing will lead to a greater proportion of false positive results. The number of tests done per day has nearly tripled since Spring 2020, in Canada, with nearly 26 million tests carried out by 13th March 2021. Up to 31st March 2021, 70% of the testing done in Canada has been carried out in Quebec and Ontario.

| Date | Total Tests done to date | Tests per day | Total cases to date |
|---|---|---|---|
| 17th April 2020 [36] | 503,003 | Not reported | 30,670 |
| 4th June 2020 [37] | 1,787,446 | 35,823 | 93,441 |
| 22nd August 2020 [38] | 5,088,437 | 47,986 | 124 629 |
| 21st November 2020 [39] | 10,824,873 | 68,503 | 326 424 |
| 13th March 2020 [40] | 25,994,162 | 102,675 | 906,755 |

**Table 2: Increase in testing done in Canada over time.**

7.3.10. Figure 7 shows the cumulative number of tests per 1000 people carried out in Canada compared with a selection of other countries. Levels have been higher than Canada in most European countries and in the United States.

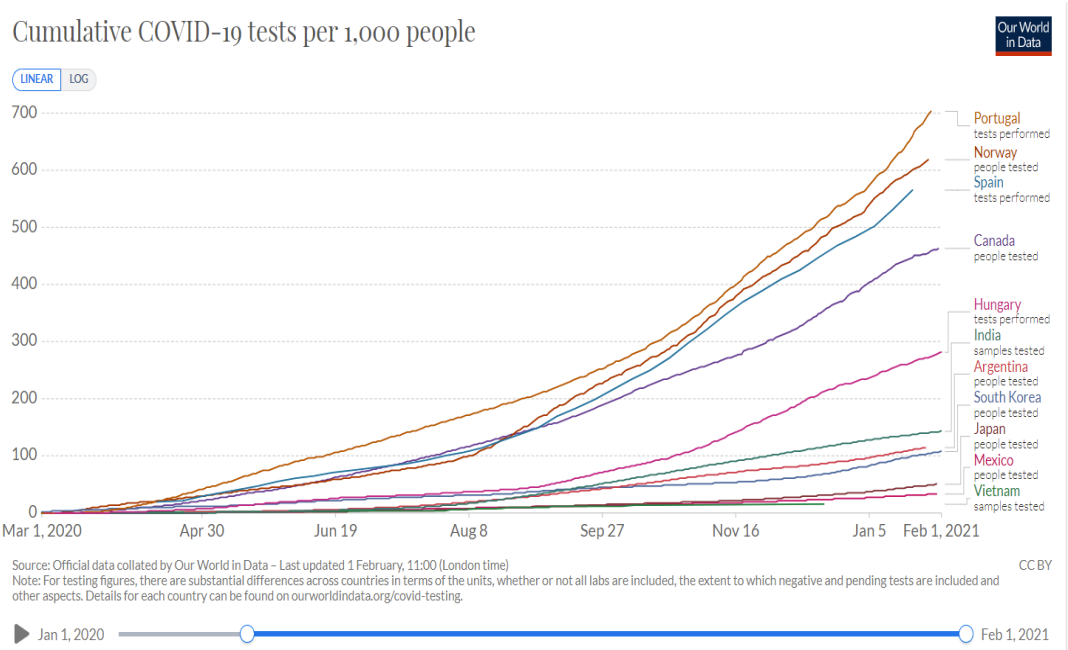



**Figure 7: Cumulative COVID-19 tests in Canada compared with a selection of other countries.**[2]

## 7.4. Pandemic Early Phase: Aim of testing

7.4.1. At the onset of a pandemic, up until peak deaths are reached, the best choice of test is a sensitive test. The aim of testing is to identify infectious contacts and reduce the risk of transmission. While this cannot stop a virus spreading, it can slow the spread of the virus. If a virus is left to spread at maximal speed then, at the point when herd immunity is reached, many people will already have caught it at the point that herd immunity is reached. These people will not be able to benefit from herd immunity, and the susceptible among them will die. However, by slowing spread, at the point when herd immunity is reached, a smaller number of people will already have caught the infection and fewer will die. This excess mortality from not delaying spread is referred to as overshoot.

7.4.2. Because testing is focused on contacts of confirmed cases the likelihood of those being tested being infectious is high. The main danger during this period is false negative results where an infectious person is incorrectly told they do not have the disease, and then they go on to infect others.

7.4.3. The risk of false positive results will be real, but can be safely accepted as collateral damage during this phase.

## 7.5. Pandemic early phase: Choice of Laboratory strategy

7.5.1. Laboratories are like any other undertaking. Restaurants can only do two of the following three things: quality food; fast food or cheap food. The same is the case for laboratories, but we can substitute quality testing, fast results and high volume throughput. During the early phase of a pandemic, when the death curve is climbing, rapid results and scaling of volume must be the two priorities. The aim of testing during this phase is to prevent overshoot. In order to achieve this, infectious contacts must be diagnosed and isolated. Having timely results is critical for that to be effective. It is also important that the volume of tests processed is sufficient to enable all those in contact with an infectious case to be tested. Therefore the quality of the testing is compromised in order to ensure fast high volume testing.

## 7.6. Pandemic in early phase: Which is the best test to use for a new virus

7.6.1. There are now many superior tests available to diagnose COVID. However, at the outset of the pandemic, a new test needed to be developed quickly and scaled up to provide adequate numbers of tests. RT-PCR (quantitative polymerase chain reaction) testing was the right choice of test for this role. It is easily adapted to new viruses and can be quickly scaled up in already existing genetic laboratories.

7.6.2. RT-PCR testing is a way of identifying parts of the genetic sequence. It is designed for DNA so when testing for SARS-CoV-2 (the virus that causes COVID), the genetic material must first be converted into DNA. Several parts of the genetic sequence are searched for using the test and, if adequate sequence is present that appears to be from SARS-CoV-2, then the test is called positive.

7.6.3. The primary problem with PCR testing during the climb of the death curve, is that it is not as sensitive as we would like. Swabbing of the nasopharynx does not always result in there being sufficient viral material on the swab to make a diagnosis. It is generally

thought that 20% of real cases will be missed on one PCR test, although it has been estimated to be as high as 30%.[41]

7.6.4. However, it was the most sensitive test available at the time, so it was the right choice at the beginning of the pandemic.

7.6.5. In order to mitigate against this risk every choice made about how testing should be carried out has been made to maximize the sensitivity of the test – to try and diagnose any possible case. This inevitably maximizes the chance of a false positive result.

## 7.7. Pandemic After peak Deaths: Aim of testing

7.7.1. When peak deaths is reached, a change in test is required to prevent a false positive problem. If testing is switched to a specific test, then cases will be missed and this is difficult to justify. However, the testing strategy can become more specific by focusing not on an individual, but on outbreaks. A failure to change testing strategy will result in problematic false positive results ultimately leading to a false positive pseudo-epidemic (see section 8).

7.7.2. It is essential that only definite outbreaks are diagnosed. To achieve this, specific testing must be used that minimizes the risk of a false positive test result. Once a definite outbreak has been diagnosed, then testing of individuals within that outbreak should be carried out with more sensitive testing to ensure that all possible individuals are diagnosed.

## 7.8. Pandemic After peak Deaths: Choice of laboratory strategy

7.8.1. It is imperative that testing quality is prioritized after peak deaths have been reached in order to prevent a problem with false positive results. That requires compromising on either volume or speed or results. Volume can safely be compromised in several ways:

7.8.2. no testing of asymptomatic people unless identified as contacts;

7.8.3. only testing those cases in a potential outbreak that reach strict symptomatic eligibility criteria;

7.8.4. using rapid antigen testing as a gateway to PCR testing (only retesting those that are positive).

7.8.5. A failure to make this change and to continue with high volume testing has resulted and continues to result in a false positive problem with PCR testing.

## 8. How testing can go wrong creating false positive pseudo-epidemics

It is our professional opinion that Canada, including Quebec and Ontario, is in a false positive pseudo-epidemic. The cases and death statistics have been inflated by false positive test results, creating the illusion of an epidemic. Being in a false positive pseudo-epidemic does not mean there is zero COVID, indeed, levels of real COVID would be expected to rise in the winter, as they do for all endemic respiratory viruses. However, the false positive problem will cause inflated case and death numbers well in excess of the underlying true cases and deaths.

### 8.1. What is a false positive pseudo-epidemic?

8.1.1. A pseudo-epidemic can be created from false positive test results. This can and has happened with any type of testing, but RT-PCR testing has a particular propensity to create a pseudo-epidemic because of the degree of faith that doctors have about its ability to correctly diagnose.

8.1.2. However, the hypothetical argument that RT-PCR testing should not be able to produce a high false positive rate does not detract from real world cases where this has happened. When it has happened, no-one has been able to fully explain why it did happen. Given that RT-PCR induced false positive pseudo-epidemics have been well recorded, the evidence that they can happen exists. The fact that the popular narrative on how RT-PCR testing works cannot explain these events does not prevent them happening again. In fact, they are more likely to happen again because this lack of understanding perpetuates the myth of how RT-PCR cannot fail.[42] [43]

8.2. **Examples of false positive pseudo-epidemics**

8.2.1. RT-PCR testing for the bacteria Bordetella Pertussis resulted in a false positive pseudo-epidemic in 2006 in a hospital in Dartmouth,[44] New Hampshire. A doctor was suspicious that his colleague had caught whooping cough so they set up a PCR test for the causative bacteria (*Bordetella Pertussis*) in their laboratory. After the PCR test was positive, they started testing all symptomatic staff and patients in the hospital. This resulted in 15% of the tests coming back positive and, as more people were tested, the increasing number of 'cases' per day took on the appearance of epidemic spread. One of the doctors insisted that further testing was carried out on those that were positive and attempts were made to grow the bacteria in culture in the laboratory. However, not one of the samples was confirmed with this more refined testing method. Consequently, 100% of the positives were false positive RT-PCR test results. In retrospect, they concluded that the cause of the symptoms was the common cold. They speculated about the cause of the false positive PCR results but the underlying cause was never fully proved or understood.

8.2.2. In 2015 a false positive pseudo-epidemic was described in Colorado[45]. In this example there was a genuine outbreak with a first wave, and then a second wave followed due to false positive test results. Of note, the total positive rate during the real epidemic was 6% but this rose to 34% during the false positive pseudo-epidemic. Only by cross checking with antibody testing and bacterial culture did they prove that the PCR testing was producing false positive results. Investigation in this case found significant sources of cross contamination[45]:

> *"B pertussis DNA was widely detected on surfaces in Clinic A (11/18, 61% of sites swabbed) and its satellite clinic, A1 (3/9, 33% of sites swabbed), compared with fewer areas at Clinic B (2/20, 10% of sites swabbed). Large amounts of DNA (Ct value 33.2) were found on nurses' laptops in Clinic A and to a lesser degree (Ct value range 35.7–41.0) on vaccine refrigerator surfaces and examination room provider areas (worktops, sink areas, glove containers, biohazard bin, stool), patient areas (couch, toys, chairs), and doorknobs, with higher densities in an examination room without a sink. At the smaller satellite, Clinic A1, DNA was detected at the nurses' station, vaccine refrigerator, and doorknobs (Ct values 39.6–39.9)."*

A sample of 39 of the cases from the second wave were investigated more thoroughly with either antibody testing, bacterial culture or PCR testing at the CDC laboratories. Not

one of these cases were confirmed on further investigation, but 17 tested positive for other respiratory pathogens. The failure to confirm the diagnosis in any of these cases means that the second wave of this pseudo-epidemic also had a PCR false positive rate of 100%.

8.2.3. Pandemic swine flu (H1N1 influenza) had a second wave that was a false positive pseudo-epidemic in the USA. In 2009 there was a genuine epidemic of swine flu. The epidemic peaked in the winter months, with the swine flu (H1N1 strain) becoming the predominant flu strain for that winter (2009/2010). However, after the total number of flu cases had fallen to summer lows and the percentage of diagnosed cases attributed to H1N1 had fallen to 20%, a false positive problem began. The percentage of flu diagnoses attributed to H1N1 rose and kept rising, reaching 63% of flu cases in August 2010. Antigen tests, which had been shown to be excellent tests, started to be discredited in the medical literature as failing to detect all the cases. In fact, the antigen testing was accurate, but the PCR testing was overcalling. The PCR pseudo-epidemic only ended because PCR testing was stopped[46] with the WHO declaring the pandemic over on 10th August 2010.[47] At the time, 63% of global flu samples were testing PCR positive for H1N1 (figure 8).

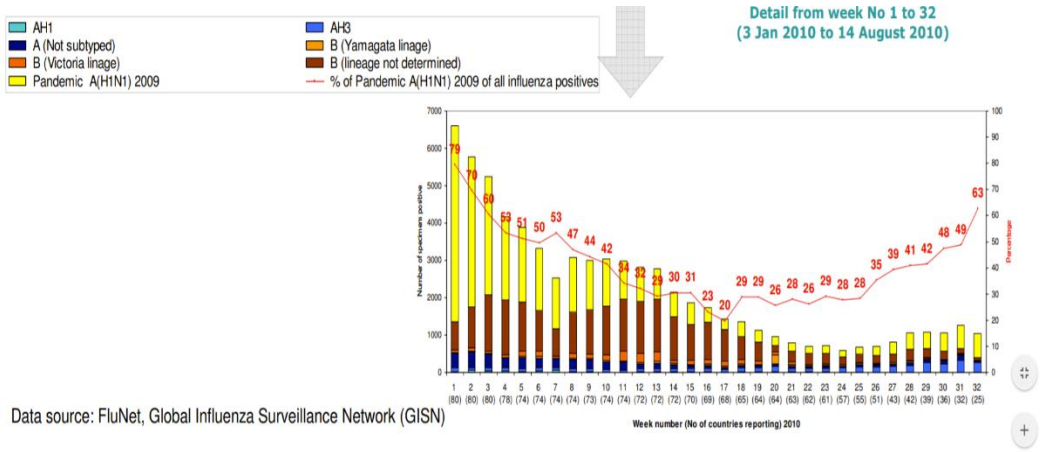



**Figure 8: The total number of flu samples over time globally in 2010 and the percentage of flu samples testing positive for H1N1 swine flu.**[48]

8.2.4. German virologist Christian Drosten, who is the primary expert advising the German government, exposed the problem of over testing; using PCR which can overcall positives and having a bad case definition when he was interviewed during the MERS epidemic. He makes the point that PCR testing can identify virus in the air that we breathe. Someone breathing out infected air could, in theory, transmit disease. However, this is not how carriers of disease are defined. A carrier of a disease would continue to be infectious over

time. We agree with comments which apply not just to MERS but any novel virus (translated from German).:[49]

*"What are the regional focuses of the disease?*

*Apart from the statement that the Arabian Peninsula seems to be very badly affected, little can be said so far. That is why there is so much research going on. The cases in Europe and the USA can all be traced back to infections in the Arab region. However, one must also be very clear: This region and especially in Saudi Arabia are currently the most intensive tests.*

*Which is not a fault in itself, is it?*

*Oh well. The fact is that there has been a clear case definition so far, i.e. a strict scheme that stipulates which patient was reported as a MERS case. This included, for example, that the patient has pneumonia that affects both lungs. When a whole series of MERS cases suddenly appeared in Jeddah at the end of March this year, the doctors there decided to test all patients and the entire hospital staff for the pathogen. And to do this, they chose a highly sensitive method, the polymerase chain reaction (PCR).*

*Sounds modern and contemporary.*

*Yes, but the method is so sensitive that it can detect a single genetic molecule of this virus. If, for example, such a pathogen flits over the nasal mucous membrane of a nurse for a day without becoming ill or noticing anything, then it is suddenly a MERS case. Where previously terminally ill were reported, now suddenly mild cases and people who are actually very healthy are included in the reporting statistics. This could also explain the explosion in the number of cases in Saudi Arabia. In addition, the local media boiled the matter up incredibly high."*

## 8.3. Faith in PCR testing amongst the medical profession

8.3.1. Most medical practitioners have substantial faith in diagnostic testing and this is usually well founded. In specialties where testing is problematic, doctors are more familiar with potential shortcomings and will use a combination of the clinical picture, multiple tests and repeat testing to ensure they make sound decisions.

8.3.2. However, PCR testing is held in great esteem by medical professionals. It is a relatively complex test. When carried out perfectly, the false positive rate is low. A UK Government

review estimated the false positive rate of PCR testing in general to be between 0.8% and 4.0% of tests carried out, which we agree is a fair estimate for PCR testing generally:[50]

> *"An attempt has been made to estimate the likely false-positive rate of national COVID-19 testing programmes by examining data from published external quality assessments (EQAs) for RT-PCR assays for other RNA viruses carried out between 2004-2019 [7]. Results of 43 EQAs were examined, giving a median false positive rate of 2.3% (interquartile range 0.8-4.0%)."* [50]

8.3.3. Consequently, medical practitioners trust PCR test results absolutely, often discounting false positive results as a possibility. The knowledge that it is a complex test is used as evidence that it cannot go wrong. Evidence that it can go dramatically wrong is often not known about or discounted because it does not fit in with their understanding of how the testing works.

8.4. **Inability to explain how false positive pseudo epidemics have occurred previously**

8.4.1. Because a clear consensus explanation of why false positives results occur is not always forthcoming, the fact they can and do occur is easily forgotten.

8.4.2. The fact that quality PCR testing usually results in a low false positive rate does not mean that all PCR testing will result in a low false positive rate.

8.4.3. The accepted dogma that PCR testing will always have a low false positive rate, while true much of the time, does not leave room to explain the false positive rate of 100% in the examples of the pseudo-epidemics given above. Both of these examples were from well resourced laboratories with skilled staff who were not working under undue pressure.[45,44]

**9. What is PCR?**

9.1. PCR is a biological technique used to amplify DNA.

9.2. It was not invented to be used as a diagnostic test. However, it has been adapted as a useful tool in confirmatory diagnosis when there is a high suspicion of disease.

9.3. Kary Mullis won a Nobel prize in 1993 for inventing the technique. He said he invented it for laboratory research, but that it was never intended to diagnose disease. That is because, while it can identify viral material, it cannot distinguish this from viral particles capable of infection. We agree with his summary when he said:[51]

> *"With PCR, if you do it well, you can find almost anything in anybody…. It tells you something about what's there. It allows you to take a very miniscule amount of anything and make it measurable...that's not a misuse. It's a misinterpretation... It doesn't tell you that you're sick and it doesn't tell you that the thing you've ended up with was going to hurt you or anything like that."*

9.4. PCR tests, even if performed correctly, cannot provide information on whether or not a person is infected with an active, viable, pathogen, capable of infecting others. We concur with the Swedish Public Health Body's summary:[52]

> *"The PCR technology used in tests to detect viruses cannot distinguish between viruses capable of infecting cells and viruses that have been neutralized by the immune system and therefore these tests cannot be used to determine whether someone is contagious or not. RNA from viruses can often be detected for weeks (sometimes months) after the illness but does not mean that you are still contagious. There are also several scientific studies that suggest that the contagion of covid-19 is greatest at the beginning of the disease period."*

To illustrate, PCR is used in forensic science to amplify residual DNA from, say hair remains, or other trace materials such that the genetic details of a perpetrator can be identified long after they have left the scene.

9.5. Even when carried out optimally, a positive PCR test does not mean that the person tested must be infected with a replicating virus and therefore capable of infecting others.

## 10. How PCR testing is carried out

10.1. COVID RT-PCR testing has six steps. Steps 2-4 are carried out simultaneously but it is easier to consider them in order:

1. **Reverse Transcription:** Any viral RNA present is **converted to DNA**, meaning that the sample then contains both the DNA created from this conversion, mixed up with all the other DNA in the sample, including that from the patient's

own cells, bacteria from the nose and mouth, other viruses and even potentially from fragments of food.

2. **First Match and Doubling:** The DNA of interest is replicated (or amplified) in a series of repeated periods of temperature alteration called cycles, where each cycle doubles the DNA from the last cycle. To ensure only the DNA we are interested in is doubled, 'primers' that match the part of the SARS-CoV-2 virus sequence being targeted are used to identify the strands to be replicated (figure 9). The primers for the target sequence are roughly 20 letters out of the total ~30,000 letters that make up the whole SARS-CoV-2 genome. The genetic strands that match these primers and the part of the sequence between the two primers will be replicated. This is usually 100 bases long.

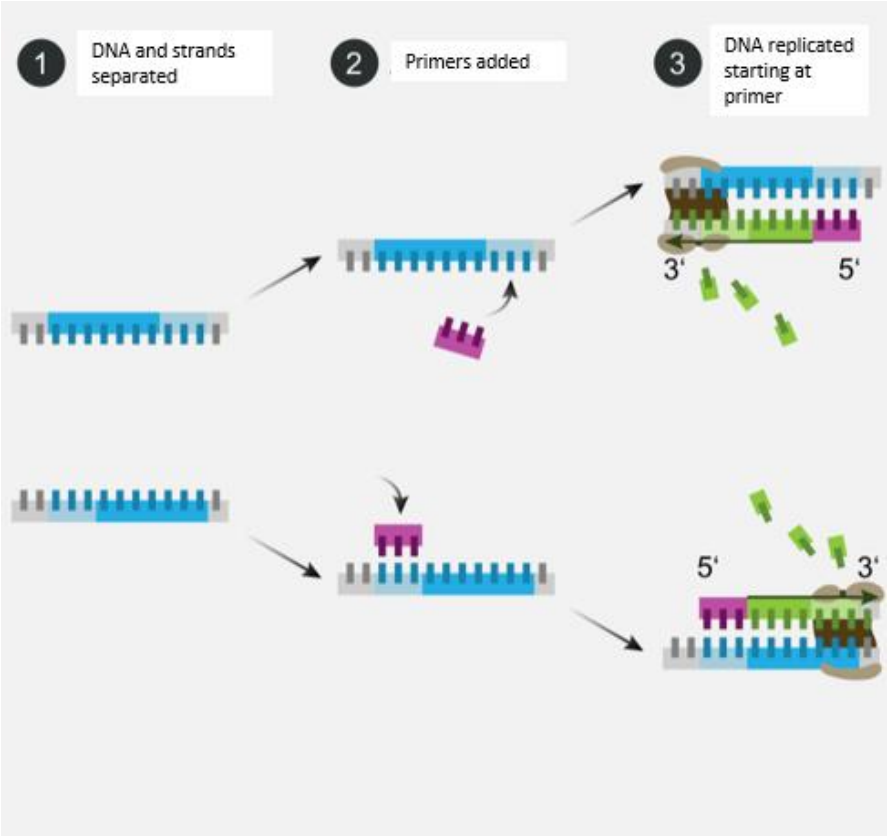



**Figure 9: The first part of the RT-PCR process selectively replicates the DNA present.**

3. **Amplification:** Doubling is then repeated many times to make billions to trillions of copies of these specific strands of DNA. The first cycle doubles the DNA, the second doubles it again. By the time there have been 25 cycles there will be 17

million copies of what was there at the beginning. By 30 cycles that will be 535 million and by 40 cycles it will be 550 billion copies. This amplification process is therefore exponential. (See figure 10)

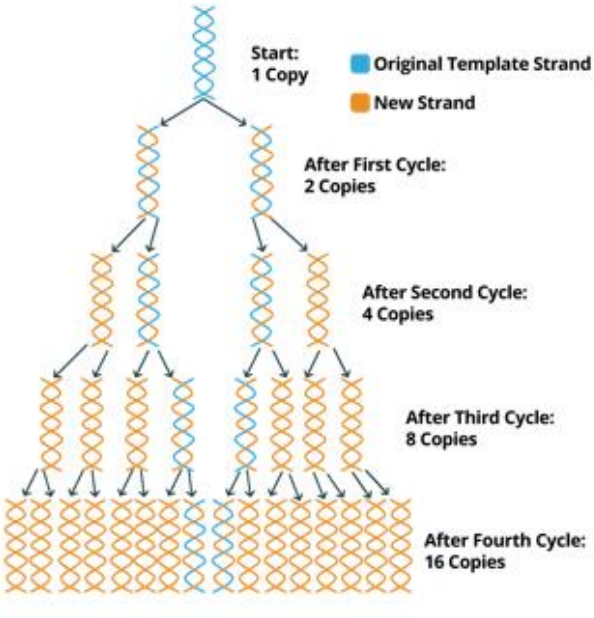



**Figure 10: showing exponential growth from doubling the DNA present.**

4. **Second Match:** The third part of determining if SARS-CoV-2 virus is present requires a detection event that is facilitated by a third fluorescently labeled piece of synthetic DNA known as a "probe". This probe must match a DNA sequence between the two primers, and as amplification occurs, the fluorescent probe is turned on in a process known as probe hydrolysis. This probe hydrolysis is catalyzed by the DNA copying enzyme known as a polymerase, and it only occurs if both primers and probe match the target sequence. Since the probe, about 25 letters long, is such a small portion of the whole SARS-CoV-2 genetic sequence (~30,000 letters), a good test requires two or three probes to detect separate genes situated in different parts of the SARS-CoV-2 genetic sequence (figure 11). Each of these probes require their own pair of primers. All these components of a reaction need to be unique to the genetic material of the virus and probing multiple locations in the viral genome is critical. This would minimize the risk of mistaking other DNA present in the sample (eg from other viruses) for SARS-CoV-2. However, in many cases, it is not possible to design an assay that would not contain elements with similarity

to genetic material of different organisms. This is because the probe and primers set has to satisfy a number of additional criteria. For example, to avoid nonspecific binding, both primers have to contain an optimal percentage of GC content relative to the total sequence. This constraint can lead to a design where cross-reactivity (binding to the wrong sequence) is possible. This is a well recognised parameter that needs to be reported.[53] Some SARS-CoV-2 assays are reported to have a potential for cross-reactivity (see section 14.39).

5. **Checks against controls:** Each test should be run including samples that we know should test either negative or positive to ensure that the test has worked.

6. **Interpretation of results:** RT-PCR requires interpretation of a signal for each target sequence (gene). A judgement must be given as to whether or not exponential replication was seen, and whether sufficient signal was present to call the result positive.

10.2. SARS-CoV-2 contains at least 20 genes. Depending on the protocol between one and three genes are tested for in the PCR test (see section 14.5). The more genes tested for, the more likely a positive result will be a true positive.

10.3. As of 4/09/2020 more than 20 different tests are on the *WHO Emergency Use Listing for In Vitro Diagnostics (IVDs)* detecting SARS-CoV-2 Nucleic Acid, most of which rely on RT-PCR detection of SARS-CoV-2. These tests target different regions of the virus. For example, TaqPath COVID-19 CE-IVD RT-PCR Kit, used in the UK Lighthouse labs, targets the ORF1a, Spike and Nucleocapsid genes of the virus (Figure 11).

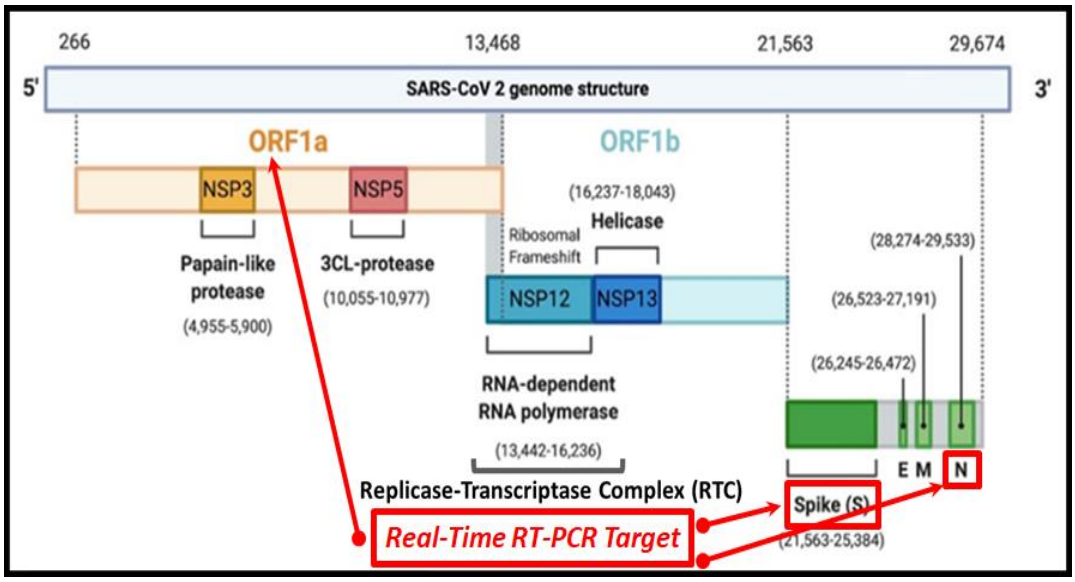



**Figure 11: Example of regions of the virus targeted by TaqPath COVID-19 CE-IVD RT-PCR Kit.**

10.4. The CDC diagnostic panel has two viral targets, both in N-gene,[54] plus a third component of the assay that targets human RNase P gene for detection of human nucleic acids. This additional control enables comparison between the amount of viral RNA present and the amount of human DNA sampled. These controls enable an understanding of the significance of the Ct value. If numerous cycles are required to detect viral RNA, and there is minimal human material in the sample, then the sample should be interpreted as negative. However, in the presence of plentiful human material, a good sample must have been taken and a small amount of viral RNA would have more significance.

10.5. Short DNA sequences called forward or reverse primers are synthesized that specifically bind to either end of the target sequence. A Taqman probe is synthesized that specifically binds to the middle of the target sequence. This probe has a fluorophore attached at one end and a quencher, which suppresses fluorescence, attached at the other end. As the polymerization reaction moves along the target sequence and meets the Taqman probe, the fluorophore is cleaved off, resulting in the emission of a pulse of light as it is no longer in the vicinity of the quencher. By using different fluorophores that emit different colours, more than one target sequence can be distinguished in a single RT-PCR reaction.

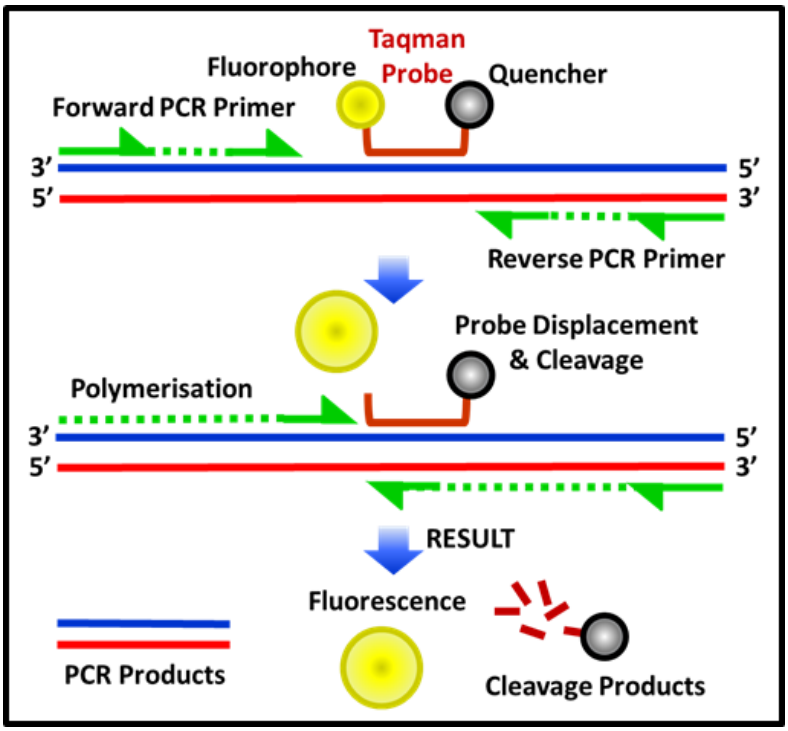



**Figure 12: Mechanism of the Real-Time Polymerase Chain Reaction.**

## 11. Manufacturer's responsibilities

11.1. Over a hundred PCR test kits exist for detecting viral RNA from SARS-CoV-2 and these tests have not passed through the usual approval processes:[55]

> "*To remove impediments for manufacturers in this time of public health need, Health Canada does not require manufacturers to provide a MDSAP certificate with their application for a COVID-19 medical device subject to the Interim Order Respecting the Importation and Sale of Medical Devices for Use in Relation to COVID-19. Manufacturers will be required to share information to demonstrate that their products are of consistent quality and effectiveness. This can be demonstrated by either providing a copy of the manufacturer's Quality Management System certificate to ISO 13485:2016, or by submitting evidence of Good Manufacturing Practices.*"

11.2. The Canadian regulatory process for new tests was called into question with doubts about test validity, safety and efficacy in September 2019.[56]

11.3. Manufacturer's sales will continue as long as the 'crisis' continues. They are therefore incentivized to find 'cases'.

11.4. No standards have been produced by public health bodies or government to determine the criteria for a manufacturer to be able to call a positive result.

11.5. 60 million tests have been distributed by TIB MolBiol in 12 months.[57] The package inserts state at the top:[58]

*"Instructions for life science research use only. Not tested for use in diagnostic procedures."*

11.6. A PCR test kit instruction manual states:[59]

*"Kits and reagents are sold for research use only. Not for use in diagnostic procedures."*

11.7. A further test kit manual states:[60]

*"This product is for research use only and is not intended for diagnostic use.*
*This product is intended for the detection of 2019-Novel Coronavirus (2019-nCoV). The detection result of this product is only for clinical reference, and it should not be used as the only evidence for clinical diagnosis and treatment."*

## 12. Interpretation of PCR test results

12.1. It is critical to make a distinction between 'colonization' of the throat with a few viruses that do not cause infection (as described by Drosten in section 8.2.4) and a genuine infection. The latter results from exponential growth of virus which leads to symptoms and the ability to infect others.

12.2. In the past viral culture was considered the gold standard test for all viral infections. It remains so for some viral[61] infections. Viral culture tests for virus that is able to enter cells and replicate before either bursting them open or changing the cell appearance in a measurable way.

12.3. Viral culture remains[35] an essential tool to calibrate PCR and other testing. The WHO have emphasized the importance of viral culture:

*"The requirement for suitably equipped NICs* [National Influenza Centres] *to conduct virus isolation must continue to be emphasized. Although RT-PCR (both real-time and conventional) is increasingly the method of choice for influenza virological surveillance, this should not distract from the crucial role of virus isolation."*

12.4. To ensure a test is measuring what you intend it to measure, calibration work must be undertaken. This can be carried out either against a better "gold standard" test or against clinical findings. The "gold standard" test for any virus test is viral culture.

12.5. Each laboratory must calibrate their own testing and if there is a change in any component of testing from chemicals, enzymes, protocols or machines, then recalibration should be carried out. Results of calibration in one laboratory cannot be used as evidence for the accuracy of testing in another laboratory.

12.6. Ct values of amplified target sequences (Figure 13). The Ct is the cycle where the fluorescence generated by the amplification of the target sequence crosses the designated fluorescence threshold (set at 5). Different doses of a virus were intravenously administered into mice. The results show that the different Ct values of the target sequence detected in the DNA isolated from the livers of treated animals, reflect the different doses administered to the mice. When there is plenty of virus present, fewer doublings are needed to reach sufficient positivity to cross the threshold and the Ct value is lowest. **The smaller the Ct value of a sample, the higher the initial amount of DNA/RNA in the test sample.** In the case of a viral test, this correlates with the amount of virus present in the sample, referred to as the 'viral load'.

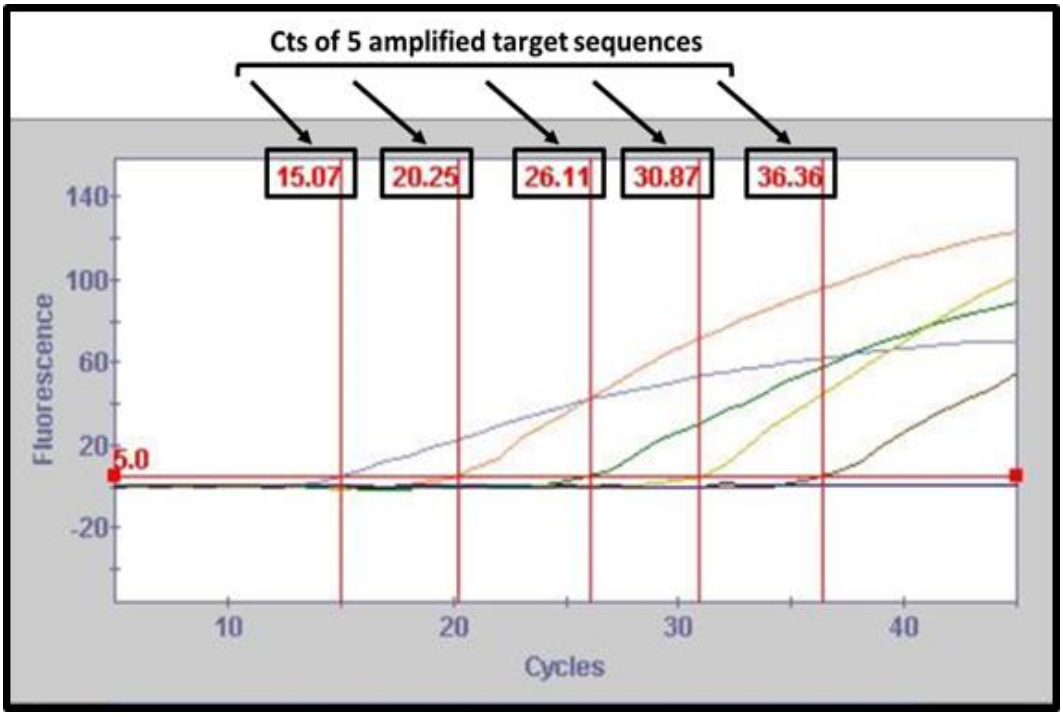



**Figure 13: Determining Ct values of amplified target sequences.**

12.7. The endpoint of the PCR test is arbitrarily set by the test kit manufacturer, using a Ct number to divide cases into "positive" or "negative." All tests, of any sort, ultimately need to set a line to determine what will be called positive. However, the evidence used by the manufacturers to determine this value, for SARS-CoV-2 testing, was minimal and the decision has not been revisited based on subsequently available evidence.[62]

12.8. Having designed a test based on hypothetical sequences, it is critical that checks are done to see how it performs in the real world against samples that should test positive.[63] Any new test must be validated against the best test available which, in this case, is viral culture. These calibration experiments measured the number of cycles required to reach the threshold (Ct value) for a positive and compared these results with viral culture. It is not good practice to assume a Ct value from other RT-PCR tests will have meaning for a new test. Therefore, calibration work, alongside gold standard viral culture testing, or confirmatory antibody testing, are the only way to interpret the Ct values in a meaningful way.[64] Without information about the correlation with viral culture for that laboratory, a Ct value is worthless as an evaluation of positivity.

12.9. A study of patients in January 2020, published by a group including Christian Drosten, demonstrated no viral culture when there were fewer than 1,000,000 copies of the virus

(viral load <$10^6$ per ml).[65] However, the tests are designed to detect approximately 1,000 copies per ml.[66] This would mean only 4 copies in a sample of 5µl. For example, this Roche test claims to be able to detect fewer than 4 copies per sample.[58] The PCR test is therefore declaring as a positive a sample with one thousandth of the concentration required to contain viable virus and be an infectious patient.

12.10. External quality control assessment has been carried out, using dilute samples, to make sure the laboratories call a positive in the presence of single digit numbers of copies of the virus in the sample.[67] Emphasizing the minimizing of false negative results will lead to consequent high false positive results. A summary of international external quality controls demonstrated this emphasis when they concluded:

> *"Laboratories that were unable to detect low-concentration samples, or whose methods showed Cq values greatly different from the provided medians, should strive to improve the sensitivity of their molecular assays to prevent false-negative results in respiratory samples with low viral concentrations from SARS-CoV-2-infected patients, e.g. during the early phase of infection."*

12.11. False positive results can look like true positive results and there will be false positive results with a low Ct value, otherwise there would be no problem identifying them all as false positives.

12.12. Figure 14 from a paper[12] comparing PCR positive results with viral culture shows that only 9% of the PCR positive samples (all dots) were positive on viral culture (black dots). That is to say that 91% of the PCR results were false positive results in that no viable virus was present. There were 129 patients tested and only 17.8% of the patients had a sample which was viral culture positive at any point. That is 82% of patients that tested positive on PCR never had successful confirmatory testing. This was carried out in Spring 2020 and many of the patients would have been in the later stages of infection. However, the relationship between viral load and infectivity is clear.

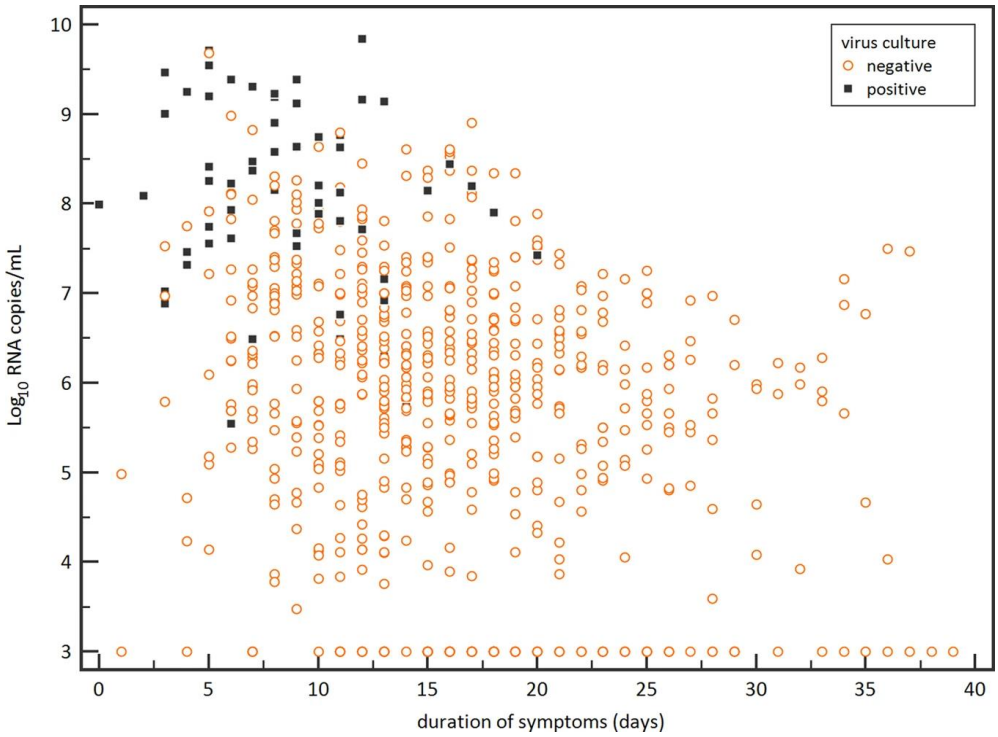



**Figure 14: Comparing PCR positive results with viral culture.**[12]

12.13. Such calibration work was described by Scola[68] et al in April 2020 and showed no viral culture above a Ct value of 34. This study, showing no viable virus above a Ct value of 34 indicates that results above this level will be false positive results and people with these results will not be capable of infecting others.

12.14. The same team published a follow up paper in September 2020.[69] The authors performed 250,566 COVID PCR tests on 179,151 patients and found 13,161 positives. Of these, 3,790 were selected for viral culture testing. Virus was only successfully cultured in 51% of the cases. The likelihood of successful culture fell with increasing Ct values. At a Ct value of 25, there was a 70% chance of there being viable, culturable virus. Above this level, the chances fell. At a Ct of 35, fewer than 3% of cultures were positive such that test results at these values would have a 97% chance of being false positives, in that they would not contain infectious virus.

12.15. The exact Ct cut off to use to ensure a meaningful result will vary depending on the laboratory carrying out the work and the kit they use.

12.16. A retrospective study repeated this work in Manitoba.[13] The study was carried out using samples collected at a time when there was not mass testing, and the overall positivity rate was high because the people being tested were very likely to have the disease. They commented

> *"the testing criteria in Manitoba had sufficient pretest probability to make the likelihood of a false-positive remote."*

However, of the 90 samples they tested, viral culture only confirmed infection in 29%. That is 71% of the samples were false positive results, even when the positivity rate per test done was high.[13] Bullard et al also noted for every 1-unit increase in Ct value, the odds of a positive culture decreased by 32%.

12.17. Bullard et al, as above in Manitoba, demonstrated that a Ct value of 24 or less was indicative of a sample containing viable virus.[13]

12.18. A South Korean study found no viable virus where the Ct value was above 28.4.[70]

12.19. National Centre for Infectious Disease Singapore stated in May 2020:[71]

> "*it is important to note that viral RNA detection by PCR does not equate to infectiousness or viable virus. A surrogate marker of 'viral load' with PCR is the cycle threshold value (Ct). A low Ct value indicates a high viral RNA amount, and vice versa. As noted above, detection of viral RNA does not necessarily mean the presence of infectious or viable virus. In a local study from a multicenter cohort of 73 COVID-19 patients, when the Ct value was 30 or higher (i.e. when viral load is low), no viable virus (based on being able to culture the virus) has been found. In addition, virus could not be isolated or cultured after day 11 of illness. These data corroborate the epidemiologic data and indicate that while viral RNA detection may persist in some patients, such persistent RNA detection represent non-viable virus and such patients are non-infectious."*

12.20. The Office of National Statistics in the UK has published evidence that people with a Ct threshold above 25 could not transmit virus within their household, whereas those with a Ct value below 25 did.[72]

12.21. The UK Scientific Advisory Group for Emergencies confirmed this conclusion that household transmission did not occur at a Ct Value above 25.[73]

12.22. In order to demonstrate vaccine effectiveness, success was defined by using a Ct value of 25 to represent real infection. Ct values of 27 in the vaccinated group were considered to be evidence that vaccine had worked.[74]

12.23. Results with Ct values above 25 should not be reported as diagnostic. Positive results above this level should be reported as equivocal positive results, pending confirmatory diagnosis by antibody testing or viral culture.

12.24. It is our professional opinion that a Ct value of 25 or less would be a pragmatic cut off to use for testing and containment of spread, having passed peak deaths, as it would reduce the false positive problem, while still enabling diagnosis of the vast majority of cases. If a case were to be missed on such testing, clinical judgement of the treating physician could be used to decide the best course of action and alternative testing, including antibody testing, could be carried out where there was continued concern.

12.25. The UK Office of National Statistics published on the Ct Values for testing of a random sample of the UK population. This showed that in May and June, between 25% and 50% of results had a Ct below 25; in July, no results were below 25, and in Autumn 2020, the figures returned to 25% to 50% of the tests done. All the tests were reported as true positives.[75]

12.26. Figure 15 shows the Ct value; number of genes that were positive and whether or not the person had symptoms in the top graph (A) and the percentage of positive tests at each Ct Value in (B).[75]

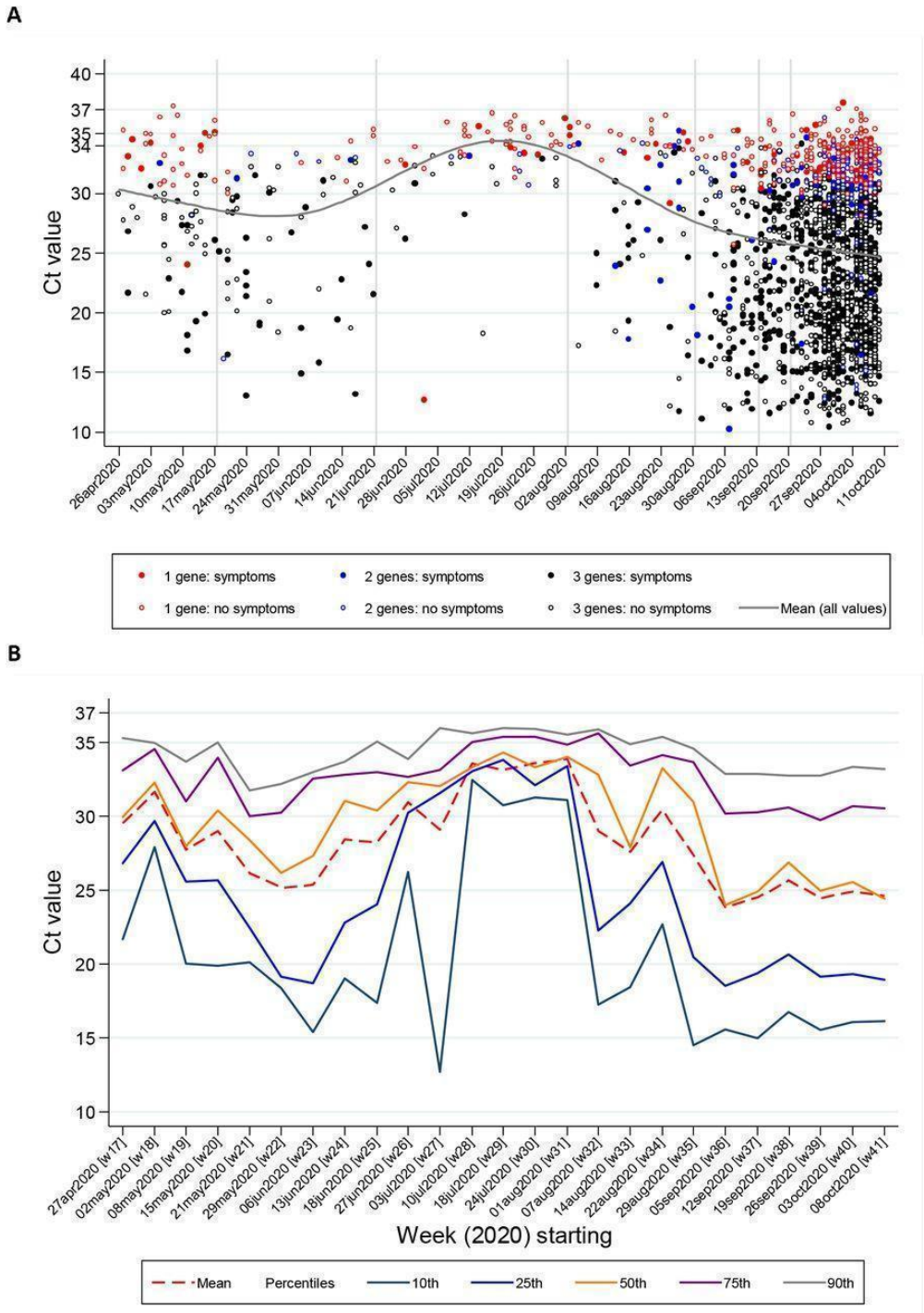



**Figure 15: Variation over calendar time in Ct values (raw values (A) and distribution (B)).**[75]

12.27. Using the testing strategy above, to detect only definite outbreaks, PCR positive results with a cycle threshold below 25 would be a reasonable cut off to use. Contacts within a confirmed outbreak could be tested with a higher threshold, say 30, as a screening test to be followed by confirmatory testing.. The exact figure would depend on the laboratory

doing the testing and calibration of their Ct values against a gold standard test, e.g. vial culture or confirmatory antibody testing, would enable a meaningful value to be selected.

12.28. The Quebec Public Health Authorities have chosen a Ct value cut off of equal to or below 37.[76] All positives below that level will be reported as real positives. However, the Ct value is set too high, which means that it brings or even guarantees positive results in situations where no viable virus could be found. This will invariably result in false positive results causing inflated case numbers leading to policy decisions based on misleading data of the extent of disease. On an individual level, people will have been and are being quarantined on the basis of false positive results. The proportion of results, which were reported at high Ct values, will have depended on how many true positives there were around at the time. Only disclosure of the Ct Values of the positive results will reveal the extent of the problem.

12.29. Public Health Ontario have stated that the cycle threshold has been set, determined not by calibrating against true positives, but rather to ensure that even a minimal, diluted, quantity of virus would be called positive. Figure 16 shows that even Ct values of up to 38 are called positive in Canada, with values of 38.1-39.9 reported as indeterminate. They suggest that patients with such results should have genetic sequencing or a repeat test with a PCR test which is even more sensitive, that is it will be able to detect even lower levels of virus.[77]

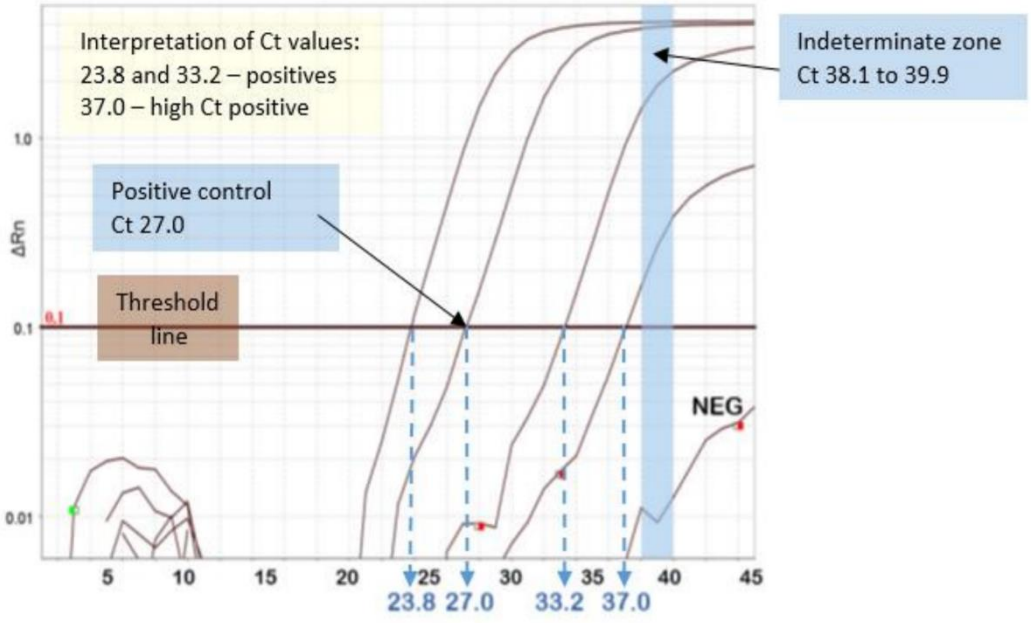



**Figure 16: Interpretation of Ct values guidance, Public health Ontario.**[77]

12.30. The PCR machines are set to run a certain number of cycles e.g. up to 45. This is a different number to the Ct value. To determine a positive result, a threshold is decided. The output from each sample is plotted as the degree of positivity over time. The threshold is drawn as a horizontal line on this graph. To read a result, the output is examined and if it is not exponential, it is disregarded. For outputs that have an exponential increase in positivity, they are compared to the threshold. If they cross the threshold, then a line is drawn from the crossing point to the x-axis to reveal the number of cycles that the sample had passed through at that point. This is the Ct value. The cycle level of the machine must not be confused with the Ct value of an individual result. It does not matter if the machines run at 45 cycles, as long as the results that have high Ct values are ignored.

12.31. The decision about what Ct value is meaningful will depend on the kit and equipment in use. It is therefore imperative that every laboratory carry out calibration work such that they know the Ct value beyond which a positive is no longer meaningful in terms of identifying infectious disease. This work was not done.

12.32. Results of a German External Quality Assessment of the laboratories, in April 2020, found, that for the same standardized sample (probe 340061) given to 463 laboratories returned results with Ct values between 15-40 for the E gene; 20-40.7 for the N gene and 19.5-42.8 for the RdRp gene.[78] These ranges indicate that material that was detected in one laboratory was not detected in others until between 1 million and 33 million more copies were present. This represents an extreme lack of test standardization within the participating laboratories, indicative of a lack of calibration of testing. Results of a repeat assessment carried out in June/July 2020 have not been published.

12.33. Dr Anthony Fauci, Chief Medical Advisor in the USA, was aware that PCR is unreliable when the Ct value is above 35. In a podcast on July 16th 2020 called This week in Virology he said (4 mins in):[79]

> *"What is now evolving into a bit of a standard is that if you get a cycle threshold of 35 or more that the chances of it being replication competent are miniscule… We have patients, and it is very frustrating for the patients as well as for the physicians… somebody comes in and they repeat their PCR and it's like 37 cycle threshold… you can almost never culture virus from a 37 threshold cycle. So I think if somebody does come in with 37, 38, even 36, you gotta say, you know, it's just dead nucleotides, period."*

12.34. RT-PCR is a highly sensitive and specific test when carried out by those with the necessary qualifications, training and expertise, and when accompanied by appropriate controls and checks. Otherwise, because it involves amplifying the material present to more than a billion copies, it is a test that is vulnerable to significant error and, therefore, the reliability of data generated can be put into doubt.

12.35. To summarise, any test needs to be calibrated to ensure that what is called positive or negative is meaningful. Each laboratory should calibrate their results against viral culture to understand which results indicate a sample from an infectious patient.

PCR testing as currently carried out is not suitable for determining infectivity.

Attempts to ensure every possible case was diagnosed at the outset of the pandemic led to protocols which were biased towards producing false positive results. It is possible to define a Ct threshold above which a positive signal no longer correlates with viable virus capable of infection. Given all the evidence published so far it is possible to create a three tiered system for interpreting test results. The cut offs would be laboratory dependent. The cut off of 35 is chosen as an absolute maximum, applicable to all laboratories, above which no cultured virus has been found.

Ct < 25: positive (viable virus present with risk of transmission)
Ct 26-35: suspicious (confirmatory testing with viral culture should be carried out)
Ct>35: negative

However, Canada, including Quebec and Ontario, continues to report positives with a Ct value up to 37, and these results are used as definitive evidence of COVID, with legal consequences for quarantining. The number of cases, many of which are most probably, if not certainly, false positives results, were consequently inflated. Policy making, on the basis of these case numbers, led to the imposition of drastic measures, such as lockdown, business closures and curfew (in Quebec).

As well as using too high a Ct value, too few genes are being tested to ensure meaningful results. Even the sequences being used for the genes being tested are questionable, given that they were created based on hypothetical sequences. In Spring 2020, inadequate

testing calibration was justified given the urgency with which testing was set up. However, despite good evidence that calibration of testing in Canada and elsewhere is severely flawed, no attempts have been made to rectify this.

## 13. What causes false positive test results? - The broad picture.

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

13.2. 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.

### Profiling Errors

13.3. Who is being tested has a significant bearing on the false positive rate. For example, any positive pregnancy test from testing children in a reception class at primary school must be a false positive. Likewise, testing asymptomatic people for COVID will result in a higher proportion of positives being 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 programs do not screen young women. For COVID, a similar unexpected level of false positives was seen in the summer 2020 in Europe with people in their 20s. The estimates from the Office of National Statistics were that there were 20,000 people aged 17-34 with COVID on 20th August 2020, rising to 73,000 by 10th September. 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 2020 across the world proves that genuine COVID outbreaks spread rapidly between age groups. This did not happen throughout August 2020, which proves that the “outbreak” amongst young people was a pseudo-epidemic made up of false positives. Figure 17 shows the

increasing levels of COVID positivity in younger age groups throughout August which did not spread to other age groups.[80]

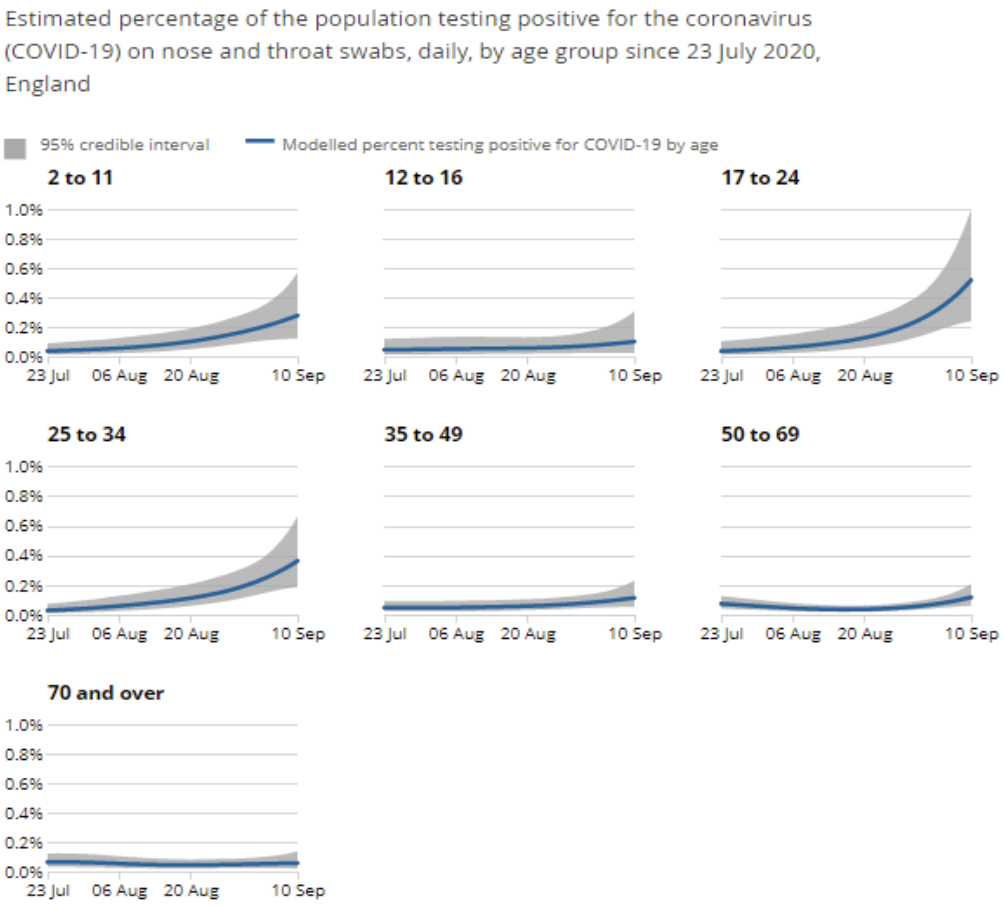



**Figure 17: Distribution of COVID positivity in late July - early September 2020, England.**[80]

It is important to target testing to people who have symptoms that provide a high clinical suspicion of the disease you are testing for. The 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.

13.4. Respiratory viruses can commonly be found at death even when they are not the cause of death. Testing of deceased over 65 year olds revealed that 7% had a coronavirus present at death and 47% had a respiratory virus of any type.[81] Only 7% had a diagnosis of a viral infection prior to death. Testing the dead or dying may therefore give a false impression of active infection and lead to misinterpretation of the cause of death.

**Mistaken Identity**

13.5. 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.

13.6. Human DNA has been mistaken for a different coronavirus when doing PCR testing.[82] 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.

13.7. A 2003 outbreak of SARS-1 in a care home in British Columbia turned out to be a common cold causing coronavirus.[83] 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.

**Contamination of the chain of evidence**

13.8. 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.

13.9. 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.

13.10. Contamination of swabs has been known to occur in factories. In Germany, a woman who worked in the swab factory and referred to as the "Phantom of Heilbronn", contaminated swabs with her DNA, and was thus linked forensically to 40 crimes, wasting 16,000 hours of police time.[84]

13.11. 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.

13.12. Prevention of cross contamination requires very competent staff, an environment designed to minimize cross-contamination and thorough use of testing of control samples.

**Equipment Errors**

13.13. 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.

**Burden of Proof**

13.14. As well as choosing a reasonable cycle threshold to reduce 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 more than one gene belonging to the SARS-CoV-2 virus. However, if positive is defined as the presence of only one gene, rather than more than one, then the false positive rate will be higher, as this is a lower bar.

13.15. 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. The five types of false positives will vary between

laboratories, so investigations as to the rate at one laboratory cannot 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. Changes in who is targeted, seasonal infections, and laboratory quality standards can lead to changes in the false positive rate over time.

## 14. What causes false positive results? - The details.

### Profiling errors

14.1. Testing in hospitals and care homes when there are symptomatic outbreaks of a COVID-like illness is good profiling, where false positive results would be a minor problem. Testing of children and university students is bad profiling, where false positive results are likely to be a major problem.

### Mistaken Identity

14.2. Similarities between the SARS-CoV-2 sequences being tested for and other viruses or even bacteria mean that, when mass testing, it is critically important to use more than one gene target.

14.3. Each gene that is tested, from the point of view of a false positive risk, can be considered to be a separate test. For example, if the three genes had false positive rates of 6%, 5% and 3% respectively, then testing 100,000 samples with a requirement that all three genes be positive would give 9 false positive results. However, if a positive in just the first gene was acceptable then there would be 6,000 false positive results.

14.4. On 13th January 2020, the WHO published guidance for PCR testing that required detection of three independent genes.[85] On 2nd March 2020, the WHO changed the requirement to only one:[86]

> "*In areas where COVID-19 virus is widely spread a simpler algorithm might be adopted in which for example screening by rRT-PCR of a single discriminatory target is considered sufficient.*"

Consequently testing for the E gene alone, including in Canada (see 14.5), has been used even at times of low prevalence.

14.5. Canadian protocols include a protocol where only a single gene is tested and two protocols with only two genes tested (figure 18).[87]

**Current Assays in Use at PHO Laboratory and Associated Gene Targets**

| Assay | Gene Targets |
|---|---|
| PHO Laboratory LDT | E gene* |
| Roche | Orf1a/b gene, E gene |
| Abbott | N gene, RdRp gene |

E – envelope; Orf1a/b – open reading frame 1a/b; RdRp – RNA dependent RNA polymerase; N – Nucleocapsid
*Specimens may also be tested using a laboratory developed RdRp gene target assay

**Figure 18: Table from Public Health Ontario testing guidelines.**[87]

14.6. While the exact sequence of molecular assays used in Canadian labs are not known, all four gene targets used have been reported in publications that characterized various problems and did not recommend it for diagnostic purposes. Jung et al reported[88]: "unexpected amplifications from NTC (non-target-control) samples were observed with the **RdRp**_SARSr (Charité) set". The NTC sample contains only water and should not produce any signal. Wernike et al also found unambiguous positive results from samples of pure water.[89] Konrad et al[90] found that: "the SARS-CoV **E gene** screening assay with the QuantiTect Virus +Rox Vial kit showed moderate to high amounts of nonspecific signals in late cycles in 61% (451/743) of the tested patient samples and also of negative extraction and NTCs(Table 1, Figure 2 of their paper), which complicated the evaluation of the RT-PCR result". Khan and Cheung[91] performed in silico analysis to test the accuracy of primer binding to SARS-CoV-2 samples which demonstrated that "the reverse primer of Charité-ORF1b shows a mismatch with all the viral sequences (a total of 17 002)." As described in section 14.39, **N-gene** assay can cause cross-reactivity with the common nasopharyngeal bacteria.

14.7. A Lancet article "Curbing false positives and pseudo-epidemics" also emphasized the importance of using multiple gene targets:[42]

> *"So-called "classical" PCR amplification, in which "positivity" is assessed based on the size of identified DNA fragments, gives "notoriously poor" results; spurious, hard-to-quantify fragments tend to cause "lots of false positives", Perlin said. By contrast, real-time PCR relies on secondary probes that are*

*sequence-specific, so the rate of false positives is considerably lower. "But the best way to reduce false positives for pathogens you're not sure about and that are difficult to grow, such as Bordetella pertussis, is to use multiple targets", Perlin emphasized. "You're not just amplifying a single fragment, but rather multiple targets to reduce the probability of error"."*

14.8. SARS-CoV-2 PCR test results are always reported as binary "positive" or "negative", a decision which is taken based on the Ct value. It is not unusual for RT-PCR testing to operate in this binary mode, if the test is utilizing a well defined volume of biological fluids, such as blood. However, the amount of RNA present in a sample sent for SARS-CoV-2 testing can vary considerably due to sampling error.[92] This is because these tests utilize nasopharyngeal swabs, and the volume of material collected is dependent on sampling technique. The amount of virus present will depend on how much material was sampled. By comparing how much virus there is per human cell, it is possible to understand how much virus is in the person, rather than just in the sample. The only way to overcome this limitation is by including an internal control. The internal control measures one of the human genes to give a baseline for how much material is present. Valid interpretation of the test result requires a knowledge of the Ct value in the context of the ratio of virus to human material. There are several well characterized regions in the human genome that can be used to measure this. One such target is a gene encoding human RNase P, recommended by the CDC and included in the SARS-CoV-2 diagnostic panel.[54]

14.9. However, there are numerous examples of countries that use a PCR assay for SARS-CoV-2 lacking such a control. Many European countries are using the Corman-Drosten panel[93] which lacks an internal control[94]. The same is true for the TaqPathCOVID-19_CE-IVD_RT-PCR Kit utilized for majority of the community testing in England[95] . Based on publicly available information we conclude that no human internal control is used in SARS-CoV-2 testing in Canada.

14.10. The WHO's assessment of PCR for Zika virus testing recommended two gene targets because of discrepant results between separate targets when tested individually.[96]

*"Various real-time and conventional RT–PCR assays specific for Zika virus have been described. Lanciotti at al described a combination of two real-time PCR assays and this*

*approach is the most commonly used for direct diagnosis of Zika virus. Two gene targets were described and equivocal positive results were mentioned that could be related to false positives; of 157 samples tested, 10 were positive for only one target while 17 were positive for both. It was not mentioned whether this was randomly observed with both assays. However, discrepant results were observed between the two targets in the French and Dutch reference laboratories as well (authors' own unpublished observations)."*

**Contamination errors**

14.11. In April 2020, test kits produced by the CDC were contaminated with SARS-CoV-2.[97] This resulted in a 33% error rate. The source of contamination was apparently minor however:

*"CDC and HHS officials disagree with Stenzel's characterization of the lab. One former CDC official who was there when he arrived said the issues were small. "It was beakers on a counter that were empty and washed within 7 feet of a negative pressure hood. He called that dirty. Was that protocol? No. But it wasn't a dirty lab."*

14.12. Reports of localized problems with false positive results include 77 professional football players who tested positive when all of them were false positives attributed to cross-contamination.[98]

14.13. 90 out of 140 people (63%) tested false positive in July in Connecticut. This was reported as being due to a "widely-used laboratory testing platform" that the state laboratory started using on 15th June 2020.[99]

14.14. The FDA issued a warning about the Becton-Dickinson test kit after that manufacturer found a 3% false positive rate. That is 3% of tests done would be false positives. If 5 out of 100 tests were positive, then 3 of those would be false positives, with only 2 being true positives. That would mean 60% (3/5) of the positive test results would be false positive results.[100]

14.15. A further warning was issued by the FDA because inadequate centrifuging was leading to false positive results using the ThermoFisher Thermo Fisher Scientific TaqPath COVID-19 Combo Kit.[101]

**Contaminated reagents**

14.16. There has been more than one report of contamination of the reagents used for testing, including the primers and probes themselves:[102] [103]

> *"It is an essential practice to assure that this control template is made at different sites, usually from alternate vendors, from those sites making the other PCR reagents, to avoid this major potential source of contamination. However, as the number of laboratories developing assays and positive control materials for the global SARS-CoV-2 pandemic is unprecedented, selecting different vendors may no longer prevent this source of contamination."*

14.17. Figure 19 comes from a report on contamination of reagents.[102] The graphs show the results plotted by the PCR machines. Each line of the graph is the positivity (y-axis) from one sample. The x-axis shows the number of cycles (doublings) to reach that level of positivity. A threshold is selected as a horizontal line across the graph. Any signal that has an exponential line and crosses this threshold is considered positive. A shows results of a negative batch of samples, where the only signal is from the positive control sample. B shows a batch with contamination of the reagents, where multiple signals appear to be positive even in the absence of SARS-CoV-2.

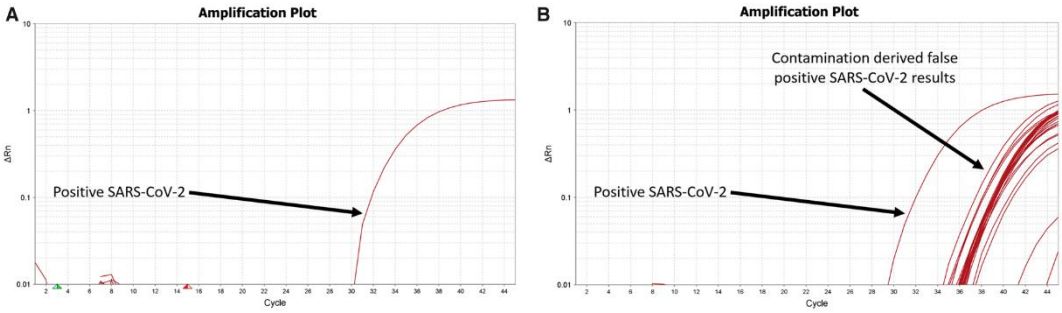



**Figure 19: Contaminated reagents generate false-positives in SARS-CoV-2 testing.**[102]

14.18. The CDC reported on contamination of reagents.[104] Ten laboratories from 8 countries in Europe reported contamination in commercially ordered primer and probe batches, which led to SARS-CoV-2 reverse transcription PCR (RT-PCR) signals in their negative controls. Five additional laboratories indicated that they received contaminated material, but did not provide details.

14.19. False positive results, for SARS-CoV-2, have been reported due to contamination of the nasal swabs themselves.[105] [106] If such swabs were contaminated with viable virus, the testing itself could have spread the disease.

**Cross contamination**

14.20. The BBC Panorama programme exposed how PCR testing was being carried out in extremely contamination prone environments with untrained personnel under time pressure in England.[107] The laboratories said in their defense that their results were comparable with all other laboratories in the country. The laboratories used in the comparison have similar issues.

14.21. The significant risk of false positive results comes from aerosols within the laboratory resulting in cross contamination of negative samples with genetic material from positive samples or the positive control. The CDC warns about that saying:[108]

> *"The most common cause of false-positive results is contamination with previously amplified DNA. The use of real-time RT-PCR helps mitigate this problem by operating as a contained system. A more difficult problem is the cross-contamination that can occur between specimens during collection, shipping, and aliquoting in the laboratory. Liberal use of negative control samples in each assay and a well-designed plan for confirmatory testing can help ensure that laboratory contamination is detected and that specimens are not inappropriately labeled as SARS-CoV positive.*

*In the absence of SARS-CoV transmission worldwide, the probability that a positive test result will be a "false positive" is high. To decrease the possibility of a false-positive result, testing should be limited to patients with a high index of suspicion for having SARS-CoV disease. For information on the indications for SARS-CoV testing, see Clinical Guidance on the Identification and Evaluation of Possible SARS-CoV Disease among Persons Presenting with Community-Acquired Illness.*

*In addition, any positive specimen should be retested in a reference laboratory to confirm that the specimen is positive. To be confident that a positive PCR specimen indicates that the patient is infected with SARS-CoV, a second specimen should also be confirmed*

*positive. Finally, all laboratory results should be interpreted in the context of the clinical and epidemiologic information available for the patient."*

**Equipment errors**

14.22. The specific RT-PCR methodology published by Drosten for SARS-CoV-2 testing and similar protocols used throughout the world contain numerous suboptimal design characteristics in the following six areas which are summarized then explained below:

14.22.1. Poor primer design - the primers specified in the Drosten paper contained unspecified parts of the sequence (uncertain or "wobbly" positions) that could result in 64 different sequence combinations, some of which do not recognise SARS-CoV-2 at all.[109] This risks primers binding to non-COVID DNA resulting in both false negative and false positive results. The primers chosen can also bind to each other risking false positive or false negative results.

14.22.2. Inadequate directions - every step of the protocol has flaws in that will maximise false positive results.

14.22.3. Poor choice of genes for testing - the genes chosen also maximise the risk of false positive results. Examples relevant to Canadian labs are examined in section 14.6.

14.22.4. Failure to thoroughly check the test will work in the real world - to ensure testing would detect infectious cases it needed to be checked against tests that show viable virus.

14.22.5. Poor recommendations for controls to mitigate against mistakes.[110]

14.22.6. Lack of advice on interpretation of the results.

14.23. Each amplification steps risk errors in both replication and binding which can result in false positives.

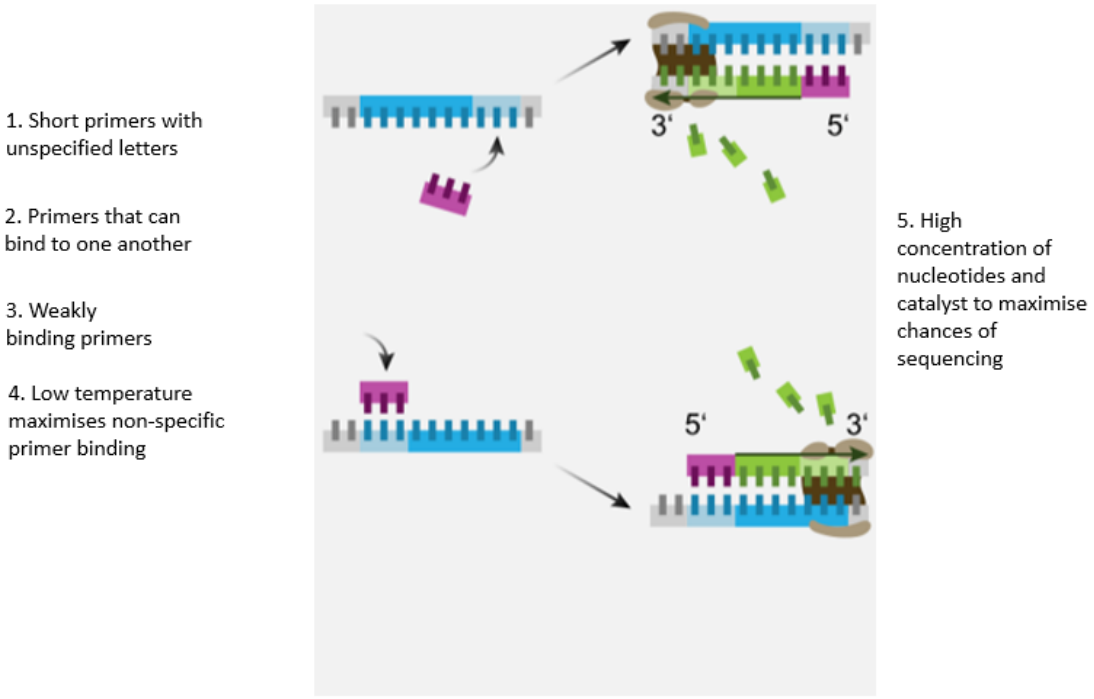



**Figure 20: Faults in amplification stages of the test.**

**Burden of Proof**

14.24. 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.[111] They found 57% of their positives were false positives in May 2020. To minimize 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 REACT study methods state: [111]

> *"We observed that the proportion of positive results from the commercial laboratory was substantially higher than from the Public Health England (PHE) laboratories. It was apparent that the commercial laboratory was routinely reporting as positive, on testing by RT-PCR, samples with high Ct values for the N-gene target, although the E-gene target was not detected.*

*To reconcile these differences, we conducted three separate calibration experiments. First, 10 RNA extraction plates were sent from the commercial laboratory to two NHS accredited laboratories for blinded re-analysis. Results were concordant for 919 negative*

*samples and all 40 controls. We detected viral RNA in 11 of the 19 samples reported positive by the commercial laboratory (N-gene Ct-value range 16.5 to 40.7); 10 of these 11 samples had an N-gene Ct value < 37. Second, the commercial laboratory conducted a serial dilution experiment of known positive samples with high viral load to assess Ct thresholds at the limit of detection. Third, a further 40 unblinded positive samples (on 19 plates) with Ct values (N-gene) > 35 (range 35.7 to 46.8) and without a signal for the E-gene were selectively re-analyzed in a PHE reference laboratory; SARS CoV-2 RNA was detected in 15/40 (38%) (2/4 with N-gene Ct value < 37). As a result of these calibration experiments, we report swab-positivity for positive samples reported by the commercial laboratory where N-gene Ct values < 37 or where virus was detected by both N-gene and E-gene targets."*

**Interpretation of the results / Cycle threshold (Ct) interpretation**

14.25. Interpretation of the results of the type of PCR carried out for COVID (RT-PCR) requires skill. The result of the testing is a trajectory showing how the signal developed with each cycle of DNA amplification. A positive test will demonstrate an exponential increase and will reach a threshold that defines positivity.

14.26. If the test is intended to identify infectious individuals, samples that only test positive once 35 cycles of doubling have taken place will be entirely false positives (in the sense that live, replicable virus is unlikely to be present) (see section 12). After 45 cycles, there will be tens of trillions of copies of the original sequence. Protocols could be adequate if combined with advice to not consider tests turning positive only after 35 cycles to be considered a positive result. Results positive after 25 cycles should not be considered diagnostic of the fact that a person has been infected with SARS-CoV-2, has COVID and is capable of infecting others. Where there is a strong clinical suspicion, with pneumonia or clotting abnormalities, then a positive result after 25 cycles should necessitate confirmatory testing, ideally with a different test. However, this has not been done.

14.27. The choice of threshold is critical to determining the correct result. A judgement must be made each time RT-PCR is run as to where this threshold lies. The decision is based on the degree of positivity of the positive and negative controls, but inevitably, the shape of graphs from the test results will also influence where a reasonable threshold may be set.

14.28. Finally, results that become positive only after minimal cycles, only after numerous cycles, or after a linear increase should be flagged, and those samples retested as unreliable results.

14.29. The decision about where the threshold is put for each test run would, in the past, be taken by a skilled scientist. The positioning of the threshold determines which cases will be considered positive and at what Ct value (see figure 16). As well as considering the signal from the positive and negative control for that run, it is also important to consider the results from the samples in that run. If there are samples with a convincing exponential rise in positivity, then the threshold will be set to ensure such samples will test positive.

14.30. However, for COVID, rather than using skilled scientists, a software is being used with artificial intelligence to determine the positioning of the threshold. UgenTec won a contract with the UK government to provide software to carry out this interpretation. Canada is also using the same software[112]. The choice of threshold and the credibility of the test result graphs is, therefore, not being determined by skilled operators and it is not clear how much manual auditing of results by skilled operators has taken place.

14.31. Medical regulators have criteria that a machine being used for diagnosis would need to pass to be approved. Clinical validation, where the device can be tested against real world clinical cases to judge its accuracy is carried out. The assumption is that the machine will remain constant and that results will be reproducible over time.

14.32. Rather than apply for approval of the software itself, UgenTec have passed the responsibility on to laboratories, such that approval must be sought for each assay using their software[113].

14.33. It is not clear whether this software includes artificial intelligence with active learning. This is where artificial intelligence continually adapts to adjust its conclusions based on a continuing supply of new information. This may result in drift of the criteria for a positive over time. It is also unclear how much manual auditing of results has taken place.

14.34. Diagnostics.ai successfully sued the UK Government for £2m because UgenTec testing had a high false negative rate.[114] If the decision tool places the threshold too high, resulting in false negatives, similar errors in decision making could result in placing it too low resulting in false positives.

**Checking against controls**

14.35. Control samples are required to calibrate the testing when using it in the laboratory for the first time and on an ongoing basis to ensure errors have not developed over time.

**Positive controls**

14.36. Positive controls are used to measure the false negative rate. A positive control should be a real patient sample to represent the full complexity of real samples, with their complex genetic makeup of human and bacterial genetic material. Synthetic RNA controls have been used for SARS-CoV-2.

14.37. Where synthetic controls are used, it is possible to draw conclusions about what Ct Value is of relevance for interpretation of the results of these controls. However, these results cannot be extrapolated to real world samples. These have much greater complexity in terms of what the sample contains, which means that they are at a higher risk of testing errors.

**Negative controls**

14.38. To measure the false positive rate, controls are needed, which should test negative. A negative control also needs to be a real patient sample and need to contain other viral or bacterial, as well as human DNA, to ensure that cross-reactivity (where one infective agent can be mistaken for another) is not occurring. The test was approved after checking against a handful of each type of bacteria or virus provides good evidence that cross-reactivity is not guaranteed to happen. However, a particular sample type may give a false positive result at a rate of 10% or fewer of samples tested. In order to identify such a problem, more than a handful of samples of this type would need to be tested. A study

of 100s to 1000s of such samples would be needed to be statistically valid. Such a study has not been carried out.

14.39. Marketing material from the TaqPath[115] COVID-19 CE IVD RT-PCR Kit, approved by WHO for emergency use, is reported by the manufacturer as containing elements that show homology to Neisseria elongata,[116] a very common nasopharyngeal bacteria. In the N-gene assay, the forward primer showed ≥80% homology, while the reverse primer and probe showed 36% homology.

## 15. The use of confirmatory testing to validate PCR

15.1. The risk of false positives from mass testing is well understood and can be minimized by using confirmatory testing.[117]

15.2. All cancer screening programs require confirmatory testing and this can be multilayered. For example, first line cervical cancer screening is carried using validated PCR testing kits manufactured to strict standards.[118] This testing has a false positive rate of between 7 and 10%.[119] The true positive rate for cervical cancer is only 9 in 100,000 i.e. 0.009%.[120] That is between 1 in 14 and 1 in 10 women being screened have a false positive PCR result. Rather than declaring 1 in 10 women being screened as being pre-cancerous based on a false positive result, further steps are taken. The women have a cervical smear performed and a colposcopy examination (where the cervix is examined directly by an experienced gynecologist), and most also have a lesion confirmed by biopsy before a diagnosis is made. The treating doctors do not use a single test to make a diagnosis. Rather, the diagnosis is a weighing up of the probability of there being a precancerous lesion. This evidence is evaluated against the probability of a false positive result. There are particular clinical scenarios where overcalling happens more frequently, and these will each be considered before a diagnosis is rendered.

### Confirmatory testing recommendations

15.3. Confirmatory testing must be carried out on all cases in order to minimize false positive results. A basic principle of mass testing is that the first test is a screening test and, for those found positive on screening, a subsequent positive confirmatory test is required to

make the diagnosis.[121] Subsequent testing carried out on only a subset of the positive results is not confirmatory testing, but external quality assurance.

15.4. The WHO set out these guidelines for confirmatory testing on 19th March 2020:[122]

*"Laboratory confirmation of cases by NAAT in areas with no known COVID-19 virus circulation. To consider a case as laboratory-confirmed by NAAT in an area with no COVID-19 virus circulation, one of the following conditions need to be met: A positive NAAT result for* ***at least two different targets*** *on the COVID-19 virus genome, of which at least one target is preferably specific for COVID-19 virus using a validated assay (as at present no other SARS-like coronaviruses are circulating in the human population it can be debated whether it must be COVID-19 or SARS-like coronavirus specific);*

*OR One positive NAAT result for the presence of betacoronavirus, and COVID-19 virus* ***further identified by sequencing partial or whole genome of the virus*** *as long as the sequence target is larger or different from the amplicon probed in the NAAT assay used. When there are discordant results, the patient should be resampled and, if appropriate, sequencing of the virus from the original specimen or of an amplicon generated from an appropriate NAAT assay, different from the NAAT assay initially used, should be obtained to provide a reliable test result. Laboratories are urged to seek confirmation of any surprising results in an international reference laboratory."*

15.5. Canada uses whole genome sequencing to confirm a proportion of the PCR positive test results. Whole genome sequencing requires a high volume of good quality DNA in the sample, so this confirmatory testing does not act as quality control for the testing as a whole, but only for the extreme cases of samples most likely to be positive.

15.6. The Canadian Consortium CanCOGen is responsible for whole genome sequencing of SARS-CoV-2 samples in Canada. By December 2020, they had sequenced 25,197 genomes, which represents only 4.5% of the positive samples reported in Canada.[123]

15.7. The 22 scientists who called for the retraction of the Corman-Drosten Paper explained how confirmatory testing is usually carried out for PCR testing:[124]

*"To determine whether the amplified products are indeed SARS-CoV-2 genes, biomolecular validation of amplified PCR products is essential. For a diagnostic test, this validation is an absolute must.*

*Validation of PCR products should be performed by either running the PCR product in a 1% agarose-EtBr gel together with a size indicator (DNA ruler or DNA ladder) so that the size of the product can be estimated. The size must correspond to the calculated size of the amplification product. But it is even better to sequence the amplification product. The latter will give 100% certainty about the identity of the amplification product. Without molecular validation one cannot be sure about the identity of the amplified PCR products…"*

## 16. False positive errors in COVID PCR testing – overview and examples

16.1. A BMJ analysis in May 2020[41] assessed the quality of PCR testing. Their estimate for false negative rates was between 2% and 29%. We concur with their following statement:

*"No test gives a 100% accurate result; tests need to be evaluated to determine their sensitivity and specificity, ideally by comparison with a "gold standard." The lack of such a clear-cut "gold-standard" for covid-19 testing makes evaluation of test accuracy challenging."*

No evidence could be referenced for the false positive rate provided, so they used an illustrative estimate of 5%.

16.2. The German External Quality Assessment carried out in April 2020 noted false positive results. Several were due to mistaking one sample for another. However, there were other false positive results and they commented (at bottom of page 20):[78]

(translated from German): "*In addition, in some cases the tests with the SARS-CoV-2 negative control samples show 340060, 340062 and 340065 indicate specificity problems that are independent of interchanges. It is to be clarified whether these false positive results are due to a specificity problem of the tests used or to a cross-contamination of SARS-CoV-2 during testing in the laboratories concerned."*

16.3. We concur with the authors of a Lancet publication, who said:[16]

"In our view, current PCR testing is therefore not the appropriate gold standard for evaluating a SARS-CoV-2 public health test."

"Once SARS-CoV-2 replication has been controlled by the immune system, RNA levels detectable by PCR on respiratory secretions fall to very low levels when individuals are much less likely to infect others. The remaining RNA copies can take weeks, or occasionally months, to clear, during which time PCR remains positive."

16.4. The CDC instruction manual for its 2019 Novel Coronavirus Real Time RT-PCR Diagnostic Panel includes these statements,[125] with which we agree:

*"Detection of viral RNA may not indicate the presence of infectious virus or that 2019 nCoV is the causative agent for clinical symptoms.*

*This test cannot rule out diseases caused by other bacterial or viral pathogens."*

16.5. Examples of false positive problems from PCR testing include:

16.5.1. a quality control study for MERS[126] testing carried out 2 years after the outbreak: 8% of laboratories had false positive results (the overall rate was not clear);

16.5.2. an outbreak of the coronavirus[83] HCoV-OC43 in a care facility was mistaken for SARS1 in 2003, thanks to false positive PCR and antibody testing results;

16.5.3. PCR testing for the HCoV-NL63 coronavirus[82] produced false positive results, when there was cross-reactivity with human X-chromosome DNA.

16.6. The more genes that are tested for, the better the test will be at identifying real COVID and not mistaking other DNA or RNA for COVID. There are likely numerous coronaviruses capable of infecting humans. As these are usually mild infections, there has been little incentive to characterize them all and only seven have a known sequence. As these are related to COVID, and will therefore have similar genetic sequences, it is critical to properly evaluate the COVID RT-PCR test against these related viruses.

16.7. Questions have been raised about RT-PCR test methods for COVID, which had been set out in a paper published by a German group led by Christian Drosten, the German virologist providing expertise to the German Government,[93] (the Corman-Drosten Paper) on 21st January 2020. A group of 22 scientists have called for the retraction of the Corman-Drosten paper[62]. These scientists identified numerous serious flaws in the design of the PCR test described in the Corman-Drosten Paper. These included using high concentrations of primers, which can then bind non-specifically, using a hypothetical sequence and leaving regions of the sequence unspecified, selecting gene targets in the region of the viral genome that is most heavily and variably replicated, choosing sequences and temperatures which would contribute to non-specific binding. These flaws together with a lack of standard checks to minimise the risk of errors, have led to worldwide misdiagnosis of infections attributed to SARS-CoV-2 and associated with the disease COVID-19.

16.8. The methods described in the Corman-Drosten paper have been used globally since. On 21st January 2020, only six COVID deaths had been announced worldwide, so the timing of this publication, in itself, was odd.

16.9. The viral test was established at a time when there was no actual viral material available. Instead "theoretical genetic sequences" of a "closely related virus" were used. This was an educated guess. The theoretical genetic sequences were from 375 "SARS related virus sequences". These sequences were matched up with each other to decide which areas would be put forward to be included in the test. When China released the first SARS-CoV-2 viral sequence, the tests they had that best matched it were chosen[93]. The Corman-Drosten Paper states:

> *"The present report describes the establishment of a diagnostic workflow for detection of an emerging virus in the absence of physical sources of viral genomic nucleic acid. Effective assay design was enabled by the willingness of scientists from China to share genome information before formal publication, as well as the availability of broad sequence knowledge from ca 15 years of investigation of SARS-related viruses in animal reservoirs."* [93]

16.10. The CDC manual on testing[125] states that they were unable to carry out quality control with viral isolates. Instead, a synthetic sequence made from the theoretical genetic sequence was used for testing the tests:

*"Since no quantified virus isolates of the 2019-nCoV were available for CDC use at the time the test was developed and this study conducted, assays designed for detection of the 2019-nCoV RNA were tested with characterized stocks of in vitro transcribed full length RNA (N gene; GenBank accession: MN908947.2) of known titer (RNA copies/µL) spiked into a diluent consisting of a suspension of human A549 cells and viral transport medium (VTM) to mimic clinical specimen."*

16.11. The WHO issued a medical product alert for PCR testing for SARS-CoV-2 on 7th December 2020.[29] stating:

*"In some cases, the IFU will state that the cut-off should be manually adjusted to ensure that specimens with high Ct values are not incorrectly assigned SARS-CoV-2 detected due to background noise."*

16.12. An updated version of this alert was published on 13th January 2021 and stated the below. (IVD means in vitro diagnostic medical device i.e. test kits and equipment and NAT stands for nucleic acid testing i.e. PCR):[127]

*"WHO guidance Diagnostic testing for SARS-CoV-2 states that careful interpretation of weak positive results is needed. The cycle threshold (Ct) needed to detect virus is inversely proportional to the patient's viral load. Where test results do not correspond with the clinical presentation, a new specimen should be taken and retested using the same or different NAT technology.*

*WHO reminds IVD users that disease prevalence alters the predictive value of test results; as disease prevalence decreases, the risk of false positive increases (2). This means that the probability that a person who has a positive result (SARS-CoV-2 detected) is truly infected with SARS-CoV-2 decreases as prevalence decreases, irrespective of the claimed specificity.*

*Most **PCR assays are indicated as an aid for diagnosis**, therefore, health care providers must consider any result in combination with timing of sampling, specimen*

*type, assay specifics, clinical observations, patient history, confirmed status of any contacts, and epidemiological information."*

17. **Evidence for false positive overcalling in COVID testing**

17.1. COVID disease and death in the spring of 2020 was more commonly seen in people of black or asian ethnicity, men and the elderly. These features of a classic COVID case have been diluted or lost.[128]

17.2. COVID hospital fatality rates fell from April 2020 to May 2020[129] after protocols to reduce ventilation, use proning and new treatments became available. However, they continued to fall through the summer of 2020 in the UK, when every hospital admission was being tested. In the winter of 2020 to 2021, the rate returned to April 2020 levels. The virus has been clinically stable over that period. There are three interpretations for this:

17.2.1. humans are more vulnerable to dying in April and December 2020;

17.2.2. admissions policy changed over that period with 60% of those admitted in summer 2020 denied admission in April and December 2020;

17.2.3. the diagnosis was being diluted with false positive results.

There is seasonality to the human immune response with resulting peak winter deaths in December each year, but the same argument cannot be made for April.[130] The majority of patients caught COVID while in hospital, so it would be impossible to alter the statistics by not admitting patients.[131] Therefore, there must have been a dilution with false positive test results.

17.3. An audit of patients in hospital with COVID in London[132] showed that by 13th May 2020, 80% of those with a COVID diagnosis did not have either acute, infectious COVID or the complications of COVID (figure 21).

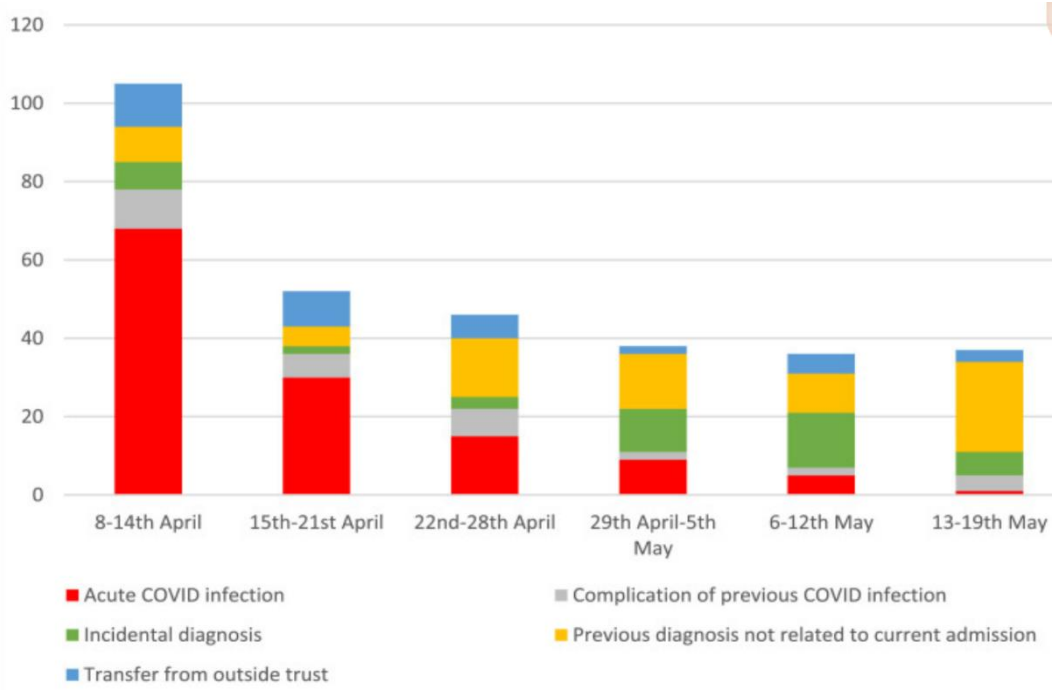



**Figure 21: Results of audit of COVID positive patients in London in Spring 2020.**[132]

17.4. The Scientific Advisory Group for Emergencies, who advise the Government in the UK, were not confident that data collection from the NHS could demonstrate which patients were readmissions or did not have acute COVID.[133] They were concerned that between a third and a half of cases did not have acute COVID in June2020. .

17.5. Cambridge university carried out testing by pooling cases and then carrying out repeat, confirmatory, testing.[134] The false positive rate for initial testing reached 100% of the positive results in some weeks.

17.6. Swansea university retested a sample of their positive results over the summer 2020 and found that 87% of their positive results were false positives.[135]

17.7. A letter from health minister in the UK, Lord Bethell, showed that experts advising Government in the UK had estimated the false positive rate to be 0.7%.[136] In Summer 2020, for six weeks, from 2nd July 2020, the total positive rate was 0.7%. In that period just over 5.2 million tests were carried out. With a false positive rate of 0.7%, a total of 36,000 false positive test results would be expected. The total number of positive test results was 35,000. This means that all of the positive results at that time were false positive results. There was low prevalence throughout the summer, so the risk of cross

contamination would have been low. The rate was likely higher at times of high prevalence.

17.8. If COVID diagnosis were identifying meaningful cases of a novel infectious disease, then the COVID-labelled deaths would be noticed as excess deaths. Excess deaths provide the most reliable measure of the impact of an epidemic.[137] In the absence of excess deaths, the implication is that COVID-labelled deaths have replaced non-COVID labelled deaths or that non-COVID deaths have been misdiagnosed. Taking all of Europe as an example, looking at the area under the curve in figure 22, there have been considerably more COVID-labelled deaths since summer 2020 than before summer 2020. However, the excess deaths curve is much smaller.

Not all excess deaths will be COVID deaths. Every winter, there are excess deaths as the baseline used is based on summer deaths. In addition, there has been restriction of access to healthcare, and that will result in excess death.

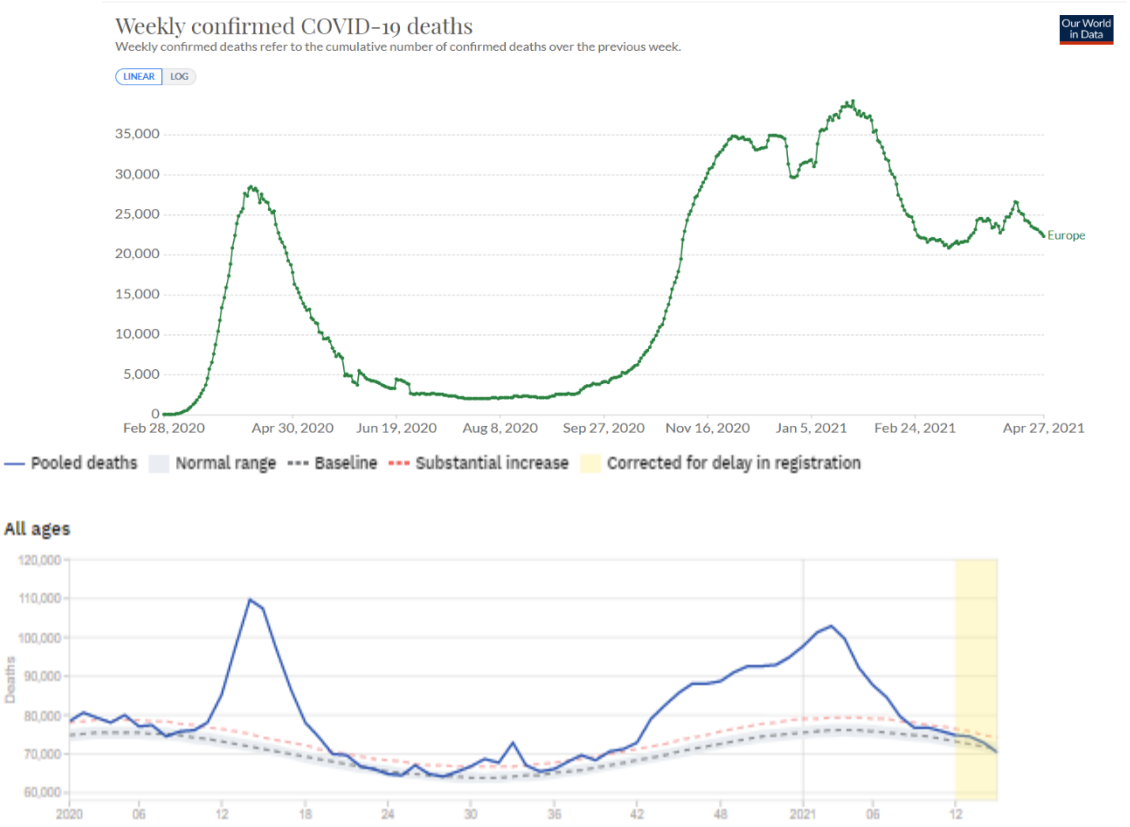
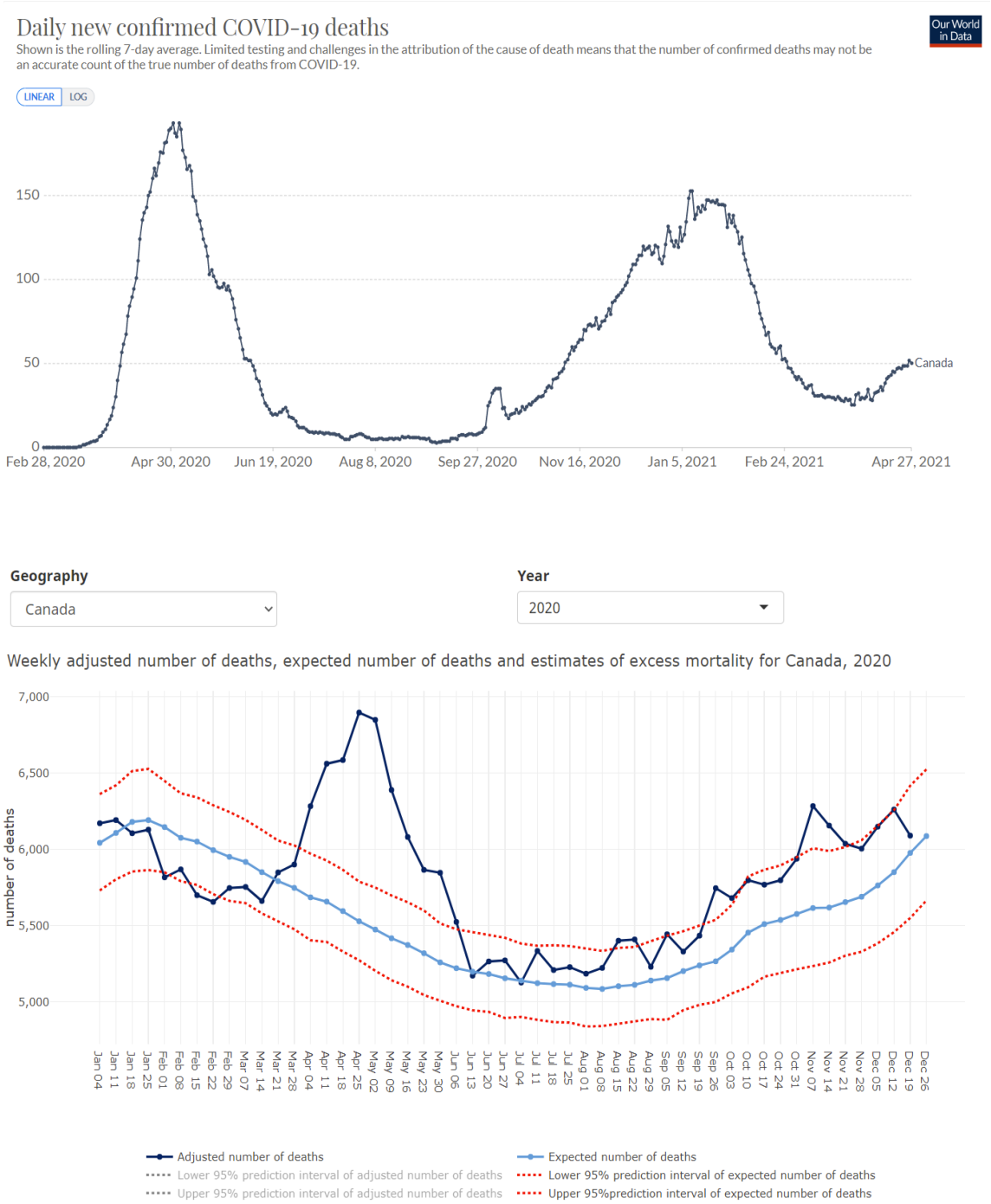



**Figure 22: COVID labelled deaths data for Europe from Our World in Data up to week 17.[2] Excess mortality data for Europe over 2020-2021 from EUROMOMO_for 2020-2021.[138] Note scale on top graph is for excess deaths and bottom graph shows total deaths.**

17.9. Canada is slow in reporting excess deaths and currently (April 2021), the latest data available is only up until January 2021. Figure 23 shows a clear pattern of excess mortality in Spring 2020, and at the beginning of the second COVID death spike there had been no similar impact on excess mortality.



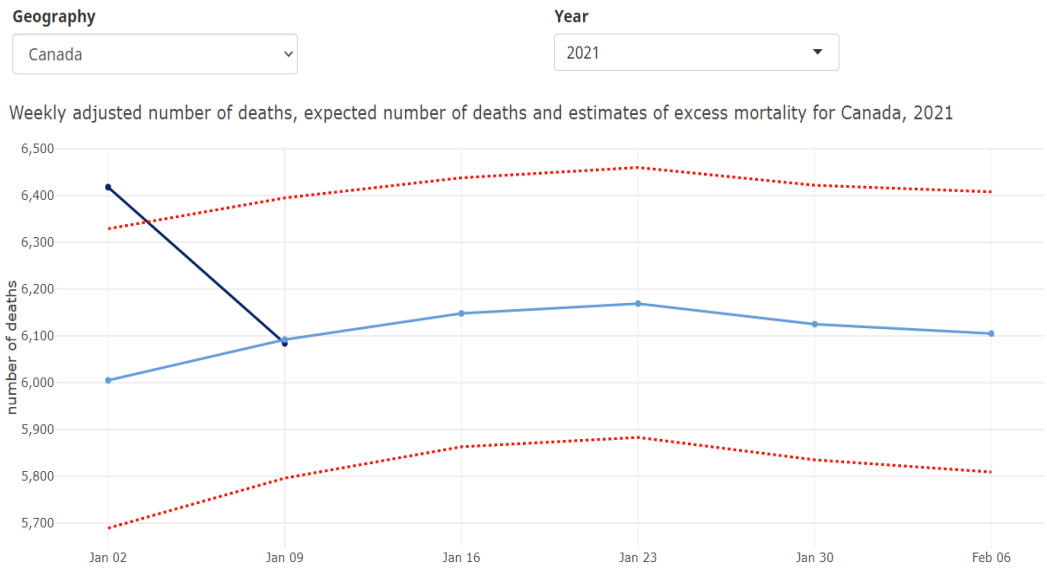



**Figure 23: COVID deaths in Canada (top)[2] and Excess deaths ( 2020 middle, 2021 bottom) total deaths (black line) compared with expected deaths 2020 (blue line).[139]**

17.10. Statistics Canada have reported on excess deaths, highlighting their concerns about non-COVID excess deaths in the young, resulting from Government policy.[140] From March to June 2020, Canada had 8,577 deaths in excess of average for previous years. 52% of these deaths were in Quebec, 38% in Ontario and 4% were in people aged under 45 years old. From mid-September until November 2020, there were 2,710 excess deaths - 21% in Quebec and 37% in Ontario. In the same period, there were 440 deaths (16% of total) in those under 45 years old. However, there have only been 50 COVID deaths in total ever in that age group. From June to September 2020, there were no overall excess deaths. However, from May to November 2020 there were 1,691 excess deaths in people under 45 years of age. As there were only 50 deaths in this age group diagnosed with COVID, the remainder of these excess deaths must be from non-COVID causes. Statistics Canada stated that these were not due to COVID: [140]

> *"…these excess deaths cannot be attributed directly to COVID-19…Some of these excess deaths may be due to the indirect consequences of the pandemic, which could include increases in mortality due to overdoses."*

17.11. The average age of a Canadian COVID death is higher than normal life expectancy (Figure 24). In 2019, over 80-year-olds accounted for 51.1% of deaths. Over 80-year-olds account for 69% of COVID labelled deaths.[141]

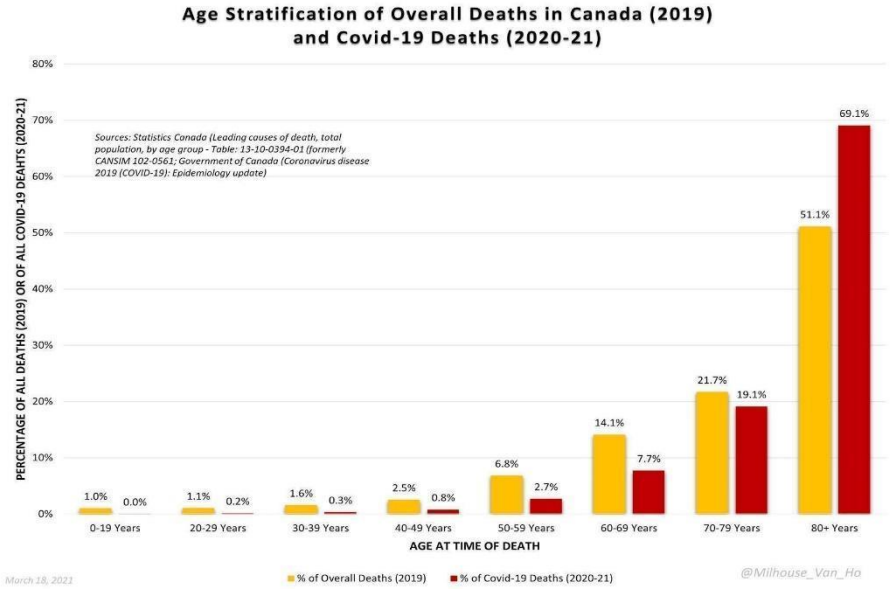



**Figure 24: Age stratification of COVID death as compared to overall mortality in Canada.**[141]

17.12. In May and June 2020, it was hoped that many countries had reached or come close to herd immunity. Antibody testing was carried out to indicate how many were immune. When designing a test, a decision must be taken as to what results should be called negative and what should be positive. The manufacturers all chose pre-COVID donor blood samples as the negative group. This meant the test would show who had been exposed to the novel coronavirus (SARS-CoV-2), but anyone who was immune before the virus arrived, would test negative. Initial results showed fewer than 2% had antibodies after the first wave.[142] An alternative test design uses blood from babies to represent a negative sample with no immunity. Using this methodology, a study in Vancouver showed that 90% of adults who had not been infected had antibodies to SARS-CoV-2 in June 2020.[143] This high level of prior immunity could explain the natural decline in mortality in Spring 2020, as the available non-immune individuals diminished. Viruses do not disappear and every winter a new cohort of vulnerable people with weakened immunity will succumb even when herd immunity is reached.

17.13. The Imperial REACT study published a graph showing the dates when 10,940 people in England, who developed antibodies without vaccination, had had symptoms.[144] This graph showed that none of these individuals had symptoms in June or July 2020. Figure 25 shows this graph, for England, overlaid with PCR diagnosed deaths that occurred 18 days later. There is a good fit until the deaths after 10th April, which continued until the end of July. This was likely from post-infectious false positive PCR results leading to misdiagnosis of cause of death. From 31st October 2020 onward there is a second deviation, increasing in the last three weeks of December 2020 before a lull until a big increase from 12th January 2021. These deviations are matched almost exactly by the dates when there were missing non-COVID deaths (figure 26). The plot of symptomatic disease is also a good fit for lateral flow positive results (see figure 30) and a much better predictor of excess death than PCR positive deaths. PCR positivity was a good predictor of symptomatic disease and excess death before peak deaths in the spring 2020, but subsequently PCR positivity has overestimated the extent of the disease. The concurrence of the other measures, including symptomatic disease and excess deaths, demonstrates that the outlier here is PCR testing.

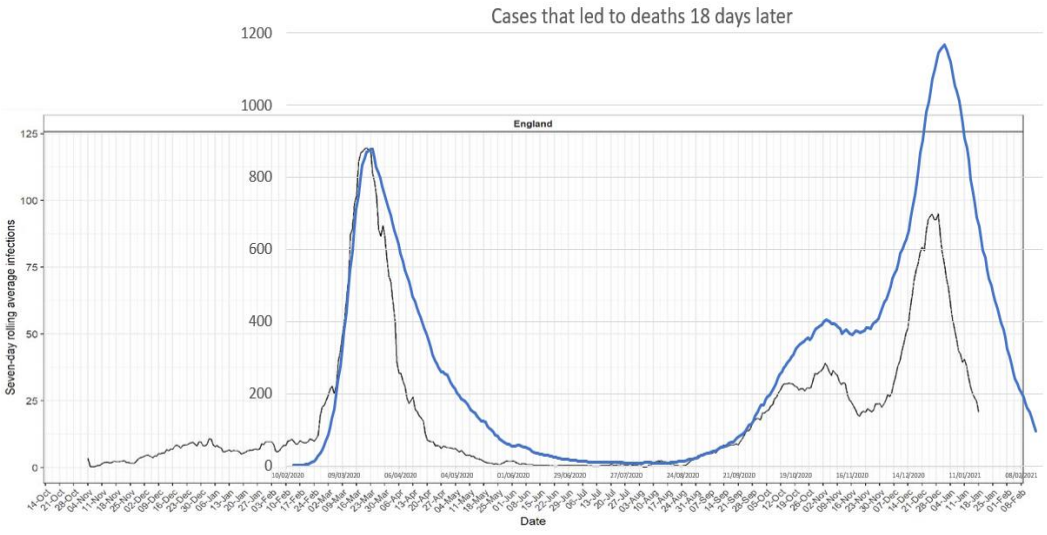



**Figure 25: REACT plot of when people who developed antibodies had their symptoms (black line) overlaid with PCR positive deaths, plotted at the time those people would have developed symptoms (blue line).**[144]

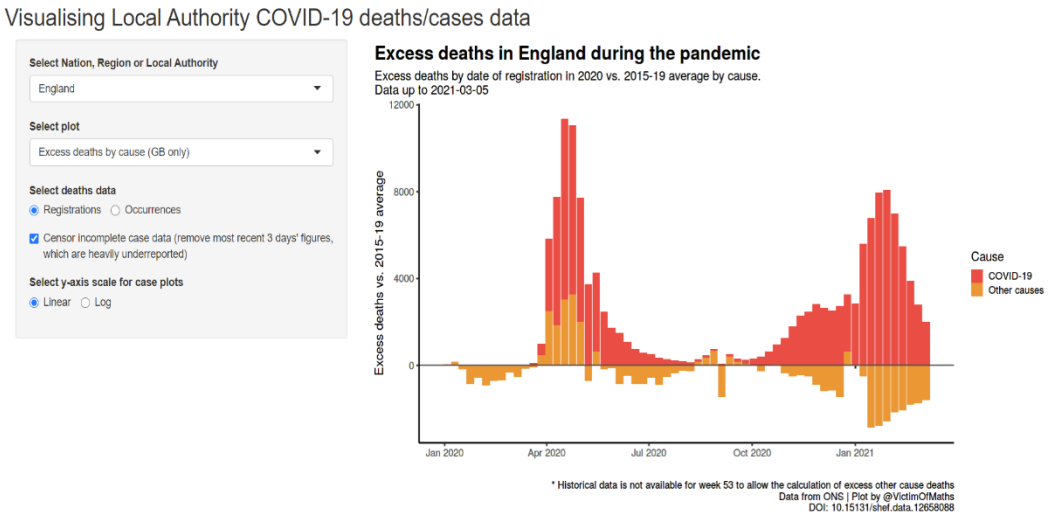
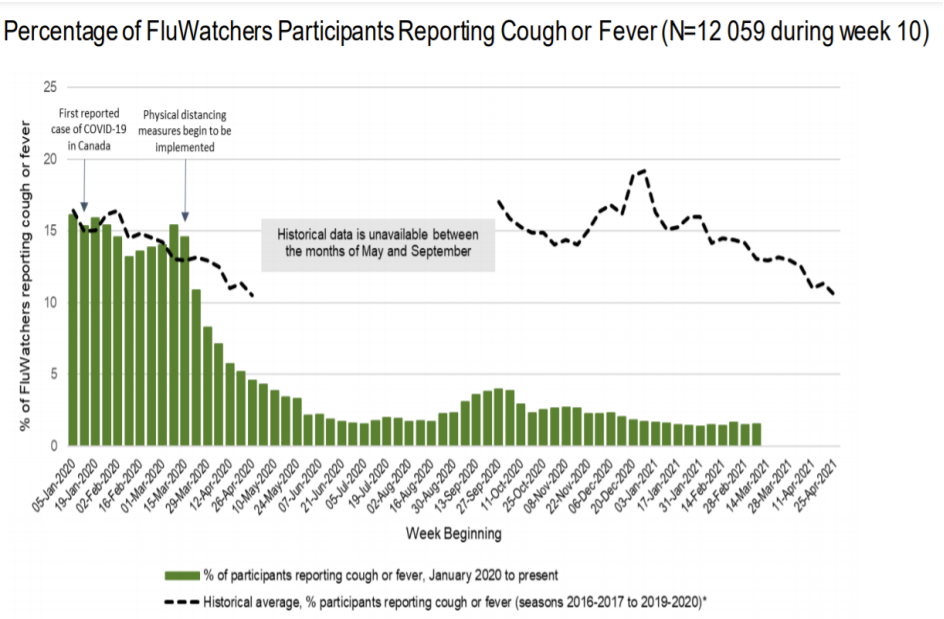



**Figure 26: Weekly deaths by date registered by ONS. Red bars show COVID deaths and orange bars show non-COVID deaths. Where orange bars are below zero, this demonstrates missing non-COVID deaths.**[145]

17.14. Canada monitors influenza-like symptoms across the country by surveying a random sample of the population. Out of a sample of 12,059 persons surveyed, there were two weeks in March 2020 when the number of people with cough or fever exceeded expected levels.[40] Subsequently, levels have been well below normal. In the week ending 13th March 2021, when about 13% of the population would normally have cough or fever, only approximately 2% of the population had symptoms. Of these, 39% were tested and only 6 positives were found. That represents only 0.05% of the overall population in the survey or 1 in 2000.[40] Symptoms from mid-December 2020 to late January 2021, were at historic lows and fell despite a rise in case numbers at that time.[2]



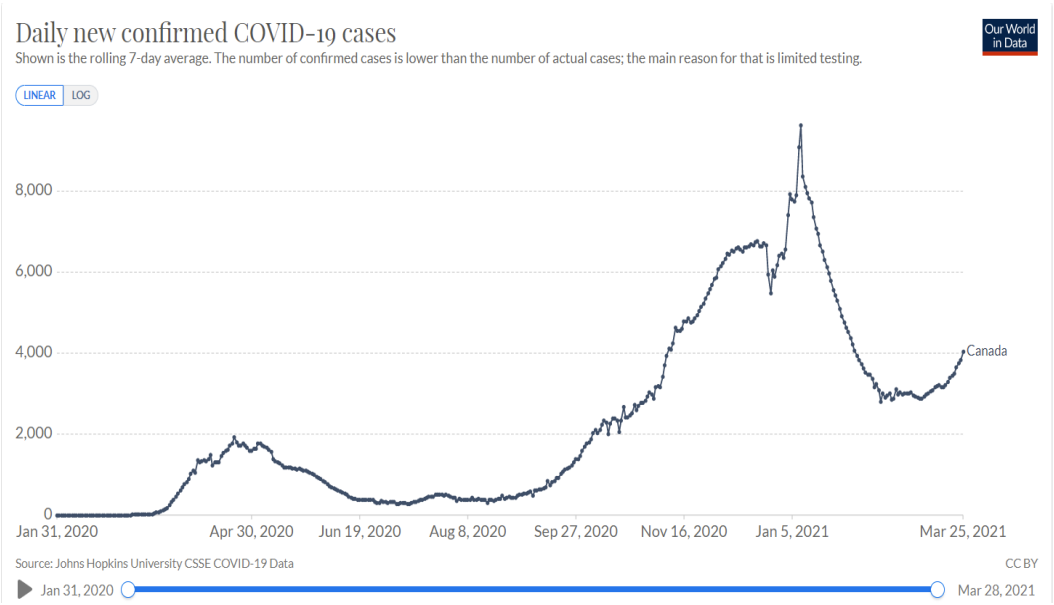




**Figure 27: Top graph: Percentage of sample of 12,059 Canadians who reported cough or fever each week (green bars), compared to historic data (dashed black lines).**[40] **Bottom graph: Daily case numbers reported in Canada, distorted by increasing test numbers, showing a rise in cases from September 2000 to a peak on 9th January 2021.**[2]

17.15. Two trials of antiviral therapies in over 65 year olds and high risk over 50 year olds found only 3% of COVID patients in the community were admitted to hospital.[146] A further study of high risk over 50 year olds found only 3.2% were admitted to hospital in the untreated group.[147] Neil Ferguson's group at Imperial estimated that the overall hospitalization rate in this age group would be 10-27% for modelling purposes.[148] Either the disease is much less severe than has been claimed, severe cases are predominantly found in patients who

catch it in hospital and community disease has been exaggerated, or these trials were finding false positive cases.

17.16. The number of cases diagnosed and the positivity rate peaked on 11th January 2020 on every continent, except Australasia (where the cases were near zero) (Figure 29). This simultaneous peak and fall in positivity is odd. If it were only Northern hemisphere countries that were affected, then seasonal factors could be the cause; however, the Southern hemisphere saw the same phenomenon in mid-summer. There was great variation in restrictions between countries; vaccination was only just beginning or had not begun and the suggestion that herd immunity was reached simultaneously across the world on the same day would be an extreme coincidence. The common denominator between countries is the testing. Swabs, reagents, testing kits are provided by a finite number of suppliers. Testing protocols and artificial intelligence algorithms may also be common factors that could be changed overnight. It is highly likely that, the reason for the simultaneous fall in cases in countries across the world was because of a change in how testing was being carried out or interpreted. If the fall was due to changes in testing, then that suggests the spike was attributable to testing too. The alternative explanations would require some unlikely coincidences.

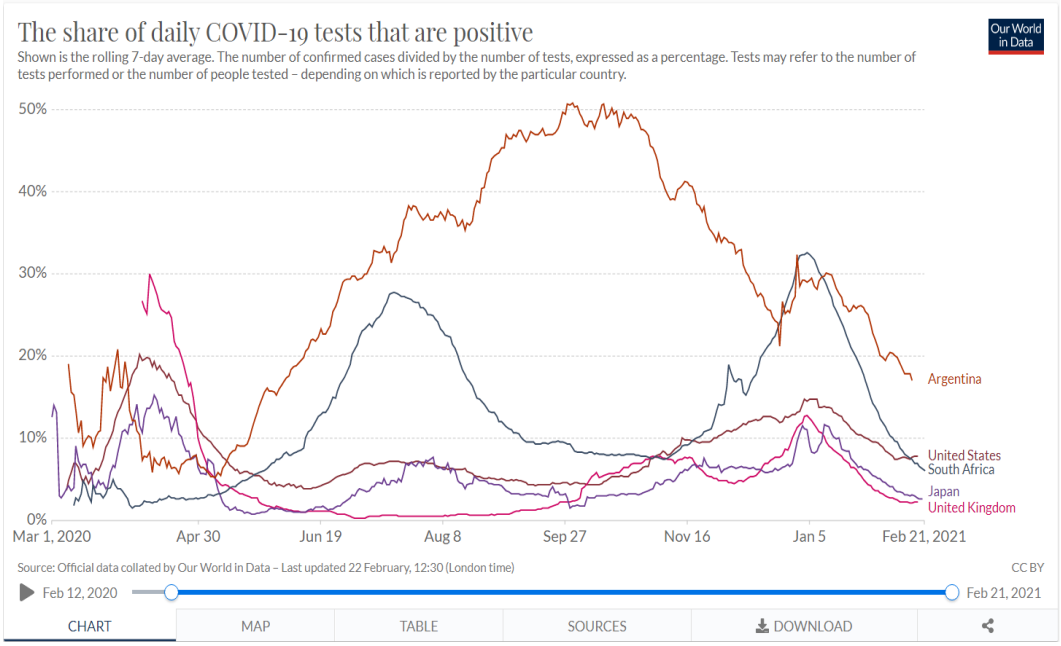



**Figure 28. Simultaneous peaks in positivity in countries on five continents.**[2]

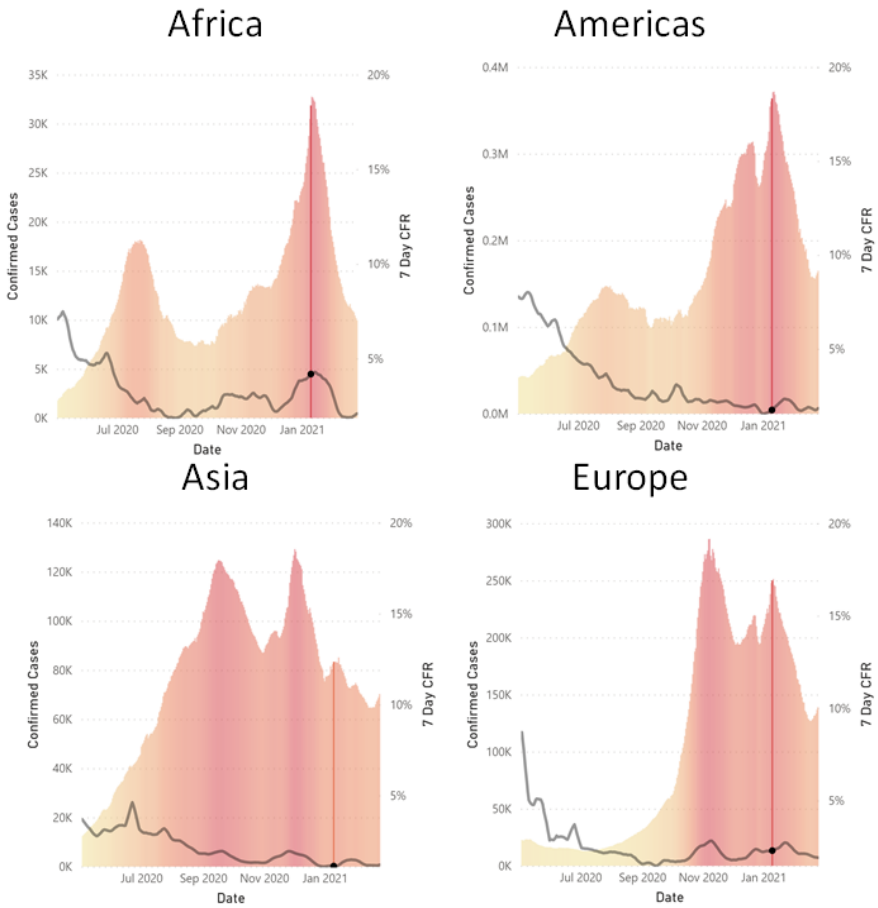



**Figure 29: The red bars show the number of cases per day with the 11th January highlighted as a darker red line.**[149]

**Antigen testing (Lateral Flow testing)**

17.17. By comparting other tests, e.g. antigen tests, to PCR, an estimate of the false positive rate for PCR can be made.

17.18. Because antigen tests are better at picking up all infective cases and only infective cases, they can be treated as an alternative gold standard to compare with PCR testing (false positive rate of 0.32% and 5% false negative rate for high viral load cases).[150] When PCR tests and antigen tests are examined head to head, there are big discrepancies. These have been interpreted as showing the LFT tests are missing real cases. However, that interpretation results in wildly different conclusions (false negative rates of 42%,[151] 51%,[152] 97%[153]) about what proportion they miss on each occasion they are compared. A more realistic explanation for the discrepancy is that PCR testing is overcalling cases and

that the supposed false negative percentages from lateral flow testing are actually the percentage of positive results that were false positives from PCR testing.

17.19. Using viral culture as a gold standard, and based on a population where 11% had the disease, then a positive antigen test meant a 90% chance of having a real infection, whereas a PCR positive test meant only a 74% chance of having infection.[154] This means the antigen test has a 10% false negative rate and PCR had a 26% false negative rate.

17.20. A separate study by a team at the CDC, also using viral culture, showed that the false negative rate for lateral flow testing was 11%.[155] Although not stated, from their figure it can be estimated that almost two thirds of the PCR positive samples were viral culture negative (including 20 with a Ct<18).

17.21. A comparison of three antigen tests, against viral culture, showed a false positive rate for lateral flow tests of under 24%:[156]

> *"the sensitivity of the examined Ag-RDTs for the SARS-CoV-2 rRT-PCR reactive samples within the standardized potential infectious range for the ORF1 gene reactive samples was 76.2% (the Nal von Minden test), with a potential of up to 100% (the Roche and LumiraDx tests)."*

Only 52% of the PCR samples were positive on viral culture.

17.22. A Cochrane review of the literature on lateral flow testing said[157]:

> "In people who did not have COVID-19, antigen tests correctly ruled out infection in 99.5% of people with symptoms and 98.9% of people without symptoms."

17.23. Mina et al have reviewed the evidence and commented that the 97% false negative rate was found based on all cases where:[16]

> *"viral loads were very low (Ct ≥29 reflecting around <1000 RNA copies per mL in the laboratory used)—when LFT should be negative."*

17.24. Lateral flow testing in the UK showed a six week period, in winter, where positivity was above the baseline false positive rate. However, prior to and after this six week period, the results indicate that there were no true positives and, therefore, no COVID in the population being tested. However, PCR positivity continued to show significant positivity.

The PCR positive rate rose and fell at times when the lateral flow positivity was static. Lateral flow tests have been restricted for use in the asymptomatic population in an attempt to identify presymptomatic cases and isolate them to prevent spread. For six weeks, presymptomatic cases were successfully identified, but no presymptomatic cases were found in weeks 45-49 and weeks 4-7 (figure 30).[158] During both these periods there would have been large numbers of post infectious patients with viral debris that could trigger a false positive test result.

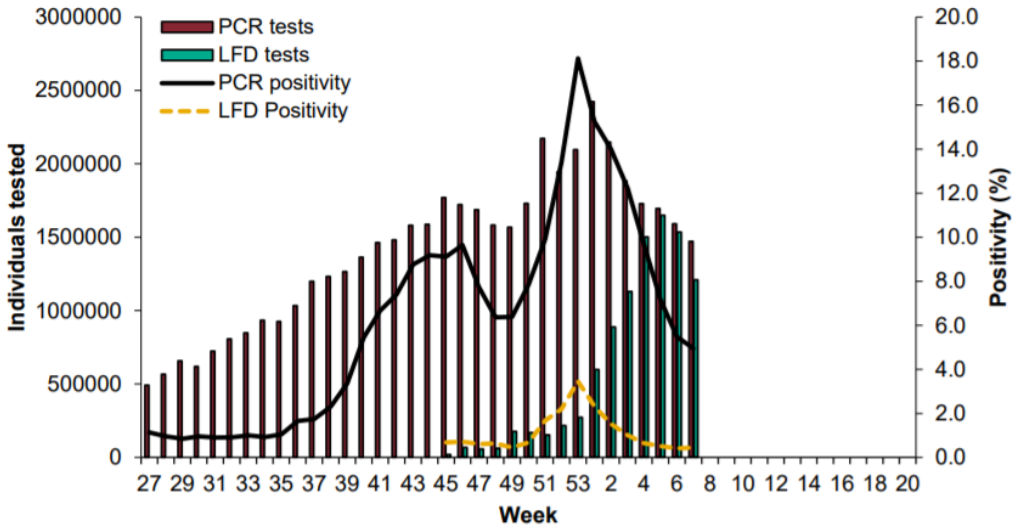



**Figure 30: Public Health England graph showing lines representing weekly positivity for LFT and PCRCOVID testing and bars for the number of tests done.**[158]

17.25. Austria carried out mass population testing of the asymptomatic population in early January 2021 using lateral flow testing. Prior to this, only PCR testing was being used on both symptomatic and asymptomatic individuals. PCR testing had a positive rate of 12% with 18,000 tests a day being carried out. After the introduction of lateral flow tests, the number of tests performed a day jumped to over 500,000 and the overall positivity rate plummeted to 0.4%.[159] This approaches the lowest recorded false positive rate for lateral flow tests (0.32%).[160] (The false positive rate will vary depending on the population being tested). This demonstrates that presymptomatic undiagnosed cases in the general population were incredibly hard to find on lateral flow testing. Where there are no presymptomatic cases in a population, the source of the PCR positive symptomatic cases is questionable. Our World in Data retrospectively altered the positivity graph to include only the PCR results, but the graph published at the time is shown in figure 31:

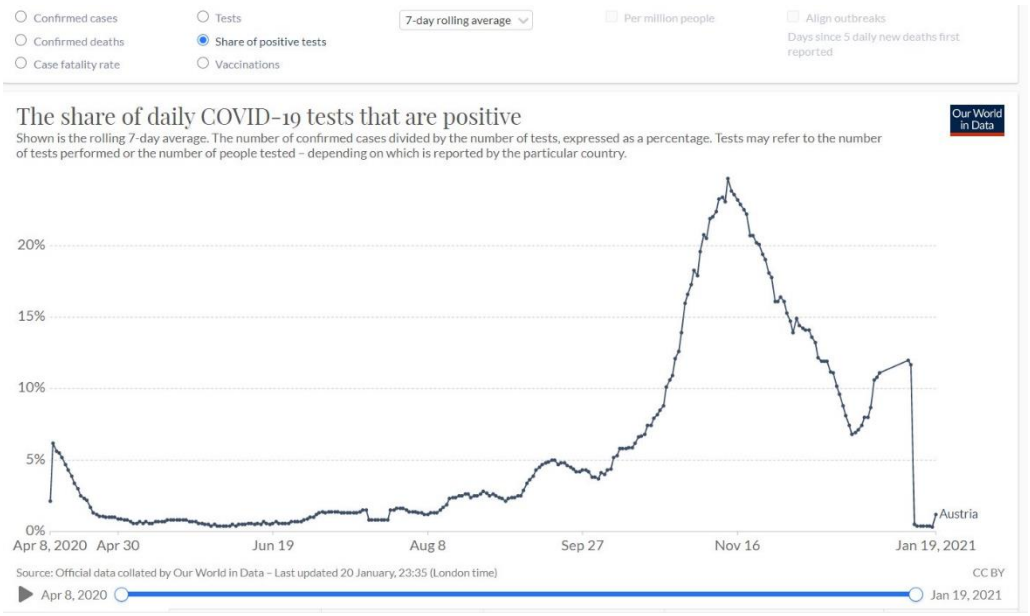



**Figure 31: The positive share of the COVID-19 tests in Austria.**[2]

17.26. The UK Office of National Statistics estimated, using random PCR testing of the population, that 1 in 250 of 12-24 year-olds had COVID on 13th March 2021.[161] Mass screening in schools took place that week using 4.5 million Lateral Flow antigen tests and positive results were only found in 0.06% i.e. less than 1 in 1500.[162] These were false positive antigen test results, which happen at a lower rate in a younger population. The mass screening demonstrated no COVID in the school aged population and exaggeration of the extent of disease by PCR testing.

17.27. Lateral flow testing is a more accurate, cheaper, faster and easier to use alternative to PCR testing that has been ignored.

**Other evidence of a PCR false positive problem**

17.28. Antibody testing can be used to demonstrate an immune response seen if someone has been genuinely infected. Of patients who were PCR positive in hospitals in a Spanish study, 87% of those in hospital for fewer than 7 days had not had COVID based on antibody testing.[163] 56% of those in hospital for a longer stay and PCR positive also did not have confirmatory antibodies. Even 53% of those who were PCR positive and on intensive care did not have confirmatory antibodies.

17.29. The Taiwan Central Epidemic Command Center adopted a policy of restricting testing to only to symptomatic patients because of the risk of false positive results.[164] Taiwan has had 1082 cases and 11 deaths in total as of 21st April 2021.[2]

17.30. On 7th December 2020, the WHO issued a warning about false positive test results:[165]

*"Healthcare providers are encouraged to take into consideration testing results along with clinical signs and symptoms, confirmed status of any contacts, etc.*

*Users of RT-PCR reagents should read the IFU carefully to determine if manual adjustment of the PCR positivity threshold is necessary to account for any background noise which may lead to a specimen with a high cycle threshold (Ct) value result being interpreted as a positive result."*

17.31. Over testing the dying has led to misdiagnosis of death, with thousands of deaths from acute and chronic respiratory conditions missing from the death data. Figure 32 shows Public Health England data for excess deaths since March 2020 for most medical conditions, but a lack of excess deaths for respiratory diseases indicating either that these deaths have been postponed or have been reclassified.[166]

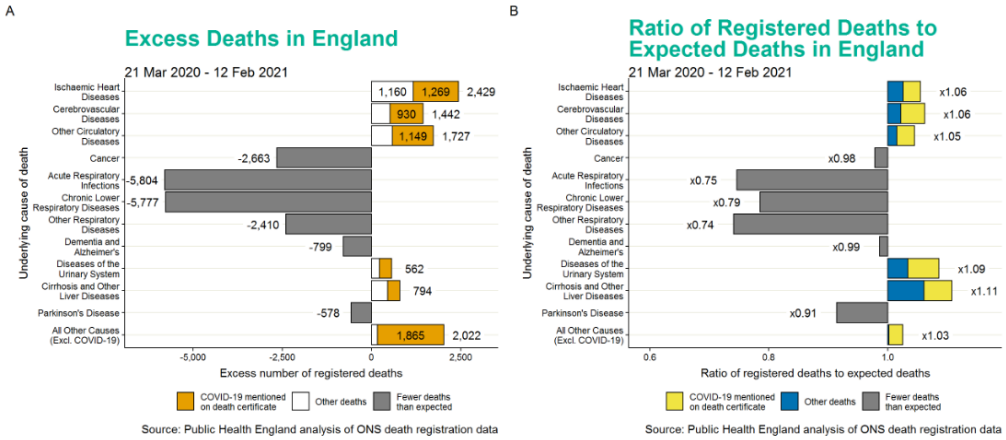



**Figure 32: Public Health England data for excess deaths since March 2020**.[166]

17.32. The spread of an epidemic is measured by estimating the number of new cases each case causes. This is called the R value. It is the ratio of new cases to old cases. SARS-CoV-2 was estimated to have an R value of between 3.6 and 6.1, in the absence of intervention. This means every case would spread disease to an average of 3.6 to 6.1 other individuals.[167] Three changes could increase the R value:

17.33. there is spread of genuine disease with an increase in true positive results;

17.34. the false positive rate increases with an increase in false positive results;

17.35. the number of tests increases with an increase in false positive results.

In the absence of disease, and all else being equal, there would be only false positive results at a constant rate i.e. the same number of old 'cases' as new 'cases'. This would lead to an R value of 1.0. In an epidemic, the R value would be high initially and then fall rapidly to below one at peak cases, because falling case numbers mean fewer new cases than old ones. The Canadian Government's estimates of the R value within Canada are shown in figure 33. The R value in Canada has deviated above or below 1.0 throughout the pandemic.[40]

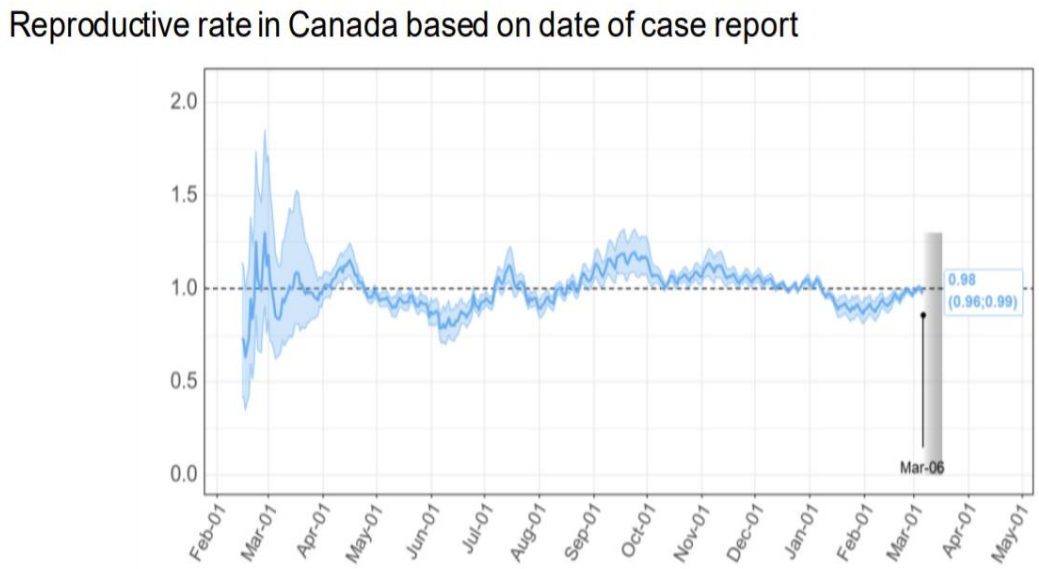



**Figure 33: Estimated reproductive rate, or R value, of SARS-CoV-2 in Canada.**[40]

17.36. The Canadian Government produces a weekly epidemiology report in which details of COVID outbreaks are recorded.[40] [38] In the spring of 2020, outbreaks were mainly centered around care homes and hospitals. The definition of an outbreak is two people who test positive and are linked to a setting. Increased testing in prisons and schools as well as extensive testing in care homes has led to increasing numbers of supposed 'outbreaks' (table 2 and 3). [40] [38]

| Outbreak setting | Total number of outbreaks reported | Total number of cases reported | Total number of reported deaths |
|---|---|---|---|
| Long-term care and seniors homes | 1 234 | 21 622 | 6732 |
| Meat production/packing facilities | 19 | 3 078 | 7 |
| Hospitals | 152 | 2 116 | 205 |
| Community/Small city/Reserve/Indigenous communities/Rural and remote | 42 | 1 939 | 21 |
| Agricultural work settings (including those with congregate living for workers)[b] | 20 | 1 732 | 4 |
| Correctional facilities | 30 | 840 | 4 |
| Mass gatherings[c] | 26 | 760 | 2 |
| Other industrial settings[d] | 49 | 748 | 2 |
| Shelters | 45 | 644 | 4 |
| Other congregate living settings | 51 | 506 | 37 |
| Retail businesses | 59 | 277 | 1 |
| Food/drink establishments | 36 | 242 | 0 |
| Child and youth care[e] | 31 | 156 | 0 |
| Rehabilitation facilities | 8 | 104 | 8 |

Source: Publically reported data as of 22 August

**Table 2: Cumulative numbers of COVID outbreaks in Canada up to 22nd August 2020.**[38]

| Outbreak setting | Total number of outbreaks reported | Total number of cases reported | Total number of reported deaths | Outbreaks Reported in past 7 days |
|---|---|---|---|---|
| Community[b] | 197 | 10 261 | 83 | 3 |
| Corrections/shelter/congregate living | 666 | 11 580 | 223 | 12 |
| Food/drink/retail | 634 | 2 161 | 3 | 4 |
| Healthcare | 700 | 10 339 | 780 | 15 |
| Industrial (including agricultural)[c] | 469 | 10 956 | 24 | 8 |
| Long term care and retirement residences | 4 252 | 65 923 | 12 337 | 61 |
| Personal Care[d] | 47 | 401 | 0 | 1 |
| School & Childcare Centre[e] | 1 349 | 7 429 | 1 | 40 |
| Other[f] | 525 | 5 059 | 6 | 6 |

Source: Publicly reported data, including Provincial and Territorial websites, as of 13 March 2021

**Table 3: Cumulative numbers of COVID outbreaks in Canada up to 13th March 2021.**[40]

17.37. Up until April 17th 2020, 76% of COVID cases diagnosed (without a history of international travel), had no known exposure to a case. Although, tracing of contacts may have failed in some instances, the proportion is so high that it is highly likely that many of these were false positive results.[36] The alternative explanation is that transmission is not person to person.

Possible exposure setting of COVID-19 cases reported in Canada

| Possible Exposure Setting | N=19 000 | |
|---|---|---|
| **Travel-Related** | **n=4 565** | **24%** |
| History of international travel | 3 795 | 83% |
| Close contact of an international traveller | 770 | 17% |
| **Community-Related** | **n=14 366** | **76%** |
| Case exposed in a healthcare facility* | 1 820 | 13% |
| Case lives in a long-term care facility | 409 | 3% |
| Close contact with case in a household | 833 | 6% |
| Close contact with case in a workplace¥ | 210 | 1% |
| Case attends/works at a school or daycare | 157 | 1% |
| Case has no known exposures† | 10 937 | 76% |
| **Pending** | **n=69** | **0%** |

*Includes healthcare workers and exposure in health care setting
¥ Excludes healthcare settings
† Includes community transmission where specific setting was not reported as well as cases where no clear exposure setting was reported

**Table 4: Exposure history for 62% of reported cases up to 17th April 2020 (detailed data not available for other cases).**[36]

17.38. Spread of COVID is primarily seen in the hospital and care home population, with up to 40% of transmission in the spring of 2020 happening in hospitals.[168] The Scientific Advisory Group for Emergencies estimated that the majority of cases were due to hospital spread on June 4th 2020.[133] Hospital spread was also a key characteristic of both SARS-CoV-1 and MERS.[169] The exaggerated case numbers, due to PCR testing, have meant that policy has focused on community cases rather than on ways to prevent hospital transmission, the key driver of spread. Figure 34 shows that the increase and decrease in COVID bed occupancy in England did not impact on total occupancy nor on spare capacity which suggests either hospital acquired infection or false positive test results or a combination of both.

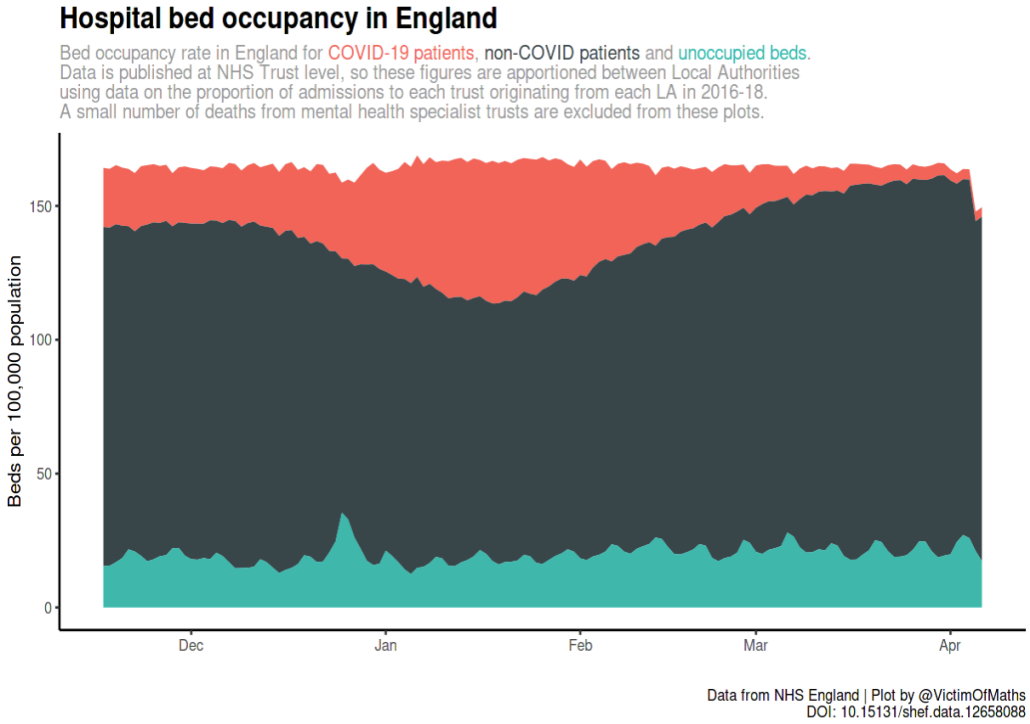



**Figure 34: Hospital bed occupancy in England, since November 2020.[170] Beds occupied by COVID patients in red; non-COVID patients in black and empty beds in green.**

17.39. To summarise, after the spring of 2020, the characteristics of the patients diagnosed as COVID reverted to levels expected in the general population and their clinical presentation was no longer that of an acute COVID infection. The small numbers of studies done with confirmatory testing indicate a significant false positive problem with PCR testing, and the PCR test results have not been confirmed when testing has been carried out with antigen tests and with antibody tests. Even the deaths diagnosed as being due to COVID are no longer predictive of excess death levels as they were in the spring of 2020. The diagnosis of death is an art and relies on the balance of probabilities based on all the information available at the time. False positive test results can therefore have a large influence on death diagnosis. Misdiagnosis, misattribution of death and over testing the dying have led to missing deaths from other respiratory causes and a higher age at death for COVID deaths than for general deaths[171]. Even substantial numbers of false positive tests, which we believe there were, would not mean that there was no real COVID present in addition. Viruses do not disappear and endemic winter COVID cases will have been present too.

## 18. Asymptomatic spread exists as an idea only because of the PCR testing strategy

18.1. The response to COVID has been predicated on the assumption that asymptomatic PCR positive individuals can spread disease.

18.2. There are three situations where someone can be PCR positive, but asymptomatic.

18.2.1. They are in the incubation period of real disease and are pre-symptomatic.

18.2.2. The test result was a false positive.

18.2.3. They have virus on board, but never develop symptoms.

18.3. The latter category used to be referred to as "immunity". This is a state where, even if a virus is inhaled and present in the respiratory tract, the person is oblivious as their immune system deals with the infection and they never develop a symptom. Rather than assume immune individuals cannot spread infection, it was worthwhile checking.

18.4. Pre-symptomatic people can spread disease and account for a maximum of 7% of cases.[172]

18.5. We concur with Dr Anthony Fauci when he said:

*"In all the history of respiratory borne viruses of any type, asymptomatic transmission has never been the drive of outbreaks. The driver of outbreaks is always a symptomatic person."*[173]

18.6. Finding people that test positive, but show no symptoms during an outbreak, is evidence of immunity, not evidence of transmission.[49] This applies to any test including PCR, antigen testing and even viral culture. Evidence of transmission requires that someone who is immune was the source of infection for someone who then developed symptoms and had disease.[174]

18.7. The proportion of people who test positive, but have no symptoms, ranges from 4%[175] to 76%.[176] This is because this is a function of how testing has been carried out, not a function of a true disease (in which case the range would have been much smaller).

18.8. Reviewing all the published meta-analyses on asymptomatic transmission reveals that the same stories have been recycled repeatedly by respectable institutions.[177] The underlying evidence for asymptomatic transmission amounts to 6 individuals who were alleged to have spread COVID to 7 others.[177]

18.9. Two of these examples may well have been one patient with the story repeated in separate publications.[178] [179] This was a situation where neither person involved in transmission had any symptoms. It therefore fails as evidence of disease spread, which requires the presence of symptoms.

18.10. Two further cases were from Vo in Italy where the whole town was tested.[180] 1% of the tests were positive in the absence of symptoms. The UK Government's own estimates for the percentage of tests that will be false positive is between 0.8-4.0% and, as this was a new test, a rate of 1% is very respectable. The alleged result of transmission again resulted in no symptoms. These were false positive PCR test results and assuming chains of transmission based on the degree of positivity of a test result is bad science.

18.11. The final two examples were both from studies in Brunei.[181] The evidence is weakened by a poor case definition (any symptom of any severity was considered real symptomatic COVID), and a high probability of false positive results. A 13-year-old girl with no symptoms was alleged to have spread COVID to an adult who had "a mild cough on one day".[182] The second was a father who remained asymptomatic, but whose wife briefly had a runny nose, and whose baby had a mild cough on one day.[182] Much of the evidence of asymptomatic spread is based on modelled data not actual evidence of spread. Excluding modelled data, reports from China and presymptomatic spread, this is the totality of the so-called evidence for asymptomatic spread related to COVID as of today.

18.12. It is therefore at least arguable that the asymptomatic diagnoses in Spring 2020 were all due to false positive test results. No testing system is perfect. Failure to acknowledge this and misinterpretation of positive results in patients with no symptoms has been hugely damaging.

18.13. There are three types of evidence for asymptomatic spread: studies showing people test positive while asymptomatic (the bulk of the work); studies measuring viral load and

concluding from it that people with no symptoms can transmit virus; and studies showing actual transmission. The first two are not proper evidence that spread can occur.

18.14. It is important to carefully distinguish purely asymptomatic (individuals who never develop any symptoms) from pre-symptomatic transmission (where individuals do eventually develop symptoms). To the extent that the latter phenomenon, which has in fact happened only very rarely, is deemed worthy of public health action, appropriate strategies to manage it (in the absence of significant asymptomatic transmission) would be entirely different and much less disruptive than those actually adopted. For example, there would be no need to lockdown the healthy population and quarantine of contacts of known true positive cases could end after 5 days, unless symptoms developed.

18.15. Many early studies, which purported to demonstrate the phenomenon of asymptomatic transmission, were from China, yet, the fact that Chinese studies are only published following Government approval must bring their reliability into question.[183] Nevertheless, the high volume of these studies spawned significant salience of the issue within the medical community, and an assumption of the likelihood of asymptomatic transmission being an important contributory factor. There then followed a number of meta-analyses examining the issue of asymptomatic transmission, which tended to aggregate and give equal weight to studies, regardless of origin or quality.[184] [185] [186] [187] In this way, these meta-analyses, given undue credibility by their association with reputable universities, amplified minimal evidence of asymptomatic spread to an importance the data did not warrant.

18.16. In a review of the literature, the papers most frequently cited in support of the existence of asymptomatic transmission were examined.[177] Despite our criticisms of the sources of the data above, we did, in fact, find only six case reports of viral transmission by people who throughout remained asymptomatic, and this was to a total of seven other individuals. However, all of these were in studies with questionable methodology. These were: In Italy, two asymptomatic cases allegedly passing the virus to two others, in Brunei, two asymptomatic cases allegedly passing the virus to three others, and in China, two asymptomatic cases allegedly passing the virus to two others (see paragraph 18.8).

18.17. In all these studies, confirmation of 'cases' was solely made via PCR testing, without regard to the possibility that any of the cases found might be false positives. The case numbers found are, in any event, extremely small and certainly not sufficient to conclusively determine that asymptomatic transmission is a major component of spread.

18.18. It is also notable that, in what would seem to represent an abrupt volte face by the Chinese Communist Party (CCP), a further (presumably Government-approved) study from China was recently published, which entirely contradicts the earlier conclusions regarding the phenomenon of asymptomatic transmission, which had been driven by Chinese data in particular, early in the pandemic.[188]

18.19. Aside from reported studies of transmission, those leading on the contact tracing response might have useful experience on the likelihood of transmission. Maria Van Kerkhove, head of the World Health Organization's emerging diseases and zoonosis unit, stated at the beginning of June 2020:[189]

> *"Countries doing very detailed contact tracing …[are]…following asymptomatic cases and following contacts and they're not finding secondary transmission onwards. It's very rare. Much of that is not published in the literature."*

**19. Consequences of current policy regarding the PCR test**

19.1. The PCR test for COVID is not a reliable test in the way it is being used. It is not a suitable or reliable test for the detection of infectious SARS-CoV-2 viruses and is a bad measure of who is an infection risk to others.

19.2. A single positive test result alone should not be used as indicative of a diagnosis of disease. Diagnosis should only be made either in the presence of a clinical picture of classic symptoms or after confirmatory testing (see section 6).

19.3. Decisions about interventions were originally based on deaths from COVID. However, as deaths reduced, the focus changed to cases. The focus is currently shifting to variants of the virus and to people with post viral symptoms, complaining of symptoms for weeks to months after COVID infection, known as "long COVID". The measure of whether there is a real public health emergency is whether there are excess deaths. The Canadian data on

excess deaths is slow to be released. Healthy people have been labelled as cases. Cases are being treated as infectious. People have been unnecessarily subject to self-isolation, quarantine, contact tracing, and places of employment have been shut down on the basis of this policy.

19.4. PCR tests cannot distinguish between exposure that was effectively controlled by the patient's immune system or from post infectious dead virus particles.

19.5. The risk of cross contamination means that, even people who have never been exposed to SARS-CoV-2 can test positive and be asked to quarantine.

19.6. Overcalling of cases has resulted from:

19.6.1. a case being defined as a positive test result;

19.6.2. the calling of PCR results with high Ct values as positives, when the likelihood of viable virus is low;

19.6.3. other causes of false positive results, meaning people are erroneously described as positive.

19.7. Testing accuracy and strategy are critical as tests determine 'cases' and this metric is used to determine business closures, school closures, event cancellations, lockdowns, withdrawal of civil rights and liberties, whether people can congregate, and mask requirements.

19.8. In Portugal, the Lisbon Appeals Court ruled that the quarantine of four foreign individuals, which was based on positive PCR results, violated Portuguese and international law. The conclusion of their 34 page ruling included the following:[190]

> *"In view of current scientific evidence, this test shows itself to be unable to determine beyond reasonable doubt that such positivity corresponds, in fact, to the infection of a person by the SARS-CoV-2 virus."*

## 20. Mass testing with Lateral Flow tests

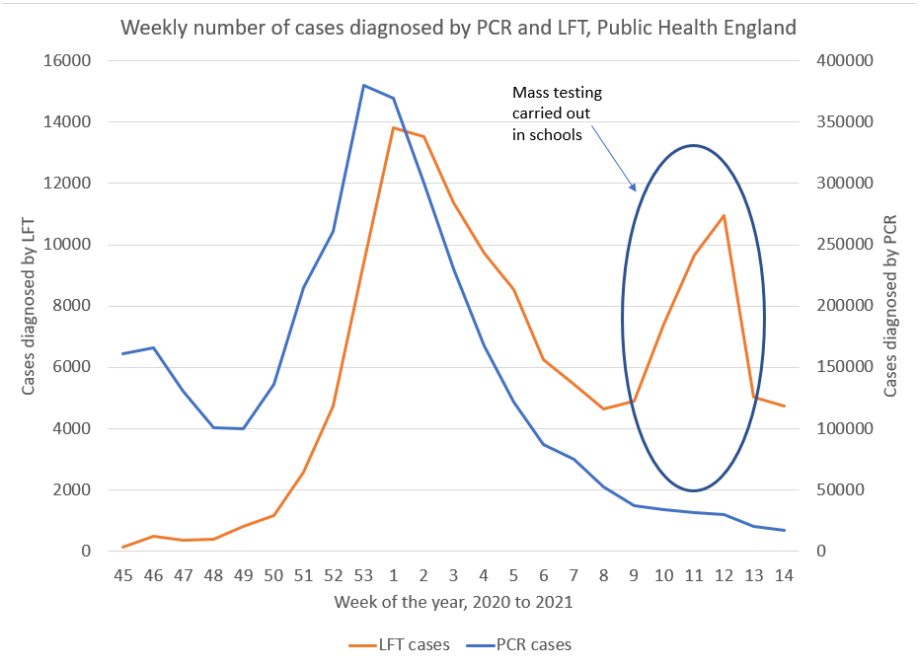
20.1. Lateral Flow testing detects viral particles particularly the outer envelope of the virus and the spike protein. However, these do not have to be intact and fragments of viral particles which contain these proteins will also test positive.

20.2. As with PCR testing, testing a population with low prevalence will result in a high proportion of the positive results being false positive even if the percentage of false positive results per test done is low.

20.3. The false positive rate for lateral flow tests is lower for students and children than for the general population with only 0.06% of secondary school children testing positive.[191]

20.4. For a school of 1000 children every round of testing will result in 6 false positive results. If testing is repeated twice weekly that will result in 1000 false positive results in a 14 week term.

20.5. We agree with Prof John Deeks that the vast majority, if not all positive tests in the UK in schools were false positives (see figure 35).[192]



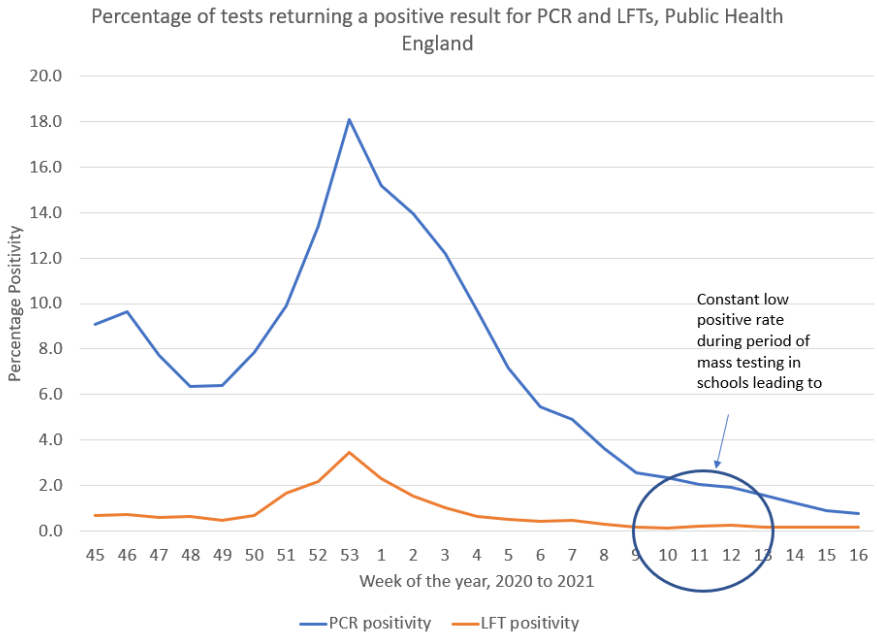



**Figure 35: Top graph, number of cases diagnosed by PCR and LFT showing clear spike on school return. Bottom graph, percentage of tests done that were positive showing that the spike was induced by increased numbers of tests not an increase in positivity (Public Health England data).**[193]

20.6. The problems with mass testing were illustrated by a Cochrane review:[157]

*"In people with no symptoms of COVID-19 the number of confirmed cases is expected to be much lower than in people with symptoms. Using summary results for SD Biosensor STANDARD Q in a bigger population of 10,000 people with no symptoms, where 50 (0.5%) of them really had COVID-19:*

*- 125 people would test positive for COVID-19. Of these, 90 people (72%) would not have COVID-19 (false positive result).*

*- 9,875 people would test negative for COVID-19. Of these, 15 people (0.2%) would actually have COVID-19 (false negative result)."*

20.7. The same Cochrane review of antigen testing concluded:[157]

*"At 5% prevalence using data for the most sensitive assays in symptomatic people (SD Biosensor STANDARD Q and Abbott Panbio), positive predictive values (PPVs) of 84% to 90% mean that between 1 in 10 and 1 in 6 positive results will be a false positive, and between 1 in 4 and 1 in 8 cases will be missed. At 0.5% prevalence applying the same tests in asymptomatic people would result in PPVs of 11% to 28% meaning that*

*between 7 in 10 and 9 in 10 positive results will be false positives, and between 1 in 2 and 1 in 3 cases will be missed."*

20.8. The cases seen in school aged children when schools reopened at the beginning of March disappeared again once schools closed and mass testing ended. There was no spread to other age groups as would be expected if these were true positive results of infectious cases (see figure 36).

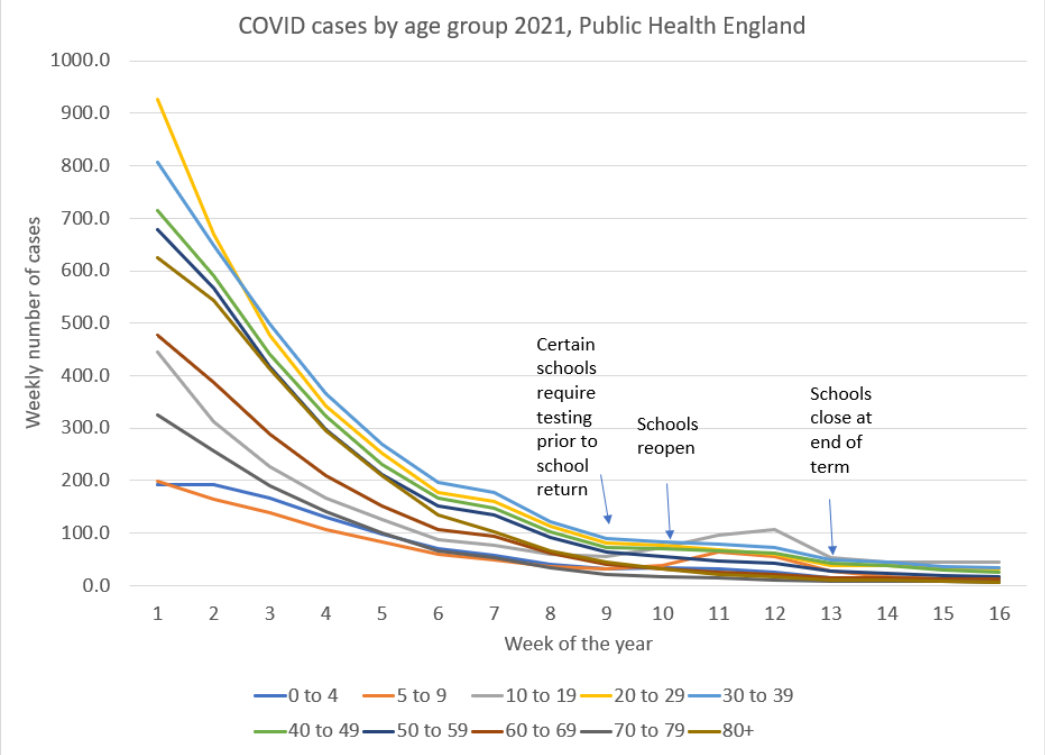



**Figure 36: COVID cases by age group in England 2021 from Public Health England data.**[193]

20.9. In Conclusion, Lateral Flow antigen tests could be a useful test for symptomatic patients. However, their use in mass testing of asymptomatic populations will results in substantially more errors than correct diagnoses. Although the false positive rate is low, the consequences of false positive results cause unnecessary harm when used on an asymptomatic population, from causing health and social care staff to isolate leading to understaffing to shutting schools.

## 21. Effects of Variants on PCR testing

21.1. Viruses mutate all the time and are under constant evolutionary pressure. Common cold coronaviruses are thought to have crossed from animal hosts to humans, starting a pandemic e.g. the Russian Flu of 1889, before evolving to become relatively trivial common colds.[194]

21.2. The word 'variant' means a mutation that is of no clinical significance[195] i.e. it has not been shown to be more transmissible or more deadly.[196] Were either to be shown then it would be named a new 'strain'. These terms and their meaning are currently being conflated.

21.3. There is evidence that results of tests from patients with new variant COVID, B.1.1.7, in the UK, have a lower Ct value.[197] From this, it was concluded that there was more virus in the sample. People have then extrapolated from that finding to say it is more transmissible, thinking that more virus in the airway should lead to more infections in people around them. Another valid interpretation is that, in order to reach the same level of symptoms in order to get tested in hospital, more virus is needed i.e. it is less disease inducing. Test results have led to confusion here as high Ct value results, interpreted as having a low viral load, may have been false positives. Although it seems intuitive, animal studies on other respiratory viruses,[198] have shown no correlation between viral load and transmissibility and showed that repeated exposure to low viral doses can cause disease.[199] Viral replication results in exponential growth, so even a small initial dose can rapidly result in significant numbers of viruses.[200] This means viral load works best as a measure of the course of infection.

21.4. There is no evidence of the new, B.1.1.7 variant being more deadly.[201] [202] A Nature paper that was much reported in the media, claimed there was an increased mortality. However, they did not control for comorbidities, a significant risk factor for deaths.[203]

21.5. Over time viruses mutate and dominant variants will change. The dominant variant changed in Summer 2020, shown in studies on the prevalence of the new variant and its transmissibility.[204] Cases were falling or remained low at the time.

21.6. Variants are identified by genomic sequencing allowing comparison of the sequence to the original sequence provided by Chinese Scientists. There is a relationship between how much sequencing a country carries out and the likelihood of finding a variant in that country.

21.7. The 'UK' variant, B.1.1.7, was first identified in the UK at the end of October 2020. By the last week of November or first week of December, it had been identified in almost every country internationally.[205]

21.8. By 30th July 2020, there had been over 5000 variants identified out of 46,723 viruses sequenced in one study.[206] A separate study demonstrated over 350,000 variants in under 49,000 samples.[207]

> *"All major clades* [families of variants] *in the global diversity of SARS-CoV-2 are represented in various regions of the world, and the genomic diversity of SARS-CoV-2 in circulation in different continents is fairly uniform."*

21.9. The current variants have 23 base pair mutations out of approximately 30,000 base pairs, so 0.08% of the base pairs are different from the original Wuhan sequence.[208] If there was a significant change in shape, then protein would fail functionally and the virus would die. Small changes in shape should not affect immunity, as each individual's immune system recognises numerous areas on each protein. The immune system does not recognise sequences but, instead, recognises the shape of the proteins that the sequences code for. Immune individuals recognised around 17 different sites on the SARS-CoV-2 virus with the population as a whole recognising over 100.[209]

21.10. The UK variant had mutations in the S-gene which codes for the spike protein. The mutation happened to be in the region of the primers or probes such that the S-gene of the TaqPath test used in some British laboratories failed. However, the other two genes tested for continued to work and no alteration was made to the testing, as the variant was still detectable. In fact, the manufacturers used the fact that the absence of the S gene could identify the variant as a selling point.[210] Canadian laboratories did not include the S gene as part of their testing (see 14.5). Therefore, PCR testing did not need to change to detect COVID, but whole genome sequencing is needed to distinguish the presence of a variant.

21.11. Variants can become dominant from evolutionary selection pressures or just randomly, as certain outbreaks prosper and others die away. The first three variants to make headlines arose in countries that carried out vaccine trials: UK; Brazil and South Africa. Subsequent variants have emerged on vaccine rollout e.g. India, Colombia, Philippines, United States. This may or may not be a causal relationship. Others have postulated a relationship to lockdowns.[211]

21.12. The UK variant was said to have caused the winter surge in COVID seen across the UK. During this period, the ONS estimated that the new variant (B.1.1.7) was the predominant strain in England, but that was not the case for the devolved nations where the old variant was still predominant. In the first few days of 2021, at peak cases, the ONS estimated that in the last week of December, the new variant was the cause of 60% of COVID cases in England; 39% in Northern Ireland; 29% in Scotland and only 17% in Wales.[212] Despite this, and despite Wales having had their highest ever levels of disease in November and December, the decline in cases was reversed in mid-December and all devolved nations had a winter peak in line with England, but driven primarily by the old variant, not the new one (see figure 37).

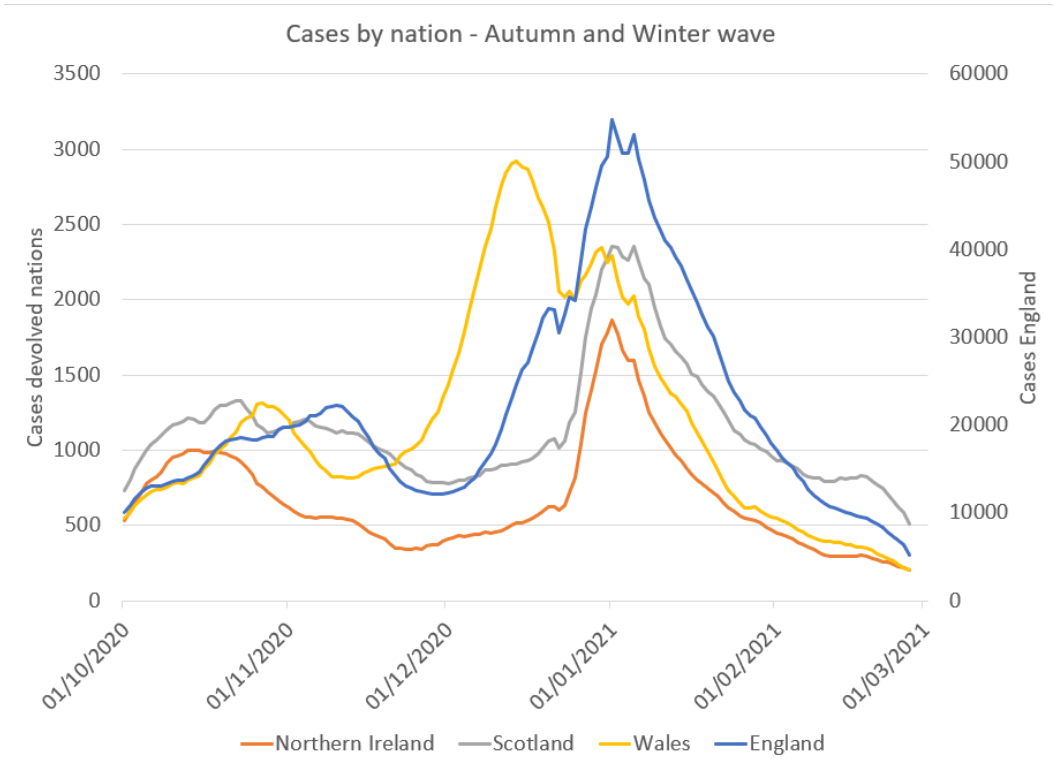



**Figure 37: Daily case numbers by nation for autumn and winter 2020.**[213]

21.13. The UK variant, B.1.1.7, was predominant in Florida in February and March 2021 and was spreading as cases dropped sharply.[214] The fact that a variant was making up a larger proportion of cases could be due to chance alone and it is the diminishing number of total cases that is what is of importance to public health.[215]

21.14. A variant with increased transmissibility leads modellers to predict sharp rises in cases. Cases rising when levels of a new variant are low and then falling as the new variant becomes predominant, does not support a position of concern about the transmissibility of that variant.

21.15. If testing failed because of a variant, then adjustments to the primer and probe sequences to detect the variant could be quickly made. Many commercial companies already have specific PCR tests on the market designed to detect particular variants.[216] The PCR-based detection of SARS-CoV2 can easily be adjusted to detect variants but would remain subject to the same possible problems and biases in PCR-testing as discussed in this report.

## 22. Interpretation of recent synchronous rises in cases and deaths

22.1. Synchronous rise in cases have been seen in every region of UK in December 2020 and in every Canadian region from March 2021. An infectious disease usually spreads from region to region with remote regions being affected last, so this pattern is odd. With COVID a regional pattern was seen and areas affected last and least in spring 2020 were the ones most affected in Autumn 2020.[217]

22.2. One interpretation is that a change in the laboratory testing that affected all regions would have led to an artefactual rise. The fact that we saw a simultaneous peak and fall across four continents in January 2021 supports this hypothesis (see section 17.15).

22.3. However, the synchronous rise in the UK coincided with the start of the vaccination rollout. No-one would predict a vaccination programme to lead to an increase in cases of the disease which it is intended to prevent. Nevertheless, given the coincidence, this explanation requires further exploration.

22.4. Figure 38 has been plotted to show the positivity rate (percentage of positive tests) as a percentage of what the rate was in that region on 1st January 2021. This is a way of comparing all regions fairly as differences due to demographics, population density, level of immunity from previous infection and other factors will be equalized using this method. The percentage of tests that were positive varied by region and in Spring and Autumn 2020 these values varied geographically, as COVID spread from one region to another. However, in winter the rise was synchronous. Figure 39 shows the positivity in Canada by region plotted as a percentage of the rate on 15th April 2021.

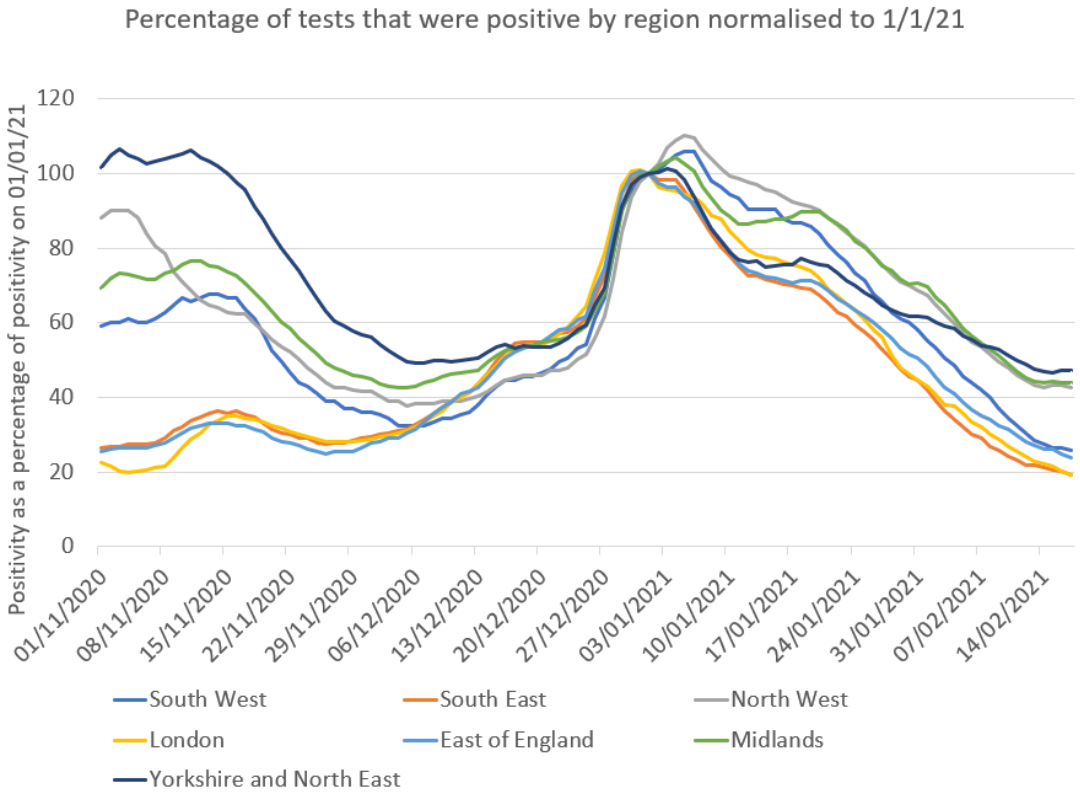



**Figure 38: The positivity rate by England regions plotted as a percentage of the rate on 1/1/21**

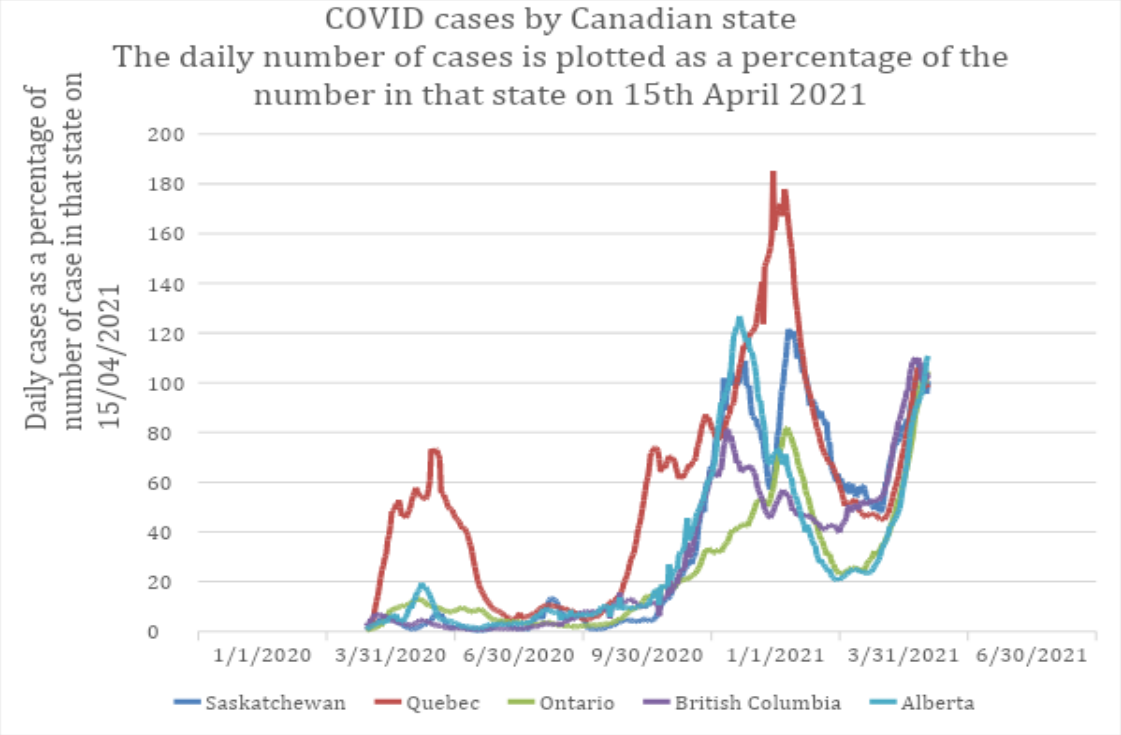



**Figure 39: The positivity rate by Canadian regions plotted as a percentage of the rate on 15/4/21**

22.5. **Simultaneous rise in COVID seen in most remote parts of UK**

Natural infection spreads regionally with remote places usually being affected last. However, after vaccine rollout, rates rose simultaneously in the most remote parts of the United Kingdom. Cornwall and the Isles of Scilly are in the South West corner of the country; the Isle of Wight is off the South Coast; the Shetland Islands are off North East Scotland and the Isle of Anglesey is in North Wales. Vaccines began everywhere on 8th December and escalated thereafter.

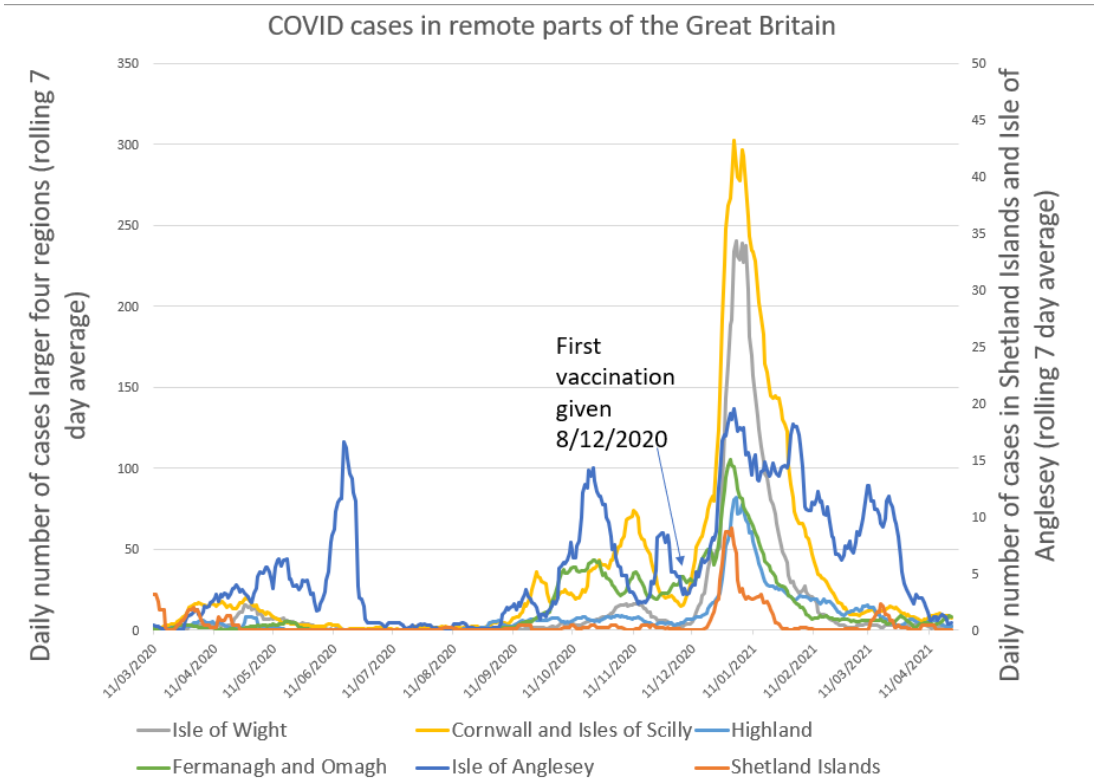



**Figure 40: Reported case numbers over time in remote regions of Great Britain.**

22.6. Vaccination with a traditional whole-virus inactivated vaccine has the potential to cause a false positive PCR result. However, the vaccines currently in use make use of mRNA or DNA to cause the patient's cells to express SARS-CoV-2 spike protein. Genetic material for this gene is therefore present, but no test relies solely on this gene in order to call a positive result. Therefore, vaccination alone would not directly result in a higher false positive rate.

22.7. Vaccination is designed to increase immunity and the trials and subsequent data do show a tentatively promising decrease in hospital admissions with the effect starting about two weeks after vaccination.[218]

22.8. In the first two weeks after vaccination, there is a rise in symptomatic COVID cases among the vaccinated. Normally vaccination should have the opposite effect.

22.8.1. Data submitted by Pfizer to the FDA after the first trial showed that there were 40% more people with "suspected COVID" in the vaccinated group than the placebo group in the first week of the trial.[219]

22.8.2. A separate Israeli study reported a doubling in daily incidence until about day 8 post Pfizer vaccine.[220]

22.8.3. A Danish paper showed a 40% increase in the vaccinated in the first two weeks, despite the bias created from not vaccinating homes that had outbreaks.[221]

22.8.4. A Public Health England study noted a 48% increase in COVID in the vaccinated arm in the first 9 days after vaccination.[222]

22.8.5. A study in Israel showed that 0.54% of healthcare workers developed symptomatic COVID up to 10 days after Pfizer vaccination.[223] They did not disclose the rate for unvaccinated healthcare workers. As SARS-CoV-2 is infectious, and at herd immunity 40% of the population would remain susceptible, this small percentage of additional infections could have a significant impact.

22.8.6. Other publications on the AstraZeneca vaccine as well as the Pfizer-BioNtech vaccine have been, at best, obtuse on infection rates in the first week after vaccination.[224] [225]

22.9. A report from the UK Government demonstrated a 400% increase in positive PCR results immediately on vaccination.[226,227]

22.10. Most other vaccine programmes have not been reported to increase rates of the disease they are meant to prevent. Live polio vaccination did cause polio cases.[228] However, the COVID vaccines themselves do not contain live virus, so the association cannot be a direct one, unless some batches are contaminated with virus.

22.11. Pfizer vaccination reduced lymphocyte white blood cell numbers for the first three days after vaccination.[229] AstraZeneca reduces neutrophil white blood cell numbers.[230] A possible mechanism for these findings is that COVID vaccination causes suppression of immunity, which leads to increased susceptibility to infection. The mechanism that causes the increased COVID rates after vaccination may or may not be related to this fall in white blood cells. The evidence of higher COVID rates after vaccination remains a fact that has been measured in multiple different studies, even if we do not understand the mechanism for that relationship yet.

22.12. There have been reports from Israel of reactivated herpes Zoster infection causing Shingles after vaccination. Chicken Pox, caused by herpes Zoster virus, is never totally eradicated from the body but lies dormant. Immune suppression can lead to reactivation in the form of Shingles. The Israeli study included 491 vaccinated individuals and 99 controls who were women aged 36 to 61 years old.[231] There were 6 cases of Shingles in the vaccinated group and all occurred in women under 61 yrs of age. Five reported Shingles symptoms within two weeks of the first vaccine, with a further case after the second dose. The incidence in the first two weeks after the first dose was 1% of the patients vaccinated. The expected incidence for this age group in that time period is 0.02%.[232] Therefore the infection rate was 50 times higher than expected. This indicates that the immune suppression post vaccination is of practical importance and that the **ability to protect from viral infection** is lost, in at least a proportion of individuals.

22.13. A UK publication by International Severe Acute Respiratory Infection Consortium - Coronavirus Clinical Characterisation Consortium, demonstrated that the mortality in the first 20 days after vaccination was higher for every vaccination priority category including the health under 50 year olds.[226]

22.14. Vaccines suppressing immunity could explain aspects of recent waves that have been attributed to new variants. Immunosuppression leads to increased susceptibility to and severity of respiratory viral infections.[233] Immunosuppression could lead to the impression of COVID being, more transmissible, having a shorter period from cases to deaths, causing reinfection of people who had been previously immune and could turn a decline in cases into a new surge despite high levels of background immunity. It is therefore important that potential vaccine effects are investigated before attributing such negative consequences to changes outside of human control. The evidence that vaccination causes immune suppression is not overwhelming at this stage and therefore it is only a hypothetical mechanism not a confirmed one (see section 22.10).

22.15. Striking correlations can be seen between vaccine rollout and increasing COVID positivity and COVID deaths across the world. While correlation does not equal causation, if this were a coincidence, we should see some countries where COVID positivity and deaths were coincidentally falling when vaccinations were started, but these examples are elusive, although, United States and Panama, and possibly Canada, in February and March 2021, may be exceptions. However, Panama has a daily rate of administration of

less than 0.5 doses per 100 people, which may be insufficient to see an effect. Australia and New Zealand have not seen a rise in COVID cases and deaths with their vaccine rollout so far. Both nations are vaccinating at a rate of well under 0.5 vaccinations per 100 people per day. United States has seen a plateauing of case which were falling in line with the United Kingdom and South Africa but then plateaued from mid-February. Certain individual states within the United States show a similar picture of increased cases on vaccine rollout e.g. Texas, Alabama, Arizona, California. South Africa has carried out only minimal vaccination and cases remain under control there. There are three observations from the data that are notable:

a) time from vaccine rollout to a return to baseline death levels;

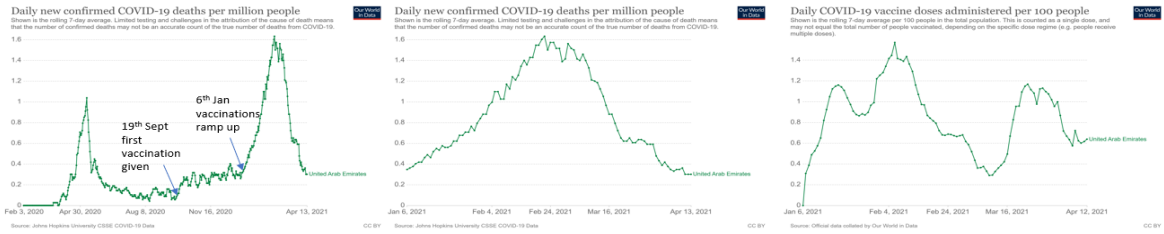
b) Israel compared to Palestine;

c) falls in deaths when vaccine rollout slows.

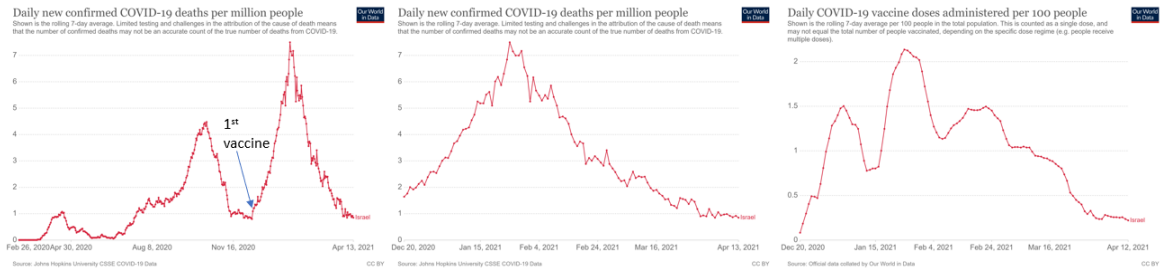
22.15.1. **Time from vaccine rollout to a return to baseline death levels**

For those countries that have had extensive vaccination programmes, there was a significant rise in deaths before a fall. After vaccine rollout, COVID deaths did not return to pre-vaccine levels for 12 weeks in Israel, 16 weeks in the United Arab Emirates, 11 weeks in the UK, 14 weeks in Ireland and 8 weeks in Portugal (see figure 41).

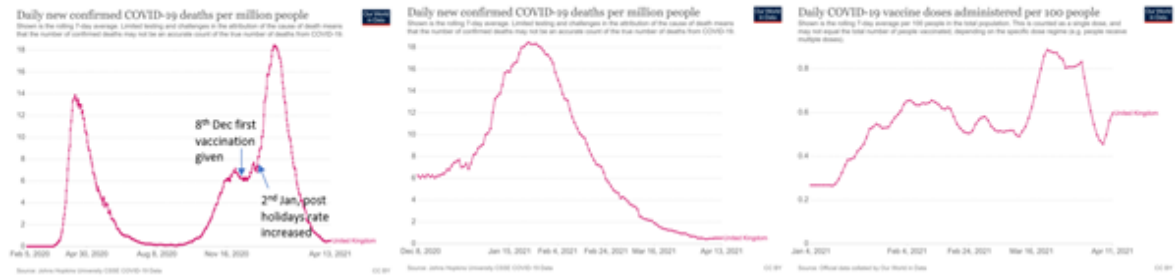
UAE



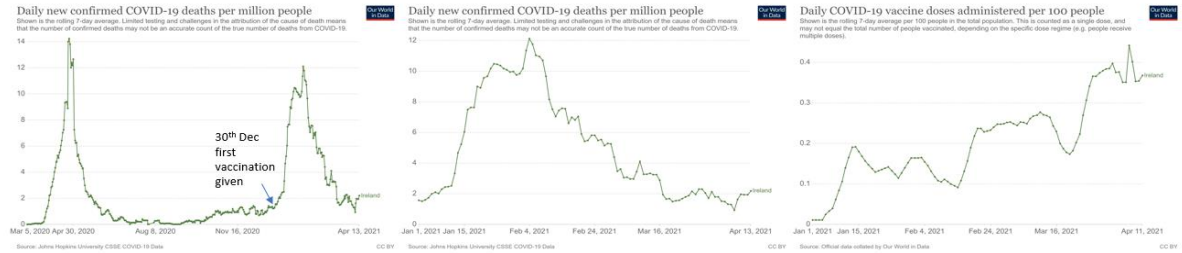
# Israel




# United Kingdom




# Ireland




# Portugal

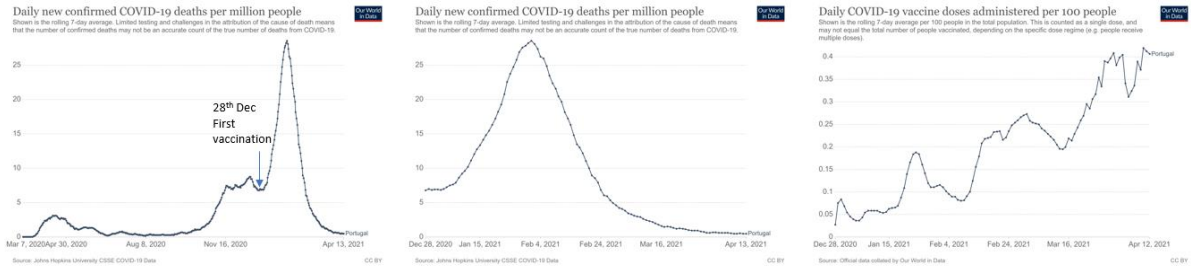



**Figure 41: Data for five countries that have passed peak deaths since vaccine rollout: Israel; United Arab Emirates; United Kingdom; Ireland and Portugal. Sets of three graphs showing on left, all COVID deaths per million people since Spring 2020; in centre COVID deaths since vaccine rollout and on right, vaccine doses given per 100 people.**[2]

22.15.2. **Israel compared to Palestine**

When vaccination was rolled out in Israel, deaths were falling in Palestine. Deaths rose and continued to rise for five weeks in Israel after vaccination began. Deaths fell and remained low in Palestine during this period until a slow start to vaccination in East Jerusalem, when deaths plateaued. Deaths rose from the beginning of March 2021 when larger numbers were vaccinated (see figure 42).

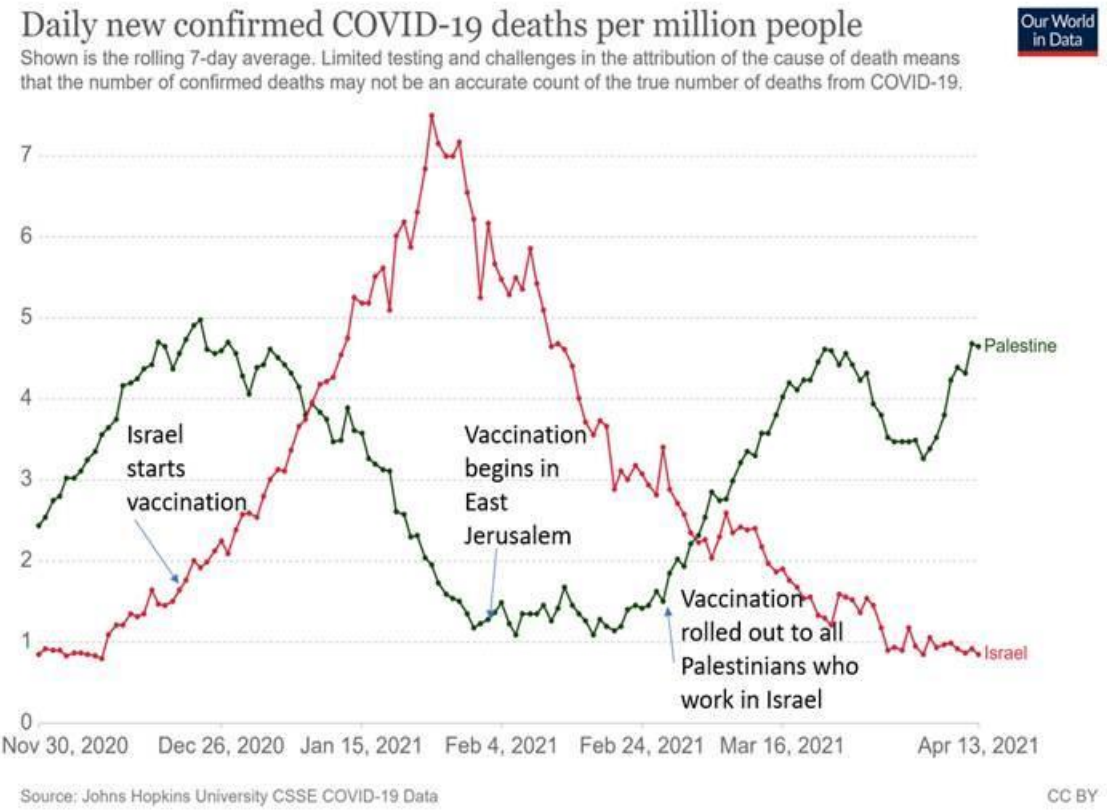
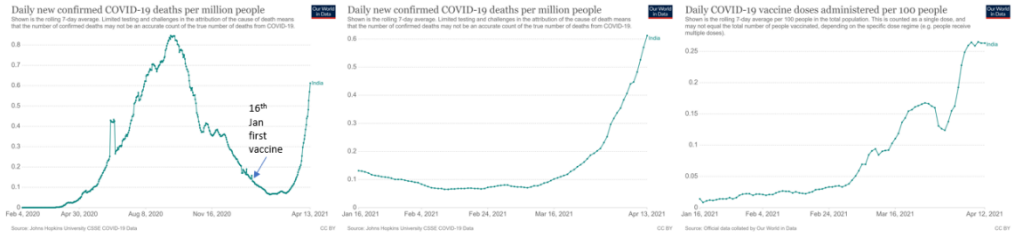
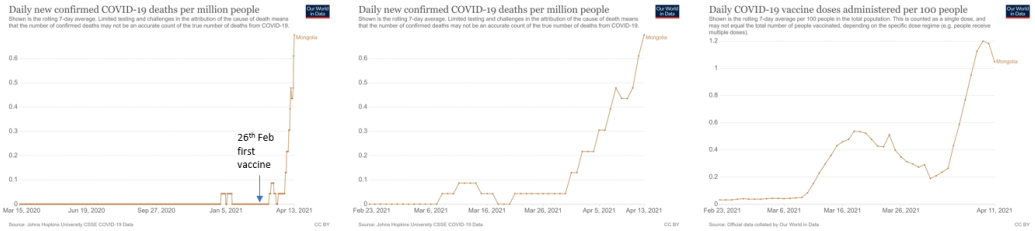



**Figure 42: COVID deaths in Israel and Palestine since November 2020.**[2]

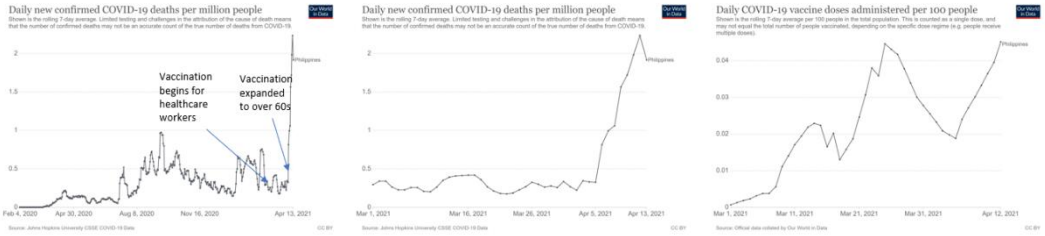
India




Mongolia




Philippines




Uruguay

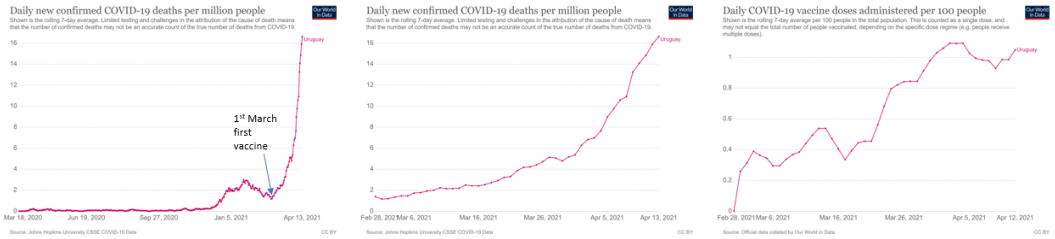
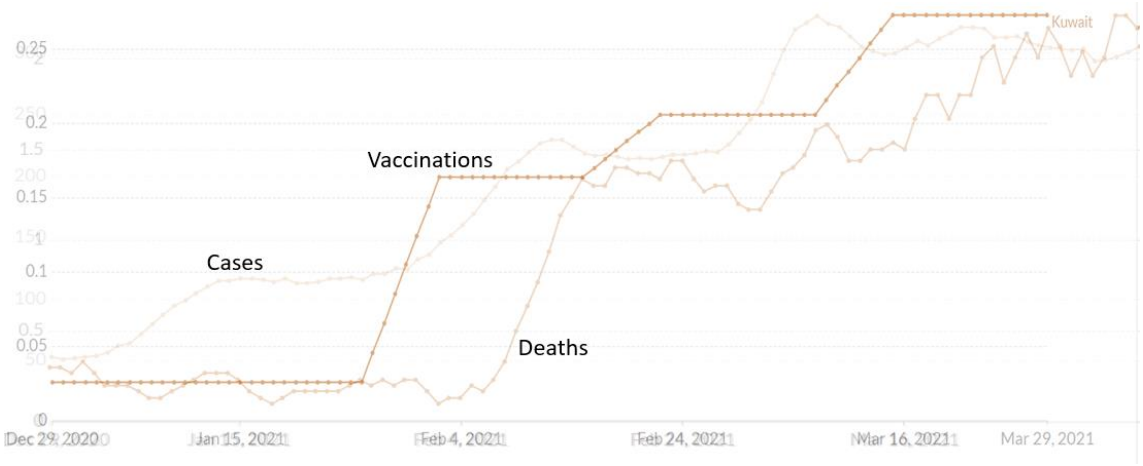



**Figure 43: Data for five countries that had a later vaccine rollout and have not yet seen a significant decline in deaths since vaccine rollout: Hungary; India; Mongolia; Philippines; Uruguay. Sets of three graphs showing on left, all COVID deaths per million people since Spring 2020; in centre COVID deaths since vaccine rollout and on right, vaccine doses given per 100 people.**[2]

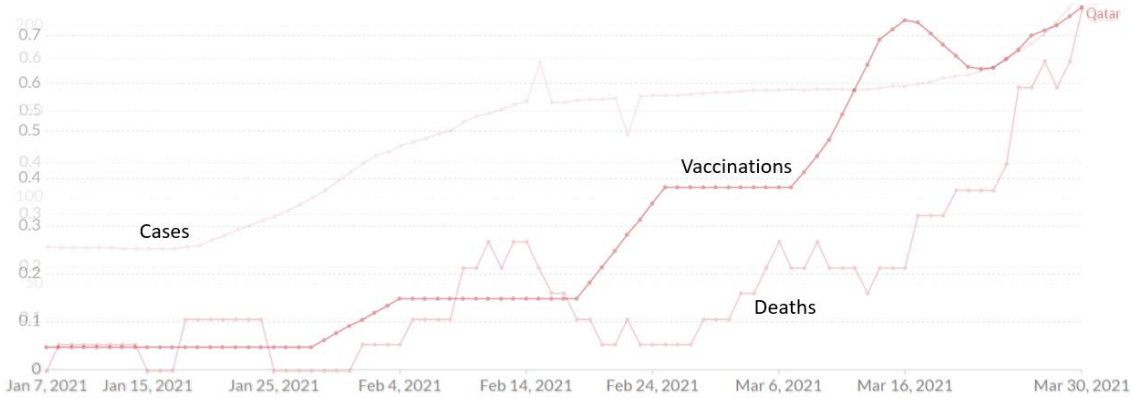
22.15.3. **Falls in deaths when vaccine rollout slows**

Looking closer at particular countries, the COVID death numbers fall when vaccine rates slow. There is a closer relationship in some countries between COVID deaths and vaccination than alleged COVID cases. However, there are examples of countries with erratic vaccination rates where the death rate is smoother and more closely follows the alleged cases, e.g. Columbia, Turkey. Correlation does not equal causation; however, in the context of other data on the effect of vaccinations on COVID, these findings are noteworthy.

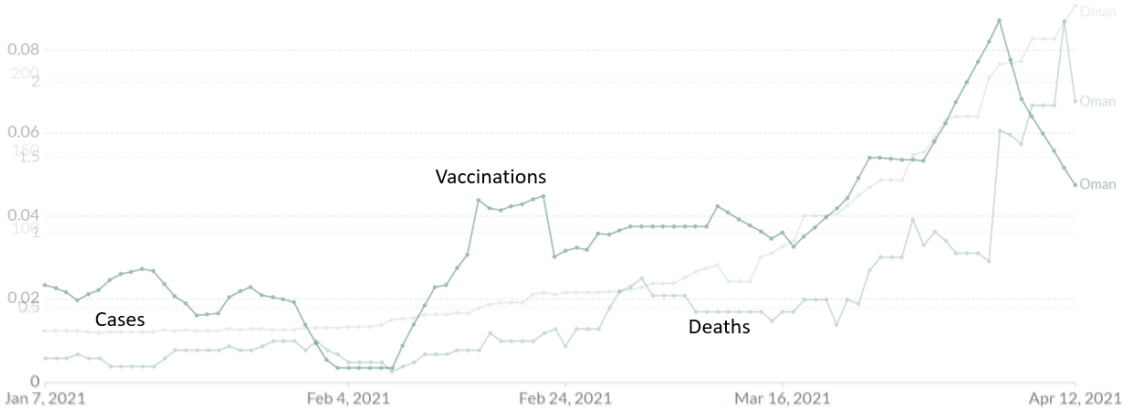
**Kuwait**




**Qatar**



**Oman**




**Sri Lanka**

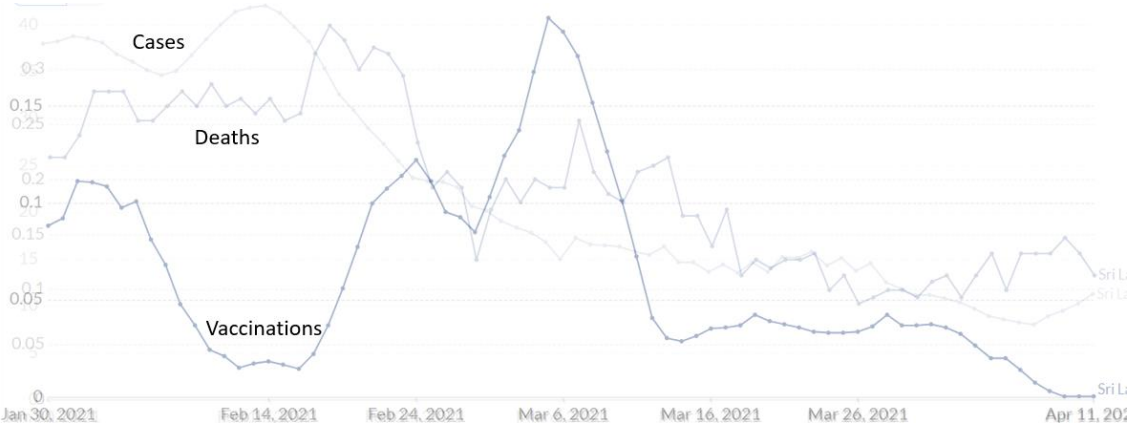



**Figure 44: Examples of countries where COVID deaths closely follow vaccination numbers. Graphs from Our World in Data for alleged cases, deaths and vaccination overlaid.**[2]

22.16. There are a number of countries with low or no vaccines rollout, that have seen recent rises in COVID cases. Often these countries are neighbours with countries that have rolled out vaccination and have seen larger rises in COVID cases. Some have said this is evidence that there are other factors at play causing the rise in cases and that the timing of vaccination rollout is therefore coincidental. However, the countries with highest COVID rates in every region are the ones vaccinating the most.

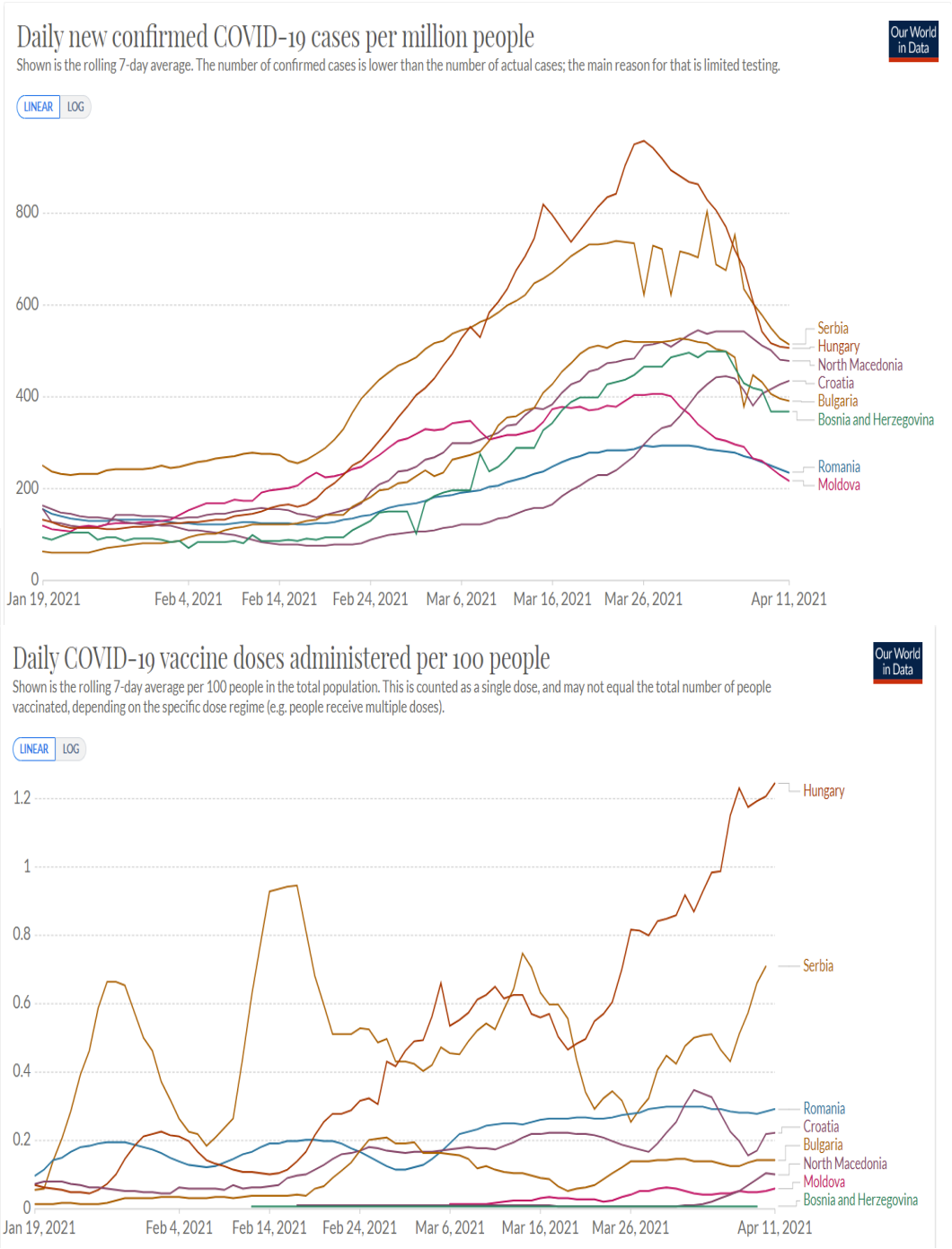



**Figure 45: Reported cases per million population in the Balkans over time compared to vaccine doses administered per 100 people.**[2]

22.17. Canada has low vaccination rates thus far, with daily rates only exceeding 0.5 per 100 people on 8th April 2021. There has been a rise in reported COVID cases following rollout of vaccination and deaths have stopped falling but have not yet risen significantly (Figure 46). The first vaccinations were carried out predominantly in healthcare workers and a small spike in reported cases was seen in early January 2021 (Figure 47). From 16th January 2021 until 13th February 2021, vaccinations plateaued and reported cases fell. However, from February 13th 2021, vaccinations of the over 80s increased and from 27th February 2021 the rate was much higher, with a rise in reported cases following.

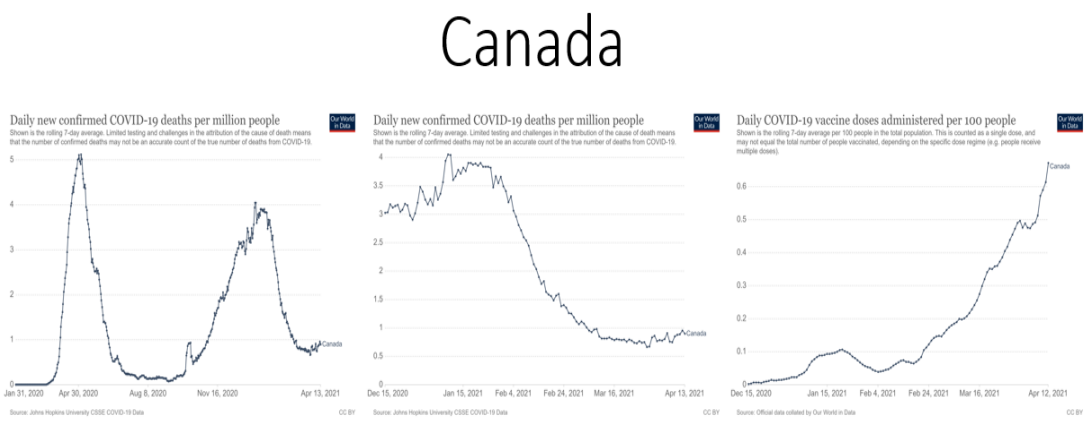



**Figure 46: Canada three graphs showing: on left, all COVID deaths per million people since Spring 2020; in centre COVID deaths since vaccine rollout and on right, vaccine doses given per 100 people.**[2]

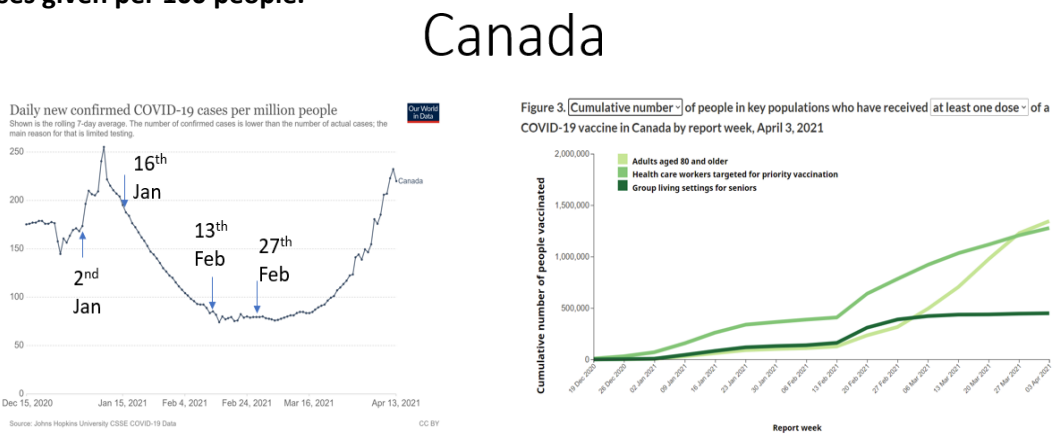



**Figure 47: Graph on left shows reported cases since vaccine rollout began from Our World in Data.**[2] **Graph on the right shows Canadian Government data on cumulative total numbers of vaccines given at each date to different groups.**[234]

22.18. There may have been a rise in genuine COVID in Canada on vaccine rollout. However, with both the current poor case definition and the lack of calibration of and confirmation of testing, it is not possible to assess what proportion of COVID 'cases' in Spring 2021 have been genuine and what proportion have been due to false positive results. Even in the presence of genuine COVID the false positive problem remains and risks of cross contamination between samples will be at their highest.

## 23. Summary

23.12. COVID is a real disease caused by the virus SARS-CoV-2. It causes deaths, but the death rate is much lower than generally perceived, particularly in the young and those with no other health problems. The disease itself has been defined by the test results instead of the other way around. The result of this has been an ever expanding case definition, with increasing numbers and variety of symptoms, and the inclusion of asymptomatic 'cases'.

23.13. There is no perfect diagnostic test, as every test must compromise between finding every possible case and only finding definite cases. A choice must be made as to which of these strategies to prioritise, and that choice must change over the course of an epidemic. A testing system designed to find every possible case will result in positive results for people who have no disease and cannot be infectious, known as false positive results.

23.14. Infected patients can shed viable virus from two days before having symptoms to up to 8 days afterwards. However, after the infectious period, people can continue to shed viral debris, including viral RNA that can result in a positive PCR test for up to 3 months, even though they are not infectious and are perfectly healthy. These post infective false positive results are a significant problem and have been thoroughly studied now. However, they are not the only cause of false positive results, the causes of which are myriad.

23.15. False positive results are inevitable with any testing and will occur at a steady low percentage of tests carried out. When designed carefully and carried out by experts, PCR testing has a low rate of false positive results. Even in these circumstances, when there is

minimal real disease present, false positives can be a significant problem. The less disease around, the higher the proportion of the positives that will be false positives. When there is no disease, all the positives, by definition, are false positives.

23.16. Although a strategy and test designed to find every possible case is justifiable at the outset of an epidemic, once peak deaths have been passed, the strategy and test design must be changed. A failure to institute such a change will result in a false positive problem. At an extreme, there have been situations of false positive results accounting for 100% of positive results in false positive pseudo-epidemics. Viruses do not disappear (with the important exception of SARS1) and a novel virus will become endemic, attacking the vulnerable in the winter, when immunity wanes. The lack of excess deaths indicates that at least the majority of 'deaths' diagnosed in winter were false positive test results. Other evidence presented here indicates that the vast majority of 'cases' diagnosed as COVID were false positive test results. In the absence of a change to the testing it is reasonable to assume the problem has continued and remains.

23.17. PCR testing is carried out by amplifying the material present before testing. Therefore, the tiniest fragments of material can trigger a positive test. This is true for all PCR, but the design of the test for SARS-CoV-2 PCR includes numerous other ways which predispose to false positive results.

23.18. To avoid errors, including false positives, tests need to be calibrated against a gold standard, in this case viral culture. Every laboratory carrying out the testing for SARS-CoV-2 with the PCR test should have carried out such calibration work which does not seem to be the case in Canada, including in Quebec and Ontario. Such work has only been carried out by a handful of laboratories and, every time, they have exposed significant problems with false positive results.

23.19. The majority of false positive results could be avoided by using a lower cut off e.g. a Ct Value of 25 or less, for calling a positive test. In Canada, including in Quebec and in Ontario, laboratories continue to use a high cut off, despite evidence that no viable virus can be found at these high levels and there is no risk of viral transmission. Further, false positive results could be avoided by ensuring that several SARS-CoV-2 genes test positive. The more genes included in the test, the less likely a false positive result would be

reported. Laboratories in Canada, are still using protocols in which only one or two genes are tested for.[87]

23.20. Further, false positive results could be avoided by the judicious use of internal controls. These should include using negative swabs, preferably containing human DNA and DNA from non-COVID respiratory viruses, and passing them through the whole testing process, from specimen reception onwards, to ensure there is no cross contamination. External quality assurance checks should use similar procedures.

The false positive problem is evidenced by the following. After the spring of 2020, the characteristics of the patients diagnosed as COVID reverted to levels expected in the general population, and their clinical presentation was no longer that of an acute COVID infection. The small numbers of studies done with confirmatory testing indicate a significant false positive problem with PCR testing and the PCR test results have not been confirmed when testing has been carried out with antigen tests and with antibody tests. Even the deaths diagnosed as being due to COVID are no longer predictive of excess death levels as they were in the spring of 2020. The diagnosis of death is an art and relies on the balance of probabilities based on all the information available at the time. False positive test results can therefore have a large influence on death diagnosis. Misdiagnosis, misattribution of death and over testing the dying have led to missing deaths from other respiratory causes and a higher age at death for COVID deaths than for general deaths. The presence of occasional real cases of COVID does not mean that the majority of 'cases' were not, in fact, false positive results.

23.21. Patients that have been labelled as having asymptomatic COVID are largely people with false positive test results. There is essentially no evidence of asymptomatic transmission leading to a severe acute respiratory syndrome, a pneumonia or anyone needing to seek medical attention of any kind. The evidence of transmission by asymptomatic people is, at best, extremely weak, with only six such people worldwide said to have transmitted infection and only two individuals developing symptomatic disease as a result of contact with someone labelled as having asymptomatic COVID. The symptoms they had were incredibly minor and common, with a runny nose in one patient, and a mild cough for one day in the other. Other papers that purport to show asymptomatic transmission have been based either on a summary of these handful of 'cases' or on modelled data.

23.22. The PCR test is not capable of accurately identifying people with COVID disease, nor people capable of infecting others with SARS-CoV-2. Overdiagnosis by PCR test has led to exaggeration of case numbers and deaths, which, in turn, has led to immense harm, including quarantining, lockdowns and business closures.

23.23. PCR test results have been used to introduce extreme policies that restrict people's freedoms and liberties. PCR testing was the right test to use at the outset of the epidemic, but since peak deaths have been passed, the strategy and technique for using it needed to be changed and has not. Other testing methods, which in conjunction with clinical diagnosis are more accurate, are available and have been underused on symptomatic patients. A body of evidence demonstrates that PCR testing has been used in ways that do not identify infectious cases and yet, people testing positive have been falsely treated as infectious.

23.24. PCR testing has resulted in inflated case numbers and misdiagnosis of deaths, which has created the illusion of a serious COVID epidemic. Concerns about PCR testing creating such false positive epidemics have been raised in the past, but the lessons have not been heeded.

**London, 4th May 2021**

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