Peek-a-Boo Flu

Is viral interference between SARS-CoV-2 and the flu a myth? And if we don't believe the PCR test can diagnose the presence of SARS-CoV-2 why should we trust it to diagnose the absence of influenza?

Mr Law, Health and Technology, Martin Neil, Jonathan Engler, Norman Fenton, and Nick Hudson
3 hr ago

A previous WATN (Where Are The Numbers) post looked into the global disappearance of the flu virus. It found that flu had not actually disappeared but had actually been playing hide-and-seek and could be found hiding in the Hindu-Kush or sunning itself in Haiti. It clearly wasn't hanging around to witness the craziness of the West's response to the new 'novel and deadly' interloper.

This post examines another part of the puzzle - the near-universal acceptance of the explanation for the disappearance of the flu: that it was out-competed by SARS-CoV-2 from Spring 2020 and failed to return until the end of 2021, just after the arrival of the SARS-CoV-2 Omicon variant. It reappeared just as quickly as it disappeared. And it did so globally and with a high degree of synchronicity across multiple countries.

Based on published empirical evidence we think that the explanation that flu disappeared because of competition from SARS-CoV-2 is wrong and, given this fact, we need to look elsewhere for an explanation for flu's disappearance.

Viral Interference

The disappearance of the flu supposedly rests on a well-accepted theory, called viral interference, whereby the circulation patterns of flu, and other viruses, fluctuate and change from year to year and hemisphere to hemisphere. Under this theory we are told to accept that this is the single and only plausible explanation for what happened to flu and that, after many decades of absolute respiratory viral dominance by flu, SARS-CoV-2 was just too fit and potent a competitor for flu to win the fight to occupy people's respiratory systems. This relationship between flu and SARS-CoV-2 has been

likened to a see-saw.

As a result, flu disappeared and only returned after the circulation of the SARS-CoV-2 Omicron variant. This did not just happen with flu but was reported to have occurred with rhinovirus and RSV, which also absconded with the flu but then returned.

The biological mechanisms for viral interference look plausible and have been around since the 1960s. A good review of the various interference mechanisms can be found here, along with a review of results from epidemiological, ex vivo and in vivo studies, which show that sequential or co-infection with one virus can interfere with, and reduce the propensity of, infection by another. It is posited that production of a strong immune response to the first virus prevents other viruses from setting in.

However, it should be noted that even if this phenomenon is accepted as credible (and we do question its evidential basis below), it is surely a huge stretch to suggest that something which appears to happen at an individual level can result in synchronized population-wide suppression of influenza globally, and it doesn't explain how it bounced back.

Empirical evidence for viral interference with SARS-CoV-2

What empirical evidence do we have that viral interference occurs between the flu, rhinoviruses (RV), respiratory syncytial virus (RSV) and SARS-CoV-2?

Piret and Boivin report on two experiments involving sequential infection of flu and SARS-CoV-2 in Syrian hamsters and ferrets but concluded that there was no detectable sign of viral interference. They concluded:

> ……previous infection with SARS-CoV-2 did not affect pH1N1 load in the lungs compared with a single infection…….further studies are needed to clarify the interactions between SARS-CoV-2 and influenza viruses.

Fage et al looked at the replication kinetics and interactions between SARS-CoV-2, A(H1N1) flu, and RSV and concluded that:

> Our results showed that during simultaneous infection, SARS-CoV-2 interferes with

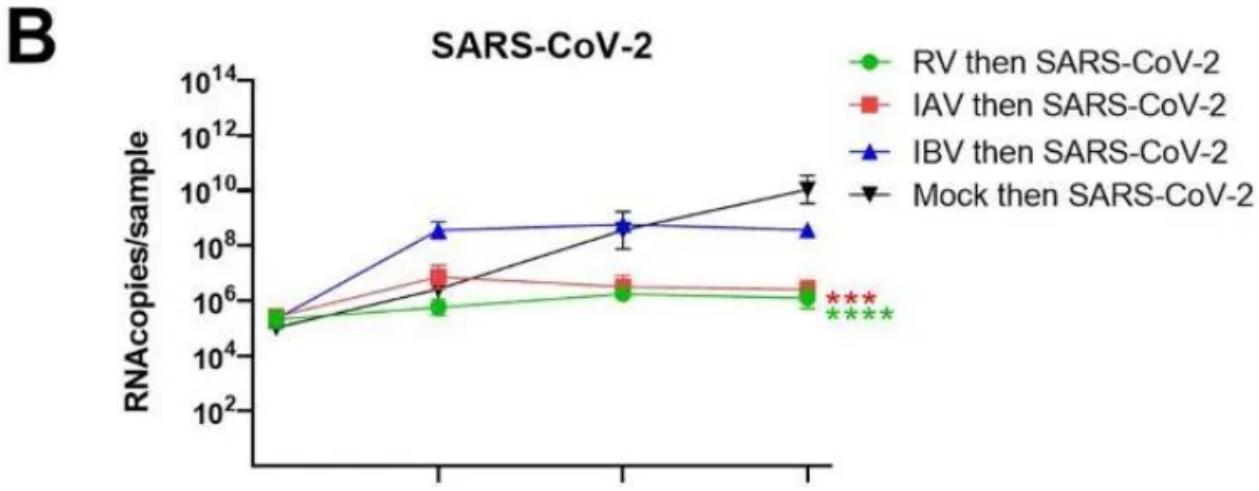
> RSV-A2 but not with A(H1N1)pdm09 replication. The prior infection of nasal HAE with SARS-CoV-2 reduces the replication kinetics of both respiratory viruses. SARS-CoV-2 replication is decreased by a prior infection with A(H1N1)pdm09 but not with RSV-A2.

Replication of influenza A was reduced in the presence of prior infection by SARS-CoV-2 and vice-versa. So, both viruses had some ability to interfere with each other but there is no evidence that it was predominately one way, favouring the dominance of SARS-CoV-2.

Essaidi-Laziosi et al investigated dual infections involving SARS-CoV-2 with RV and Influenza A and B viruses (IAV and IBV), using reconstituted repository airway epithelial cells and stated that:

> We found that SARS-CoV-2 replication was impaired by primary, but not secondary, rhino- and influenza virus infection. In contrast, SARS-CoV-2 had no effect on the replication of these seasonal respiratory viruses.

In the viral interference theory if SARS-CoV-2 was infected first and then followed by another, secondary, infectious agent, we would expect that the effect of primary infection by SARS-CoV-2 would *decrease* the presence of the secondary infection. However, Essaidi-Lazios's experimental results did not match these theoretical expectations. As their charts show what they found was that primary infection by SARS-CoV-2 did not affect the infection trajectory of RV or flus at all.



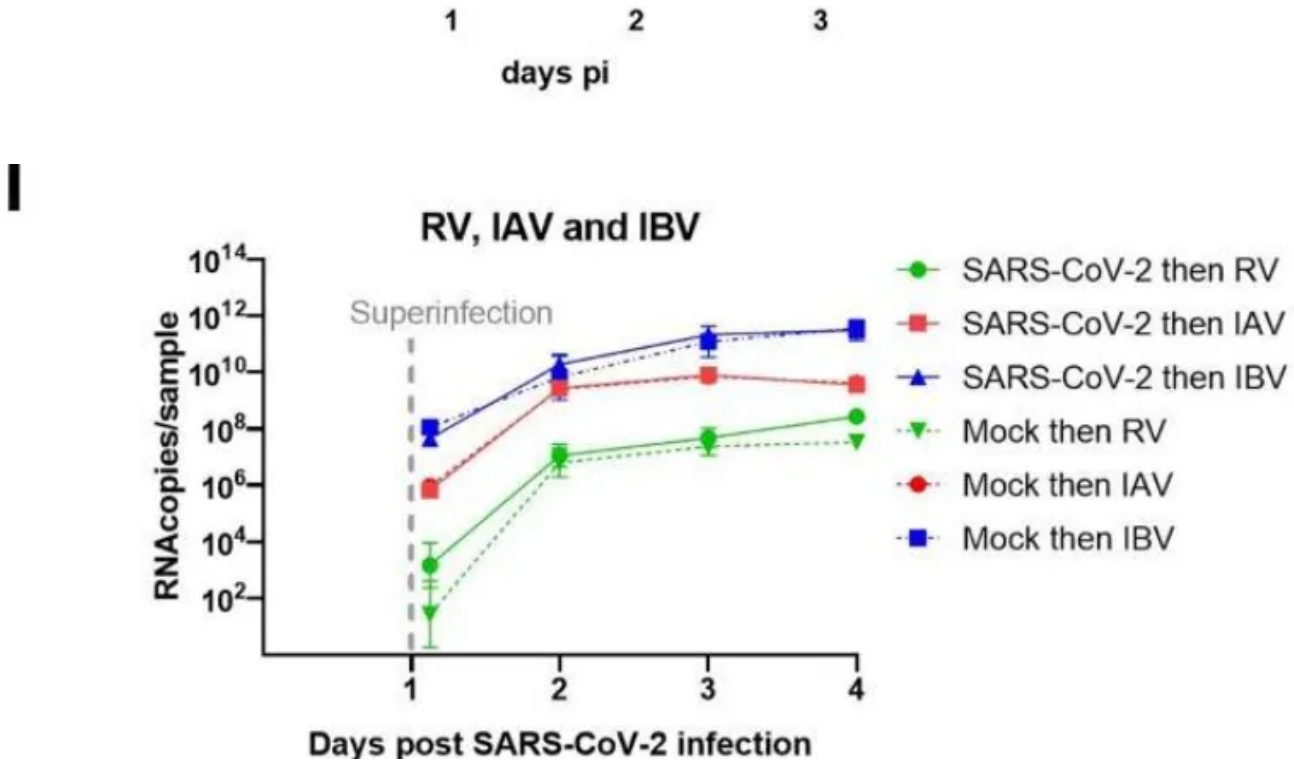


Chart (B) SARS-CoV-2 replication in single infection versus tissues pre-infected by RV, IAV and IBV and mock solution: four experiments each involving secondary infection of SARS-CoV-2 preceded by primary infection by RV or Influenza A or B or a mock solution. The y-axis is the growth in the SARS-CoV-2 virus and the x-axis is calendar days.

Chart (I) RV, IAV and IBV replication in single Infection (dotted lines) and in the presence of SARS-CoV-2 pre-infection (solid lines): three experiments each involving primary infection of SARS-CoV-2 followed by a secondary infection of RV or Influenza A or B. Plus, three experiments with mock solution then infection by RV or Influenza A or B.

(Chart (B) x-axis is a typo in the original paper)

To hammer the point home, they concluded (my emphasis):

> While infecting first with RV, IAV and IBV and then 48 h later with SARS-CoV-2 led to reduced SARS-CoV-2 replication even when inoculated with 2 logs higher

> multiplicity of infection (approximate MOI 0.1 for SARS-CoV-2 versus 0.001-0.002 for seasonal viruses), **no such effect was seen when the order of infection was inverted**, even when the incubation time between the two infections was shortened (in order to establish a co-infection during the exponential phase of SARS-CoV-2 infection). Our results indicate that the sequence of infection events influences the fate of SARS-CoV-2 infection. Regardless the order of infections …, no adaptation was observed in SARS-CoV-2 after co-infection (data not shown).

So, is the theory that viral interference caused the eradication of the flu a myth?

Observational studies

One observational study by Stowe et al reported interactions between SARS-CoV-2 and influenza, and the impact of co-infection on disease severity. They used data for influenza and SARS-CoV-2 collected from England's national surveillance systems between 20 January 2020 and 25 April 2020.

In their paper they conclude two things:

- The risk of testing positive for SARS-CoV-2 was 58% lower among influenza-positive cases and
- Patients with a co-infection had a risk of death of 5.92 (95% confidence interval: 3.21–10.91) times greater than those with neither influenza nor SARS-CoV-2. The odds of ventilator use, or death and intensive care unit admission or death were greatest among coinfected patients.

So here we see lower co-infection rates, but significant numbers of co-infections were indeed discovered. However, the study sampled people who were tested for both influenza and SARS-CoV-2 within 7 days of each other, without recording the order of the tests, so we can conclude little about whether previous infection with SARS-CoV-2 prevented infection by flu.

It is notable that in Spring 2020 there was up to a 10-times higher risk of death in people with a SARS-CoV-2 co-infection with flu. And this correlated with ventilator use. However, with hindsight we now know that, as a matter of protocol rather than genuine health needs, many covid patients were unnecessarily put on ventilators leading to

increased risk of their death.

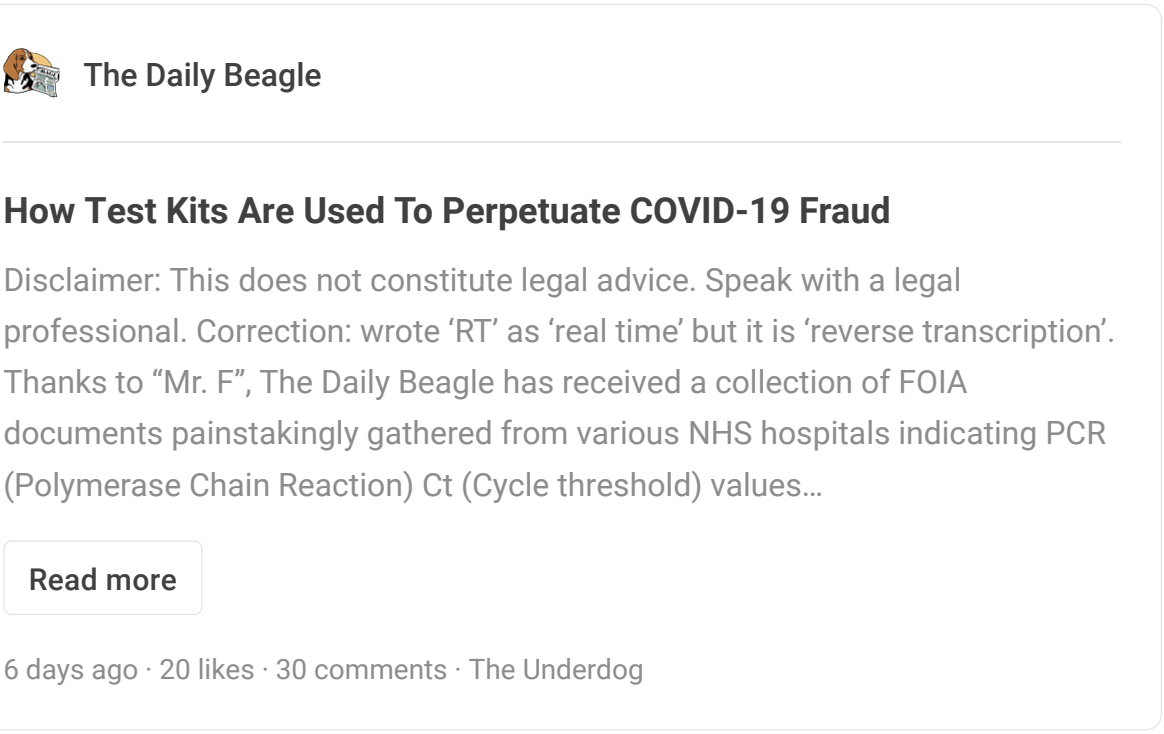
Of course, tracking of both flu and SARS-CoV-2 was routinely performed worldwide by national health bodies. The independent newspaper reported for Public Health England (PHE):

> …of the 685,243 samples that have been reviewed at PHE's laboratories since the first week of January, not a single one has tested positive for influenza. In the week up to 31 December 2020, just one case of flu was confirmed by laboratory analysis.

Think about this. Nearly seven hundred thousand tests and they are all negative, except one. And that single positive was confirmed to be a true positive. So, there was not one single FALSE positive test result. This just is not possible for any test, as it implies a specificity of 100%, zero chance of cross contamination and perfect laboratory conditions, which we know cannot possibly be true.

PCR Testing

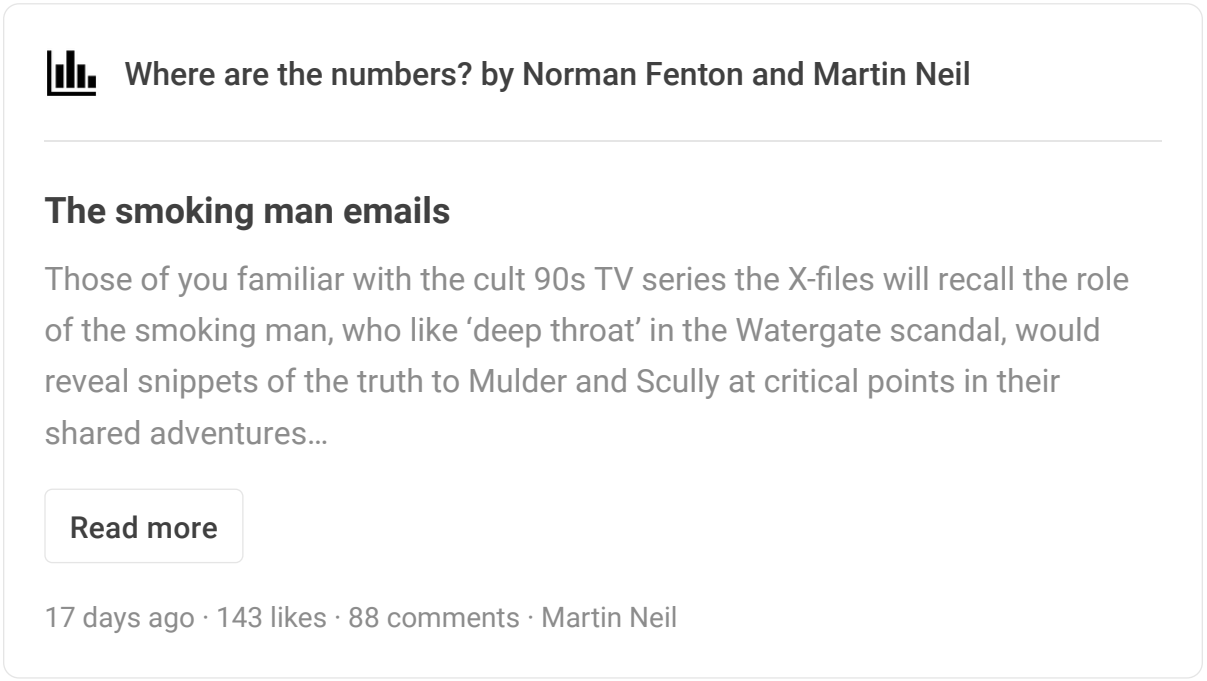
We are all painfully aware of the inaccuracy of using PCR to test for SARS-CoV-2, and a useful review of SARS-CoV-2 PCR can be found here:



Another recent publication by Collateral Global highlights the PCR scandal in the UK. Our interpretation of their conclusions is that PCR testing in the UK is not effectively regulated, and that PCR testing is effectively as opaque as a black box.

Much of the discussion in the Daily Beagle focused on cycle thresholds which might determine whether there is SARS-CoV-2 in the sample or not. But focusing on this alone side-steps questions of cross-reactivity, non-specificity, cross contamination or some outcome synergistic with high amplification. These are central to whether we can determine whether another pathogen (such as flu) might be the actual cause of a false positive test result for SARS-CoV-2.

This article noted that the possibility of cross reactivity with flus, other coronaviruses and bacterial contamination was actually the reality, and this reality was recognised as far back as 2020. However, it appears that the magnitude of the problem was underappreciated and misunderstood at the time.



There is so much PCR kit heterogeneity that it can be difficult to know which PCR test kits can be trusted and which cannot. Some PCR kits claim to be perfectly accurate, with no cross reactivity, such as GeneXpert , GenMark and BioFire. However, in June 2020 this Australian validation of the Beijing Genomics Institute (BGI) test kit reveals a

specificity of 97.5% at one laboratory. Also, this study that appeared in the Journal of Clinical Virology looked at the accuracy of the Australian Diagnostics multiplex kit, which also tests for flus, and found a specificity of 92%.

We should be wary of taking PCR manufacturer data at face value when we know that viruses continually mutate and are a moving target. As they mutate the potential for cross reaction and non-specificity obviously increases and the test, invented at a particular point in time, inevitably become progressively less trustworthy.

The central question about PCR is therefore this:

If we don't believe the PCR test can diagnose the presence of SARS-CoV-2

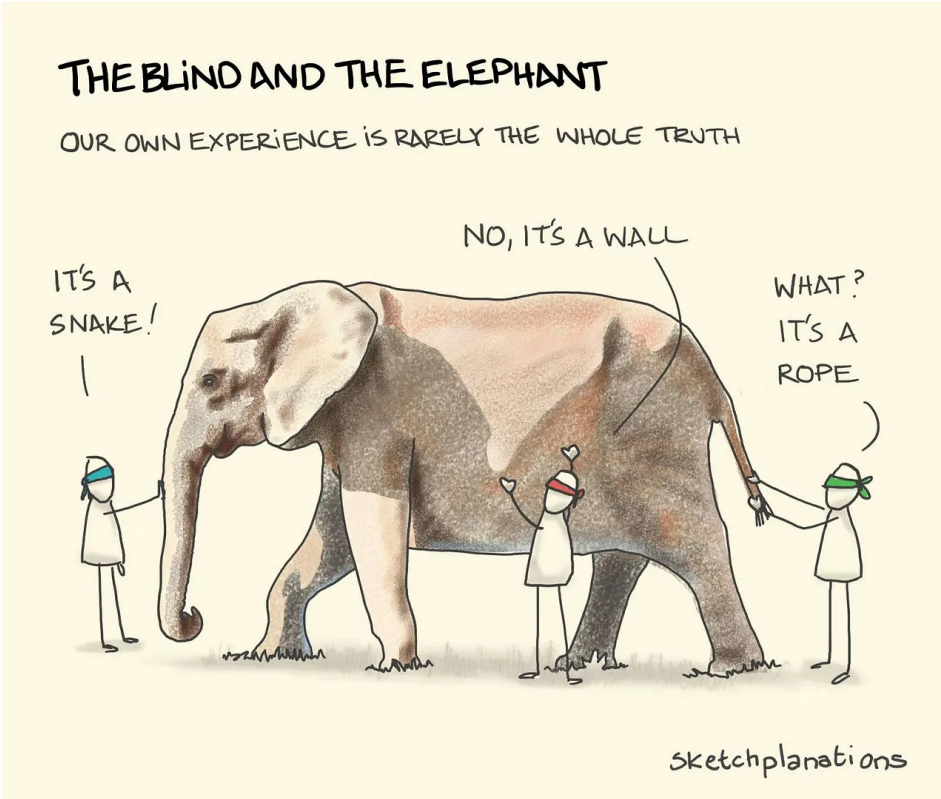
why should we trust it to diagnose the absence of influenza?

Australia in 2020 is used by some as the basis to claim that SARS-CoV-2 PCR kits are perfect as they had a long stretch of 1:10K positivity off-season [1]. In response to an FOI request the ONS deployed the same lazy logic with regards PCR testing in the UK:

"*We know the specificity of our test must be very close to 100% as the low number of positive tests in our study over the summer of 2020 means that specificity would be very high even if all positives were false.*"

The ONS are claiming that because the number of PCR positives were so low in the summer, when SARS-CoV-2 was not circulating, then the tests must therefore be perfectly specific. However, this claim only makes logical sense if the PCR tests undertaken were actually subject to challenge by other circulating viruses or bacteria that had the capacity to trigger a non-specific false positive result. In the absence of a competing challenge then a negative test result would be inevitable and proves nothing. Further, given that both SARS-CoV-2 and the flu circulate during winter then the absence of both in summer would logically lead to a high rate of true negative PCR test results in summer.

To put it another way if SARS-CoV-2 PCR cross reacts with flu then when flu is present during the winter this will generate PCR false positives for SARS-CoV-2. If flu is absent in the summer but other non-seasonal pathogens or contaminants were circulating, that caused false positives, we would observe a high false positive rate during the summer season. The fact that we did not see high false positive rates during the summer logically means that the kits are predominately picking up flu in the winter when it is circulating. We could use similar arguments for cross reaction with other competing winter coronaviruses (which as far as we know continued to circulate and were unaffected by viral interference).



Back in December 2020 we raised the issue of the role of confirmatory testing being done in the summer but not in the winter flu season in the UK. By performing confirmatory testing for SARS-CoV-2 during a period of low prevalence the false positive rate would depress case rates to make the PCR testing look accurate and, when confirmatory testing ceases, it will inflate the SARS-CoV-2 case rate.

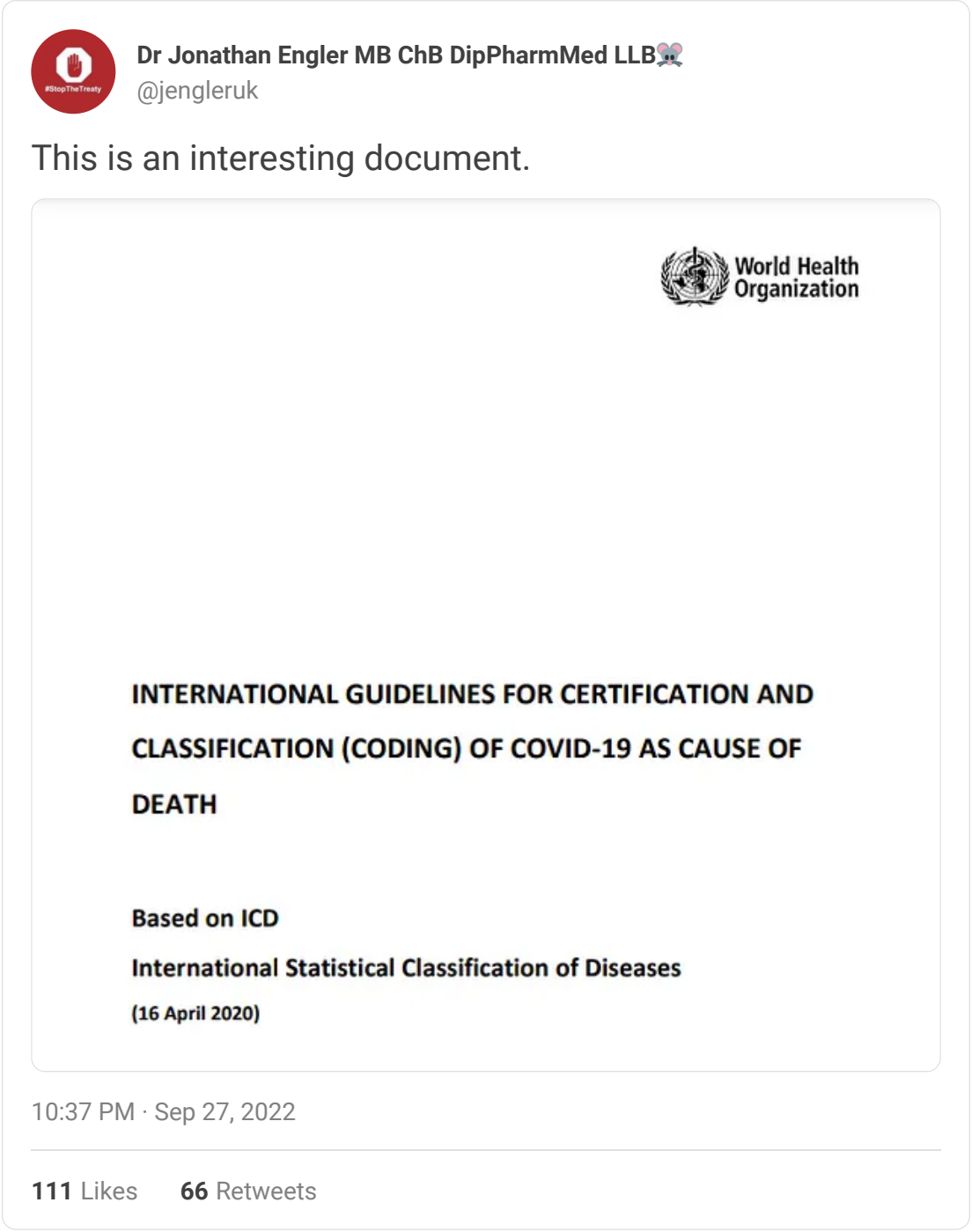
On false positives in COVID19 testing again: we are being misled over confirmatory testing

It has long been claimed that many of the COVID19 'cases' reported (where a 'case' is simply a positive test result) are false positives. This short article addresses an aspect of the problem not widely discussed before and suggests that many of the very large number of new 'cases' reported amid great hysteria each day could be people who do not have CO…

Read more

2 years ago · Norman Fenton

In the early part of the pandemic doctors were incentivised to diagnose SARS-CoV-2, where the symptoms are indistinguishable from flu, for symptoms which would have hitherto been attributed to Influenza-like-illnesses (ILIs). That incentive was achieved by a combination of authoritative diktat by the WHO, who mandated that a respiratory death could be certificated as covid-19 deaths on the flimsiest of grounds, and the all-pervasive fear caused by the ceaseless propaganda about a novel and deadly virus. And this despite the fact that the UKHSA (Health Security Agency) had ruled that SARS-CoV-2 was not a High Consequence Infectious Disease.



PCR Multiplex kits

In early 2020 we assume influenza and SARS-CoV-2 testing was performed by different PCR kits but by July 2020 the CDC approved the first multiplex (multi-virus) kits under EUA to detect both influenzas and SARS-CoV-2. After their near universal global roll-out flu disappeared over winter 2020/21. This may be a coincidence.

It seems to us that single virus, rather than multi-virus test kits, that are sensitive and specific to a single organism, would surely reduce the risk of shared failure modes and common causes of error. Diverse types of PCR kits specialising in the diagnosis of separate and different viruses would reduce the risk of cross-contamination or confusion about whether a positive means a covid positive or an influenza positive or both.

Note that we have not discovered a smoking gun that exposes systemic problems with ALL multi-virus PCR kits. Some of the early PCR kits we know to be unreliable but after the CDC EUA approval of multi-viral kits many were declared to have perfect specificity. We have no idea how and why there was a step change in reliability for these kits, if indeed there was actually any real improvement. In any case, given the huge variety of kits available, of unknown provenance, we cannot simply assume perfection across the board.

There are some potential failure modes worth investigating that might provide some insight into what might be going on:

- Co-infection with both flu and SARS-CoV-2 may occur at the same time. Is a positive for SARS-CoV-2 somehow prioritised by the tests? Perhaps by SARS-CoV-2 masking the existence of flu or the tests showing this?
- Often when people think of PCR they think of a biological/chemical reaction without considering that it takes place within a wider system involving technology, people, procedures and policies. Each and all of these have a potential role to play in generating results and are thus potential sources of systematic or random error. One potential vulnerability is that PCR equipment uses proprietary software algorithms and are connected to the internet. Yet we do not know whether the software is independently audited. Likewise, we do not know whether the chain of custody for samples, or their reporting, is respected. It is therefore not inconceivable that these, and more, vulnerabilities exist in this wider system that might be exploitable.

Clearly, we are speculating here. But things do not add up.

Year	Flu Cases	Covid Cases
2010-2011	21m	0
2011-2012	9m	0
2012-2013	34m	0
2013-2014	30m	0
2014-2015	30m	0
2015-2016	24m	0
2016-2017	29m	0
2017-2018	41m	0
2018-2019	29m	0
2019-2020	36m	0
2020-2021	0	57m

Flu and covid-19 cases in the USA from 2010 to 2021.

Sources: CDC and Our World in Data

Discussion

In theory there is no difference between theory and practice,

……while in practice there is.

Microbiology or virology theory is not our area of expertise hence we have not presented any arguments here rooted in theory. Instead, we have taken the sceptical option and asked - where is the empirical evidence? Anyone, no matter their credentials, can and should be able to ask this question.

We have found there is little empirical evidence that proves SARS-CoV-2 interferes with the flu in a dominant way. Therefore, there is no support for the widespread assumption that SARS-CoV-2 prevents flu's transmission or infection. This is one of the central planks of the covid crisis and it looks to be wrong.

Flu did not globally disappear since we know it was playing hide-and-seek in some far-flung places. If we accept flu was in circulation, then we must entertain the possibility of alternative explanations, not for the disappearance of flu, but for the disappearance of *positive* flu test results, especially false positive results.

Also, recall that flu disappeared simultaneously just as SARS-CoV-2 appeared simultaneously across the globe. The omicron variant of SARS-CoV-2 appeared at the end of 2021, and it did so in near synchronicity across the globe. Coincidentally flu then reappeared and did so simultaneously globally with no evidence of transmission from place to place. The sequence of these events does not concord with another central plank of virology - the idea of viral spread. A seasonal trigger is often touted as an explanation for the synchronous appearance of flu at the end of 2021, yet this does not explain the fact that flu had not disappeared from Haiti, Afghanistan, Pakistan, Bangladesh and Laos.

Despite the similarity of the symptoms of flu with those of SARS-CoV-2 it was, at least initially, the infection fatality rate for SARS-CoV-2 that differentiated it from the flu - its novelty was dependant on its perceived elevated lethality. However, over time the infection fatality rates for SARS-CoV-2 have converged on that for the flu and now the deadliness of one is indistinguishable from the other. Why then do we, three years later, do we consider SARS-CoV-2 to be more novel than flu or any other respiratory viral infection? Given that the symptoms of both overlap to an extent which makes each completely indistinguishable from the other based on clinical presentation, legitimate questions have been raised as to the circumstances that led SARS-CoV-2 to be identified as a novel virus in the first place.