# Executive Summary: COVID-19 29th April 2020



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The Executive Summary is produced weekly and contains in-depth analysis. International SOS publishes a COVID-19 <u>Daily Case Summary</u>.

# **INTRODUCTION**

#### In this week's edition of the International SOS COVID-19 Executive Summary we explore:

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  - An epidemic of firearms-related suicide in the USA?

#### WHAT IS GOING ON IN AFRICA?

"We are at the beginning in Africa," Dr Mike Ryan, the Executive Director of the WHO's Health Emergencies Programme, <u>said last week.</u>

The number of COVID-19 cases in Africa has jumped 45% in the last week and the World Health Organization (WHO) warned that the continent of 1.3 billion people is poised to potentially become the next epicenter of the highly infectious and deadly disease.

<u>Matshidiso Moeti</u>, WHO Regional Director for Africa, said the spread of the viral disease from capital cities to rural areas in the continent should be addressed as a matter of urgency to prevent a public health crisis. "Tackling cases in rural areas that often lack the resources of urban centers will pose an immense challenge for the already strained health systems in Africa. There is a critical shortage of treatment facilities for critical cases of COVID-19 in Africa."

Africa's <u>first diagnosed case of COVID-19</u> was reported in Egypt on 13 Feb. Now, more than 32,000 cases have been recorded across the world's second-largest continent in nearly all 54 nations. Officially, the <u>Africa Centers for Disease Control and Prevention</u> (CDC) report 33,566 cases, 1,469 deaths and 10,152 recoveries.

So far it has been difficult to <u>fully grasp the extent of the spread of the disease in Africa</u>, as testing has been patchy. Djibouti has recorded 98.6 cases per 100,000 people, the highest prevalence on the continent, but the tiny country of one million has conducted just over 10,000 tests, as many as neighbouring Ethiopia, which has more than 100 million people.

South Africa, which currently <u>has the highest number of cases</u> in sub-Saharan Africa, with more than 4,000 cases is conducting up to 10,000 tests every day in a bid to find and isolate the disease before it can take hold in the crowded townships where up to a third of the 56 million population live.

#### Of the 54 African countries:

- Only 10 report more than 1,000 cases, and
- Twenty-three report less than 100 cases.

<u>A report from the Economic Commission for Africa</u> on 17 April stated that "anywhere between 300,000 and 3.3 million African people could lose their lives as a direct result of COVID-19, depending on the intervention measures taken to stop the spread."

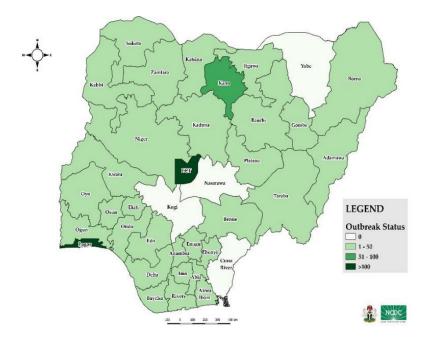


Wafaa and Justman in an article in the NEJM on 17 April said, "Africa has so far been largely spared the kind of impact that has thrown China, the United States, and Europe into chaos...despite the slow arrival of COVID-19, a storm is building, and the 1.2 billion people living in Africa are at tremendous risk...the obstacles are not limited to care and treatment of people who are sick. In many communities, people live together in close quarters, which makes social distancing, a critical prevention strategy, more difficult. Millions of people live without access to clean running water, which makes frequent handwashing all but impossible."

We note the paucity of reporting on the COVID-19 situation in Africa in the international media.....

#### FOCUS ON NIGERIA: IS A SIGNIFICANT COVID-19 EPIDEMIC GOING UNDETECTED?

#### Situation in Kano State



Map of Nigeria showing 32 states and FCT affected by COVID-19: Nigeria Centre for Disease Control

On 21 April, the <u>Daily Trust</u> newspaper reported that over 150 people died in Kano last weekend (24-25 April) and have been buried in three cemeteries. Undertakers, who double as grave diggers, in the affected cemeteries said the frequency at which they received corpses on these days was unusual when compared to before the coronavirus outbreak.

Doctors in Kano say they have seen a surge in fatal cases of pneumonia. But local authorities have denied that COVID-19 is responsible, variously blaming malaria, meningitis, hypertension and other illnesses for the increased mortality. However, the Governor, Abdullahi Umar Ganduje, stated on 28 April, "so far there's been nothing to suggest that they are linked with COVID19."

Khalil Muhammed, a driver in Kano city, said many people were scared. "Four of my neighbours have died, all in the last week, so we know the government is not understanding this thing. Two weeks ago in my area, people were burying, burying. I was thinking, what is this? I have been staying at home with my children and wife. What can I do? I know something is very wrong," he said.

On 27 April, Nigeria's President announced an immediate <u>two-week lockdown in Kano</u>, the largest city in the north, after the <u>mysterious deaths</u> of 640 people over the last two weeks.

# Information from International SOS, Nigeria

International SOS Medical Director in Lagos, Dr. Raymond Ruthven, explained that private medical facilities are not permitted to treat or manage basic COVID-19 cases and thus are not overwhelmed. There has been no reported increase in flu-like or other febrile illnesses, except for malaria, but some have attributed this to a reduction in antimalaria medications occasioned by the lockdowns. However, there is a tendency to over-diagnose malaria and there may be a bit of an overlap in symptoms with COVID-19, especially early in the illness.



Dr. Ruthvin worries that the low levels of testing in Nigeria may be masking something bigger. He supplied this table:

	NIGERIA	GHANA	
Population	196 million	30 million	
Total tests	12,004	100,622	
Tests/1m Pop	53	3,238	
Total Pos	1,337	1,550	
Pos Rate	12.2%	1.5%	

<sup>&</sup>quot;We also know that NCDC tests only about half of the patients we refer," Dr. Ruthvin said. "Soon we will have RDT's and I suspect we will then pick up a lot."

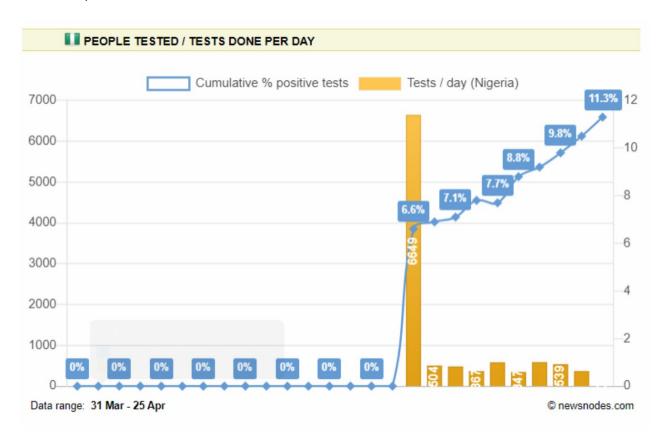
Dr Ruthvin continued, "The Federal Government takes the lead in formulating overall policies; these guide the states. Screening measures have been ramped up across all the 36 states with isolation and treatment centers being set up and equipped.

"The NCDC is working closely with some private laboratories to expand the testing capacity. The inclusion of two more laboratories into the country's COVID-19 network brings the total number of laboratories in to 17.

"Personal hygiene, social distancing and screening protocols have been reinforced by both government and private organizations alike. Face masks in public are now compulsory, though this varies between states."

# More testing needed

On 25 April, the Director of the Nigeria Centre for Disease Control, Chikwe Ihekweazu, made <u>an open plea on Twitter</u> for more kits to expand testing. The Tweet included a graph from <u>newsnodes.com</u> showing 11% of recent tests to be positive.



# ICU & ventilators in Nigeria

<u>The Federal Government</u> has announced a strategy of "test, treat, trace and isolate". Before the pandemic, Nigeria had only 350 ventilators, most in the private sector. Around 100 more have been bought in recent weeks, though many other bottlenecks, such as a critical lack of specialised healthcare workers, remain.



#### Lockdown and food shortages

Dr Sani Aliyu, <u>Nigeria's national coordinator of the COVID-19 Presidential Task Force</u>, said officials were keenly aware of the problems of lockdown in a country where many of the 200 million inhabitants need to leave home every day to earn enough for basic subsistence.

To ease the threat of food shortages, the Government has released huge quantities of grain from the national reserves, and distributed 100 trucks of rice across the country, along with approving conditional cash transfers. But Aliyu admitted that such assistance was "probably going to be a drop in the ocean compared to what is needed".

#### Lockdown lifting in some areas

<u>BBC reports</u> that Nigeria will begin a "gradual easing" of coronavirus-related lockdowns for millions of people in its largest city, Lagos, and the capital, Abuja. President Muhammadu Buhari said the lockdowns, which had been due to end on Monday, needed to continue until 4 May.

He also ordered new nationwide measures against COVID-19, including a night-time curfew and mandatory face masks. The moves would ensure the economy functioned "while still maintaining our aggressive response", Mr Buhari said. The easing will apply to Abuja, Lagos and the neighbouring Ogun state, where collectively more than 25 million people have been under lockdown since 30 March. Other states have introduced their own measures.

# IMF Executive Board Approves US\$ 3.4 Billion in Emergency Support to Nigeria

On 28 April, the IMF (International Monetary Fund) approved US\$3.4 billion in emergency financial assistance under the Rapid Financing Instrument to support the authorities' efforts in addressing the severe economic impact of the COVID-19 shock and the sharp fall in oil prices.

# IS SCHOOL SAFE FOR STUDENTS AND TEACHERS?

In Australia, the <u>National Centre for Immunisation Research and Surveillance has reported</u> on an enhanced investigation of the transmission of SARS-CoV-2 in schools in New South Wales in early March, 2020.

"Schools are among the safest places that we have," lead investigator Professor Kristine Macartney said.

# Details of the study

- 18 individuals (nine students and nine staff) from 15 schools (10 high schools and 5 primary schools) were confirmed as COVID-19 cases. All had an opportunity to transmit the virus to others in their schools
- 735 students and 128 staff were close contacts of these initial 18 cases.

# Summary of results

- One child from a primary school and one child from a high school may have contracted COVID-19 from the initial cases at their schools
- No teacher or staff member contracted COVID-19 from any of the initial school cases.

#### Details: High schools

• A total of 12 COVID-19 index cases (8 students and 4 staff) were identified who had attended 10 high schools while infectious. The total number of close contacts in these 10 high schools was 598 students and 97 staff (total of 695 contacts). Nose/throat swabs were taken from one third (n=235) of contacts, all of which tested negative. In one high school, of the 75 close contacts who underwent blood testing at approximately 1 month after contact with the initial cases while infectious, only 1 student had antibodies detected, indicating infection had occurred. Overall, as shown in Figure 2, only one of 695 individuals was identified to have been infected following close contact with a school case in these 10 high schools.

#### Details: Primary schools

A total of six initial cases (comprising one student and five staff) were identified in five primary schools. The
total number of close contacts in these five primary schools was 137 students and 31 staff (total of 168
contacts). Nose/throat swabs were taken from one third (n=53) of contacts. Only one secondary case
(nose/throat swab positive) was identified in the 168 close contacts. In the same primary school that had this



secondary case, 21 close contacts underwent blood testing. The same student whose nose/throat swab tested positive also had antibodies detected through serology testing, consistent with their known recent infection. Overall, as shown in Figure 3, only one of 168 individuals was identified to have been infected following close contact with a school case in these five primary schools.

# Does the age of school children modify the number of contacts and so the risk?

A letter in <u>Eurosurveillance</u> estimated contact patterns of children of different ages using radio-frequency identification (RFID) technology. It was reported that:

- Young French children (age 6 years) in a primary school had a median of 500 contacts per school day and a median of 300 minutes of cumulated contact per day.
- Older children (age 10–11 years) had a median of 300 contacts per day and a median of 250 minutes of cumulated contact per day.

The comment was that in an emergency context, such as the COVID-19 pandemic, where scientific knowledge regarding the virus is still lacking, total closure of a school was reasonable and reassuring for parents.

# U.K. review finds school closures likely to have little impact on the spread of coronavirus

Research at University College London, reviewed 16 studies of recent outbreaks of other coronaviruses, including the 2003 Sars epidemic in mainland China, Hong Kong and Singapore, and found that school closures did not help control the epidemic.

"We know from previous studies that school closures are likely to have the greatest effect if the virus has low transmissibility and attack rates are higher in children. This is the opposite of COVID-19," said the lead author, Prof Russell Viner, of UCL Great Ormond Street Institute of Child Health.

"Data on the benefit of school closures in the COVID-19 outbreak is limited but what we know shows that their impact is likely to be only small compared with other infection-control measures, such as case isolation, and is only effective when other social isolating measures are adhered to."

Viner, who is President of the Royal College of Paediatrics and Child Health, said the benefit gained from closing schools had to be weighed against the costs. "Children's education is damaged and their mental health may suffer, family finances are affected, key workers may need to stay home to look after children and vulnerable children may suffer most."

# **MORE ABOUT MASKS**

#### Germany's states make face masks compulsory

On Monday, new regulations went into effect across Germany requiring residents to cover their noses and
mouths while traveling with public transportation or while shopping. Each of Germany's 16 states, which are
entitled to make their own decisions under Germany's federal system, drew up their own set of regulations —
meaning that the rules are slightly different depending on the region.

# A cluster randomised trial of cloth masks compared with medical masks in healthcare workers

This study is the first RCT of cloth masks, and the results caution against the use of cloth masks. This is an
important finding to inform occupational health and safety. Moisture retention, reuse of cloth masks and poor
filtration may result in increased risk of infection. Further research is needed to inform the widespread use of
cloth masks globally. However, as a precautionary measure, cloth masks should not be recommended for
healthcare workers, particularly in high-risk situations, and guidelines need to be updated.

# Adding A Nylon Stocking Layer Could Boost Protection From Cloth Masks, Study Finds

• Researchers at Northeastern University have reported in a pre-print that adding an outer layer made from nylon stockings to a homemade face covering can boost its ability to filter out small particles in the air by creating a tighter seal between the mask and the wearer's face. A "particulate matter counter" was used in



the analysis. In some cases, that extra nylon layer helped homemade cloth masks match or exceed the filtering capability of medical-grade surgical masks.



Image credit: Northeastern University

# **HOW MIGHT A "SECOND WAVE" OCCUR?**

# Opinion of Christian Drosten, Director of the Institute of Virology at the Charité Hospital, Berlin. The "prevention paradox"

• When asked what will happen when Germany starts to unwind its lockdown, he replied: "At the moment, we are seeing half-empty ICUs in Germany. This is because we started diagnostics early and on a broad scale, and we stopped the epidemic – that is, we brought the reproduction number below 1. Now, what I call the "prevention paradox" has set in. People are claiming we over-reacted, and there is political and economic pressure to return to normal. The federal plan is to lift lockdown slightly, but because the German states, or Länder, set their own rules, I fear we're going to see a lot of creativity in the interpretation of that plan. I worry that the reproduction number will start to climb again, and we will have a second wave."

NOTE: it is worth reading the entire Q&A with Prof Drosten.

# CDC Director warns second wave of coronavirus is likely to be even more devastating

• "There's a possibility that the assault of the virus on our nation next winter will actually be even more difficult than the one we just went through," <u>CDC Director Robert Redfield said in an interview with The Washington Post</u>. "And when I've said this to others, they kind of put their head back, they don't understand what I mean. We're going to have the flu epidemic and the coronavirus epidemic at the same time," he said.

# Projecting the transmission dynamics of SARS-CoV-2 through the post-pandemic period

We used estimates of seasonality, immunity, and cross-immunity for betacoronaviruses OC43 and HKU1 (cause
the common cold) from time series data from the USA to inform a model of SARS-CoV-2 transmission. We
projected that recurrent wintertime outbreaks of SARS-CoV-2 will probably occur after the initial, most severe
pandemic wave. Absent other interventions, a key metric for the success of social distancing is whether critical
care capacities are exceeded. To avoid this, prolonged or intermittent social distancing may be necessary
into 2022.



#### **Opinion of Professor John Oxford**

It is unclear if the so called "Second Wave" during the 1918 influenza pandemic was caused by a mutated virus making those already infected in the first wave again susceptible. This scenario is less likely during a coronavirus pandemic due to its general lack of mutation.

#### **JOURNAL / ARTICLE ROUND UP**

#### First U.S. Virus Death Came Weeks Before Previously Thought

• The <u>first U.S. death</u> from COVID-19 probably occurred in California on 6 February. Previously, the first report of a U.S. death from COVID-19 was on 29 February in Washington state.

# Antibody testing suggests virus hit DC weeks earlier than estimated

 A <u>woman in NYC developed fever and chills on 16 February</u>, a day after returning from a ski trip to northern Italy. Tests for flu and mononucleosis were negative. On 22 April, the woman tested positive for antibodies to SARS-CoV-2.

# National alert as coronavirus-related condition may be emerging in children

An <u>alert to GPs in the UK</u> says that in the "last three weeks, there has been an apparent rise in the number
of children of all ages presenting with a multisystem inflammatory state requiring intensive care across
London and also in other regions of the UK". It adds: "There is a growing concern that a [COVID-19] related
inflammatory syndrome is emerging in children in the UK, or that there may be another, as yet unidentified,
infectious pathogen associated with these cases."

# Guillain-Barré Syndrome Associated with SARS-CoV-2?

• During a three-week period from February to March, <u>five patients in three hospitals in northern Italy developed Guillain–Barré syndrome</u> after the onset of COVID-19. Four of the patients had a positive nasopharyngeal swab for SARS-CoV-2 at the onset of the neurologic syndrome, and one had a negative nasopharyngeal swab and negative bronchoalveolar lavage but subsequently had a positive serologic test for the virus. Detailed case reports are provided in the Supplementary Appendix.

#### Returning Qantas crew members tested positive for coronavirus but were exempt from quarantine

• Four <u>Qantas crew members</u> who operated a repatriation flight from Chile have tested positive for the coronavirus but unlike their passengers, who were put into isolation in city hotels, they did not go into quarantine due to a special exemption. The flight from Santiago landed in Sydney on 29 March.

# New CDC advice: If you have any of these emergency warning signs for COVID-19 get medical attention immediately:

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion or inability to arouse
- Bluish lips or face

These take into account the "silent hypoxics" - findings that many with COVID-19 have a low level of oxygen in their blood, without being aware.



#### A VIEW FROM THE LABORATORY: PROFESSOR JOHN OXFORD

We have reviewed previously (Fenner and White textbook, for example) the wider family of six coronaviruses that can infect humans in an attempt to predict immune response to the new virus COVID-19 and its longevity. Could a vaccine response be relied upon to give protection, or even, could such a response enhance disease in some way like dengue and animal coronavirus?

Now there is a very comprehensive 57-page paper authored by Derrick Cummings and co-authors from Florida and Cambridge University. I would not attempt a blow-by-blow analysis of the data presented. There are over 100 papers in the reference list. I found this paper most relevant to immunity not the least being reminded of scientific papers published by my counterpersons Sylvia Reed, Paul Beare, Dr Callow and David Tyrrell.

# A systematic review of antibody mediated immunity of Coronaviruses

This study reviewed 1,281 abstracts in the world literature and classified 322 manuscripts to five areas:

- 1. Antibody kinetics
- 2. Correlates of protection
- 3. Immune pathogenesis
- 4. Antigenic diversity
- 5. Population seroprevalence.

The review covers viruses OC43, 229E (the two early isolates), HKU1, NL63 and most recently SARS COV-2. They searched PubMed databases. Each abstract was reviewed by two authors.

For antibody tests, the most commonly used was a binding assay. Fifty-six studies described antibody kinetics which was rarely reported during the acute illness. Robust antibodies were detected after 2-3 weeks to 229E, MERS, SARS and SARS-CoV-2. Early work at the Common Cold Unit in Salisbury in the 1960's and 1970's studied IgA and IgG in volunteers infected with the 229E virus in quarantine. The antibody peak was around 14 days.

To bring us up to date with COVID-19, IgM is detected on day seven, peaking on day 28. IgG appeared by day 10 and peaked on day 49. A study of 173 patients showed seroconversion at 12 days (IgM), 14 days IgG, and neutralising antibody at 11 days. Most studies showed waning IgM. In the early volunteer study by Callow with 229E virus antibody waned between 11 weeks and 52 weeks.

Potentially there is elevated antibody response in severe infections with COVID-19. Rather unexpected was the recent study with COVID-19 where neutralising antibody was higher in severe cases.

Very important, I feel, was the early Callow study. Not unexpectedly, data for protection was only available for analysis following challenge of past patients. Seven of eight volunteers with neutralisation titre of <5 excreted virus were protected compared to  $\frac{1}{4}$  with pre exposure antibody titre of  $\frac{1}{40}$ . There was a correlation here between dose of challenge and symptoms. Higher doses (>  $\frac{10^{1.2} \text{ TCID}_{50}}{10^{1.2} \text{ TCID}_{50}}$ ) were more likely to cause colds. Barrow found that lower proportions of individuals with high neutralising antibody experienced significant colds. The Callow study (229E challenge) found that serum IgG, nasal IgM were protective for clinical severity.

Several studies exposed volunteers to two challenges many weeks apart. On the first challenge all six volunteers developed symptoms (Callow *et al*). On re-challenge 67% were re-infected a year later but without respiratory symptoms and moreover had reduced excretion of virus.

To recap, the alpha coronavirus grouping has 229E and NL63 viruses, and multiple 229E strains have been detected. The <u>beta</u> coronaviruses have four lineages, OC43, HKU1 and the lineage SARS and SARS-COV-2 (COVID-19).

Other coronaviruses cause human disease, including enteric disease in children and zoonotic infections. In essence, these experiments at the Common Cold Unit tell us that post-infection immunity can last months and reduce symptoms. Furthermore, high levels of antibody are protective to challenge.

#### The 'repurposed' antivirals are not showing signs of working

Of the handful of drugs pulled from the medicine cupboard to test at this desperate time, the one with the most science testing behind it, at least in the laboratory, was the nucleotide analogue remdesivir.



There had been some animal modelling with coronavirus in primates and also in vitro studies. A controlled clinical trial of 237 patients has failed to show benefits, according to a draft document on the WHO website. The manufacturer, Gilead, (who have a history of effective antivirals against, for example, influenza), are still considering a trial with less seriously ill patients.

In the present clinical trial carried out in China, 158 patients were randomly in the remdesivir group whilst 79 others were given "standard" care. Approximately 14% of remdesivir patients died, compared to 13% placebo. Furthermore, the drug was stopped early in 18 patients because of adverse effects versus four in the placebo group.

Previous uncontrolled studies of 125 patients, as is quite common with a threatening virus, were treated and could be discharged early. But there was no control group for comparison.

Other repurposed drugs tested are hydroxychloroquine, an anti-malarial drug and protease inhibitors from the HIV medicine cupboard.

It must be admitted that these are "long shots" and we all await data, especially laboratory modelling from yet to be discovered, and specific, anti-COVID-19 inhibitors. Undoubtedly this means that effective antivirals will be at least one year away and probably more.

Meanwhile we have to rely on what our ancestors did in the Spanish influenza; good nursing, social distancing, masks (usually home made with cotton) and control of large groups. In 1918 most patients died quietly at home, at least in Europe, where the hospitals were full of wounded soldiers, as were hotels and houses along the coastlines of Southern England.

# An epidemic of firearms related suicide in the USA?

I end my report on a rather depressing note, which actually I most often try not to do.

Rebekah Mannix and colleagues in Annals of Internal Medicine (23rd April 2020), discuss the topic of gun suicide. They note that since February 2020, more than 2.5 million firearms were used in the USA.

It is known in the USA that sales of handguns correlate with suicide. The authors point to a 'Tsunami' of COVID-19 + unemployment + social separation. From 2006 to 2018, gun suicide rates increased 25%. In 2018 there were 24,482 firearm suicides in the USA. However, the authors point to a new figure - namely an 85% increase in gun sales between March 2019 and March 2020, the highest sales ever recorded.

It is known that possession of a handgun at home is a 2-10 times increased risk of attempted suicide (applies to the entire household) and lasts for years. As of 16<sup>th</sup> April 2020, more than 22 million Americans applied for unemployed "insurance". The authors conclude "we are therefore a society now primed for a suicide epidemic triggered by COVID-19".

Unfortunately, firearm suicide has a fatality 40 times that of drug poisoning, for example. The authors conclude that "Advancing social connecting should be a local national public heath priority in the coming months. Only 16 states have effective firearm legislation. A federal buyback programme could be an appropriate area for people to dispose of guns whilst offering economic incentives. Clinicians have a role to play by counselling and distribution of lock-up boxes. It read like the novel "1984", but we have a serious group here from Harvard Medical School and a serious medical journal.

And finally, I note today that hospital coronavirus deaths in the UK passes 20,000 in the 51 days since the first case was identified. Rather as in China, and I suspect like other countries, we have underestimated total deaths as elderly persons have not been included in those figures.

Globally, 200,000 have died and 2.8 million cases have been confirmed. On an "optimistic note" this is many fewer than in the flu pandemics of 1957 (5 million deaths worldwide) and 1968 (2 million deaths worldwide) and, of course, 1918 where there were 50 million deaths within the year 1918-1919! Sometimes we can reflect positively on history.

In Finchley (my suburb in London) we all go out to the road each Thursday and applaud the nurses and doctors and other dedicated scientific workers.

My own group and other quarantine groups in the EU and USA are discussing clinical quarantine trials. Work with RSV and flu will continue because these viruses have not gone away either!



We still have to be very cautious about the willingness of "volunteers" for a COVID-19 challenge until we know exactly how pathogenic the virus is. On the other hand, surrogate viruses like OC-43 and 226E might give relevant data safely as they did in the 1960's.

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