Twitter Thread by Deepti Gurdasani

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Thread on the recent report on the possible risk of increased death associated with the new UK variant (B117)- with a discussion of the evidence around this, and what this means.

First, there is strong evidence to support increased transmissibility of B117 - current estimates of increased transmissibility range between 30-70% - from epidemiological evidence examining the differential rate of growth of B117 with respect to other variants & increase in R

There is also evidence from PHE contact studies that the risk of transmission from those carrying the B117 variant is ~50% greater than with other non-B117 variants.

Increased transmissibility, even if a variant has the same fatality rate can increase deaths substantially, because the rate of growth of cases is higher- & more cases means more deaths.

Increased fatality rates also increase deaths- but do so linearly.

https://t.co/nqV3udZByu

> How dangerous are the B.1.1.7 and 501Y.V2 hyper-transmissible strains?
> by @AdamJKucharski @CFR_orghttps://t.co/aycWMN3b5h
> h/t @Karl_Lauterbach pic.twitter.com/JlaFzzP06t
>
> — Eric Topol (@EricTopol) January 11, 2021

So how was risk of death with the variant studied?
We don't routinely sequence all samples for the virus. We've found that the variant has a particular deletion which means that some PCR tests on samples with the variant give a different read-out when the variant is present.

They show something called 'spike dropout'. This is because a gene in the virus that's targeted by the PCR is changed by the mutation, so the PCR can't pick up this particular part of the virus. But the PCR test targets multiple parts of the virus, so we still get a +ve test.

Not all commercial PCR tests are able to detect this, as only some PCRs target this part of the virus showing 'spike dropout' when this key mutation is present. PHE data show that spike dropout is a good proxy for the B117 variant, when the frequency of the variant is high.

Given this limitation, we can only study deaths among those who have been tested with a specific PCR test that is able to identify spike dropout. Only 8% of deaths had these data available (Only 1/3rd of tests carried out through pillar 2 have these data), so these were studied.

The analysis carried out in a number of different ways mainly compare 28 day deaths among people whose samples showed spike dropout to those whose samples didn't (tested with tests that could identify dropout).

Given the different transmissiblity of B117, it is possible that differences in deaths may be down to people infected by B117 being different in some way - e.g age, socio-economic status, living in an area where critical care capacity was under pressure.

To try and reduce the impact of these factors, comparisons were matched for age, gender, deprivation scores, time of testing & location.

Different analyses carried out with the data in slightly different ways suggested a ~1.3x increase in risk of death.

Could this increase be attributed to pressure on the NHS during the past month?
Unlikely. The people with the B117 variant were matched to controls by age, specimen data, and location - so they would've been compared with people infected at the same time, in the same area.

They also did additional analyses to adjust further for NHS pressure - by including ventilation capacity, occupancy, and staff sickness factors. These did not change the result, suggesting that the increase is not down to differences in NHS pressure.

Could there be other reasons we see this?
Possibly. A theoretical reason is that people who are infected with the new more transmissible variant are different in some other way- that makes them more likely to die anyway were they infected with any variant.

E.g. if the variant was more likely to result in clusters of infection in care homes rather than the community, just adjusting for age may not account for the relatively greater frailty of a person in a care home vs someone in the community of the same age.

This is unlikely to explain the findings, given we see a uniform increase in risk of fatality across all age groups. So if there is an alternative explanation, it would need to apply to all age groups.

This is possible but would mean transmission dynamics of the strain consistently lead to more infection in people in groups who are *already* at greater risk. In this case the variant wouldn't *cause* the increase in deaths, but would be infected those already at higher risk.

E.g. if the variant was more likely to infect deprived population. But the models have adjusted for many factors that could explain this - including deprivation. So we can't rule out this possibility completely, but the modelling has tried to account for this.

What does this mean?
To me, this highlights the gambles we take when we follow an approach which allows high levels of transmission to continue in the community for long periods of time. The UK govt has consistently minimised the risk posed by COVID-19, which is why we're here.

What's worse is that we now also have the variant from South Africa circulating - a variant that has raised legitimate concerns about vaccine effectiveness - based on early studies showing poorer neutralisation of the strain with antibodies in the laboratory.

While this doesn't necessarily translate to lower vaccine effectiveness, can we really afford to take this risk? No.
Hoping for the best, and dealing with variants after they get out of hand doesn't work. We need to proactively contain these.

Whitty in the briefing yesterday seemed to suggest that the variant from SA coming into the UK was inevitable. It wasn't. Our travel restrictions were put in place several days after the SA variant was reported. Our border restrictions are still extremely lax.

People can exit quarantine on day 5 after a -ve rapid test. This is not grounded in any evidence & is exactly the sort of policy that would lead us to where we are now.

Australia imported the UK variant, but they acted aggressively to prevent it establishing in the community

We now have not one- but at least 2 (if not more) variants of concern circulating in the community. There are >70 cases of the variant linked to SA. What have we done to contain spread? This should have been treated as an emergency.

We don't understand the properties of many of these new variants until much later. We can't risk more virus adaptation & spread. Our health, and even our vaccine resources depend on eliminating the virus. It's the idea that we can 'live with the virus' that's led us here.

There is no way to live with the virus. It's clear virus adaptations can and will continue to occur if we allow this. And the idea that this will make the virus somehow less fit or less likely to cause death isn't grounded in evidence or reality.

We must urgently move to elimination. The case for this has been clear for months, but recent events emphasise this even more. Hoping for the best isn't a strategy- it's a recipe for disaster.