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21 Dec · 22 tweets · [mugecevik/status/1341094836682838021](https://twitter.com/mugecevik/status/1341094836682838021)



There are several reasons to think that the new UK [#SARSCoV2](#) variant is an important one as it might be more contagious than other variants, but there are also some uncertainties. So much misinformation is being circulated, so this thread brings key data together. 🧵

1- Genomic data

In the UK, COG-UK undertakes sequencing of SARS-CoV-2 samples from ~ 10% of positive cases. This is an enormous effort, and helps scientists to identify mutations and track them over time. Here are some variants being tracked in the UK. 1/ https://www.cogconsortium.uk/wp-content/uploads/2020/12/Report-1_COG-UK_20-December-2020_SARS-CoV-2-Mutations_final.pdf

Table 1a. Priority mutations being tracked by COG-UK

Mutation	Predominant Lineage	Reasons for tracking	Cumulative number in UK	Number over last 28 days (13/11/2020 - 10/12/2020)
D614G	B.1	Moderate effect on transmissibility	118,906	11,447
A222V	B.1.177	Fast growing lineage but no evidence of mutation effect	46,710	7,856
N439K	B.1.141 B.1.258	1) Increased binding affinity to hACE2 receptor 2) Escape to some mAbs	3,320	246
Δ69-70	B.1.1 B.1.258	1) Evasion immune response 2) Diagnostic failure in some assays targeting the S gene including the three-target TaqPath assay and the two-target Biofire assay	3,504	1,228
N501Y	B.1.1.7	Fast growing lineage & increased binding affinity to hACE2 receptor	2,057	1,182
N501Y + Δ69-70	B.1.1.7	Likely to maintain characteristics described for N501Y and 69-70del	1,524	1,034
N439K + Δ69-70	B.1.258	Likely to maintain characteristics described for N439Y and 69-70del	1,895	176
Y453F	B.1.1 B.1.1.298	1) Increase binding affinity to hACE2 receptor 2) Escape to some mAbs Human/mink associated	0	0

Over time, scientists have identified this new variant, called B.1.1.7 or VUI – 202012/01 (the first Variant Under Investigation in December 2020), which looked different than others. It has acquired 17 mutations compared to its most recent ancestor. 2/



N:
D3L
S235F

Preliminary genomic characterisation of an emergent SARS-CoV-2 line...
 Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations Report written by: Andrew Rambaut¹, Nick Loman², Oliver Pybus³, Wendy Barcla...

<https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-...>

- UK's newest fast growing lineage, B.1.1.7:

Defined by multiple spike protein mutations: 69-70del, 144-145del, N501Y, A570D, D614G, P681H, T716I, S982A & D1118H.

Image from report by Sebastian Maurer-Stroh at GISAID.

3D structural visualisation of the spike glycoprotein with mutations identified in the query sequence shown as colored balls

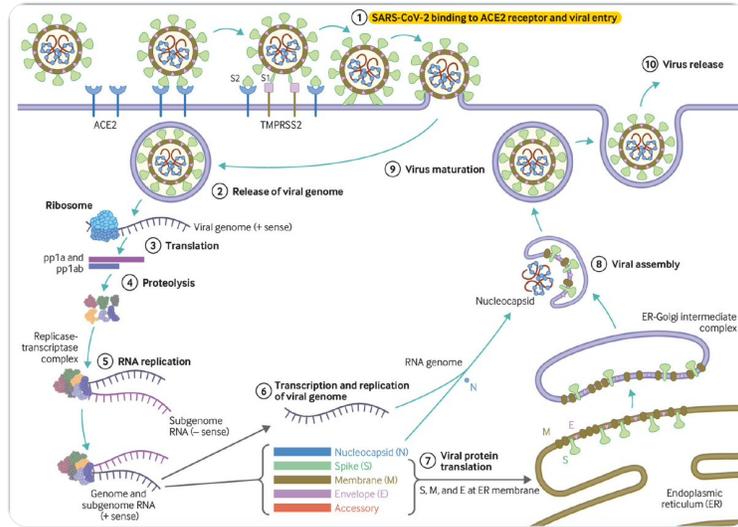
Spike glycoprotein (PDB: 6W01) (N 501Y) with RBD in down conformation. Spike glycoprotein (PDB: 6W01) (N 501Y) in complex with host cell receptor ACE2 (green ribbon).

Many of these mutations are on the gene that encodes the spike (S) protein on the surface of SARS-CoV-2, through which the virus binds to and enters human cells, that is the first step in the viral cycle (first step in this diagram) 3/

Virology, transmission, and pathogenesis of SARS-CoV-2

What you need to know Since the emergence of SARS-CoV-2 in December 2019, there has been an unparalleled global effort to characterise the virus and the clinical course of disease. Coronavirus d...

<https://www.bmj.com/content/371/bmj.m3862>



There is experimentally-predicted and plausible biological consequences of some of these mutations seen in this variant but we don't know the combined effect of all these 17 mutations together. Here is a paper detailing this by [@arambaut](#) et al. 4/

A570D P681H T716I S982A D1118H ORF8: Q27stop R52I Y73C N: D3L S235F	
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Preliminary genomic characterisation of an emergent SARS-CoV-2 line...

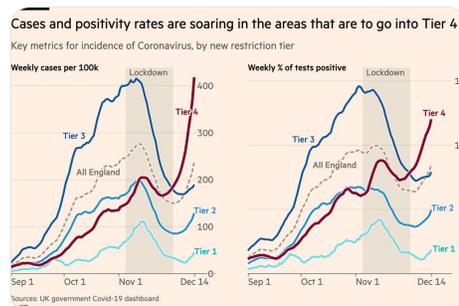
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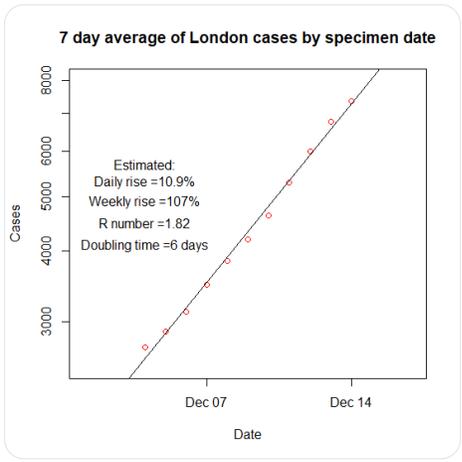
<https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-...>

2- Epidemiological data

Over the last 3 wks there has been a steep increase in cases in some regions in England, mainly London & East of England & a further increase seen after the end of restrictions in these areas now put into Tier 4. 5/

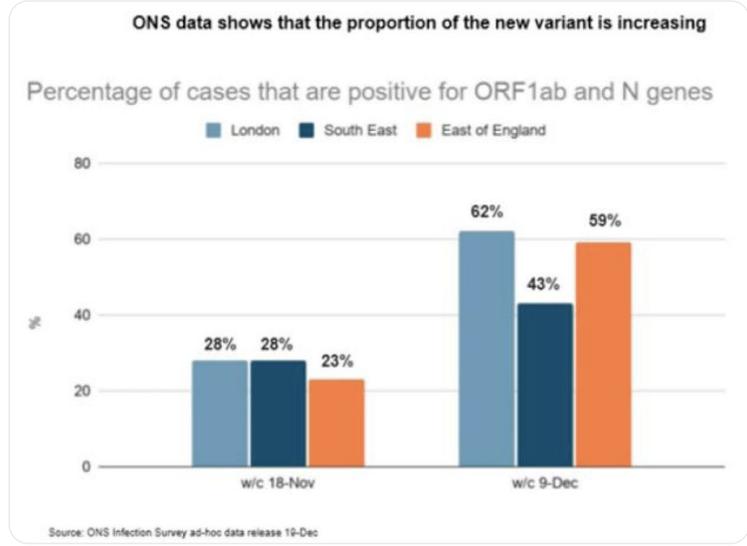
<https://www.ft.com/content/538a640b-2b2e-4039-9b11-9749be3fa579>



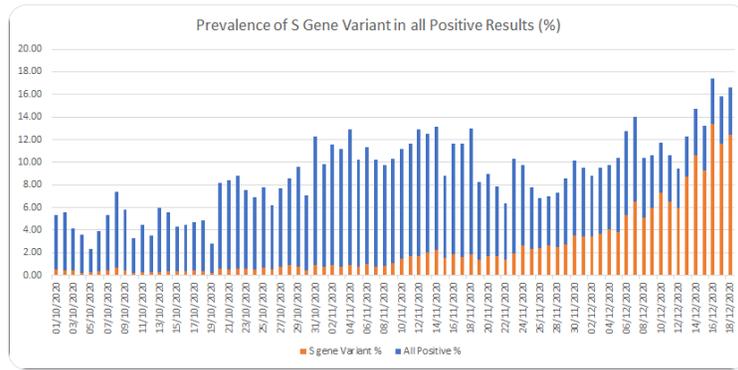


Importantly, the new variant is now dominant in London and the East of England. So, it's rapidly replacing other variants. This figure shows that by w/b of the 9th of December over 60% of all the cases were the new variant compared to 30% in November. 6/

<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/adhocs/12690percentageofcovid19casesthatarepositivefororf1abandngenes>



National testing data shows increased prevalence of the variant in positive cases over time. This is detected incidentally by the commonly used 3-gene PCR test because 69-70del leads to a negative signal. But this does not effect the results of the test. 7/ h/t @The Soup Dragon



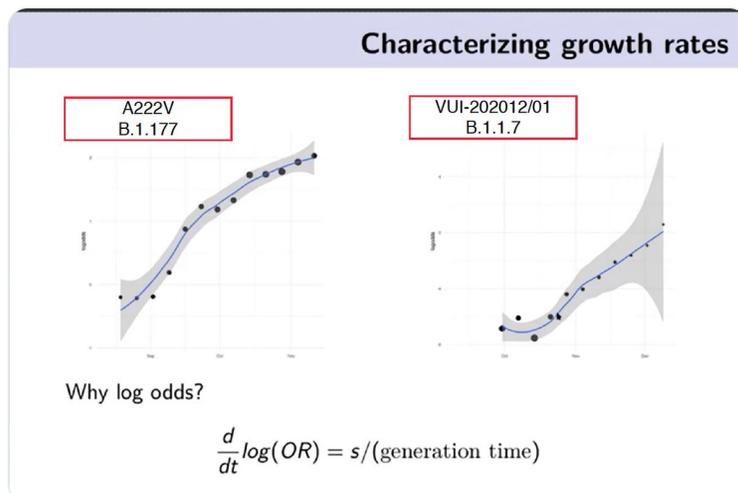
So, putting all these observations together, we can make an assumption that there might be a correlation between the new variant and increased rates of infection. But how can we know whether the increasing frequency reflects the fitness advantage or chance ? 8/

3- Modelling data could help

Here you can see growth rates of two different variants based on modelling. A222V (left): rapid rise over summer up to Nov vs. B.1.1.7 (right): the new variant, 1 month data & growth rate seems to be larger. @erikvolz 9/



<https://www.youtube.com/embed/G3CT9N89L-c>

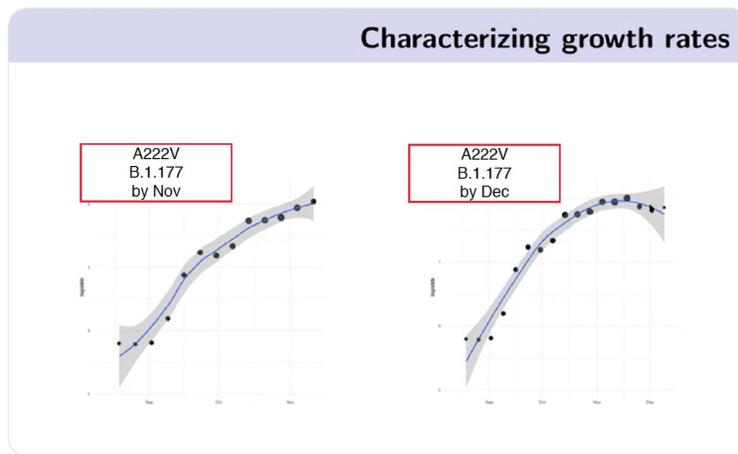


However, the trend observed early on may not pan out later on. For example, A222V showed a steep increase initially over summer but then this increase settled by December. Details in this COG-UK event presented by [@erikmvolz](#)

10/



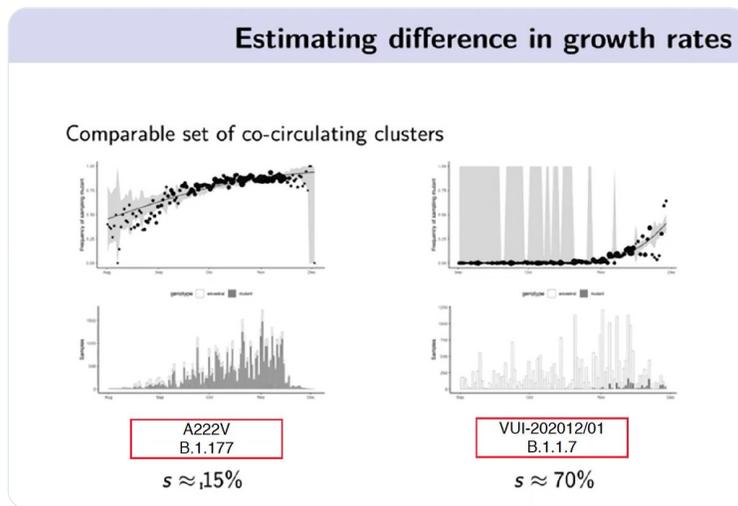
<https://www.youtube.com/embed/G3CT9N89L-c>



But does it mean the new variant (B.1.1.7) is circulating faster (more transmissible)? In this logistic regression model, comparing the rate of increase of B.1.1.7 vs other variants, B.1.1.7 is estimated to grow faster. Although data is too noisy. 11/



<https://www.youtube.com/embed/G3CT9N89L-c>



Further modelling studies of correlation between R-values and detection of the variant estimates an increase in the R between 0.39 to 0.93. So, time varying reproduction number is correlated with the increase in fraction of new variant. ^{12/}
<https://khub.net/documents/135939561/338928724/SARS-CoV-2+variant+under+investigation%2C+meeting+minutes.pdf/962e866b-161f-2fd5-1030-32b6ab467896?t=1608491166921>

4- Virology data

Early virological studies suggest a decrease in Ct value of ~ 2 (higher viral load) associated with the new variant. Viral load inferred from number of unique genome reads suggests increase in viral load (0.5 increase in median log₁₀) in Y501 vs N501. ^{13/}

In summary: these data suggest that there are lineages with this variant associated with more rapid spread. The concern is that the mutations may be causing this. Although it is possible that this variant may be more transmissible, we don't know how much w/absolute certainty. ^{14/}

Whilst the full significance of the mutations is yet to be determined, the main concern

is the rapid rise in infections alongside this distinct variant, which has a previously unseen combination of mutations that are known or likely to have biological effects.

15/

And it's important to note that this variant has also been identified in other European countries. In addition, in South Africa, scientists also identified a lineage separate from the U.K. variant that also has the N501Y mutation. @Tuliodna et al. 16/

<https://www.krisp.org.za/publications.php?pubid=315>

However, there are many unknowns. We don't know if it will influence the severity of illness, reinfection, effectiveness of vaccines and treatments. So, there's still a lot of work to be done, including lab experiments, contact tracing studies & genomic surveillance. 17/

For instance, we don't know how it may influence transmission in kids. If it's more transmissible overall, we would of course expect more transmission across all age groups. However, key unknown is relative effect on transmission among children (if any). 18/

Another worry, of course, is that the virus may mutate to become resistant to the vaccines. But for that to happen, it will likely take years & more mutations - a good discussion by @apoorva_nyc contributions from @firefox66 @GuptaR_lab @trvrb & me. 19/



The Coronavirus Is Mutating. What Does That Mean for Us?

Officials in Britain and South Africa claim new variants are more easily transmitted. There's a lot more to the story, scientists say.

<https://www.nytimes.com/2020/12/20/health/coronavirus-britain-variant.html>

But according to what we already know, it does not alter the effectiveness of social distancing, face masks, hand washing, hand sanitisers and ventilation. Important to continue following these measures. #HandsFaceSpace 20/



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Over the last 6 months, we've learned a lot about how SARS-CoV-2 spreads 🦠

What does the evidence so far tell us about SARS-CoV-2 transmission dynamics, high-risk activities and environments?

Thread 📖 (1/n)

papers.ssrn.com/sol3/papers.cf...

4:26 PM · Sep 21, 2020



9.7K



See the latest COVID-19 information on Twitter

We've got to be really careful especially as scientists and doctors because there's already a lot of speculation and misinformation about this particular variant and getting answers may take a few weeks or months. I will update this thread as more data becomes available 21/

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