

COVID-19 Update

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Daily new confirmed COVID-19 cases per million people



Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.





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Delta is the dominant variant in the UK (almost 100% of cases). But Delta has continued to mutate & there are several subtypes in the UK (all start with AY). The most common is called AY.4 - almost 80% of sequenced cases in UK are this type





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- So far, no Delta subtype has seemed to have had much of an advantage over the others & non-Delta variants aren't getting anywhere
- But AY.4 has developed a new mutation (S:Y145H) & that variation (AY.4+S:Y145H) has been growing in the UK since July
- This version low labeled AY.4.2
- A222V and not Y145H may be the mutation of interest

AY.23 (Delta sub-lineage) in Singapore



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Time to Panic?

- New UK variant possibly only fractionally more transmissible than the original Delta variant
- Immune dodging and severity not known
- The spike Y145H and A222V mutations:
 - Don't fall in the Receptor Binding Domain and are not obvious candidates for immune escape, increased transmissibility or higher virulence
 - They are also not mutations found in other Variants of Concern (VoCs)
 - A222V was found in the B.1.177 lineage that swept Europe in the summer of 2020, but likely having no inherent transmissibility advantage
 - Y145H is an uncommon mutation (<0.02% outside AY.4.2) that pops up here and there and has been found in various genetic backgrounds. The mutation was first observed in March 2020. The two mutations have been found together in some strains dating back to April 2020



What does this all mean?

- The new AY.4.2 worth watching but not (yet) a Variant of Concern (VOC)
- Likewise, for AY.23 in Singapore
- However, SARS-CoV2 will continue to mutate we just don't know whether there is a new combination of mutations that will cause another major global surge of cases and deaths.
- So, in the meantime:



Get Vaccinated 3rd Dose/Booster when due



Wear your mask in public

Make sensible choices!



How is it all going to end?



 Endemic state - once the (more or less entire) population has immunity to the virus, blunting transmission and disease relative to the pandemic state



- Will happen at different times around the world
- Will be a gradual transition not the flip of a switch
- Even when the entire population of a region has immunity (infection or vaccination) there may still be significant circulation of the virus due to waning immunity and viral evolution
 - Like the flu everybody over 3 has immunity but it still infects 10% of the population and kills 30-60K
- The key parameters that will determine the endemic state are:
 - **R0**
 - Waning immunity
 - Antigenic drift
 - Infection to fatality rate (IFR)



• R0 is the average number of secondary infections in a fully naive population.

- R0 of seasonal flu is around 2.
- R0 of Wuhan-like SARS-CoV-2 was around 3 and with Delta it's now perhaps 5 or 6.
- Higher R0 should correspond to greater circulation all other things being equal
- Waning immunity:
 - Although, other seasonal coronaviruses appear to cause reinfections every ~3 years it's hard to extrapolate to SARS-like coronaviruses
 - There will be at least some waning of immunity to infection season-toseason in endemic state



^Adjusted for age group, sex and epi-week

- Antigenic Shift (mutations/Variants)
 - Although there's been relatively little antigenic drift in SARS-CoV-2, we've seen rapid adaptive evolution in the S1 domain of spike protein as selection pressure has driven increased transmissibility
 - Partial immune escape in the Beta, Gamma and ²
 Mu variants spike protein mutations
 - When selection pivots to be primarily immune driven likely see steady antigenic drift
 - Recent adaptive evolution has been occurring at a faster rate than H3N2 influenza - median scenario would be we see sustained antigenic evolution at a similar pace to influenza H3N2





- High R0
- Waning immunity
- Antigenic drift

20% or 30% of the population infected each year



- Circulation does not necessarily translate to disease burden
 - Based on robust vaccine effectiveness against severe outcomes, guess would be that infection to fatality rate (IFR) drops 10-fold from its original ~0.6% to a flu-like ~0.06%
 - Estimate 40k or 100k deaths per year in the US from COVID at endemic state
 - Most infections would be relatively mild (just like flu), but there's enough of them that even a small fraction of severe outcomes add up
 - 30% attack rate and IFR of 0.1% = 100K deaths
 - 20% attack rate and IFR of 0.06% = 40K deaths
 - Likely season-to-season variability



- Endemic COVID-19 is not cancer or heart disease, but it's still a substantial public health burden
 - Hospitalizations
 - Deaths
 - Long COVID
- What we can do:
 - Yearly boosters with modified vaccines like the flu vaccine
 - Therapeutics e.g., molnupiravir
 - Rapid testing
 - Improved ventilation
 - Mask use





Questions

Upcoming NEBGH virtual events:

- Oct. 21 Improving Equity in Mind-Body Healthcare There's an App for That!
- Oct. 25 Weekly Monday COVID-19 Update: The Ins and Outs of Vaccine Mandates, Exemptions, Accommodations and More
- Nov. 2 Navigating the New Gateways to Access Mental Health
- Nov. 3 Hospital Price Transparency Requirements and Employers
 - **Dec. 9 -** Pharmacy Benefits Strategies for Now and Later