Notes on COVID-19

Part 10: 2020-06-08 to 2020-06-17

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2020-06-17

2020-06-08 A survey by Mullard in The Lancet of vaccine candidates, where they are in trials, and near-mid-term prospects for development of vaccines https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31252-6/fulltext

2020-06-08 Hsiang et al (largely from Berkeley) have looked in a paper in Nature at the effect of large-scale public anti-contagion policies on the Covid-19 pandemic https://www.nature.com/articles/s41586-020-2404-8_reference.pdf From the abstract: "*Here, we compile new data on 1,717 local, regional, and national non-pharmaceutical interventions deployed in the ongoing pandemic across localities in China, South Korea, Italy, Iran, France, and the United States (US). We then apply reduced-form econometric methods, commonly used to measure the effect of policies on economic growth, to empirically evaluate the effect that these anti-contagion policies have had on the growth rate of infections. In the absence of policy actions, we estimate that early infections of COVID-19 exhibit exponential growth rates of roughly 38% per day. We find that anti-contagion policies have significantly and substantially slowed this growth.*"

2020-06-08 Similarly, Flaxman et al (largely from Imperial College) have looked at the effects of non-pharmaceutical interventions in 11 European countries until 4 May https://www.nature.com/articles/s41586-020-2405-7 "*We estimate that, for all the countries we consider, current interventions have been sufficient to drive the reproduction number R_t below 1 (probability $R_t < 1.0$ is 99.9%) and achieve epidemic control. We estimate that, across all 11 countries, between 12 and 15 million individuals have been infected with SARS-CoV-2 up to 4thMay, representing between 3.2% and 4.0% of the population. Our results show that major non-pharmaceutical interventions and lockdown in particular have had a large effect on reducing transmission*."

2020-06-08 To et al in The Lancet Microbe looked at the seroprevalence of SARS-CoV-2 in Hong Kong and residents evacuated from Hubei province https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30053-7/fulltext "*The seropositivity rate in Hubei returnees indicates that RT-PCR-confirmed patients only represent a small proportion of the total number of cases. The low seroprevalence suggests that most of the Hong Kong and Hubei population remain susceptible to COVID-19. Future waves of the outbreak are inevitable without a vaccine or antiviral prophylaxis.*"

2020-06-09 Peter Daszak, president of EcoHealth Alliance, which works with governments and other organisations to analyse and prevent pandemics, has written in TheG that it is clear that SARS-CoV-2 is of zoological origin and not artificially manipulated https://www.theguardian.com/commentisfree/2020/jun/09/conspiracies-covid-19-lab-false-pandemic A paper is due soon in Nature Communications.

2020-06-10 The European Commission has said that Russia and China are behind a "huge wave" of Covid-19 disinformation. EC Vice-President Věra Jourová gave a press conference about it on Wednesday https://www.theguardian.com/world/2020/jun/10/eu-says-china-behind-huge-wave-covid-19-disinformation-campaign

2020-06-12 Neil Ferguson told the UK House of Commons Science and Technology Committee on Wednesday 2020-06-10 that "*[h]ad we introduced lockdown a week earlier we'd have reduced the final death toll by at least half*", which means some 20,000 deaths averted https://www.theguardian.com/world/2020/jun/10/uk-coronavirus-lockdown-20000-lives-boris-johnson-neil-ferguson Sir David King, former Chief Scientific Advisor to the HMG and convenor of the Independent SAGE committee went further on a TV interview on the Good Morning Britain show in 2020-06-11, available at https://www.dailymail.co.uk/video/coronavirus/video-2189770/Video-David-King-Earlier-lockdown-cut-deaths-10-000.html He thinks that going into lockdown a week earlier could have resulted in about 10,000 deaths rather than the 40,000-some the UK has now suffered. This suggestion is consistent with the estimates of James Annan and John Dagpunar reported in my Notes Part 7 on 2020-05-20.

2020-06-12 Pybus et al on behalf of the Covid-19 Genomics UK Consortium (COG-UK) have analysed the transmission lineages of the virus in GB https://virological.org/t/preliminary-analysis-of-sars-cov-2-importation-establishment-of-uk-transmission-lineages/507 Most came in through international travel into the country. The researchers found 1356 lineages and believe this is an underestimate. Some of the lineages seem to have "died out" already. "*We estimate that ≈34% of detected UK transmission lineages arrived via inbound travel from Spain, ≈29% from France, ≈14% from Italy, and ≈23% from other countries. The relative contributions of these locations were highly dynamic.*" There is a useful summary by Hannah Devlin in TheG on 2020-06-11 https://www.theguardian.com/world/2020/jun/11/british-clampdown-on-non-essential-travel-came-a-week-too-late Interestingly, "*[t]he study also found that individual events, such as Liverpool's controversial match against Atletico Madrid, on 11 March, probably made little difference to the overall number of imported cases. An estimated 3,000 fans travelled to watch the game, but at the time around 20,000 inbound passengers were arriving from Spain every day anyway.*"

2020-06-15 Okell et al consider in The Lancet on 2020-06-11 the observed declines in Covid-19 cases and deaths in various countries, and use the data to amplify two possible causes: extensive developed immunity ("herd immunity"), and social distancing mechanisms. The available data support the distancing mechanisms as cause, and not any developed immunity, which is still of relatively low prevalence. "*… there are large differences in patterns of per-capita deaths in different countries that are difficult to reconcile with herd immunity arguments but are easily explained by the timing and stringency of interventions. Seroprevalence studies also provide an independent source of information that is highly consistent with mortality data. The herd immunity argument is therefore at odds with both mortality and seroprevalence data, whereas the intervention argument provides a parsimonious explanation for both.*

…….epidemiological data suggest that no country has yet seen infection rates sufficient to prevent a second wave of transmission, should controls or behavioural precautions be relaxed without compensatory measures in place."

2020-06-15 Stringhini et al in The Lancet on 2020-06-11 study the seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva (a study called SERO-CoV-POP). They enrolled just under 2800 participants from just over 1300 households and studied them weekly from 2020-04-06 to 2020-05-09. In the first week, a seroprevalence of 4·8% was estimated; increasing to 8·5%, 10.9%, 6.6% and 10.8% in the subsequent weeks. "*Individuals aged 5–9 years ….and those older than 65 years …. had a significantly lower risk of being seropositive than those aged 20–49 years.*" The key observation: "*we estimated that for every reported confirmed case, there were 11·6 infections in the community.*" Their interpretation: "*These results suggest that most of the population of Geneva remained uninfected during this wave of the pandemic, despite the high prevalence of COVID-19 in the region (5000 reported clinical cases over <2·5 months in the population of half a million people). Assuming that the presence of IgG antibodies is associated with immunity, these results*

highlight that the epidemic is far from coming to an end by means of fewer susceptible people in the population."

2020-06-15 Ooi and Low comment in The Lancet Infectious Diseases on two independent studies of people from the Diamond Princess cruise ship who were asymptomatic when tested for the presence of SARS-Cov-2. "*Of the 43 individuals positive for SARS-CoV-2 on RT-PCR who were asymptomatic at admission to a hospital in Tokyo, Japan, ten developed COVID-19, including severe pulmonary disease. Of the 215 asymptomatic individuals who returned to Hong Kong for further quarantine and were enrolled in the study by Hung and colleagues, eight became RT-PCR positive and three of them eventually developed symptoms; a ninth individual was seropositive for SARS-CoV-2 and had abnormalities on chest CT scan but remained asymptomatic….. these studies describe two remarkable features. First, the presence of comorbidities did not appear to increase susceptibility to symptomatic infection or even disease outcome in these studies. Instead, older age appeared to be the only demographic factor that differentiated symptomatic from asymptomatic outcome in the individuals in Hong Kong, as well as differentiating severe from mild cases in the Japanese hospital. Second, about 50% of asymptomatic individuals showed radiographic abnormalities, including ground-glass opacities on chest CT scans.*" The Japanese study by Tabata et al in The Lancet Infectious Diseases on 2020-06-12 is https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30482-5/fulltext and the Hong Kong study by Hung et al , in the same journal also on 2020-06-12, is https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30364-9/fulltext Also see the letter to the NEJM on 2020-06-12 by Sakurai et al https://www.nejm.org/doi/full/10.1056/NEJMc2013020?query=featured_coronavirus , which reports that out of 96 a- and presymptomatic travellers on the Diamond Princess transferred to a hospital in Central Japan, 11 subsequently developed symptoms.

2020-06-15 A colleague asked about the chances of dying if he was ill enough to be admitted to hospital. There was a BMJ study by Argenziano et al on 2020-05-18 about the experience at one NYC hospital. From the first 1000 admitted, 211 died, just over a fifth https://www.bmj.com/content/369/bmj.m1996 But caution is required in extrapolating. The CFR is very, very different in different countries and regions: see Notes Part 7, entry on 2020-05-23. The NYC experience is not the London experience, and significant regional differences in the UK have already been noted. Just the fact that the CFRs are so very different needs explaining.

2020-06-15 Almost any interview with Anthony Fauci is worth reading, and this by Jennifer Abbasi published on 2010-06-08 more than most https://jamanetwork.com/journals/jama/fullarticle/2767208

2020-06-16 Ieva Ilves advises the government of Latvia on digital technology for contact tracing. Latvia has until now a fairly good record of suppressing Covid-19. Latvia has apparently tried to use the Apple-Google app infrastructure but it does not fulfil the needs (either epidemiological or political) and she queries whether it is appropriate for foreign technology companies to be telling democratic governments what they can do and what not. It is an important discussion https://www.theguardian.com/commentisfree/2020/jun/16/google-apple-dictating-european-democracies-coronavirus

2020-06-16 Good news! Dexamethasone reduced the death rate of Covid-19 by 1/3 in an RCT. A result of the Recovery trials in GB. "*The study enrolled 2,100 participants who received dexamethasone and tracked how they fared in comparison with about 4,300 people who received standard care. For people on ventilators, it reduced deaths by about one-third. For patients needing*

oxygen, it cut the risk of death by one-fifth. The drug seems to reduce the damage from a ... cytokine storm." (Nature Briefing email). https://www.nature.com/articles/d41586-020-01824-5 This stuff is not special – you can get it at your local pharmacy. A 4mg tablet costs less than €1 if you buy in bulk. Of course, when you are ill enough that it helps, the hospital will be giving it to you. And there is no question that they will have enough of it. Cheap and plentiful, both advantageous over remdesivir.

2020-06-17 It is well known that if you have a test which is quite accurate, but tests for a rare event, that erroneous results overwhelm accurate ones. Say a test for human-condition X is 98% accurate, with a 2% false-positive rate (it says you have X when you do not). And say condition X is present in roughly 1% of the population. Then if you test 100 people, you would expect two people to test positive when they do not have X, and one person A to have X. So, whether or not A tests positive, the proportion of people mistakenly identified to have X is at least twice as high as the proportion of people identified to have X when they do. This may not matter for 100 people, but it certainly matters for a few million people if handling X is very resource consuming, as people all over the world in lockdown against Covid-19 can attest. Martyn Thomas brought to my attention an example from California which makes this clear https://www.npr.org/sections/health-shots/2020/06/15/871186164/what-zebra-mussels-can-tell-us-about-errors-in-coronavirus-tests?t=1592393125639&t=1592403323037 The best part is the very last sentence.

2020-06-17 Trish Greenhalgh has been arguing in the medical literature for general use of face masks as source control for Covid-19 transmission, as well as in TheG. Source control means preventing emissions of the wearer from distributing in the environment, specifically exhaled droplets in the case of Covid-19. Her contributions have attracted criticism, not least because much of the literature on face covering is concerned with infection control, namely how such coverings protect the wearer, which, as she points out, is a different kettle of fish. She published a response to critics in the Journal of Evaluation in Clinical Practice on 2020-05-26 https://onlinelibrary.wiley.com/doi/10.1111/jep.13415 and notes a preprint from the German organisation IZA, the Institute of Labor [sic] Economics, which estimated the requirement for face masks in Germany reduced transmission https://www.iza.org/publications/dp/13319/face-masks-considerably-reduce-covid-19-cases-in-germany-a-synthetic-control-method-approach

I really don't know why this proposal of Greenhalgh could be controversial. Videos show drops spreading, and being hindered by face coverings. When I was a kid in the 1950's, putting your hand in front of your mouth when coughing or sneezing, to protect others from your effluent, was considered courteous. Nobody felt the need to ask "is it *really* so?", or "how well does it work?" Nobody seriously wondered whether "sneezing into an atmosphere with lots of people in it is not noticeably different from covering your mouth as you do so." Nobody thought it pertinent that "it is not perfect; some drops are going to get around your hand anyway." Nobody suggested RCTs, even if anyone could figure out how to design one when the environment consists predominantly of obviously confounding variables. It was not because we were incurious. It was because it was obvious that putting something physical in the air/droplet stream hindered the spread of aerial effluent. The question now appears to be not about coughing or sneezing, but talking (and singing). The videos show similar, but not as dramatic, effect.