## **Notes on COVID-19**

Part 2: 2020-03-21 to 2020-03-31

Peter Bernard Ladkin 2020-04-02

2020-03-23 The NYT is reporting that loss of a sense of smell is associated with Covid-19, even in people who are otherwise asymptomatic <a href="https://www.nytimes.com/2020/03/22/health/coronavirus-symptoms-smell-taste.html">https://www.nytimes.com/2020/03/22/health/coronavirus-symptoms-smell-taste.html</a> The article includes advice on this from Professor Claire Hopkins, President of the British Rhinological Association, and Prof Nirmal Kumar, President of ENT UK <a href="https://www.entuk.org/loss-sense-smell-marker-covid-19-infection">https://www.entuk.org/loss-sense-smell-marker-covid-19-infection</a>. ENT UK is a British association of ear, nose and throat physicians. The American Academy of Otolaryngology refers to it on their WWW site, citing ENT UK <a href="https://www.entnet.org/content/coronavirus-disease-2019-resources">https://www.entnet.org/content/coronavirus-disease-2019-resources</a>. It has been reported in 2/3 of the people talking to Hendrick Streeck, a Uni Bonn virologist interviewing people in Heinsberg. It was also commented by Prof. Clemens Wendtner of LMU.

2020-03-23 TheG live blog <a href="https://www.theguardian.com/world/live/2020/mar/23/coronavirus-live-updates-uk-us-italy-germany-europe-outbreak-cases-meetings-bans-update-latest-news">https://www.theguardian.com/world/live/2020/mar/23/coronavirus-live-updates-uk-us-italy-germany-europe-outbreak-cases-meetings-bans-update-latest-news</a> has a short note about Singapore at 1402 UTC. Singapore has 509 infected "cases", of which 65 are students who have returned from the UK, 12.77% of the total infected. That seems to suggest that there may well be undetected pockets of infection in the UK. It is hard not to bring that in correlation with the different attitudes to testing for the virus in the UK and in Singapore.

2020-03-24 NYT 's Pam Belluck is reporting that a calculation from the Wuhan epidemic is showing symptomatic mortality rate (sCFR) of 1.4% <a href="https://www.nytimes.com/2020/03/19/health/wuhan-coronavirus-deaths.html">https://www.nytimes.com/2020/03/19/health/wuhan-coronavirus-deaths.html</a> Authors are from Hong Kong and Harvard, including Joseph Wu, Gabriel Leung and Marc Lipsitch. <a href="https://www.nature.com/articles/s41591-020-0822-7">https://www.nature.com/articles/s41591-020-0822-7</a>. Leung has been proposing a sCFR of around 1.4% for a while (see the note on his press conference from 2020-03-06). The numbers, though, are worrying from the point of view of control&mitigation. The sCFR was 2.6% for those 60 and older, 0.5% for those 30-59, and 0.3% for those under 30. Not only that, but people showing symptoms were twice as likely in the 60-and-over group as in the 30-59 group, and those under 30 have 1/6 (0.16) the chance of developing symptoms. (These numbers were not sensitive to the probability of developing symptoms after infection, Psym. They are roughly the same with a Psym of 0.5, 0.75 or 0.95) That suggests many younger asymptomatic carriers among people least likely to conform to social distancing requirements.

2020-03-24 An article in Science by Jon Cohen reports the gathering of HIV/AIDS pioneers at Cold Spring Harbor Laboratory. <a href="https://www.sciencemag.org/news/2016/10/gathering-hivaids-pioneers-raw-memories-mix-current-conflicts">https://www.sciencemag.org/news/2016/10/gathering-hivaids-pioneers-raw-memories-mix-current-conflicts</a> The article isn't dated, but it is from 2016-10-26. Amongst other things is the story of how Anthony Fauci got to NIAID. He was frustrated by the slow pace of his own work on HIV/AIDS and the relative lack of support, and wanted to get things done. He has headed NIAID since 1984. The article is a salient reminder of "turbulent times" (Warner Greene). Those that suggest that there is "the science" and politicians and other non-experts should listen to it tend to forget the battles between NCI and Institute Pasteur of the 1980's. Robert Gallo missing out on a Nobel despite establishing definitively the link between HIV and AIDS, then being found guilty of "scientific misconduct" by a USG inquiry, and subsequently being exonerated on appeal.

2020-03-25 A "Perspective" (opinion article) from David J. Hunter of the Nuffield Department of Population Health at the University of Oxford on the British government's puzzling initial response to the Covid-19 outbreak, published last Friday, 2020-03-20 <a href="https://www.nejm.org/doi/full/10.1056/NEJMp2005755">https://www.nejm.org/doi/full/10.1056/NEJMp2005755</a>

2020-03-25 A "Viewpoint" on the apparently-high CFD in Italy, by Onder, Rezza and Brusaferro <a href="https://jamanetwork.com/journals/jama/fullarticle/2763667">https://jamanetwork.com/journals/jama/fullarticle/2763667</a>. They point out that the sCFD of the Italian data and Chinese data are very similar up to the age categories 70-79 and 80-and-older. And over half the number of Italian deaths up to 2020-03-17 were in the 80-and-older category, as compared with only 20% of the Chinese cohort. They also performed a detailed chart review of 255 patients who died: mean age nearly 80, and mean number of comorbidities was 2.7 (SD 1.6). Only 3 patients had no preexisting conditions. They point out that these comorbidities might have increased the chance of death even without Covid-19 infection. However, in Italy, every death of a SARS-CoV-2-positive individual is counted as a death due to Covid-19. This broad definition of Covid-19 death might affect the numbers also. Finally, they suggest testing strategies might have affected the results. Testing of asymptomatic people and those with only mild, limited symptoms was generally not performed after the initial stage of the epidemic in Italy – the CFD on February 24th was 3.1% and on March 17th 7.2%. They compare with Korea, where there was largely blanket testing, and a CFD of 1.0%.

One factor they do not include is that it is widely reported that the health system in Lombardy is overwhelmed. There are not enough ICU places for all those sick, so triage is being performed and people dying who might otherwise have lived with the appropriate care. Of course, we don't know how much that was the case in China.

2020-03-25 Neil Ferguson is giving evidence to the House of Commons science committee. TheG is reporting on its live blog at 10:38 UTC that the UK has "surged" its capacity in critical-care beds; there are now more than twice the number of places that there were. He says that, with the new social-distancing measures and the new capacity, he thinks the UK will be able to cope across the system. He is expecting the peak hospital demand in the next two-and-a-half to three weeks.

2020-03-25 TheG live blog at 1105 is reporting that Jaap van Dissel, head of the Netherlands' public health institute, has told parliament that the "infection rate per carrier" was now on or below 1. This is ten days after the social-distancing measures were put in place – no mass gatherings; restaurants, bars, schools and coffee shops closed. Getting the transmission rate under 1 is key. It is good to know that can happen in ten days, somewhere. TheG refers to this newspaper report: <a href="https://www.dutchnews.nl/news/2020/03/dutch-coronavirus-measures-may-be-slowing-growth-health-chief-tells-mps/">https://www.dutchnews.nl/news/2020/03/dutch-coronavirus-measures-may-be-slowing-growth-health-chief-tells-mps/</a>

2020-03-25 Oxford's Blavatnik School of Government has launched a government-response tracker. News at <a href="https://www.bsg.ox.ac.uk/news/worlds-first-covid-19-government-response-tracker-launched-today">https://www.bsg.ox.ac.uk/news/worlds-first-covid-19-government-response-tracker-launched-today</a> and tracker at <a href="https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker">https://www.bsg.ox.ac.uk/news/worlds-first-covid-19-government-response-tracker-launched-today</a> and tracker at <a href="https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker">https://www.bsg.ox.ac.uk/news/worlds-first-covid-19-government-response-tracker-launched-today</a> and tracker at <a href="https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker">https://www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker</a> Invaluable, I anticipate. Various types of social distancing are currently the only methods available to us to dampen the pandemic. (Obviously people are interested in the site – it has a very slow response time.)

2020-03-25 The Robert Koch Institut (without an "e") is the German public health organisation. They are using a version of the JHU CSSE Dashboard to show the infections and deaths in Germany, not only by Bundesland (state) but by Landkreis (administrative district). Its titles and subtitles are in German, of course

https://experience.arcgis.com/experience/478220a4c454480e823b17327b2bf1d4/page/page\_1/ I have looked at Bielefeld, where I live, as well as all of the surrounding districts, which are

Gütersloh (SW to NW, named after the city of the same name, home to Bertelsmann, the largest English-language publisher in the world, as well as the home-equipment manufacturer Miele), Lippe (SE, a largely rural district with a historic town Detmold, with a stately home right in the middle and a world-famous music academy) and Herford (NE, with an old town centre ranging about the River Werra). The numbers are interesting:

•	Bielefeld:	36 cases,	pop. 333, 786,	rate 10.79 cases per 10K population
•	Gütersloh:	190 cases,	pop. 364, 083	rate 52,19 cases per 10K
•	Lippe:	162 cases,	pop. 348, 391	rate 46.50 cases per 10K
•	Herford:	102 cases,	pop. 250,783	rate 40,67 cases per 10K

Other nearby districts are similar:

•	Osnabrück I	157 cases,	pop. 357,343	rate 43.94 cases per 10K
•	Osnabrück II	135 cases,	pop. 164,748	rate 81.94 cases per 10K
•	Minden-Lübb	ecke 177 case	es pop. 310,710	rate 56.97 cases per 10K

The question is why the Bielefeld rate is one-fourth that of the next-lowest district. On Friday 2020-03-13, the Bielefeld mayor cancelled all planned public events, effective Sunday morning 2020-03-15 at 00.00 until April 30 at 24.00. At that point, there were reported to be 15 Covid-19 cases in Bielefeld https://www.t-online.de/region/bielefeld/news/id 87515566/coronavirus-bielefeld-stadtuntersagt-alle-oeffentlichen-veranstaltungen.html . At the same time, the state government acted to close schools and kindergarten, as well as child-care facilities, from Monday 2020-03-16 until 2020-04-19. Restaurants had to close state-wide at 1500 from Tuesday 2020-03-17 on. Now they are completely closed; things have been further regulated by the Federal Government since Sunday 2020-03-22, no more than two people not in the same household may meet, etc.

I wonder if Bielefeld being just a few days ahead of everywhere else has made the difference? It is plausible from the mathematics of exponential growth, and a fine piece of foresight by our mayor if it is so. I think so. For the details, and a histogram, see CoV-Notes-3 with date 2020-04-02. Figures used there are taken from the local newspaper, rather than the Robert Koch Institute which also publishes figures but those figures are often delayed by a few days so the histograms are distorted.

The figures from the local newspaper up to 2020-03-24 (the day of the figure; the day of publication is the next one. Saturday's figures together with Sunday's appear in Monday's paper, so are not available separately).

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2020-03-24
                 104
                        Diff:
                               6
   2020-03-23
                 98
                               5
•
   2020-03-22
                 93
                              11
   2020-03-21
                 n/a
   2020-03-20
                 72
                              15
   2020-03-19
                 57
                               8
   2020-03-18
                 49
                               6
   2020-03-17
                              15
                 43
   2020-03-16
                 28
                               1
   2020-03-15
                 27
                               8 Date on which social distancing measures came into force
   2020-03-14
                 n/a
   2020-03-13
                 19
                               <4
   2020-03-12
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>15 cases reported. Date of mayor's social distancing measures

## • 2020-03-07 1st case reported

The decision to cancel all events was taken on Thursday 2020-03-12, presumably on the basis of Thursday's figure of "more than 15 infected". Before that, only events with more than 1,000 participants, for example football games of the local team Arminia Bielefeld, had been cancelled.

The mayor said "the number of infected is doubling about every 24 hours" (NW, 2020-03-15). There is of course uncertainty about who is infected, because there is no serological test, and general guidelines on testing only those who have been in contact with a known infected person, or have been in regions of the world identified as risky within the previous 14 days, let me talk about those "identified as infected" (IaI). The mayor is obviously talking about IaI. His statement did not apply to Bielefeld: if the first IaI was on Saturday 2020-03-07, as reported, then by that reckoning on Thursday there would have been at least 26 = 64 IaI, but there were only about a quarter of that. He was likely talking about Germany in general. For general conclusions, and the histogram to 2020-04-01, please see the entry on 2020-04-02.

2020-03-26 Smith and Prosser have a bullet-point list of possible amelioratory drug options for treating Covid-19 <a href="https://www.elsevier.com/\_data/assets/pdf\_file/0007/988648/COVID-19-Drug-Therapy\_Mar-2020.pdf">https://www.elsevier.com/\_data/assets/pdf\_file/0007/988648/COVID-19-Drug-Therapy\_Mar-2020.pdf</a>

2020-03-26 The "Oxford model" of Sunetra Gupta is at <a href="https://www.dropbox.com/s/oxmu2rwsnhi9j9c/Draft-COVID-19-Model%20%2813%29.pdf?dl=0">https://www.dropbox.com/s/oxmu2rwsnhi9j9c/Draft-COVID-19-Model%20%2813%29.pdf?dl=0</a>

2020-03-26 The Bielefeld figure for 202-03-25 is 120 IaI, 16 more than the day before. The BI population is 333,786 according to the RKI Dashboard, yielding a proportion of 35.95 per million people, which is somewhat under a national rate of 29,000 (assuming Germany's population is 80m), whereas Germany is showing 39,502 IaI according to the JHU dashboard. So BI is showing <sup>3</sup>/<sub>4</sub> of the average rate of IaI in Germany.

2020-03-26 Remuzzi and Remuzzi wrote on March 12 (paper published March 13, to which I referred in my Notes 1), concerning the exponential growth they had seen, that "If this trend continues for 1 more week, there will be 30 000 infected patients." That would have been March 19. The JHU Dashboard shows that this level was reached earlier: 28K on March 16 and 31.5K on March 17. On March 19, there were 41k IaI. They also said "If the Italian outbreak follows a similar trend as in Hubei province, China, the number of newly infected patients could start to decrease within 3–4 days, departing from the exponential trend. However, this cannot currently be predicted because of differences between social distancing measures and the capacity to quickly build dedicated facilities in China." Spot on! New IaI peaked two days later on March 21 at 6.6K, and have been going generally down since then. The IaI count first went over 100 on Wednesday 26th February. There followed three and a half weeks of exponential growth to the high point of new IaI on March 21 and now it is slowly going down.

2020-03-26 Continuing with observations from the JHU Dashboard, in Germany, the 100-point was reached rather spectacularly on March 5, with 220 new IaI. It peaked on March 20, only two and a half weeks later, with 4.5k new IaI. It is still roughly up there (although over the weekend March 21-22 the numbers were down), but slightly lower. Grounds for hope for Germany.

2020-03-27 Actually, not. New IaI yesterday were 6.6k, according to JHU Dashboard. That is an almost 50% rise over any previous day.

2020-03-27 BI has 132 IaI as of Thursday March 26th, 12 more than the previous day.

2020-03-27 Fine article by Tomas Pueyo on strategies and policy, referencing the Imperial work and doing some analysis of their own (a bunch of people worked on it) <a href="https://medium.com/@tomaspueyo/coronavirus-the-hammer-and-the-dance-be9337092b56">https://medium.com/@tomaspueyo/coronavirus-the-hammer-and-the-dance-be9337092b56</a>. (Thanks to Martyn Thomas for the pointer.)

2020-03-27 The Financial Times has extruded certain important commentary from behind its firewall <a href="https://www.ft.com/coronavirus-latest">https://www.ft.com/coronavirus-latest</a>

2020-03-28 The peaks in the German rise in IaI are at 2020-03-13 (1.6k), 2020-03-20 (4.5k), 2020-03-26 (6.6k) and 2020-03-27 (6.9k). That is a sublinear rise in peaks: between 13<sup>th</sup> and 20<sup>th</sup> the rise averaged 410 per day, between 20<sup>th</sup> and 26<sup>th</sup> averaged 350 per day, and between 26<sup>th</sup> and 27<sup>th</sup> 300. Between 20<sup>th</sup> and 25<sup>th</sup>, the daily rise was 4500 or lower, leading some such as myself to hope we had peaked on 20<sup>th</sup>, but it was not to be. For comparison, the IaI per day in Italy appears to have peaked and stabilised. Highest was 6600, on March 21<sup>st</sup> and it hasn't been to 6000 since.

2020-03-28 I missed this last week. The first results of a general screening in Iceland reported on March 23<sup>rd</sup> <a href="https://nordiclifescience.org/covid-19-first-results-of-the-voluntary-screening-in-iceland/">https://nordiclifescience.org/covid-19-first-results-of-the-voluntary-screening-in-iceland/</a> and reported by the government on March 16<sup>th</sup>, updated on March 21<sup>st</sup> <a href="https://www.government.is/news/article/2020/03/15/Large-scale-testing-of-general-population-in-Iceland-underway/">https://www.government.is/news/article/2020/03/15/Large-scale-testing-of-general-population-in-Iceland-underway/</a> At the time of those reports, there were 473 sIaI (for "symptomatic IaI") and 48 testing positive from 5,571 tests on the asymptomatic population (aIaI, or "asymptomatic IaI"). Wikipedia is telling me the population of Iceland numbers 364,260. That means that about one sixty-fifth of the asymptomatic population has been tested, and if that sample is representative, that means just over 3100 people in the general population are asymptomatic SARS-CoV-2 carriers. People are saying (e.g., <a href="https://www.theguardian.com/us-news/2020/mar/23/have-i-already-had-covid19-coronavirus">https://www.theguardian.com/us-news/2020/mar/23/have-i-already-had-covid19-coronavirus</a>) that that means 50% of the infected are asymptomatic. I do not quite understand that arithmetic.

2020-03-28 The Financial Times is making all coronavirus articles free to read. Some observations from Undercover Economist Tim Hartford, and an extended essay by the recently retired neurosurgeon Henry Marsh, author of a highly-praised and by now well-known book on his medical experiences, Do No Harm, and the article on emerging drug therapies are well worth a read <a href="https://www.ft.com/coronavirusfree">https://www.ft.com/coronavirusfree</a>. Hartford points out that the comprehensive testing in Vò found that 50% of viable-virus carriers were asymptomatic. In fact, Crisante and Cassone gave the figure of "a good 70%" for "asymptomatic or quasi-symptomatic" IaI in TheG on 2020-03-20 <a href="https://www.theguardian.com/commentisfree/2020/mar/20/eradicated-coronavirus-mass-testing-covid-19-italy-vo">https://www.theguardian.com/commentisfree/2020/mar/20/eradicated-coronavirus-mass-testing-covid-19-italy-vo</a> 50% is said to be the figure derived from the Icelandic experience also.

2020-03-28 Richard Horton in The Lancet is scathing about Britain's lack of preparedness, and points out that the country was explicitly warned in an article by Joseph Wu and colleagues in The Lancet on January 31, and its chief medical officers could have used February to prepare – and inexplicably didn't. <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30727-3/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30727-3/fulltext</a>

2020-03-28 Rajgor et al. in correspondence in The Lancet point out that the Diamond Princess situation was unique, has by now resolved, and yields a CFR of 0.99%. And that from a population skewed towards more elderly people. Numbers: "3711 passengers and crew were onboard, of whom 705 became sick and tested positive for COVID-19 and seven died". But note a reservation: only symptomatic cases were tested, so the CFD is 0.99% of sIaI. If we acknowledge the Vò and Icelandic experience of having half or less of IaI being sIaI, as well as the bias on the ship towards older passengers, it would follow that the CFD for Diamond Princess passengers and thus for the general population is almost certainly lower than 0.99%.

2020-03-28 Sarah Dalglish points out in The Lancet that in the 2019 Global Health Security Index, which supposedly measures preparedness and ability to deal with a public-health crisis, the US was ranked first, the UK second, South Korea ninth and China fifty-first. As she says, "things look different now." <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30739-X/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30739-X/fulltext</a>

2020-03-28 On Friday 2020-03-27 in BI, there were 142 IaI, 10 hospitalised and 2 on ventilators. 10 IaI more than on Thursday.

2020-03-28 Shen and colleagues report in JAMA on March 27<sup>th</sup> on treating 5 critically-ill Covid-19 patients with plasma transfusions from convalescent patients. Convalescents will have developed appropriate antibodies, and these will be in the plasma. This treatment led to clinical improvement. 4 of the patients were mechanically ventilated, and one ECMO. Concurrently they received interferon and lopinavir/ritonavir treatment.

https://jamanetwork.com/journals/jama/fullarticle/2763983 Roback and Guarner discuss the limitations and implications of this observation https://jamanetwork.com/journals/jama/fullarticle/2763982

2020-03-30 The NewYorker's Isaac Chotiner conducted an interview with Richard Epstein, a lawyer with NYU and the Hoover Institution, who has an interest in epi/pandemics. The interview was published today, and turned out to be pretty testy

 $\underline{https://www.newyorker.com/news/q-and-a/the-contrarian-coronavirus-theory-that-informed-the-\underline{trump-administration}}$ 

I think it is worth some detailed discussion, because Epstein makes a number of scientific claims that he suggests justify his estimate. He is an obvious academic high-flyer of some eminence (else he wouldn't be at Hoover), a lawyer who believes he understands epidemiology. The interviewer is not necessarily sympathetic, but that goes with the territory. Chotiner does fact-check. Two weeks on, we can fact check a little more. The interview was conducted on Wednesday, March 18<sup>th</sup>, two weeks ago. Epstein's modified prediction is 5,000 US dead. This will either be right or wrong, very quickly.

[Added 2020-04-02. The JHU Dashboard says the total deaths in the US are 5,137 (at 1119 MEST = UTC+2 = 0919 UTC) and looking at the US "daily increase" histogram, it is still looking as if it is in the exponential-growth phase. Given the Imperial College estimate of 17.8 days between onset of symptoms and death, and allowing for a couple of days before confirmation, there is about a two-week delay between confirmation of a case and death, in case of death. From which it follows that US deaths will still be increasing, likely parallel to the confirmed-case graph with a two-week lag. Which suggests exponential growth in deaths for at least another two weeks yet. That is the view of another cod-epidemiologist, namely me, but it is not on the Hoover Institution WWW site. But these numbers aren't a "view"; they are, rather, fact. And they show that Epstein is wrong.]

Epstein thinks (thought) all the fuss about Covid-19 (indeed, about epidemics in general) is overblown. He wrote a couple of short on-line articles (blog posts) about it on the Hoover Institution WWW site (referenced below), apparently in reaction to an NYT piece by Nicholas Kristof and Stuart Thompson on March 13<sup>th</sup>.

The Kristof/Thompson (K&T) NYT article is worth reading. It has some nice interactive graphics <a href="https://www.nytimes.com/interactive/2020/03/13/opinion/coronavirus-trump-response.html">https://www.nytimes.com/interactive/2020/03/13/opinion/coronavirus-trump-response.html</a>. K&T built the graphical model informed by epidemiologists Ashley Tuite and David N. Fisman at the Dalla Lana School of Public Health at the Uni Toronto. It gives the usual curve of undamped

epidemic spread and how social/political measures can "flatten" it.

In response, Epstein published <a href="https://www.hoover.org/research/coronavirus-isnt-pandemic">https://www.hoover.org/research/coronavirus-isnt-pandemic</a> with a further commentary a week later <a href="https://www.hoover.org/research/coronavirus-overreaction">https://www.hoover.org/research/coronavirus-overreaction</a>. He suggested an original estimate of 500 US deaths (later amended to 5,000 .... but the follow-up post still includes the 500 figure).

Epstein thinks the "standard model" is wrong. He refers to the K&T graphs as an example.

The standard model is based on the basic reproduction number R0 (the average number of people an infected person will further infect) and the serial interval (the average length of time it takes to pass the infection on). Let us assume a constant rate of personal contacts of infectious-person X and therefore opportunities for transmission, say C contacts per day. Let us also assume that people who have been infected become (after the disease has run its course) immune. So, no repeat infections. At the very beginning, X will contact C people not yet infected, and 0 people already infected. As time goes on and the prevalence of the disease in the population increases, the proportion of personal contacts of X who have already been infected goes up, say to PT. So, in a day, X will contact C.PT already-infected people, and, correspondingly, C.(1 - PT) people not yet infected. X has thus continuously-lowering opportunity to pass the infection on. The true infection number (technically known as the effective repreoduction number), RT at time T, thus decreases with increasing time T, and when it goes below 1 the epidemic begins to recede. That is the "standard model" of undampened transmission. The K&T graphs show this, and they also show how this can be "dampened" over time by reducing C, say by so-called "social distancing". The idea is that this dampening extends the time period over which infection continues to spread, but it reduces the peak number of diseased people at any given time, and thus aims not to overwhelm at any one time the health-care resources available, which cannot be ramped up anywhere near as quickly as diseases can spread. There is no need for me to illustrate this graphically – K&T have already done so.

What the Kristof/Thompson graphics show is also what all the more sophisticated models show. All the more sophisticated models I have seen are tweaks of this "standard model", which consider variations in data collection per subpopulation (for example, differing by country or region, travellers or on-location cases, comprehensive cohort screening or clinical presentation) and differences in subpopulations, as well as introducing the effect of various factors which the simple standard model ignores. Such as the opportunity for repeat infection.

The "standard model" is pretty well explained (as one would expect) in the first week of the short course the LSHTM is putting on at the moment (3 weeks, 4 hours/week).

Epstein suggests three ways in which this "standard model" is wrong. First, there is an "adaptive response". Second, there is with Covid-19 an increased "vulnerability of infection for older people". Third, the model assumes that "the strength of the virus remains constant, when it does not."

It is notable that his notes do not refer to any of the epidemiological analyses already in the literature. He is also not using standard terminology, which means one has to inquire further what he means.

First, "adaptive response". It is not clear whether he means social/political response or whether he is referring to a physical response of the human body. If he is talking about social/political response then that is exactly what the K&T graphs show. It is part of the standard model, and it is not clear why Epstein might think this could be wrong. It obviously isn't. If he is saying "these distancing measures" are actually much more effective than people think, then let us genuinely hope

so. That is, ultimately, a political and social issue. Radical distancing measures seem to have been very effective in Wuhan, where people are also reported sometimes to have been welded in to their apartments to prevent them from leaving! In contrast, it is not clear how well New Yorkers or Californians are willing or able to comply with injunctions to stay at home and well away from other humans. Evidence from Florida during university/college "spring break" doesn't show that young Americans are taking it very seriously at all.

If Epstein is referring rather to a physical response of the human body, I don't know of any reported evidence that any human body is reacting to the virus differently on March 18th than it would have on January 1st, all other things being equal.

Second, the "vulnerability of infection for older people". It is not clear what he means (using standard terminology would help here). One interpretation is that older people are more likely to become infected. I don't know of any evidence for that. Indeed, the latest, most comprehensive study from the Imperial College group (see 2020-03-31) assumes the infection attack rate is uniform across ages. Another interpretation could be that older people are more likely to have severe reactions to the disease including death. There is generally-accepted evidence that the CFR is far higher for older people, and the Imperial study confirms that. But it seems odd to describe that wellknown concept as "vulnerability of infection"; it does not have to do with infection, but rather with the disease. It could be that lots of people get infected, but few (of any age group) get the symptoms of the disease – they remain asymptomatic. And that could be true of older people also – there is no good age-classified estimate of the prevalence of asymptomatic infection yet, as far as I know. Early data from Singapore suggested asymptomatic carriers to be about a third of carriers. I believe. The experience of Vò, one of the first outbreaks in Italy, a small town of about 3,000 people where everyone was systematically tested by Uni Padua researchers, has suggested it is about half. Initial experience from Iceland, where a local biomedical company is helping the government conduct extensive tests of the general population, is also that asymptomatic carriers are about half the infected. None of that data is age-striated.

Finally, maybe he rather means "vulnerable to the disease", the consequences of symptomatic Covid-19. Any estimate of who is more vulnerable in this sense, and who less, should surely note that older people are radically more likely to die from it. So how many "older people" are there in the US? In 2016, there were 6.9m aged 85 or older, and 37.2m aged 65 or older, so it follows 30.3m aged 65-84. With a CFD amongst the over-80's of almost 13.4% (see the Imperial figures from 2020-03-21), to achieve Epstein's (modified) figure of 5,000 deaths even amongst just this age group, you would need to ensure that, to the nearest thousand, at most 37,000 of those 6.9m develop Covid-19, an infection rate of 5.4%. That is, that fewer than one in nineteen over-84-year-olds become sympomatically infected. Possible? Maybe. But not predictable from any current model of which I am aware.

Third, Epstein criticises an assumption that "the strength of the virus remains constant, when it does not". It is not clear what he means by "strength". If he means virulence, then there is currently no evidence that any strain of SARS-CoV-2 is less or more virulent than any other strain. He cites HIV as an example. As far as I know, HIV is exactly as virulent as it always was over the last 40 years. What has changed is propylaxis and treatment. Maybe he is alluding to a phenomenon also described by retired pathologist John Lee in The Spectator recently [2020-03-28 – see 2020-04-02] <a href="https://www.spectator.co.uk/article/The-evidence-on-Covid-19-is-not-as-clear-as-we-think">https://www.spectator.co.uk/article/The-evidence-on-Covid-19-is-not-as-clear-as-we-think</a>, that "most infections tend to decrease in virulence as an epidemic progresses." Unfortunately, Lee does not amplify on what he said.

In conclusion, it is hard to see what Epstein means. But whatever he might mean, he is almost certainly wrong in the prediction to which his thoughts led him, and the next couple of weeks are

likely to show that definitively.

2020-03-30 A new respiratory-help machine has been devised by UCL researchers and the Mercedes F1 engineers, called Continuous Positive Airway Pressure, or CPAP. It doesn't require sedation or intubation, so can hopefully keep people out of ICU. Mercedes can make 1,000/day if it works. TheG live blog at -03-03 07:09 BST (UTC+1)

https://www.theguardian.com/world/live/2020/mar/30/coronavirus-live-news-us-deaths-could-reach-200000-uk-warned-six-month-lockdown-covid-19-latest-updates

2020-03-30 NW says 146 sIaI in BI on Sunday, 4 more than on Friday. (RKI says 123 reported to them.)

2020-03-31 The Imperial College group has produced the most detailed study yet of case fatality ratio and infection fatality ratio of Covid-19, using data on 70k individuals in China and various data from elsewhere than China, and attempting to correct for biases derived from observation (for example, calculating from hospitalised cases misses many if not most symptomatic cases; and calculating from symptomatic cases misses asymptomatic infections).

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/fulltext

They obtain an overall CFD of 1.38% (1.23-1.53) in China. (The crude CFD from the Chinese data is 3.67% (3.56-3.8), showing the difference if you just calculate from lab- and clinically-confirmed cases.) However, the data are very age-dependent. They found "substantially higher ratios in older age groups (0.32% [0.27-0.38] in those aged <60 years vs 6.4% [5.7-7.2] in those aged  $\geq$ 60 years), up to 13.4% (11.2-15.9) in those aged 80 years or older. Estimates of case fatality ratio from international cases stratified by age were consistent with those from China (parametric estimate 1.4% [0.4-3.5] in those aged  $\leq$ 60 years [n=360] and 4.5% [1.8-11.1] in those aged  $\leq$ 60 years [n=151])."

The estimated overall infection fatality ratio for China was 0.66% (0.39-1.33). They also estimated the proportion of infected individuals likely to be hospitalised, which increased with age up to 18.4% in those 80 years old and over.

The underlying assumption is that the attack rates do not vary with age. The infection attack rate they estimated at 80% for an unmitigated epidemic.

2020-03-31 (actually noted yesterday) Using the Imperial CFR of 1.38%, LSHTM CMMID researchers have estimated the effective detection/reporting rate in various countries <a href="https://cmmid.github.io/topics/covid19/severity/global\_cfr\_estimates.html">https://cmmid.github.io/topics/covid19/severity/global\_cfr\_estimates.html</a> Italy, Spain, France and the UK are all under 10% (in 2.5%-97.5% confidence range), the US is 13%-18%, Germany is 51%-84%, South Korea 58%-100% and Norway 63%-100%.

2020-03-31 Cases in Bielefeld 164 (NW) on Monday or 169 (RKI). 18 more on Monday than on Sunday. (Reminder, only 4 over the weekend.)