Notes on COVID-19

Part 4: 2020-04-16 to 2020-04-23

Peter Bernard Ladkin 2020-04-23

2020-04-16 Helen Ward, Professor of Public Health at Imperial College London, is scathing about the British government response in early-mid March to expert advice it was being given on what to do about the Covid-19 pandemic, in an article in TheG

 $\underline{https://www.theguardian.com/comment is free/2020/apr/15/uk-government-coronavirus-science-who-advice}$

2020-04-17 William Hanage is a Brit who is now a professor at Harvard's T. H. Chan School of Public Health https://www.hsph.harvard.edu/william-hanage/. He wrote a short, striking opinion article for The Observer newspaper on 2020-03-15 on the UK government then-approach with the title "I'm an epidemiologist. When I heard about Britain's 'herd immunity' coronavirus plan, I thought it was satire". The Observer is TheG's sunday paper, although it is a lot older, founded in 1791. His latest opinion piece in TheG today crunches a few simple numbers to suggest that, far from being almost over, the pandemic is just starting

https://www.theguardian.com/commentisfree/2020/apr/16/number-coronavirus-pandemic The numbers are as follows. There are about 100,000 recorded infections in the UK at present. He cites the BMJ editorial from 2020-04-02 (https://www.bmj.com/content/369/bmj.m1375, referenced in Notes Part 3) which discussed initial data from China suggesting that maybe 4/5 of cases are asymptomatic. That would give 500,000 UK infections. If the UK is at "peak infections", assume there will be at least as many "going down" the curve as "coming up". That gives 1m infected after this wave – and 65m not yet infected. Under optimistic assumptions about transmissibility and immunity, Hanage observes that "you would need half your population to have been infected to achieve a level of population immunity that would stop the epidemic continuing to grow and overwhelming healthcare systems." That is 33 times what would have happened in the first wave. So we would need 30 waves to get to that point. About 10,000 have died so far. Assuming equal numbers of deaths "going down", that would be 20,000 deaths in the first wave. And you need 30 of them I strongly doubt there are going to be thirty waves at 2-3 months a pop. That is over 7 years total time; the progression of the disease will be better understood and managed; there will likely be pharmacological mitigants, and, as things seem now, likely a vaccine or two. AIDS has been around for almost forty years without an HIV vaccine; lifestyle changes and pharmacological and physical mitigants have held it somewhat in check.

2020-04-17 And here is the Australian epidemiologist Gideon Meyerowitz-Katz also explaining why the herd-immunity idea is bonkers, using Australian numbers https://www.theguardian.com/commentisfree/2020/apr/17/herd-immunity-is-a-fatal-strategy-we-should-avoid-at-all-costs

2020-04-17 An article from the Financial Times on the UK's decision making processes using not only Covid-19 but also some recent history concerning the BSE/vCJD and H1N1 incidents https://amp.ft.com/content/1e390ac6-7e2c-11ea-8fdb-7ec06edeef84 (thanks to Martin Newby for the reference).

2020-04-17 Here is the list of contributors to the program budget of the World Health Organisation https://www.weforum.org/agenda/2020/04/who-funds-world-health-organization-un-coronavirus-pandemic-covid-trump/ The UK and Germany are the third and fourth biggest contributors, after

the US and the Bill and Melinda Gates Foundation. On top of this, WHO gets further donations for specific purposes, such as dealing with specific outbreaks of infectious disease, such as at present.

2020-04-17 The UK has set up the world's largest controlled trial of drugs for help with Covid-17, called Recover, which has recruited 5,000 participants in a month. It is led by Peter Horby, Chair of UK NERVTAG, and Martin Landray and is hosted at Oxford's Jenner Institute. https://www.theguardian.com/world/2020/apr/17/world-biggest-drug-trial-covid-19-uk Recruits amount to 10% of UK Covid-19 patients. They are trying out most everything we've heard of, except remdesivir because they couldn't get enough of it (it is already in trials in the US and China, and other supplies are going for compassionate use). They haven't yet but will decide on an IL-6 antagonist to cope with the cytokine-storm-like phenomenon with Covid-19. I pointed out some discussion in The Lancet with respect to baricitinib in Notes Part 3 on 2020-04-04. Recover is looking at toxilizumab. Maybe also plasma? And there is hope for monoclonal-antibody approaches, but nothing specific on the table.

2020-04-17 Philip Oltermann is reporting on TheG live blog

https://www.theguardian.com/world/live/2020/apr/17/coronavirus-live-news-trump-says-29-states-could-reopen-relatively-soon-as-global-deaths-near-145000 at 1118 BST (= MEST -1 = UTC -2) that German Health Minister Jens Spahn has claimed the outbreak is "controllable". Daily newly-infected have been fewer than daily newly-recovered since Sunday April 12th. The head of the Robert Koch Institute, Germany's public-health body, has said the effective reproduction rate R_t is currently 0.7. But the mortality rate is up to 2.9%.

2020-04-17 BI figures. NW reported 269 infected on Thu 9th April. Good Friday morning the paper was distributed with this figure, and the next edition came out on Tuesday 14th April, contained the figure for Easter Monday 13th April.

I give the figures differently.

I am starting to give the "ill" figure is in three parts: <infected>/<hospitalised>/<in intensive-care>. And I now include the figure for recovered. Note that the "Diff" for 2020-04-13 is over the four days 2020-04-10 to 2020-04-13 inclusive.

•	Date	inf/hosp/ICU	Diff	Recovered
•	2020-04-16	336/16/8	36	176
•	2020-04-15	300/18/9	6	169 (?)
•	2020-04-14	294	0	170
•	2020-04-13	294	25	122

2020-04-17 TheG live blog at 0616 BST (= MEST - 1 = UTC - 2) is giving numbers from the JHU Dashboard of the 10 countries with the largest number of (declared) infections. These include the newly upward-revised figures for Chinese deaths. They are (quote):

• US: 667,225 (33,286 deaths)

• Spain: 184,948 (19,315 deaths)

• Italy: 168,941 (22,170 deaths)

• France: 147,091 (17,941 deaths)

• Germany: 137,698 (4,052 deaths)

• United Kingdom: 104,145 (13,759 deaths)

• China: 83,403 (4,636 deaths)

• Iran: 77,995 (4,869 deaths)

Turkey: 74,193 (1,643 deaths)Belgium: 34,809 (4,857 deaths)

Using the simple (and wrong, for reasons discussed in Notes Part 1) calculation of mortality rate as <recorded deaths>/<number of infections>, we arrive at

- US 4.9%
- E 10.4%
- I 13.1%
- F 12.1%
- D 2.9%
- GB 13.2%
- China 5.5%
- Iran 6.2%
- Turkey 2.2%
- B 13.9%

These figures will obviously be lower than <deaths>/<deaths + recoveries> which was discussed in Part 1 as a possibly more accurate estimate. All these figures depend on the pervasiveness of testing and on which deaths are recorded. Two sources of inaccuracy that have arisen in multiple jurisdictions are deaths of elderly people in care homes, and deaths of people in their own homes. Some jurisdictions have only been counting hospital deaths. Some jurisdictions have not been testing all those displaying symptoms, and some of those people have gone on to die at home and were not posthumously tested.

However, these figures are likely a good guide to the following situation: f you get Covid-19 so badly that you are RT-PCR-tested and hospitalised, these would be close to your chances of dying. Dying is of course not the only bad thing which could happen to you. Damage and partial failure of heart, liver, kidneys and lungs have been recorded.

2020-04-18 An important data point. The crew of the USS Theodore Roosevelt, which docked in Guam after a number of Covid-19 cases, is being tested https://www.reuters.com/article/us-health-coronavirus-usa-military-sympt-idUSKCN21Y2GB?
https://www.reuters.com/article/usa-health-coronavirus-usa-military-sympt-idUSKCN21Y2GB?</

2020-04-18 A Stanford immunoassay of 3,330 residents of Santa Clara County, led by Eran Bendavid, with some eye-opening results has been posted on 2020-04-17 to MedrXiv https://www.medrxiv.org/content/10.1101/2020.04.14.20062463v1 "The unadjusted prevalence of antibodies to SARS-CoV-2 in Santa Clara County was 1.5% (exact binomial 95CI 1.11-1.97%), and

the population-weighted prevalence was 2.81% (95CI 2.24-3.37%). Under the three scenarios for test performance characteristics, the population prevalence of COVID-19 in Santa Clara ranged from 2.49% (95CI 1.80-3.17%) to 4.16% (2.58-5.70%). These prevalence estimates represent a range between 48,000 and 81,000 people infected in Santa Clara County by early April, 50-85-fold more than the number of confirmed cases. Conclusions The population prevalence of SARS-CoV-2 antibodies in Santa Clara County implies that the infection is much more widespread than indicated by the number of confirmed cases." TheG report on this says that "[a]t the time of the study, Santa Clara county had 1,094 confirmed cases of Covid-19, resulting in 50 deaths." https://www.theguardian.com/world/2020/apr/17/antibody-study-suggests-coronavirus-is-far-more-widespread-than-previously-thought

There is the question, as always, of how reliable the test is. The study has taken that expressly into account, adjusting for "test performance characteristics" in three ways, using manufacturer's data, a sample of 37 positive and 30 negative controls tested at Stanford, and a combination of those.

2020-04-18 Julian Peto and many others, including the Nobel Economics Laureate Paul Romer, have suggested an exit strategy from lockdown consisting of universal weekly serological testing, with isolation of positives and their families. They suggest it can be started in cities of 200,000 – 300,000 population https://www.thelancet.com/lancet/article/s0140-6736(20)30936-3

2020-04-18 A report in The Lancet by Richard Lane on the work on recombinant Covid-19 vaccine technology by the group of Sarah Gilbert at the Jenner Institute in Oxford. The institute has stopped work on all other vaccines to concentrate on Covid-19 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30796-0/fulltext

2020-04-18 On 2020-04-16, Judith Glynn of LSHTM notes in The Lancet that the Imperial College analysis from Chinese data, adapted to the age distribution of the UK, suggest that, if the over-70's are successfully "cocooned", about two thirds of Covid-19 deaths can be expected to occur in the 60-69 age group https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30311-X/fulltext She thereby questions the policy of bringing recently-retired health-care workers out of retirement to aid in Covid-19 care.

2020-04-18 Wynants et al surveyed predictive models of Covid-19 disease progression. They included 27 studies with 31 prediction models, all but one based on patient data from China https://www.bmj.com/content/369/bmj.m1328. They concluded that "[p]rediction models for covid-19 are quickly entering the academic literature to support medical decision making at a time when they are urgently needed. This review indicates that proposed models are poorly reported, at high risk of bias, and their reported performance is probably optimistic."

2020-04-18 Here is Jeffrey Aronson of Oxford's Nuffield Department on how good the models are. His summary: "We should therefore recall George Box's <u>wise words</u> about statistical models: "All models are wrong but some models are useful". Or as he put it elsewhere, less dramatically but morespecifically: "Models, of course, are never true, but fortunately it is only necessary that they be useful. For this it is usually needful only that they not be grossly wrong". But the models being used to estimate the reproduction numbers of SARS-CoV-2 may be "grossly wrong"."

2020-04-20 In Bielefeld:

•	Date	inf/hosp/ICU	Diff	Recovered
•	2020-04-19	349/-/-	6	214
•	2020-04-18	n/a		
•	2020-04-17	343/17/9	7	190

2020-04-21 I read in the NW paper this morning that Bielefeld data are now no longer coming from the city administration, but are being distributed by the state of North Rhine Westfalia (NRW). The

change in compilation of data is also noted on the city WWW site

https://www.bielefeld.de/de/covi/ (in German, but the graph shows the a gap between 2020-04-19 and 2020-04-20 representing the "change in registration procedure"). There used to be three sets of numbers – one from the city administration, and different numbers assembled by NRW and RKI. There are inevitably going to be delays with the new numbers. Those hospitalised and those in ICU are no longer being reported. This seems like a retrograde step. Grown-ups know numbers are likely to be different, and why they are likely to be different. I would like to know what my city thinks its numbers are. Why should they have to be quiet about it?

2020-04-21 The UK Office for National Statistics (ONS) has a page representing deaths involving Covid-19. There are careful explanations of their methodology, how they gather and record the data, what it represents and what it might not represent

 $\frac{https://www.ons.gov.uk/people population and community/births deaths and marriages/deaths/bulletins/deaths involving covid 19 england and wales/deaths occurring in march 2020$

March is the first month for which there are a significant number of deaths connected with Covid-19. Excluding those deaths which are subject to investigation by the coroner, there were 3,912 deaths involving Covid-19 in England and Wales, of which 3,372 had Covid-19 listed as the underlying cause. Of all those deaths, 91% had at least one pre-existing condition. The rate was 68.6 deaths per 100,000 population – higher in England at 69.7 and lower in Wales at 44.5, less than two-thirds of that in England.

For comparison, RKI is reporting the *infection rate* in Bielefeld at 101.26 per 100,000. There have been 2 deaths, on 2020-04-02 and 2020-04-17 (actually between late afternoon on -04-16 and late afternoon on -04-17). Given the population of Bielefeld at just over 333,000, this gives Bielefeld a mortality rate so far of 0.6 per 100,000, one hundred times less than that of England in March.

Figure 2 on the ONS page is informative. On 2020-03-31, the number of Covid-19 deaths at 491 was almost exactly 1/3 of the 5-year average of 1,452. The total deaths of 1,740 are 20% higher than the 5-year average. These numbers are given for each day of March. For each day from 2020-03-21, the total number of 2020 deaths exceeds the 5-year average. On that day, there were 93 Covid-19 deaths. It seems worthwhile to compare the number of Covid-19 deaths per day with the excess number of deaths over the 5-year average on that day. On average, the excess deaths per day are 72% of the Covid-19 deaths (that is, the mean value is 72%).

It is tempting to conclude from that figure that just over a quarter of the people dying with Covid-19 involvement would have died anyway. But this would not be correct, because it does not take some characteristics of March 2020 into account. From 2002-03-02 until 2002-03-14, when there were just 11 deaths from Covid-19, less than 1% of the daily total, the March 2020 deaths lay on average 177 under the 5-year average. The average value of the 5-year average over this period is 1,588 deaths per day, so the March 2020 death rate lay some 11% under the 5-year average for the first almost-half of the month, when there were few Covid-19 deaths to take into account.

It would be wise to take this initially-lower death rate for March into account also. But how? I will leave it to those more adept or motivated than I, but I note that the February 2020 deaths were down 4.9% on those of February 2019, so the lower March figure appears to be part of a longer trend, not just a couple of weeks of happenstance

https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/monthlyfiguresondeathsregisteredbyareaofusualresidence

2020-04-21 Yaron Ogen of Martin Luther University in Halle-Wittenberg led a study which has shown that, across 66 administrative regions in Italy, France, Germany and Spain, 78% of the Covid-19 deaths in just 5 regions, and these were the most polluted with NO2. https://www.theguardian.com/environment/2020/apr/20/air-pollution-may-be-key-contributor-to-covid-19-deaths-study.

2020-04-21 A boy who caught Covid-19 from Steve Walsh in the chalet at Les Contamines Montjoie did not pass on the infection to any of the 170 or so contacts he subsequently made. A newspaper report is https://www.theguardian.com/world/2020/apr/21/boy-with-covid-19-did-not-transmit-disease-to-more-than-170-contacts. The original paper by Danis et al. is downloadable at https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa424/5819060 (open access).

2020-04-22 Superstar public health academic Devi Sridhar looks at different national policies towards Covid-19 https://www.theguardian.com/commentisfree/2020/apr/22/flattening-curve-new-zealand-coronavirus In almost all scenarios, countries trying to keep the lid on it as well as they can come off best.

2020-04-22 The UK Office of National Statistics published its figures on deaths up to April 10 yesterday. The "excess deaths" have starkly rised since the end of March. There is some speculation that they will have peaked on April 8 (I don't know the basis for this). The Financial Times has the best summary I have yet read https://www.ft.com/content/67e6a4ee-3d05-43bc-ba03-e239799fa6ab

The numbers are not final – the dates include holidays, which slow down the registration of figures (deaths are registered up to four days later, except for those which require a coroner's intervention).

The FT extrapolates from these figures up to April 21 to arrive at an estimate of 41,000 deaths by April 21. This may be too high if April 8 was peak, since extrapolation from a peak figure will overestimate. On the other hand, as suggested by the ONS, the figure for calendar week 15 could be an underestimate of the final figure, due to late reporting because of Good Friday and then Easter Monday.

2020-04-22 The Oxford vaccine is about to start Phase I trial on Thursday. This trial is to evaluate the safety of the vaccine (no drastic side-effects). Oxford's Jenner Institute has been working on recombinant technology which can be adapted to target previously-unknown disease. (A computer scientist would say "parametrised") The "platform" is called ChAdOx, and the specific vaccine developed using this platform and entering trial is named ChAdOx1 nCoV-19. https://www.telegraph.co.uk/global-health/science-and-disease/oxford-university-coronavirus-vaccine/

2020-04-22 A reminder of the useful graphical presentations of the figures by the Financial Times on a free-to-read page https://www.ft.com/coronavirus-latest

2020-04-23 D'Arienzo and Coniglio estimate R₀ associated with the Italian outbreak to be between 2.43 and 3.1 https://www.sciencedirect.com/science/article/pii/S2590053620300410