

Notes on COVID-19

Part 3: 2020-04-01 to 2020-04-15

Peter Bernard Ladkin

2020-04-15

2020-04-01 A clear, uncompromising view from Gregory Poland of the Mayo Clinic, in The Lancet, of what must be done, now, to stem the spread of Covid-19 as far as possible

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30250-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30250-4/fulltext) Poland says that social distancing is the only measure and we have to engage in it. Both parts of that are obviously right.

2020-04-01 CEPI is coordinating the search for vaccines for SARS-CoV-2. They describe the current situation in the NEJM (published March 31)

<https://www.nejm.org/doi/full/10.1056/NEJMp2005630>

2020-04-01 The University of Southern California tested patients presenting with mild flu-like symptoms in mid-March over a 3 day period for SSARS-CoV-2. 131 tests were performed and 7 were positive, giving a rate of 5.3%, with a 95% CO of 2.2-10.7%. 6 of those presented with fever, 5 with myalgias, and only 1 with cough. <https://jamanetwork.com/journals/jama/fullarticle/2764137>

2020-04-01 British American Tobacco, of all organisations, has announced it has a vaccine in pre-clinical testing and will be able to produce 1m-3m doses a week, beginning in June. Apparently it cloned a part of the virus RNA, produced an antigen, and is reproducing it in fast-growth tobacco plants. Well, who'd have thought - smoking will cure you of Covid-19?

<https://www.theguardian.com/business/2020/apr/01/british-american-tobacco-plant-based-coronavirus-vaccine>

2020-04-01 Updated figures for BI, from the local Neue Westfälische newspaper (NW).

• 2020-04-01	177	Diff:	13
• 2020-03-31	164		0
• 2020-03-30	164		18
• 2020-03-29	146		4
• 2020-03-28	n/a		
• 2020-03-27	142		10
• 2020-03-26	132		8
• 2020-03-25	120		16
• 2020-03-24	104		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	43		15
• 2020-03-16	28		1
• 2020-03-15	27		8
• 2020-03-14	n/a		

- 2020-03-13 19 <4
- 2020-03-12 >15
-
- 2020-03-07 1st

The histogram is given below in Figure 1. Put a ruler on the graph from -03-15 to -03-22, you'll notice the plot "corners" lie about equally to the left and right sides of the ruler. That means essentially linear growth over those 8 days (indeed, about 9 a day). From the first case on -03-07 to -03-15, there is missing data; it might be linear but a slight upward bend looks more plausible, superlinear growth. The 9-a-day slope of the subsequent linear growth from -03-15 to -03-22 is steeper. Notice then the change in scale (in red). 2020-03-23 is shown on both scales. Putting the ruler on the 8 days -03-23 to -04-01, you see all the plots appearing to the left of the ruler. So this is a convex curve and sublinear growth.

The social distancing measures were announced by the mayor on -03-12, to take effect from Sunday -03-15. There is slight concavity from -03-15 to -03-23. If we take the serial interval to be somewhere between 5 to 7 days, this is exactly what we would expect: concave growth continuing for 5-7 days after the measures are introduced. If the measures are having the desired effect, we would then expect to see at least flattened concavity, but preferably linear or sublinear growth – and indeed we see convexity. So, hurray! The measures appear to be working.

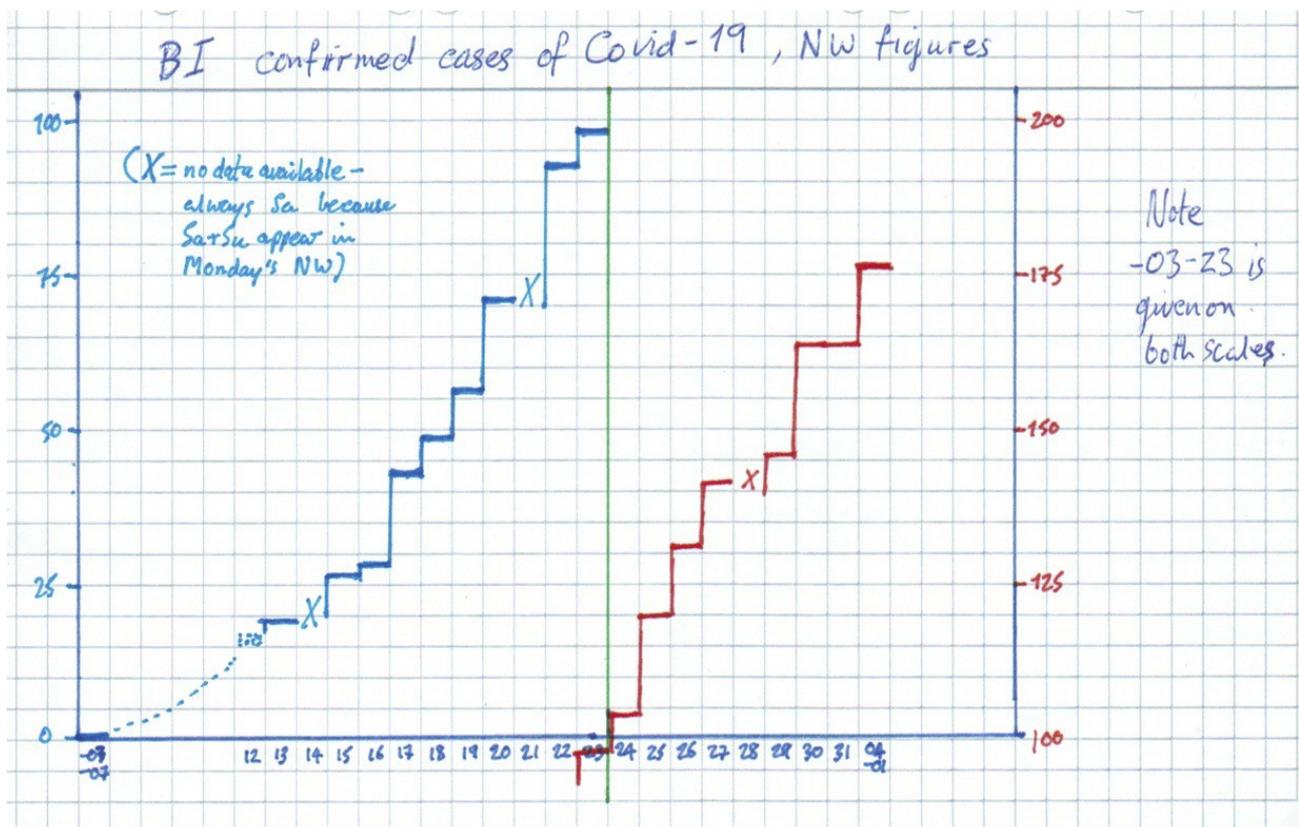


Figure 1: The Bielefeld figures on confirmed Covid-19 cases, announced in the local newspaper (NW); first case on 2020-03-07; “more than 15 cases” up to and including 2020-03-12; daily figures are from 2020-03-13 onwards; Sat+Sun figures are displayed as Sun figures only, with Sat as “X”

2020-04-02 John Lee, a recently retired professor of pathology and HMS consultant pathologist published an article in The Spectator on Saturday 2020-03-28 noting the there were many

interpretations of the situation with Covid-19 consist with the data we are seeing.

<https://www.spectator.co.uk/article/The-evidence-on-Covid-19-is-not-as-clear-as-we-think> He made three main points.

First, the excess deaths we might expect to be seeing from a virulent new disease are, in fact, lost in the noise (as of date of writing). In GB, deaths linked to Covid-19 are 0.8% of expected deaths at this time of year. Globally, they are 0.14% of expected deaths.

Second, the figures we are obtaining about the disease are distorted (in comparison with other diseases). People with underlying health problems who encounter respiratory problems and die are not necessarily tested for precisely which respiratory disease led to their demise (flu or some other). But since Covid-19 is notifiable, they are and it is recorded. Also, testing based on hospitalisation overestimates virulence. And since deaths which occur through non-Covid-19-related respiratory problems are not so recorded, such deaths are systematically under-recorded in comparison with those related to Covid-19.

Third, the evident death rates calculated from the data we have are highly variable, even in nominally comparable European countries. Italy, 9.9%. Germany, 0.5%. Spain, 7.1%, France, 4.3%, Switzerland 1.3%. How so? One suspects amongst other things different criteria for recording. In the US and South Korea, it is currently 1.3% (as in Switzerland) and in Iran (where recording has long been suspect) 7.3%. And Iceland, where about 50% of the cases appear to be asymptomatic, it is 0.3%. It is surely hard to draw any reliable conclusions from such disparities. But these data, with their wildly different characteristics, are the figures from which the mathematical modellers are drawing their conclusions.

All good points. He suggests that basing draconian social-distancing measures on “evidence” from such variable data sets is a risky business. Indeed so. But the evidence is not just numerical. Italy, Spain, and increasingly France, are overwhelmed by caring for people with severe respiratory disease at the moment. Is it just that, according to equilibrium theory, they have facilities appropriate to the “usual problems”, and then when another comes along on top of that, they are overwhelmed, beyond the “tipping point”? Even if the newcomer is only like a new type of seasonal flue? And because the newcomer is “notifiable”, it gets all of the blame for a somewhat overstressed system which had not reckoned with anything except the “usual problems”? Maybe. Someone will surely have to figure that out at some point. Because it speaks to a public health policy of planning for “the usual problems + one more”. Experts have been saying forever that new diseases leading to pandemics are inevitable, but have mostly been worried about a new type of influenza. Is it really beyond the capabilities of human politics to anticipate something which we have been told forever is inevitable?

To the chorus of those wondering about the reliability of the data can be added the Stanford epidemiologist John Ioannides, writing in mid-March <https://www.statnews.com/2020/03/17/a-fiasco-in-the-making-as-the-coronavirus-pandemic-takes-hold-we-are-making-decisions-without-reliable-data/> He refers to the situation aboard the Diamond Princess

“The one situation where an entire, closed population was tested was the Diamond Princess cruise ship and its quarantine passengers. The case fatality rate there was 1.0%, but this was a largely elderly population, in which the death rate from Covid-19 is much higher.

Projecting the Diamond Princess mortality rate onto the age structure of the U.S. population, the death rate among people infected with Covid-19 would be 0.125%. But since this estimate is based on extremely thin data — there were just seven deaths among the 700 infected passengers and crew — the real death rate could stretch from five times lower (0.025%) to five times higher (0.625%). It is also possible that some of the passengers who

were infected might die later, and that tourists may have different frequencies of chronic diseases — a risk factor for worse outcomes with SARS-CoV-2 infection — than the general population. Adding these extra sources of uncertainty, reasonable estimates for the case fatality ratio in the general U.S. population vary from 0.05% to 1%.”

That is reasonable argumentation. It adds to Lee's point about very variable data sets, and picking one from which to draw conclusions about (in this case) US social/political policy in face of Covid-19. He warns, as Lee does, about drawing too-drastic conclusions about what must be done.

However, the experience of Italy, Spain, and, increasingly, France is incontrovertible. If Lee and Ioannides are right and we shouldn't be worrying that much about Covid-19 itself, the experiences of these three countries surely lead us to be extremely worried about encountering “the usual problems plus one” and becoming overwhelmed, as these countries are. As we are also increasingly hearing New York is. Whether it is the case that SARS-CoV-2 is particularly virulent and dangerous, or whether it is the case that Covid-19 is “lost in the noise” and the current experience is just “the usual problems plus one”, with many countries being unable to handle the “...plus one”, there exists a major public health issue which has to be dealt with in the here and now.

We will surely have time later to contemplate which of these scenarios is more accurate, and we have plenty of academics and politicians able and willing to do so. But surely, for now, drastically inhibiting social contact and thereby the means of transmission of the disease is the justifiable thing to do. Of course, this is socially far harder on some people than on others (and I confess to being among those who do not currently find it such an imposition).

2020-04-02 John Chisholm chairs the BMA medical ethics committee. In the case of greater demand for life-saving resources than supply, how do you choose who gets what? Chisholm has some words to that <https://www.theguardian.com/commentisfree/2020/apr/01/doctors-choose-life-saving-treatment-ethical-rules> Moral philosophers have of course been discussing such issues for hundreds of years. For example, Jeremy Bentham's “the greatest good of the greatest number”, proposed 231 years ago. How do you measure “good”, and in what proportion? Live saved? For how long, under what constraining conditions? Saving the life of someone who is in permanent coma, versus saving the life of someone who is conscious but will in any case die soon? How does one measure the relative “benefit” of mechanical ventilation under sedation? That of a relatively-young rock musician with a heroin problem compared with that of an older still-active Nobel-prize-winning scientist? All of a sudden, these “academic”, “theoretical” problems are to become the subject of practical decisions. Is there much evidence that medical-ethics councils have absorbed the best of the last few hundred years of moral-philosophical thinking? Or that individual doctors have done so? What is certain is that these decisions will not occur under any public scrutiny, unless they are seen to be egregious by colleagues who then publicise it. I worry that careful moral thinking will be sidelined.

2020-04-03 The NW reports that Bielefeld has 188 cases as of April 2nd, 11 more than on April 1st. Oddly, the RKI Dashboard thinks we have 316. Just yesterday, they thought we had half that.

2020-04-03 Chin et al. report in The Lancet on 2020-04-02 on the stability of SARS-CoV-2 on various surfaces [https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247\(20\)30003-3/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30003-3/fulltext) The virus is stable at 4°C, but undetectable after 5 minutes at 70°. On printing paper and tissue paper, undetectable after 3 hours; wood and cloth, undetectable on Day 2; glass and banknotes, on Day 4; stainless steel and plastic, on Day 7, except some was detected on the outside of a surgical mask on Day 7. In standard disinfectants, undetectable after 5 mins, except for soap.

This suggests that any food cooked for 5 minutes or longer has no viable virus, and that standard

ways of disinfecting surfaces suffice. It is likely useful also to know on what surfaces viable fomites last the longest, as this tells us.

2020-04-03 A useful Lancet article on the development of antibody tests

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30788-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30788-1/fulltext) A key feature is to ensure that there is not cross-reactivity with other coronaviruses, yielding false positives for immunity. For some coronaviruses are responsible for the common cold; those who have had such a cold should not be judged immune to SARS-CoV-2 because of cross-reactivity. There is an expectation that immunity to SARS-CoV-2 is lifelong (Hibberd, LSHTM). Some SARS survivors have maintained immunity 17 years after illness.

2020-04-03 Wong, Yang and He point out that the initial guidance for use of chloroquine in treatment of Covid-19 in China was 500mg twice per day for 10 days. That it has deleterious side effects. And that a lethal dose is about 5g. And that chloroquine hangs around in the body, with an elimination half-life of 20-60 days. Dangerous stuff, in possibly dangerous doses. The guidelines were subsequently revised. Caution, with this and other proposed treatments, is warranted, they suggest. Indeed so. [https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30093-X/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30093-X/fulltext)

2020-04-03 Imperial MRC CGIDA's latest Report (No. 13) looks at 11 European countries and tries to model progression of Covid-19 in an attempt to assess the efficacy of policy reactions (mainly forms of social distancing to reduce the effective reproduction number R_T).

<https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-13-europe-npi-impact/> They assume that each intervention has the same effect across different countries. An interesting factoid is that they suggest that R_T dropped to below 1 in Italy around the time of the lockdown on 11th March, although this is accompanied by a high degree of uncertainty.

2020-04-03 LSHT CMMID have an analysis of the Diamond Princess cohort which is rather more sophisticated than that by Ioannides referenced above

https://cmmid.github.io/topics/covid19/severity/diamond_cruise_cfr_estimates.html

2020-04-03 It is not just Wuhan that can do it. The NHS Nightingale hospital, at the Excel Centre in East London, with 500 beds and capacity for up to 4,000, was built in two weeks and has been opened today. (There was, of course, already a building in place on the site.)

2020-04-04 Tomas Pueyo's latest essay, from Thursday 2020-04-02

<https://medium.com/@tomaspueyo/coronavirus-out-of-many-one-36b886af37e9>

2020-04-04 A fine news piece by David Adam in Nature, published on 2020-04-02, on the use of modelling, and the types of models (equation-based or agent-based)

<https://www.nature.com/articles/d41586-020-01003-6>. (Thanks to Martin Newby for the pointer.) It is one of the few pieces I have read which gets the contribution of Sunetra Gupta's group in Oxford right.

2020-04-04 An aside. I found the Gupta group's contribution easy to understand from the first. They pointed out that there are a number of key parameters which are *completely* unknown, but which radically affect the prognosis of severe illness and deaths from Covid-19. In particular, the proportion/number of asymptomatic or only lightly symptomatic infected individuals who do not go on to develop further disease. That is obviously right. No one else had pointed it out in public at the time. I have previously noted Kucharski's grudging acknowledgement of this in TheG. Twenty years ago, there was an incident at Oxford when Roy Anderson disparaged Gupta, for which he apologised and resigned his Oxford post (as well as other appointments) and went to Imperial with

some of his team. <https://www.nature.com/articles/35016213> I wonder whether the residue of that incident is still affecting perceptions, twenty years later?

2020-04-04 There is some further information related to the Gupta group's suggestions. China has been testing arrivals from overseas, and published their first data for April 1. 130 of 166 new infections (78%) were asymptomatic. This was reported and commented in the BMJ on Thursday 2020-04-02 <https://www.bmj.com/content/369/bmj.m1375> Written reference is BMJ 2020;369:m1375. The South China Morning Post has said that China has already found 43,000 asymptomatic cases through contact tracing. Those data are said to be classified. Recall the studies in Vò and Iceland which indicated 50% or more of those infected were asymptomatic. There is more on Vò and the work that was done there in the BMJ on 2020-03-23 <https://www.bmj.com/content/368/bmj.m1165> The BMJ written reference is BMJ2020;368:m1165.

2020-04-04 The Lancet is launching a new journal, The Lancet Planetary Health, which will consider studies that integrate interconnected domains which have traditionally been handled separately. For example, the obvious concerns about social distancing measures necessary to mitigate Covid-19 and their deleterious effect upon economics. Or about bush-meat and “wet” markets and the emergence of virulent human disease.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30742-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30742-X/fulltext)

2020-04-04 There has been some concern in severely-ill Covid-19 patients that, as the virus becomes less detectable, a phenomenon similar to a “cytokine storm” can occur, and finally kill patients. Broadly speaking, you want an immune-system response to counter the infection, but there is such a thing as too much. Stebbing and colleagues suggested possible use of a drug, baricitinib, that might block the biochemical signalling leading to this phenomenon. Favalli et al. urge caution [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30262-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30262-0/fulltext) and Anderson et al. respond [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30270-X/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30270-X/fulltext)

2020-04-04 The current crisis is drawing almost everyone's attention, not least that of technical people with the mathematical skills to understand the modelling. It is clear to those of us who have taught math and computer science for almost half a century that many, even most, people still have trouble understanding the concept of exponential growth, for example. A computer scientist at Purdue, Li Ninghui, was disturbed early on by the nonchalant US response to the pandemic, and wrote this note to the Risks Forum Digest, to which I also contribute observations about system safety <https://catless.ncl.ac.uk/Risks/31/63#subj1> But Li is not content to explain, he also wants to revise. He has a “simplified model” of infectious-disease spread which he suggests is easier to communicate than the “standard model”. He suggests using “Base Doubling Rate”, “Cumulative Fatality Rate” and “Mortality Rate” instead of, for example, CFR. I doubt that will work any better than the standard model, but leave it up to the reader to devise their own critique, because I think that misses the main point. Li is addressing a matter of what I call mathematical rhetoric: how an issue is conceptualised mathematically. I can understand the math, however it is communicated and with whichever concepts. But I see the main issue as this. The math is very sensitive to slight changes in some parameters, because of the effect of exponential growth on differences. So if you guess this value for a parameter, you have 5,000 deaths in the US (see Epstein), but with a slightly different guess, you have 100,000-200,000 (see current USG hopes), and with a slightly different guess you have tens of millions. That is so, no matter what basic concepts you use. The mathematical rhetoric is surely subsidiary to this uncertainty about parameters. It is coping with this uncertainty that governs the political issue of determining a response, not the way you phrase the issue in terms of parameters. Which is inter alia why the establishment of the venue The Lancet Planetary Health is welcome.

Indeed, concerning the “standard model” parameter CFR, there has been recent discussion (2020-

03-31) of the calculation of CFR in The Lancet. Baud et al. Suggested on 2020-03-12 a variant calculation to estimate CFR [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30195-X/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30195-X/fulltext) Kim et al. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30234-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30234-6/fulltext) and Spychalski et al [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30246-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30246-2/fulltext) , as well as Lipsitch [https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099\(20\)30245-0.pdf](https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30245-0.pdf) responded critically to that suggestion, and Baud et al. replied [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30255-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30255-3/fulltext)

2020-04-04 An editorial from 2020-04-01 by Harvey Fineberg in the NEJM on how to “crush” Covid-19 in 10 weeks in the US. https://www.nejm.org/doi/full/10.1056/NEJMe2007263?query=featured_home The ideas about testing everyone and getting enough PPE and breathing help/ventilators out there are points which now seem to be unanimous around the globe. The difficulty lies in doing so.

2020-04-04 For 8 days now, since 2020-03-26, Germany has been recording between 6,000 and 7,000 new cases per day (on Sunday 2020-03-29 and Monday 2020-03-30, there were fewer than 5,000 new cases, but that trend did not persist through the week). That looks stable, but I don't know whether it will be within the capacity of the health system to handle. Worldometer is indicating 5% of cases are severe or critical, so that is 300-350 per day which will become so in Germany. There are 28,000 ICU positions in the country, of which I understand the Health Minister Jens Spahn said on Monday about half are available <https://www.zdf.de/nachrichten/politik/coronavirus-spahn-intensivstationen-100.html> The WHO-China Joint Report says severe or critical cases stay 3-6 weeks in hospital but those who die do so in very variable time, 2-8 weeks: p14 of <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf> Some simple arithmetic. If 14,000 positions are available in ICU, it takes 3 days to fill 1,000 beds at the rate of 300-350/day, so 6 weeks to use up available capacity of 14,000 beds. With a 3-6 week stay per patient, that capacity is going to suffice if infections stay at current levels and severe/critical cases also at current levels. Some such arithmetic is probably why the German government is reported to be somewhat reassured. The issue is not going to be the positions. It is going to be staffing them. ICU specialist nurses are highly skilled. I have it on personal authority that it takes months to train ICU specialists. The kit and care is complex. It is not just a matter of a couple of weeks repurposing an already-experienced nurse – it is a lot more than that.

2020-04-04 My colleague Harold Thimbleby, who specialises in the use and misuse of digital equipment and computers in medicine, noticed that the Imperial College Covid-19 Response Team had apparently based some part of their work, on which it appeared HMG was basing policy, on unverified, monolithic computer code written in C. That is a red flag for us software engineers. Harold's paper is at <http://www.harold.thimbleby.net/reliable-models.pdf>

I can imagine a telephone conversation.....

"Professor Ferguson?"

"Yes. Who am I speaking with?"

"This is Computer Monthly. We are writing an article about your work and we'd be grateful if you had a minute or two to talk with us."

"Sure. That is very flattering. What's the title?"

" "Senior scientist admits that UK government policy on Covid-19 relies on spaghetti code." "

Jokes aside, I doubt that Harold was the only software engineer to latch on to Neil Ferguson's tweet. The article by David Adam in Nature, referenced above, has Ferguson suggesting that Microsoft will help him (re)engineer the code.

There is a perspective that it seems was not apparent to those relying on this computational artifact. The model used has two components. One is the mathematical modelling technique, which is the one described in the accompanying papers and most carefully considered by peers. The other is the implementation of this mathematics in computer code, here in C. It is equally important to show that this code implements the mathematics as described. But this task is often ignored by people who are not specialists in dependable software engineering. It is non-trivial. Ladkin and Thomas refer to investigations of professional programming in the 1980's by SEI's Watts Humphrey, who noted that programmers “inject a defect about every ten lines of code.”

https://www.researchgate.net/publication/339697246_Software_Quality_Its_Nature_and_the_Cultures_of_Building_It Let us hope that in this case the engineering of the software is improved, because this model, and the code which implements it, has essentially the status of a public good, as indeed do all worthy models, at Imperial and LSHTM and the other specialist institutions. Please, everyone, make sure your code indeed does what your math says it should do! If you don't know how to do that, ask people such as myself.

2020-04-05 An editorial in the BMJ by Pollock et al. on 2020-03-30 bemoans the UK policy so far <https://www.bmj.com/content/368/bmj.m1284> (Thanks to Martin Newby for drawing my attention to this.) “Classic” public-health measures involve testing, contact-tracing, isolation and quarantine and they were not/are not being followed rigorously in the UK as WHO has been recommending. There is an interesting factoid about the Feb 12 change in Chinese accounting. Apparently the Chinese went from lab-confirmation alone to (lab-confirmation OR clinical symptoms) because the RT-PCR lab tests they were using were returning 40-50% false negatives (references 12 & 13). The article provoked a storm of letters (“rapid responses”), mostly supportive <https://www.bmj.com/content/368/bmj.m1284/rapid-responses> However, Chambers and Rouse suggest that contact tracing would be an infeasible task. Harvey suggests all those students and other people not able to pursue their normal everyday tasks could be recruited, supported by Redgrave et al.

2020-04-06 Reliable data is hard to come by, because of reporting oddities. For example, the RKI was reporting a very low figure for Bielefeld cases, some 30 or so when it was well up over 100, according to the local newspaper; then there was a sudden spike in Bielefeld cases reported on the RKI Dashboard (which uses the JHU software, I think), to over 300. Whereas the NW reported as in the graph above.

Thursday's figure (2020-04-02) was 188 cases, Friday's figure (2020-04-03) was 200 cases.

So there is quite a discrepancy, which has been there for some days now. There was an article in the NW newspaper on Saturday remarking it and trying to get an explanation of what is going on (and failed, at least for this reader).

There is a note in TheG live blog today that many cases, including deaths, in the US are likely going unreported, because many rural areas are not equipped with SARS-CoV-2 tests that they can use.

Also in France, the reported numbers might not provide an accurate view. Here are numbers from France, reported by Kim Willsher on TheG live blog, entry at 0748 UTC+1 (= BST = MEST -1) <https://www.theguardian.com/world/live/2020/apr/06/coronavirus-live-news-boris-johnson-admitted-to-hospital-as-trump-again-touts-hydroxychloroquine>

These numbers are admissions to hospital, followed by admissions to ICU within hospital

- 05/04: +748 (+140 in IC)
- 04/04: +711 (+176 in IC)
- 03/04: +1,186 (+263 in IC)
- 02/04: +1,607 (+382 in IC)
- 01/04: +1,882 (+452 in IC)
- 31/03: +1,749 (+458 in IC)
- 30/03: +1,654 (+475 in IC)
- 29/03: +1,734 (+359 in IC)

It sure looks as if those are going down. But no one should be surprised that social distancing is having an effect.

2020-04-06 There is some question about the efficacy of the serological tests that Britain has acquired. From TheG's "Monday Briefing"
<https://www.theguardian.com/world/2020/apr/06/monday-briefing-boris-johnson-in-hospital-for-as-long-as-needed> "Scientists in the UK have warned that the testing kits ordered by the government and described by Johnson as a "game-changer" could be unreliable and might only detect 50-60% of milder cases."

50% is by no means enough. I wrote a note yesterday, A Hard Constraint on the Efficacy of Serological Tests. Assume social distancing is perfect (i.e., $R_t = 0$ amongst subpopulations practicing social distancing), and you wish to use a serological test to determine who is already immune, in order to allow them then to mingle freely. The test must yield proportionally at least $(1 - 1/R_0)$ true-positive results in order to keep R_t lower than 1 amongst the false-positive subpopulation, because false-positives are not immune and will transmit the disease if one of them is infected. With an R_0 of 2.3 (at the lower end of estimates), this means the test must be at least 56.5% efficient to keep R_t lower than 1 amongst the false-positive subpopulation. 50% effectiveness will not do. Given that social distancing is not perfect, it seems to me to be very doubtful whether even 60% will do.

2020-04-07 Monteleone et al in The Lancet describe anti-cytokine therapy as used for immune-mediated disorders in which patients take cytokine blockers
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30092-8/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30092-8/fulltext) This would normally render such patients more susceptible to viral diseases, but "surprisingly" there has been no increase in SARS-CoV-2 pneumonia in such patients so far. This raises the question of whether the blockers help; whether such patients are resistant to Covid-19 disease. "Analysis of the cytokine profile characterising severe cases of COVID-19 suggests this assumption might be the case."

2020-04-07 A major review of intensive care management of Covid-19 by Phua et al.
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30161-2/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30161-2/fulltext) A comment on this review by Vincent and Taccone says it raises the issue of how to interpret the reported CFR
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30165-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30165-X/fulltext) , especially in those jurisdictions which only report one cause of death.

2020-04-08 A report by Reuters journalists Stephen Gray and Andrew MacAskill about scientific advice on pandemic modelling given to the British government <https://www.reuters.com/article/us-health-coronavirus-britain-path-speci-idUSKBN21P1VF> It is detailed, and rings true. Two main players would not be interviewed: Sir Chris Whitty, Professor at LSHTM, Chief Medical Officer for England and Chief Medical Advisor to HMG, and Neil Ferguson, Professor at Imperial College.

2020-04-08 Boccia, Ricciardi and Ioannidis give their views on what can be learnt from the Italian experience, in JAMA on 2020-04-07 <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2764369> They say “*The number of cases and deaths cannot be explained simply because of the epidemic starting in Italy earlier compared with other countries besides China. It is important to understand why death rates were so high in Italy to learn how to best prepare and how to plan for optimal actions in other countries. Some contributing factors may be immutable (eg, age structure of the population), but even these need to be laid out carefully in preparedness assessments. Some other contributing factors are potentially modifiable.*” The median age of those dying has been 80, and “*Italy has a high proportion of patients with history of smoking and high rates of chronic obstructive pulmonary disease and ischemic heart disease.*” They suggest it is “likely” that the overwhelming number of cases in Bergamo had to do with attendance at the Atalanta vs. Valencia football match on February 19th, before the first case in Italy was identified in Codogno on February 21st. They note that “*[i]t is difficult to differentiate between deaths with SARS-CoV-2 infection and deaths caused by SARS-CoV-2 infection because the vast majority of patients who have died had 1 or more other major pathologies (98.8% with at least 1 comorbidity, and 48.6% having 3 or more diseases) that contributed to their death.*” They also claim that, in Lombardy, Covid-19 became “*largely a nosocomial infection*” and as of March 30 almost 9,000 medical personnel had become infected.

2020-04-08 The BMJ has a news article on whether wearing cloth face masks amongst the general public is of any use in hindering the spread of the disease. Summary: there is no evidence for it. <https://www.bmj.com/content/369/bmj.m1422>

2020-04-08 An article on the “cluster effect” in TheG <https://www.theguardian.com/world/2020/apr/09/the-cluster-effect-how-social-gatherings-were-rocket-fuel-for-coronavirus> They mean superspreading events: Carnival in Gangelt on -02-15; the football match in Bergamo; the party on Bondi Beach in Sydney; Mardi Gras in New Orleans. All associated with local outbreaks of Covid-19.

2020-04-08. TheG's Philip Oltermann attended the video press conference this morning of the preliminary results of Hendrick Streeck's Heinsberg research project. They have evaluated about half the results. 14% of the population had developed immunity. Previous guesses were around 5%. Mortality is 0.37%. (In contrast, Oltermann put the latest figures from JHU for Germany as a whole at 1.98%.) I guess that is under the assumption that Professor Streeck's serological test doesn't yield many false positives.

2020-04-10 Continuing figures for Bielefeld:

- 2020-04-09 269 Diff: 18
- 2020-04-08 257 22
- 2020-04-07 233 11
- 2020-04-06 224 2
- 2020-04-05 222 22 (over two days)
- 2020-04-04 n/a
- 2020-04-03 200 12
- 2020-04-02 188 11

No data are available yet for Friday 2020-04-10 (a public holiday) nor will there be any until next Tuesday April 14th because of public holidays. The NW paper does not print from Maundy Thursday (which of course is only a British festive day) until Tuesday after Easter. On Wednesday 8th I was prepared to say there was approximately a linear increase, but in fact the numbers have gone from just over 10 a day for the first 7 days of April to around 20 a day on Wed-Thu April 8-9.

That is not great. The NW “celebrated” Bielefeld's comparatively low figures in its edition of Fri April 10th, written of course on Thursday 9th, but this view may need to be revised once we see new figures on Tuesday.

2020-04-11 Susan Jaffe reports in the Lancet on the decision by US and France to allow use of hydroxychloroquine and chloroquine in treating hospitalised Covid-19 patients. The EU regulator and WHO say the science does not support the decision

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30817-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30817-5/fulltext)

2020-04-11 The JHU Dashboard reported more cases for Germany as a whole on Wednesday 2020-04-08 than on the preceding days. This alerted me to the following phenomenon, which is more clear a couple of days later. If you look at the JHU figures for Germany over the month of March until today, you can see three weekly “waves”. One is Thu-Fri-Sat, March 26-28 with 6.6K, 6.9K and 6.8K new cases; one is Wed-Thu-Fri April 1-3, with 6.1K, 6.9K and 6.4K new cases, and one lesser one this week on Wed-Thu April 08-09, with 5.6K and then 4.9K. Otherwise, new cases have been lower than 5K per day. Some of that may be the characteristics of reporting. For example, reporting at the weekends might be different from reporting during the “working week”. Some of it may very well be cyclical public behaviour. The weather was very pleasant at weekends recently. Wednesday is 5 days from Saturday and 4 days from Sunday. That is median incubation period. But then there is also the period between applying for a test (getting recommended by your doctor), taking it (same-day, at least in Bielefeld at the moment) and waiting for the results (a positive result is communicated the next day. A negative result takes days to be reported to the testee, presumably because that is less important and there are more of them).

Italy has four “waves: Thu-Sun March 19-22, Thu-Sat March 26-28, Wed-Fri April 01-03, Wed-Fri April 8-10. Three of those waves coincide with Germany's. Spain has two, with a third one-day increase: Wed-Sat March 25-28 (Wed was the peak of new cases in Spain), then Mon-Thu March 30 – April 2, then a one-day increase on Wed April 8 in a generally-decreasing trend. Those periods also generally cohere with German and Italian new-case peaks.

All three countries have very different experience with Covid-19 and coping with it, as well as different reporting regimes. So what is going on with these waves? Where do they come from?

2020-04-12 TheG live blog is reporting at 0149 BST that EC president Ursula von der Leyen suggested that “elderly people” might have to stay isolated until the end of the year, by which time there is some hope that a vaccine might be available

<https://www.theguardian.com/world/live/2020/apr/12/coronavirus-live-pope-easter-lockdown-us-death-toll-uk-boris-johnson-donald-trump-> I think she means me, although I have never thought of myself as fitting in this category until the age-stratification figures for Covid-19 deaths came out. Uugh.

2020-04-12 TheG live blog is also reporting that John Horton Conway has died from Covid-19 (note at 0702 BST). Apparently he was only taken ill on Wednesday.

<https://www.theguardian.com/world/live/2020/apr/12/coronavirus-live-pope-easter-lockdown-us-death-toll-uk-boris-johnson-donald-trump->

I first heard him lecture in 1971 in Cambridge. I was an end-first-year undergraduate at Oxford and because I was fascinated by mathematical logic I had been given some money by my college to attend the annual Logic Colloquium of the Association for Symbolic Logic, that year in Cambridge. He talked about his Game of Life, which he had invented the previous year. I was fascinated. I remember the chalk he used came out of his jacket pocket. Always prepared....

Two years later I was in Berkeley. Where there was Elwyn Berlekamp. I never got much into combinatorial games, but Elwyn's book with Conway and Richard Guy became what amounts to a best-seller – it was called *Winning Ways for you Mathematical Plays* and is of course still in print. There are four volumes of it now, it seems.

Apart from the fun, Conway was a finite-group theorist, and has four groups named after him https://en.wikipedia.org/wiki/Conway_group Three of them are sporadic. That is, not part of any more general class of groups in the classification of finite simple groups (strictly speaking, in a class by themselves). There are a total of 26 sporadic simple groups, according to Wikipedia. So Conway found just over a tenth of all of them. That was all at a time when finite-group theorists were considered the hard core of mathematicians – an exceptionally hard subject with, as far as anyone could see then, no application at all except for a few well-known basic ones. I had a pal in graduate school who was doing his PhD in group theory and moaned at least once a week that he was working full time on something that couldn't ever get him a job and he couldn't understand why he was so perverse. Then came computer security with its need for one-way functions – functions easy to compute (determine the value of the function given the arguments) but hard to invert (given the value of a function to infer its arguments). It turns out that finite groups are a rich source of one-way functions. There was a job in it after all.

Conway's Game of Life founded the study of what are now called cellular automata. Consider a two-dimensional grid – like a sheet of graph paper, but going on for ever in each direction. Pick a region somewhere, and color-in some of the squares, say with red (it is usually done with black, but I prefer colours). Each square has eight “neighbors”, squares which share an edge or a corner with it. The game proceeds in discrete steps. There are rules for coloring-in a square, respectively erasing its color, depending simply on how many neighbors are coloured, respectively empty. A step of the game consists in applying these colouring/erasing rules once, to evolve a new configuration. Playing the game consists in performing such steps one after another, continuously. The patterns formed by the colored squares evolve, and can be designed to do all sorts of animate-looking things, as if they were alive. Hence the name of the game. It is pure combinatorics, but it is fascinating. Animated gifs work well to show cellular automata evolving. There are some on the Wikipedia page https://en.wikipedia.org/wiki/Conway%27s_Game_of_Life

2020-04-12 Sylvia Richardson and David Spiegelhalter have a worthy guide in TheG to trusting and not trusting numbers <https://www.theguardian.com/world/2020/apr/12/coronavirus-statistics-what-can-we-trust-and-what-should-we-ignore>

2020-04-13 The Süddeutsche Zeitung has a piece on Friday 2020-04-10 about the preliminary results of the study led by Hendrick Streeck in Gargelt, where apparently they measured that 15% of the tested people had antibodies to SARS-CoV-2. <https://www.sueddeutsche.de/wissen/heinsberg-studie-herdenimmunitaet-kritik-1.4873480> (in German). First, there are doubts whether the test is sufficiently discriminatory, so that maybe antibodies to relatively-harmless common-cold coronaviruses are sometimes being detected (and we are at the end of the season for these). Second, the study selected households and tested everyone in the household. People in a household with an infected person are more likely to be (have been) themselves infected. It is not at this point clear how this lack of independence was controlled for in calculating the 15% number that was expressed in the press conference. These are relatively obvious characteristics which the Streeck study needs to control for; I would be surprised if no attention had been paid to them. But without a document including such details, the questions remain open.

2020-04-14 On request of the US Office of Science and Technology Policy and the Office of the

Assistant Secretary for Preparedness and Response, the US National Academies of Science, Engineering and Medicine have formed a Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats <https://www.nationalacademies.org/our-work/standing-committee-on-emerging-infectious-diseases-and-21st-century-health-threats#sectionCommittee> . The Committee has just published four Rapid Expert Consultations on 2020-04-08. One is on the effectiveness of cloth masks in inhibiting infection of others (not protecting the wearer). National Academies of Sciences, Engineering, and Medicine 2020. *Rapid Expert Consultation on the Effectiveness of Fabric Masks for the COVID-19 Pandemic (April 8, 2020)*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25776> or <http://nap.edu/25776> . “Overall, the available evidence is inconclusive about the degree to which homemade fabric masks may suppress spread of infection from the wearer to others.” There is also a Rapid Expert Consultation on the potential for seasonality of Covid-19: National Academies of Sciences, Engineering, and Medicine 2020. *Rapid Expert Consultation on SARS-CoV-2 Survival in Relation to Temperature and Humidity and Potential for Seasonality for the COVID-19 Pandemic (April 7, 2020)*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25771> or or <http://nap.edu/25771> , one on laboratory testing for SARS-CoV-2 National Academies of Sciences, Engineering, and Medicine 2020. *Rapid Expert Consultation on SARS-CoV-2 Laboratory Testing for the COVID-19 Pandemic (April 8, 2020)*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25775> or <http://nap.edu/25775> , and one on viral shedding and antibody response: National Academies of Sciences, Engineering, and Medicine 2020. *Rapid Expert Consultation on SARS-CoV-2 Viral Shedding and Antibody Response for the COVID-19 Pandemic (April 8, 2020)*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25774> or <http://nap.edu/25774> .

2020-04-14 In Bielefeld there were according to the NW on Monday 2020-04-13 294 people with Covid-19, and 122 recovered.

2020-04-15 A major study from Harvard by Kissler et al. models the transmission dynamics of the virus SARS-CoV-2 through the period following the pandemic, up to 2025 <https://science.sciencemag.org/content/early/2020/04/14/science.abb5793> The key modulator affecting the dynamics is population immunity, whether it wanes, and at what rate. Accurate serological testing is required to establish these parameters. The authors consider the effects of intermittent social distancing, seasonal variation, and management to keep incidence within the capacity of health care systems.

In general, Science is making its coronavirus articles open-access, at <https://www.sciencemag.org/collections/coronavirus>

2020-04-15 Jon Cohen's March interview with NIAID Chief Anthony Fauci, which has been referred to everywhere <https://www.sciencemag.org/news/2020/03/i-m-going-keep-pushing-anthony-fauci-tries-make-white-house-listen-facts-pandemic>

2020-04-15 Jon Cohen's article about vaccine research and trials, from 2020-04-03 <https://science.sciencemag.org/content/368/6486/14>

2020-04-15 A comment in The Lancet on the importance of health literacy from Paakkari and Okan [https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667\(20\)30086-4/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30086-4/fulltext) Okan is a Bielefeld researcher.

2020-14-15 A New York Times opinion article by Harvard epidemiologist Marc Lipsitch is well worth reading <https://www.nytimes.com/2020/04/13/opinion/coronavirus-immunity.html>

2020-14-15 A visceral, harrowing account of her recent experience by Helen Ouyang, a doctor and

professor at Columbia, who has been tending to sick people in New York. Only read it if you are feeling strong <https://www.nytimes.com/2020/04/14/magazine/coronavirus-er-doctor-diary-new-york-city.html>