

The corona puzzle

There is still plenty we don't understand about the virus

DR JOHN LEE



In announcing the most far-reaching restrictions on personal freedom in the history of our nation, Boris Johnson resolutely followed the scientific advice that he had been given. The advisers to the government seem calm and collected, with a solid consensus among them. In the face of a new viral threat, with numbers of cases surging daily, I'm not sure that any prime minister would have acted very differently.

But I'd like to raise some perspectives that have hardly been aired in the past weeks, and which point to an interpretation of the figures rather different from that which the government is acting on. Solid consensus in science can be dangerous — especially a consensus forged by fast-moving events, guided by incomplete data, and framed by a narrative that was expecting something *exactly like this* to happen. There is room for different interpretations of the current data. If some of these other interpretations are correct, or at least nearer to the truth, then conclusions about the actions required will change correspondingly.

The simplest way to judge whether we have an exceptionally lethal disease is to look at the death rates. Are more people dying than we would expect to die anyway in a given week or month? Statistically, we would expect about 51,000 to die in Britain this month. At the time of writing, 422 deaths are linked to Covid-19 — so 0.8 per cent of that expected total. On a global basis, we'd expect 14 million to die

over the first three months of the year. The world's 18,944 coronavirus deaths represent 0.14 per cent of that total. These figures might shoot up but they are, right now, lower than other infectious diseases that we live with (such as flu). Not figures that would, in and of themselves, cause drastic global reactions.

Initial reported figures from China and Italy suggested a death rate of 5 per cent to 15 per cent, similar to Spanish flu. Given that cases were increasing exponentially, this raised the prospect of death rates that no healthcare system in the world would be

Any testing regime that is based only in hospitals will overestimate the virulence of an infection

able to cope with. The need to avoid this scenario is the justification for measures being implemented: the Spanish flu is believed to have infected about one in four of the world's population between 1918 and 1920, or roughly 500 million people with 50 million deaths. We developed pandemic emergency plans, ready to snap into action in case this happened again.

At the time of writing, the UK's 422 deaths and 8,077 known cases give an apparent death rate of 5 per cent. This is often cited as a cause for concern, contrasted with the mortality rate of seasonal flu, which is estimated at about 0.1 per cent. But we

ought to look very carefully at the data. Are these figures really comparable?

Most of the UK testing has been in hospitals, where there is a high concentration of patients susceptible to the effects of any infection. As anyone who has worked with sick people will know, any testing regime that is based only in hospitals will overestimate the virulence of an infection. Also, we're only dealing with those Covid-19 cases that have made people sick enough or worried enough to get tested. There will be many more unaware that they have the virus, with either no symptoms, or mild ones.

That's why, when Britain had 590 diagnosed cases, Sir Patrick Vallance, the government's chief scientific adviser, suggested that the real figure was probably between 5,000 and 10,000 cases, ten to 20 times higher. If he's right, the headline death rate due to this virus is likely to be ten to 20 times lower, say 0.25 per cent to 0.5 per cent. That puts the Covid-19 mortality rate in the range associated with infections like flu.

But there's another, potentially even more serious problem: the way that deaths are recorded. If someone dies of a respiratory infection in the UK, the specific cause of the infection is not usually recorded, unless the illness is a rare 'notifiable disease'. So the vast majority of respiratory deaths in the UK are recorded as bronchopneumonia, pneumonia, old age or a similar designation. We don't really test for flu, or other seasonal infections. If the patient has, say, cancer,

motor neurone disease or another serious disease, this will be recorded as the cause of death, even if the final illness was a respiratory infection. This means UK certifications normally under-record deaths due to respiratory infections.

Now look at what has happened since the emergence of Covid-19. The list of notifiable diseases has been updated. This list — as well as containing smallpox (which has been extinct for many years) and conditions such as anthrax, brucellosis, plague and rabies (which most UK doctors will never see in their entire careers) — has now been amended to include Covid-19. But not flu. That means every positive test for Covid-19 must be notified, in a way that it just would not be for flu or most other infections.

In the current climate, anyone with a positive test for Covid-19 will certainly be known to clinical staff looking after them: if any of these patients dies, staff will have to record the Covid-19 designation on the death certificate — contrary to usual practice for most infections of this kind. There is a big difference between Covid-19 causing death, and Covid-19 being found in someone who died of other causes. Making Covid-19 notifiable might give the appearance of it causing increasing numbers of deaths, whether this is true or not. It might appear far more of a killer than flu, simply because of the way deaths are recorded.

If we take drastic measures to reduce the incidence of Covid-19, it follows that the deaths will also go down. We risk being convinced that we have averted something that was never really going to be as severe as we feared. This unusual way of reporting Covid-19 deaths explains the clear finding that most of its victims have underlying conditions — and would normally be susceptible to other seasonal viruses, which are virtually never recorded as a specific cause of death.

Let us also consider the Covid-19 graphs, showing an exponential rise in cases — and deaths. They can look alarming. But if we tracked flu or other seasonal viruses in the same way, we would also see an exponential increase. We would also see some countries behind others, and striking fatality rates. The United States Centers for Disease Control, for example, publishes weekly estimates of flu cases. The latest figures show that since September, flu has infected 38 million Americans, hospitalised 390,000 and killed 23,000. This does not cause public alarm because flu is familiar.

The data on Covid-19 differs wildly from country to country. Look at the figures for Italy and Germany. At the time of writing, Italy has 69,176 recorded cases and 6,820 deaths, a rate of 9.9 per cent. Germany has 32,986 cases and 157 deaths, a rate of 0.5 per cent. Do we think that the strain of virus is so different in these nearby countries as to virtually represent different diseases? Or

that the populations are so different in their susceptibility to the virus that the death rate can vary more than twentyfold? If not, we ought to suspect systematic error, that the Covid-19 data we are seeing from different countries is not directly comparable.

Look at other rates: Spain 7.1 per cent, US 1.3 per cent, Switzerland 1.3 per cent, France 4.3 per cent, South Korea 1.3 per cent, Iran 7.8 per cent. We may very well be comparing apples with oranges. Recording cases where there was a positive test for the virus is a very different thing to recording the virus as the main cause of death.

Early evidence from Iceland, a country with a very strong organisation for wide testing within the population, suggests that as many as 50 per cent of infections are almost completely asymptomatic. Most of the rest are relatively minor. In fact, Iceland's figures, 648 cases and two attributed deaths, give a death rate of 0.3 per cent. As population testing becomes more widespread elsewhere in the world, we will find a greater and greater proportion of cases where infections have already occurred and caused only mild effects. In fact, as time goes on, this will become generally truer too, because most

Do we think that the strain of virus is so different in nearby countries as to virtually represent different diseases?

infections tend to decrease in virulence as an epidemic progresses.

One pretty clear indicator is death. If a new infection is causing many extra people to die (as opposed to an infection present in people who would have died anyway) then it will cause an increase in the overall death rate. But we have yet to see any statistical evidence for excess deaths, in any part of the world.

Covid-19 can clearly cause serious respiratory tract compromise in some patients, especially those with chest issues, and in smokers. The elderly are probably more at risk, as they are for infections of any kind. The average age of those dying in Italy is 78.5 years, with almost nine in ten fatalities among the over-70s. The life expectancy in Italy — that is, the number of years you can expect to live to from birth, all things being equal — is 82.5 years. But all things are not equal when a new seasonal virus goes around.

It certainly seems reasonable, now, that a degree of social distancing should be maintained for a while, especially for the elderly and the immune-suppressed. But when drastic measures are introduced, they should be based on clear evidence. In the case of Covid-19, the evidence is not clear. The UK's lockdown has been informed by modelling of what might happen. More needs to be known about these models. Do they correct for age, pre-existing con-

ditions, changing virulence, the effects of death certification and other factors? Tweak any of these assumptions and the outcome (and predicted death toll) can change radically.

Much of the response to Covid-19 seems explained by the fact that we are watching this virus in a way that no virus has been watched before. The scenes from the Italian hospitals have been shocking, and make for grim television. But television is not science.

Clearly, the various lockdowns will slow the spread of Covid-19 so there will be fewer cases. When we relax the measures, there will be more cases again. But this need not be a reason to keep the lockdown: the spread of cases is only something to fear if we are dealing with an unusually lethal virus. That's why the way we record data will be hugely important. Unless we tighten criteria for recording death due only to the virus (as opposed to it being present in those who died from other conditions), the official figures may show a lot more deaths apparently caused by the virus than is actually the case. What then? How do we measure the health consequences of taking people's lives, jobs, leisure and purpose away from them to protect them from an anticipated threat? Which causes least harm?

The moral debate is not lives vs money. It is lives vs lives. It will take months, perhaps years, if ever, before we can assess the wider implications of what we are doing. The damage to children's education, the excess suicides, the increase in mental health problems, the taking away of resources from other health problems that we were dealing with effectively. Those who need medical help now but won't seek it, or might not be offered it. And what about the effects on food production and global commerce, that will have unquantifiable consequences for people of all ages, perhaps especially in developing economies?

Governments everywhere say they are responding to the science. The policies in the UK are not the government's fault. They are trying to act responsibly based on the scientific advice given. But governments must remember that rushed science is almost always bad science. We have decided on policies of extraordinary magnitude without concrete evidence of excess harm already occurring, and without proper scrutiny of the science used to justify them.

In the next few days and weeks, we must continue to look critically and dispassionately at the Covid-19 evidence as it comes in. Above all else, we must keep an open mind — and look for what is, not for what we fear might be.

John Lee is a recently retired professor of pathology and a former NHS consultant pathologist.