Comparisons between countries are essential for the control of COVID-19

Neil Pearce[1], Deborah A Lawlor[2], Elizabeth B. Brickley[1]

(1) London School of Hygiene and Tropical Medicine, London, UK

(2) MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, UK; Population Health, Bristol Medical School, University of Bristol, Bristol, UK

May 2020

[1499 words]

The first author (NP) will act as Guarantor of the paper.

This material has not been published previously in a substantively similar form

On 6 May 2020, the UK Prime Minister, Boris Johnson, quoted statistician David Spiegelhalter, arguing that it was not appropriate to compare the COVID-19 death rate in the UK with other countries[1]. Within a few hours, Spiegelhalter tweeted a request for the Prime Minister to stop quoting him and affirmed that "of course we should now use other countries to try and learn why our numbers are high" [2].

The issue was that, although it is difficult to reliably compare COVID-19 population fatality rates between countries, it is also quite clear that some countries (e.g. UK, USA, Italy, Spain, Belgium, France) have markedly higher burdens of COVID-19 mortality than others (e.g. New Zealand, Australia, Singapore, South Korea, Germany). While one could not say definitively that the UK was the worst in the world, it was performing worse than some countries which had tried alternative control strategies, and there are things that we can learn from that contrast.

Indeed, epidemiology is built on the idea of studying differences between populations. Much of what we have learnt about the causes of disease has had its origins in comparisons of countries[3, 4]. For example, in the 1950s, it was realised that colorectal cancer risks were high in Europe and low in Africa, possibly due to dietary differences in fibre from fruit and vegetable intake. Similarly, liver cancer was common in Asia, which eventually provided a link to hepatitis B. International differences in cervical cancer incidence and mortality suggested an infectious cause, later established as human papillomavirus (HPV).

COVID-19 is different. The causative agent, SARS-CoV-2, is clear; the task is to learn how to best block the virus's transmission and to prevent infections from progressing to severe disease and death.

As the pandemic unfolds, there are numerous natural experiments in progress, as countries adopt different approaches. Although international comparisons are often disparaged because of different data quality and fears of the 'ecological fallacy', if done carefully they can play a major role in our learning what works best for controlling COVID-19 [3]. Furthermore, these natural experiments are yielding clear results within weeks or months (e.g. on the success of the Asian approaches). Thus, there needs to be more thoughtful and thorough analyses of country differences, done by experienced epidemiologists, as it is probably the most important and most valid evidence for informing COVID-19 policy in real time

And after all, what is the alternative? It is impossible or unethical to randomize a lockdown, or other aspects of physical distancing. There could be trials of intensive population testing(5), or prophylactic treatment of household contacts, but few have been launched to date. And all the time, the COVID-19-clock ticks relentlessly on, accumulating more deaths and more survivors with debilitating long-term health problems.

Perhaps the biggest global difference has been the approach taken to the timing and intensity of testing and social distancing. Learning from their experiences of the coronavirus that causes SARS(6), governments in Asia (e.g. China, Hong Kong, Taiwan, Singapore, South Korea), soon followed by Australia and New Zealand (which is the only country to publish an elimination strategy(7)), took action early and decisively. There are differences across Asian countries, with most favouring rapid lockdowns, while South Korea, for example, quickly mobilized intensive mass testing and contact tracing without the need for a full-scale lockdown; Taiwan also avoided the need for a lockdown and has achieved some of the lowest population infection rates recorded(8). In contrast, many European and North American countries were ready (more or less) to tackle pandemic influenza, but were not prepared for a coronavirus pandemic, even though the possibility of such a pandemic had been often discussed. Many countries took action too late and/or indecisively (with important exceptions such as Greece and Germany). They lost critical time, and the delays to action have cost lives. As the virus now spreads across nations in South America and Africa, the lessons from these differences in response take on even greater importance.

However, appropriate inter-country comparisons are not going to be easy. Sweden has been an outlier in its relaxed approach to lockdowns. But who should Sweden be compared to? The population fatality rate in the UK (472 per million on 11/5/2020) is, at this time, higher than Sweden (322); but maybe Sweden, as a Scandinavian country with some 'innate physical distancing' and a different socio-economic structure is more comparable to Denmark (92), Norway (40), Finland (49) or even Australian and New Zealand (4). The comparisons are not helped by major differences in case definitions and quality – for example, the death rate in Belgium is among the highest in the world, but likely because it includes *suspected* COVID-19 deaths in the totals, whereas many other countries do not. Other data problems include COVID-19 deaths being missed due to lack of testing or poor test sensitivity, and deaths misclassified as being *from* COVID-19 rather than just *with* COVID-19(9). This has led some to argue that the only reliable data on the pandemic's impact on mortality will be measures of excess total mortality, which account for COVID-19 deaths that have not been

identified, as well as deaths from other causes related to the lockdown and/or changes in health service provision (10). Even then, there are issues as to the time periods to consider. The advocates of Sweden's startling approach have argued that the country's apparently high death rate simply reflects deaths brought forward (i.e. individuals who were going to die later in the year anyway) and that other countries are just trying to delay the inevitable. This seems to be an extremely risky approach(11), and preliminary UK data suggests that COVID-19 deaths are not all 'deaths brought forward', and that each death on the average, represents about 13 years of healthy life lost (12).

As time goes on and lockdowns are lifted, more international differences will become apparent. For example, there are policy differences in whether face masks are recommended or required in public places. And there are major questions about how schools should be opened, who should return to work, and what aspects of physical distancing should be maintained. Some of these questions can be answered within countries with epidemiological studies such as the test-negative design(13), but some require country-to-country comparisons. Of course, we will know more in a year, but we have to take decisions now (as the Danish philosopher Kierkegard noted in 1843: *"Life can only be understood backwards; but it must be lived forwards"*). Policymakers must look to other countries' actions and outcomes from this first wave of infection and put themselves in a better position to prepare for the next.

So what are the post-Covid-19 implications for epidemiology?

Firstly, international collaboration has been essential for making rapid progress on COVID-19(14). There has been a remarkable alliance of health researchers internationally who have worked together to tackle the problem (often while politicians have not). We need to strengthen these international ties, and build more international collaborations, particularly between high-income-countries and low-and-middle-income countries(15, 16), rather than staying within our national silos(17).

Secondly, we must ensure that the scientific advisory committees include diverse voices, including a range of epidemiological approaches. In the early stages of the epidemic, the evidence from Asia on the effectiveness of lockdowns and mass testing was largely overlooked by countries such as the UK (which initially did not even consider these options), where the advisory committees were (and are) dominated by infectious disease modellers, behavioural scientists and laboratory scientists. There is a notable lack of other infectious

disease epidemiologists who are experienced at collecting and analysing real data (e.g. population surveys of infection prevalence which provide essential information for policy(9), and analyses of interventions such as those that had already been done in Asia); there is also a notable lack of public health specialists with on-the-ground experience in epidemic control (including mass testing).

Thirdly, there is an unmet need for effective global surveillance systems for both infectious and chronic diseases (18, 19). Many of these cannot be validly identified from routine health system data in low-and-middle-income countries, so worthwhile initiatives like the Global Burden of Diseases (GBD) will not pick them up. Regular population disease monitoring is also important so that surveillance systems are in place when epidemics occur. Of course, it is not possible to conduct comprehensive surveys of all health conditions all of the time. However, many low-and-middle-income countries are already conducting surveys such as WHO's STEPS(20), as well as surveys of particular diseases(21). These provide an infrastructure which can be the basis for more integrated surveillance systems, which can be used to quickly conduct population surveys in an epidemic, thus allowing the estimation of important important quantities such as the infection fatality rate and attack rate, and ongoing monitoring of the epidemic (9).

Finally, the COVID-19 epidemic shows the need for epidemiology to go back to its roots – thinking about populations(3). Studying disease occurrence by person, place and time (often referred to as "descriptive epidemiology") is usually taught in introductory courses, even if this approach is then paid little attention subsequently. COVID-19 is a striking example of how we can learn a great deal from comparing countries, states, regions, time trends, and persons, despite of all of the difficulties. Epidemiology is a process of discovery(22) and testing of multiple hypotheses, putting diverse sets of information together. Population comparisons provide the basis for this process, and a 'reality check' for almost everything else we do subsequently. The first questions we should always be asking are "who gets the disease, and who doesn't, and what can we learn from this?"

References

1.   Spiegelhalter D. Coronavirus deaths: how does Britain compare with other countries? The Guardian. 2020 30 April 2020.
2.   Spiegelhalter D. Author of Guardian article on death tolls asks UK government to stop using it. The Guardian. 2020 6 May 2020.
3.   Morris JN. Uses of epidemiology. Edinburgh: Livingstone; 1957.
4.   Saracci R, Wild C. International Agency for Research on Cancer : the first fifty years - 1965-2015. Lyon: International Agency for Research on Cancer; 2015.
5.   Peto J, Alwan NA, Godfrey KM, Burgess RA, Hunter DJ, Riboli E, et al. Universal weekly testing as the UK COVID-19 lockdown exit strategy. The Lancet. 2020;395:1420.
6.   Wilder-Smith A, Chiew CJ, Lee VJ. Can we contain the COVID-19 outbreak with the same measures as for SARS? Lancet Infectious Diseases. 2020;20:e102-7.
7.   Baker MG, Kvalsvig A, Verrall AJ, Telfar-Barnard T, Wilson N. New Zealand's elimination strategy for the COVID-19 pandemic and what is required to make it work. New Zealand Medical Journal. 2020;133:10-4.
8.   Wang CJ, Ng CY, Brook RH. Big data analytics, new technology and proactive testing. Journal of the American Medical Association. 2020 323:1341-2.
9.   Pearce N, Vandenbroucke JP, VanderWeele T, Greenland S. Accurate statistics on Covid-19 are essential for policy guidance and decisions. American Journal of Public Health. 2020:in press.
10.   Banerjee A, Pasea L, Harris S, Gonzalez-Izquierdo A, Torralbo A, Shallcross L. Estimating excess 1- year mortality from COVID-19 according to underlying conditions and age in England: a rapid analysis using NHS health records in 3.8 million adult. MedRxiv. 2020:doi.org/10.1101/2020.03.22.20040287.
11.   Robinson C. The truth about Sweden and its Covid 19 coronavirus choices. New Zealand Herald. 2020 11 May 2020.
12.   Hanlon P, Chadwick F, Shah A, Wood R, Minton J, McCartney G, et al. COVID-19 – exploring the implications of long-term condition type and extent of multimorbidity on years of life lost: a modelling study. Wellcome Open Research. 2020;5:75.
13.   Vandenbroucke JP, Brickley EB, Vandenbroucke-Grauls CMJE, Pearce N. Analysis proposals for test-negative design and matched case-control studies during widespread testing of symptomatic persons for SARS-Cov-2. arXiv. 2020:2004.06033v1.
14.   WHO. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Geneva: WHO; 2020.
15.   Pearce N. Epidemiology in Latin America: an opportunity for a global dialogue. Journal of Epidemiology and Community Health. 2008;62(9):762-3.
16.   Pearce N. Global epidemiology: the importance of international comparisons and collaborations. Open Access Epidemiology. 2012;1:15.
17.   Hunter D. Covid-19 and the Stiff Upper Lip — The Pandemic Response in the United Kingdom. New England Journal of Medicine. 2020;382:e31.
18.   Caplin B, Jakobsson K, Glaser J, MNitsch D, KJha V, Singh A, et al. International collaboration for the epidemiology of eGFR in low and middle income populations: Rationale and core protocol for the Disadvantaged populations eGFR epidemiology study (DEGREE). BMC Nephrology. 2017;18:DOI 10.1186/s12882-016-0417-1.
19.   Ellwood P, Asher MI, Billo NE, Bissell K, Chiang C-Y, Ellwood EM, et al. The Global Asthma Network rationale and methods for Phase I global surveillance: prevalence, severity, management and risk factors. European Respiratory Journal. 2017;49:1601605.
20.   WHO. STEPwise approach to surveillance. Geneva: WHO; 2020.
21.   Ruwanpathirana T, Senanayake S, Gunawardena N, Munasinghe A, Ginige S, Gamage D, et al. Prevalence and risk factors for impaired kidney function in the district of Anaradhapura, Sri Lanka. BMC Public Health. 2019;19:763.

22.   Vandenbroucke JP, Pearce N. From ideas to studies: how to get ideas and sharpen them into research questions. Clinical Epidemiology. 2018;10:253-64.