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Multiple testing and the effect of NPIs on the spread of SARS-CoV-2

You Li and colleagues¹ estimate average associations between imposing and lifting eight non-pharmaceutical interventions (NPIs)

and the reproduction number (R) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the first half of 2020 across 131 countries through a regression analysis with daily data. Since changes in the status of different NPIs often occurred either jointly or in close temporal proximity within each country, their individual associations are generally difficult to disentangle from observational data and are naturally subject to substantial statistical uncertainty.² This uncertainty is unfortunately not adequately captured by the 95% CIs reported by Li and colleagues.¹ In particular, they do not reflect the fact that multiple NPIs are considered simultaneously, and they do not account for possible temporal and spatial dependence between datapoints.

To see the scope of the simultaneity issue, consider the association between NPI-status changes and the percentage shift in R after 28 days. With lengths between 30 and 72 percentage points, the corresponding 95% CIs reported in the right column of table 1 in the Article are quite wide to begin with. But with 16 estimates to account for in this case alone, a simple Bonferroni correction³ would further widen each 95% CI by about half. Although there are other statistical adjustments that might not result in quite as much stretch, it is safe to predict that 95% CIs that correctly account for multiple comparisons would be much wider than the ones presented in table 1, and would overlap substantially.

It is therefore not possible to deduce from this kind of data with conventional levels of statistical certainty that imposing or lifting any particular NPI is associated with a non-zero change in R after 28 days, or that any particular NPI works better than any of the others under consideration (analogous comments apply to estimates for other timepoints). Given the substantial statistical uncertainty,

individual point estimates should also not be interpreted as precise predictions of the effect of future interventions.

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Why development of outbreak analytics tools should be valued, supported, and funded

The COVID-19 pandemic has brought infectious disease modelling to the forefront, with mainstream media uncovering the good, the bad, and sometimes, the ugly in a field of research that is being used more than ever to inform public health decision-making. A dramatic example is the code release of Imperial College London's COVID-19 simulations, which sparked waves of criticisms for its poor coding practices, although the results themselves were later found to be reproducible.¹

Does good coding matter in science? If by good coding we mean using practices that make the code clear and easy to reuse, maintain, expand on, and test—in short, reliable—then the answer is yes. And it matters even more when the corresponding piece of software is used to inform public health operations. Unfortunately, scientific software development has struggled to gain recognition,^{2,3} and there has been little incentive so far

for academic researchers to make code free to access and transparent in infectious disease modelling.

The issue is not limited to modelling. The emergence of outbreak analytics as a new field of research emphasises the need for high-quality, freely available, and open-source software tools for informing the response to infectious disease outbreaks, from data collection to advanced statistical analyses.⁴

Nor is the issue new. Development of tools for outbreak analytics has been chronically undervalued and underfunded. Despite the emergence of initiatives, such as the R Epidemics Consortium,⁵ to promote open-source software for outbreak response, such projects typically fall outside the scopes of health-research funders, lying somewhere between theoretical modelling work and interventions.

As a result, we have faced an absurd situation where data scientists involved in outbreak responses have encountered the same issues at every new outbreak, without ever being able to focus on developing software tools to solve these problems once and for all. While it is frustrating to see this issue finally acknowledged during the biggest public health crisis in recent times, it is not too late for a cultural shift to take place.

Solutions are simple. The development of high-quality scientific software must be as valued as other academic outputs. Dedicated career profiles for scientific software engineers must be created to build long-term capacity in academic institutions. Last, and perhaps most importantly, funders need to lead—not follow—this cultural shift by acknowledging the development of outbreak analytics tools as a field deserving recognition and support.

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Keeping childhood immunisation rates stable during the COVID-19 pandemic

Vaccination teams all over the world grew concerned about how to ensure stable childhood immunisation rates once local COVID-19 outbreaks turned into national outbreaks. Childhood immunisation team members in the Lothian area of Scotland were equally concerned. Lothian comprises Edinburgh and the surrounding area; it has a population of around 900 000 people and around 10 000 births per year. In previous years, attendance at the five routine vaccination appointments in children (aged 0–5 years) has been very high, leading to coverage of more than 95% (as recommended by WHO¹) for most vaccines.²

During the first wave of the COVID-19 pandemic in spring, 2020, 22% of infants in the WHO European Region had their vaccination courses interrupted.³ A drop in vaccination rates of almost 20% during the first UK lockdown was reported in England.⁴ However, in Lothian, attendance at childhood immunisation clinics remained stable in the weeks during lockdown (appendix).

When the Scottish Vaccination Transformation Programme was designed in 2018, a strong emphasis was placed on the needs of children and adults who require vaccinations.⁵ This programme provided the foundation for local adaptations to immunisation efforts by the childhood immunisation team in Lothian during the first wave of the COVID-19 pandemic. Several adaptations had an important role in keeping attendance rates stable.

First, vaccinations were delivered via fixed-point clinics at various locations that were accessible by public transport. Children who could not attend clinics owing to shielding could be vaccinated by mobile teams. All vaccinations were delivered with appropriate personal protective equipment in place, in line with guidance at the time.

Second, changes were made to how data were collected. All vaccination data are held centrally in the Scottish Immunisation Recall System. Public Health Scotland collects and publishes vaccination uptake data for Scotland.² Data published in previous years began with vaccinations completed when children reached 12 months of age. By contrast, during the pandemic, much shorter periods of time were required to monitor immunisation clinic attendance (appendix) and uptake of vaccinations.

Third, efforts were made to establish trust and ensure that children and their families felt looked after. All families received a personal reminder via telephone from a trained operator on

See Online for appendix



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