Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Authors' reply

Senjuti Saha and Samir Saha make the excellent point that the scope of vaccine impact goes beyond the deaths that are directly averted by immunisation activities. In this we agree. We aimed to quantify the deaths averted by vaccination for ten diseases in 98 low-income and middle-income countries.[1] However, there are wider benefits of vaccination—for example, in reducing the burden on health-care services. With many low-income and middle-income countries having minimal health-care capacity, the impact of vaccination might far outstrip the current best estimates.

COVID-19 has emphasised the ramifications of a health-care capacity that is resource-limited as countries have seen the pandemic saturate possible treatment space, with the introduction of vaccines relieving some of this burden. We noted that vaccination activities reduced overall mortality by 45% between 2000 and 2019, for the countries and pathogens that were studied. However, these data do not capture the reduction in morbidities that are associated with vaccine-preventable diseases, nor the benefits of strengthened health systems and equity.

Quantifying the wider effects of vaccination has been attempted, particularly in an economic sense. Chang and colleagues[2] assessed the role of vaccination in reducing medical impoverishment, noting a 9% reduction in the number of people in low-income countries whose income is below the World Bank poverty line. The burden of vaccine-preventable diseases disproportionately affected the lowest income quintiles, showing the potential equalising nature of vaccination activities. Vaccination has also been linked with productivity, shown by a measurable improvement in cognitive outcomes in later childhood.[3] Improved educational achievements are generally linked with increased social mobility and economic development.[4]

Given the wide-ranging impact of vaccination, why are epidemiological and health economic studies so focused? In our study, 16 modelling groups provided estimates that considered heterogeneity in data, transmission, and health access both geographically and, in some cases, temporally. To provide robust, well calibrated estimates of disease burden, focused analysis is required. This requirement motivates the structure of the Vaccine Impact Modelling Consortium, which brings together modelling groups to capture the latest insights in disease transmission and vaccine impact. Despite this motivation, uncertainties remain in both the natural history of the pathogens that are studied and the input data relating to vaccination and demography. As such, we need to balance the need for robust and focused results, data scarcity, and the huge and far-reaching ramifications of such an effective intervention as vaccination. It is an area of continued study and improvement that will potentially be accelerated by the ongoing COVID-19 pandemic.

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Inclusion and diversity in the PRINCIPLE trial

We welcome the call from Paramjit Gill and colleagues[1] for diverse participation in clinical trials like PRINCIPLE.[2]

We initiated many inclusive recruitment strategies, including the appointment of a leading and national pharmacist expert working with minority ethnic communities who was tasked with targeting socio-economically deprived areas, minority ethnic communities, and people with learning difficulties; developing UK-wide relationships with community and religious organisations (including places of worship); collaborating with universities and national and regional health-care institutions; and gathering nationwide support from minority ethnic leaders, health professionals, and their organisations (appendix).

We consistently promoted the trial in many languages, via local and UK national media channels, the internet, and social media platforms. Our pharmacy networks and general practice networks helped establish PRINCIPLE footprints in approximately 7500 community pharmacies UK-wide, with more than 1000 general practice co-investigators helping with participant recruitment from a range of settings.

This strategy contributed to the inclusion of 55 (4·0%) South Asian and seven (0·5%) Black participants in our analysis of azithromycin for treatment of suspected COVID-19,[2] which was comparable to 3·7% Asian ethnicity and 1·6% Black ethnicity among people older than 50 years (PRINCIPLE's target age group) in England and Wales.[3] The proportions of participants' in Index of Multiple Deprivation (IMD) quintiles were (from most to least socioeconomically deprived): 352 (26%) of 1375 in IMD1; 267 (19%) of 1375 in IMD2; 270 (20%)


Adaniel Leal-Olivas/Getty Images

For the **Vaccine Impact Modelling Consortium** see https://www.vaccineimpact.org/

See **Online** for appendix