¹ Edward Ford Building (A27), School of Public Health, University of Sydney, NSW 2006, Australia

² Institute for Evidence-Based Healthcare, Faculty of Health Sciences and Medicine, Bond University, Robina, QLD 4226, Australia

³ Department of Epidemiology and Data Science, Amsterdam Public Health, Amsterdam University Medical Centers, Amsterdam, Netherlands

katy.bell@sydney.edu.au

Cite this as: *BMJ* 2021;372:n435

<http://dx.doi.org/10.1136/bmj.n435>

Published: 12 February 2021

COVAX ALLOCATION OF COVID VACCINES

Equity and evidence during vaccine rollout: stepped wedge cluster randomised trials could help

Katy J L Bell,¹ Paul Glasziou,² Fiona Stanaway,¹ Patrick Bossuyt,³ Les Irwig¹

Herzog and colleagues raise the thorny issue of allocating scarce vaccines, comparing the proportional allocation model with a fair priority model.¹ Regardless of what is used for prioritisation between and within countries, there will be a long period of rollout before most of the world's population are offered vaccination. For groups of equivalent priority, a fair and equitable way to decide on the order of rollout is to use a lottery, or system of random choice.² Such randomised sequential rollout of vaccines could be delivered through stepped wedge cluster randomised trials (SW-CRTs).³

Although constrained by the absence of placebos,⁴⁻⁶ SW-CRTs might provide valuable information related to uncertainties about different vaccine effects, including:

- Effectiveness in preventing transmission of SARS-CoV-2 infection from vaccinated patients to others, and whether this differs across genetic variants of the virus including new, more infectious, strains
- Effectiveness in preventing SARS-CoV-2 asymptomatic or paucisymptomatic infection: the Oxford-AstraZeneca vaccine was estimated to have only 27.3% (–17.2 to 54.9) efficacy in preventing infection that is asymptomatic or when symptoms are unknown,⁷ and the efficacy of Pfizer and Moderna vaccines for this outcome has not been reported^{8,9}
- Safety of vaccines in terms of risk of clinically important adverse events
- Comparative safety and effectiveness of different vaccines, including combinations of vaccines
- Comparative safety and effectiveness of different intervals between first and second dose of vaccine.¹⁰

Just as the benefits and harms of other population interventions can be assessed through randomised trials in population health programmes,¹¹ the benefits and harms of SARS-CoV-2 vaccines could be assessed through randomised trials in population rollouts. The SW-CRT study design might be the only randomised evaluation possible outside of phase III placebo controlled vaccine trials, as phase IV parallel randomised controlled trials (cluster or individual) might not be feasible because of logistics or acceptability. The likely alternative is non-randomised sequential rollout, which is a less fair way to decide on the order of offering vaccination and will result in evidence with a higher risk of bias.

Competing interests: None declared.

- 1 Herzog LM, Norheim OF, Emanuel EJ, McCoy MS. Covax must go beyond proportional allocation of covid vaccines to ensure fair and equitable access. *BMJ* 2021;372:m4853. doi: 10.1136/bmj.m4853 pmid: 33402340
- 2 Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of covid-19. *N Engl J Med* 2020;382:2049-55. doi: 10.1056/NEJMs2005114 pmid: 32202722
- 3 Hemming K, Talaard M, McKenzie JE, et al. Reporting of stepped wedge cluster randomised trials: extension of the CONSORT 2010 statement with explanation and elaboration. *BMJ* 2018;363:k1614. doi: 10.1136/bmj.k1614 pmid: 30413417
- 4 Rid A, Lipsitch M, Miller FG. The ethics of continuing placebo in SARS-CoV-2 vaccine trials. *JAMA* 2021;325:219-20. doi: 10.1001/jama.2020.25053 pmid: 33315080
- 5 Krause PR, Fleming TR, Longini IM, et al. WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation. Placebo-controlled trials of covid-19 vaccines — why we still need them. *N Engl J Med* 2021;384:e2. doi: 10.1056/NEJMp2033538 pmid: 33264543
- 6 Krause P, Fleming TR, Longini I, Henao-Restrepo AM, Peto R. World Health Organization Solidarity Vaccines Trial Expert Group. Covid-19 vaccine trials should seek worthwhile efficacy. *Lancet* 2020;396:741-3. doi: 10.1016/S0140-6736(20)31821-3 pmid: 32861315
- 7 Voysey M, Clemens SAC, Madhi SA, et al. Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397:99-111. doi: 10.1016/S0140-6736(20)32661-1 pmid: 33306989
- 8 Polack FP, Thomas SJ, Kitchin N, et al. C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. *N Engl J Med* 2020;383:2603-15. doi: 10.1056/NEJMoa2034577 pmid: 33301246
- 9 Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2020; doi: 10.1056/NEJMoa2035389. pmid: 33378609
- 10 Iacobucci G, Mahase E. Covid-19 vaccination: what's the evidence for extending the dosing interval? *BMJ* 2021;372:n18. doi: 10.1136/bmj.n18 pmid: 33408068
- 11 Bell KJL, Bossuyt P, Glasziou P, Irwig L. Assessment of changes to screening programmes: why randomisation is important. *BMJ* 2015;350:h1566. doi: 10.1136/bmj.h1566 pmid: 25825377

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.