Randomization during vaccine deployment

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MEGA-SCALE randomisation during deployment

In the established UK breast screening program, AgeX has individually randomised 4 million women to have, or not have, 1 extra screening invitation.

The primary analysis is of outcome (by electronic health records) among those who had attended their previous cancer screening invitation

Pandemics: Could this example be of any relevance to randomising some aspect of vaccination in some population to get rapid, totally unbiased results?

COVID (and future pandemics)

Even without importantly new variants, there would be uncertainties about the choice of vaccines, of vaccination schedules, of target populations, and of when, whether, or to whom, to offer a booster.

Could mega-scale randomisation during vaccine deployment help study some of these issues?

A key requirement in such a study is that it must not interfere with ordinary vaccination.

Nothing extra should be added to what the vaccinators have to do with each individual.

Follow-up depends on what's locally possible; electronic records may well not be available.

As newer vaccines target new variants, further uncertainties are likely to arise.

Could large-scale randomisation during deployment help address some of them?

(NB Trials assess effects on individuals, not any effects on viral evolution rates.)

Example: A large-scale randomised study with clinical endpoints could compare intervals of 4 weeks vs 12 weeks between vaccine doses.

Example: A mega-scale randomised study with clinical endpoints could have compared intervals of 4 weeks versus 12 weeks between COVID vaccine doses.

In a population where mass vaccination was being offered to many millions, with dose 2 at week 12, a million of those already given dose 1 could have been randomly chosen to be invited back at week 4.

The comparison would have been strictly randomised, but as placebo injections would not have been given, follow-up would have emphasised hard endpoints.

Another example: If two vaccines are each being given to millions of people in a country, can really large numbers be randomised between them, with genotyping of failures?

Final example:
2023 COVID booster shots

Instead of offering a COVID booster shot to everyone in a population of many millions,

why not randomise at least 2 million in some sub-population where the appropriateness of offering a booster is substantially uncertain?

Massively large randomised comparisons need not be expensive, and could NIMBLY AND RAPIDLY resolve SOME uncertainties.

They may usefully complement observational studies of clinical outcomes and lab studies of immunological responses, especially if many of the vaccine failures in trials get genotyped.

The chief obstacles to mega-trials during vaccine deployment are bureaucratic

At present, there are double standards between what is needed for mass deployment of a vaccine, and what would be needed for mass randomisation.

Pandemic preparedness during the years between pandemics should involve revising trial regulation to make mass randomisation as easy as mass vaccination

Wherever it's practicable to randomise in rollout, give randomisation a chance to work its magic

If large numbers are randomised, the magic of randomisation always yields trustworthy evidence; so-called "real-world" evidence may well not do so.

The Magic of Randomization vs
the Myth of Real-World Evidence
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