Trial designs to evaluate additional vaccines

Richard Peto
Nuffield Department of Population Health
University of Oxford, UK
UK breast screening program: 4 million women were randomly allocated to get, or not to get, one extra screening invitation (www.agex.uk)

Could this example be of any relevance to randomising a new, or modified, vaccine in one particular country, seeking **rapid** results?
Even without importantly new variants, there would be uncertainties about the choice of vaccines, of vaccination schedules, and of target populations.

Could large-scale randomisation during deployment help study some of them?
A key requirement in such a study is that it should 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.)
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The comparison would be strictly randomised, but as placebo injections would not be given, the results would be really reliable only for reasonably hard endpoints (got by monitoring hospital records and death registries).
Example (2): Testing a novel vaccine in a population that would not otherwise be vaccinated for many months.

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For high compliance, consent teams first cover a small area house-to-house. Randomisation (by household??) lists those to be vaccinated promptly by house-to-house vaccination team visits, and those to be vaccinated later.
Example (3): If two vaccines are each being given by a state system to millions of people, could really large numbers be randomised between them?
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 such trials get genotyped.
With large numbers randomised & unbiased follow-up, the magic of randomisation will yield reliable evidence; so-called “real-world” evidence may not *

* The magic of randomization vs the myth of “real-world” evidence

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