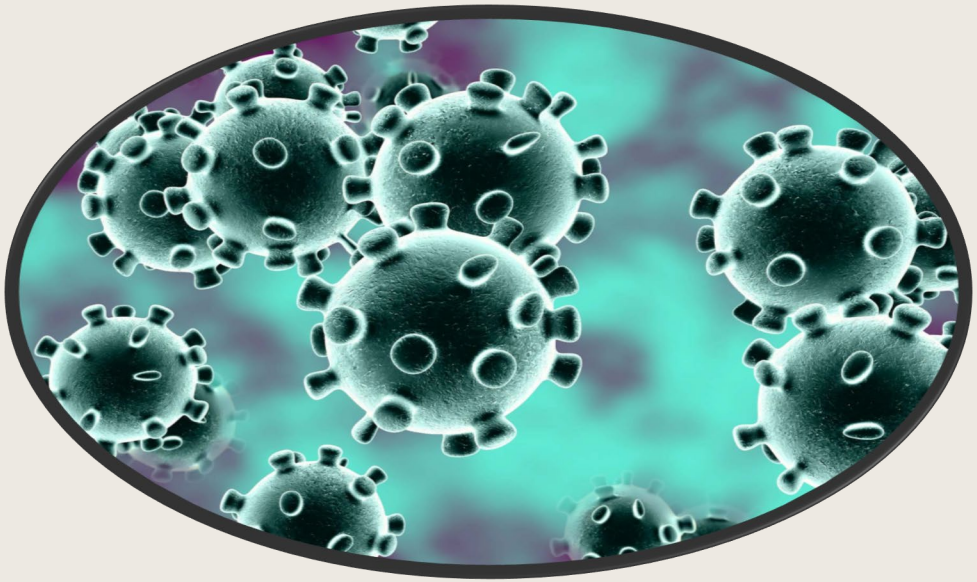

Achieving timely and reliable evaluation of promising candidate vaccines

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ALL vaccine candidates need to be evaluated

35 candidates in clinical phase

9 already in Phase 3 trials

145 candidates in pre- clinical phase

The world needs efficient, speedy, and reliable evaluation of many candidate vaccines against COVID-19.

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How can WHO help ensure ALL vaccines are evaluated?

Establishing robust and transparent processes to assess preclinical evaluation and rigorously identify the few vaccines with the greatest promise to join Phase 3 trials

Convening international experts to design robust trial designs

Working with partners, clinical research networks and sites to find solutions to the needs and addressing the challenges for implementation

How can WHO help ensure ALL vaccines are evaluated?

In comparison with individual trials for each of many different vaccines:

- **the costs of a "platform trial" approach** will be a fraction of the cost of of several separate trials.
- **continuous use of established clinical trial infrastructure in a "platform trial" of several vaccines** could save time and effort, accelerating the discovery of some safe and effective vaccines.
- **high enrolment rates facilitated by flexible trial design and hundreds of study sites in high-incidence locations** could yield results on short-term efficacy within just a few months of including a vaccine.

Approval and deployment of a vaccine of only modest efficacy could do more harm than good

Regulators, researchers and policy makers should seek not just proof of **some** efficacy, but transparent proof of **worthwhile efficacy** in humans.

COVID-19 vaccine development is different

Adverse consequences of using a weakly effective vaccine

- Use of weakly effective vaccine interferes with evaluation of better vaccines
- Large numbers would be immunized before the mistake is apparent

- Resources used on a poor vaccine reduce resources available to make better ones
- Timeliness of proper vaccine testing and deployment is critically important

3 issues are crucial in planning COVID-19 vaccine trials

(1)whether to demand not only proof of some vaccine efficacy but also proof of **worthwhile efficacy**;

(2)whether the initial trials of vaccine against placebo should prioritise not only single-vaccine trials but also **a multivaccine trial**; and

(3)whether to assess safety, protection against severe disease, and **duration of protection** by continuing blinded follow-up of the vaccine and placebo groups after definite evidence of short-term efficacy has emerged, but before an effective vaccine has been deployed locally in the general population.

Twofold WHO COVID efficacy requirements

Not only **apparently halving** disease incidence,

but also **guaranteeing > 30%** reduction

Example:

Observing 50 vs 100 cases apparently halves risk, and guarantees > 30% efficacy

Reliable evidence is also needed about vaccine safety, longer-term efficacy, and protection against severe COVID-19

Trials of sufficient size and duration are needed to provide this,

- Need to determine whether the vaccine can make COVID-19 more hazardous (so-called disease enhancement).
- Assessments of safety in multivaccine trials can determine directly whether particular vaccines have adverse effects not shared by other vaccines.

Trials that assess only immunological endpoints cannot provide this evidence, and human challenge studies in young, otherwise healthy, adult volunteers might not provide sufficient evidence of safety or efficacy in other populations.

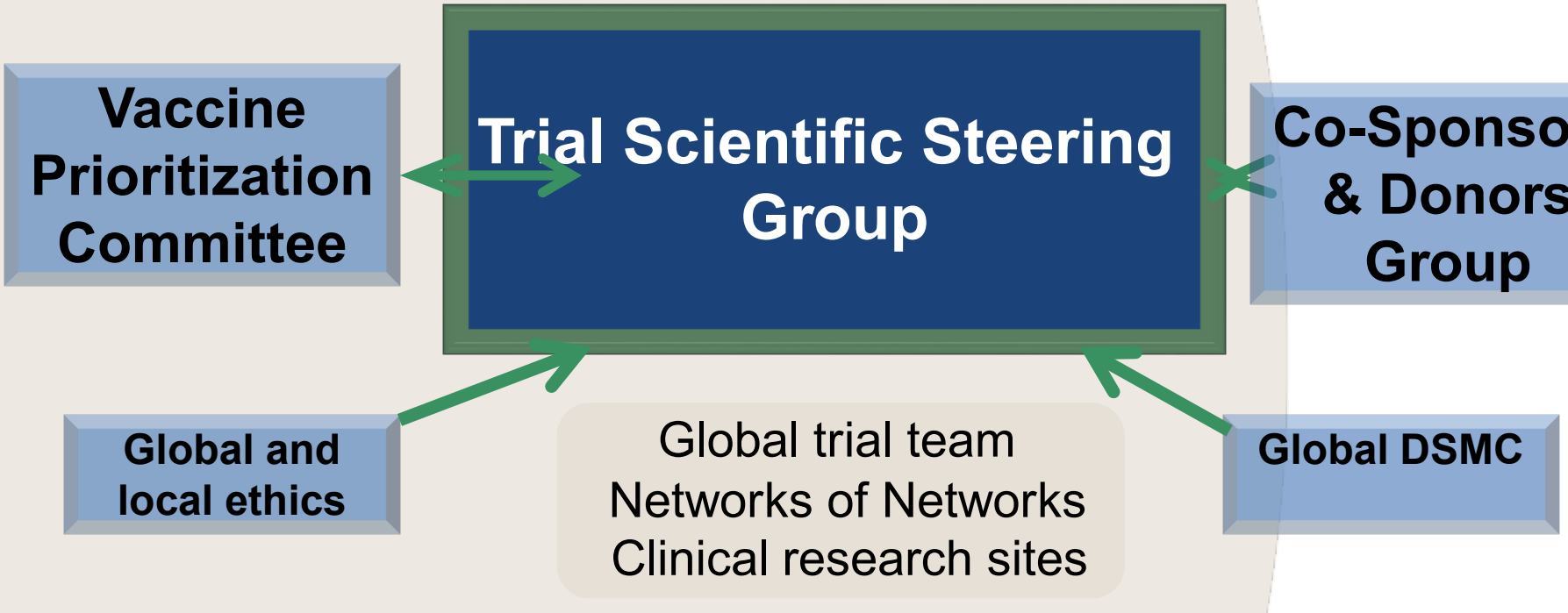
WHY an international RCT of several candidate vaccines ?

Solidarity trial for vaccines

Evaluating several different candidate vaccines	Expeditiously enrolling participants at sites with high rates of COVID-19	Eliminating inefficiency of designing and conducting separate trials	International collaboration and countries' commitment
permitting selected vaccines to enter the trial whenever ready	flexible mix of fixed sites and pop-up sites	shared placebo group increases efficiency and attractiveness	fosters participation of sites with high COVID-19 rates
vaccines selection for trial assessed using a priori criteria	sufficient enrollment to assess efficacy and safety of all vaccines	If placebo can no longer be used, another vaccine becomes comparator	any effective vaccines will be tested at all sites
all vaccines selected for trial are eligible for testing at all sites	adaptive design accommodates unanticipated circumstances	ineffective vaccines don't much hinder evaluation of better vaccines	paves the way for international distribution of effective vaccines
INCREASING THE LIKELIHOOD OF FINDING SEVERAL EFFECTIVE VACCINES	**RAPID ACCUMULATION OF DATA TO SUPPORT RIGOROUS EVALUATION**	**RESULTS WITHIN 3-6 MONTHS AFTER EACH VACCINE IS READY FOR INCLUSION**	**FOSTERS INTERNATIONAL DEPLOYMENT WITH EQUITY OF ACCESS**

Criteria for site selection
>1% incidence forecast in next few months
Access to laboratory for case confirmation
Potential to enroll rapidly and to follow up
Previous experience in clinical research
Support and resources from Ministry of Health
National regulatory and ethics support

Governance framework



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Conclusions

Reliable evaluation of COVID-19 vaccines is essential

- Studies must be able to exclude weakly effective vaccines

Prompt evaluation of **MOST** vaccines is also critically important

Global Collaboration in Vaccine development and further deployment is a win-win

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Additional information can be found here

https://www.who.int/teams/blueprint/covid-19