Key Criteria for the ethical acceptability of Covid-19 human challenge studies

Principales criterios para la aceptabilidad ética de los estudios de exposición con seres humanos en el contexto de la COVID-19

On behalf of:

WHO Working Group for Guidance on Human Challenge Studies in COVID-19

WHO Global Health Ethics Unit

World Health Organization

Challenge studies / Estudios de exposición

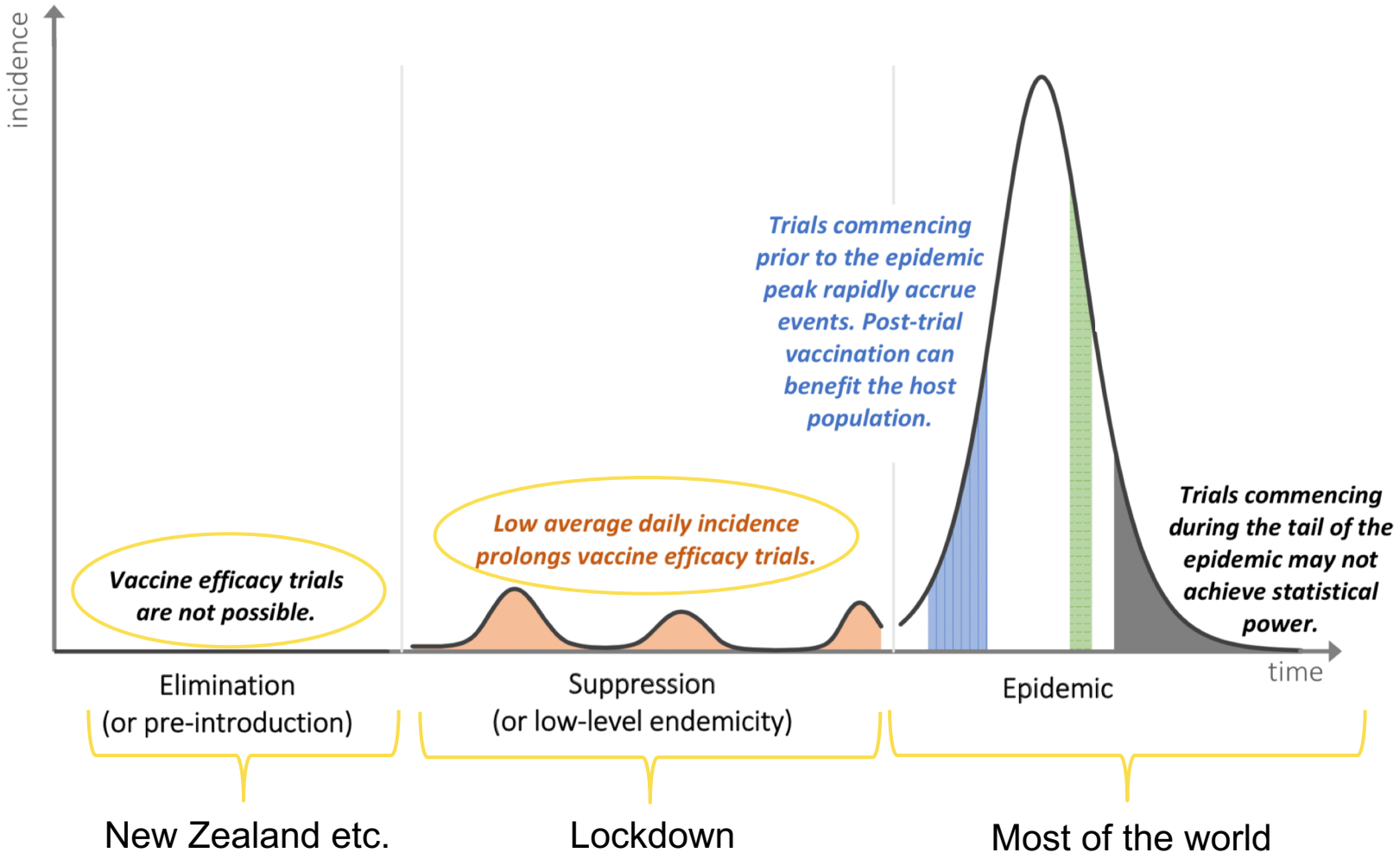
A type of research involving:

1. Intentional infection of research participants
2. With aim to
    a) Test vaccines / drugs
    b) Study infection / immunity
    c) Develop models of infection
3. In a highly controlled setting

Challenge studies / Estudios de exposición

- >100 Covid-19 vaccine candidates
- Complexities of vaccine field trials
  - Involve >10,000 participants
  - Require months-years (depend on local transmission levels)
- Uncertainties of public health measures
  - Based on incomplete knowledge re: infection & immunity
- Infection in young adults >1000 times less risky than older people

Vaccine field trials: when and where?



Heriot & Jamrozik, Medical Journal of Australia, 2020

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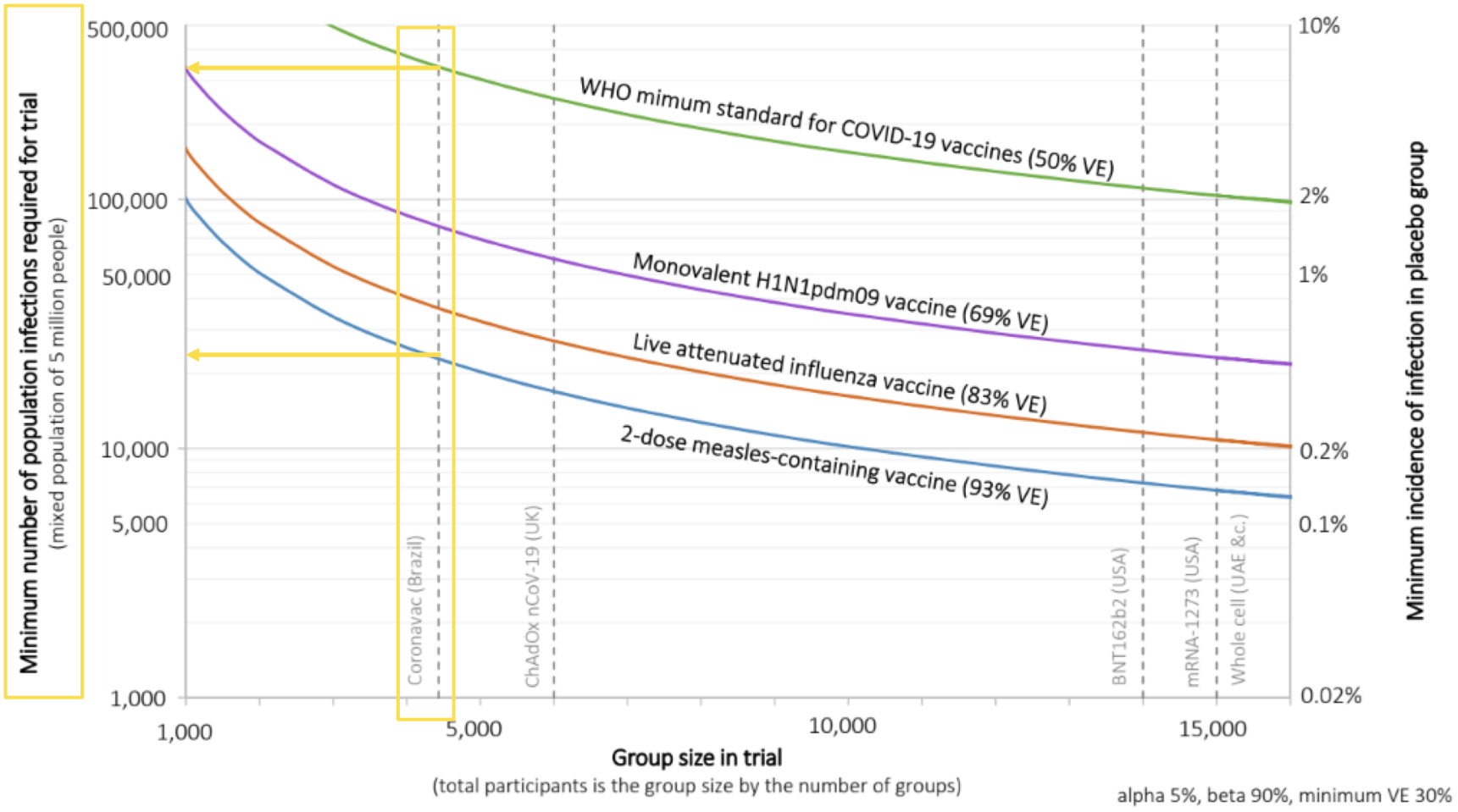
Size of epidemics for field trials



Heriot & Jamrozik, Medical Journal of Australia, 2020

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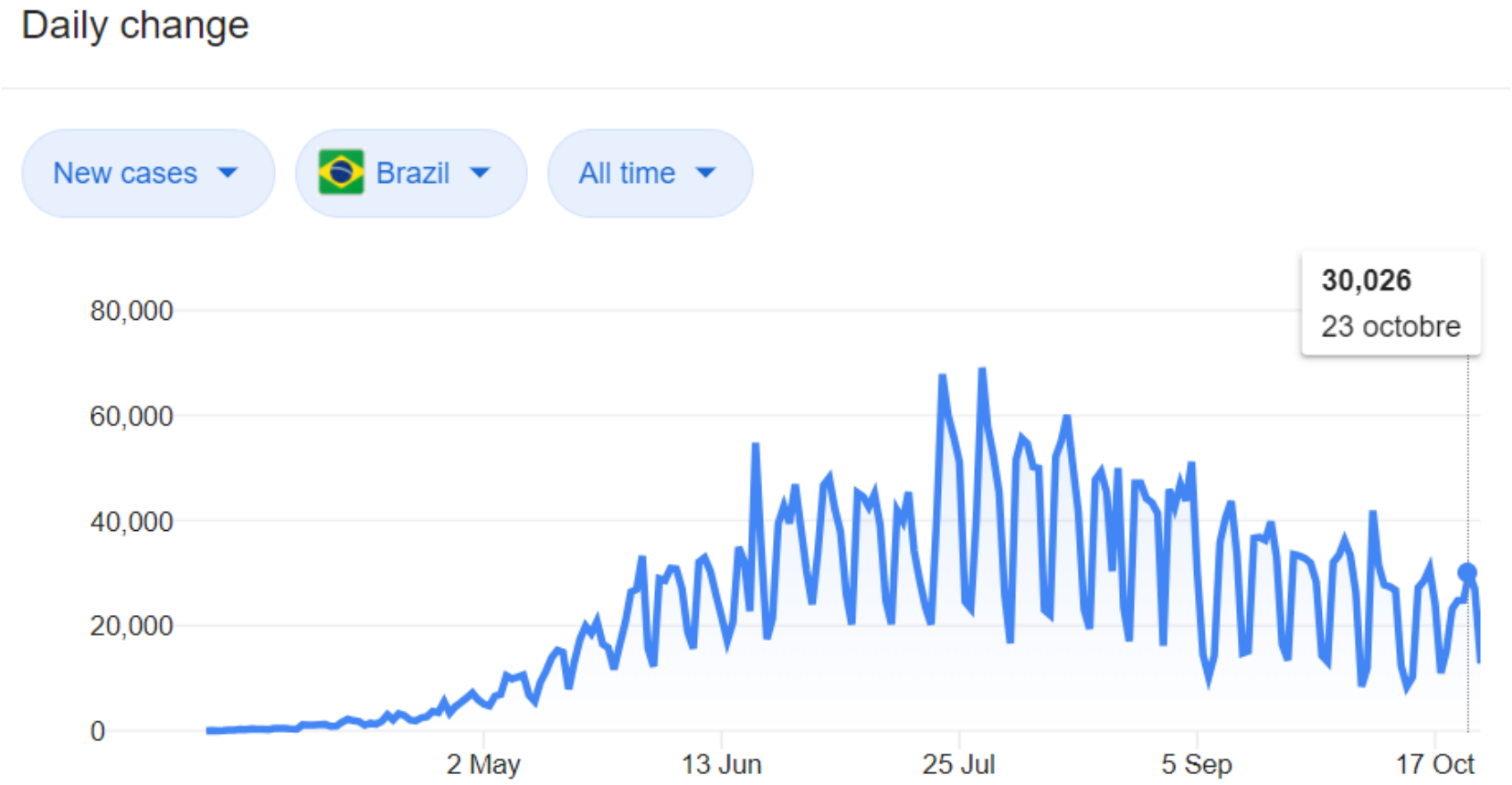
Daily confirmed cases: Brazil



Daily confirmed cases: UK

1 Scientific Justification / Justificación científica

SARS-Cov-2 challenge studies must have strong scientific justification

Los estudios de exposición al SARS-CoV-2 deben tener una justificación científica poderosa.

- Aim for important results , e.g.,
  - Selecting vaccines
  - Informing public health measures (e.g. with data regarding infection & immunity)
- Specify role in development pathways
- Aim to obtain maximum scientific knowledge per individual challenged

2 Risk-benefit assessment / Evaluación de riesgos y posibles beneficios

It must be reasonable to expect that the potential benefits outweigh risks

Debe ser razonable prever que los posibles beneficios de los estudios de exposición al SARS-CoV-2 superen los riesgos.

- Especially systematic assessment
- Where possible, benefits and risks should be:
  - Inclusive of benefits & risks to participants, third parties, and society in general
  - Quantified
  - Compared with alternative study designs
- Risks should be minimized, expected benefits should be maximized

3 Consultation & Engagement / Consulta e involucramiento del público

The research should be informed by engagement with the public, relevant experts, and policy-makers

Los programas deben basarse en consultas e involucramiento del público, así como de los expertos y los responsables de formular políticas pertinentes.

- Consultation
  - Ensure ethical criteria met
  - Ensure research designs optimised in light of expert consensus and public engagement
- Public engagement
  - Assess local acceptability & respond to concerns
  - Maximize transparency
  - Understand the potential impact of the research

4 Co-ordination / Coordinación

Co-ordination should involve researchers, funders, policy-makers, and regulators

Debe haber una estrecha coordinación entre investigadores, financiadores, responsables de formular políticas y reguladores.

- Situate studies within coherent international programmes of research
- Aim to maximize public health benefits, safety, efficiency
- Must be pre-registered, ideally standardized (insofar as possible)
- Appropriate co-ordination with local public health response

5 Site selection / Selección de los centros

Site selection should ensure
the highest scientific, clinical and ethical standards

Deben realizarse en lugares donde la investigación pueda llevarse a cabo de acuerdo con los estándares científicos, clínicos y éticos más rigurosos.

- Initial SARS-CoV-2 challenge studies only in experienced centres
- Ideally centres with community engagement capacity
- Consideration of local conditions
  - Background risk
  - Disruption of public health response
    (e.g., clinicians & PPE diverted to challenge study research)

6 Participant selection / Selección de los participantes

Participant selection criteria should limit and minimize risk

Deben asegurarse de que los criterios para la selección de participantes en estudios de exposición al SARS-CoV-2 limiten y minimicen el riesgo.

- Selection should aim to make participation as safe as possible
- Initial studies limited to young healthy adults 18-30years
- Other considerations
  - Exclusion of vulnerable individuals
  - Background risk
  - Generalisability of results

7 Expert review / Revisión por expertos

Review by a specialized independent committee

deben ser revisados por un comité independiente especializado.

- In addition to or in conjunction with standard local ethics review
- Review procedures:
  - High levels of expertise
  - Rapid, without compromising stringency
  - Ideally at the national or international level
- Ongoing consultation between investigators and ethics committee(s)

8 Informed consent / Consentimiento informado

Rigorous informed consent

deben siempre contar con un proceso riguroso de consentimiento informado.

- Designed to ensure information understood
- Incorporate tests of understanding
- Include best available data on risks and uncertainties
- There should be “virtually no doubt that participants comprehensively understand the potential risks of participation and that consent is voluntary”

Conclusion 1: Impact of Key Criteria

- Set timely standards for challenge studies (May 2020)
- Influenced development of WHO technical report*
- All 8 requirements incorporated in challenge study designs
- Co-ordination requirement aligned with other pandemic research norms (e.g. SOLIDARITY)
- Widely cited in ethical and scientific debates

*See Levine et al., CID 2020, DOI: 10.1093/cid/ciaa1290

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Conclusion 2: Progress in meeting Criteria

1.	**Scientific justification**	-	Plausibly strong
2.	**Risk-benefit assessment**	-	Plausibly favourable
3.	**Consultation & engagement**	-	Commenced
4.	**Coordination**	-	Commenced
5.	**Site selection**	-	Commenced
6.	**Participant selection**	-	As per Key Criteria
7.	**Expert review**	-	Commenced
8.	**Informed consent**	-	As per Key Criteria

Thank you !

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