Strengthening capacities to generate evidence to inform policies: Learning from pandemic responses

Alejandro Cravioto

Facultad de Medicina, Universidad Nacional Autónoma de México

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- **policy**

- **1**
- **a: prudence or wisdom in the management of affairs**
- **b: management or procedure based primarily on material interest**

- **2**
- **a: a definite course or method of action selected from among alternatives and in light of given conditions to guide and determine present and future decisions**
- **b: a high-level overall plan embracing the general goals and acceptable procedures especially of a governmental body**

What is health policy?

Health policy is defined by the World Health Organization as the decisions, plans, and actions that are undertaken to achieve specific healthcare goals within a society.

IMPROVING HEALTH THROUGH STRONGER SYSTEMS

Improved health service delivery. ...

Health workforce development. ...

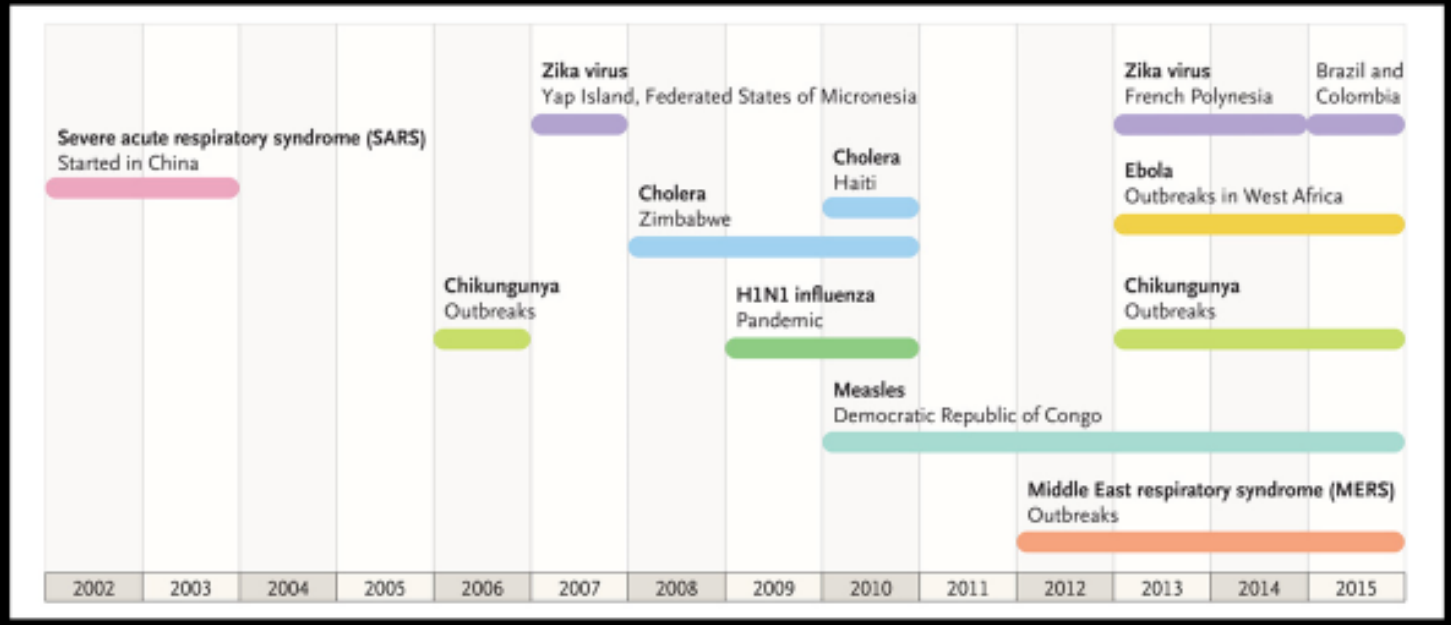
Information systems. ...

Access to essential medicines. ...

Health system financing. ...

Leadership and governance.

Major Emerging and Reemerging Infectious-Disease Outbreaks, Epidemics, and Pandemics, 2002 through 2015.



Sands P et al. N Engl J Med 2016;374:1281-1287.

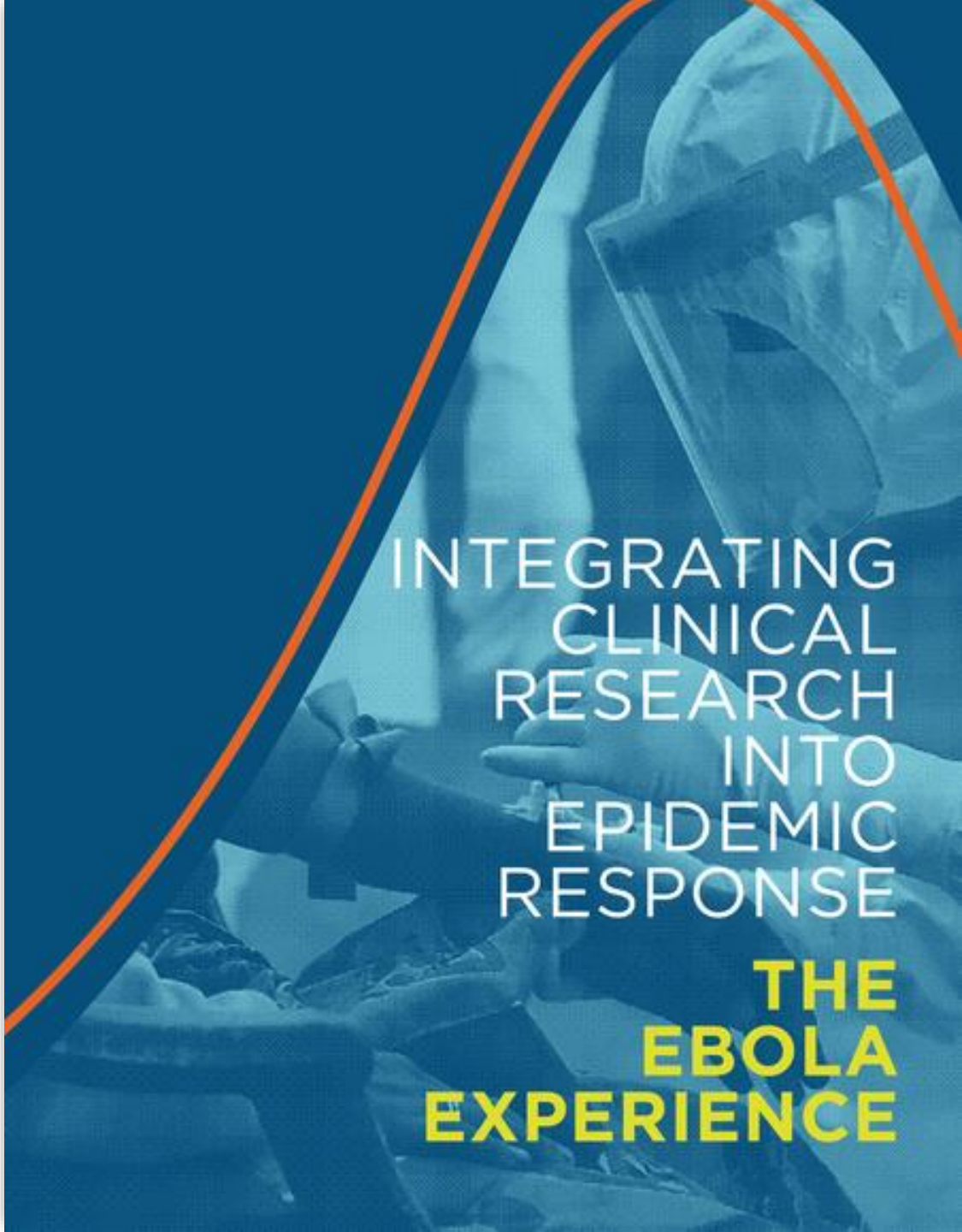
The NEW ENGLAND JOURNAL of MEDICINE

National Academies of Sciences, Engineering, and Medicine;

Health and Medicine Division; Board on Global Health; Board on Health Sciences Policy; Committee on Clinical Trials During the 2014-2015 Ebola Outbreak;

Gerald Keusch, Keith McAdam, Patricia A. Cuff, Michelle Mancher, and Emily R. Busta, Editors

Chapter 5 Strengthening Capacity for Response and Research



Conclusion 5-1 In order to better respond to future outbreaks and recognize an emerging epidemic in time to effectively mount a response, including conduct of clinical trials, it is critical that surveillance, outbreak investigation, and diagnostic capacity be strengthened in low- and middle-income countries. The mandate to ensure compliance with IHR 2005 core capacity for surveillance, reporting, and initial response rests with the WHO; however, two-thirds of countries have not yet reached the minimal required standards, which represents a major gap in global readiness.

Recommendation 1

Support the development of sustainable health systems and research capacities—Inter-epidemic

To better prepare low-income countries to both respond to future outbreaks and conduct foundational research, during the inter-epidemic period (as covered in 2005 International Health Regulations [IHR 2005]), major research funders and sponsors and development agencies should collaborate with the World Health Organization and regional centers of excellence to:

1. **Assist in monitoring and evaluating the development of national and regional core capacities under IHR 2005, and**
2. **Provide financial and technical assistance to the extent possible or establish a financing mechanism, to help build sustainable core capacities at the intersection of health systems and research (e.g., diagnostics, surveillance, and basic epidemiology).**

Conclusion 5-2 To effectively promote the health of a population, every country requires a well-integrated functional health care and health research system. The separation of the responsibility to care for the sick, which is the humanitarian mandate of medicine, from the responsibility to continually learn and improve the quality of care, or the research mandate, adversely affects the potential to fully meet both imperatives. Mechanisms for training (and the stable support of) key personnel, laboratories, and medical care facilities are essential to establishing an effective clinical research environment.

Conclusion 5-3 Researchers conducting clinical trials during epidemics in low-resource settings will require substantial logistical support from organizations that build and operate treatment centers (including international humanitarian organizations and national health systems), and these organizations should be included in strategic planning for clinical research activities during the inter-epidemic period.

Conclusion 5-4 In an epidemic context, particularly with a highly lethal contagious pathogen in a low-resource setting, recording detailed clinical data is a resource-intensive process that may be seen as diverting attention from patient care. However, despite the difficulties, it is imperative to systematically and comprehensively collect basic information on patient characteristics and clinical outcomes in order to document the natural history of the evolving epidemic and to provide clues to better patient management.

Recommendation 2a

Develop memoranda of understanding to facilitate data collection and sharing—Inter-epidemic

Research funders, sponsors, national governments, and humanitarian organizations should work together with the World Health Organization to develop memoranda of understanding during the inter-epidemic period to improve capacity to collect and share clinical data, with all necessary provisions to protect the privacy of individuals and anonymize data for epidemiological research.

Recommendation 2b

Provide resources to enable data collection and sharing—Epidemic

At the start of an outbreak, developed countries, research funders, and sponsors should work together with national and international health care providers responding to an outbreak, to provide the additional resources and personnel needed to enable systematic data collection on routine care practices and outcomes. Data collection should begin as soon as possible, and data should be shared and coordinated in a central database to advance an understanding of the natural history of the disease and of the best practices for standard of care. This information should also be used to inform protocols for clinical trials.

Conclusion 5-5 Helping low- and middle-income countries expand their capacity for the ethics review of human research protocols, regulatory oversight, and the legal review of clinical trial agreements, material transfer agreements, data sharing, and post-trial benefits could reduce bottlenecks in the clinical trial setup process during epidemics and greatly speed up the time to enrollment of the first participant.

Recommendation 3

Facilitate capacity for rapid ethics reviews and legal agreements—Inter-epidemic

Major research sponsors should work with key stakeholders in low- and middle-income countries to

•Build relationships between local ethics boards and entities that could provide surge capacity for ethics review in the event of an emergency situation. Such efforts would include strengthening networks of ethics boards in a region or connecting local and outside ethics boards, agencies, or experts. Memoranda of understanding setting forth who will provide what services and how decisions will be made should be executed in the inter-epidemic period.

Recommendation 3

Facilitate capacity for rapid ethics reviews and legal agreements—Inter-epidemic

Major research sponsors should work with key stakeholders in low- and middle-income countries to

- **Establish banks of experts in negotiation of clinical trial and material transfer agreements, and other essential components of collaboration, who are willing to offer pro bono advice and support to counterparts in countries affected by outbreaks.**
- **Develop template clinical trial agreements reflecting shared understandings about key issues such as data sharing, post-trial access to interventions, storage and analysis of biospecimens, and investments to build local capacity.**

Conclusion 5-6 When conducting research in settings with weak public health, clinical care, and health research infrastructure, efforts to strengthen research capacity without improving the general public health and clinical care infrastructure may inadvertently create the perception that research is more important than care of patients and will ultimately undermine the acceptance of clinical research by the population.

Recommendation 4

Ensure that capacity-strengthening efforts benefit the local population—Epidemic

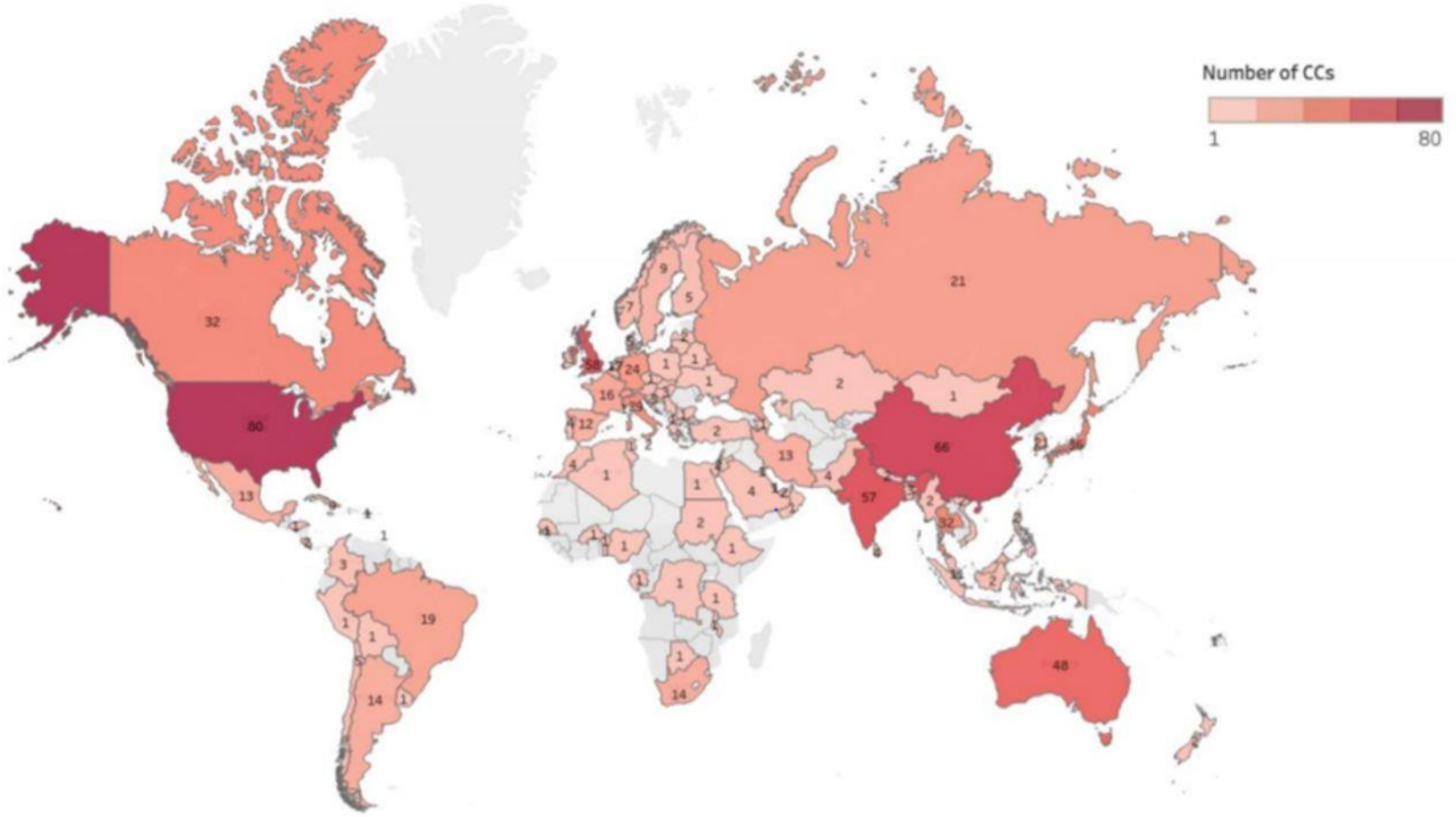
When the health care services of a population need to be enhanced or augmented in order to support the conduct of research, development organizations, international bodies, and other stakeholders should partner with national governments to ensure that capacity-strengthening efforts are not limited to services that solely benefit study participants.

Recommendation 5

Enable the incorporation of research into national health systems—Inter-epidemic

National governments should strengthen and incorporate research systems into their emergency preparedness and response systems for epidemic infectious diseases. **The multilateral institutions (the World Health Organization and the World Bank Group), regional and international development agencies, and foundations working in global health, should support national efforts by providing expertise and financing.**

Global distribution of WHO collaborating centres (WCCs) (WCCs=WHO Collaborating Centres).



Zsuzsanna Jakab et al. BMJ Glob Health 2021;6:e006852

BMJ Global Health

Urgent lessons from COVID-19: why the world needs a standing, coordinated system and sustainable financing for global research and development

Nicole Lurie, Gerald T Keusch, Victor J Dzau

The research and development (R&D) ecosystem has evolved over the past decade to include pandemic infectious diseases, building on experience from multiple recent outbreaks. Outcomes of this evolution have been particularly evident during the COVID-19 pandemic with accelerated development of vaccines and monoclonal antibodies, as well as novel clinical trial designs. These products were developed, trialled, manufactured, and authorised for use in several countries within a year of the pandemic's onset. Many gaps remain, however, that must be bridged to establish a truly efficient and effective end-to-end R&D preparedness and response ecosystem. Foremost among them is a global financing system. In addition, important changes are required for multiple aspects of enabling sciences and product development. For each of these elements we identify priorities for improved and faster functionality. There will be no better time than now to seriously address these needs, however difficult, as the ravages of COVID-19 continue to accelerate with devastating health, social, and economic consequences for the entire community of nations.

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Coalition for Epidemic Preparedness Innovations, Oslo, Norway (N Lurie MD); **Harvard Medical School, Boston, MA, USA** (N Lurie); **National Emerging Infectious Diseases Laboratory, Boston University, Boston, MA, USA** (G T Keusch MD); **National Academy of Medicine, Washington, DC, USA** (V J Dzau MD)

Correspondence to:
Dr Gerald Keusch, National Emerging Infectious Diseases Laboratory, Boston University, Boston, MA 02118, USA
keusch@bu.edu

Introduction

2020 will long be remembered as the year of COVID-19, not only for its devastating health, social, and economic consequences around the world, but for forcing the world to consider the implications of the pandemic for solidarity and equity. It will be remembered as a year that exposed the fragility of our global system of preparedness and response to pandemics, and the fragmentation of our pharmaceutical industry to expedite the translation of science into breakthrough therapies by enabling "all of us in the biomedical community to work together more effectively than ever before".[6] The idea soon evolved into one of an R&D ecosystem, to connect the talent and resources wherever they resided in academia, government, competitors in the biopharmaceutical industry, and patients or patient advocates in unique partnerships,

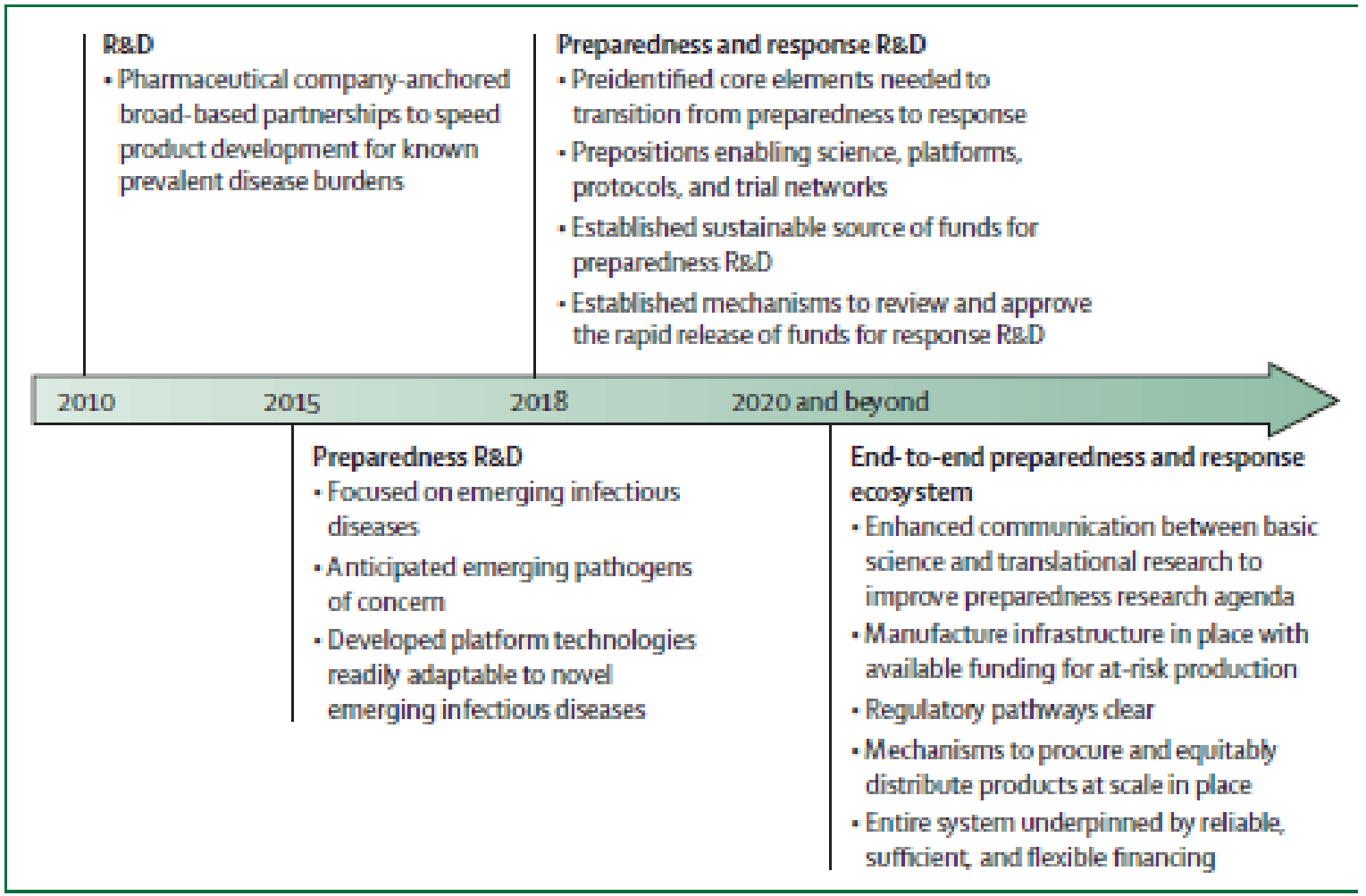
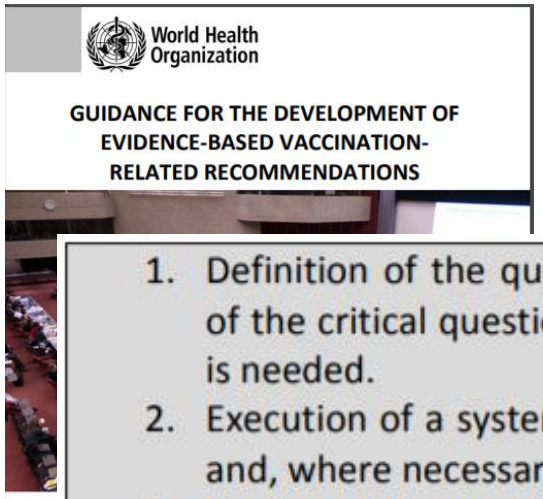


Figure: **Evolution of the R&D ecosystem, 2010–20 and beyond**
R&D=research and development.

https://www.who.int/immunization/sage/Guidelines_development_recommendations.pdf?ua=1

Appendix 1. Specific factors which underpin the development of SAGE recommendations [16]

Main factors	Specific elements
Epidemiologic features of the disease	-disease burden, including age specific mortality, morbidity, and social impact. -specific risk groups. -epidemic potential. -disease occurrence over time (i.e. secular trends). -serogroup or serotype distribution (for serogroup or serotype specific vaccines). -changes in epidemiological features over time.
Clinical characteristics of the targeted disease	-clinical management. -disease severity and fatality. -primary/secondary/tertiary care implications. -long-term complications and medical care requirements.
Other options for disease control and prevention	-existence of other prevention and control options.
Vaccine and immunization characteristics	-efficacy. -effectiveness and population impact of the vaccine (including herd immunity). -safety (serious adverse events and reactogenicity profile). -indirect effects (potential impact on strain selection, herd immunity, potential safety concerns of live attenuated vaccines in contacts of vaccines, serotype replacement). -cold chain and logistical concerns. -vaccine availability. -vaccine schedule(s). -social and programmatic acceptability of the schedule(s). -ability to reach the target populations. -ability to monitor programme impact.
Economic considerations	-cost of illness. -vaccine and vaccine delivery costs. -potential for vaccine price reductions. -cost-effectiveness of immunization programmes. -affordability of immunization.
Health system considerations	-possible interactions with other interventions and control strategies. -possible impact of vaccine introduction on the wider health system.
Social impacts	-possible impact on social equality and inequality.
Legal considerations	-possible legal requirements for implementation.
Ethical considerations	-possible ethical considerations.



1. Definition of the questions to inform recommendations including identification of the critical questions and outcomes for which an in-depth review of evidence is needed.
2. Execution of a systematic review of the literature with or without meta-analysis and, where necessary, commissioning research to address gaps in evidence.
3. Review of the quality of the evidence, in particular through assessment of the risk of bias and confounding.
4. Rating of the quality of the evidence (using the GRADE approach for data on safety and effectiveness).
5. Reflection of benefits & harms, values, resource use, equity, acceptability and feasibility considerations of the intervention within Evidence to Recommendation tables.
6. Discussion and deliberation leading to the development of proposed recommendations.
7. Presentation of proposed recommendations, along with their supporting evidence to the entire SAGE membership at SAGE meetings.
8. SAGE discussion, deliberation and decision regarding the proposed recommendations to WHO.

https://www.who.int/immunization/sage/Guidelines_development_recommendations.pdf?ua=1 page 22

Parameter
Recommendation(s) for use
Benefits
Harm
Feasibility
Resource Use
Values & Preferences*
Equity*
Acceptability
EUA/ WHO EUL and PQ status

*from the sample
SAGE Evidence to Recommendation table

PPC/TPP ↔ PPoC/TPoP ↔ VIS

Registration

PPC/TPP

Parameter
Indication for use
Contraindications
Target population
Efficacy
Durability of protection
Safety & reactogenicity
Dose regimen
Route of administration
Co-administration
Product stability and storage
Formulation/presentation
Accessibility
EUA/WHO EUL PQ

Source: WHO TPP for COVID-19 vaccines

Policy

PPoC /TPoP

Parameter
Recommendation(s) for use (Burden / recommended targeted risk population(s) by epi setting(s); other populations (permissive /contraindicated); geographies (regional, national, subnational), etc)
Benefits (pre-clinical and clinical; *direct*: effectiveness / preventable disease, and duration of protection; *indirect:* herd effect; etc)
Harm (pre-clinical and clinical; safety/ tolerability; benefit-harm-acceptance assessment; etc)
Feasibility (implementation considerations: regimen, route, setting(s); storage, delivery, etc.)
Resource Use (*Costs:* illness; product & implementation; *Cost-effectiveness; Supply and wastage:* vaccine & delivery considerations; etc.)
Values & Preferences (related to intervention & comparative health outcomes)
Equity (Vaccine access; health, social, economic security, human rights/civil liberties, etc.)
Acceptability (by stakeholders; affordability, etc)
EUA/ WHO EUL and PQ status

Source: SAGE Guidelines development recommendations

Finance

VIS

Parameter	
Health impact	Ranking criteria
Value for money	Ranking criteria
Equity & social protection impact	Ranking criteria
Economic impact	Ranking criteria
Global health security impact	Ranking criteria
Other impact	Secondary criteria
Gavi comparative advantage	Secondary criteria
Implementation feasibility	Secondary criteria
Alternate interventions	Secondary criteria
Broader health system benefits	Secondary criteria
Vaccine cost	Financial
Operational cost	Financial
Additional implementation costs	Financial

Source: Gavi Vaccine Investment Strategy