2nd Global **Clinical Trials** Forum

Action for impact

2 – 3 April 2025, Geneva

GCTF
Global clinical trials forum
WHO Managed Network

World Health Organization

From agreed actions to impact: implementing the WHO clinical trials guidance

Vasee Moorthy
Research for Health Department
Science Division

2 April 2025

Document link:

Vasee Moorthy MD PhD | LinkedIn

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Major Milestones achieved in last 12 months

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Improving the clinical trial environment and infrastructure: moving from global resolution to action

Several changes have occurred recently in the clinical trials landscape. A Series of six papers published in the *Lancet Global Health* updates readers on current advances and calls for urgent improvements in areas where progress is lacking.[1–6] This Series follows the World Health Assembly resolution 75.8 adopted in 2022 on strengthening clinical trials and WHO guidance for best practices for clinical trials published in September, 2024.[7] The WHO guidance provides a global framework for

See Series page e716, e732, e740, e749, e759 and e769

Focusing on solutions to key barriers

Poor trial design and implementation lead to uninformative trials wasting valuable resources.

Well-designed trials lead to **high quality evidence**

Lack of engagement and non-inclusive clinical trials restrict generalizability of evidence and translation to effective policy and practice.

Patient Involvement/ Community engagement and addressing **under-represented populations** are placed centrally

Major gaps in trial infrastructure and capabilities in many countries with high disease burden hinder research to address key needs.

New framework to improve **clinical trial infrastructure and capabilities**

Inefficiency in regulatory and ethics approval and oversight costs time and money, and demotivates research and trials.

New framework for **enabling environment for clinical trials**

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WHO guidance for best practices for clinical trials: Online training course coming in 2025

Good clinical trials

- ✓ are designed to produce scientifically sound answers to relevant questions
- ✓ respect the rights and well-being of participants
- ✓ are collaborative and transparent
- ✓ are feasible for context
- ✓ manage quality effectively and efficiently

The guidance is relevant to all clinical trials addressing any health intervention for commercial or non-commercial purpose, for any role involved and in any health system setting.

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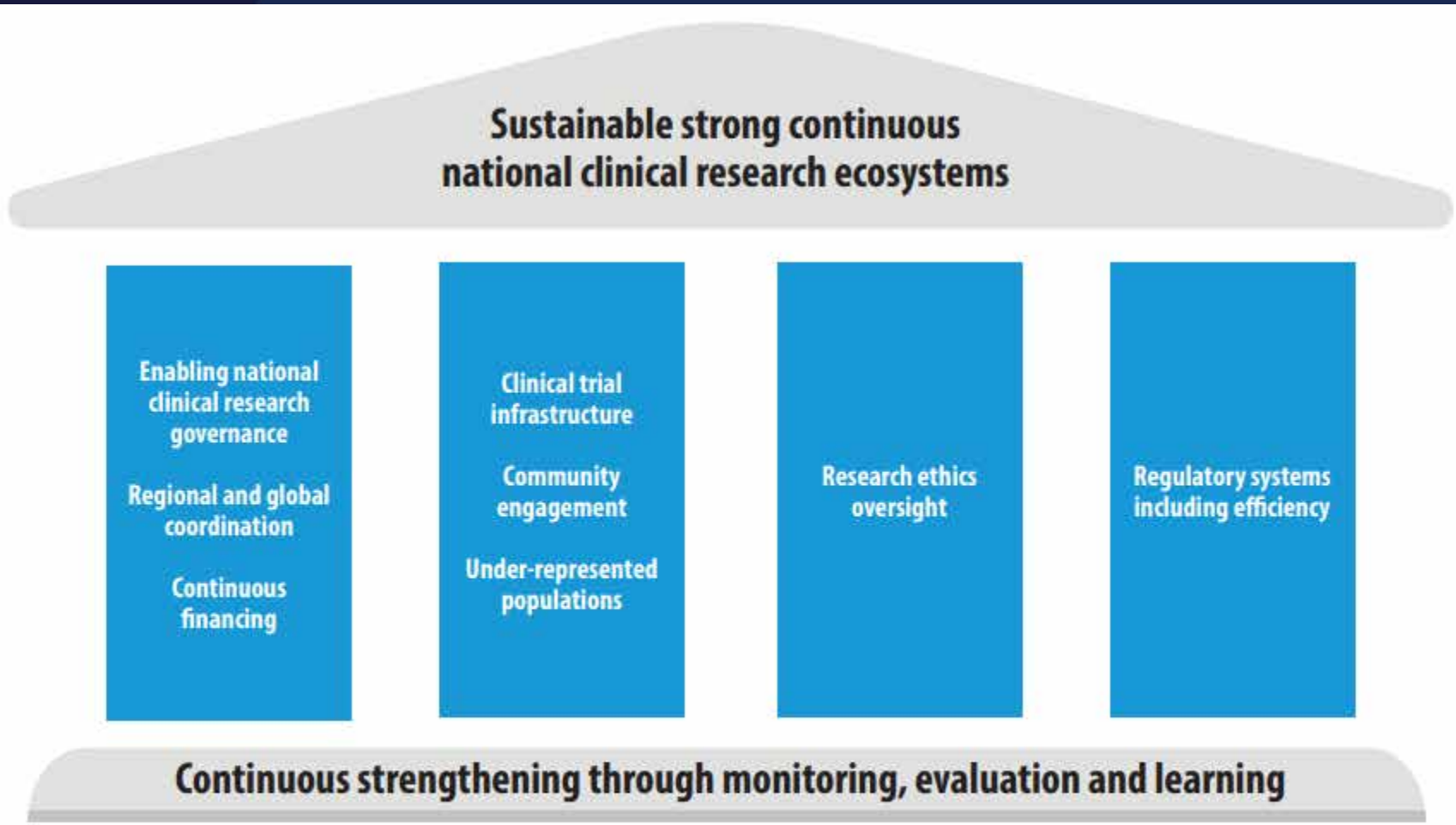
Document link:



Source: Moorthy V, Abubakar I, Qadri F, Ogutu B, Zhang W, Reeder J, et al. The future of the global clinical trial ecosystem: a vision from the first WHO Global Clinical Trials Forum. The Lancet. 2024 Jan 13;403(10422):124–6 (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)02798-8/fulltext).

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Document link:

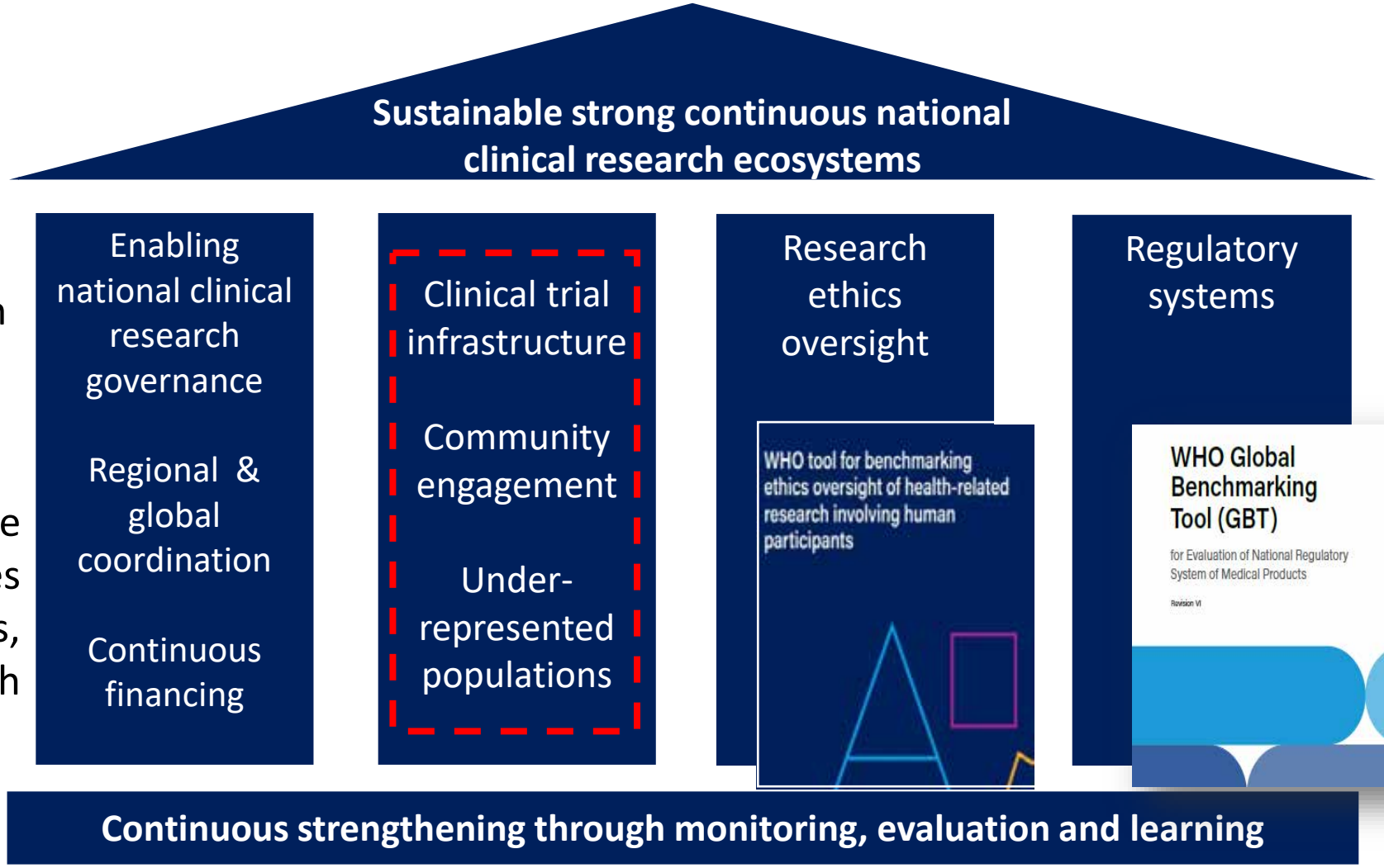
Develop practical tool to benchmark maturity of clinical trials units

- **Objective:**

The framework aims to support benchmarking of infrastructure, capabilities, and capacities of institutions in conducting clinical trials and related clinical research activities.

- **Target audience:**

The primary target users of the framework are research institutes involved in clinical trial activities, and national health research agencies.



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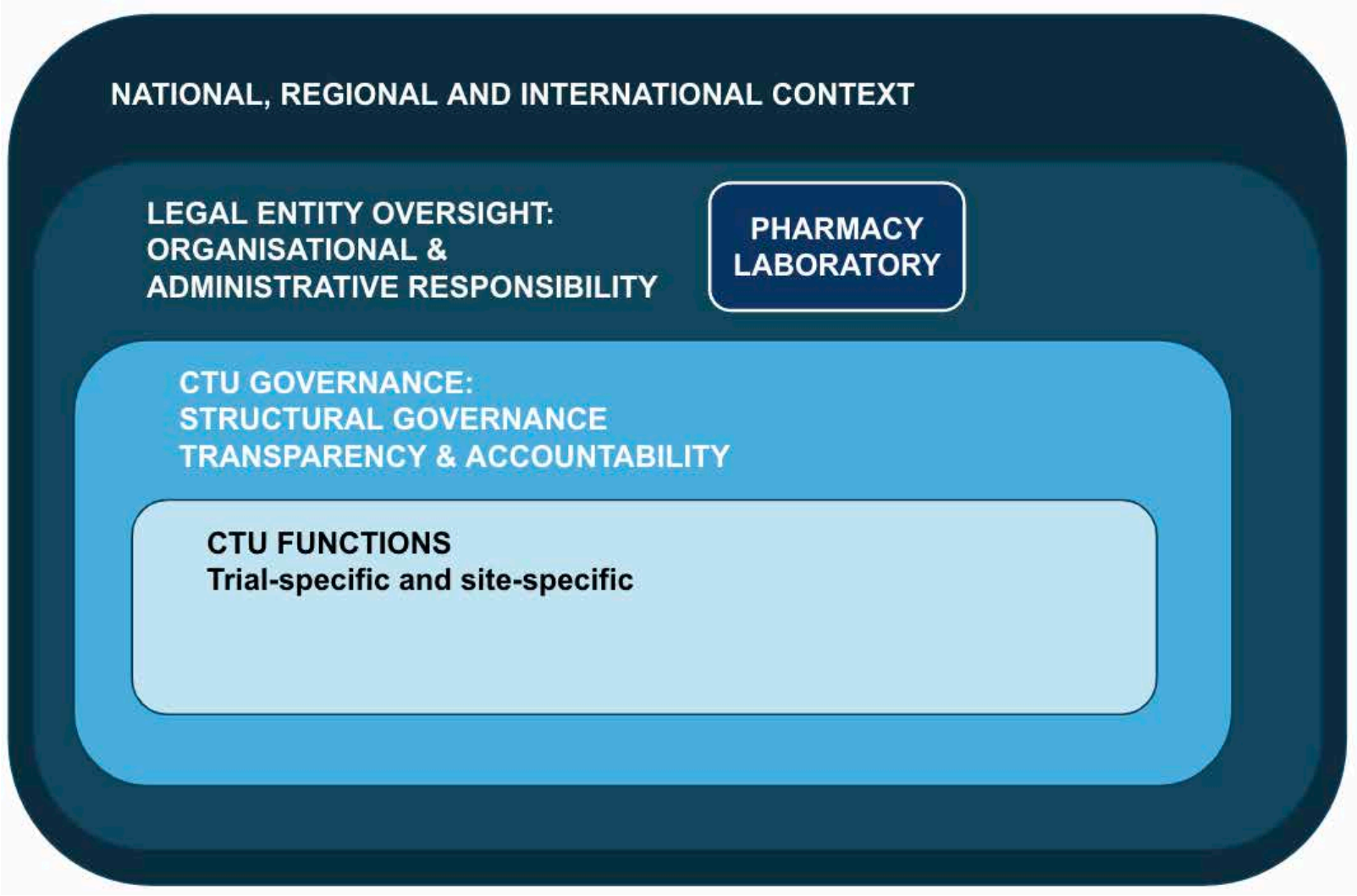
What does draft include? – For Consultation

1. **CTU Maturity Framework**
   - 4 major domains with subdomains
   - List of useful definitions for clinical trials and CTUs

2. User Guide



Domains and subdomains - Draft

Domain 1: National, regional and international context	Domain 2: Legal entity oversight	Domain 3: CTU Governance	Domain 4: CTU Functions / Services
Pharmacy and Laboratory **Pharmacy** • Operations • Facilities, Resources and Accreditation **Laboratory and Biobank** • Operations • Facilities and Procedures	1. Legal, Regulatory and Ethical Compliance 2. Human Resource Management 3. Insurance and Indemnity 4. Financial Management and Sustainability 5. Facilities Management 6. Research Facilitation and Support 7. Sponsorship	1. Patient and Public Involvement and Engagement 2. Information Sharing 3. Performance Evaluation 4. Research Excellence 5. Governance and Organisation 6. Strategic Development	1. Protocol Development and Research Design 2. Biostatistics and Analysis 3. Ethics and Safeguards 4. Regulatory 5. Clinical Trial Operations and Mngmnt. 6. Safety Monitoring 7. Quality Management 8. Data Lifecycle

Global action plan for clinical trial ecosystem strengthening

Strengthen local leadership and national support for sustained infrastructure and funding

Enhance involvement and engagement with patients, communities and the public in clinical trial lifecycle

Address barriers to clinical trials in under-represented populations

Enable effective trials through adoption of innovative designs and digital technologies

Accelerate access to fit-for-purpose training packages for clinical trials

Improve coordination and streamlining regulatory and ethics review

Engage clinical practitioners to integrate clinical trials into health systems and practices

Step up the use of trial registries to improve research transparency

Expand international health research and clinical trial collaboration

Outcome measures to monitor how reforms can accelerate generation of quality evidence

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Activities to advance actions

1	Strengthen local leadership and national support for sustained infrastructure and funding	1.1 Case study (demonstration) of exemplar national initiatives to improve clinical trial governance and oversight enabled by good practices (EMRO, WPRO, AFRO, EURO) 1.2 Research funders joint statement includes sustained support for clinical research infrastructure linked to health systems and aligned with locally relevant priorities
2	Enhance involvement and engagement with patients, communities and the public in clinical trial lifecycle	2.1 Research funders joint statement includes a focus on patient involvement and community engagement in clinical trials without causing inappropriate burden to researchers, and as appropriate 2.2 Competency maps and gaps in patient and community involvement and engagement in clinical trial conduct 2.3 Improving comprehensibility of and shortening informed consent forms
3	Address barriers to clinical trials in under-represented populations	3.1 Research funders joint statement supports inclusion of under-represented population groups without causing inappropriate burden to researchers, and as appropriate 3.2 Recommendations of good practices for design and implementing clinical trials with older people 3.2 Prioritization of clinical trials to address unmet needs in children's health 3.3 Toolkit for inclusion of pregnant women in clinical trials 3.4 Maternal immunization research framework

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Activities to advance actions

5	Accelerate access to fit-for-purpose training packages for clinical trials	5.1 WHO clinical trial training resource hub, including training-of-trainer network 5.2 WHO regional clinical trial resource portals (PAHO, AVAREF)
6	Improve coordination and streamlining regulatory and ethics review	6.1 Joint regulatory and ethics review in African region, and regulatory reliance network (AVAREF) 6.2 Single digital clinical research application review system (SEARO) 6.3 Analysis of methods to enable contracting for large multi-site trials (PAHO)
7	Engage clinical practitioners to integrate clinical trials into health systems and practices	7.1 Lancet Global Health paper with analysis of next steps to advance RCTs in primary care
8	Step up the use of trial registries to improve research transparency	8.1 Research funders joint statement includes focus on registration, updating and results reporting 8.2 Exploring updates and enhancements to ICTRP 8.3 Expand availability of site maps using registry data
9	Expand international health research and clinical trial collaboration	9.1 Enabling work of large scale clinical trials networks through information sharing on best practices

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Cancer work through ICTRP: data to inform actions

- **89,069** interventional cancer trials analyzed (1999-2022).
- Distribution by geography, economic development status, and disease burden (globally and by geography).
- Characterization of cancer clinical trials based on multiple variables of interest.
- Identification of trends, major gaps, and persistent disparities.

1. **WHO global report on cancer clinical trials** (in progress)
2. **Report on cancer R&D in the EU27 Region** (finalized)
3. **Global landscape analysis of cancer clinical trials** (revision in Nature Medicine)
4. **Snapshots**

Cancer research and development landscape

Overview of 1999–2022 period

To soon be launched

Research and development landscape for childhood cancer: a 2023 perspective

Already published

Foundation for the development of a comprehensive WHO strategy aimed at promoting well-designed, patient-centered, locally relevant, and equitable cancer clinical trials.

Monitor improvements

Numbers of countries/regions with national CT ecosystem strengthening initiatives employing WHO tools

Patient involvement/ community & public engagement implemented by KSC

Inclusion of under-represented populations implemented by KSC

Prospective design review in place prior to submission; Innovative designs supported by KSC

Resource training hub available with gaps mapped by KSC

Monitoring against target timelines for approval, initiation, recruitment, and completion

Case studies of trials embedded into health systems

Digitization of RAS; single submission systems
Results reporting implemented by KSC;

Monitoring of rate-limiting steps for international trials

Outcome measures to monitor how reforms can accelerate generation of quality evidence

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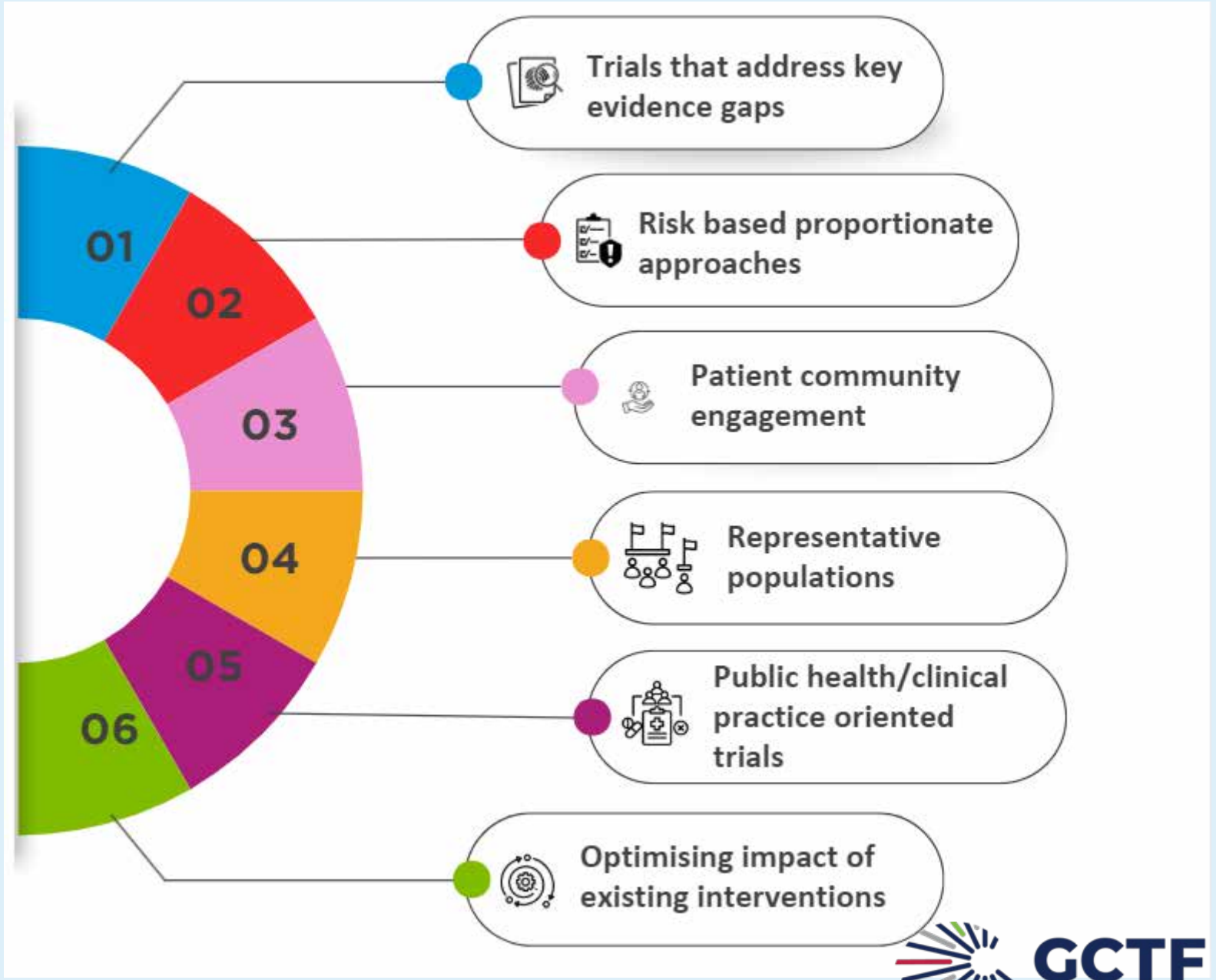
Implementing change



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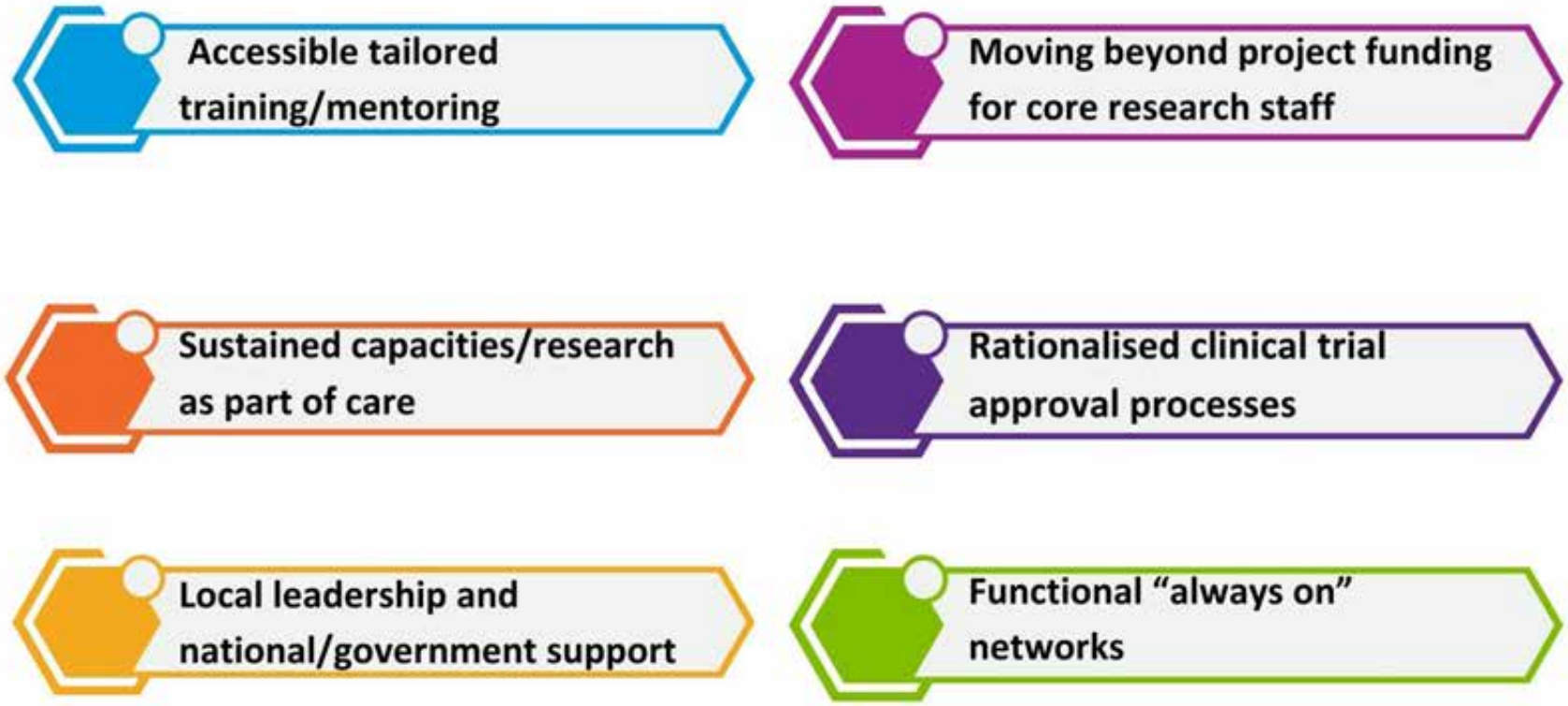
Enabling environment



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Document link:

Next steps

A global network of partners with shared objectives – **The Global Clinical Trial Forum (GCTF)**

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Global clinical trials forum
WHO Managed Network

Translations into French, Portuguese, Spanish, Arabic, Chinese, Russian

Developing training material suitable to different contexts and audiences

Developing and piloting implementation tools

6 regional workplans led by colleagues in WHO regional offices

Impact of the new guidance depends on engagement with stakeholders worldwide

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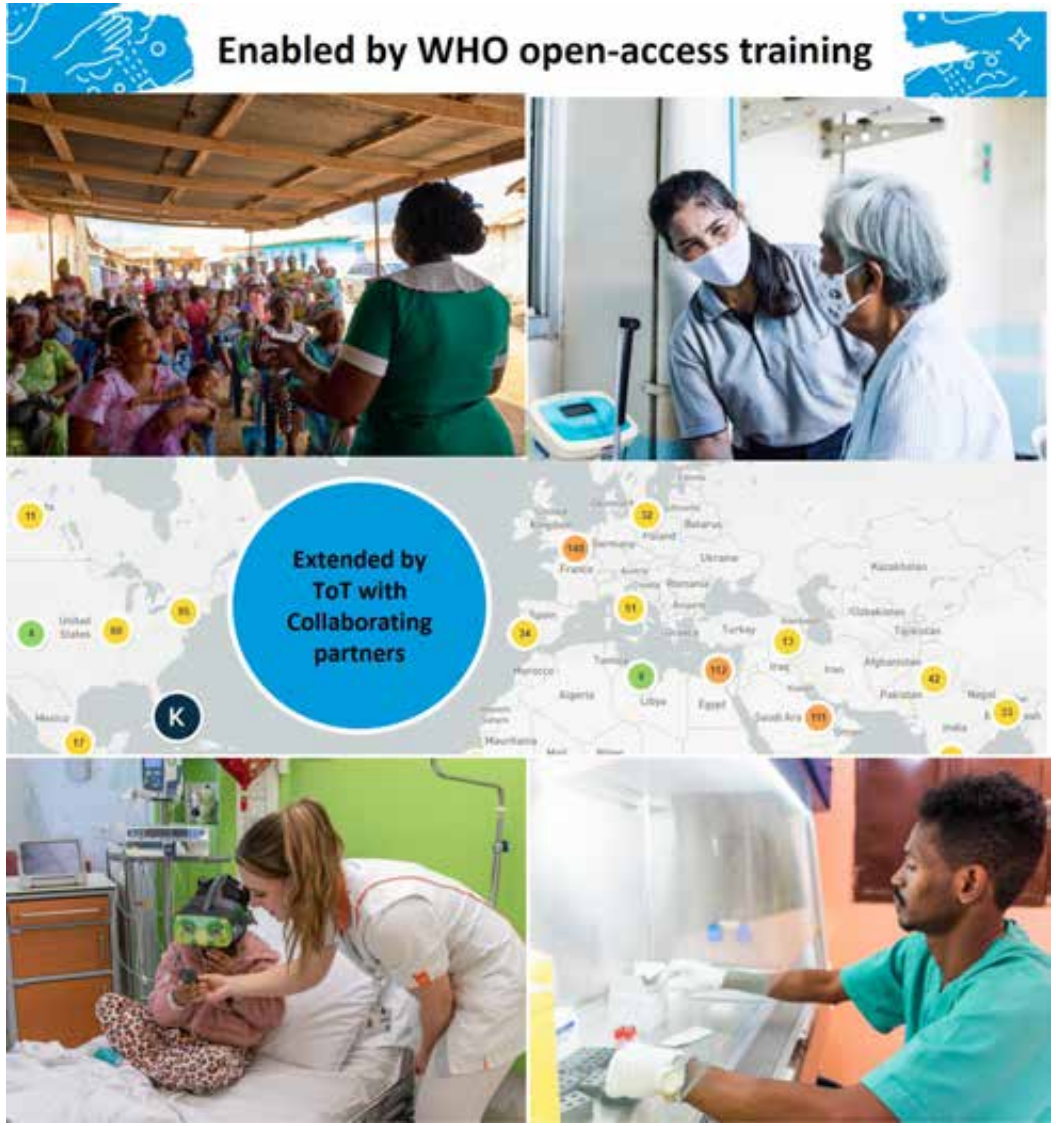
WHO training for clinical trials

- **Objective:**

The training aims to contextualise the principles and best practices outlined in the normative guidance in real-life scenarios. It aims to provide continued learning experience and sustained peer support to disseminate and implement the best practices.

- **Target audience:**

While sponsors and investigators are key audiences for the training on trial design and implementation, the training will also address individuals and organizations working in the ecosystem such as governance, regulation, oversight, monitoring, auditing, funding of clinical trials.



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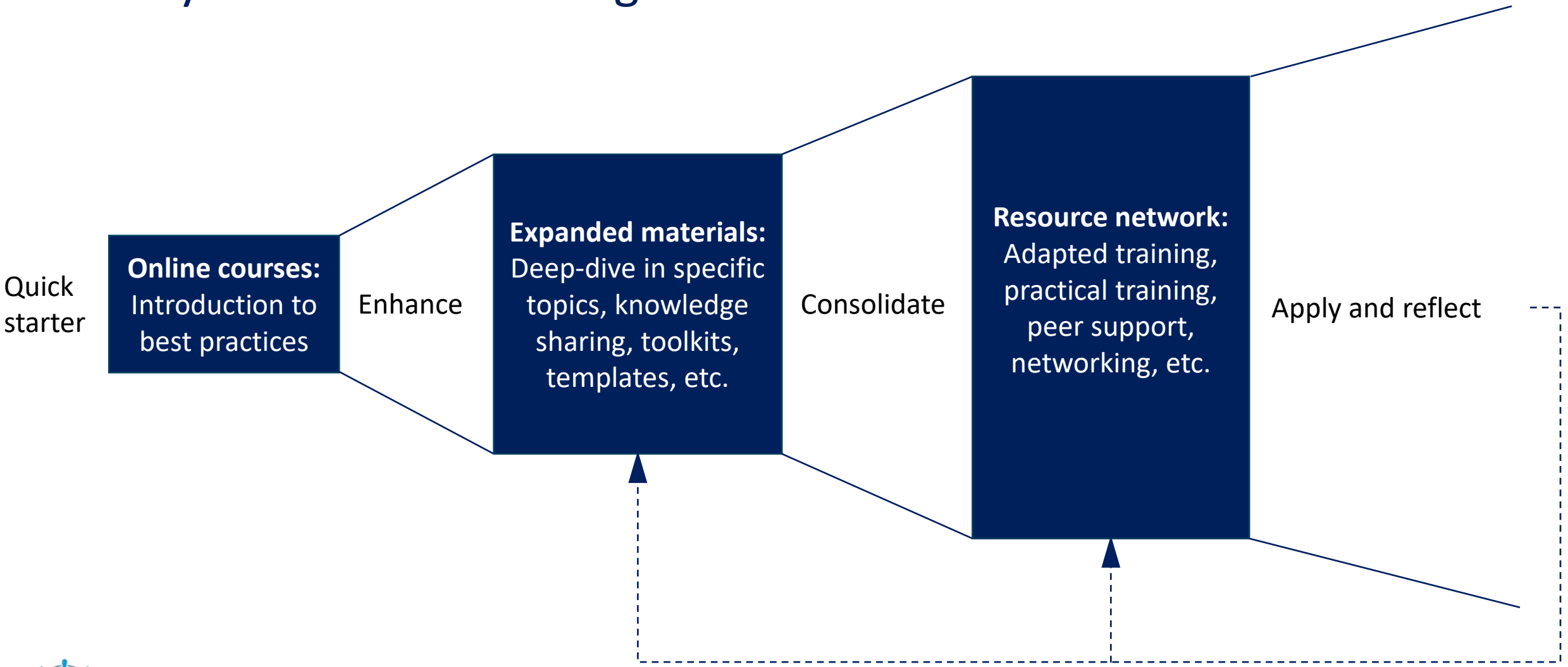
Delivery of effective training



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Online course: Introduction to ethical and scientific principles for clinical trials

Module 1: Introduction to the WHA75.8 resolution, and well-designed and well-implemented RCTs

Module 2: Design principles

Module 3: Avoiding bias through trial conduct

Module 4: Analyzing and monitoring data

Module 5: Effective participant communication and consent

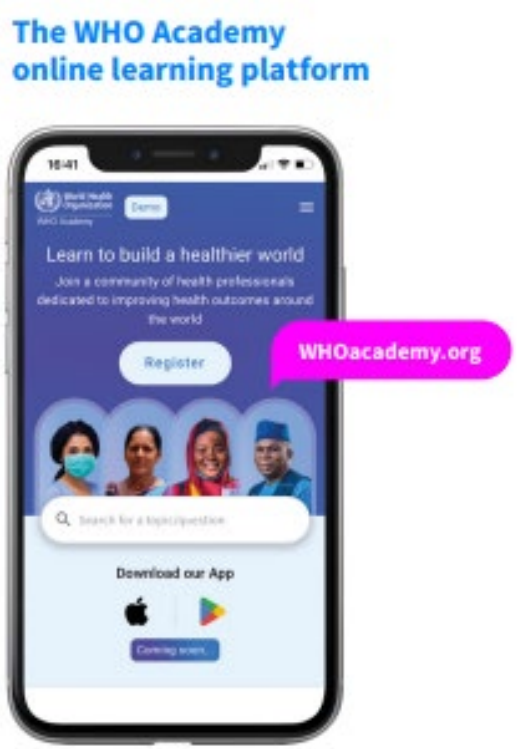
Module 6: Protecting participants

Module 7: Collaboration and transparency

Module 8: Feasibility

Module 9: Managing quality effectively and efficiently

Module 10: Reviewing the principles and course re-cap



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Milestones

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Funding and collaboration

Donors

EDCTP

FUNDED BY NIHR National Institute for Health and Care Research

UKaid from the British people

BILL & MELINDA GATES foundation

Department of Health & Social Care

Collaborating Center

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

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The guidance incorporated or adapted guidance from

CIOMS

good clinical trials

GCTF Global clinical trials forum WHO Managed Network

The CTU Maturity Framework Consortium

Project Team

oucru

Tulane University

ISARIC

UNIVERSITY OF OXFORD

ZIAUDDIN UNIVERSITY

Expert Framework Working Group

TDR For research on diseases of poverty

anzic research centre

SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

MRC SOUTH AFRICA

PATH

THE GLOBAL HEALTH NETWORK

Enabling research by sharing knowledge

UNIVERSITY OF TORONTO

Expert Writing Group

KEMRI

Wellcome Trust

Rinda UBUZIMA

ecrin

MORU Tropical Health Network

advanceid.

oucru

LIVEN

Team Acknowledgements

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John Owuor – Dissemination/Outreach
Zainab Eleiba – Training
Ghassan Karam – ICTRP Manager

Management

John Reeder – Director, Research for Health Department

Jeremy Farrar – WHO's Chief Scientist

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Organizations contacted

- Gates Foundation
- Saint John College, Bangalore
- Malaysia NIH
- Cochrane
- Drugs for Neglected Diseases initiative
- EUPATI
- European & Developing Countries Clinical Trials Partnership
- European Clinical Research Infrastructure Network (ECRIN)
- European Organisation For Research And Treatment of Cancer
- George Institute for Global Health
- Indian Council of Medical Research
- INA CRC Indonesia Clinical Research
- International Vaccine Institute
- Kenya Medical Research Institute
- National Research Institute - Ghana
- Kwame Nkrumah University of Science and Technology
- Mahidol Oxford tropical Medicine Research Unit (MORU)
- ACT Canada
- Medicines for Malaria Venture

National Centre for Cardiovascular Diseases
NIHR
Nepal Health Research Council
Nuffield department of medicine, Uni of Oxford
Good Clinical Trials Collaborative
Nuffield department of population health, Uni of Oxford
NUS Saw Swee Hock School of Public Health.
Paediatric European Network for Treatment of AIDS
Science for Africa Foundation
South Africa Medical Research Council
The AGA Khan University, Medical college
Wellcome Trust
Tata Memorial Hospital
John Hopkins University
CERCLE
CEPI
Christian Medical College Vellore
IFPMA

Organization pending FENSA clearance

Cochrane
ecrin
EUPATI
International Vaccine Institute
VACCINES FOR A SAFER FUTURE
EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy
BECAUSE OF ME
HE SHALL LIVE
जीविष्यति मयैवासौ
NUS
National University of Singapore
protas
St. John's
National Academy of Health Sciences

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Thank you

Vasee Moorthy MD PhD | LinkedIn

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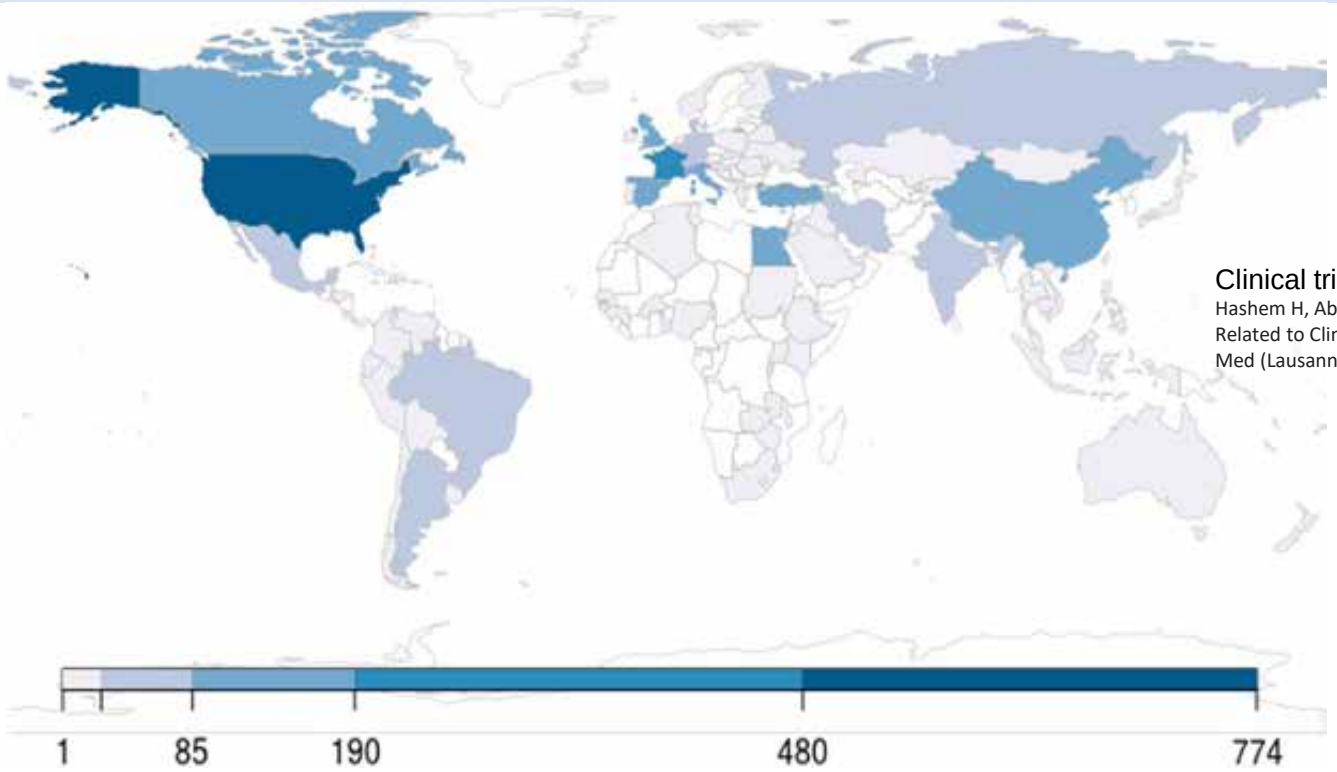
Mainstreaming Ethics to effectively implement the Global Action Plan



Clinical trials listed on ClinicalTrials.gov in 2020

Hashem H, Abufaraj M, Tbakhi A, Sultan I. Obstacles and Considerations Related to Clinical Trial Research During the COVID-19 Pandemic. Front Med (Lausanne). 2020 Dec 23;7:598038

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Addressing unmet local needs to find solutions that are affordable, evidence based, accessible

Roli Mathur **Ross Upshur** **Katherine Littler** **Andreas Reis**

Revisions to the Declaration of Helsinki, Oct 2024

Ethical Principles for Medical Research Involving Human Participants

- Ethics ≠ Ethics Review; 37 clauses (ONLY 1 on REC)
- Scientific & Ethics rigor and integrity
  - Avoid Research Waste
  - Scientific, Safe, Meaningful, Minimize risk, Inclusions, Accountable, Transparent
- Ethics Guidelines are not just for RECs!

WMA DECLARATION OF HELSINKI – ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN PARTICIPANTS

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013
and by the 75th WMA General Assembly, Helsinki, Finland, October 2024

PREAMBLE

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human participants, including research using identifiable human material or data.

   The Declaration is intended to be read as a whole, and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. While the Declaration is adopted by physicians, the WMA holds that these principles should be upheld by all individuals, teams, and organizations involved in medical research, as these principles are fundamental to respect for and protection of all research participants, including both patients and healthy volunteers.

GENERAL PRINCIPLES

3. The WMA Declaration of Geneva binds the physician with the words, "The health and well-being of my patient will be my first consideration," and the WMA International Code of Medical Ethics declares "The physician must commit to the primacy of patient health and well-being and must offer care in the patient's best interest."

4. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

5. Medical progress is based on research that ultimately must include participants.

1 of 3

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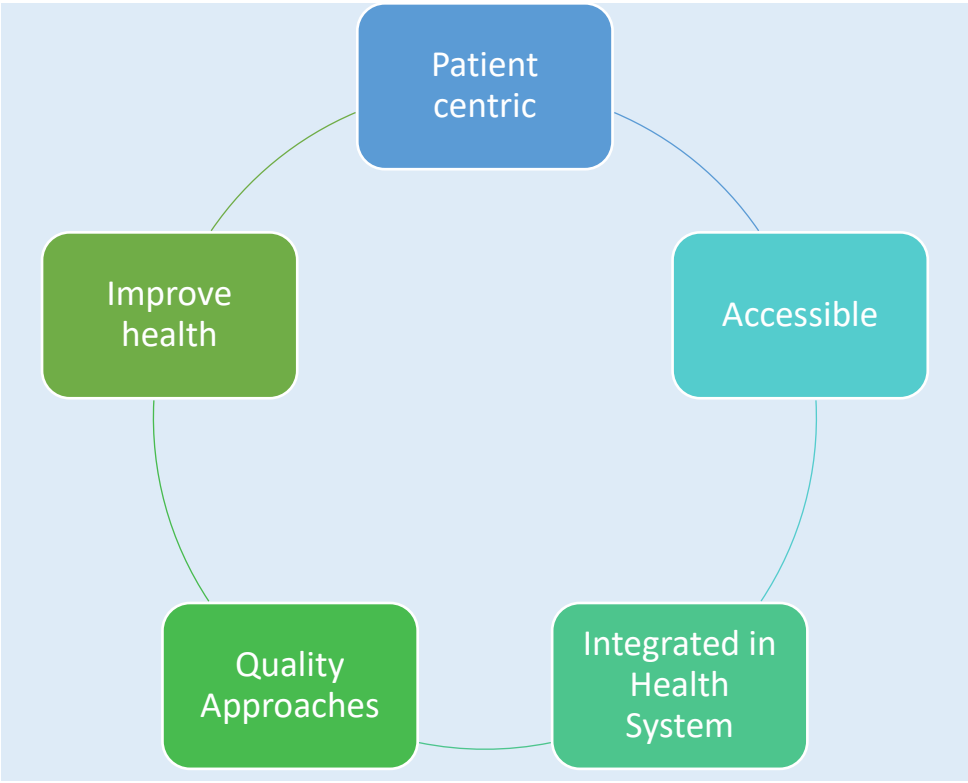
Emphasizes obligations of researchers

Integrating Ethics in the Global Action Plan

- Adequately powered, avoid duplications
- Prioritization, Minimizing risks, Monitoring
- Inclusivity, Societal Connect, Engagement
- Understood -inf consent/ increase support
- High-quality publications and Avoid Infodemics
- Creating Opportunities/ Updates/ Investments



Ethics Review: Evolved, Efficient & Enabling

- Poorly designed research is a challenge to EC
  - Of >2000 COVID-19 trials worldwide, only 5% were designed/ executed with rigor

Reis AA. Key Revisions of Dec of Helsinki 2024. *JAMA.* 2025;333(1):20–21.

- Paragraph 23:
  - REC- funding, inst support, commitments, approvals in Sponsoring & host countries
- Capacity Building:
  - researchers, reviewers, RECs (SMART)
- Common Ethics Review & Networking of CT centres
  - Monitoring

Committing resources, efforts & time

- Capacities, equipped, Innovation, Tools for Submission/ reviews
- Adaptability -Remote
- Integrated Platforms, Data Sharing with safeguards
- Monitoring
- Improve Access, Transparency, Communication

Addressing gaps in guidance

- Guidance on AI, Tools, Trainings, REC Guidance
- Guidance on DCT, Adaptive Platform Trials, RWE, Human Challenge Studies
- SOPs/ training materials on generic protocols
- Support inclusion on under-represented populations in research
- Potential financing models for ERCs
- Models for ethical oversight of multicentre studies

Addressing gaps in implementation/practice

- Review current guidance, evidence gaps, modalities of oversight and implementation materials
- NECs & building on work during COVID-19 on mutual recognition models
- Research systems & climate change, including specific focus on RECs/IRBs
- Focusing on Issues of Diversity, Equity, Inclusion (DEI)/ Under-representation
- Fair & equitable research collaboration
- Tools: Benchmarking tool, Common Forms for ethics reviews, Informed Consent Formats, Master Agreements, insurance systems to meet untoward events

ICMR GUIDELINES FOR COMMON REVIEW OF MULTICENTRIC RESEARCH

ICMR Bioethics Unit

- Common ethics review by Designated Ethics Committee at Coordinating Site
- Expedited approvals at local participating Sites
- Part of initiative for Ethics Preparedness

Streamline the review processes and save time

Prevent duplication of effort

Improve quality of ethical review

Improve coordination in a multicentre research

Maintain highest ethical standards

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Model for common ethics review can be replicated

Conclusion

“Ethics is integral to the successful implementation of the global action plan”

In view of the constitutive nature of ethics in clinical trials, ethical considerations are critical in protecting the safety of participants and the legitimacy of results and these obligations extend to all stakeholders in the clinical trials ecosystem,

RECs are not the only place where ethics matters!

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Thank You

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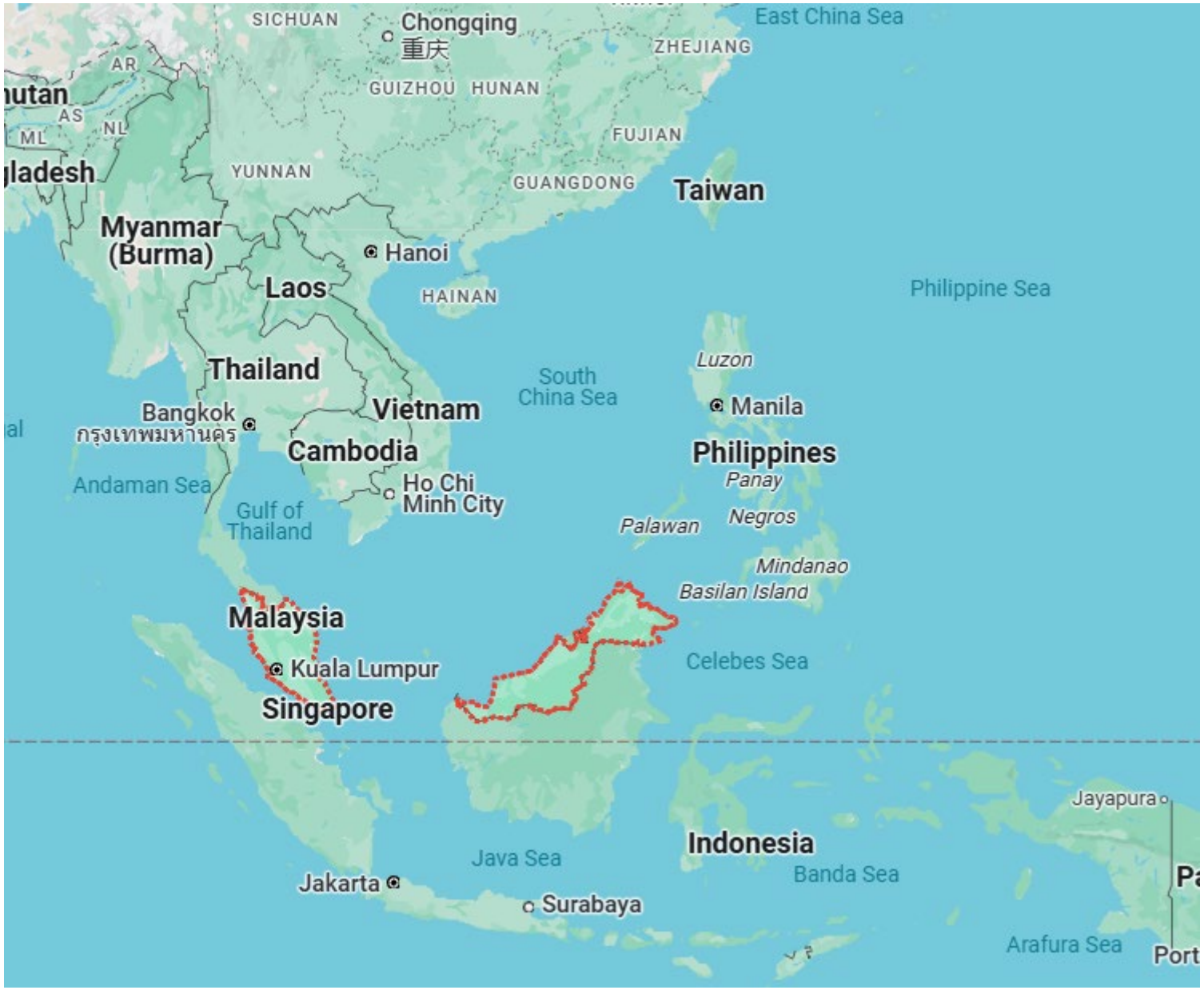
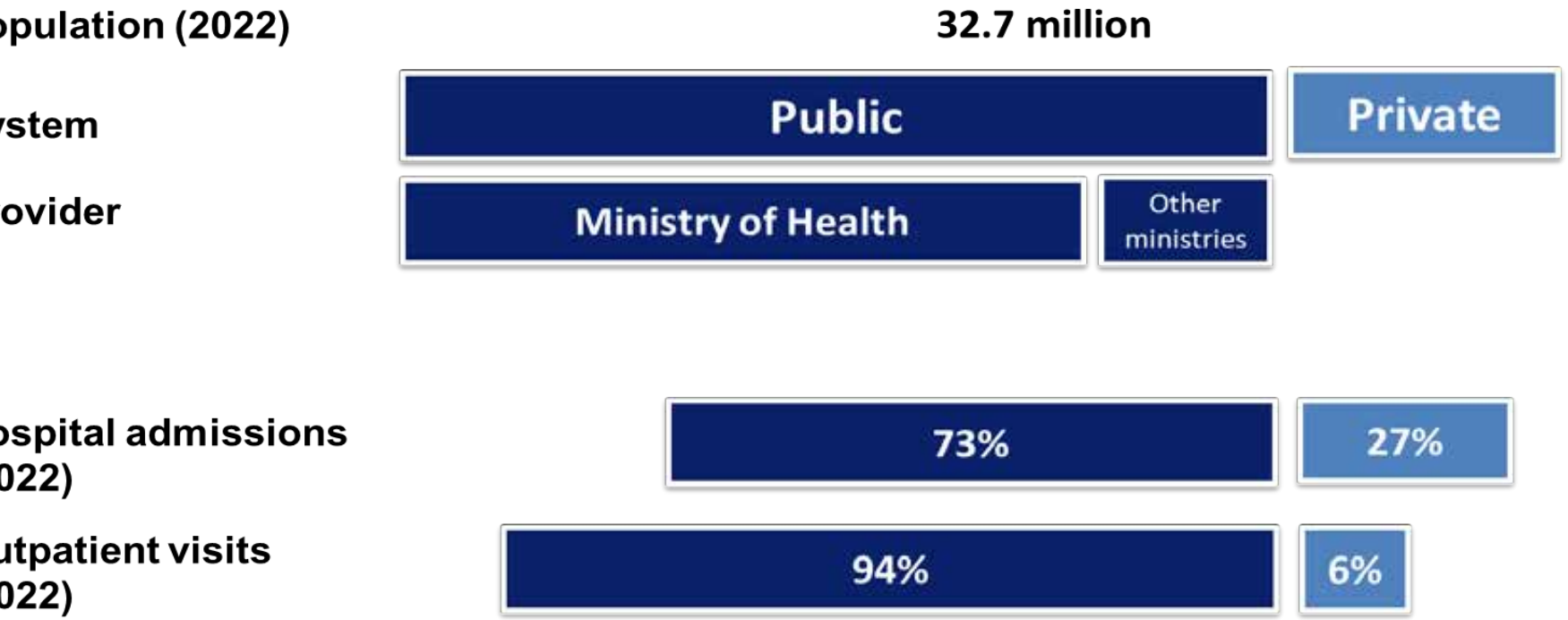
Strengthening Local Leadership and National Support for Clinical Trials in Malaysia

Carren Teh
Director of ICR-NIH

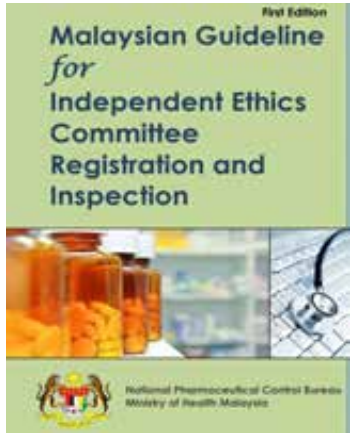

SICHUAN
Chongqing
重庆
East China Sea
ZHEJIANG
GUIZHOU
HUNAN
FUJIAN
YUNNAN
GUANGDONG
Taiwan
Myanmar
(Burma)
Hanoi
Laos
HAINAN
Philippine Sea
Thailand
Luzon
South
China Sea
Vietnam
Manila
Bangkok
กรุงเทพมหานคร
Cambodia
Philippines
Andaman Sea
Ho Chi
Minh City
Panay
Gulf of
Thailand
Palawan
Negros
Mindanao
Basilan Island
Malaysia
Kuala Lumpur
Celebes Sea
Singapore
Jayapura
Indonesia
Java Sea
Banda Sea
Jakarta
Surabaya
Arafura Sea

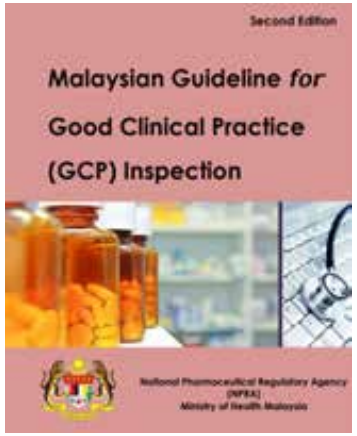
Developing and Strengthening Clinical Trial Capabilities in Malaysia

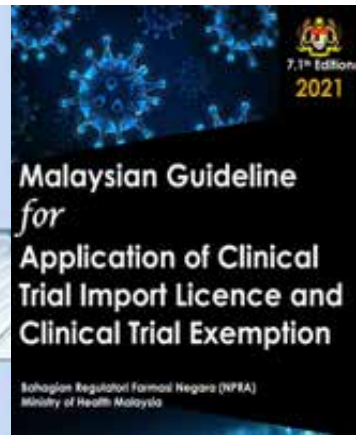
Healthcare in Malaysia

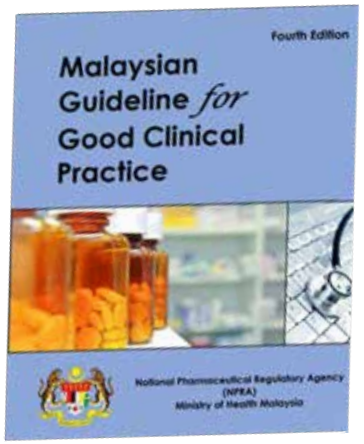


Health Facts 2023, Health Informatics Centre, MOH









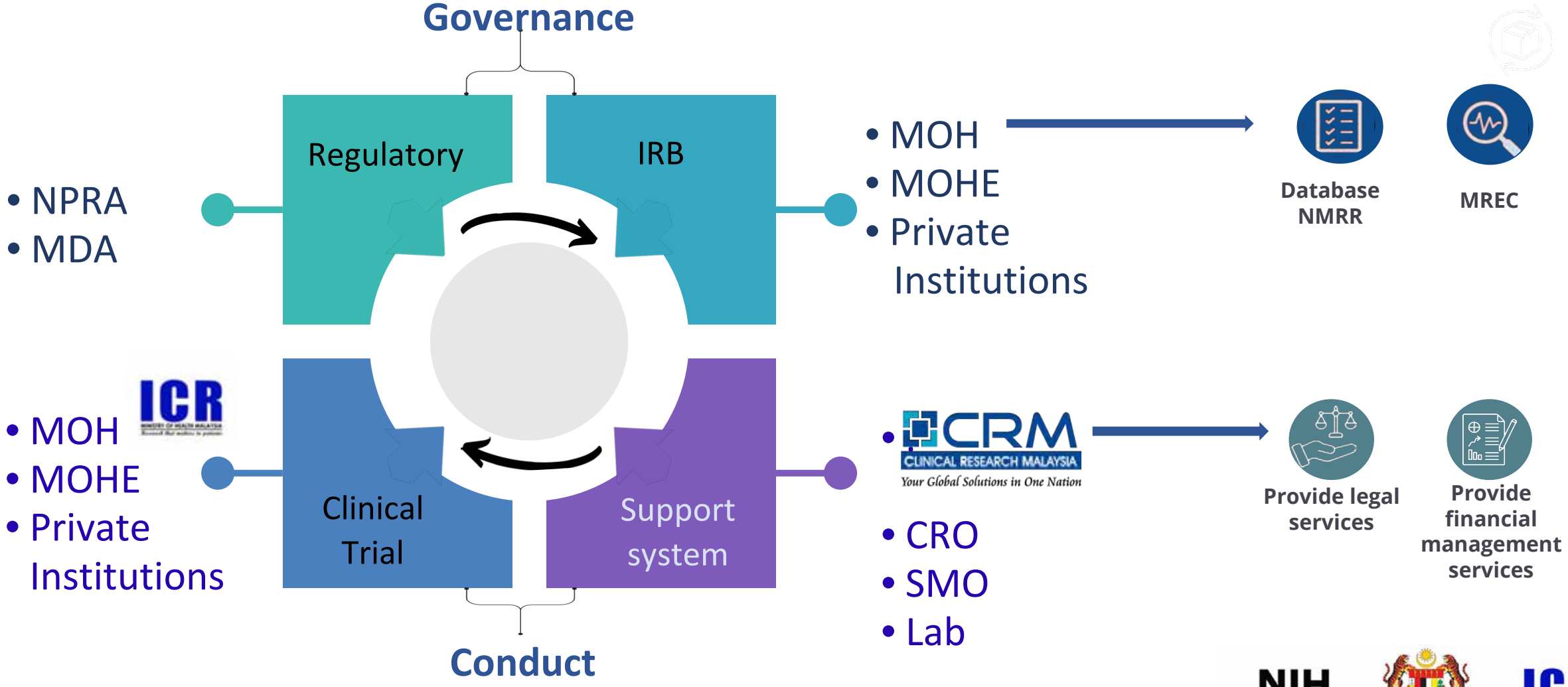
Strengthening national support for clinical trial infrastructure and sustainability of funding

12th Malaysia Plan-Health Research Priorities

- Serve as a guideline and generic assistance for planning health research budget and processes.
- Health research priority-setting processes may assist researchers and policymakers in efficiently targeting researches that have the maximum potential to benefit public health.

Improving coordination and streamlining regulatory and ethics review with our mature

CLINICAL TRIAL ECOSYSTEM:



Enhancing engagements with patients, the public and communities throughout the clinical trial process via our ICR and 37 CRCs nationwide

NIH INSTITUT KESIHATAN NEGARA NATIONAL INSTITUTES OF HEALTH

KEMENTERIAN KESIHATAN MALAYSIA INSTITUT PENYELIDIKAN KLINIKAL

ICR MINISTRY OF HEALTH MALAYSIA

Global implementation efforts of WHA 75.8

Selangor Consensus

21-22 March 2024 : 24 participants from 11 countries achieved consensus on strengthening clinical trials for local public health in the Western Pacific

1. **Developing robust clinical trial ecosystems** with networks and registries to support multi-country trials.
2. **Enhancing research capacity** by integrating clinical trials into health systems, particularly in low-resource settings.
3. **Ensuring equity and inclusivity** in multi-country trials while respecting cultural diversity.
4. **Building trust in clinical trials** by engaging stakeholders early and acknowledging countries' varying readiness.
5. **Addressing cross-cutting challenges** by removing administrative barriers.

1. Workshop On National Clinical Trial Ecosystem in Malaysia

30 Sept 2024

Situational Analysis

Report on the Conduct of Clinical Trials based on the Pillars with Malaysia's Challenges and Opportunities

2. Policy Brief

24 March 2025: A project involving 9 countries that will highlight the Return-On-Investments of clinical trials

3. Maturity Framework

27 March 2025: Testing out the new WHO CTU Maturity Framework in Malaysia

4. Training

Clinical trial Statistics and Ethics training as part of the 25 year ICR anniversary program

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INSTITUT PENYELIDIKAN KLINIKAL

ICR
MINISTRY OF HEALTH MALAYSIA

STRENGTHENING NIGERIA'S CLINICAL RESEARCH ECOSYSTEM: PROGRESS AND REFORMS

Dr. Lola Dosunmu Adeyemi

Special Adviser on Research and Innovation to the Honorable Minister of State for Health & Social Welfare, Nigeria

WHO 2nd Global Clinical Trials Forum

April 2nd, 2025

THE NATIONAL RESEARCH GOVERNANCE REFORMS

Re-establishment of the National Health Research Ethics Committee (NHREC) and the National Health Research Committee (NHRC)

Providing oversight and guidance for health research , clinical trials and ethics in Nigeria

Collaboration between NAFDAC and NHREC

Establishing regular and synergistic communication channels between the two major bodies responsible for the review and approval of clinical trials

Digitization of Research Ethics Review

Creation of the National Health Research Ethics Portal (NHREP) to streamline the submission, review, and approval process

Improved Efficiency, Transparency and Accountability

Establishing clear timelines, tracking metrics, and reporting requirements for the research ethics review process

Nigeria's research governance reforms are enhancing the country's capacity to conduct high-quality, ethical, and relevant health research to address pressing public health needs.

STRENGTHENING THE NATIONAL CLINICAL RESEARCH ECOSYSTEM

De-centralized Clinical Trial Ethics Review

Establishment of a National Research Ethics Committee (NRHEC) to streamline the ethics review process, reducing timelines from 6 months to 8 weeks

Capacity Building

Training programs for researchers, administrators, and ethics committee members, and development of guidelines and SOPs for ethical review

Digitalization and Automation

Adoption of digital technologies to enhance efficiency of research application and review process, including development of national databases and automated workflow

Improved Transparency and Accountability

Establishment of a public registry of approved research projects and regular reporting on performance and outcomes of the reformed ethics process

The reforms are poised to streamline the approval process, enhance transparency and accountability, and facilitate increased participation of diverse populations in clinical trials, positioning Nigeria as a leader in clinical research within the region.

DE-CENTRALIZED ETHICS REVIEW FOR CLINICAL TRIALS

1. Clarified differences between ethical and regulatory oversight

Adhered to international standards for ethical and regulatory frameworks

2. Re-constituted the National Research Ethics Committee (NHREC)

To coordinate ethics review process for multi-center trials and other research

3. Reduced average ethics review timeline

From 6 months to 6-8 weeks

4. Enabled parallel regulatory and ethics review processes

Where appropriate to accelerate review

5. Improved clinical trial timelines and experience

An accelerated clinical trial registration and ethics review process and improved stakeholder experience

DIGITALIZATION AND AUTOMATION

Nigeria has adopted digital technologies to enhance the efficiency of its research and clinical trial application and review process. The country has integrated its research application system with national research databases, enabling seamless data exchange and automation of workflow steps. This digitalization effort has significantly streamlined the review and approval process, reduced administrative burdens and improved overall efficiency.

NHREC RESEARCH ETHICS E-PORTAL

- **Fully Automated Digital Platform**

  Transformed manual, error-prone processes to a modernized, secure, and fully digitized system for handling clinical research and trial protocols

- **Workflow-Driven Research Ethics Portal**

  Web-based platform embedded into the NHREC website that digitizes the end-to-end lifecycle of protocol submission, review, feedback, amendment, approval, and renewal

- **Unified Platform for All Stakeholders**

  Applicants, desk officers, reviewers, and the committee chairman interact within a single platform, eliminating email bottlenecks and centralizing all research ethics processes

- **Secure and Compliant Infrastructure**

  Scalable platform with 99.9% uptime, robust database, secure document storage, regular backups, and disaster recovery, all compliant with NDPR regulations

- **Built-In Intelligence and Analytics**

  Automated submission and review cycles, real-time notifications, progress tracking, analytics dashboards, and satisfaction surveys

Management Structure of health research ethics in Nigeria

❖ HRECs and IRBs are registered by NHREC and categorized as follows

Authorization	Category/ Colour Code	Exclusions
All types of research (NHREC Only)	**A**	None
Phases II, III and IV clinical trials, vaccines and biological products trials, genetic, social and behavioural research, alternative and complementary medicines and epidemiological studies. Trials in vulnerable populations	**B**	Novel products with potential nation-wide religious, social and security implications and research including use of radioactive pharmaceuticals should be referred to NHREC
Phases III and IV clinical trials, social and behavioural research, alternative and complementary medicines and epidemiological studies. Trials in vulnerable populations	**C1**	Exclusions for categories A and B, Phase I and II clinical trials, vaccines and biological research, genetic research
Same as C1 IF also approved by the HREC at the Clinical Sites where the studies are to be conducted.	**C2**	Exclusions for categories A and B, Phase I and II clinical trials, vaccines and biological research, genetic research.
Phases III and IV clinical trials excluding those in vulnerable populations, social and behavioural research and epidemiological studies.	**D1**	Exclusions for A, B C1, and C2,
Same as D1 IF also approved by the HREC at the Clinical Sites where the studies are to be conducted.	**D2**	Exclusions for A, B C1, and C2
Authorised to review only epidemiological, social and behavioural studies. No clinical trials authorization	**E**	In addition to exclusions for categories above, this committee is not allowed to review ANY clinical trial

CAPACITY BUILDING

Ethics Committee Member Training

Training opportunities for members of the National Research Ethics Committee to ensure consistent and high-quality ethical review of research proposals.

Guidelines and SOPs Development

Establishment of comprehensive guidelines and standard operating procedures (SOPs) for the ethical review process, promoting transparency and standardization across the national research ecosystem.

Researcher Training Programs

Comprehensive training programs developed for clinical researchers to build their skills in areas such as study design, data management, and ethical conduct of research.

Research Administrator Training

Specialized training offered to research administrators on effective project management, regulatory compliance, and streamlining research application processes.

NEXT 12 - 18 MONTHS

Q1 2025

Training of State and National HRECs and E-portal Training at F2F meeting

Q2 2025

Update SOPs and Ethics review guidelines

Q3 2025

NHRC F2F meeting and strategy session - Public research database launch

Q4 2025

National Research Bill approval

CONCLUSION AND CALL TO ACTION

- The reforms undertaken in Nigeria's clinical research ecosystem have led to significant improvements in the efficiency, timeliness, and rigor of the research ethics review process.
- These efforts have streamlined the approval process, enhanced transparency and accountability, and facilitated the increased participation of diverse populations in clinical trials.
- The country's commitment to strengthening its national research governance continues to drive progress and position Nigeria as a leader in clinical research within the region.
- NHREC's digitalization strengthens Nigeria's research ecosystem.
- Sustained funding & collaboration are crucial.
- Join us in advancing funding, regulatory and ethical oversight!
- **Contact:** adeyemi.lolade@health.gov.ng; ladeyemi@hmeoffice.com

MANAGEMENT
BENEFITS
OVERSIGHT
ACCOUNTABILITY
REGULATIONS
NIGERIA
EQUITY
QUALITY
CAPACITY
STAKEHOLDERS
INTERNATIONAL
MONITORING
PROTECTION
PARTICIPANTS
DATA
NAFDACS
CLINICAL
THANKYOU
NHREC
NHRC
CONSENT
ETHICS
STANDARDS
SUSTAINABILITY
RESEARCH
COLLABORATION
TRIALS
GUIDELINES
POPULATIONS
RISK
INNOVATION
INFORMED
COMMUNITY
COMMITTEES
VULNERABLE
ENGAGEMENT
TRANSPARENCY

Accelerating Clinical Trials (ACT) Canada Consortium

P.J. Devereaux, MD, PhD
Nominated Principal Applicant of ACT Consortium
CEO and Scientific Director of the World Health Research Trust
Deputy Director of the Population Health Research Institute

ACT AEC
Accelerating Clinical Trials
Accélérer les Essais Cliniques

ACT AEC Accelerating Clinical Trials Accélérer les Essais Cliniques

Accelerating Clinical Trials (ACT) Canada

Funded by CIHR to improve ecosystem for conducting RCTs in Canada

Contracts

- Contracts are major bottleneck in conducting RCTs in Canada
- ACT has implemented Data and Samples Sharing Agreement in 53 Canadian centres
- Finalizing master clinical trial agreement for CIHR funded trials

Creating greater democratization of access to participate in clinical trials

- Borrowing from successful UK portfolio system
- Activated 20 ACT Portfolio hospitals

Pan-Canadian, distributive, single REB approval process with strict timelines for multi-centre RCTs

- February 2024: held meeting of leaders in research ethic boards, institutional leaders, and patient representatives
  - discussed establishing national, distributive, single REB review and approval process with strict timelines
- May 2024: announced RFA for group to set up and run process; application deadline was Aug 16, 2024
- Standardized scoring system for written application
  - groups that scored ≥70/100 invited to interview stage
- Interview consisted of presentation and questions
  - standardized process

Selection committee

- Megan Singleton (co-chair)
  - Associate dean human research protections at John Hopkins, operationalizing single REB for multiple sites
- Matt Westmore (co-chair)
  - Chief exec UK health authority, national REB service that has been running for ~12 years
- John Alexander
  - Cardiologist, clinical investigator at Duke university, co-chair clinical trial training initiative in US
- Gordon Bernard
  - physician scientist at Vanderbilt University Medical Center has led development of single IRB, iREx portal, which helps to organize multicenter IRB oversight
- Deborah Cook
  - McMaster, trialist in critical care, local REB experience, broaden acceptable rigorous ethical consent models for vulnerable patients and co-enrolment
- Adeera Levin
  - International leader in renal clinical research, Head of Division of Nephrology at UBC
- Chris MacKnight
  - Executive chair Nova Scotia health REB, member of REB board for Atlantic Canada, retired geriatrician

CanReview

- Leadership team consisting of experts from 8 Provinces and Territories
- Will utilize digital platforms for ethics approval which have already been audited and approved by both Health Canada and FDA
- https://canreview.ca/

Growing funding pie

- Canadian trialists need to help support and grow Canadian biotechnology industry by evaluating their products in RCTs
- Held 2 national meetings bringing >100 Canadian biotech companies and >300 researchers together to learn about Canadian biotechnologies
- Held 2 granting opportunities that funded trials evaluating Canadian biotechnologies

Immediate upcoming work

- Driving implementation of single national distributive REB model with strict timelines (CanReview)
- Master clinical trial agreements for CIHR funded trials
- Implementation of WHO guidance

Enhancing Clinical Trials Landscape in Pakistan

Report of the 1st Clinical Trials Summit of Pakistan 2025

17th and 18th of February 2025

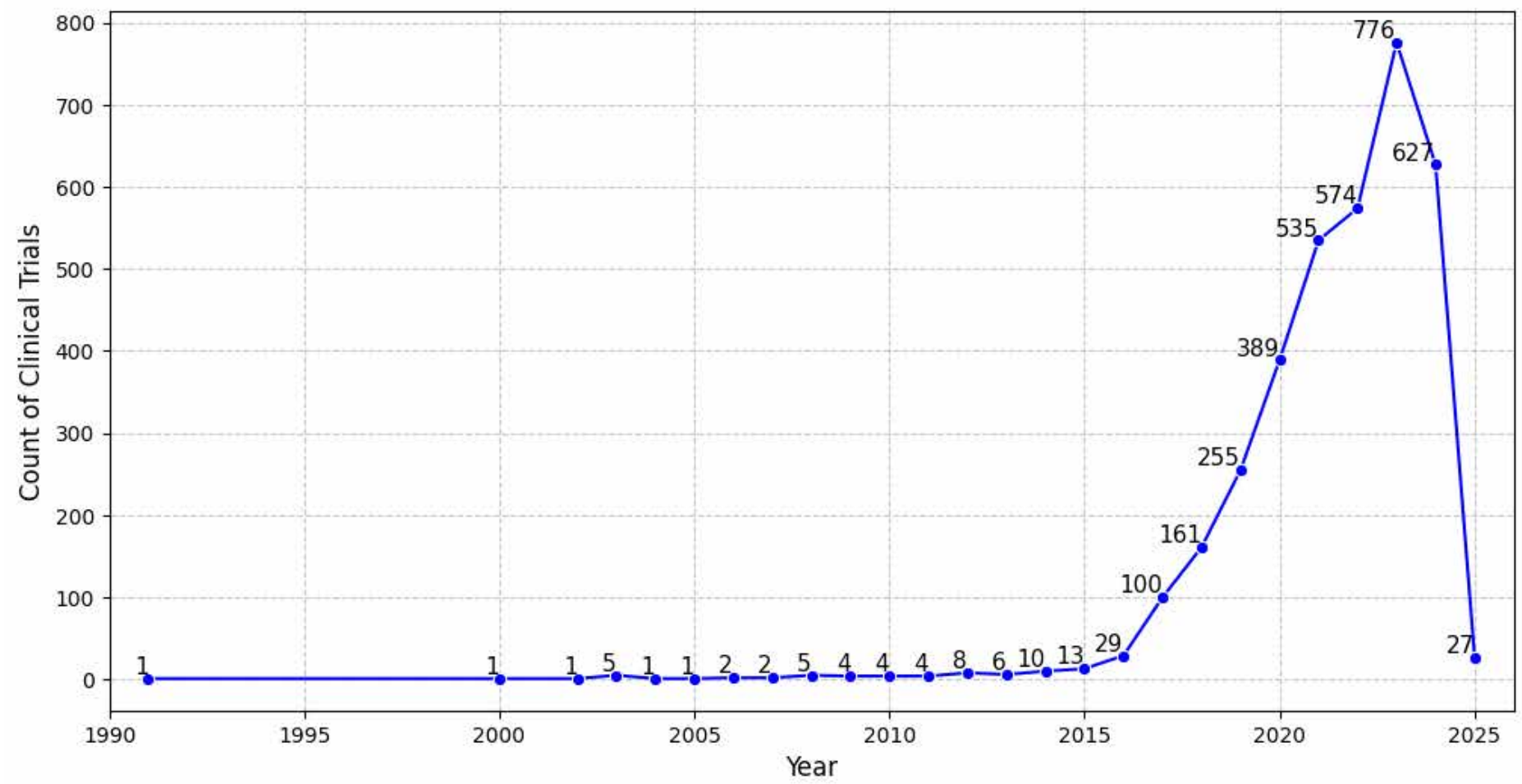
Dr Saeed Hamid
Prof of Medicine
Director CTU,
Aga Khan University
Karachi, Pakistan.

Objectives

Pakistan has significantly lagged behind countries in the region in performing and participating in large randomized clinical trials that would result in changes in clinical practice and the care provided to patients.

- The aim of the summit was to assemble all the high-level stakeholders on one platform to try and develop further the clinical trials ecosystem in Pakistan.
- To harness the post-COVID surge in clinical trial activities in Pakistan, with an increase in trial sites and reputable Contract Research Organizations (CROs) establishing a presence and ongoing efforts to align with global standards (ICH and WHO guidelines) but requiring further enhancement.
- Coupled with that is the dialogue and exchange of ideas and solutions that have developed in unison with the regulatory agencies.
- Attendees- members of the global and national regulatory and ethics bodies (DRAP, NBC, MOH, EMA, FDA, CRN Malaysia), global public health agencies, sponsors, industry, clinical trials units and independent researchers.

Trend of Clinical Trials Over Time in Pakistan

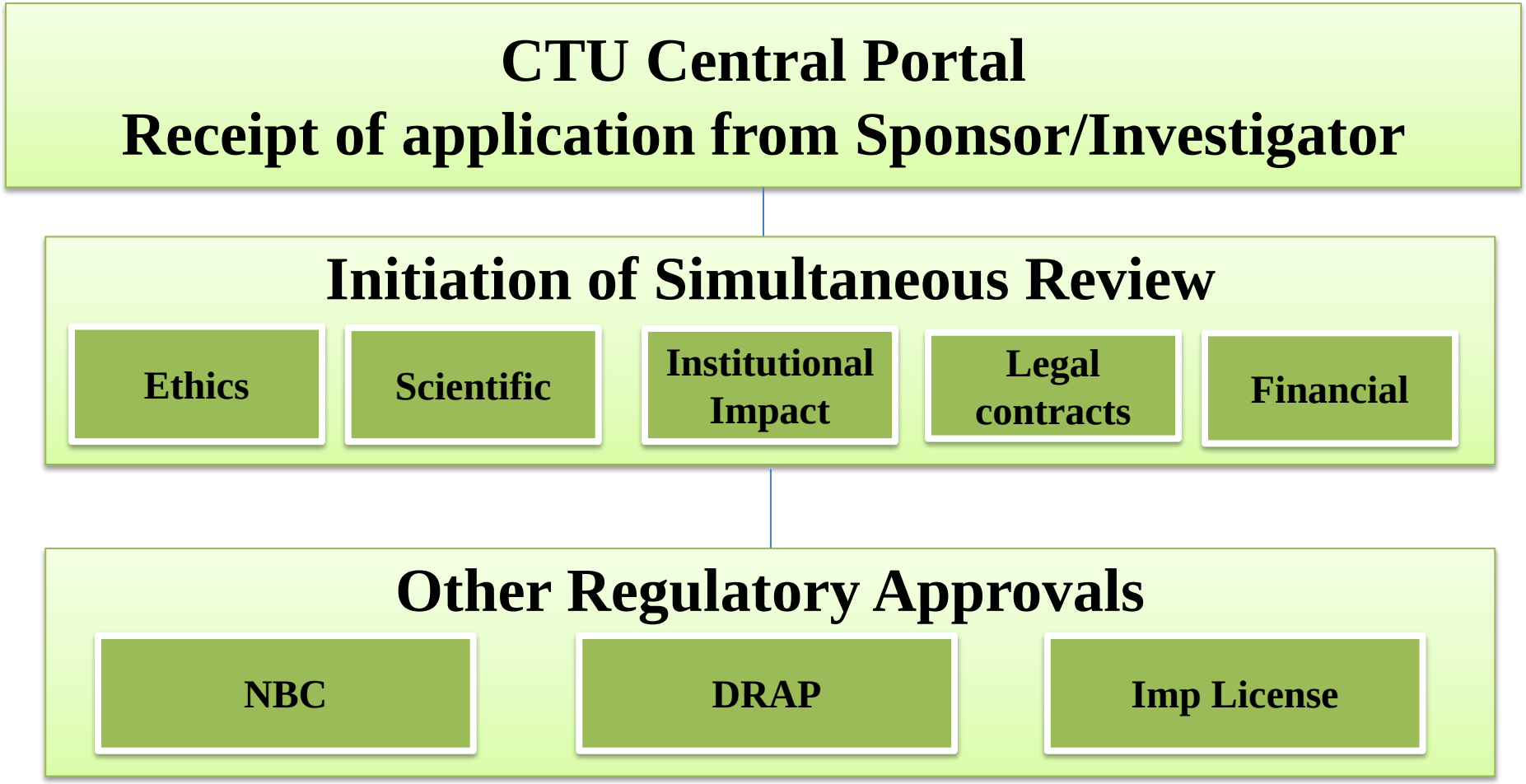


🔷Source– ClinicalTrials.gov

📅 Search Date: Feb 11, 2025.

Nasim, Z, HDSC, AKU

Clinical Trial Approval Process/ Work flow (Cont.)



Key Challenges

- **Regulatory Barriers**

  Processes not aligned - Approvals take a longer than expected.

  Relatively unstable regulatory setup, with frequent movement of personnel.

  Multiple ethics reviews.

- **Limitations in Local Data gathering and analysis.**
- **Infrastructure and Capacity Issues**

  Few well established Clinical Trials set ups.

  Under-staffed and under-funded regulatory capacity.

- **Conducting useful trials & optimizing the impact of existing interventions**

  Lack of community and public engagement

- **Industry Engagement and Investment.**

  Large international sponsors have gradually moved away from the country.

Opportunities for Improvement

- **Strengthening Regulations**

  Online submissions-standardized forms.

  Parallel submissions allowed- However application only considered after NBC approval.

  National Registry of approved clinical trials set up.

  An openness to learn and adopt international best practices.
- **Improvements in data gathering and assessments.**

Opportunities for Improvement

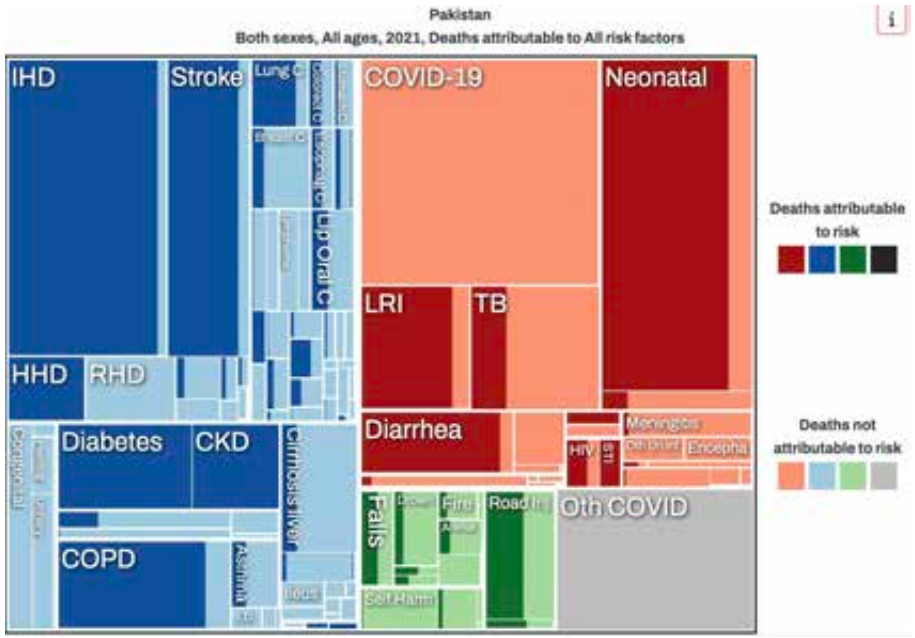
- **Strengthening Regulations**

  Online submissions-standardized forms

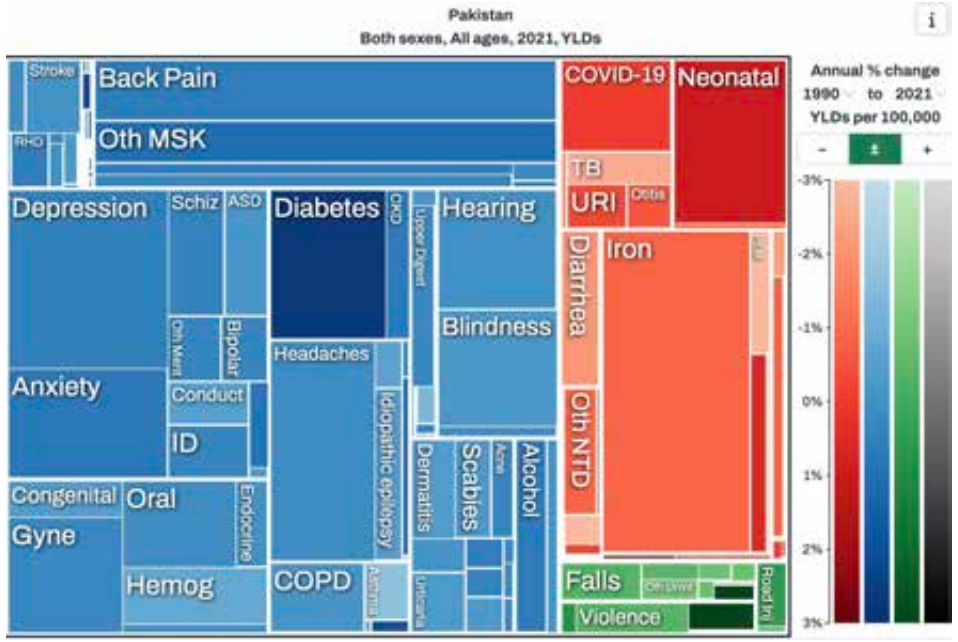
  Parallel submissions allowed- However application only considered after NBC approval.

  National Registry of approved clinical trials set up.

- **Improvements in data gathering and assessments.**



Deaths attributable to Risk - 2021



Years with Disability – Pakistan

IHME, University of Washington

Opportunities for Improvement

- **Strengthening Regulations**

  Online submissions-standardized forms

  Parallel submissions allowed- However application only considered after NBC approval.

  National Registry of approved clinical trials set up.
- **Improvements in data gathering and assessments.**
- **Developing a national clinical trials infrastructure**

  Develop clinical trials networks/consortia.

  Defining common operational processes.

  Use CTU Maturity Frameworks to enhance capacity
- **Enhancing patient and community engagement**

  Establishment of a patient and public involvement group -2024
- **Encouraging Industry & Global Collaboration**

DRAP Guidelines

GUIDELINES TO CONDUCT CLINICAL RESEARCH IN PAKISTAN

Document No: PHSR/GL/CT/002
Document History: 2nd Edition
Effective Date: 14-03-2024

Drug Regulatory Authority of Pakistan
Islamabad - Pakistan

Guidelines to Conduct Clinical Research in Pakistan

- 1st Edition in 20-May-2022
- 2nd Edition in 18-Mar-2024

Guidelines for Conduct and Reporting of Good Clinical Practice Inspections

- 1st Edition in 20-May-2022
- 2nd Edition in 18-Mar-2024

DRAP Mandate

Drugs → Therapeutic Goods

Human Drugs (Pharmaceuticals)	**Veterinary Drugs** (Pharmaceuticals)
Human Drugs (Biologicals including vaccines)	**Veterinary Drugs** (Biologicals including vaccines)
Health & OTC (Alternative medicines)	**Medical Devices** (Class A, B, C & D)
Controlled Drugs (Quota and consumption)	**Clinical Trials** (CROs, Protocols)

Transformation in the role of NBC

from the advisory body- reorganized as regulatory through “Act of Parliament”

essential part of Health Research Institute- NIH

mandated to

- ensuring ethical oversight over human subject research
- promoting responsible research practices
- policy frameworks

Patient & Public Involvement and Engagement- Pakistan First PPIE Summit

community role in health research

PUBLIC ENGAGEMENT EXPERTS, HEALTHCARE PROFESSIONALS PARTICIPATED

Ziauddin University hosts 'Public & Patient Engagement Summit'

Daily The Spokesman

Wednesday, August 21, 2024

Ziauddin University Hosts Public & Patient Engagement Summit

Next Steps:

- Establish a monitoring committee to oversee implementation of these recommendations.
- Host annual follow-up summits to evaluate progress and refine strategies.
- Publish the Pakistan Clinical Trials Landscape Report to engage international stakeholders.

Progress in the national clinical research ecosystem – South Africa

Prof. Catherine Orrell
Unit Director, HIV and Infectious Diseases Research Unit (HIDRU)
South African Medical Research Council

2-3 April 2025

saMRC advancinglife

SAMRC history and health STATEMENT

The South African Medical Research Council recognises the catastrophic and persisting consequences of colonialism and apartheid, including land dispossession and the intentional imposition of educational and health inequities.

Acknowledging the SAMRC's historical role and silence during apartheid, we commit our capacities and resources to the continued promotion of justice and dignity in health research in South Africa.

transformation
WORKING TOGETHER FOR EXCELLENCE

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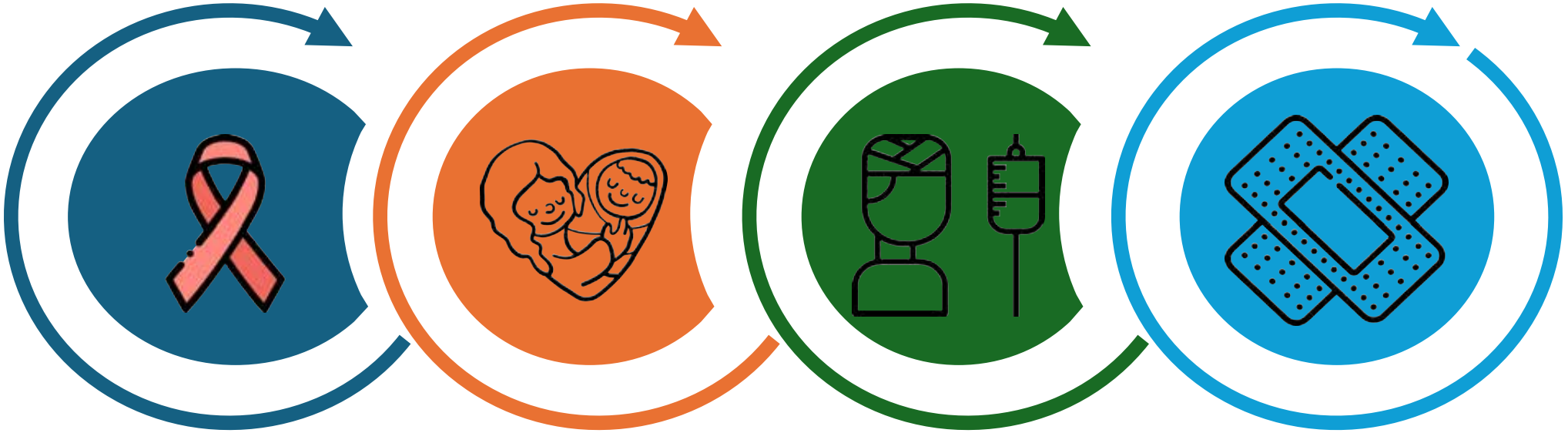
South African Quadruple Burden of Disease



HIV/AIDS and TB

Maternal, newborn and child health

Non-communicable diseases

Violence and Injury

PROGRESS SINCE NOVEMBER 2023

Action 1: Strengthen local leadership and national support for sustained infrastructure and funding

Strong leadership in the clinical trial space:

- Larger NIH-funded Clinical Trial Units – attached to larger institutions (e.g. SAMRC, CAPRISA, UCT, WITS, UStellenbosch). Network studies, some pharma.
- Non-profit research organisations – more investigator–driven research (e.g. Ezintsha, Desmond Tutu HIV Foundation, PharmOVS).

Well-designed studies, high impact publications.

eClinicalMedicine
Part of THE LANCET *Discovery Science*

PLOS Global Public Health

NEJM GROUP COVID-19 Collection

saMRC advancinglife

PROGRESS SINCE NOVEMBER 2023

Action 1: Strengthen local leadership and national support for sustained infrastructure and funding

- Domestic public financing:

  Multiple calls for local investigator-driven research e.g. Strategic Health Innovation Partnerships (SHIP); SAMRC/NIH-R01.

- Capacity building:

  Existing consortia building research skills in LMIC.

EDCTP

ViiV Healthcare

Unitaid
Innovation in Global Health

MERCK

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Strategic research Initiatives

South Africa-US Program for Collaborative Biomedical Research
18 joint SA-US projects

For the global development and delivery of antibiotic treatments for drug-resistant bacterial infections
3 projects funded

BRICS STI COVID response – 7 projects
AMR diagnosis and treatment
Simulation and big data analytics
BRICS TB Research Network

Hosting agreement
Co-funding for Malaria & HIV projects

OTHER

Research partnership with India on HIV and TB

Partnership with Sweden on inequalities in health, health systems and health systems policies

Global research collaboration for infectious disease preparedness

Public research funding agencies addressing prevention and treatment of non-communicable diseases

Partnership with the BGI to establish a genomics sequencing facility in Africa

Participation in the EU-Africa Personalized Medicine Consortium and the Joint Transnational Funding Call 2022

PROGRESS SINCE NOVEMBER 2023

ACTION 3: ADDRESS BARRIERS TO CLINICAL TRIALS IN UNDER-REPRESENTED POPULATIONS

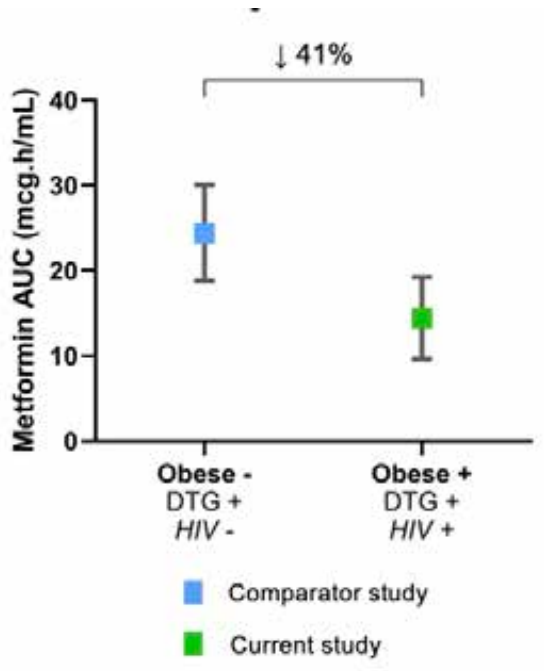
- Parental consent waiver for older adolescents (16-17 years); with community approval.
- Inclusion of pregnant and breastfeeding women.
- Justification for inclusion age restrictions.

PROGRESS since November 2023

Still requiring effort:

- Action 6: improving efficiencies in approval processes (Regulatory vs Ethics vs Institutional vs local DOH).

- Little early phase research capacity (FIH, phase I-II): pharmacogenetics of Southern African population not the same as US/Europe; dose-finding important in local populations,



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CATHERINE. ORRELL@MRC.AC.ZA

thank you

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good clinical trials

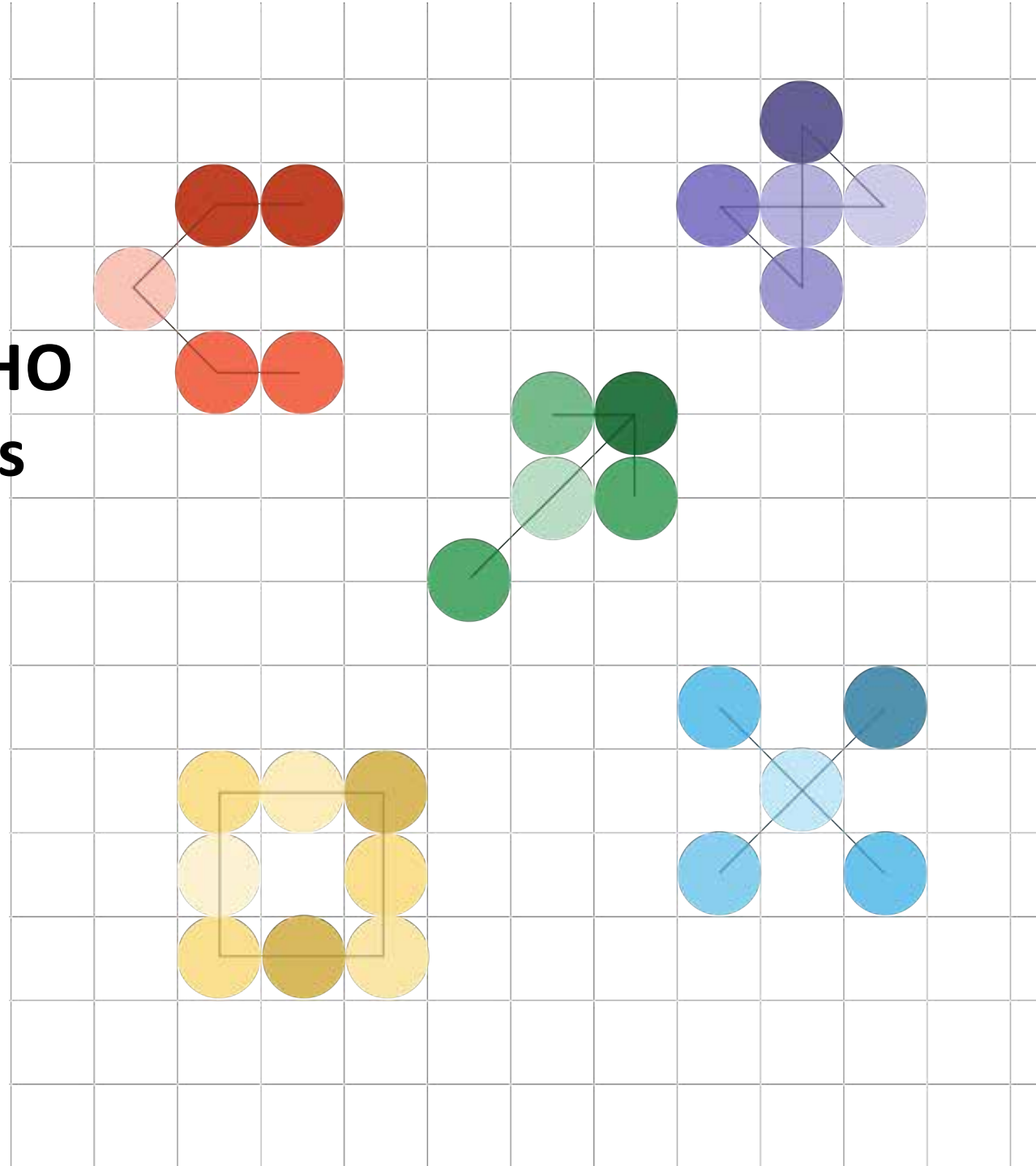
Enabling implementation of WHO Guidance on Good Clinical Trials

Martin Landray

Chair, Good Clinical Trials Collaborative www.goodtrials.org

Chief Executive Officer, Protas www.protas.co.uk

Prof of Medicine & Epidemiology, Oxford Population Health



wellcome

BILL & MELINDA GATES foundation

Context

- Arbitrary use of unproven treatments and failure to develop novel treatments damages patient care & public health
- Randomized trials are a critical component of high quality clinical care
- Compelling results change practice
- Regulatory, policy & clinical decision making is better (& easier) if evidence is clear
- But trials must be:
  - Designed to deliver a reliable answer to a relevant question
  - Designed to be feasible for patients and clinical staff
  - Designed to take advantage of technology & data
  - Designed with the full range of interested parties
- **Obstacles & burdens to randomized clinical trials damage patient care, medical innovation, public health, and the trustworthiness of the health system**

VIEWPOINT

Benefits of Streamlined Point-of-Care Trial Designs
Lessons Learned From the UK RECOVERY Study

Robert M. Califf, MD
US Food and Drug Administration, Silver Spring, Maryland.

Patrizia Cavazzoni, MD
US Food and Drug Administration, Silver Spring, Maryland.

Janet Woodcock, MD
US Food and Drug Administration, Silver Spring, Maryland.

JAMA Internal Medicine

Recent findings from the UK Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial group present an important learning opportunity for the clinical and clinical research communities.

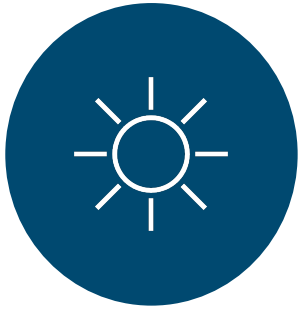
Given the resources, technology, and talent in the US, our knowledge of the risks and benefits of interventions could be greatly enhanced with focused, pragmatic point-of-care trial designs. Streamlining and quality are not opposed; rather, by applying quality-by-design principles, reliable evidence can be developed with planned, measurable quality when researchers focus on ensuring both the quality of data that address important research questions and trial conduct that protects patient safety.

What does good guidance look like?

good clinical trials

Good science & ethics

Focused on issues that materially influence the well-being of trial participants & reliability of the results

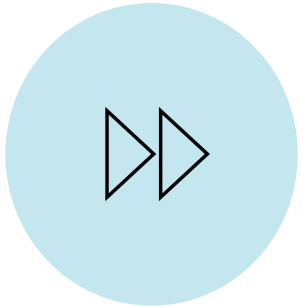


Clear and concise

Promotes critical thinking and application through accessibility and decision-making support.

Inclusively developed

Co-developed with regulators, funders, commercial & academic trialists, clinicians, patients & public.



Progressive & durable

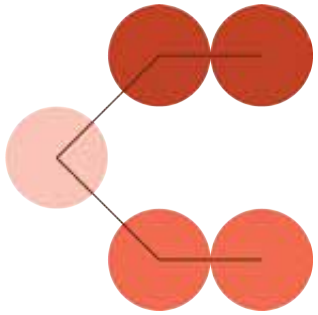
Forward looking and applicable across disease areas, intervention types, development phases, trial designs, geographies & time

www.goodtrials.org

Turning guidance into practice:
Focus on the “Why”- not who, what, where, or how

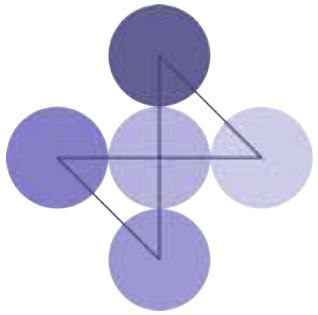
- Focus on the principles
- Recognise that many trials pose little or no additional risk to participants compared to normal clinical practice
- Recognise the strengths of the routine healthcare system & the standards to which organizations & individuals are held
- Encourage efficient & effective solutions (even if they are unfamiliar)
- Discourage excessive or defensive practices
- Remember: Documentation is not the same as quality

Good Trials: Produce a scientifically sound answer to a relevant question



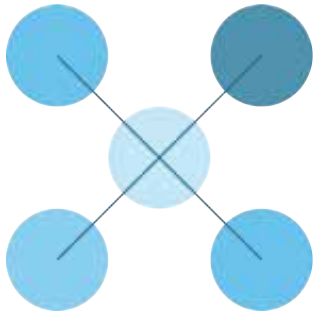
Produces a scientifically sound answer to a relevant question

1. Trial population
2. Allocation
3. Adequate size
4. Blinding
5. Adherence
6. Follow-up
7. Measuring outcomes
8. Data capture
9. Ascertainment
10. Statistical analysis
11. Assessing effects
12. Emerging information



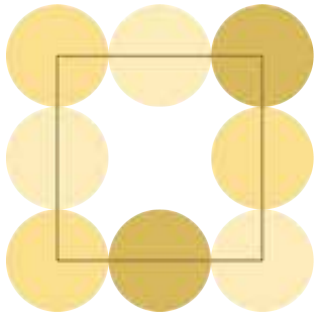
Respects the rights & well-being of participants

13. Appropriate participant communication
14. Relevant consent
15. Changing consent
16. Implications of changing consent
17. Safety of individual participants
18. Communication of new information



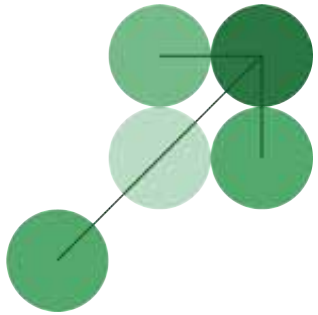
Collaborative and transparent

19. Working in partnership with patients and communities
20. Collaboration among organizations
21. Transparency



Feasible for the context

22. Setting and context
23. Use of existing resources



Manages quality effectively and efficiently

24. Competent advice and decision-making
25. Protecting trial integrity
26. Planning for success and focusing on issues that matter
27. Monitoring, auditing and inspection of study quality

good clinical trials

www.goodtrials.org

WHO guidance for best practices for clinical trials: Key scientific and ethical considerations

Good clinical trials

- ✓ are designed to produce scientifically sound answers to relevant questions
- ✓ respect the rights and well-being of participants
- ✓ are collaborative and transparent
- ✓ are feasible for context
- ✓ manage quality effectively and efficiently

The guidance is relevant to all clinical trials addressing any health intervention for commercial or non-commercial purpose, for any role involved and in any health system setting.

World Health Organization

Guidance for Good Randomized Clinical Trials Evaluation Tool

A tool to support application of the key principles of good RCTs

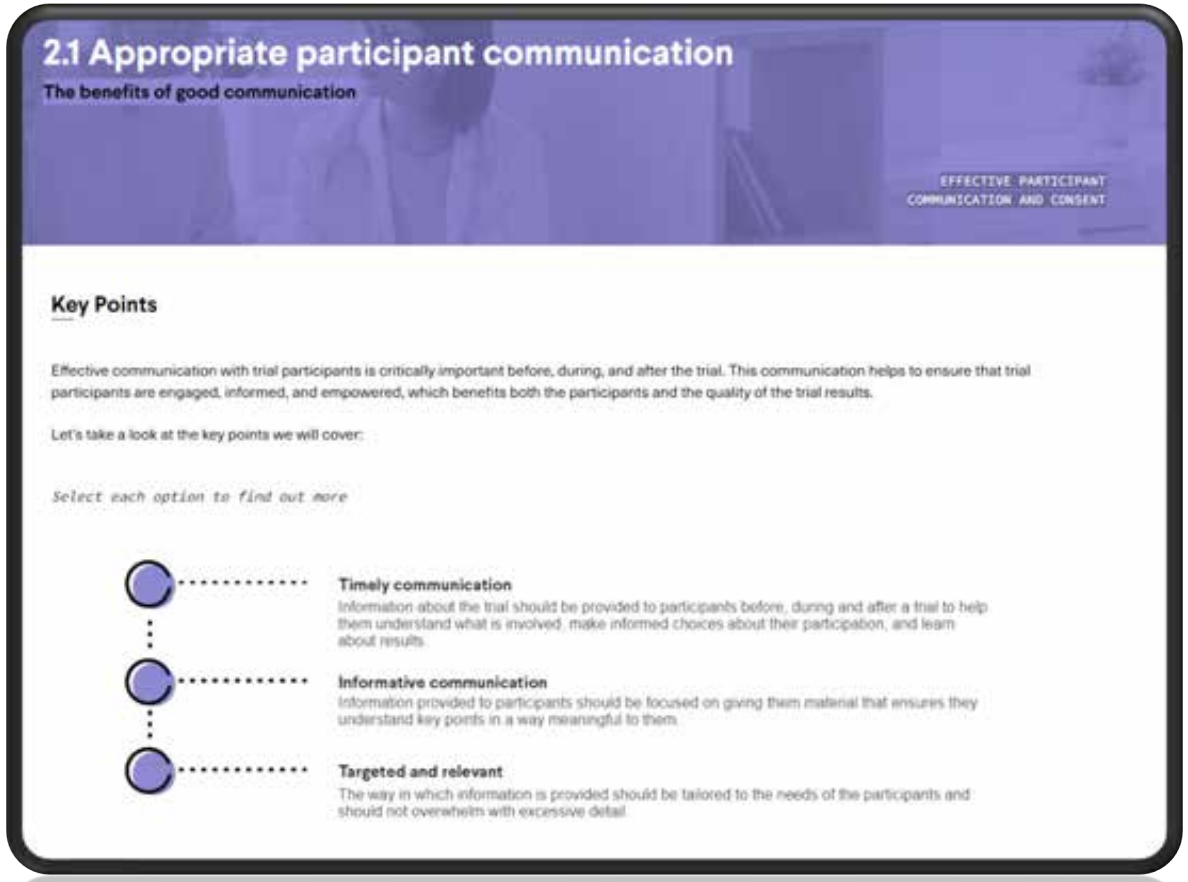
Principle 03

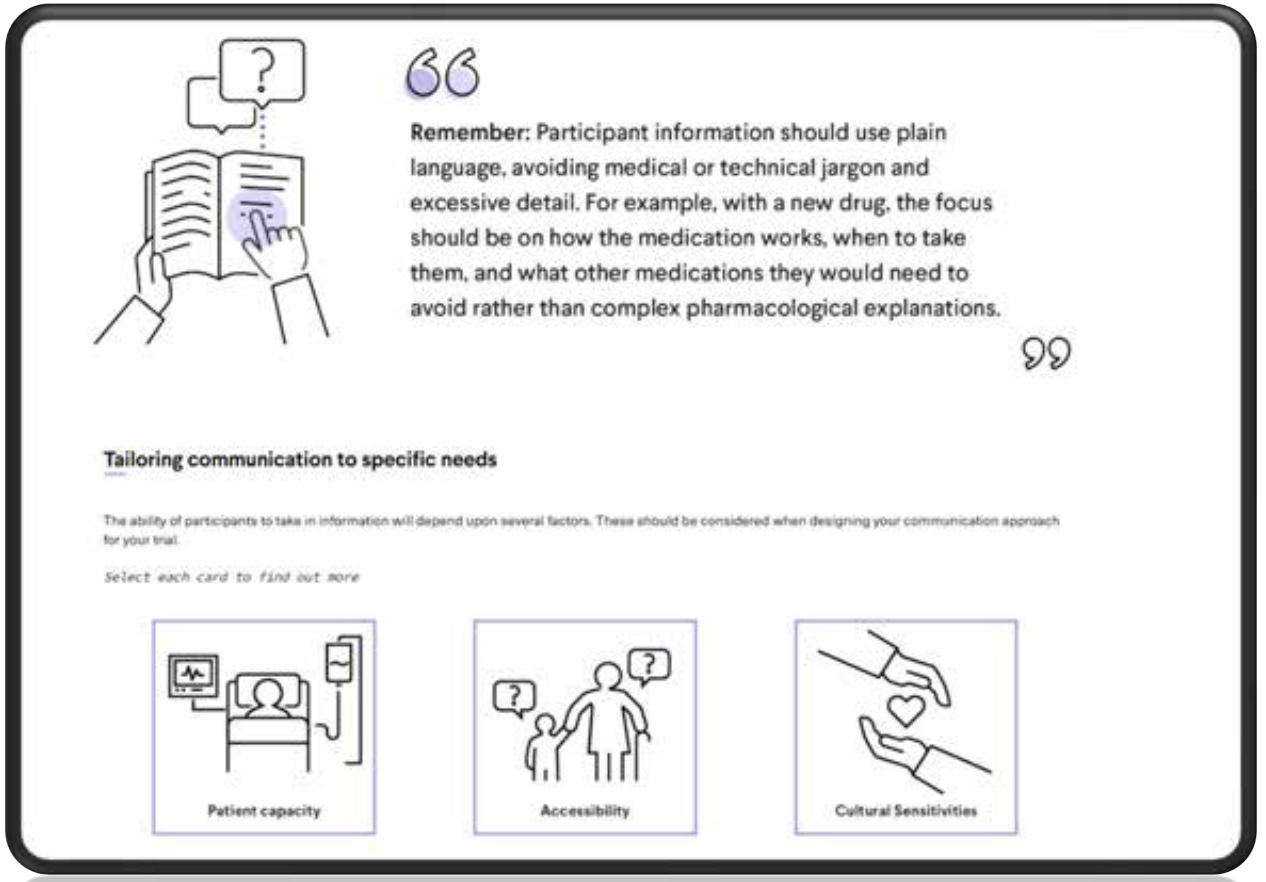
Good RCTs are **collaborative and transparent**

Sub-principle	Key points to consider	Fulfilled?	Comment
3.1 Working in partnership with patients and communities	Potential participants and/or members of the relevant community have been able to contribute to the design, execution, and interpretation of the trial.	☐ Yes ☐ No ☐ Partially	
3.2 Collaboration among organizations	Broad-based collaboration and engagement of a range of relevant individuals and/or organisations to identify and address those factors that are critical to trial quality and enable a delivery approach that is appropriate to the trial setting and context.	☐ Yes ☐ No ☐ Partially	
3.3 Transparency	a. Trial registered on a publicly available database prior to enrolment of the first participant.	☐ Yes ☐ No ☐ Partially	
	b. Additional trial information, including the trial protocol and other trial documentation, is made publicly available if feasible.	☐ Yes ☐ No ☐ Partially	

https://www.goodtrials.org/resources/evaluation-tool/

E-learning course





Launching April 2025

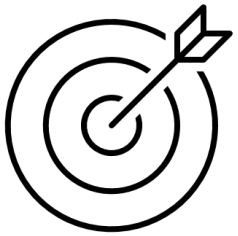
II. PRINCIPLES OF ICH GCP

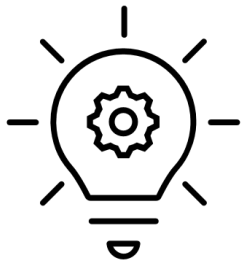
Clinical trials are a fundamental part of clinical research that support the development of new medicines or uses of existing medicines. Well-designed and conducted clinical trials help answer key questions in healthcare and drug development. Their results are essential for evidence-based healthcare decisions. Trials with inadequate design and/or poorly conducted trials may place participant safety at risk, yield inadequate or unreliable results and are unethical. They waste resources and the efforts and time of investigators and participants.

The Principles of GCP are designed to be flexible and applicable to a broad range of clinical trials. This guideline, along with ICH E8(R1), encourages thoughtful consideration and planning to address specific and potentially unique aspects of an individual clinical trial. This includes evaluation of trial characteristics, such as the design elements, the investigational product being evaluated, the medical condition being addressed, the characteristics of the participants, the setting in which the clinical trial is being conducted, and the type of data being collected. Careful consideration of factors relevant to ensuring trial quality is needed for each clinical trial.

The Main Concern
- Over-interpretation & Rigid Implementation -

Rigid interpretation will prevent appropriate flexibility & innovation, impair feasibility, and reduce quality of participant experience and information generated for future patients





Quality

Quality is the absence of errors that have a material impact on the safety, rights & well-being of participants or the reliability of the results (and thereby impact the care of future patients)

Proportionality

Focusing efforts on issues that would have the greatest influence on quality (and deprioritising or stopping activities of little value or that create burden & distraction)

Implications & implementation

WHO Guideline for Best Practices for Clinical Trials:

- Sets out the principles that make a trial a good trial
- Guides interpretation & implementation of ICH E6 (R3) “Good Clinical Practice”
- Informs investment and prioritisation decisions

Ways to implement:

- **Adoption into funding guidance & decisions** – guiding grant reviewers and panels
- **Advocacy** – to drive improvements to commercial & non-commercial trials ecosystem, infrastructure, regulation and bureaucracy
- **Training & capacity strengthening** – helping the next generation of clinical trialists to think for themselves and equipping them to deal with new challenges, technology & contexts
- **Put into practice** – the principle of efficiency and minimising additional burden applies both to those who design and conduct clinical trials and those who fund, administer and monitor them
- **Demonstrations** – there is nothing like exemplars to show what is possible and change practice

What do we need?

Methods & systems

Establish & support trials infrastructure: sustainable investment in people, skills, partnerships, data & technology, policy & processes

Optimise use of data: accessible, analysable, interpretable, acceptable

Quality by Design: an up-front approach to avoid issues that would have a material on participant safety & well-being and reliability of results for future patients

Culture

Collaboration: across organisational, sector & disciplinary boundaries and with patients & public

Integration with health service: clinical trials are a core part of good clinical care

Integration with routine life: most patients are not patients most of the time

Imagination & careful thought

Regulation & innovation as joint enablers: emphasise principles not process; focus on quality not documentation; embrace flexibility & innovation

Moving forward: Building a global action plan for enhancing community involvement in clinical trials

Nina Gobat, Senior Technical Officer, WHO Health Emergency Program

Stuart Nicholls, Scientist, Ottawa Hospital Research Institute

Maria Dutarte, Executive Director, European Patients' Academy on Therapeutic Innovation (EUPATI)

WHA75.8 Strengthening Clinical Trials Resolution

World Health Organization

SEVENTY-FIFTH WORLD HEALTH ASSEMBLY
Agenda item 16.2

WHA75.8
27 May 2022

Strengthening clinical trials[1] to provide high-quality evidence on health interventions and to improve research quality and coordination

The Seventy-fifth World Health Assembly,

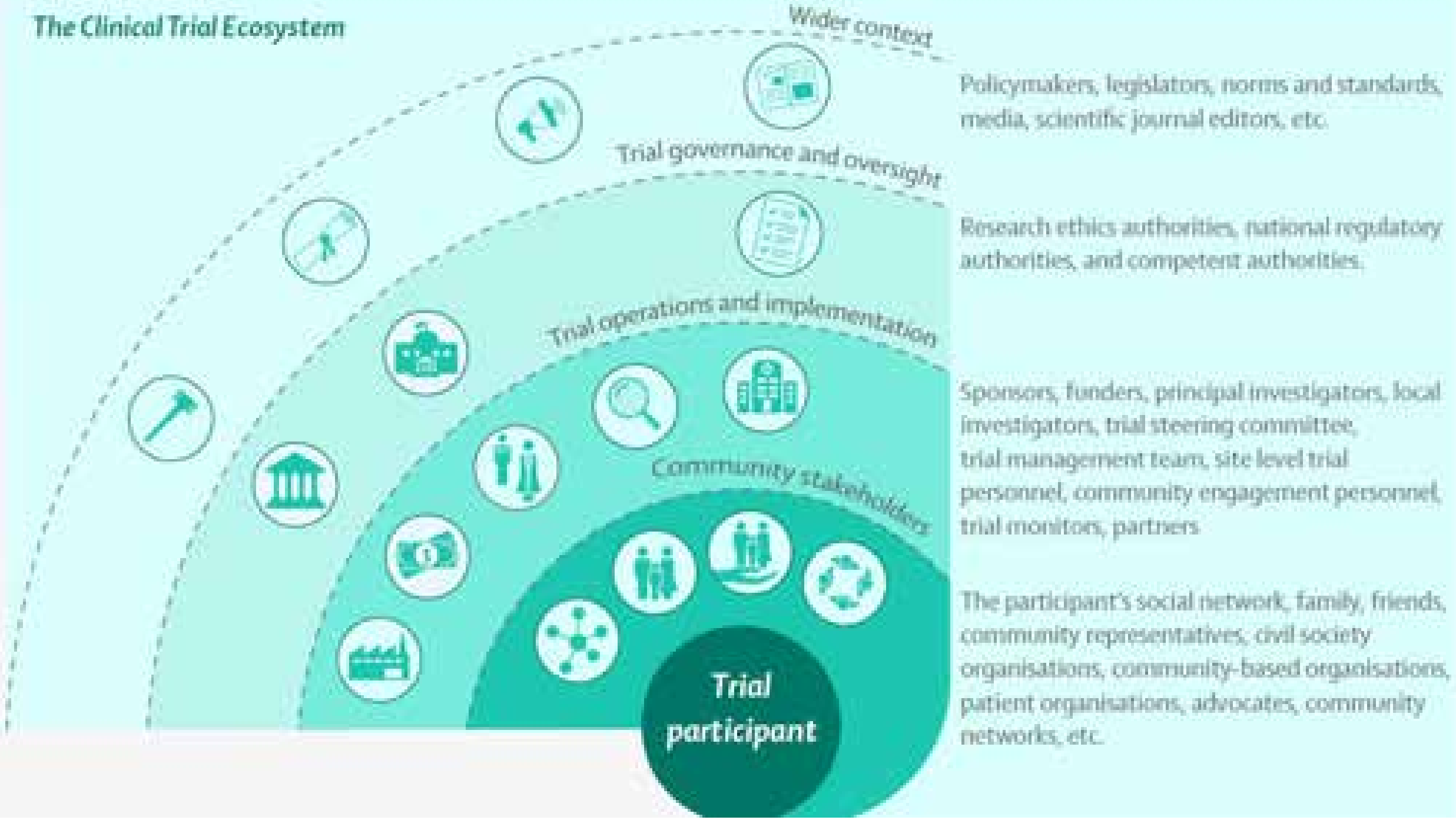
Recalling resolutions WHA58.34 (2005) acknowledging that high-quality, ethical research and the generation and application of knowledge are critical in achieving internationally agreed health-related development goals, WHA63.21 (2010) outlining WHO's role and responsibilities in health research, WHA66.22 (2013) and WHA69.23 (2016) on the follow-up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination, WHA67.20 (2014) on regulatory system strengthening for medical products, WHA67.23 (2014) on health intervention and technology assessment in support of universal health coverage, WHA74.6 (2021) on strengthening local production of medicines and other health technologies to improve access, and WHA74.7 (2021) on strengthening WHO preparedness for and response to health emergencies, which notes the importance of basic and clinical research and recognizes the critical role of international collaboration in research and development, including in multicountry clinical and vaccine trials, as well as rapid diagnostics test and assay development, while acknowledging the need for further rigorous scientific evidence;

Noting the recommendations made by the Independent Panel for Pandemic Preparedness and Response in their review "COVID-19: make it the last pandemic"[2] relating to health research and development, including clinical trials;

[1] "A clinical trial is defined by WHO as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials may also be referred to as interventional trials. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process of care changes, preventive care, etc. This definition includes Phase I to Phase IV trials." Joint statement on public disclosure of results from clinical trials, 2007 (https://www.who.int/news/item/18-05-2017-joint-statement-on-registration, accessed 27 May 2022).

[2] Independent Panel for Pandemic Preparedness and Response. COVID-19: make it the last pandemic. 2021 (https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf, accessed 31 May 2022).

Calls on **member states** to increase capability for " … **well designed** and **well implemented**…" clinical trials that include " … all the major population groups the intervention is intended to benefit.." and " … that are **developed in collaboration with affected communities**, with a view to addressing their public health needs …"


The Clinical Trial Ecosystem
Wider context
Policymakers, legislators, norms and standards, media, scientific journal editors, etc.
Trial governance and oversight
Research ethics authorities, national regulatory authorities, and competent authorities.
Trial operations and implementation
Sponsors, funders, principal investigators, local investigators, trial steering committee, trial management team, site level trial personnel, community engagement personnel, trial monitors, partners
Community stakeholders
The participant's social network, family, friends, community representatives, civil society organisations, community-based organisations, patient organisations, advocates, community networks, etc.
Trial participant

Strengthening the capacity of patients, communities and the public through training

Training and education are important for building the capacity and capability of patients/community to contribute to the design, execution and interpretation of the results of clinical trials.

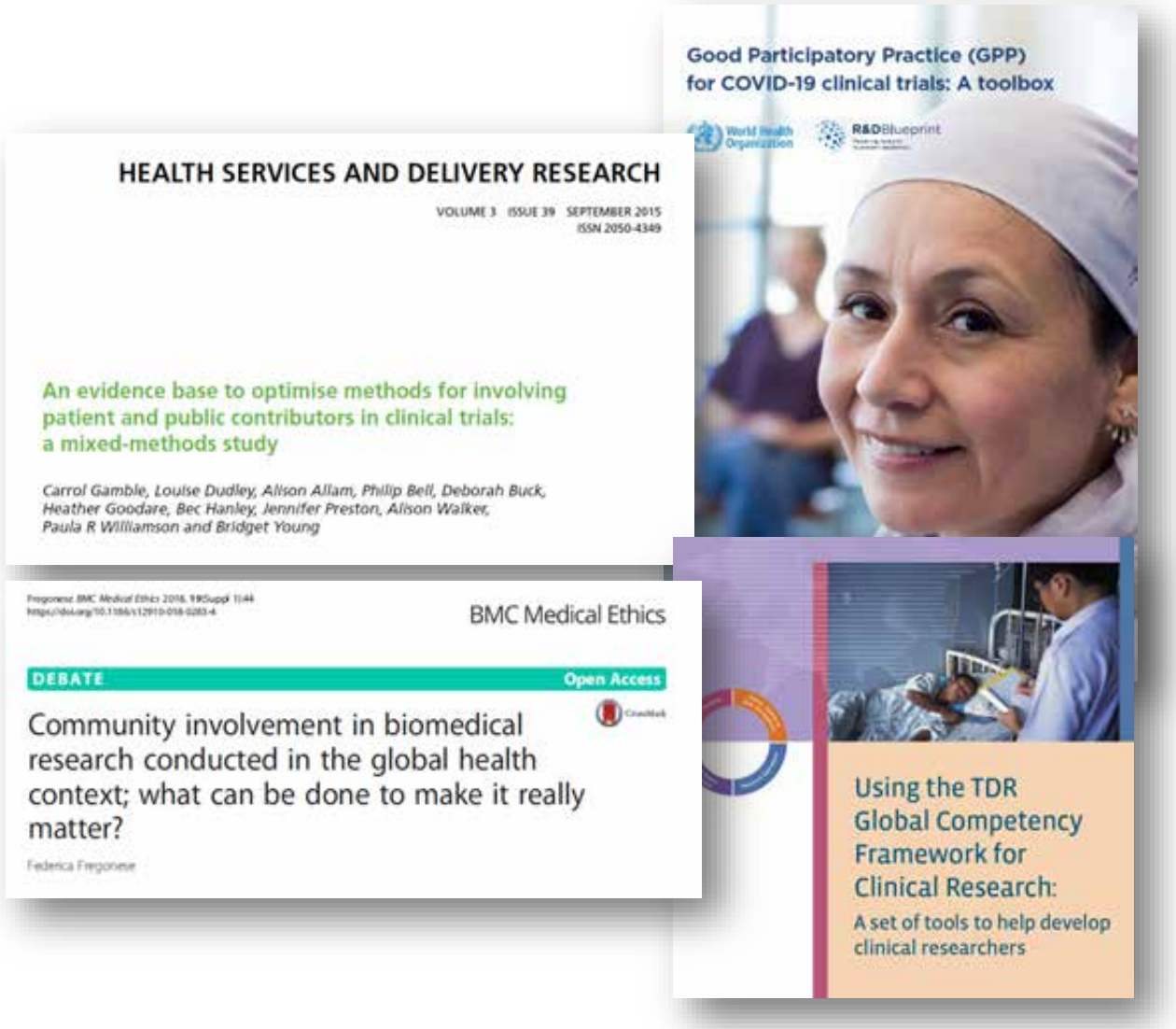
- **knowledge of clinical research**

- Knowing the critical **points for patient input** and how to contribute

There are existing trainings provided by patient organisations, international/regional educational initiatives but scaling up of these efforts and tailoring to different country/community contexts needed

A rapid scoping review of guidance regarding training and competencies

- Identifying proposed and implemented knowledge, skills & attitudes training or competencies
- Academic and grey literature
  - Up to December 2024
- Focused on clinical trials
  - Not general involvement or training
- To be completed spring 2025



The Ottawa Hospital Research Institute | L'Hôpital d'Ottawa Institut de recherche

ACT AEC Accelerating Clinical Trials / Accélérer les Essais Cliniques

Starting point: Actors and actions across the trial ecosystem

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(24)00521-7/fulltext

Examples

- Actors

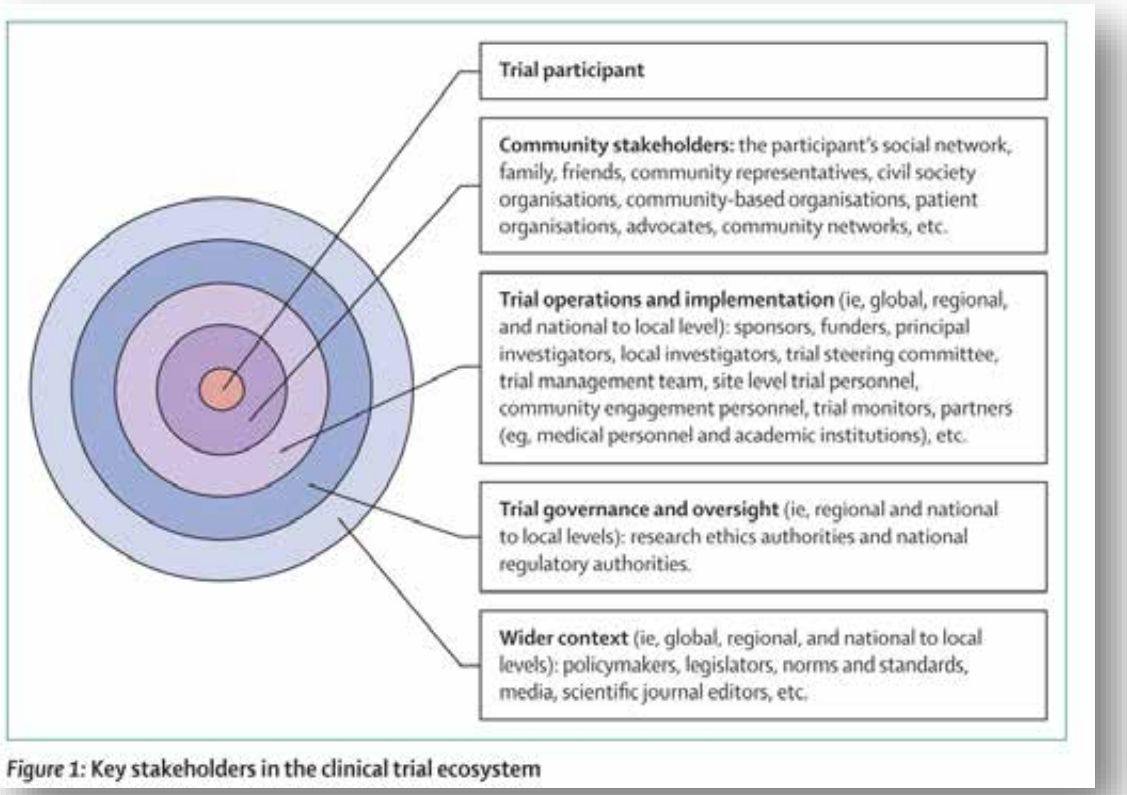


Figure 1: Key stakeholders in the clinical trial ecosystem

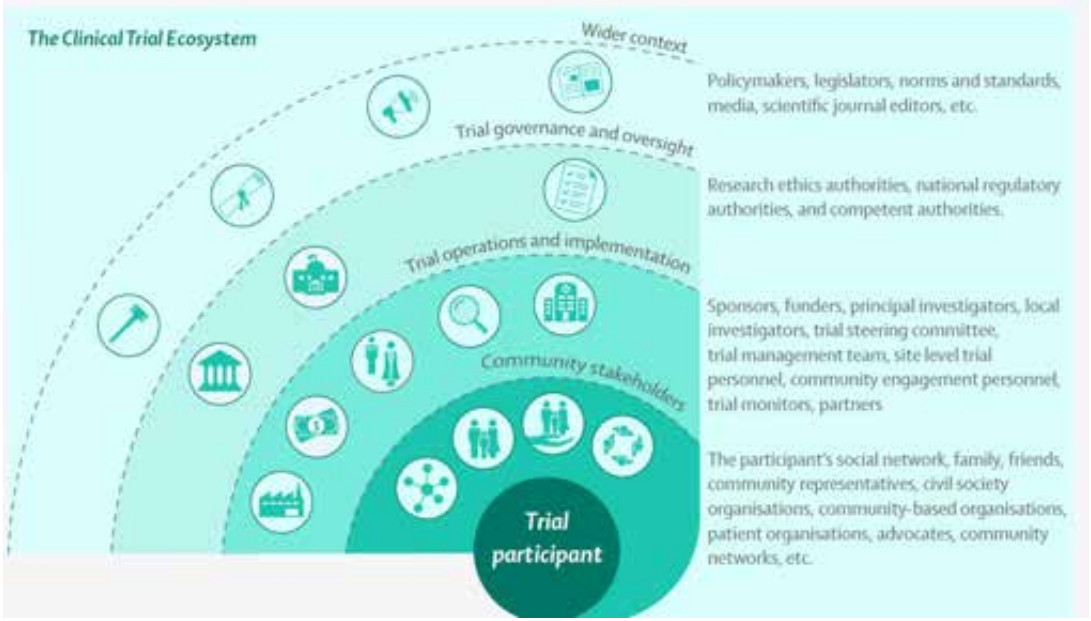
- Actions (examples)
  - Require papers reporting clinical trials to describe participant engagement activities
    - Example: BMJ section of "Patient and Public Involvement"
  - Provide ongoing training on engagement support tailored to different internal stakeholders without engagement expertise
  - Develop REC forms (eg, application forms and renewal forms) that prompt trialists to describe their engagement plans
    - UK REC process includes Q14-1"In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?" https://www.myresearchproject.org.uk/help/hlpcollatedqsg-iras.aspx#2296

Gobat, N., et al (2025). "Better engagement, better evidence: working in partnership with patients, the public, and communities in clinical trials with involvement and good participatory practice." Lancet Global Health.

Questions for further discussion

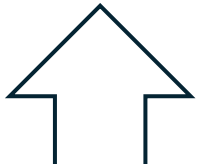
Building a global action plan for enhancing community involvement in clinical trials

How? Who? When?



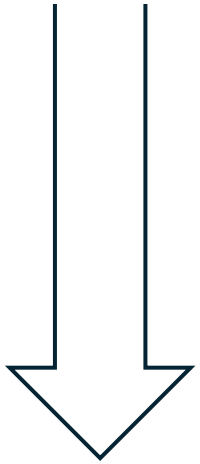
- Strengthening policies
- Enhancing funding mechanisms
- Improving regulatory oversight
- Advocacy
- Education of all stakeholders about engagement
- Promoting strong culture of engagement

Community involvement cuts across all areas of work



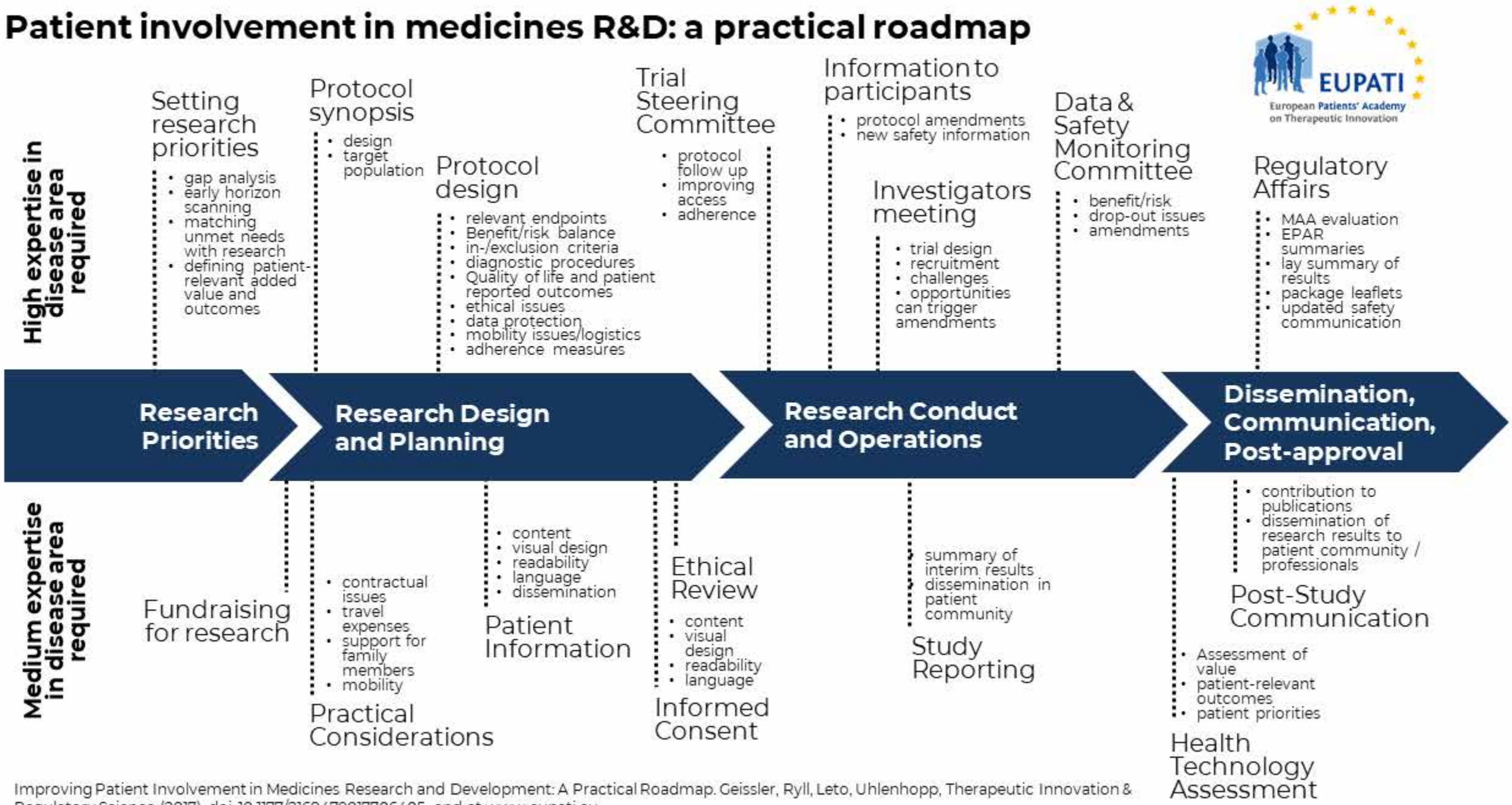
Action 1: Strengthen local leadership and national support for sustained infrastructure and funding

Action 2: Enhance engagement with patients, communities and the public in trial life cycle



Action 3: Address barriers to clinical trials in under-represented populations
Action 4: Enable effective trials through adoption of innovative designs and digital technologies
Action 5: Accelerate access to fit-for-purpose training packages for clinical trials
Action 6: Improve coordination and streamlining regulatory and ethics review
Action 7: Engage clinical practitioners to integrate clinical trials into health systems and practices
Action 8: Step up the use of trial registries to improve research transparency
Action 9: Expand international health research and clinical trial collaboration

Patient involvement in medicines R&D: a practical roadmap



Improving Patient Involvement in Medicines Research and Development: A Practical Roadmap. Geissler, Ryll, Leto, Uhlenhopp, Therapeutic Innovation & Regulatory Science (2017), doi: 10.1177/2168479017706405, and at www.eupati.eu

Thank you

2nd Global Clinical Trials Forum, 2-3 April 2025
WHO Science Division, Geneva, Switzerland

Tackling underrepresented populations

Judd Walson

On behalf of

Members of the dedicated working groups as well as Per Ashon, Matteo Cesari, Katherine Litter, Yasir Nisar, Martina Penazzato and Mariana Widmer

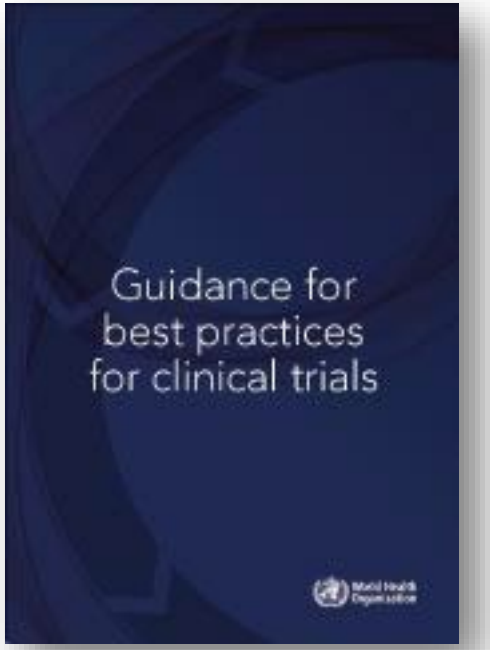
World Health Organization

Why are we focusing on underrepresented populations?

- WHA75.8/associated guidance identified needed reforms to allow for inclusion of underrepresented populations. This includes the need to focus on:
  - Research prioritisation
  - Equitable representation in evidence generation
  - Appropriate sampling, inclusion/exclusion criteria
  - Post-trial access & benefit sharing

- Guidance doesn't define populations but identifies 3 factors:
  - Demographic, social & economic factors & health status
  - Challenges associated with identifying & defining these populations

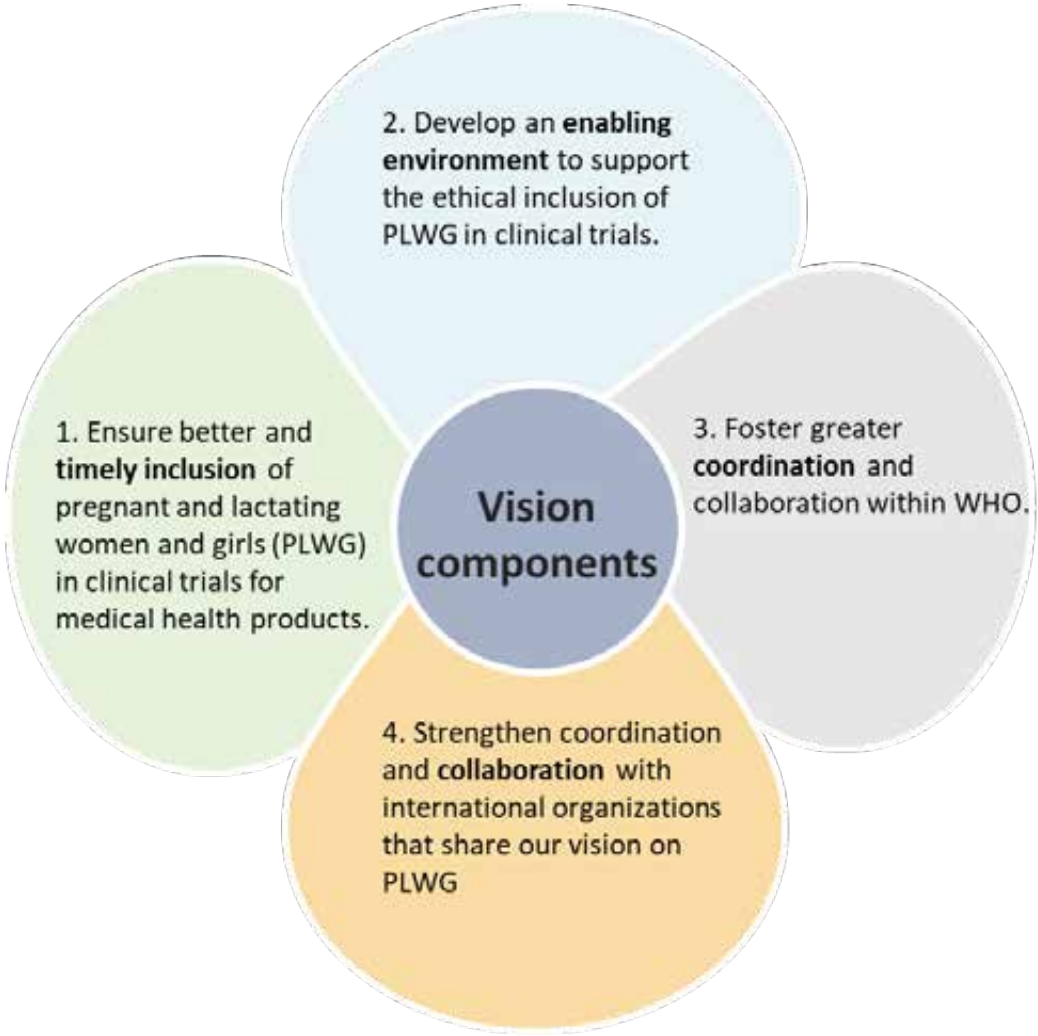
- Present on key initiatives in pregnant women, paediatrics and older people, also working on people with disabilities & migrant/refugee populations
- Breakout groups: discuss opportunities/challenges & future workplan



World Health Organization

Update 1- Pregnancy: WHO Pregnant and Lactating Women Task Force

- **Aim**: To align approaches and foster cooperation across WHO units and its partners in delivering core activities related to the WHA resolution 75.8.
- **Vision**: To achieve by 2030 timely and ethical inclusion of pregnant and lactating women in clinical trials for medical health products, by creating an enabling environment and fostering collaboration with international partners.
- **Priority activities**:
  - WHO observatory (technical advocacy and monitoring)
  - Call to action with disease agnostic framework
  - Disease agnostic toolkit
  - Language harmonization



World Health Organization

Call to action and framework

- Discuss the framework and its applicability to a set of priority diseases
- Adapt the HIV framework to highlight ‘common denominators’ (disease agnostic)
- Public consultation to get feedback from broad community of different stakeholders
- Publication, dissemination and advocacy

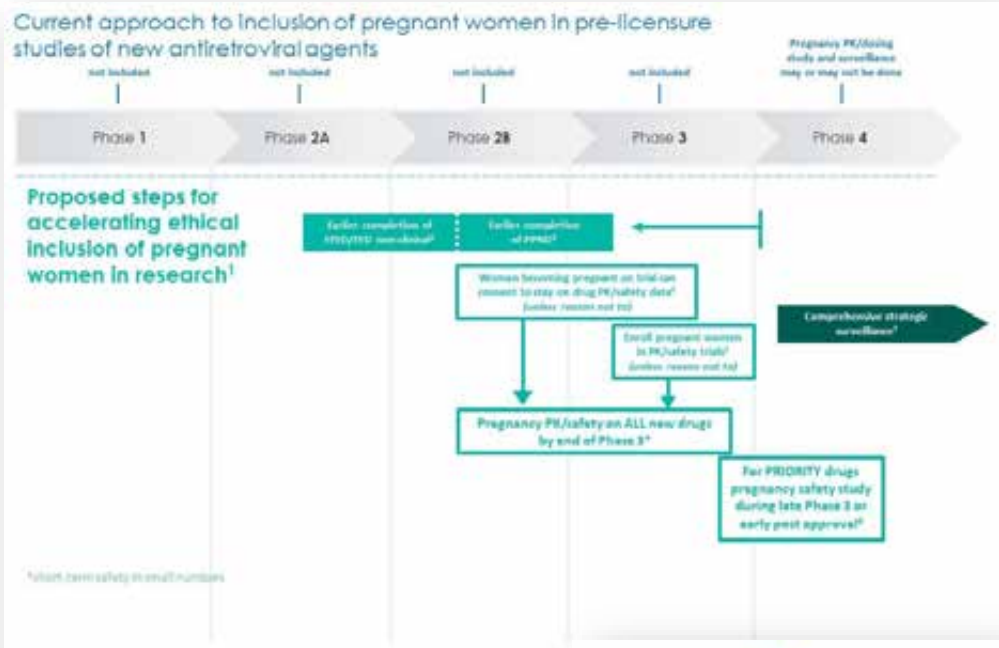


Figure 1. Framework and approaches to expedite the timeline for the study of
of childbearing potential living with HIV from the identification of research
and dissemination of results. (2) Perform non-clinical developmental and re
development for all new HIV agents. Fertility and early embryonic developm
should be completed during or no later than the end of the phase 2 registr
studies should be completed during early phase 3 or no later than the end of
nant in registrational trials should be given the option to make an informed
and EFD studies are completed, with no negative signals and dosing is establi
specific studies to determine pharmacokinetic (PK) and preliminary safety as
no negative signals for all new HIV agents. (6) Investigate adverse maternal, p
safety studies for all new priority HIV agents identified through CADO as soo
ous active safety surveillance studies to enable systematic and rapid detectio
defects associated with exposure to antiretrovirals during pregnancy.

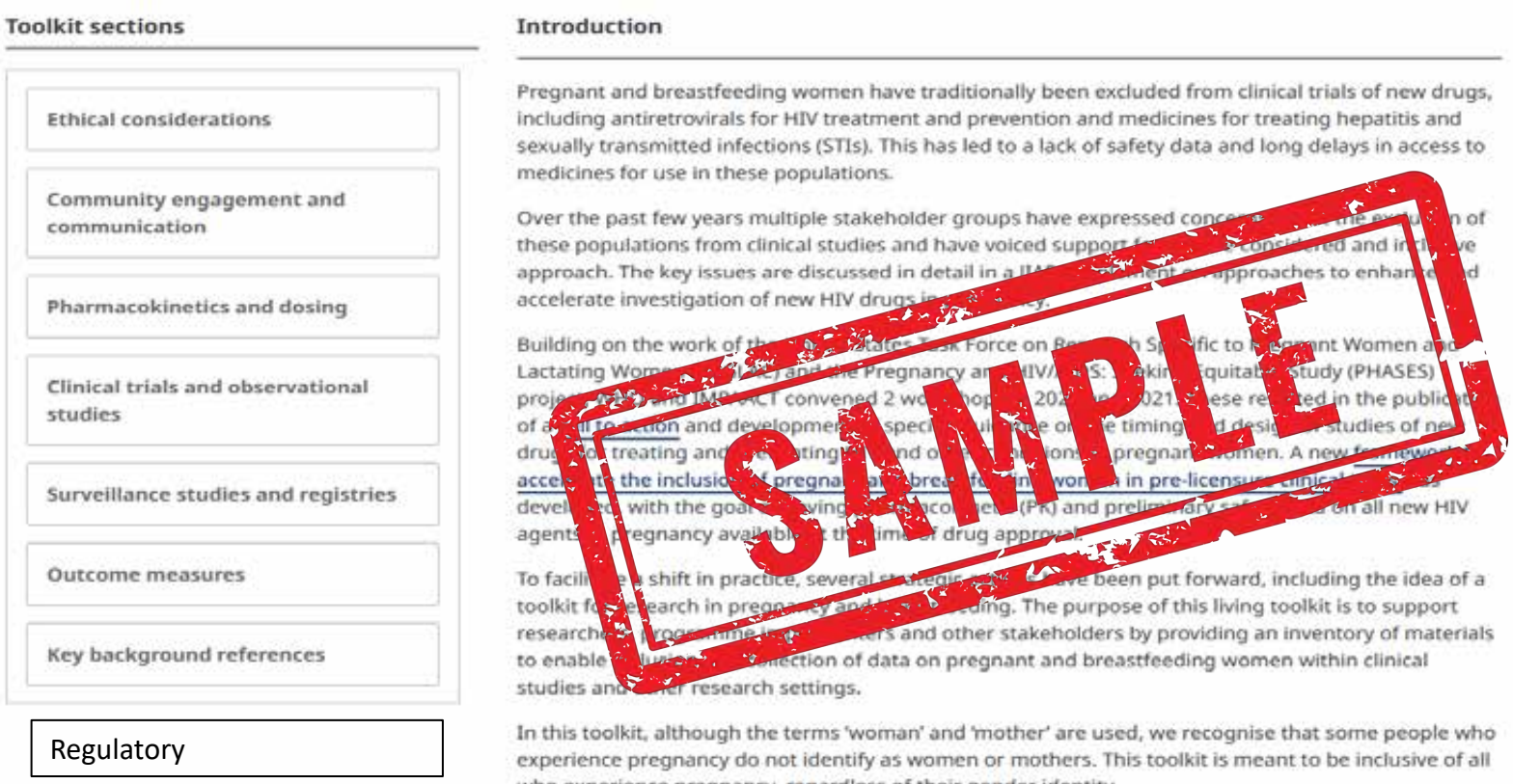
https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/call-to-action-to-accelerate-study-of-new-arv-for-pregnant-breastfeeding-women.pdf?sfvrsn=bb4febdc_14

World Health Organization

Generic research toolkit initial draft proposal

Guidance and resources to accelerate the inclusion of pregnant and breastfeeding populations in research.

- Design the structure
- Review HIV toolkit and select what to retain as generic content
- Discuss with Web-developer
- Signpost existing disease specific toolkits (i.e. HIV, TB, IVB)
- Initiate thematic specific modules (i.e. Malaria, antibiotics, maternal products, NTD, NCD, etc.)



HIV & STI

TB

Malaria

Maternal products

Antibiotics

NCD

IVB

NTD

World Health Organization

Update 2- Children: We have progressed with implementing the solution framework included in the Lancet series

Solution framework towards impactful evidence for children

Addressing shared barriers across groups

- Data & biospecimen governance
- Research leadership and capacity
- Infastructure & logistics
- Trial methodology
- National leadership and stewardship

Addressing barriers that are unique to children or particularly affect children

- Children are included
- Paeds specificities are considered
- Research Priority setting for policy change
- Coordination and collaboration to deliver accelerated high-quality research
- Enablers (ethics, funding, regulatory)


Series

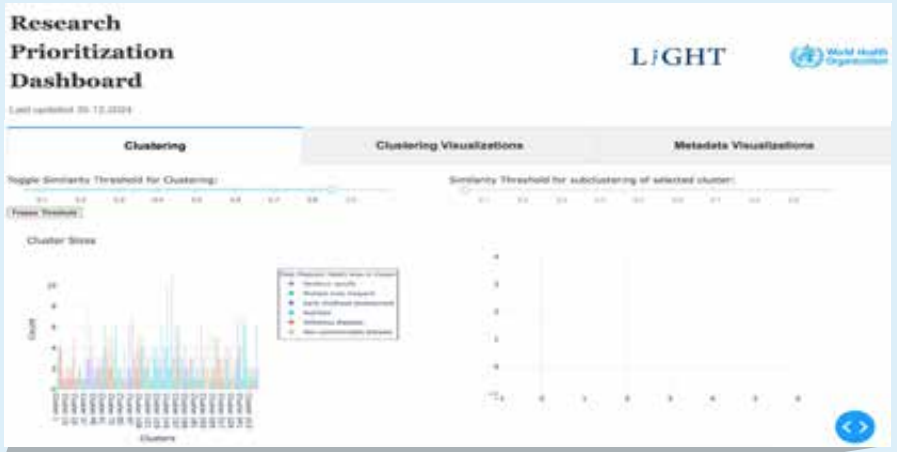
Clinical Trials in Global Health 2

Strengthening the paediatric clinical trial ecosystem to better inform policy and programmes

World Health Organization

Source: J. A. Berkley at al. Lancet Glob Health 2025; 13: e732–39

We completed a CHINRI process to prioritize research questions



653 considered for AI Clustering

Establish process managers, expert steering group & define context and scope
1

Global call for research questions
2

AI clustering, cleaning data, review & consolidation of question list
3

Scoring of research questions & data analysis
4

Stakeholder consultation: implementation considerations & actions
5

>380 respondents with 688 questions submitted

221 RQ after WHO / SG review & consolidation

171 research questions sent for scoring

World Health Organization

Scoring participants

Community / Advocate

7%

National health Authority / Programme managers

20%

Researcher

35%

Child health expert / practitioner

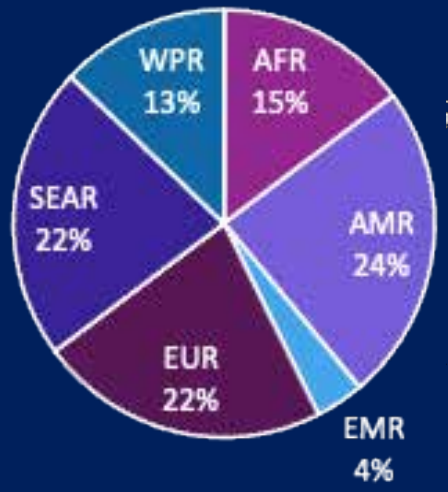
37%

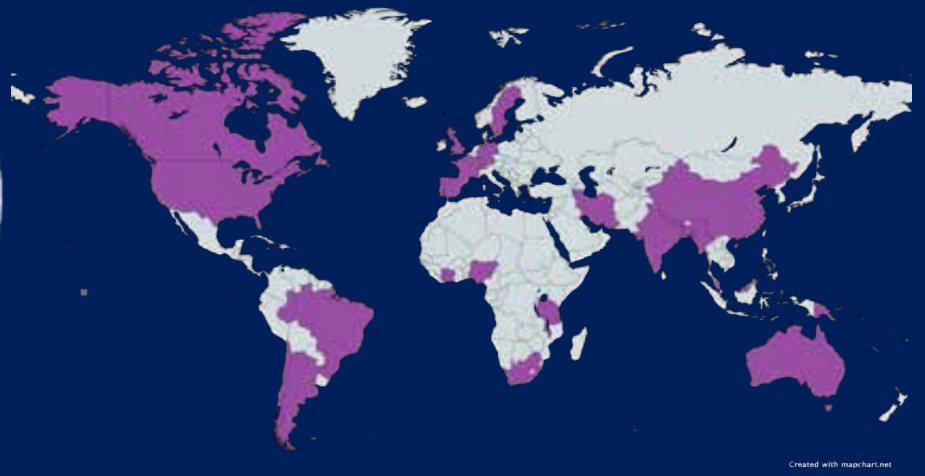
Shared with 99 external experts working in field of child health: researchers, programme managers/national health authorities, community representatives, implementing partners

57% Female

43% Male

Response rate:
54.5% (54/99)





Regional representation

World Health Organization

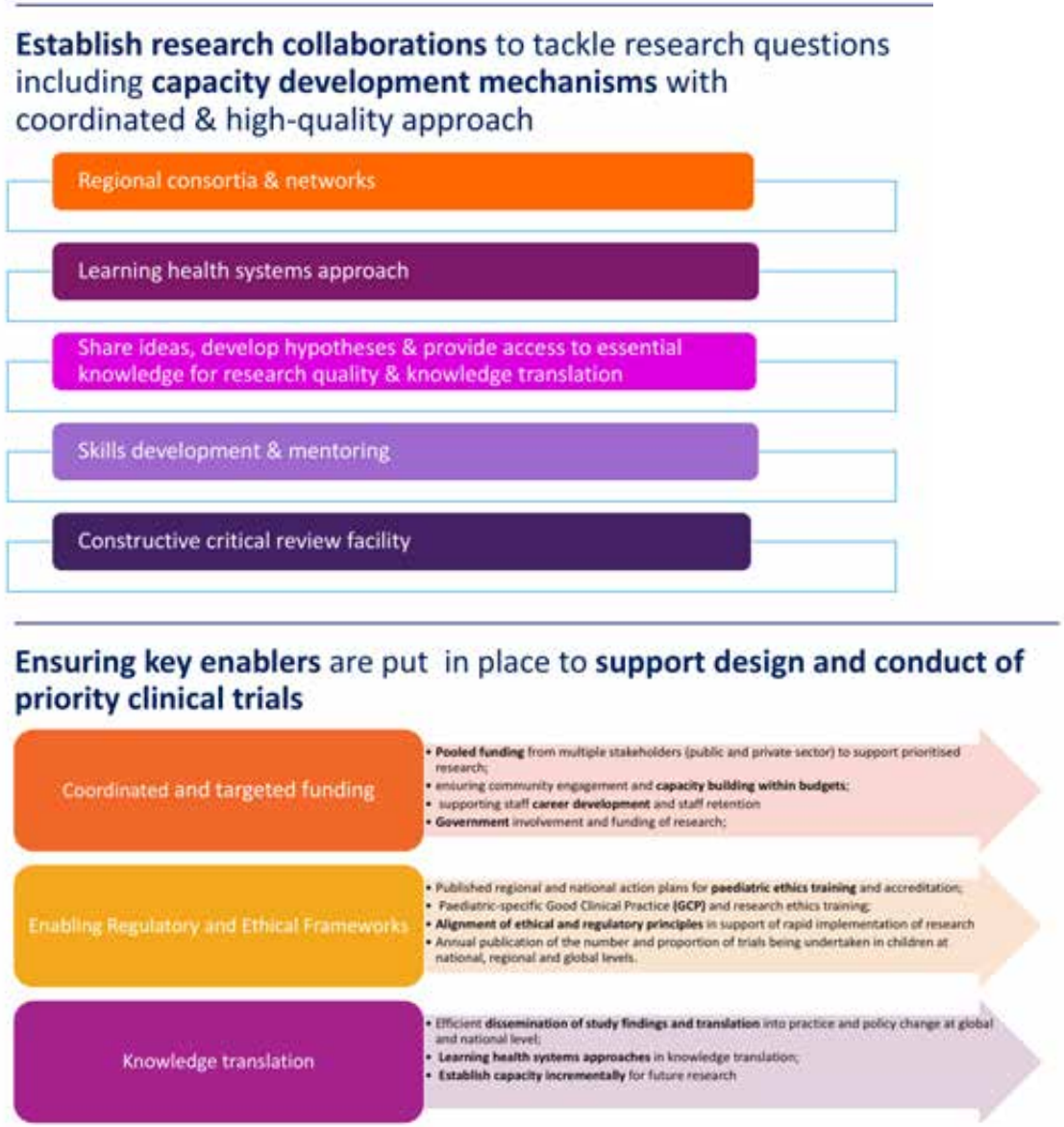
128

Top 5 ranked research questions: Overall

Rank	Research question	Health area	Impact	Equity	Answerability	Feasibility	Able to deliver and scale	Scientific value	AEA (%)	RPS (%)
1	What is the most effective and safest **fluid management** approach in children with wasting, presenting with severe dehydration and/or shock, when comparing slow IV rehydration to standard care? What is the associated impact on mortality at 24 hours, 28 days, and 6 months?	ID	0·95	0·93	0·98	0·90	0·94	0·93	95·2	93·8
2	In children under 5 years of age with **sickle cell disease**, does the implementation of malaria vaccination reduce mortality in the following 12 months?	NCDs	0·92	0·96	0·91	0·95	0·85	0·91	87·2	91·7
2	Can a simplified MUAC (mid-upper arm circumference) based treatment protocol, to admit children to treatment and to prescribe RUTF (ready-to-use therapeutic food) according to MUAC, be safely used to treat all children with **acute malnutrition**?	Nutrition	0·95	0·93	0·93	0·91	0·92	0·86	91·9	91·7
4	What is the effectiveness of **new ARV formulations** including long-acting injectables on viral suppression and drug resistance selection in children living with HIV?	ID	0·93	0·91	0·93	0·97	0·82	0·92	92·1	91·4
5	What is the effectiveness of combined Seasonal Malaria Chemoprevention (SMC) and Mass Drug Administration (MDA) with piperaquine/dihydroartemisinin (PA) and ivermectin on **malaria transmission and incidence** in children?	ID	0·95	0·92	0·96	0·91	0·88	0·86	92·1	91·2

Next steps to finalize prioritization and advance key enablers

- Refine prioritization among top 20 accounting for
  - Impact
  - Changing financial and global health landscape
  - Epidemiology
  - Ongoing research
- Develop training package for paediatric clinical trials to streghten clinical trial capacity
- Clinical trial site mapping and network of networks
- Leverage ongoing initiatives (ie WHO-supported trials, EDCTP funded trials, GAPf network etc) to promote



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Update 3: Methodology of Clinical Trials Involving Older People

Objective: Identification of critical recommendations aimed at improving the methodology of clinical trials in older persons

Research question of the scoping review (Scopus, Embase, PubMed):

"What are the critical recommendations for the conceptualisation, design (including how to reach older persons for recruitment), conduct, reporting, and dissemination of clinical trials in older persons?"

More than 4,700 articles screened to finally define 80 as of interest.

World Health Organization

Methodology of Clinical Trials Involving Older People

A total of 120 recommendations were retrieved by the scoping review.

Most highly cited recommendations from the literature

- Adopt broad eligibility criteria
- Consider meaningful outcomes for older persons
- Multistakeholder co-design of the clinical trial
- Consider alternative designs
- Consider stratifying the recruitment
- Consider the Comprehensive Geriatric Assessment in the evaluation
- Simplify the accessibility of the protocol methodology
- Specific training of research staff
- Multiple channels of communication for recruitment
- Plan strategies to ensure retention and adherence
- Offer pre-planned alternatives to full clinic visits
- Plan subgroup analyses (e.g., age, gender, race, frailty)

Additional recommendations from experts in LMICs

- Ensure age-friendliness of the research site
- Standardise nomenclature for clarity and consistency
- Use locally validated, culturally sensitive instruments
- Be aware of low literacy and cognitive impairment
- Community sensitisation before the recruitment
- Assess socioeconomic status, access to care, and health insurance status
- Define plans for clinical follow-up of participants
- Consider the burden on family and informal caregivers
- Ensure equitable access to research (i.e., transportation)
- Check local guidelines about using incentives
- Representative group for sample size calculation
- Subgroup analyses to compare rural vs urban areas

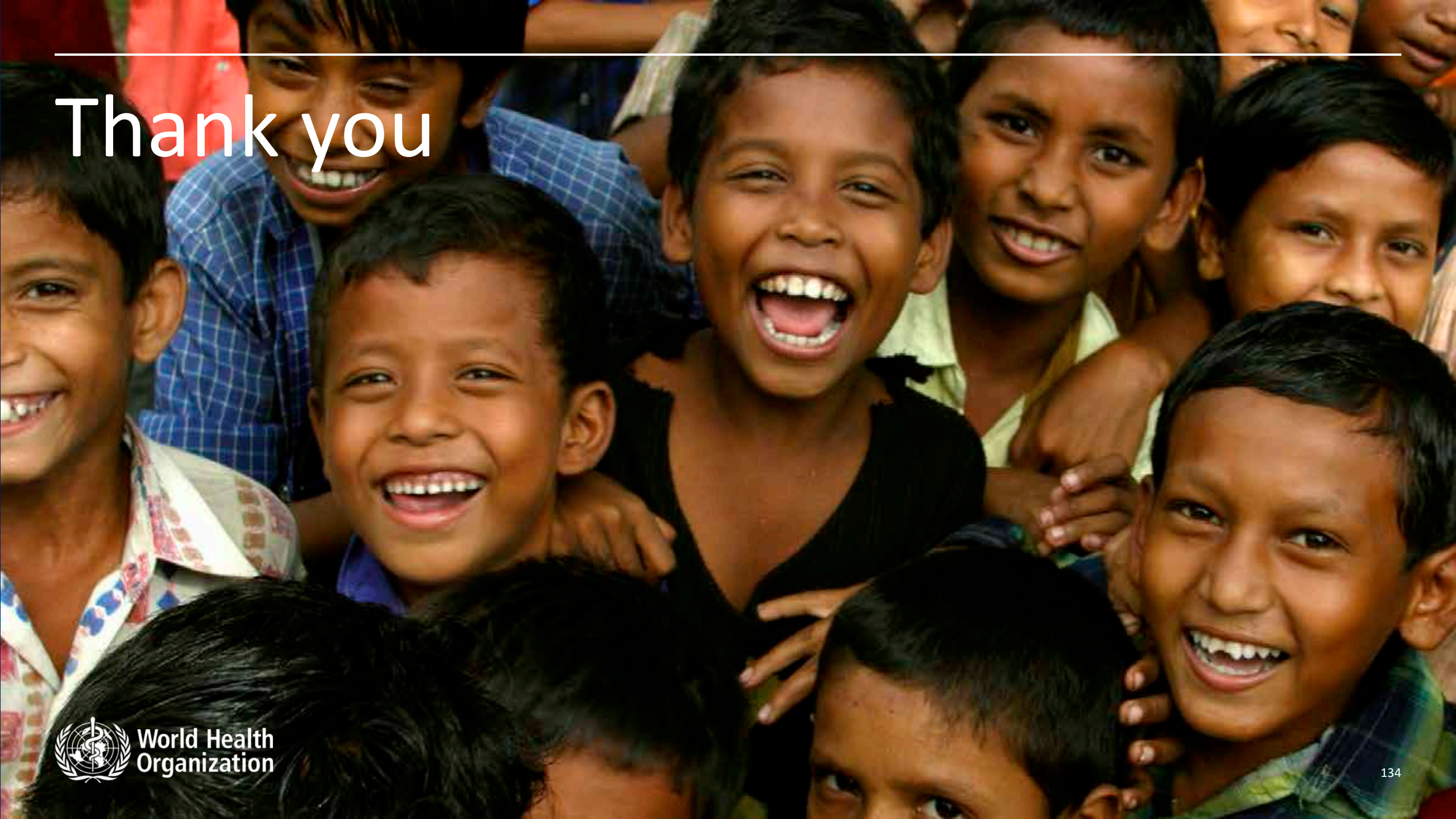
World Health Organization

What is next?...defining and promoting key enablers

Now that normative guidance is available how do we implement guidance so that regulators, funders, researchers routinely address the needs of under-represented populations?

World Health Organization

Thank you



World Health Organization

Draft disease agnostic framework

Objective: To guide stakeholders on key considerations for including pregnant women in clinical trials, ensuring robust clinical data that supports evidence-based decisions on the safe and effective use of medicines for this population and their healthcare providers.

World Health Organization

Considerations

- Sponsors are encouraged to consider strategies to generate data to support informed decisions on the safety, dosing, and efficacy of medicinal products during pregnancy and breastfeeding.
- Consultations with regulatory authorities on the plans for the participation of pregnant women in clinical trials is advised.
- It is important to evaluate the risks and benefits based on all available data, with appropriate risk mitigation and scientifically robust study design.
- If the sponsor determines that proceeding with trials in pregnancy is not yet reasonable, they should seek to obtain further data unless there is a rationale for not studying the investigational product in pregnancy.
- PK data should be used to determine appropriate dosing for pregnant women. It is essential to include in the protocol whether pregnant participants should receive the same or a different dose than non-pregnant participants.
- If the sponsor determines that proceeding with trials in pregnancy is appropriate, the following specific approaches should be integrated into the development strategy :
  - For pregnant women-only studies: conduct dedicated studies specifically designed to be conducted in pregnant women if needed
  - For studies with women without mandatory contraception: allow continued participation of women who become pregnant during clinical trial.
  - For studies with women under mandatory contraception: Remove mandatory contraception requirements in ongoing and/or subsequent clinical trials.
- A decision must be made regarding whether women who become pregnant despite mandatory contraception should continue the investigational product. While continuation is often inappropriate, exceptions may exist. Factors to consider in the decision-making are:
  - Existing safety data
  - Participant's health status: current health, pregnancy status and underlying condition.
  - Risks of treatment suspension: potential disease exacerbation, suitability or teratogenicity of alternative treatments, or impact of the disease on pregnancy.
  - Loss of potential benefit: possible effectiveness of the investigational product in improving the underlying condition.

Accelerate access to fit-for-purpose training packages for clinical trials.

What training is available where? What are the barriers to access and implementation… what's missing ?

Denis Xavier – Professor & Head, Pharmacology; Clinical Research & Training St. John's Medical College and Research Institute, India

Trudie Lang, Director. The Global Health Network,

Nick Medhurst – Head, Good Clinical Trials Collaborative, Protas, UK

Jean Bourbeau, Professor of Medicine, **Julie Dessureault,** Chief Transformation Officer, **Lisa Goos** – Chief Operating Officer, CANTRAIN, Canada

Barbara Bierer – Faculty Director, Multi-Regional Clinical Trials Center (MRCT), Harvard University, USA

Mo Yin – Senior Lecturer, NUS Saw Swee Hock School of Public Health; Consultant, Division of Infectious Diseases, National University Hospital, Singapore

Our Underpinning Principles

The WHA resolution; the WHO guidance for clinical trials and the ICH GCP revision R3

Together present the most significant opportunity for decades to level the playing field in where trials happen & who benefits

Adaptable incl. Wider application

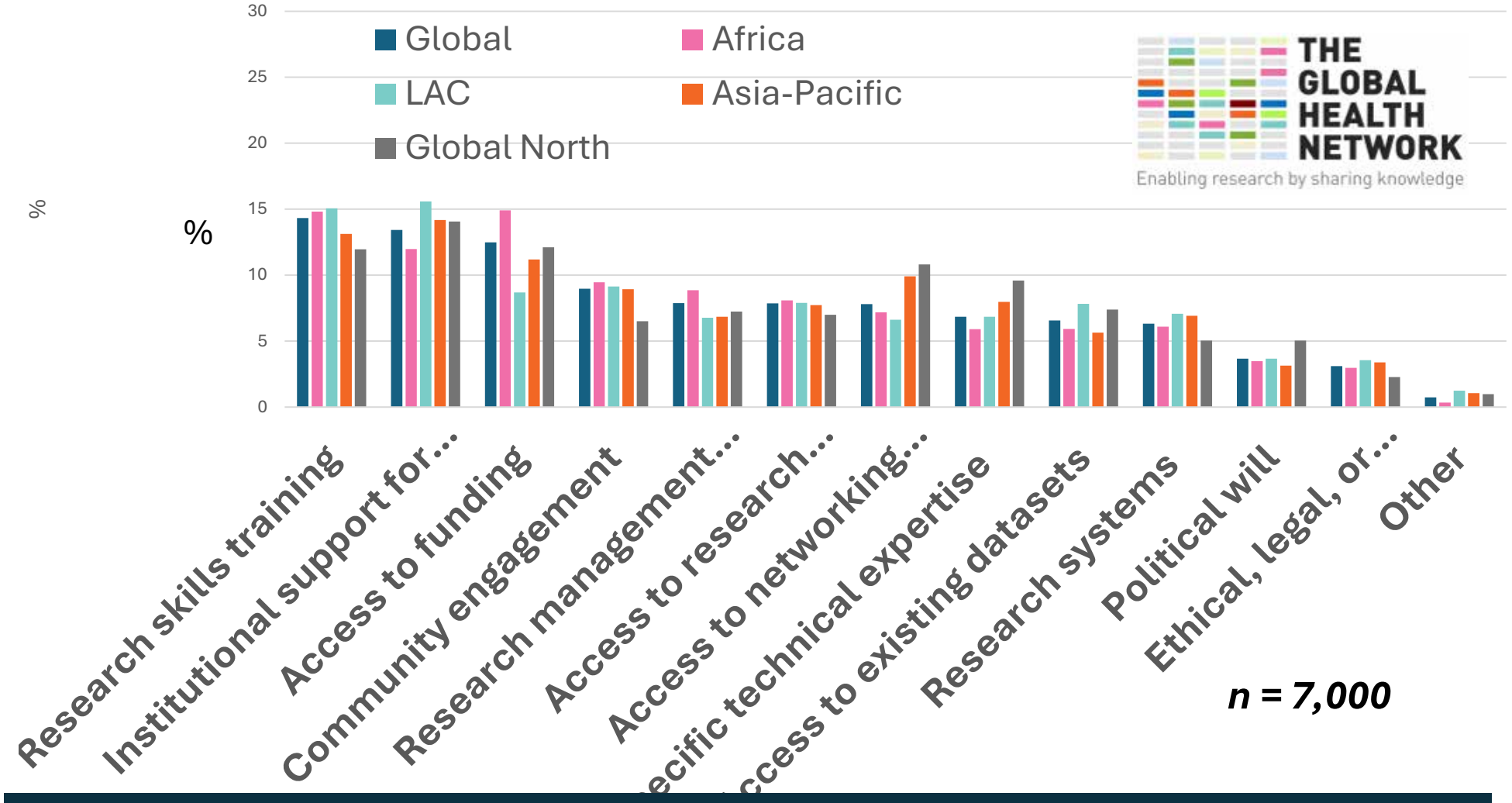
IF equitably taken up globally
- could be transformational.
If **NOT**– the gap could widen

Data Science

Need to ensure training and resources are accessible, everywhere for maximum Implementation and everyone benefits

Community engagement

Training is the highest barrier to clinical trials



THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

Many groups are tackling these gaps – how can these training initiatives be better taken up?

What is important to enable effective implementation across various research settings to ensure equitable uptake and benefit?

Training includes more than formal instruction:

Access to tools, guidance & resources

Goal: Equip research teams to adapt and apply

Align with new ICH-GCP R3

Learning should be ongoing & responsive – appropriate for different roles, step and career

We need to better understand to tackle Barriers to Training and Implementation – these could include:

- Local requirements vary widely
- Limited access and high costs
- Lack of awareness and necessary permissions
- Language, access to screens….

There is free, high, quality training :
WHO setting up a clinical trials training hub

- **Repository of what is where**
- **Be inclusive, agile and responsive**
- **Signposting and filling the gaps**
- **Training and also implementation tools**
- **Input sought …. Come to the breakout!**

Barriers for CT training : A quick survey

St John’s Medical College and Research Institute, Bangalore ran a quick survey (ongoing)

Interim results: 286 responses from 16 counties (75% India).

Women 47%; participated in a clinical trial 47% ;

formal education (degree or diploma) in research/ CTs 12%

Regarding CT courses (formal or short term), aware 47%

Barriers for CT training : A quick survey

Perceived barriers (in order)

1. Inability to find the right course
2. Insufficient time
3. Funding
4. Institutional support
5. Personal motivation

Factors influencing choice of course (in order)

1. Hands-on training and mentorship
2. Faculty expertise
3. Content of course
4. Career advancement
5. Certification

This is down to us all

Collective responsibility to implement WHO guidance effectively

Request for contributions: ideas, tools, collaboration – who is doing what and where

Please join us in the breakout session

Streamlining Regulatory and Ethics Review in Indonesia

Indri Rooslamiati Supriadi

Director of National Center for Biomedical and Health Genomics and Indonesia Clinical Research Center (INA-CRC)
The Ministry of Health of Indonesia

The 2nd WHO Global Clinical Trials Forum

Geneva, 2 April 2025

Enhancing Clinical Trial Ecosystem through Indonesia Clinical Research Center (INA-CRC)

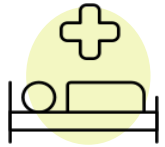
Indonesia Clinical Research Center

INA-CRC serves as **the primary contact for sponsor-initiated multicenter clinical research** activities in Indonesia

VISION INA-CRC

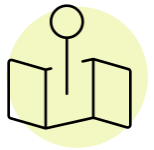
Indonesia as **a center of excellence for clinical research** in the Asian region

MISSION INA-CRC



Clinical research facilitator

Capacity building of Clinical Research Unit (CRU)



Clinical Trials Agreement negotiation support

- The new regulation **recommends hospitals to establish a Clinical Research Unit (CRU)** to strengthen the research ecosystem
- Integrating **Primary Health Care** as clinical research and trial sites

Improve **speed**

Improve **resources**

Build **public trust**

The Ministry of Health is working to continuously simplify the Regulatory Landscape, to improve transparency and accelerate approval process

Material Transfer Agreement (MTA) Services

Type of the MTA	Criteria
EXEMPTED (6-11 WD)	**Less/No Risk** Laboratory quality control, external quality assessment, proficiency testing services
EXPEDITED (9-24 WD)	**Medium Risk** Research for non-clinical trial For education
FULL BOARD (16-26 WD)	**High Risk** Multicenter clinical trials, complex procedures, commercialization, Data Transfer Agreement

https://mta.kemkes.go.id/

National Health Research Ethical Committee

- Ethical approval for multicentre research **(single approval for multi sites trials)**
- Independent
- Guidance to other Health Research Ethics Committees

Indonesia Clinical Research Registry (INA-CRR)

- Clinical Research Registration is a **mandatory**
- Managed by the Ministry of Health
- Integrated into the National Health Information System

https://ina-crr.kemkes.go.id/

Clinical Trial Approval

- For **drugs and vaccines issued by BPOM (The Indonesian FDA)**
- For **medical devices issued by The MoH**
- **20 working days** to each respond

https://siap-uk.pom.go.id/

Synergy for Strengthening the Clinical Research Ecosystem

Patients and community

- Community engagement
- Building research literacy
- Easy access to medicine
- Benefits for patients/community

Hospitals/CRUs

- Hospital's commitment
- Develop infrastructure
- Improve human resources capacity
- Conduct clinical trials

Government

- Simplify regulations
- Coordination with BPOM (the Indonesian FDA)
- Capacity building of CRU
- Incentives clinical trials at its hospitals
- Digitalization (EMR, MTA application, INA-CRR)

Other stakeholders

- Sponsor
- CRO
- Central Lab
- Pharmaceutical company
- Health tech-start up
- Professional association

Kemenkes

Acknowledgement

- Directorate General for Advanced Healthcare
- Directorate General for Pharmaceutical and Medical Devices
- BPOM (Indonesian FDA)
- Material Transfer Agreement Committee
- National Health Research Ethical Committee

INA-CRC Team

Kemenkes

2nd Global Clinical Trials Forum, 2-3 April 2025
WHO Science Division, Geneva, Switzerland

A roadmap for fostering timely regulatory and ethics approvals of international clinical trials in support of global health research systems

Marco Cavaleri, Claudiosvam M Alves de Sousa, Adam Hacker, Elisabeth S Higgs, Murray M Lumpkin, Christiane S Maia, Roli Mathur, Adam M Fimbo, Andreas Reis, Kyoung Seung Shin, David W Vaughn, Wei Zhang, Vasee Moorthy

World Health Organization

VISION

- ***Enable across countries and regions consistent and timely regulatory approval of clinical trials that are scientifically sound and can generate meaningful evidence to trigger regulatory and/or public health authorities decisions***

- ***Regulatory and ethics communities need to remain updated and informed to actively support innovations, new tools, and approaches to increase trial efficiency by streamlining their conduct***
- ***Prepardedness for emergencies: always on and always ready***

- ***A roadmap of actions and reforms is proposed to improve the ecosystem of clinical trials at global level***

A roadmap for fostering timely regulatory and ethics approvals of international clinical trials in support of global health research systems - ScienceDirect

World Health Organization

Proposed Roadmap

Leveraging existing clinical trial networks and capacity building

- Build capacity to enhance sustainable clinical trial infrastructure following maturity level three clinical trial oversight indicators.
- Maintain always active clinical trial networks.
- Develop experience in areas of weakness within the ethics and regulatory authorities.
- Create a forum for discussion among regulators, ethicists, and research community

Advancing the single Research Ethics Committee (REC) model per country for multicountry trials

- Map established processes, timelines, and legislation in place with respect to RECs in all countries.
- Benchmark REC capacities with the use of the WHO Ethics Committee global benchmarking tools
- Provide central reviews by a Designated Central RECs for core information when variable portions undergo local ethics review.
- Develop approaches for mutual recognition and reliance of trusted ethics review committees' decisions.

World Health Organization

Proposed Roadmap

Move to parallel regulatory and ethics reviews for clinical trials as a norm

- Provide joint pre-submission meetings and scientific advice between trial sponsors, ethics committes, and regulatory authorities.
- Map the overall clinical trial approval process in countries including roles, responsibilities, fees, and timelines.
- Institute any needed regulatory and legal changes to allow parallel review by ethics and regulatory bodies within a country.

Implementation of joint review for clinical trial application (CTA) between relevant NRAs and RECs for priority multi-country trials

- Strengthen regional clinical trial application assessment forums such as African Vaccine Regulatory Forum.
- Establish similar forums to African Vaccine Regulatory Forum in other regions if not available.
- Establish inter-regional forums to simplify the connections and interactions across regulators from different regions.

World Health Organization

Proposed Roadmap

Transparency as to documents needed for NRA or REC approvals per country through a public database

- Develop a global database that would define regulatory and ethics requirements and timelines in all 195 WHO member states
- Develop a common CTA technical document (analogous to the common technical document for marketing authorisations) with a core national module.
- In a second step, consider moving to a single electronic submissions system per country or even across countries for the core part

Informed consent forms and process should be simplified and standardised to the extent possible

- Define and develop models for patient-centric informed consent.
- Update templates.
- Raise example of simplification to foster streamlined approach and better subject comprehension.

World Health Organization

World Health Organization

World Health Organization

African Region

AVAREF
African Vaccine Regulatory Forum

AVAREF's role in improving the coordination and streamlining of regulatory and ethics reviews in Africa

2 April 2025

Kwasi Nyarko
AVAREF Secretariat
WHO-AFRO, Brazzaville

UHC/UCN
Universal Health Coverage/Communicable and Noncommunicable Diseases

Outline

- AVAREF – Role in Regulatory and Ethics Reviews
- Next steps in improving efficiency/coordination of clinical trial approval processes?
- Conclusion

AVAREF – Role in Regulatory and Ethics Reviews

AVAREF – Role in Regulatory and Ethics Reviews

- Using an ecosystem and life-cycle approach, AVAREF, through its capacity building activities and platform enhances excellence, harmonization, and strengthening of regulatory and ethics systems for clinical trials in the 55 member states in Africa.
- AVAREF's Signature offerings for member states, developers, and sponsors include:
  - Multi-country Joint Reviews and/or Scientific Advice for Clinical Trial Applications
    - Essential Medicines for Africa, Neglected Tropical Diseases
      - Malaria vaccines, Lassa fever, Tuberculosis, etc.
  - Facilitated Registration of therapeutics during public health emergencies
    - Ebola, COVID-19, Mpox
  - Clinical Trial Ecosystem Optimization Assessments
    - Increase timelines for decision making, quality of reviews, NRA/NEC collaboration
      - Rwanda, Ghana, Nigeria, Kenya, Uganda, Ethiopia, Zambia

Next steps improving efficiency/coordination of clinical trial approval processes?

- Evidence informed activities and initiatives including:
  - A priority on human resource capacity strengthening – Applied biostatistics for reviewers.
  - A focus on francophone and Lusophone member states including offering continuing education in French, and Portuguese.
  - Integration of emergency preparedness into capacity building.
- AVAREF Clinical Trial Pilot Project as a 16-member country reliance network.
- Enhanced partnerships and alliances for results:
  - NRAs such as EMA, PEI, AUDA-NEPAD, EDCTP, Gates Foundation, Wellcome Trust, CEPI, etc.
- Increasing the number of clinical trials in Africa.
- Alignment with operationalization of the African Medicines Agency (AMA).
  - AVAREF as precursor for regulatory and ethics oversight for clinical trials.

World Health Organization

African Region

THANK YOU

AVAREF

African Vaccine Regulatory Forum

UHC/UCN

Universal Health Coverage/Communicable and Noncommunicable Diseases

NIHR | National Institute for Health Research

2nd April 2025, Geneva

Advancing Clinical Trials in Primary Health Care

Strengthening the Evidence Base for Universal Healthcare

Professor Andrew Farmer

Primary Care Health Sciences, University of Oxford
Programme Director NIHR Health Technology Assessment Programme
Emeritus NIHR Senior Investigator

Declarations

I have no competing interests.

I am employed by the University of Oxford, receive grant funding from NIHR and am the Director of the UK's NIHR Health Technology Assessment funding programme.

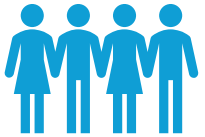
The views expressed are those of the presenter and not necessarily those of the NHS, the NIHR or the Department of Health.

The case for primary health care clinical trials

…"75% of the projected health gains from attaining the Sustainable Development Goals could be achieved through primary health care…"

Primary care trials drive cost-effective, scalable health improvements

Real-world evidence from primary care trials improves policy and practice



Research needs to include people for those who would benefit if effective

Stronger primary care reduces hospital admissions and improves life expectancy

Case Study: STRETCH

Articles

Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial

Lara Fairall, Max O Bachmann, Carl Lombard, Venessa Timmerman, Kerry Uebel, Merrick Zwarenstein, Andrew Boulle, Daniella Georgeu, Christopher J Colvin, Simon Lewin, Gill Faris, Ruth Cornick, Beverly Draper, Mvula Tshabalala, Eduan Kotze, Cloete van Vuuren, Dewald Steyn, Ronald Chapman, Eric Bateman

- Question arose from patient activism and agency
- Embedded in routine systems
- No individual consent
- Routinely collected data as follow up
- Results embedded into routine care, strengthening PHC system
- Influenced policy to save many lives

Panel 2: Innovation in HIV care delivery

The Streamlining Tasks and Roles to Expand Treatment and Care for HIV trial addressed the urgent problem in South Africa of high mortality and morbidity among people with HIV whose initiation of antiretroviral treatment (ART) was delayed by shortages of doctors authorised to prescribe it. The trial evaluated a complex intervention comprising nurse initiation and monitoring of ART (NIMART), supported by a clinical decision guide, staff training, organisational strengthening, and managerial and clinical support. The trial was conducted in all 31 primary health-care clinics that provided ART in one province, 16 of which were randomised to receive the intervention. Use of electronic medical records to identify eligible participants and measure outcomes enabled rapid recruitment of over 15 000 participants and completion of the trial in 2 years. With research ethics committee approval, participants' consent was not sought because it was not feasible and because it would not affect the care individuals received. The trial showed that the intervention did not affect mortality or virological suppression but was associated with better health and HIV programme outcomes. These improvements were despite unanticipated real-world problems including some intervention clinics being unable to deliver NIMART, and a temporary moratorium on ART initiation because of financial restrictions. The trial results coincided with and supported the change of national policy on NIMART, leading to rapid expansion of ART to millions of people with HIV in South Africa, and task shifting in HIV care in other low-income and middle-income countries. Policy relevance and effect was strengthened by long-standing engagement between the researchers and provincial and national health departments, with senior government officials represented on the trial steering committee. This primary care trial exemplifies pragmatic design, efficient use of medical records, appropriate ethical regulation, and timely production of results to influence policy.[23]

Funding: UK Medical Research Council, Development Cooperation Ireland, and Canadian International Development Agency

ENHANCE

EvideNce led co-created HeAlth systems interventioNs for MLTC-M CarE

Funding: UK NIHR

PANORAMIC

Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 In the Community

65 Hubs, 4509 GP practices

>120,000 Screened

25,708 randomised to molnupiravir vs usual care

Funding: UK National Institute for Health and Care Research (NIHR)

Strengthening primary health care requires both impactful research and the right conditions to make that research possible

- Responsiveness to Population Health Needs
- Integration with Primary Care Systems
- Strategic Engagement and Incentivization:
- Workforce Development

NIHR Clinical Research Network Primary Care Strategy, 24 February 2022

https://www.thelancet.com/series/clinical-trials

Challenges for building primary care research capacity

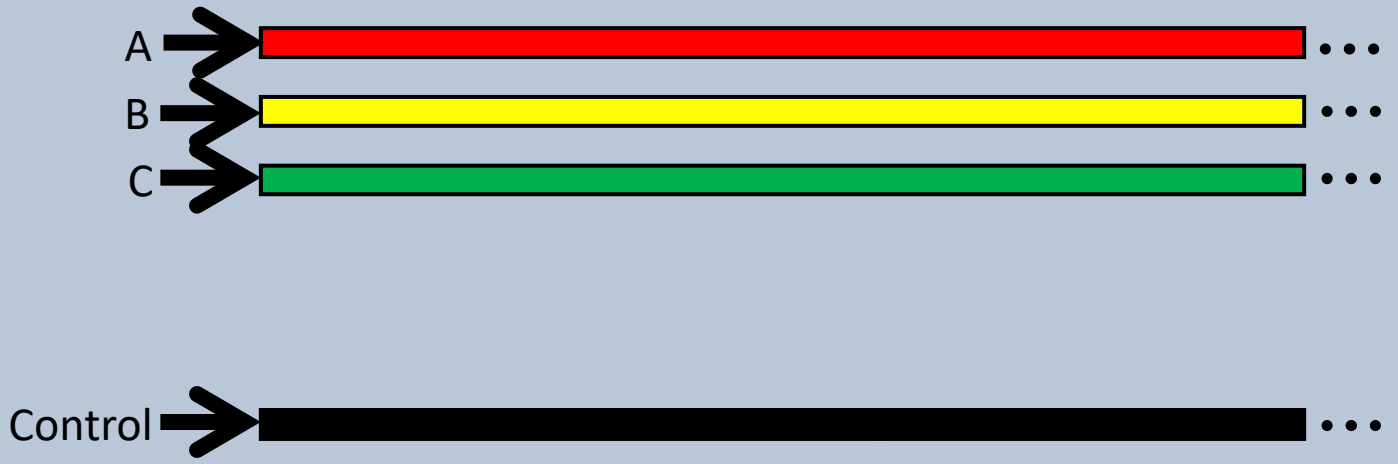
Based on - Ponka D et al: BMJ *Global Health* 2020;5:e002470.

- Need to provide mentorship and accountability for training
- Advocacy for protected research time
- Formal training and remote support
- Cross appointments needed across disciplines
- Consortia and equitable partnerships

Innovation in Participant Recruitment

“Patient comes to the research”	**“Taking trials research to the patient** (TTRTP)”
GP practices set up as sites Hub and Spoke model	UK wide access through website: clinicians, care homes, patients themselves register potential participant
Paper/practice record, face-to-face consent	Online consent
Site clinician confirms eligibility	Central eligibility check using summary care record or information form patient and GP
Study medicine stored at every study site and issued to patient by study clinicians	Medicine and study materials couriered to patient’s home
	Follow up by study team, online, telephone, trial partner, routinely collected data

Adaptive Platform Trial have the potential for faster, more efficient, flexible and data-driven decision-making



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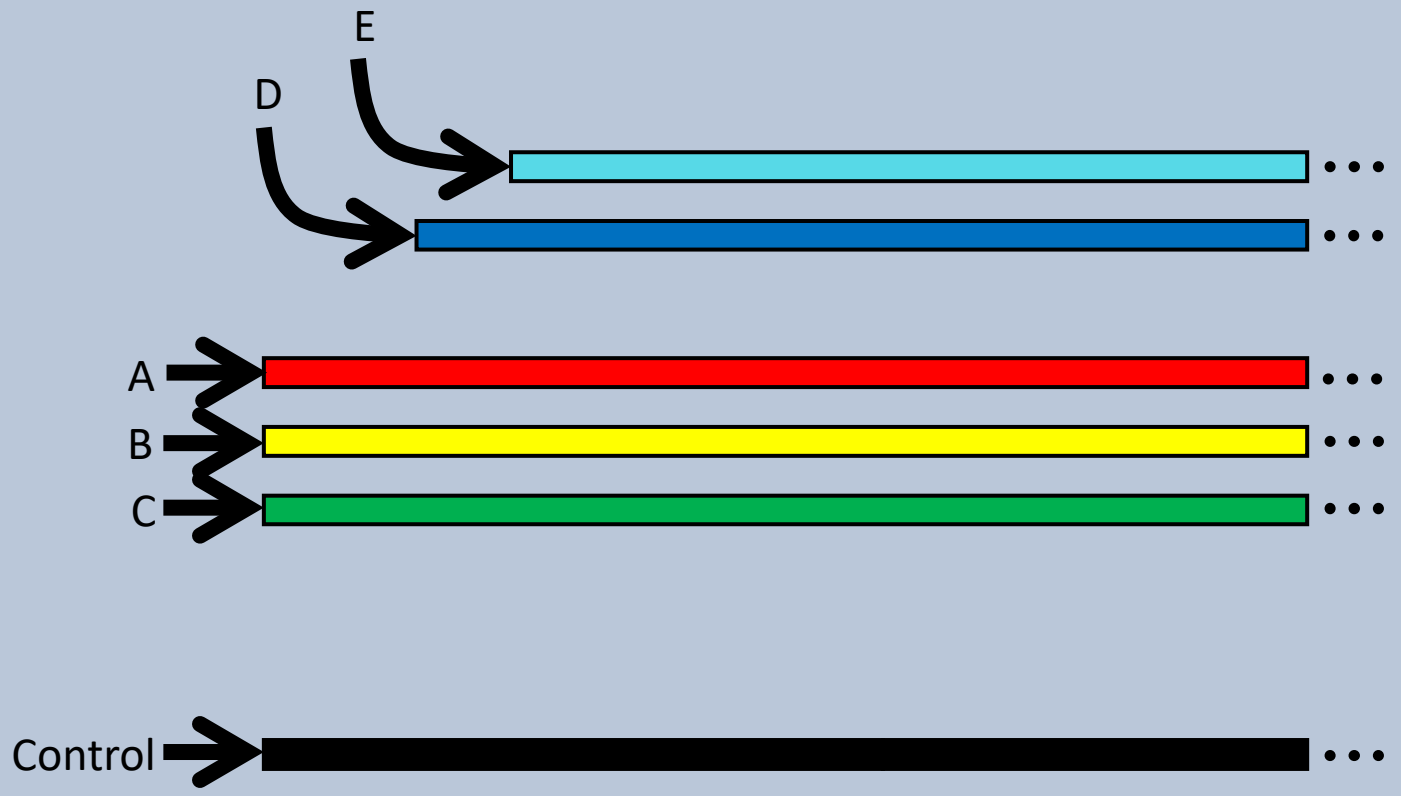

UNIVERSITY OF OXFORD

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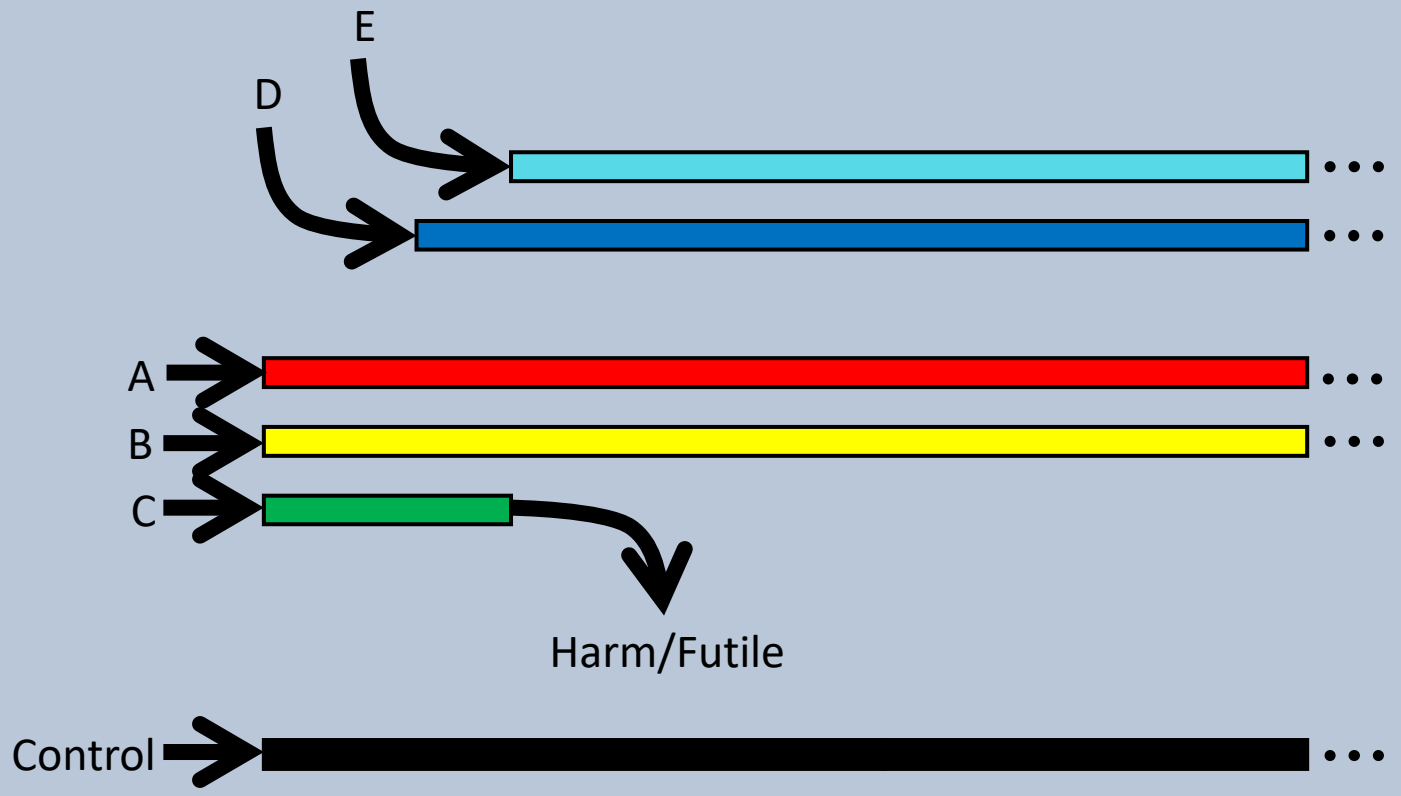

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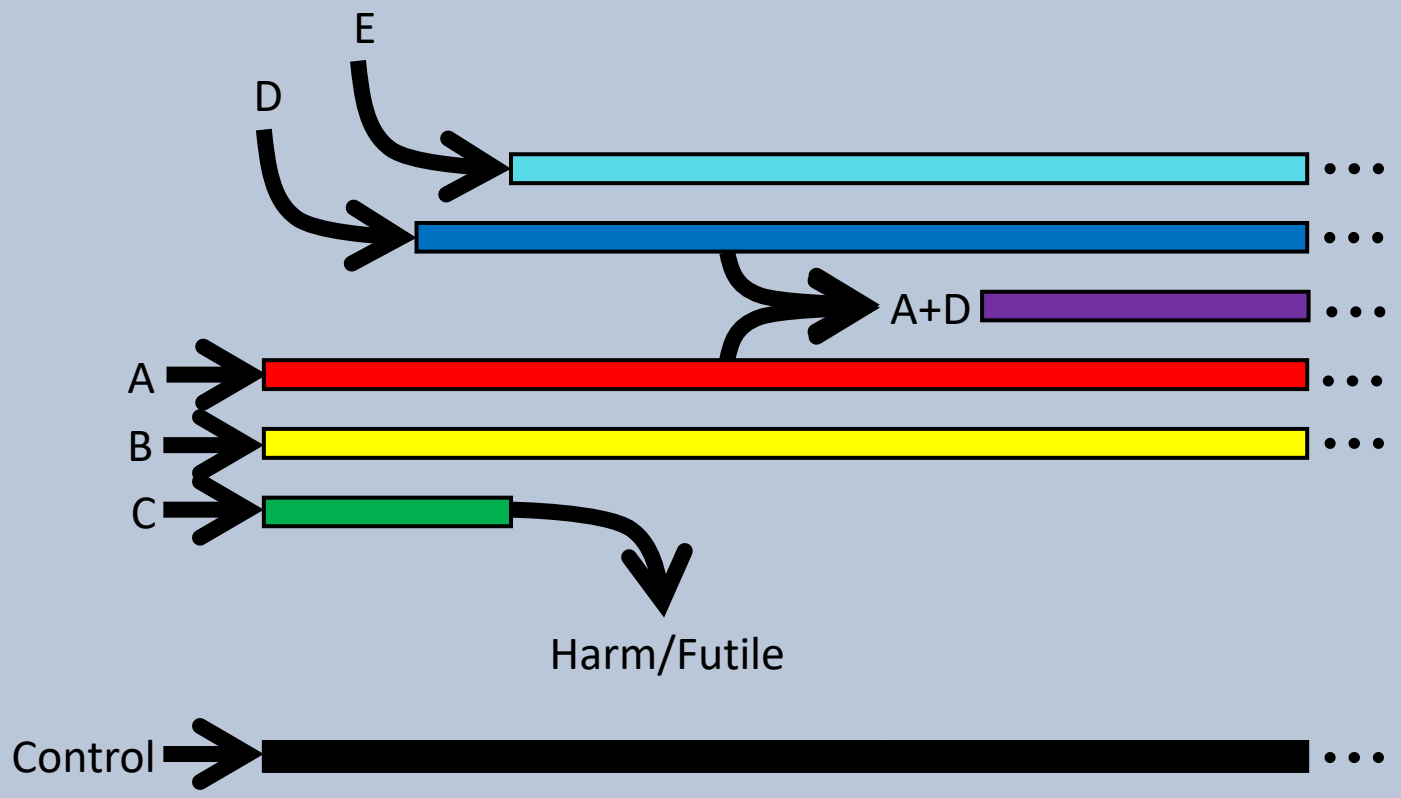

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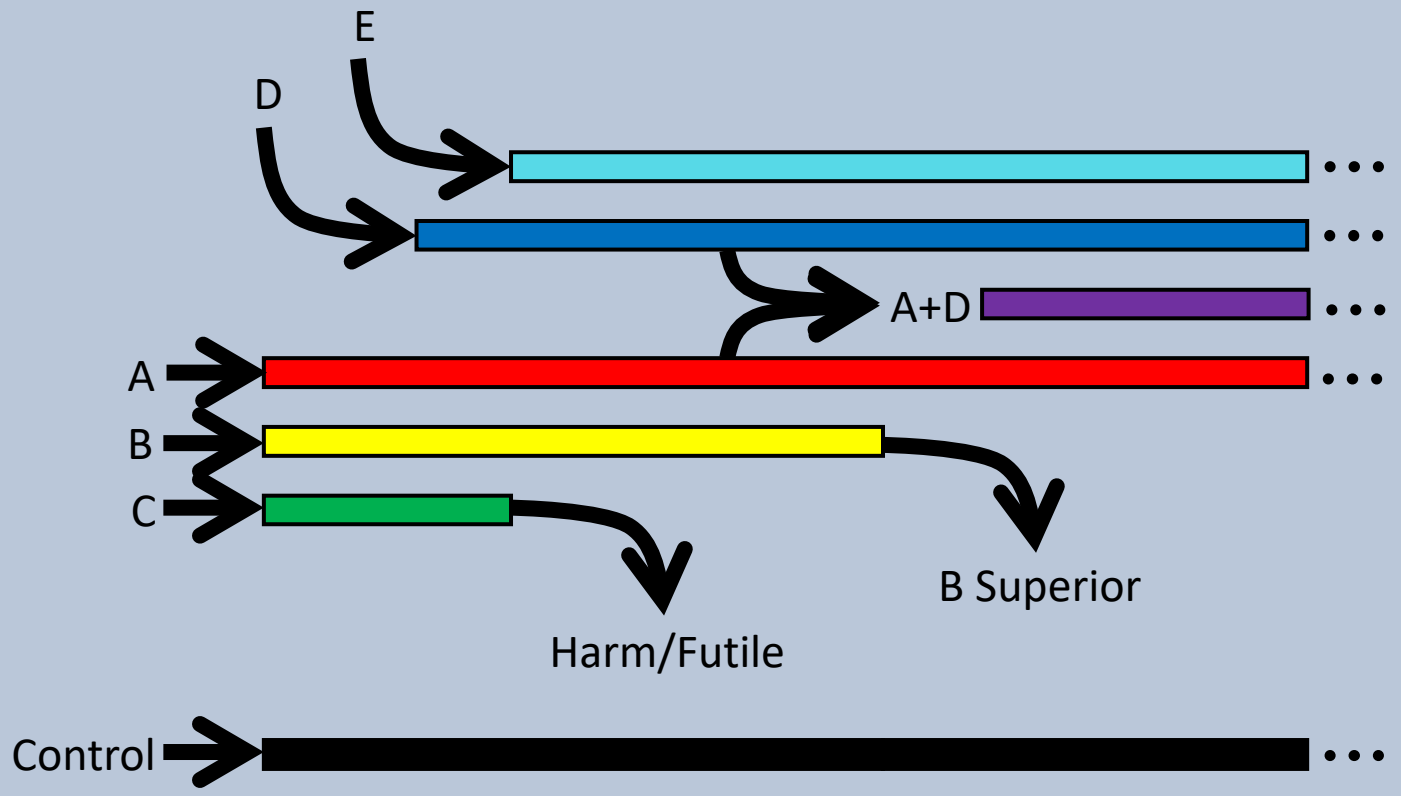

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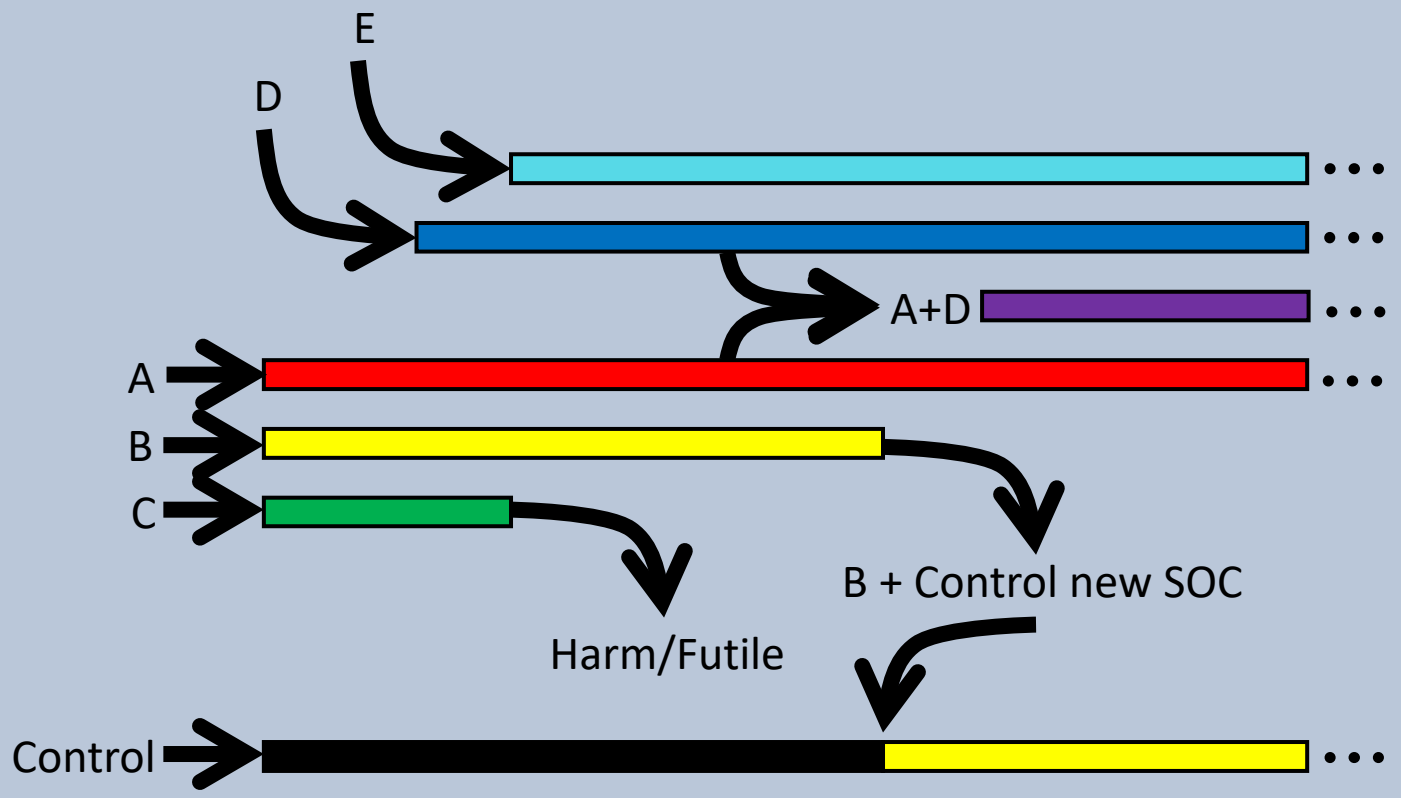


UNIVERSITY OF OXFORD

Patients and communities engaged at all stages of research

- Involving patients, the public and communities in research
- Community engagement must meet the needs of those who would benefit from the research
- Partnerships with patients and the community needed to build trust
- Community engagement needs to be long-term

Primary healthcare research can appear fragmented with underpowered trials that lack wide applicability

- Large scale, impactful, embedded trials need to thrive in the settings where the findings can be used
- We need globally coordinated studies that tackle shared challenges—ageing populations, disease prevention, and the future of care delivery.

Next steps to advance clinical research in primary health care

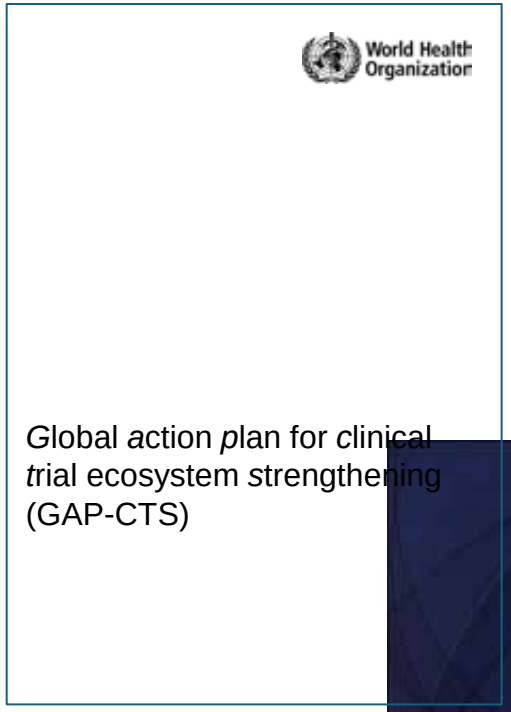
- Identify the resources already available globally that could work synergistically
- Size the opportunity of the CTS initiative to develop networks and actions
  - Convene and collaborate communities of primary health care clinical trial researchers
- Shared tools
  - Information sharing
  - Recruitment strategies
  - Master protocols (including capacity for contextualising trials e.g. service delivery models
  - Innovations in primary care delivery
- Embed trials in clinical care – develop novel designs for primary care clinical trials
- Identify the rate limiting steps
  - Lobby for implementation of the principles set out in WHO globally
  - Work on coordinating approval processes for trials across countries
  - Increase visibility of primary care research
  - Exemplify “equitable partnerships” in day-to-day working
- Empowering carers, communities, and health systems in research

"…convene … in continued advocacy and dissemination of norms and standards for clinical trials and provide peer support on implementing good practices to strengthen clinical trial ecosystem."

Global action plan for clinical trial ecosystem strengthening

There is a need to…

"… establish a unified global identity for primary care clinical trials research—building a global alliance to foster collaboration, amplify our collective voice, and ensures primary health care is central to shaping the future of clinical trials."




Series

Clinical Trials in Global Health 4

Democratising clinical trials research to strengthen primary health care

Thank you for your time.

Any questions?

Stepping up the use of trial registries

April 2, 2025

An-Wen Chan, MD DPhil

Chair, WHO Advisory Group, International Clinical Trials Registry Platform

Professor, Dept. of Medicine, University of Toronto

WHO International Clinical Trials Registry Platform

Global standards

19 registries

1 million trials

Transparent reporting of clinical trials

What trials exist? - Trial registration

What are their results? - Reporting results in registries

Are the results valid and applicable? - Full protocol in registries

What trials exist?

Prospective trial registration

- Standards: WHO Trial Registration Data Set
- Compliance
  - Two-thirds of all trials
  - Two-thirds of countries have regulatory requirement

What are the results?

Results reporting in registries

- Standards
  - 2015 WHO Statement on public disclosure of results
  - 2025 WHO guidance on reporting results
- Compliance
  - Half of all trials
  - 40% of countries have regulatory requirement

www.thelancet.com/lancetgh Vol 13 April 2025

Reporting summary results in clinical trial registries: updated guidance from WHO

An-Wen Chan, Ghassan Karam, Justin Pymento, Lisa M Askie, Luiza R da Silva, Ségolène Aymé, Christopher Marc Taylor, Lotty Hooft, Anna Laura Ross, Vasee Moorthy

- Study protocol
- Completion status
- Key dates
- Participant flow
- Baseline characteristics
- Outcome results
- Harms
- Conflicts of interest

Are the results valid and applicable?

Access to full trial protocol

- Standards: 2025 WHO guidance on reporting results
- Compliance: 15% of registered trials

Data quality

- Variability across registries
  - Content
  - Format
  - Terminology
- Missing data

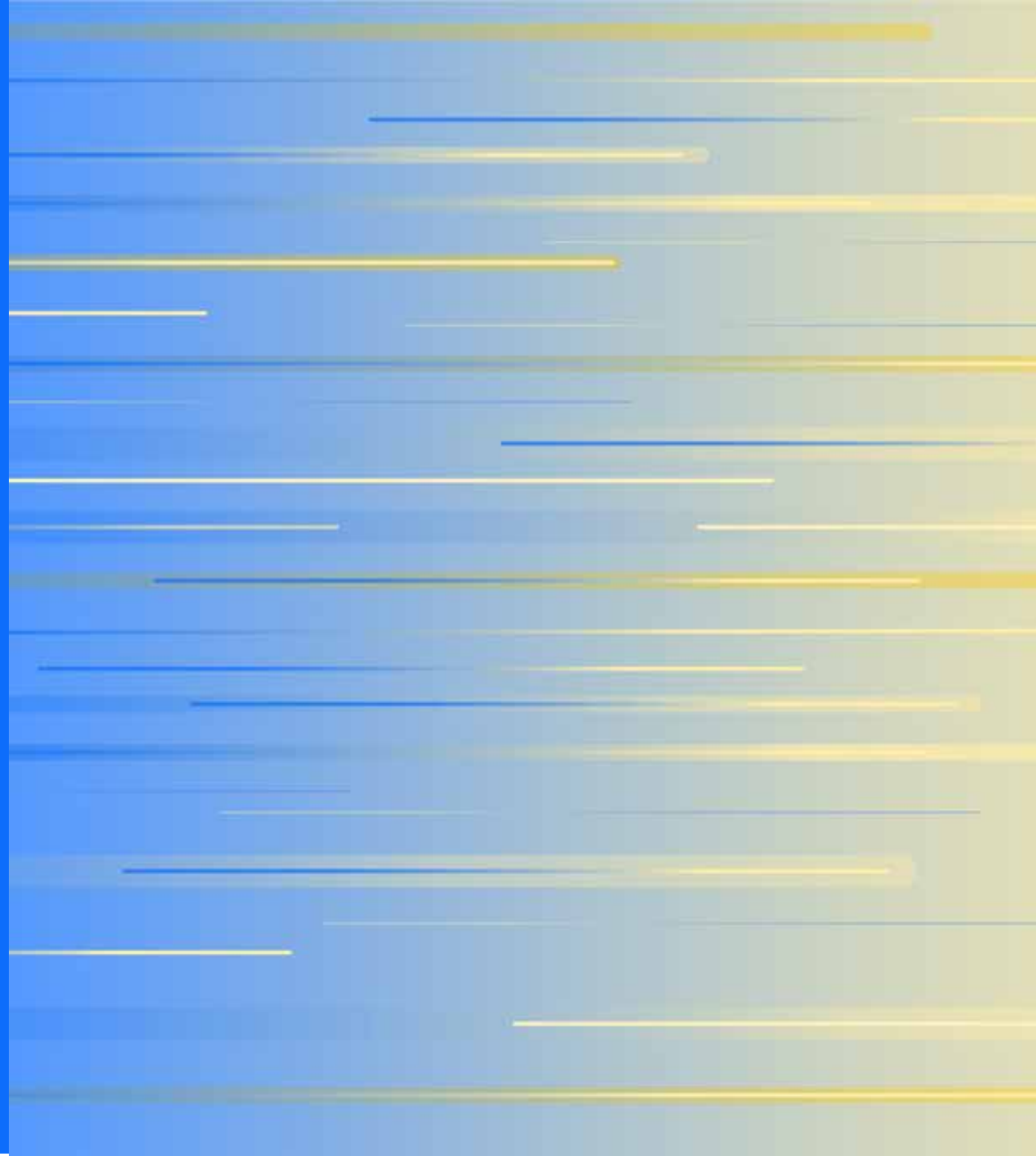
Key actions

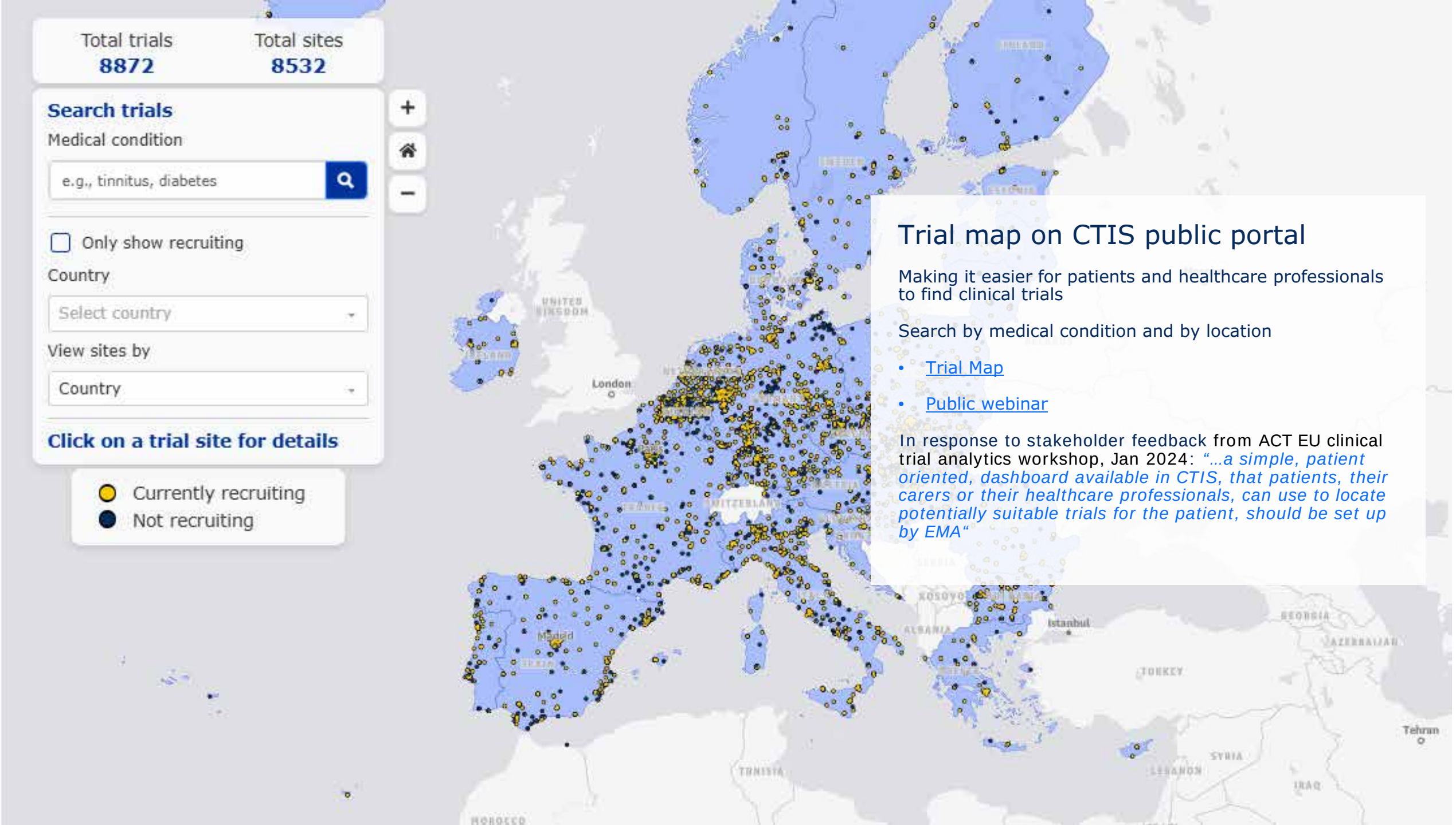
1) Legislators, funders, ethics committees, regulators, sponsors, journals:
   - Register trials prior to enrolment
   - Report results in registries within 12 months
2) WHO Registry Network: Implement harmonized, structured data fields
   - WHO Trial Registration and Results Data Set
3) Registry funders: Ensure adequate resources for registries

The ACT EU Trial Map

The 2nd WHO Global Clinical Trials Forum

Presented by Ana Zanoletty
Data Analytics and Methods Task Force
European Medicines Agency




Total trials
8872
Total sites
8532
Search trials
Medical condition
e.g., tinnitus, diabetes
Only show recruiting
Country
Select country
View sites by
Country
Click on a trial site for details
Currently recruiting
Not recruiting
Trial map on CTIS public portal
Making it easier for patients and healthcare professionals to find clinical trials
Search by medical condition and by location
Trial Map
Public webinar
In response to stakeholder feedback from ACT EU clinical trial analytics workshop, Jan 2024: "…a simple, patient oriented, dashboard available in CTIS, that patients, their carers or their healthcare professionals, can use to locate potentially suitable trials for the patient, should be set up by EMA"
London
Madrid
Istanbul
Tehran

Key benefits of the ACT EU Trial Map

Empowers patients and healthcare professionals:

- Provides easy **access to information** about clinical trials operating in their area
- Gives an overview of site distributions to **support advocacy efforts** regarding clinical trial access
- Improves **access to trials** by making it easy to find the contact information for each clinical trial site
- Increases **findability of trials** by allowing for medical condition searches in lay language (through the Consumer Health Vocabulary)

Currently only supports searches in English, with more EU languages to be available in the future

Thank you

ACTEU@ema.europa.eu

Global Health
EDCTP3

The 2nd WHO Global Clinical Trials Forum

Dr Jean Marie Vianney Habarugira,
Senior Scientific Officer, Global Health EDCTP3

Geneva, 2-3 April 2025

Co-funded by
the European Union

Global Health EDCTP3 - Strategic approach

Vision

- Reduce the socioeconomic **burden of infectious diseases** in sub-Saharan Africa by promoting the development and uptake of new or improved health technologies.
- Increase **health security** in sub-Saharan Africa and globally, by strengthening the research- and innovation-based capacities for preparedness and response to control infectious diseases.

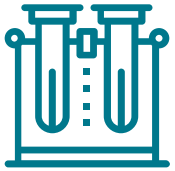
Mission

To support global collaborative research, capacity strengthening, and international initiatives **to accelerate the development, evaluation, and implementation** of interventions to prevent, identify, and treat infectious diseases including emerging/re-emerging infections in SSA to reduce overall mortality and morbidity.

Global Health
EDCTP3

Global Health EDCTP3 - Strategic approach

How do we align with the areas of the Global Action Plan ?



Advance biomedical interventions towards improved overall health

Research capacity development

Enhance coordination and alignment of countries around a common SRIA

Strengthen capacity for outbreaks/ epidemic/ pandemic preparedness

Networking, building partnerships and strategic alliances

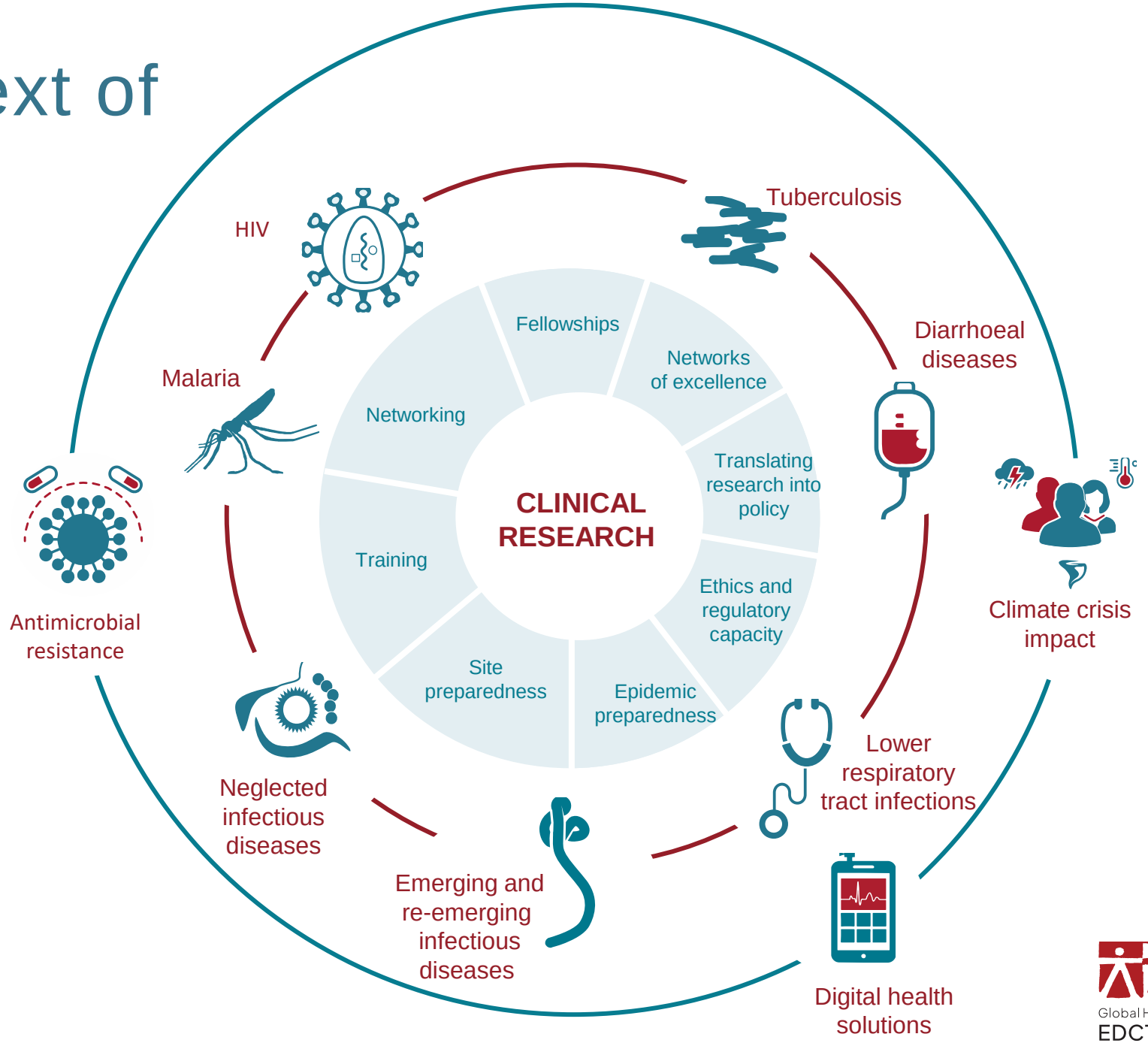
Global Health EDCTP3

Scope in the context of the Global Clinical Trials Ecosystem

We focus on the **major infectious disease threats** facing sub-Saharan Africa.

We tackle all stages of clinical evaluation but particularly **later-stage studies** with a special focus on vulnerable population groups.

We strengthen and build **research capacities** in sub-Saharan Africa.



Global Health EDCTP3

Global Health
EDCTP3

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for your attention!

https://www.global-health-edctp3.europa.eu/

info@global-health-edctp3.europa.eu

Co-funded by
the European Union

The ODYSSEY story

Accelerating global availability of treatment for children with HIV

Once daily **D**OLUTEGRAVIR in **y**oung people (and children) versu**s** **s**tandard th**e**rap**y**

MRC Clinical Trials Unit

Smarter Studies
Global Impact
Better Health

UCL

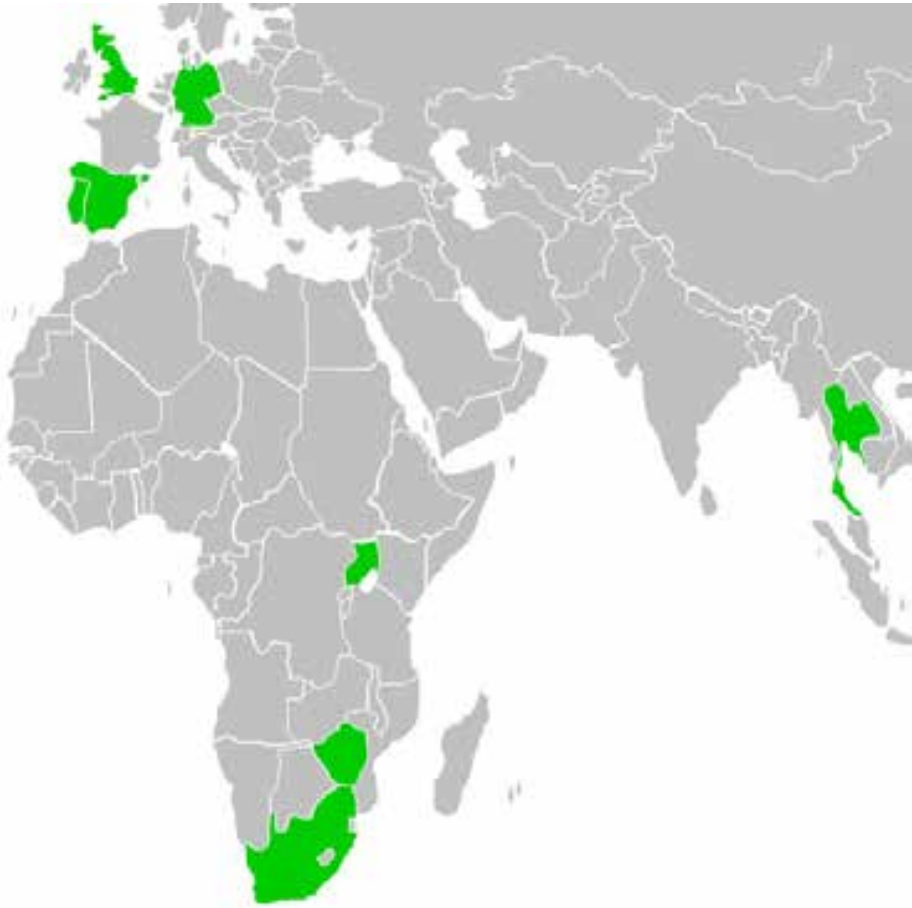
Origins of ODYSSEY

PENTA ID

Paediatric European Network for Treatment of AIDS (Infectious Diseases)

Think Big and Wide: with an eye on impact

- Dolutegravir as part of BOTH first- and second-line Rx
  - Basket design
  - Adolescents and children down to 3kg, even though baby formulation not yet ready
  - Longterm (96-week) follow-up (especially in view of toxicity profile)
- Global trial across varied settings (Africa, Asia, Europe)
  - first major collaboration between PENTA & African Centres



- Evaluate simplified WHO weight-band DTG dosing using minimal number of formulations
  - Adult 50mg tablet & baby 5mg dispersible
  - Nested PK substudies in real-time
- Wide collaborations and teamwork:
  - Viiv Healthcare, IMPAACT, Paediatric Antiretroviral Working Group of WHO, CHAI, Indian generics (Mylan), African MOHs

3 months to <18 years old,
Starting 1st line or switching to 2nd line
N = 792

ODYSSEY A:
First-line ART
N=383

ODYSSEY B:
Second-line ART
N=409

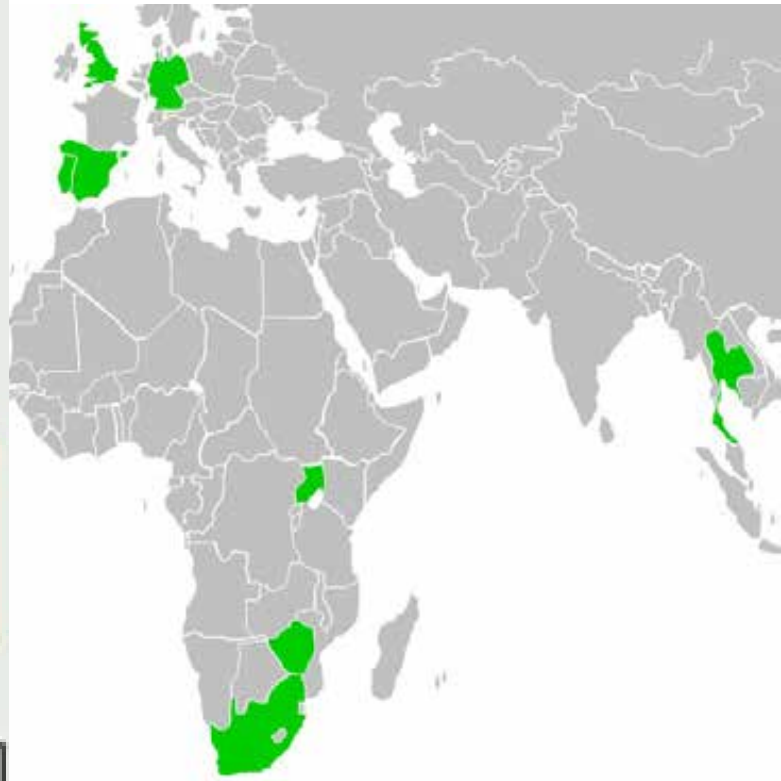
DTG
N=189

SOC
N=194

DTG
N=203

SOC
N=206

Primary endpoint: virological or clinical failure*



Simplified dolutegravir dosing for children with HIV weighing 20 kg or more: pharmacokinetic and safety substudies of the multicentre, randomised ODYSSEY trial

Pauline D J Bollen, Cecilia L Moore, Hilda A Mujuru, Shafic Makumbi, Adeodata R Kekitiinwa Elisabeth Kaudha, Anna Parker, Godfrey Musoro, Annet Nanduudu, Abbas Lugemwa, Pauline Amuge, James G Hakim, Pablo Rojo, Carlo Giaquinto, Angela Colbers, Diana M Gibb, Deborah Ford*, Anna Turkova*, David M Burger*, and the ODYSSEY trial team†

Summary

Background Paediatric dolutegravir doses approved by stringent regulatory authorities (SRAs) for children weighing 20 kg to less than 40 kg until recently required 25 mg and 10 mg film-coated tablets. These tablets are not readily available in low-resource settings where the burden of HIV is highest. We did nested pharmacokinetic substudies in

Lancet HIV 2020; 7: e533-44
See Comment page e522
*Joint last authors

Dolutegravir dosing for children with HIV weighing less than 20 kg: pharmacokinetic and safety substudies nested in the open-label, multicentre, randomised, non-inferiority ODYSSEY trial

Hylke Waalewijn, Man K Chan, Pauline D J Bollen, Hilda A Mujuru, Shafic Makumbi, Adeodata R Kekitiinwa, Elizabeth Kaudha, Tatiana Sarfati, Godfrey Musoro, Annet Nanduudu, Abbas Lugemwa, Pauline Amuge, Cecilia L Moore, Pablo Rojo, Carlo Giaquinto, Angela Colbers, Diana M Gibb, Deborah Ford*, Anna Turkova*, David M Burger*, ODYSSEY Trial Team†

Summary

Background Dolutegravir-based antiretroviral therapy is a preferred first-line treatment for adult with HIV; however, very little pharmacokinetic data for dolutegravir use are available in young cl aimed to evaluate dolutegravir dosing and safety in children weighing 3 kg to less than

Dolutegravir twice-daily dosing in children with HIV-associated tuberculosis: a pharmacokinetic and safety study within the open-label, multicentre, randomised, non-inferiority ODYSSEY trial

Anna Turkova, Hylke Waalewijn, Man K Chan, Pauline D J Bollen, Mutsa F Bwakura-Dangarembizi, Adeodata R Kekitiinwa, Mark F Cotton, Abbas Lugemwa, Ebrahim Variava, Grace Miriam Ahimbisibwe, Ussanee Srirompotong, Vivian Mumbiro, Pauline Amuge, Peter Zuidewind, Shabinah Ali, Cissy M Kityo, Moherndran Archary, Rashida A Ferrand, Avy Violari, Diana M Gibb*, David M Burger*, Deborah Ford*, Angela Colbers*, on behalf of the ODYSSEY Trial Team†

Summary

Background Children with HIV-associated tuberculosis (TB) have few antiretroviral therapy (ART) options. We aimed

Lancet HIV 2022; 9: e627-37

Pharmacokinetic Studies nested in ODYSSEY

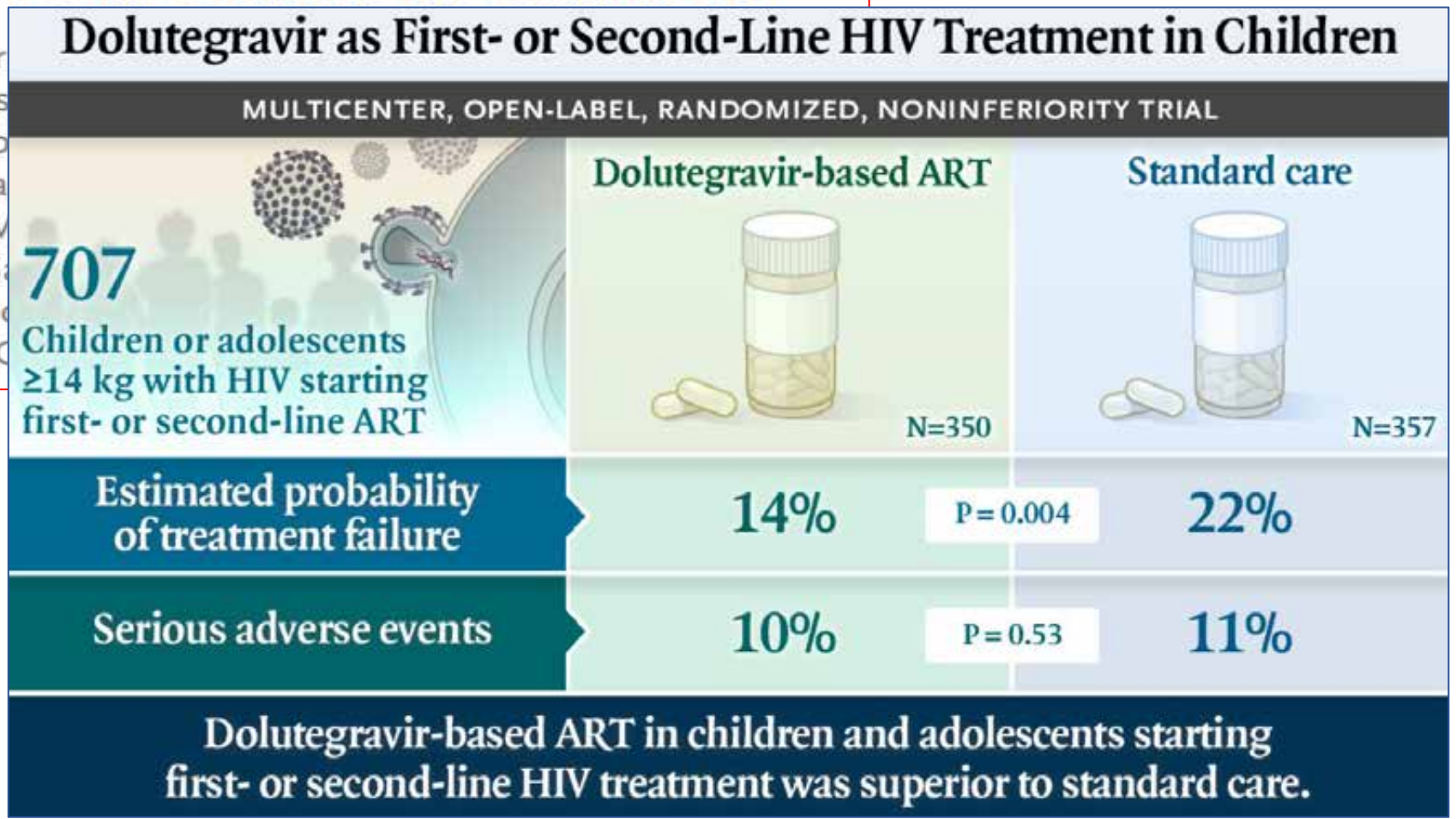
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dolutegravir as First- or Second-Line Treatment for HIV-1 Infection in Children

A. Turkova, E. White, H.A. Mujur
A. Lugemwa, T.R. Cressey, P. Mus
T. Puthanakit, O. Behuhuma, R. Kob
P. Amuge, E. Kaudha, L. Barlow-Mosha
G. Musoro, L. Atwine, A. Liberty, V
S. Chalermpantmetagul, S. Ali, T. S
N. Klein, S. Bernays, Y. Saïdi, A. Coelh
P. Rojo, D. Ford, and D.M. C

December 30, 2021
N Engl J Med 2021; 385:2531-2543
DOI: 10.1056/NEJMoa2108793



Innovate: analysis of the younger children

(Becky Turner, Ian White, Debbie Ford: MRC CTU at UCL)

Question: How should we estimate the treatment effect comparing DTG to SOC in children weighing <14kg?

- Option 1: use the data from the younger children in a standalone analysis (underpowered).
- Option 2: assume the treatment difference is identical in older and younger children, and combine the two data sets in a pooled analysis (90% would be >14kg).
- Option 3: 'borrow' information from older children to increase the precision of results in younger children; 'downweight' information from older children using clinical opinion in a Baysean analysis

Innovate: analysis of the younger children

(Becky Turner, Ian White, Debbie Ford: MRC CTU at UCL)

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Turner *et al.*
BMC Medical Research Methodology (2022) 22:49
https://doi.org/10.1186/s12874-022-01539-3

BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

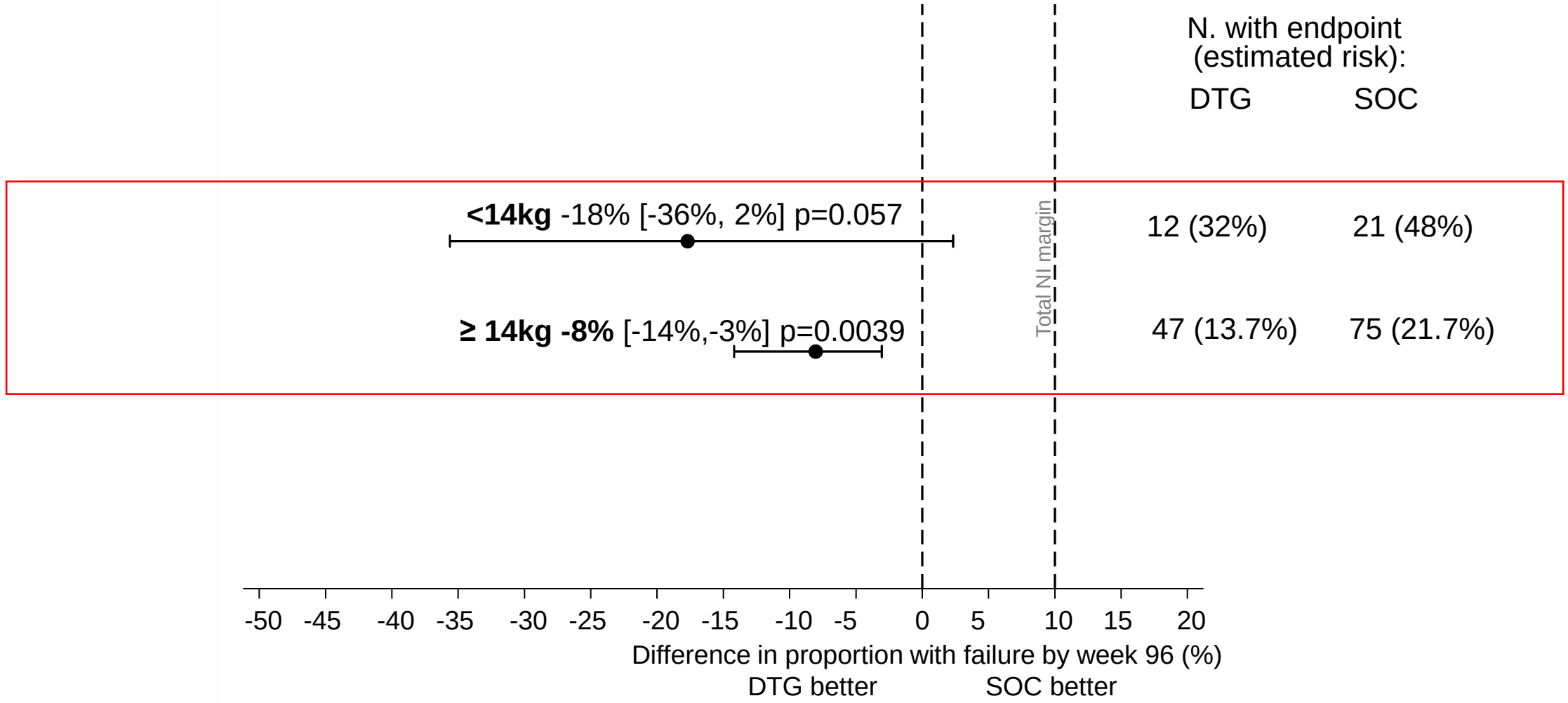
Borrowing information across patient subgroups in clinical trials, with application to a paediatric trial

Rebecca M. Turner[1*], Anna Turkova[1], Cecilia L. Moore[1], Alasdair Bamford[1,2,3], Moherndran Archary[4,5], Linda N. Barlow-Mosha[6], Mark F. Cotton[7], Tim R. Cressey[8,9], Elizabeth Kaudha[10], Abbas Lugemwa[11], Hermione Lyall[12], Hilda A. Mujuru[13], Veronica Mulenga[14], Victor Musiime[10,15], Pablo Rojo[16], Gareth Tudor-Williams[17], Steven B. Welch[18], Diana M. Gibb[1], Deborah Ford[1†], Ian R. White[1†] and and the ODYSSEY Trial Team

Abstract

Background: Clinical trial investigators may need to evaluate treatment effects in a specific subgroup (or subgroups) of participants in addition to reporting results of the entire study population. Such subgroups lack power to detect a treatment effect, but there may be strong justification for borrowing information from a larger patient group within the same trial, while allowing for differences between populations. Our aim was to develop methods for eliciting expert opinions about differences in treatment effect between patient populations, and to incorporate these opin-

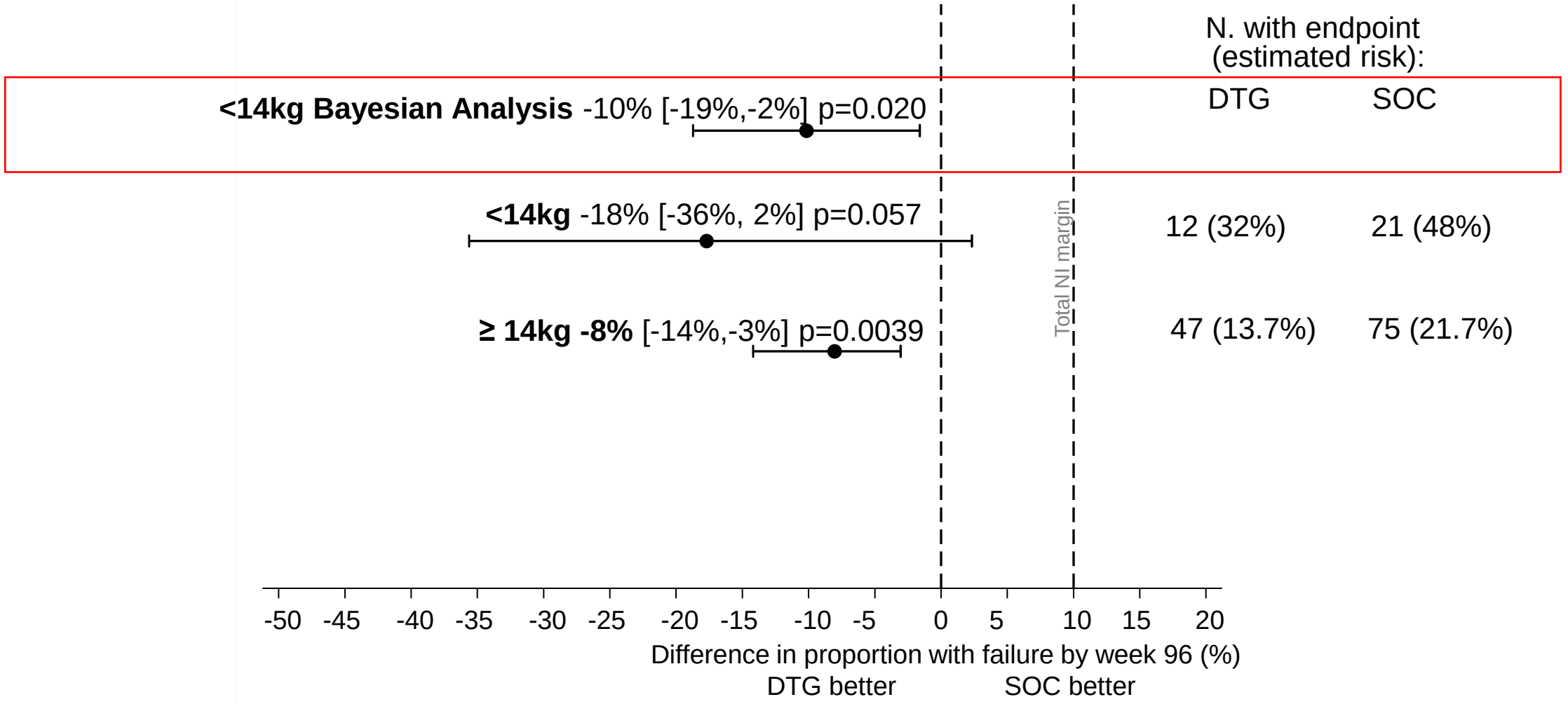
Primary outcome (children <14kg and ≥14kg): virological or clinical failure by 96 weeks



Penta

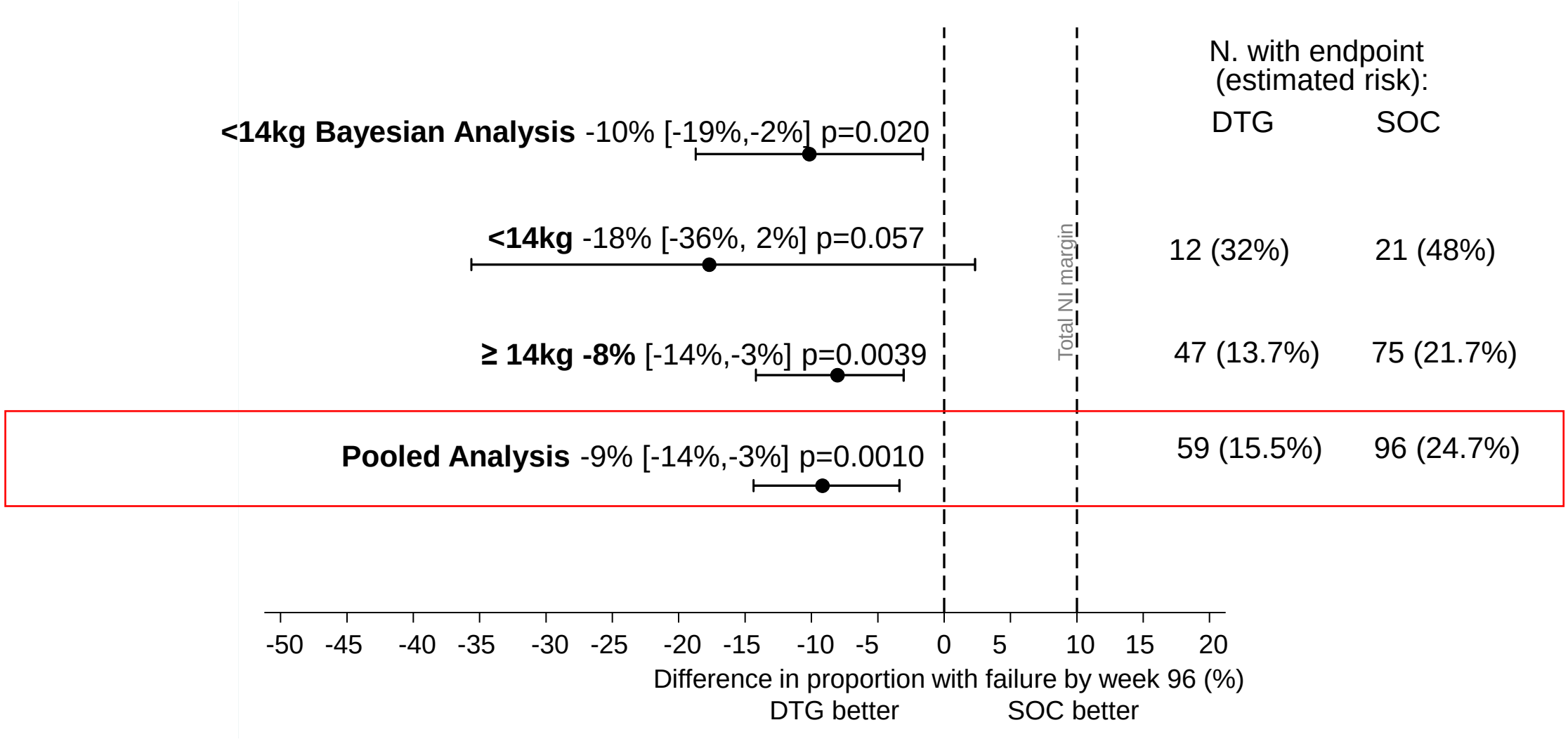
SOC= standard of care

Primary outcome (children <14kg and ≥14kg): virological or clinical failure by 96 weeks



SOC= standard of care

Primary outcome (children <14kg and ≥14kg): virological or clinical failure by 96 weeks



Penta

SOC= standard of care

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Once-daily dolutegravir-based antiretroviral therapy in infants and children living with HIV from age 4 weeks: results from the below 14 kg cohort in the randomised ODYSSEY trial

Pauline Amuge*, Abbas Lugemwa*, Ben Wynne, Hilda A Mujuru, Avy Violari, Cissy M Kityo, Moherndran Archary, Ebrahim Variava, Ellen White, Rebecca M Turner, Clare Shakeshaft, Shabinah Ali, Kusum J Nathoo, Lorna Atwine, Afaaf Liberty, Dickson Bbuye, Elizabeth Kaudha, Rosie Mngqibisa, Modehei Mosala, Vivian Mumbiro, Annet Nanduudu, Rogers Ankunda, Lindiwe Maseko, Adeodata R Kekitiinwa, Carlo Giaquinto, Pablo Rojo, Diana M Gibb†, Anna Turkova†, Deborah Ford†, on behalf of the ODYSSEY Trial Team‡

Lancet HIV 2022; 9: e638–48

See Comment page e600

Summary

Background Young children living with HIV have few treatment options. We aimed to assess the efficacy and safety of dolutegravir-based antiretroviral therapy (ART) in children weighing between 3 kg and less than 14 kg.

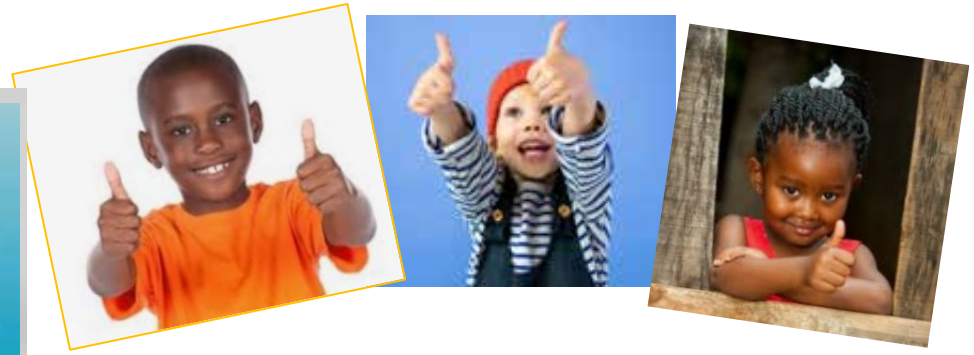
https://www.picturinghealth.org/dolutegravir-children-hiv/

ODYSSEY data informed licensing: DTG & ABC/3TC

- **Dolutegravir:**
  - FDA and EMA updated DTG approval:
    - children ≥20kg can take adult tablets – Jun /Nov 2020
    - 5mg dispersible tablets dosing for children ≥3kg –Jun /Nov 2020
  - 10mg dispersible tablet manufactured by Viatris (Mylan) approved by the FDA Nov 2020
- **Dispersible ABC/3TC 120/60mg tablets** manufactured by Mylan approved in South Africa in Feb 2021

DISPERSIBLE TABLETS

Strawberry flavour children ≥3kg



FILM-COATED TABLETS

For ≥20kg – 1 tab daily

ODYSSEY data informed guidelines

- WHO paediatric guidelines 2019
  - Recommended DTG adult tablets for children ≥20kg
  - Recommended DTG double dosing for children treated for HIV-TB

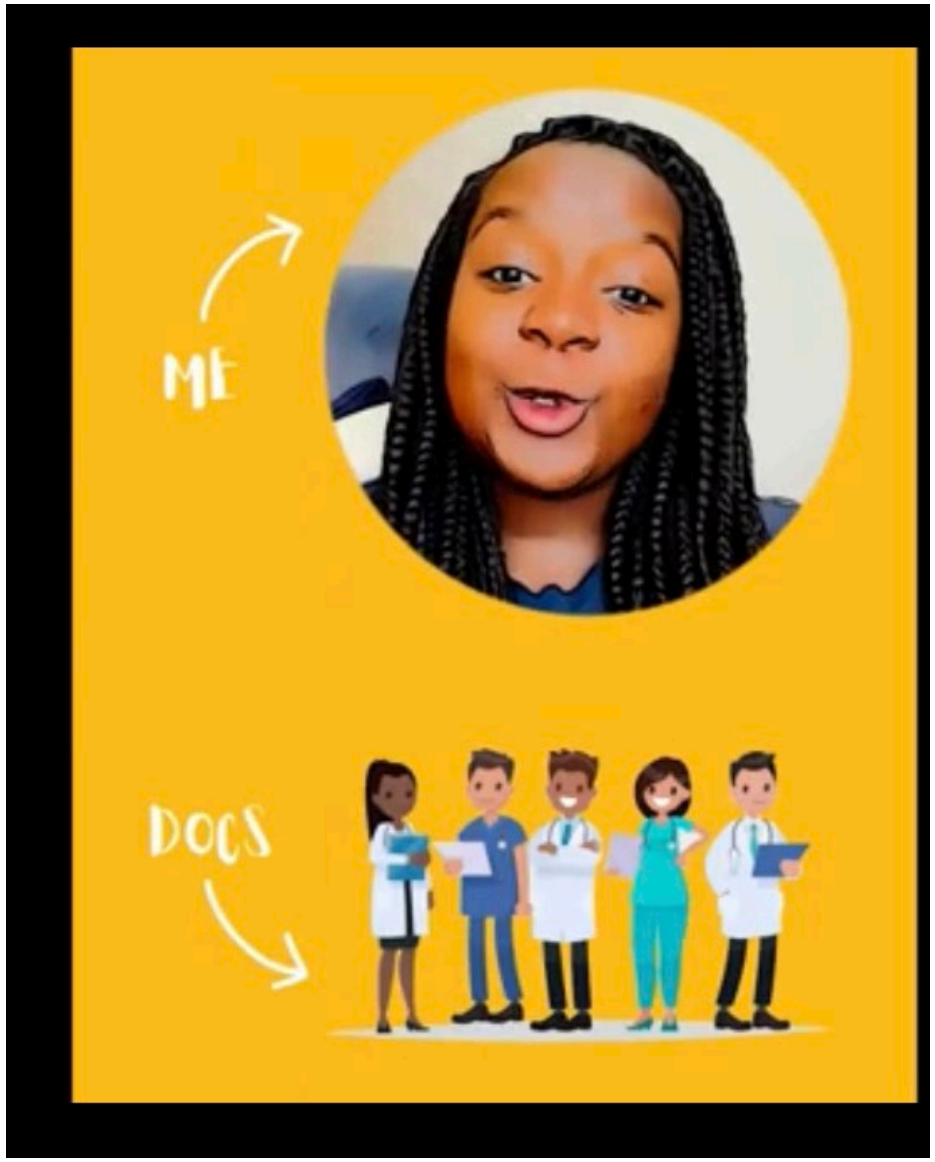
- WHO Policy brief July 2020
  - updated DTG dosing for children 3-20kg

https://www.aidsdatahub.org/sites/default/files/resource/who-considerations-introducing-new-antiretroviral-drug-formulations-children-2020.pdf

Youth Trial Board Videos on Odysseytrial.org

ODYSSEY trial findings videos

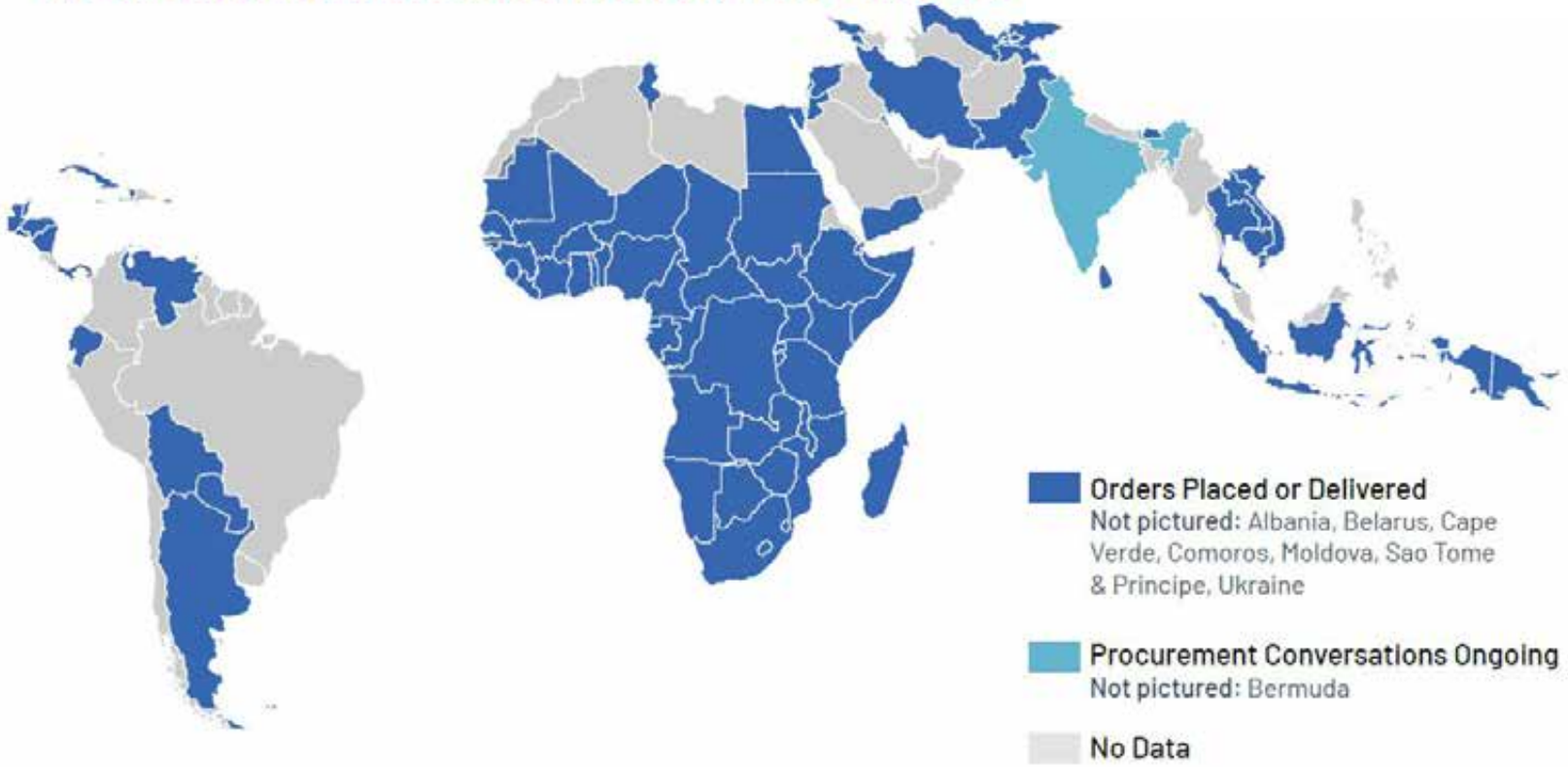
The **young people** involved in the ODYSSEY trial created **a three-part video series** to explain the trial's main findings. These videos were created in collaboration with influencers living with HIV..



Roll out of Dolutegravir in Children

- pDTG had the shortest regulatory approval on record for a generic HIV product, and is now used by 160,000 CLHIV in GA LMICs

FIGURE 33: PEDIATRIC DTG ADOPTION MAP, APWG, AS OF Q3 2023[c]



ODYSSEY - Looking Forward

- Five-year follow-up
- Combined analyses of ODYSSEY and CHAPAS 4 trials and further substudy results to come
- Some children switched to other trials of long-acting injectables or weekends off dolutegravir

- **Approach to analysis of Baby ODYSSEY may pave the way to a <u>new approach to Paediatric Trials</u>**
  - **Smaller numbers required but provide PK, and <u>COMPARATIVE</u> Safety and Efficacy**
  - **Accelerate drug approval and access for kids**

Reflections on doing a useful trial

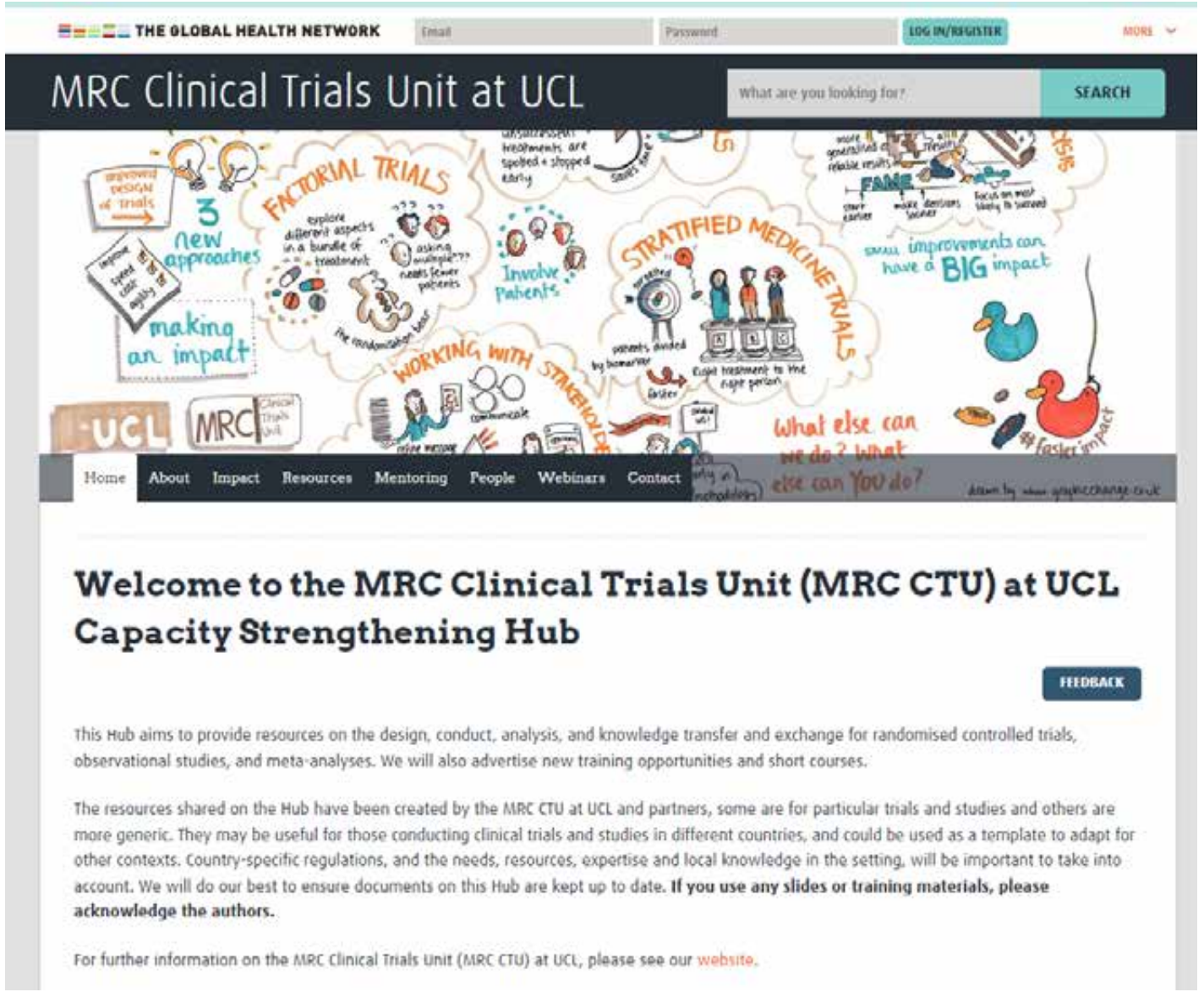
- **Asking the right question(s) and thinking about new designs to be efficient**
  - Involve people on the ground, including the community
  - Go ‘on the ground’ - They will ‘own’ the trial and its results
  - Involve methodologists early
- **Engage decision-makers early**
  - Stakeholder mapping
  - Involve decision-makers throughout – eg on Trial Steering Committee
  - Write about the rationale for the trial etc
- **Nest substudies to help explain and to implement possible result scenarios:**
  - E.g. Pharmacokinetics, basic science, social science, health economics
  - Don’t let substudies overwhelm the trial! Keep under control, and approved by committees
  - Put health economics in the main paper if possible and relevant
- **Trial isn’t just ’the publication’:**
  - Dissemination plan to internal and external stakeholders, including timing - particularly locally
  - Use wide variety of media and involve local stakeholders (they will be first to take up new results)
  - Dissemination to participants and their families and community
- **Be aware of pitfalls for guidelines and implementation:**
  - Stakeholders who may/may not like results; ‘Peoples’ prior beliefs’
  - Psychology of ‘taking away’ for example maybe different vs ‘shiny new’ intervention
  - How easy (and costly) would results be to implement

Online Knowledge Hubs

MRC Clinical Trials Unit at UCL Capacity Strengthening Hub

Aims to strengthen clinical trials capacity in LMICs

https://mrcctu.tghn.org/



THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

"NOVEL TRIAL DESIGNS FOR OLD PROBLEMS"

WEBINAR

FRIDAY 19TH MAY 10-11AM

Webinar for the official launch of the MRC Clinical Trials Unit (MRC CTU) at UCL Capacity Strengthening Hub on The Global Health Network digital platform

SARAH WALKER

Professor of Medical Statistics & Epidemiology, FMedSc

UKRI MRC Clinical Trials Unit

UCL

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

Reflections on running a trial

- What makes trials fail?
  - Failure to recruit; poor retention
    - The ‘three Rs’ of a good trial: ***recruitment, randomisation, retention***
- Needs champions amongst clinicians and end users (Patient-public involvement (PPI))
- Great if ‘the stars align’ as in the ODYSSEY trial
- ‘things move on’; beware of the landscape and whether the trial is still relevant
  - Don’t have a trial going on forever!
- Communication is vital
- Be ready for the trial which stops early: CHAP, CHER, FEAST
- Wonderful opportunity for capacity strengthening of all staff (‘on the job learning’)

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The 2nd WHO Global Clinical Trials Forum

Dr Jean Marie Vianney Habarugira,
Senior Scientific Officer, Global Health EDCTP3

Geneva, 2-3 April 2025

Co-funded by
the European Union

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Case studies of key international studie

AMBITION-cm, and STOP studies (STOP, STOP2, STOP2030)

Co-funded by
the European Union

Case study 1: Simpler and safer treatment of cryptococcal meningitis (AMBITION-cm)

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Cryptococcal meningitis is a leading cause of AIDS-related death globally

UNAIDS

PRESS RELEASE
Millions of lives at risk as progress against AIDS falters

"The AIDS pandemic ***took a life every minute*** in 2021, with 650 000 AIDS deaths despite effective HIV treatment and tools to prevent, detect, and treat opportunistic infections"

In Danger. UNAIDS Global AIDS Update 2022

Nearly all of these deaths are among people with ***advanced HIV disease*** (those with severe immune suppression)

UNAIDS Data 2021

3 leading causes of AIDS-related deaths:


Cryptococcal meningitis


Tuberculosis


Bacterial infections

Reducing cryptococcal meningitis deaths is essential to end AIDS by 2030

UNAIDS Political Declaration on HIV and AIDS 2021: Ending Inequalities and Getting on Track to End AIDS by 2030

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Treatment Call by EDCTP2 (2017)

The AMBITION-cm project

Project: AMBITION-cm trial

Project lead: Professor Jo Jarvis, London School of Hygiene and Tropical Medicine, UK

Countries involved: Botswana, France, Malawi, South Africa, Uganda, United Kingdom, Zimbabwe

Target population(s): Adults with HIV

Year funded: 2017

EDCTP funding: €9.9 M

Grant agreement: TRIA2015-1092

- Infection of the brain by Cryptococcus, a fungal pathogen, can lead to a potentially fatal meningitis. Globally, cryptococcal meningitis is the second most common HIV-related cause of death, and most deaths occur in sub-Saharan Africa.
- Old treatment was based on a one-week course of two drugs, amphotericin B deoxycholate and flucytosine.
- However, use of amphotericin B deoxycholate is associated with blood, kidney and other abnormalities, requiring careful patient monitoring, which may not be feasible in many resource-poor settings where the burden of disease is highest.

The study results

The AMBITION-cm trial is the largest HIV-associated cryptococcal meningitis treatment trial ever undertaken.

The phase III AMBITION-cm trial, in five African countries, compared use of single-dose liposomal amphotericin B and flucytosine with the current recommended treatment, recruiting 844 patients with confirmed cryptococcal meningitis. Survival was not markedly different in the two arms (24.8% mortality in the liposomal amphotericin B group versus 28.7% in the control group) and fewer serious side effects were seen with liposomal amphotericin B.

These results, in the New England Journal of Medicine on 23 March 2022, argue in favour of use of liposomal amphotericin B, which would be easier to deliver in resource-poor settings, have fewer treatment complications and could potentially reduce the duration of hospital stays for some patients

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Rapid advice by the WHO (2022) and the economic analysis

In April 2022, the WHO issued a rapid advice to update guidance on treatment of cryptococcal meningitis based on the findings of the AMBITION-cm study.

the AMBITION-cm project published an economic analysis in The Lancet Global Health demonstrating the cost and cost-effectiveness of the single, high-dose liposomal amphotericin (L-AmB) regimen for cryptococcal meningitis in five countries in Eastern and Southern Africa.

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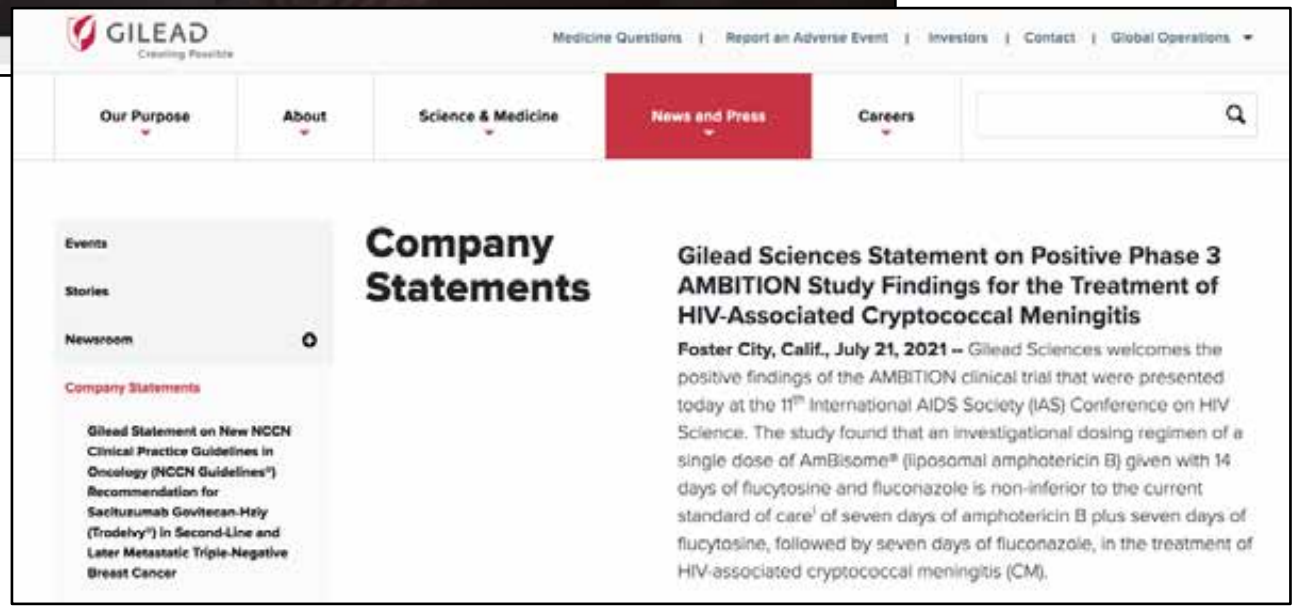
The AMBITION trial – pathway to global impact



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Case 2: The STOP studies

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The STOP and STOP2 (EDCTP2, 2018 and 2020)

STOP

Towards the interruption of transmission of soil-transmitted helminths: Clinical research development of a fixed-dose co-formulation of ivermectin and albendazole

Fundación Privada Instituto de Salud Global (ISGlobal), Barcelona, Spain with partners from Ethiopia, Kenya, Mozambique, Netherlands, Spain, and the United Kingdom.

Project Coordinator: Dr José Muñoz Gutiérrez, ISGlobal, Spain

Starting date: 1 October 2018

Duration: 60 months

Grant amount: EUR 4,899,488

Grant agreement: RIA2017NCT-1845

STOP-2

Towards the interruption of transmission of soil-transmitted helminths: Safety of a fixed-dose co-formulation of ivermectin and albendazole *

Fundación Privada Instituto de Salud Global (ISGlobal), Barcelona, Spain with partners from Kenya, the Netherlands, Spain, and the United Kingdom.

Project Coordinator: Dr José Muñoz Gutiérrez, ISGlobal, Spain

Starting date: 1 October 2020

Duration: 12 months

Grant amount: EUR 1,665,298

Grant agreement: PSIA2020-3072 – STOP-2

* This project is funded by the **United Kingdom as an independent contribution to the EDCTP2 programme, a so-called Participating States' Initiated Activity**. The study follows up on the EDCTP-funded STOP study.

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Regulatory pathway: The STOP project

The STOP Project has been done in collaboration with EMA fo WHO/Africa:

- WHO prequalification approval for generic IVM 3 mg (Liconsa)
- 3 CHMP at European Medicines Agency (EMA): Article 58 (EU-M4all)

o A Scientific Advice was submitted by April 3rd 2019 (answer 17th October 2019)
o A Follow-up to Scientific Advice was submitted by February 4th 2020 (answer 28th May 2020)
o A second Follow-up to Scientific Advice was submitted by August 29th 2021 (answer November 11th 2021)

A **safety study was needed** before embarking into a phase III trial, to further evaluate the safety of high doses of ivermectin in FDC in the study population.

An **adaptive pase II/III clinical trial** was considered the best solution.

STOP- 2: Towards the interruption of transmission of soil-transmitted helminths: Safety of a fixed-dose coformulation of ivermectin and albendazole

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The STOP-2 project

Main objective

To evaluate the **safety, pharmacokinetics and palatability and acceptability** of a fixed-dose co-formulation of IVM and ALB (from now onwards FDC) as a single dose or three-dose regimen for the treatment of *T. trichiura* in paediatric population in a unicentric randomized phase II clinical trial.

Secondary objectives

- To undergo **EMA Scientific Advice** to pursue future marketing authorization of the FDC
- To incorporate recently developed and validated **DNA detection-based molecular diagnostic tools** (PCR) for measuring the efficacy of anthelmintic drugs in clinical trials.
- To set up a **procurement system and a quality control process** to be implemented in the phase III trial.
- To ensure **fully operational infrastructure** and staffing KEMRI in order to develop and maintain the capacity for **conducting phase II clinical trials**
- To explore provider and recipient perceptions on **acceptability and feasibility** of the FDC as a single dose or three-dose regimen for school-based deworming

ISGlobal Barcelona Institute for Global Health

KEMRI Kenya Medical Research Institute

London School of Hygiene & Tropical Medicine

CHEMO

LUMC Leiden University Medical Center

Global Health EDCTP3

Demostrate safety and efficacy of FDC: The STOP project

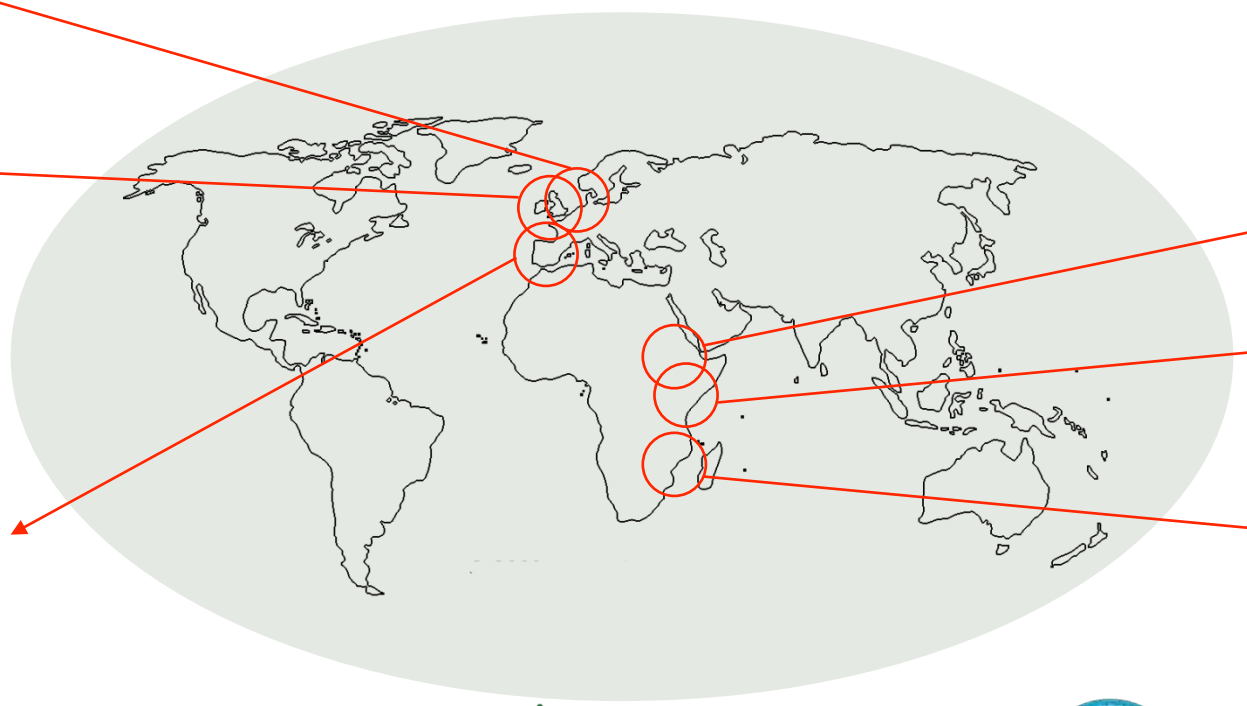
The Netherlands:
University of Leiden

United Kingdom:
London School of Hygiene and Tropical Medicine

ISGlobal

Spain:
Laboratorios Liconsa

Spain:
Universidad de León



Ethiopia:
Bahir Dar University

Kenya:
KEMRI

Mozambique:
CISM

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New treatment against parasitic worm infections funded by EDCTP receives positive opinion by the European Medicines Agency

STOP 2030 by Global Health EDCTP3

- This project, STOP2030, seeks to complement the results of the safety and efficacy trial with a field-based safety and effectiveness clinical study, acceptability studies in Ghana and Kenya, modelling and cost-effectiveness exercises.
- The resulting information will be consolidated to build a multidisciplinary package for policy making and WHO guidance with the support of advocacy and communication activities to reach stakeholders and maximize the exploitation and impact of the FDC for STH control and elimination.
- The Consortium assembled to execute the STOP2030 proposal combines expertise in complementary fields from program assessment and implementation through Ministries of Health in sub-Saharan African countries, advocacy, state of the art technology, leadership in clinical research and a pharma that has shown commitment for generating access to drugs against NTDs and has recently obtained WHO prequalification for generic ivermectin.

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Thank you
for your attention!

https://www.global-health-edctp3.europa.eu/

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The end of the slides

World Health Organization