WHO-EM/RPC/054/E

Summary report on the

Expert consultation on strengthening national capacity for the conduct of randomized controlled trials and large-scale studies in countries of the Eastern Mediterranean Region

Cairo, Egypt
14–15 November 2023

World Health Organization
Eastern Mediterranean Region

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1. Introduction

In 2022, the Seventy-fifth World Health Assembly endorsed resolution WHA75.8 on strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination. The resolution, among other things, called upon WHO to prepare global guidance on best practices to help guide Member States' implementation of scientifically and ethically sound clinical trials, as well as guidance on best practices for non-State actors in the design and conduct of clinical trials and in strengthening the global clinical trial ecosystem. The development of this guidance started in January 2023, following a public consultation organized by the Secretariat in October–November 2022. The Secretariat coordinated the development of the guidance with advice from a technical advisory group, comprising leading global experts in clinical trials and health research methodology, regulation and research ethics. The guidance was developed in close consultation with a WHO steering committee consisting of representatives from all relevant WHO technical units.

As part of the implementation of resolution WHA.75.8, the WHO Regional Office for the Eastern Mediterranean held an expert consultation on 14–15 November 2023 in Cairo, Egypt.

The objectives of the expert consultation were to:

- inform the Member States and stakeholders in the Region about the resolution and the guidance development process;
- discuss the draft guidance based on the regional challenges and priorities;
- identify areas of action on which WHO can provide strategic support for Member States; and
- discuss initiatives led by Member States and stakeholders in the Region for implementation of the resolution and the way forward.

During the two days of the consultation, more than 15 experts, with extensive experience from academia and ministries of health in the Region, shared their insights and provided guidance on strengthening the randomized control trial (RCT) and clinical trial ecosystem in the Region, and developed a set of key recommendations.

Dr Arash Rashidian, Director of the Department of Science, Information and Dissemination at the WHO Regional Office for the Eastern Mediterranean, welcomed the participants and thanked the Secretariat at WHO headquarters for supporting the expert consultation. He said the advice of the gathered experts would greatly help to strengthen national capacity for the conduct of RCTs and large-scale studies in the Region.

Dr Rana Hajjeh, Director Programme Management, WHO Regional Office for the Eastern Mediterranean, in her opening remarks, highlighted the importance of the establishment of a network for clinical trials and infectious diseases research, which had not happened previously due to the scarcity of reliable data. She also noted the dearth of nurses well-trained to support clinical trials in the Region, which was also true for other WHO regions. She stressed the need to build capacity and bring the subject to the attention of policy-makers and decision-makers through better coordination. She further noted that the role of WHO was not to conduct clinical trials but to assist countries in coordination, training and capacity-building.

2. Summary of discussions

The consultation covered a range of key areas related to RCTs, clinical trials and large-scale studies. Five sessions focused on: i) governance, ii) capacities and conduct, iii) large-scale studies, iv) strengthening of

the RCT ecosystem: academic and technical capacity, and v) the strengthening of the RCT ecosystem: regulatory functions by ministries of health and drug authorities.

Governance

The 2008 version of the Declaration of Helsinki mentions that all clinical trials must be registered in a publicly accessible database before recruiting the first subject. The WHO International Clinical Trials Registry Platform (ICTRP) emphasizes that all interventional clinical trials should be registered and publicly disclosed to ensure transparency. The 24 items in WHO's ICTRP Trial Registration Data Set are based on the items proposed by the International Committee of Medical Journal Editors (ICJME).

WHO has tried in the past to establish clinical trial registries in the Eastern Mediterranean Region, but this has not been very successful. If a registry is established, it should be in languages that are prevalent in the Region, for example, Arabic, French, Persian and Urdu. The practicalities of maintaining a registry need attention, especially ensuring adequate resources such as human resources and dedicated time.

The role of national bioethics committees in RCTs, clinical trials and large-scale studies is a crucial one. They have to ensure that the research has scientific merit and is conducted in an ethical manner and that the dignity, rights and welfare of research participants are protected and secure. However, these committees face a number of challenges, including a lack of adequate guidelines, legislation and regulations and logistical difficulties in undertaking oversight of RCTs or working in emergency settings and conflict zones. Moreover, there is often a conflict of interest

for some committee members. The overall governance landscape can be improved through better coordination of all key stakeholders.

Capacities and conduct

In the last two decades, clinical and large-scale research is increasingly being undertaken low- and middle-income countries (LMICs) because it is cheaper. However, attractive incentives often lead to inappropriate enrolment and there may be sub-par standards of care.

Many factors are involved in implementation of RCTs in LMICs. This includes the scarcity of funding and insufficient infrastructure, and the need for strong leadership, greater trust and awareness, and ensuring no compromises on ethical standards. It is crucial to understand the perception of clinical trials among the Region's populations and address deep-rooted cultural beliefs. However, these challenges not impossible to overcome. With the help of training programmes, research grants, collaboration, the engagement of communities and stakeholders, local leadership involvement and better feedback loops, much can be achieved.

The role of technology in data collection and implementation of RCTs has recently gained global traction. For example, mobile applications are simplifying data collection and entry. Telemedicine emerged as a gap filler during the COVID-19 pandemic and is helping in remote monitoring. However, while the digitization of data, including medical records, is very useful, the risks related to access must not be overlooked. Successful RCTs that are technology-driven and implemented in resource-limited settings should be disseminated through case studies.

There is the potential to forge bilateral educational, clinical and research partnerships that can transform RCTs and clinical trials in the Eastern Mediterranean Region. At the same time, the regulatory environment must be upgraded to international standards. Local health research should be aligned with local health needs and priorities and involve equitable research collaboration with international organizations.

Large-scale studies

Large-scale cohort studies can be of immense value to the Eastern Mediterranean Region as they can provide valuable insights into trends and disease patterns specific to the Region, which can help in the design of interventions. These studies not only provide high-quality Region-specific data but help in the long-term monitoring of health outcomes which can provide data to help improve the impact of public health programmes. However, conducting large-scale studies in the Region faces many challenges, including those presented by the numerous emergencies.

A multifaceted approach is required to promote cohort studies in the Region. This could involve policy advocacy, raising public awareness, increasing the allocation of resources, fostering regional and international collaboration, undertaking capacity-building, enhancing data quality and establishing a research consortium.

The key features of effective large-scale studies include having relevant research questions, an appropriate study design, the engagement of communities, research that fits the context, dimensions of data and scale that are proportionate to the research questions, and effective data monitoring. The research should also be aimed at building local capacity, not just enhancing research.

The COVID-19 effectiveness studies undertaken in the Region provided many valuable lessons. One of the key reasons for these studies was that the existing information was only reflective of data collected under the controlled conditions of RCTs (vaccine efficacy) as opposed to real-world scenarios from the field. There were also very few studies in the Region on COVID-19 vaccine effectiveness.

The challenges for the studies included the changing landscape of COVID-19 epidemiology and vaccination during the studies and the cost-benefit value of using certain tests to evaluate vaccine effectiveness, such as serology or antibody and gene sequencing for novel variants. At the country level, many countries faced difficulties in data quality, infrastructure and supply, and an inability to achieve sample size, leading to adjustments in study implementation.

Strengthening of the RCT ecosystem: academic and technical capacity

In group work, participants identified challenges and suggestions in strengthening the required operations, personnel and infrastructure for RCTs, as outlined opposite.

Challenges	Suggestions
Operations	
• Inadequate medical record keeping • Non-availability of source documents	• Develop hospital digital health records • Strengthen data management systems
Personnel	
• Mapping of staff (numbers, capacity, institutional affiliation) • Training • Retention: personnel trained on RCTs or clinical trial are lost once the trial concludes • Stakeholder knowledge (ministries of health, ethics committees, principal investigators)	• Identify institutions and research personnel with capacity in countries • Provide technical support to countries through: – online courses – certificate programmes • Conduct training of trainers (based on the WHO African Region's model for the Expanded Special Project for Elimination of Neglected Tropical Diseases) • Identify regional training centres • Develop standardized guidelines for the Region on trials, consent and data quality
Infrastructure	
• System barriers, such as multiple institutional review boards (IRBs), need for high-level approval from the ministry of health and facility-based approval • Lack of clinical trial experts on ethics committees • Dearth of bioethics experts • Issues with consent/assent processes (cultural issue related to sharing of medical information) • Too much focus on pharmaceutical or industry-led trials • Delays in seeking ethical clearance, especially in emergency situations	• Conduct a critical review leading to improvements in the ethics review system • Include a patient care component in clinical trials • Base clinical trials and research questions on country needs • Develop separate ethics guidance for new drugs or interventions • Consider option of adding external experts in ethics committees/IRB when needed • Create network of bioethics researchers

Strengthening of the RCT ecosystem: regulatory functions of the ministry of health and drug authorities

In group work, participants identified challenges and suggestions in strengthening the regulatory functions for RCTs of the ministry of health and drug authorities

Challenges	Suggestions
Regulatory	
• Adaptive designs • Ad-hoc committees • Knowledge of existing infrastructure (trial, manufacturer) • Ethical approvals	• Develop strategy for communication with stakeholders • Develop strategy for engagement with political and administrative leadership • Leverage existing infrastructure • Enable IRBs/Ethics Review Committees to give expedited ethical clearance for trials during public health emergencies • Develop a data-sharing framework
Operational	
• Quality and rigour • Ethical control • Dissemination	• Ensure effective and efficient quality management • Develop standardized SOPs • Provide clarity on protocols • Develop a dissemination strategy
Emergencies	
• Pandemics • Armed conflicts • Climate disasters	• Engage communities (leadership, target groups)
Funding	
• Lack of funds	• Secure funding for framework planning • Secure funding for preparedness

3. Recommendations

The expert consultation concluded with a set of recommendations to help strengthen the Region's clinical trials ecosystem.

To Member States

1. Develop a clinical trials unit, including specialized clinical trials.
2. Take collective action in the areas capacity-building, infrastructure development, research and governance for RCTs and clinical trials.

To WHO

3. Follow-up this consultation by engaging in dialogue with national authorities and ministries to deepen understanding of the issues and identify solutions.
4. Map the clinical research centres in the Region.
5. Develop a regional framework for strengthening the regional RCT and clinical trial ecosystem.
6. Develop a regional strategy to encourage the development of clinical research organizations.
7. Develop a regional certification system to build the trust of the public in RCTs and clinical trials.
8. Develop a toolbox or a grading system for clinical trials.
9. Mobilize resources to support work in this area.
10. Provide support to countries in the areas of capacity-building, infrastructure development, research and governance.

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