




WHO's support for COVID-19 research and knowledge management in the Eastern Mediterranean Region

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ABSTRACT

Health research, innovation and knowledge management remain major priorities of the WHO's response to the COVID-19 pandemic. WHO's Eastern Mediterranean Regional Office (EMRO) supports priority research initiatives that address gaps in current knowledge regarding the COVID-19 pandemic. Through a specific call for proposals, 122 research proposals were received and reviewed in 2020, of which 17 were recommended for funding from eight countries. Ten countries in the region participated in the global solidarity trial to assess potential therapies for COVID-19. In addition, WHO advocated for early serological and epidemiological investigations ('COVID-19 Unity Studies') on the general population, healthcare workers, pregnant women and neonates, and extending technical, financial and material support for them.

Starting in early 2020, scholarly articles on COVID-19 have been published in every issue of the *Eastern Mediterranean Health Journal*. More than 6300 publications on COVID-19 were made available on the WHO knowledge management portal in the last year alone. WHO is also supporting countries in conducting studies to assess the field effectiveness of vaccines deployed nationally. To build and strengthen country capacities, regional webinars and intercountry meetings were conducted on research ethics, national health information systems and evidence-based health policy making. With support from WHO EMRO's new research and knowledge management pillar, countries in the region were well equipped to contribute to a global understanding of the novel virus's characteristics, as well as employ a national response based on informed evidence.

INTRODUCTION

COVID-19 could be accurately described as a novel 'high-impact' disease. Emergence of the disease and its designation as a pandemic by the WHO are indications of the potential and actual impact of this disease on the lives and livelihood of people.^{1 2} This was arguably more palpable in a region already affected by

SUMMARY BOX

- ⇒ WHO in the Eastern Mediterranean Regional Office region followed an innovative approach to establish a distinct pillar for 'research and knowledge management' in its COVID-19 Incident Management Support Team structure.
- ⇒ This enabled consolidation of all research-related activities of COVID-19 in the region under one coordinating umbrella and resulted in better resource generation and capacity building at regional and country levels.
- ⇒ The pillar focused on 'enhancing capacity for evidence generation at national level', 'timely provision of available evidence to support pandemic response' and 'enhancing capacity and experience sharing in use of evidence'.
- ⇒ The enhanced processes and capacities for high-profile research and use of research outcomes in national policies will enable further enhancement of such efforts in countries of the region beyond the COVID-19 pandemic.

conflicts, resulting in a slow progress towards achieving health-related Sustainable Development Goals.^{3 4}

Within the WHO, it was clear from the start that supporting pandemic response requires generation of new knowledge, timely awareness of emerging evidence from research and country data, and proper use of best available evidence for provision of advice and recommendations to countries around the world.⁵ While such mechanisms were developed at different levels of the organisation, the WHO office for the Eastern Mediterranean Regional Office (EMRO) took a unique approach and established a dedicated pillar for 'research and knowledge management' within its Incident Management Support Team (IMST) structure. This allowed for concentration of efforts and better coordination, as well as use

of existing structures within the WHO in support of emergency response. These areas of work can be categorised under three main umbrellas: (1) 'enhancing capacity for evidence generation at national level', (2) 'timely provision of available evidence to support pandemic response' and (3) 'enhancing capacity and experience sharing in use of evidence'.

In this practice article, we highlight the areas of work and achievements of the research and knowledge management pillar of the Eastern Mediterranean Region (EMR) IMST during the COVID-19 pandemic response. We also address challenges and lessons learnt from this new enterprise and potential ways forward to prepare for future pandemics.

ENHANCING CAPACITY FOR EVIDENCE GENERATION AT NATIONAL LEVEL

Early epidemiological studies and seroepidemiology surveys

The recent emergence of COVID-19 means that understanding of transmission patterns, severity, clinical features and risk factors for infection was limited, whether among the general population, for health workers or in household and other settings. Studies to assess the epidemiology and clinical characteristics of cases in different settings were therefore critical to furthering our understanding of this virus and associated disease. They would also provide the robust information needed to refine the parameters to feed into forecasting models. With the support of expert advisors, WHO adapted the influenza and Middle East respiratory syndrome coronavirus protocols to help enhance understanding of clinical, epidemiological and virological characteristics of COVID-19.⁶

Such studies are particularly important to be conducted in the EMR. WHO advocated for early seroepidemiological investigations ('Unity Studies') on the general population, healthcare workers, pregnant women and neonates, and extended technical, financial and material support for them to ministries of health, agencies and academic institutions. By late 2021, 17 seroepidemiology studies were supported by WHO under the global Unity Studies initiative in 13 EMR countries (Afghanistan, Pakistan, Egypt, Tunisia, Lebanon, Jordan, Yemen, the occupied Palestinian territory, Syria, Somalia, Sudan, Saudi Arabia and Iran), in close collaboration with high-level policymakers in ministries of health, and with the engagement and support of national academic institutions, providing key evidence for action. The implementation and use of seroprevalence results at different stages of the pandemic allowed for monitoring of the distribution of the COVID-19 pandemic by place, time and person characteristics at national level and estimate levels of immunoglobulins by age, gender, history of disease and symptoms and recently according to vaccination status. The study results were discussed in IMST meetings for regional implications and at national level, as a source for tuning the pandemic response, including for refining national testing strategies and estimating

under-reporting of cases and deaths due to COVID-19. In certain occasions, the results were also used for forecasting and projection of the disease at national and regional levels, especially in countries that conducted more than one round of serosurveys (eg, Jordan and Pakistan).^{7,8} Some countries, particularly countries facing complex humanitarian emergencies, such as Afghanistan and Yemen, used results for advocacy for increasing financial support for vaccine introductions.⁹ To that end, WHO is also supporting countries in conducting studies to assess the field effectiveness of vaccines deployed nationally (table 1).

A key element of the support for ensuring quality and standardised study methodology (for result pooling regionally and globally) of the studies was the procurement and distribution of standardised immunoassay tests (Wantai SARS-CoV-2 Ab ELISA; sensitivity $\geq 95\%$ and specificity $\geq 99\%$ in multiple independent evaluation studies¹⁰) to participating study groups. EMRO's Dubai Hub was instrumental in delivering this support to countries (in the region and globally), while technical experts in WHO guided the laboratory technicians on the use of the immunoassay tests and results' interpretation. Moreover, three countries (Afghanistan, Pakistan and Yemen) volunteered to use a rapid immunoassay test (Orient Gene Biotech COVID-19 IgG/IgM Rapid Test Cassette) alongside the Wantai ELISA test, with the support of WHO, in order to reach remote areas and contribute to the global evaluation of the SARS-CoV-2 rapid diagnostic tests.

Pregnant women and neonates cohorts

The COVID-19 and pregnancy longitudinal cohort study is designed to assess the impact of SARS-CoV-2 infection on pregnancy and the risk of mother to child transmission, to describe the viral presence in various body fluids in pregnant women and newborns, and to characterise the clinical course and disease spectrum of COVID-19 during pregnancy.¹¹ The study is currently being implemented in seven hospitals in Pakistan, with an expected sample size of 2944, with a second cohort planned in a Tunisian hospital covering a sample size of 436.

Vaccine effectiveness studies

The rapid development of COVID-19 vaccines has been the most effective way to prevent casualties.¹² Vaccine effectiveness studies aim to estimate the effectiveness of vaccines in the field, as compared with reported efficacy from trials. This integrated approach has been taken by EMRO to assess vaccine effectiveness in order to establish a regional network to measure COVID-19 vaccine effectiveness and a sustainable, easily adaptable platform to monitor the effectiveness and impact of other vaccines, such as seasonal and pandemic influenza and diseases of childhood such as respiratory syncytial virus (RSV). By early 2022, four countries of the region were ready to start conducting such studies at large scale (Egypt, Iran, Jordan and Pakistan). This is particularly important as

Table 1 Implementation of population-based age-stratified seroepidemiological Unity Studies in the Eastern Mediterranean Region with WHO support

Country	Date	Type of study	Sample size	Outcome/status
Afghanistan (two rounds)	June 2020	Household	9546	25%
	February 2021	Household	22 000	Preparation
Jordan (three rounds)	July 2020	Household	4467	0.3%
	October 2020	Household		7.4%
	December 2020	Household		39%
Pakistan (two rounds)	July 2020	Convenient open market	5035	11.1%
	October 2020	Household		7.1%
Palestine	January 2021	Household	6151	39.7%
Somalia	August 2020	Convenient health facilities	3600	Ongoing in two regions
Syria	February 2021	Convenient health facilities	10 000	Implementation
Yemen (Aden)	January 2021	Household	2001	27.4% (RDT qualified ELISA)
Egypt	February 2021	Household	6000	Data collection completed. Awaiting report
Tunisia	March 2021	Household	10 000	Data collection completed May 2021 (31%)
Lebanon	March 2021	Random phone calls	~3700	32%
Libya	March 2021			Preparation
Sudan	April 2021	Household	15 000	Proposal review
United Arab Emirates	August	Household	8831	Completed

some of the vaccines used in EMR are not subjected to such studies in other parts of the world.

Supporting national-level research studies on priority COVID-19-related topics

WHO/EMRO held a special call for proposals related to ‘Research in Priority Areas of Public Health (RPPH)’¹³ in the fields of disaster preparedness and response, epidemiology and surveillance, health systems and services, community engagement, infection prevention and control. Consequently, 122 research proposals were received and reviewed during 2020, of which 17 were recommended for funding from eight countries (Egypt, Iran, Jordan, Pakistan, the occupied Palestinian territory, Qatar, Sudan and the United Arab Emirates (UAE)). In addition, two other calls for proposals were released during 2021. The first was on ‘migration health research’,¹⁴ for which 90 research proposals were received and reviewed, of which 14 were recommended for funding from 10 countries (Egypt, Iran, Jordan, Lebanon, Morocco, Oman, Pakistan, Palestine, Sudan and Syria). The second was for proposals on ‘international health regulations and health security preparedness’,¹⁵ for which we received 50 proposals, of which 12 were recommended for funding from nine countries (Iran, Jordan, Lebanon, Pakistan, Palestine, Qatar, Sudan, UAE and Yemen). WHO is also supporting countries in research priority setting at the national level (Egypt, Jordan and Pakistan), including COVID-19-related priorities.¹⁶ Moving forward, we will focus on additional areas of research, such as the impact of misinformation on countries’ responses to the pandemic and postintroduction vaccine effectiveness studies to guide vaccination plans and policies for the future.

Support for conduct of solidarity trials and other clinical studies

To gain updated knowledge on the clinical management of COVID-19, WHO and partners launched the global ‘Solidarity’ trial,¹⁷ a global randomised controlled trial (RCT) with nearly 12 000 participants in 500 hospitals over 30 countries. WHO EMRO supported 10 countries (Bahrain, Egypt, Iran, Jordan, Kuwait, Lebanon, Morocco, Oman, Pakistan and Saudi Arabia) to join the global Solidarity trial to help find effective treatments for COVID-19.

WHO is currently supporting a WHO O2CoV2 study (WHO Respiratory Support Research): Oxygen requirements and approaches to respiratory support in patients with COVID-19 in low- and middle-income countries.¹⁸ From the region, the following five countries were selected for full participation in the study: Egypt, Iran, Jordan, Lebanon and Pakistan. WHO also supported three countries (Jordan, Kuwait and Saudi Arabia) to contribute to the WHO Global Clinical Platform for COVID-19 inpatient data.¹⁹

Assessment of COVID-19-related randomised controlled trials in the region

As a snapshot of the situation of COVID-19 related RCTs, 300 RCTs registered in EMR countries were reviewed. These were mainly conducted in Iran (60%), Egypt (23%), Pakistan (4%) and in 10 other EMR countries. A majority (70%) had a targeted sample size of below 100, while 17% focused on ‘herbal/traditional medicines’. These results, once collated, will be used to support future priority setting and provide insights on research governance.

Research ethics and standards

In spite of the dire need for local evidence to be generated on the EMR's response to the COVID-19 pandemic, all proposals recommended for WHO funding (eg, RPPH, migration health and IHR proposals referred to earlier) passed through two tiers of ethical review, that is, national/institutional ethical review and WHO's regional ethical clearance, using expedited review processes for research during emergencies.²⁰ Four regional webinars on ethics in research in the context of COVID-19 were conducted during 2020, in collaboration with bioethics, WHO collaborating centres and representatives of national ethics/bioethics committees in EMR countries.²¹ Moreover, the work plans of these WHO collaborating centres were amended to fit COVID-19 response, particularly in the fields of bioethics, infection prevention and control, non-communicable diseases and mental health.²²

Excess mortality and health information system support

All-cause mortality registration systems are key to determining the actual impact of the COVID-19 pandemic on human life. For a considerable time, a great deal of effort has been made to improve mortality registration systems, particularly data collected in EMR countries.^{23 24} Sixteen EMR countries currently report annual mortality data by cause of death to WHO. However, the urgent need for more frequent data reporting to monitor instantaneous changes in mortality has emerged since the start of the COVID-19 pandemic.

WHO developed and built capacity of countries to report weekly mortality data on an online platform by all causes (natural and non-natural) and COVID-19 deaths. Several meetings with mortality focal points were conducted to introduce innovations around the implementation of mortality surveillance systems and collection of data by age and sex. Capacity building workshops were also organised to train country teams responsible for health information systems on the use of excess mortality calculator and interpretation of results.²⁵ This has enabled setting weekly benchmarks and the opportunity to assess excess mortality in 2020, compared with previous years.²⁶ Countries with strong health information platforms, such as Oman, managed to develop weekly mortality curves by age and sex and identified excess mortality in 2020. Lebanon has also made tremendous improvement in its death registration system. Despite its limited infrastructure, the country used available mortality data by all causes of death, to validate COVID-19 deaths and assess the true impact of the COVID-19 pandemic. Tunisia also reported monthly total deaths and identified excess deaths in 2020, in comparison to 2019.

TIMELY PROVISION OF AVAILABLE EVIDENCE TO SUPPORT PANDEMIC RESPONSE

Evidence summaries and updates on vaccines and COVID-19 therapeutics

In order to enhance the understanding of evolving epidemiology, potential therapeutics and vaccine research

and development, and to inform decision-making in the region, evidence summaries from the region and globally were generated and progress of key research studies were reported to the IMST. Information on key topics such as treatment options, vaccine efficacy and effectiveness, and the impact of public health measures has been systematically documented.

By end of 2021, over 50 research and evidence briefing presentations were delivered in weekly IMST sessions. Additional presentations were conducted on specific topics of interest identified by IMST, including the use of traditional medicine in COVID-19, variants of concerns, vaccine booster dose, etc. These updates also included the outcomes of studies supported by the WHO at the national level, noted above.

Role of the *Eastern Mediterranean Health Journal*

Starting early 2020, scholarly articles on COVID-19 continue to be published in every issue of the *Eastern Mediterranean Health Journal* (EMHJ). These articles include original research articles, commentaries and editorials on COVID-19 from scientists and research groups of different EMR countries and beyond. We have also noticed that the EMHJ submissions, readership and access to its web pages²⁷ have also substantially increased during this period, attributed in part to increasing interest in accessing up-to-date research evidence.

Health knowledge management portal

The EMRO Health Knowledge Management Portal was developed as a new model of knowledge management to enhance the efficiency of using supportive informatics and knowledge bases for policy formulation by decision-makers and mid-level managers. The portal has been fully functional since February 2020 with COVID-19 epidemic-related information that captures, evaluates, shares and disseminates reliable and updated information. More than 100 e-Alert messages for COVID-19-related information including more than 8000 hints to relevant publications selected from recent relevant publications, news and information resources were distributed semiweekly. In addition, the Index Medicus of the Eastern Mediterranean Region²⁸ provides access to more than 239 000 citations published in more than 750 peer-reviewed journals from 20 EMR countries.

ENHANCING CAPACITY AND EXPERIENCE SHARING IN USE OF EVIDENCE

Support for innovations in response to the COVID-19 pandemic

EMRO conducted a regional survey on health innovations in response to the pandemic in the fields of education, community engagement and communication, workforce development and economic support, prevention, detection and testing, emergency communication, management, vulnerable groups, data platforms, and policy and practice.²⁹ In addition, solar-powered medical oxygen production was coordinated in Somalia to respond to

increasing mortality in remote areas, with preliminary data showing about 30 lives saved in the first month following its implementation.³⁰ Other specific innovations include telehealth/telemedicine applications including online consultation, referrals to diagnostics and inpatient care and management (eg, in Egypt); use of mobile applications for UHC, diagnosing and managing patients (that is, maternal and child health (e-MCH) and non-communicable diseases (e-NCD)) by United Nations Relief and Works Agency for Palestine Refugees (UNRWA) in Jordan, Palestine (Gaza, West Bank), Syria, Lebanon³¹; home delivery of medicines: especially for NCDs; digital contact tracing with caveats of ethics, security and confidentiality (Tunisia-Ehmi); Artificial Intelligence for Mental Health: Emotion Sensing Recognition App (Qatar); and e-Census: implementation of e-Census in Sep 2020 (Oman). WHO also recently launched a landmark publication on ‘ethics and governance of artificial intelligence for health’.³² Nevertheless, legal and privacy concerns as well as challenges in sustainability of such innovations at national, provincial or facility level may hinder their use. These challenges as well as interventions to enhance digital health and other innovations at national level in EMR countries are the focus of an ongoing effort, which is planned to be presented to the Eastern Mediterranean Regional Committee of the ministers of health in October 2022.³³

Use of evidence in national decisions

Various treatment regimens (including investigational and authorised medicines) have been recommended for COVID-19.³⁴ However, national treatment protocols in the EMR have shown inconsistency in terminologies and definitions used, inadequate coverage of medication safety information and discrepancies in pharmacotherapy recommendations compared with those set by WHO guidelines. Hence, a study was conducted to assess publication date, references, task force composition, coverage of medication safety and discrepancies in pharmacotherapy recommendations in NTPs. Based on this review, serious recommendations were made to countries which were timely for effective policy making.

Efforts were also made to document use of evidence in national policies in response to the COVID-19 pandemic. WHO is currently supporting 12 case studies in seven countries of the region (Iran, Jordan, Oman, Pakistan, Somalia, Sudan and Yemen), and further such studies are being discussed with colleagues in Afghanistan, Morocco and Syria. The case studies are expected to shed more light on challenges in use of evidence and facilitators of success in evidence-informed policy making (box 1). This work is coordinated through WHO’s Regional Network for Evidence and Data to Policy, which was established in 2020.^{35 36}

Medication safety

‘Adverse events due to unsafe medical practice’ is 1 of the 10 leading causes of death and disability in healthcare

Box 1 Example of case studies conducted by countries on use of evidence in national COVID-19 response

- ⇒ Establishment of a national rapid response system in response to the COVID-19 pandemic.
- ⇒ National prioritisation of vaccination plans and protocols.
- ⇒ COVID-19 vaccine hesitancy among health workers.
- ⇒ Implementing Friday curfews to control the spread of COVID-19.
- ⇒ Automation of PCR testing during the COVID-19 pandemic.
- ⇒ Strengthening the public health reference labs for COVID-19.
- ⇒ Establishment of online teaching systems for continuing medical education during COVID-19.
- ⇒ Risk communication and community engagement to respond to COVID-19.
- ⇒ Use of evidence for policy making in surveillance in response to the COVID-19 pandemic.
- ⇒ Management of COVID-19.
- ⇒ Local authority response to the COVID-19 pandemic.

systems worldwide with approximately two-thirds of all adverse events occurring in low-income and middle-income countries. Studies under this theme seek to assess medication safety issues related to common COVID-19 treatment regimens in the EMR in order to help prevent serious adverse events/medication errors. This analysis shows that safety information is noticeably overlooked in national/regional treatment protocols and by physicians treating COVID-19. Efforts by national health experts to ensure the accuracy and timely dissemination of safe and effective pharmacotherapy recommendations will be essential to ensuring medication safety for COVID-19 now and in the future.

Infodemics and the challenge of low-quality research

Low-quality research can lead to misinformation on vital public health topics distributed to policy makers and the public.³⁷ Our assessment demonstrates that there is an abundance of small cross-sectional and interventional studies that may have been used for making policy recommendations. The results of the assessment were presented in IMST meetings, as well as two regional and one global event, advocating for more proactive involvement of national research governance mechanisms in COVID-19-related research oversight. Challenges around appropriate information and research are manifested via the actions of different groups of key players including some clinicians, scientists and policy makers and are not limited to sections of the public or journalistic media.³⁸ Recent research on infodemics has suggested a number of priority research areas that can help us to better prepare for and respond to health-related infodemics.³⁹

CONCLUSIONS

We note the activities and lessons learnt in all three levels of EMR’s research and knowledge management pillar activities for COVID-19 response, including generation of evidence at the national level, timely provision of all evidence in areas of focus to WHO leadership at

regional and national levels, and enhancing capacity for documentation and sharing of experience and innovation between countries. Related efforts have resulted in enhanced capacity, especially in countries with less experience in these areas, to plan and conduct large-scale studies in response to policy needs. Still certain areas of work were not the direct focus of the work we are reporting here (mainly due to limited resources and less demand from countries). Future work should give more attention to social aspects of pandemic response and the way the response can affect the social determinants of health.

It remains a focus for the WHO to continue to work with the countries in enhancing their capacities for generation, translation, dissemination and use of evidence for health policy making. Future work will give more focus to the shortcomings observed in research governance and the use of evidence in national policies in accordance with the decisions made by countries of the region. COVID-19 has demonstrated many pitfalls in national and international levels in response to a pandemic. However, it has also generated opportunities for improved action. The additional focus given to the importance of national health information systems and research evidence is unprecedented, and such opportunities should be seized by ministries of health and the WHO to generate additional resources and institutional capacities for better action. For the success of pandemic response, collaboration and coordination between countries and between United Nations agencies is key.³

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