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Abstract

Background: Vaccine effectiveness studies provide evidence on the effects of vaccines for preventing disease and the adverse outcomes following a vaccination rollout programme in a country or a specific population.

Aims: To document the technical and capacity-building support provided by WHO to countries in the Eastern Mediterranean Region to conduct COVID-19 vaccine effectiveness studies.

Methods: WHO implemented interventions to enhance the capacity of EMR countries to conduct COVID-19 vaccine effectiveness and similar epidemiological studies. The intervention consisted of several components, including methodological and technical support as well as data and project management at national and regional levels. Two WHO generic protocols were adopted: cohort study among healthcare workers and test-negative design in severe acute respiratory infections surveillance sites.

Results: Egypt, Islamic Republic of Iran, Jordan, and Pakistan participated in the programme. The research protocols were adjusted to country context and settings. WHO provided technical, financial and infrastructure support, including the establishment of quality assessment approaches, study conduct, data management, report development, statistical data analysis,

and experience-sharing between the countries. Technical capacity-building was also offered to other countries not involved in the vaccine effectiveness studies.

Conclusion: COVID-19 pandemic provided an opportunity to enhance the research capacities of EMR countries for the conduct of vaccine effectiveness studies. The WHO consolidated efforts and its collaboration with countries resulted in enhancement of capacity and research infrastructure, especially in the 4 countries that were supported by this programme. The capacities acquired through the programme would be very useful for other vaccine-preventable communicable diseases, thus better informing national immunization programmes and policies in EMR countries.

Keywords: vaccine effectiveness, capacity-building, COVID-19, vaccination, vaccine-preventable diseases, immunization, Eastern Mediterranean

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Background

While randomized controlled trials (RCTs) provide the evidence required for assessing efficacy of vaccines against comparator groups (e.g. placebo or other vaccines) in a study setting, vaccine effectiveness studies provide evidence on the effects of vaccines in preventing disease and the adverse outcomes following the rollout of vaccination programmes in countries or specific populations. Significant technical expertise and resources are needed to conduct vaccine-related RCTs and vaccine effectiveness studies. Such studies were rarely being conducted in the Eastern Mediterranean Region (EMR) countries due to a combination of factors such as the lack of technical expertise, limited research infrastructure, limited financial

resources, and a lack of policy interests. As a result of the urgent needs for such studies due to COVID-19 pandemic, the World Health Organization Regional Office for the EMR (WHO/EMRO) embarked on a programme to enhance the capacity of EMR countries to conduct vaccine effectiveness studies. The programme enhanced technical expertise and strengthened research infrastructure, leveraging existing respiratory disease surveillance systems.

Since being declared a Pandemic by the WHO on 11 March 2020, COVID-19 became a global health priority (1). The EMR includes 22 countries that have variable healthcare and health research capacities and infrastructure (2–4). The COVID-19 pandemic was a major public health challenge to the Region, in addition to the existing risks that negatively affected health and health outcomes in Member States (5,6).

As of March 2023, the WHO/EMRO media centre had reported at least 350 000 deaths due to COVID-19 in the EMR (7,8), while COVID-19 vaccination coverage remained lower than expected in most countries of the Region (9). Excess COVID-19 deaths in Eastern European countries had been shown to be associated with weaker implementation of COVID-19 regulations and lower vaccine coverage (8).

WHO and its partners have been committed to supporting countries in accessing COVID-19 vaccines by addressing delivery and storage challenges (10), while working closely with ministries of health to ensure that vaccine hesitancy among populations is addressed through the dispelling of misinformation.

While RCTs have demonstrated adequate efficacy of a few COVID-19 vaccines in controlled settings, it is worth noting that many factors, including differences in country demographics and disease profiles, suboptimal cold chain capacity, variation in dose intervals, interchangeability of different vaccine products, off-schedule and incomplete delivery of doses, could affect vaccine effectiveness in the field (11). These factors can cause differences in vaccine effectiveness when compared to vaccine efficacy results from the controlled conditions of RCTs.

Vaccine effectiveness studies provide opportunities to assess the durability of vaccine-mediated immunity over longer periods, their effectiveness in sub-groups of the population not adequately represented in RCTs, as well as any side-effects and potential risks.

The frequent emergence of SARS-CoV-2 variants of concern require ongoing monitoring of vaccine effectiveness against such variants (11,12). Thus, studies are needed to measure vaccine effectiveness against serious outcomes such as long-term protection against serious disease, hospitalization or deaths at population level as well as within different risk groups (e.g. the elderly and those with comorbidities) and for different vaccine products. These studies will also monitor potential side-effects and harms over time and, hence, alleviate public concerns about such risks. Sustainable vaccine effectiveness platforms provide ongoing assessment and long-term monitoring of vaccines, which will in turn provide manufacturers, national health authorities and regulators with essential data to understand vaccine impact and better inform national immunization policies.

As of September 2022 there were at least 172 COVID-19 vaccine candidates undergoing clinical trials worldwide, with 199 candidates in pre-clinical development stages (13). A variety of COVID-19 vaccines, mostly inactivated and protein products, were being produced by or being used in EMR countries (e.g. Sinopharm, Covaxin, Spikogen, Barekat, etc.), for which vaccine effectiveness data was limited compared to other vaccines (e.g. Pfizer-BioNTech, Moderna and Oxford-AstraZeneca,) which had been more widely researched (14,15).

The importance of context-specific vaccine-effectiveness data, as well as the complexity of impact assessment for novel vaccines, created an urgent need for vaccine effectiveness studies by countries in the Region; the proper design and implementation of which warranted careful epidemiological considerations that required technical support and capacity-building in countries for conducting such studies (16).

There is limited evidence of vaccine effectiveness studies (e.g. for flu vaccines) being conducted in the Region prior to the COVID-19 pandemic. As a result, subsequent to the pandemic, the leadership of WHO/EMRO raised the issue within its incident management support team, following which it was collectively decided for the research and knowledge management pillar and the vaccine pillar to lead and support an initiative to enhance the conduct of COVID-19 vaccine effectiveness studies in the EMR (17). Alongside the WHO efforts, certain research teams also conducted key vaccine effectiveness studies, which informed national and global policies (18–21).

The design and implementation of the vaccine effectiveness studies required enhancing the research infrastructure and the technical capacity of ministries of health and investigators, as well as strengthening existing surveillance systems, such as sentinel surveillance sites for other respiratory infectious diseases in the countries. These would in turn facilitate evaluation of COVID-19 vaccine effectiveness and generate valid evidence for policymaking in national and

regional immunization programmes.

This paper presents a brief description of the technical and capacity-building support provided by WHO to EMR countries to conduct the vaccine effectiveness studies.

Methods

Since 2020, WHO has adopted the following interventions to enhance the capacity of EMR countries to evaluate COVID-19 vaccine effectiveness and to conduct similar epidemiological studies:

1- Enhancing processes and structures in the Region

a. Establishment of the multidisciplinary regional COVID-19 vaccine effectiveness technical team

An interdisciplinary technical team of WHO experts from various backgrounds including epidemiology, medicine, pharmacy, laboratory science, health management, economics and health policy developed a roadmap for the selection and support for the conduct of the studies. The team served as the coordination hub, providing institutional direction and insight to the national research teams. External consultants with expertise in epidemiology, statistics and data management, and extensive experience in conducting vaccine effectiveness studies were commissioned to provide further technical support.

b. Development of the COVID-19 vaccine effectiveness studies dashboard for EMR

A COVID-19 vaccine effectiveness studies dashboard was developed to serve two purposes: (i) enable WHO to keep track of all proposals received from countries seeking WHO support for conducting national COVID-19 vaccine effectiveness studies, and (ii) track other COVID-19 vaccine effectiveness studies conducted and published by EMR countries. The dashboard included data related to the country of study, study design, sample specifications, vaccines under the study, and the dominant variants of SARS-CoV-2 virus during the study.

c. Standardization of study design and data analysis

WHO developed guidance documents outlining the requirements for conducting COVID-19 vaccine effectives studies by countries using two main methods: cohort study design among healthcare workers (22), and test-negative case-control design in severe acute respiratory infections (SARI) surveillance sites (23). These protocols had advantages. They could be adapted to local settings and capacities in each country and they allowed researchers to engage in a multinational study. Subsequently, standardization was done to harmonize study procedures (designs and methods) among the various proposals received from different

institutions, and standardized code books were developed to collect comparable data. This in turn allowed pooling of results across national studies and reporting regional COVID-19 vaccine effectiveness estimates.

d. Issuance of regional ethical clearance

A regional ethical clearance was obtained through the Eastern Mediterranean Research Ethics Review Committee for the duration of the study. National studies were required to obtain national research ethics clearance as well as the regional clearance.

e. Development of the regional data entry platform

A central data entry platform was established within Research Electronic Data Capture (REDCap) to collect anonymized disaggregated data from national studies. REDCap is a web-based application designed to support data capture for research studies while providing: (a) an intuitive interface for validated data entry, (b) audit trails for tracking data manipulation and export procedures, (c) automated export procedures for seamless data downloads using common statistical programs, and (d) procedures for importing data from external sources (24).

2- Building national technical capacities in countries

Four region-wide capacity-building workshops and two country-specific interactive training sessions were held virtually from September 2021 through December 2022. The first series of region-wide capacity-building workshops were held in December 2021. It focused on the WHO-approved protocols (study designs/methods) and required criteria for conducting COVID-19 vaccine effectiveness research. The second series of region-wide workshops were held in November 2022 and were dedicated to important considerations for investigators in conducting COVID-19 vaccine effectiveness research given the updates in WHO guidance on the evaluation of COVID-19 vaccine effectiveness and study results worldwide. Two country-specific workshops were held in March 2022, which were tailored to train the research teams from participating countries in the Region on the use of REDCap for data management of their respective study results.

In addition to the region-wide workshops, the regional COVID-19 vaccine effectiveness technical team held interactive meetings and individual consultation sessions with investigators of participating countries. The meetings were tailored to their respective needs and specific requests and the goal was to address any challenges in designing and conducting COVID-19 vaccine effectiveness studies, either during proposal development or study implementation.

Results

Overall, 93 participants from Bahrain, Egypt, Islamic Republic of Iran, Jordan, Kuwait, Lebanon, Oman, Pakistan, Qatar, Sudan, Syria, and the United Arab Emirate attended the region-wide workshops, as well as Ethiopia from the WHO/AFRO Region. Following the workshops and a call for proposals for COVID-19 vaccine effectiveness research, the technical team received 12 expressions of interest from the countries. After several rounds of technical evaluation and feedback from the team, proposals from 4 countries were selected for inclusion in the regional study. The investigators of the studies attended country-specific workshops in Egypt, Jordan, Islamic Republic of Iran, and Pakistan (Table 1).

Four country-specific questionnaires were adapted based on the generic WHO vaccine effectiveness protocols and the specific needs of each country, and these were uploaded to the regional data entry platform. Authorized investigators from participating countries were given access to the platform for data entry and trained for regular assessment and quality check of their respective study inputs and data. The use of REDCap provided the opportunity for secure and timely assessment of the data entry processes and helped in addressing technical issues encountered by the countries. The platform facilitated pooling of study results across countries for statistical data analysis and reporting on vaccine effectiveness. Table 2 summarizes key planning and operational challenges observed during the conduct of the studies at different stages.

Discussion

Towards the end of 2022, some 20 COVID-19 vaccine effectiveness studies had been published by EMR countries, 17 (85.0%) of which were from 3 high-income countries (Kuwait, Qatar and UAE), while the remaining were from Egypt, Lebanon, Morocco, and Tunisia (25). This shows that far less COVID-19 vaccine effectiveness data is being generated from low- and middle-income countries (LMICs) in EMR, underscoring the importance of WHO’s support for robust vaccine effectiveness studies in the Region, especially because 16 of the 22 EMR Member States are LMICs (26).

Of the 20 published studies, the authors or collaborators of 14 (70.0%) were affiliated with the ministries of health or other government health institutions of their respective countries. This indicates that the results of these studies are more likely to influence national immunization policies and programmes (27). Therefore, capacity-building for conducting vaccine effectiveness studies and establishing a sustainable network of investigators and decision-makers in the Region is anticipated to help generate long-term quality results that could ultimately be used for evidence-informed policymaking (28). This highlights the need to ensure that investigators conducting national COVID-19 vaccine effectiveness studies receive pertinent technical support and training as part of capacity-building programmes.

Apart from the many advantages of the regional study, we encountered several technical and operational challenges in the process of designing and implementing this multinational COVID-19 vaccine effectiveness study. Some of these were due to the emerging nature of the disease and the study designs (29), while others were due to coordination issues across the region or countries (Table 2). WHO supported countries in addressing and overcoming these challenges, although quality assurance of the study processes continues to be challenging.

There have been different approaches to the response to the COVID-19 pandemic, including enhancing capacity for policy-oriented research (17). Countries need to further invest in vaccine effectiveness studies and ensure that it becomes a part of the routine assessment for current and emerging vaccines.

WHO adapted the guidance for global influenza surveillance and response system for the purpose of integrated sentinel surveillance of influenza and SARS-CoV-2 (as well as other respiratory viruses with epidemic and pandemic potential) (30). Currently, the influenza surveillance network leveraged for COVID-19 surveillance is active in 19 out of 22 EMR countries, which provides further opportunity for vaccine effectiveness studies, noting the enhanced technical and infrastructure capacities in the Region. The SARI surveillance network for influenza in the Region contributes to the establishment of a sustainable platform for monitoring and evaluating COVID-19 vaccine effectiveness; a capacity that is amplified by the infrastructure and technical expertise developed for the regional COVID-19 vaccine effectiveness studies.

Vaccine effectiveness studies are a key source of evidence for national vaccination-related decisions. Hence, the investigators and research teams should strengthen their links with policymakers to identify the key policy questions that need to be answered by research, as well as the timely and effective presentation of the results to the relevant national bodies.

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Renforcement des capacités pour la réalisation d'études sur l'efficacité des vaccins contre la COVID-19 afin d'améliorer l'élaboration de politiques reposant sur des bases factuelles dans la Région de la Méditerranée orientale

Résumé

Contexte : Les études sur l'efficacité des vaccins fournissent des données probantes concernant les effets des vaccins sur la prévention des maladies et les résultats indésirables à la suite d'un programme de déploiement de la vaccination dans un pays ou dans une population spécifique.

Objectif : Documenter l'appui technique et le soutien au renforcement des capacités fournis par l'OMS aux pays de la Région de la Méditerranée orientale pour la réalisation d'études sur l'efficacité des vaccins contre la COVID-19.

Méthodes : L'OMS a mis en œuvre des interventions visant à renforcer la capacité des pays de la Région de la Méditerranée orientale à mener des études sur l'efficacité des vaccins contre la COVID-19 et des études épidémiologiques similaires. L'intervention comprenait plusieurs composantes, notamment l'appui méthodologique et technique ainsi que la gestion de données et de projets aux niveaux national et régional. Deux protocoles génériques de l'OMS ont été adoptés : une étude de cohorte auprès des agents de santé et une méthodologie de test négatif dans les sites de surveillance des infections respiratoires aiguës sévères.

Résultats : L'Égypte, la République islamique d'Iran, la Jordanie et le Pakistan ont participé au programme. Les protocoles de recherche ont été adaptés à la situation et aux contextes des pays. L'OMS a apporté un appui technique, financier et infrastructurel, notamment pour la mise en place d'approches d'évaluation de la qualité, la réalisation d'études, la gestion des données, l'élaboration de rapports, l'analyse des données statistiques et l'échange de données d'expérience entre les pays. Des activités de renforcement des capacités techniques ont également été proposées à d'autres pays qui n'ont pas participé aux études sur l'efficacité des vaccins.

Conclusion : La pandémie de COVID-19 a permis de renforcer les capacités de recherche des pays de la Région de la Méditerranée orientale pour la conduite d'études sur l'efficacité des vaccins. Les efforts consolidés de l'OMS ainsi que sa collaboration avec les pays ont permis de renforcer les capacités et les infrastructures de recherche, en particulier dans les quatre pays qui ont bénéficié du soutien de ce programme. Les capacités acquises par le biais du programme pourraient être très utiles dans le cadre d'autres maladies transmissibles évitables par la vaccination, ce qui permettrait de mieux informer les programmes et politiques de vaccination au niveau national dans les pays de la Région.

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6. Memish ZA, Brennan RJ, Rashidian A, Abubakar A, Khan W, Ghaffar A. COVID-19 pandemic response in one of the world's most complex and vulnerable settings. BMJ Global Health 2022;7(Suppl 3):e009911. DOI: http://dx.doi.org/10.1136/bmjgh-2022-009911.

7. World Health Organization. WHO Regional Director's statement on COVID-19. World Health Organization Regional Office for the Eastern Mediterranean, 2022. http://www.emro.who.int/health-topics/corona-virus/index.html.

8. Ylli A, Burazeri G, Wu YY, Sentell T. COVID-19 excess deaths in Eastern European countries associated with weaker regulation implementation and lower vaccination coverage. East Mediterr Health J 2022;28(10):776–780. DOI: https://doi.org/10.26719/emhj.22.074.

9. Hasan Q, Elfakki E, Fahmy K, Mere O, Ghoniem A, Langar H, et al. Inequities in the deployment of COVID-19 vaccine in the WHO Eastern Mediterranean Region, 2020–2021. BMJ Glob Health 2022;7(Suppl 4):e008139. DOI: http://dx.doi.org/10.1136/bmjgh-2021-008139.

10. World Health Organization. Inequitable COVID-19 vaccination coverage in the Eastern Mediterranean Region is a missed opportunity to protect people from severe disease and death. World Health Organization Regional Office for the Eastern Mediterranean, 2021. http://www.emro.who.int/media/news/inequitable-covid-19-vaccination-coverage-in-the-eastern-mediterranean-region-is-a-missed-opportunity-to-protect-people-from-severe-disease-and-death.html.

11. World Health Organization. Evaluation of COVID-19 vaccine effectiveness - Interim Guidance (17 March 2021). Geneva: World Health Organization, 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-measurement-2021.1.

12. World Health Organization. Guidance on conducting vaccine effectiveness evaluations in the setting of new SARS-CoV-2 variants: Interim guidance. Geneva: World Health Organization, 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-variants-2021.1.

13. World Health Organization. The COVID-19 vaccine tracker. Geneva: World Health Organization, 2022. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.

14. World Health Organization. Status of COVID-19 vaccines within WHO EUL/PQ evaluation process. Geneva: World Health Organization, 2022. https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_26May2022.pdf.

15. Kudlay D, Svistunov A. COVID-19 vaccines: an overview of different platforms. Bioengineering. 2022;9(2):72. DOI: https://doi.org/10.3390/bioengineering9020072.

16. Teerawattananon Y, Anothaisintawee T, Pheerapanyawaranun C, Botwright S, Akksilp K, Sirichumroonwit N, et al. A systematic review of methodological approaches for evaluating real-world effectiveness of COVID-19 vaccines: advising resource-constrained settings. PLoS ONE. 2022;17(1):e0261930. DOI: https://doi.org/10.1371/journal.pone.0261930.

17. Rashidian A, Wu K, Al Ariqi L, Aly E, Mandil A, Barakat A, et al. WHO's support for COVID-19 research and knowledge management in the Eastern Mediterranean Region. BMJ Glob Health 2022;7(Suppl 3):e008737. DOI: http://dx.doi.org/10.1136/bmjgh-2022-008737.

18. Heidarzadeh A, Moridani MA, Khoshmanesh S, Kazemi S, Hajiaghabozorgi M, Karami M. Effectiveness of COVID-19 vaccines on hospitalization and death in Guilan, Iran: a test-negative case-control study. International Journal of Infectious Diseases 2023;128:212–222. DOI: https://doi.org/10.1016/j.ijid.2022.12.024.

19. Alali WQ, Ali LA, AlSeaidan M, Al-Rashidi M. Effectiveness of BNT162b2 and ChAdOx1 vaccines against symptomatic COVID-19 among healthcare workers in Kuwait: a retrospective cohort study. Healthcare 2021;9(12):1692. DOI: https://doi.org/10.3390/healthcare9121692.

20. Al Kaabi N, Oulhaj A, Ganesan S, Al Hosani FI, Najim O, Ibrahim H, et al. Effectiveness of BBIBP-CorV vaccine against severe outcomes of COVID-19 in Abu Dhabi, United Arab Emirates. Nat Commun 2022;13(1):3215. DOI: https://doi.org/10.1038/s41467-022-30835-1.

21. Belayachi J, Obtel M, Razine R, Abouqal R. Long term effectiveness of inactivated vaccine BBIBP-CorV (Vero Cells) against COVID-19 associated severe and critical hospitalization in Morocco. PLoS One 2022;17(12):e0278546. DOI: 10.1371/journal.pone.0278546.

22. World Health Organization. Cohort study to measure COVID-19 vaccine effectiveness among health workers in the WHO European Region: guidance document. World Health Organization Regional Office for Europe, 2021. https://apps.who.int/iris/handle/10665/340217.

23. World Health Organization. Estimating COVID-19 vaccine effectiveness against severe acute respiratory infections (SARI) hospitalisations associated with laboratory-confirmed SARS-CoV-2: an evaluation using the test-negative design (TND): guidance document World Health Organization Regional Office for Europe, 2021. https://apps.who.int/iris/handle/10665/341111.

24. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. Journal of Biomedical Informatics 2019;95:103208. DOI: https://doi.org/10.1016/j.jbi.2019.103208.

25. VIEW-hub by IVAC. Vaccine Product (current/planned). VIEW-hub by IVAC, 2022. https://view-hub.org/covid-19/?set=vaccine-product-current-planned&group=vaccine-introduction&category=covid.

26. The World Bank.The World by Income and Region. World Development Indicators, 2022. Washington DC: The World Bank. https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html.

27. International Vaccine Access Center (IVAC). Vaccine effectiveness studies - Eastern

Mediterranean Region. Baltimore: Johns Hopkins Bloomberg School of Public Health, 2022. https://view-hub.org/covid-19/effectiveness-studies?field_region=eastern-mediterranean.

28. Steffen CA, Henaff L, Durupt A, Omeiri NE, Ndiaye S, Batmunkh N, et al. Evidence-informed vaccination decision-making in countries: Progress, challenges and opportunities. Vaccine 2021;39(15):2146–2152. DOI: https://doi.org/10.1016/j.vaccine.2021.02.055.

29. Shi X, Li KQ, Mukherjee B. Current challenges with the use of test-negative designs for modeling COVID-19 vaccination and outcomes. American Journal of Epidemiology 2023;192(3):328–333. DOI: https://doi.org/10.1093/aje/kwac203.

30. World Health Organization. Maintaining surveillance of influenza and monitoring SARS-CoV-2 - Interim Guidance. Geneva: World Health Organization, 2020. https://apps.who.int/iris/rest/bitstreams/1316069/retrieve.

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