WHO-EM/CEH/174/E

Summary report on the

# Regional training workshop on building country capacities in estimating the health impacts of air pollution using time series analysis

Amman, Jordan
25–28 February 2024

World Health Organization
Eastern Mediterranean Region

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## 1. Introduction

The WHO Eastern Mediterranean Region has the highest levels of ambient air pollution compared to other WHO regions. In 2019–2023, annual concentrations of particulate matter (PM) with an aerodynamic diameter equal to or less than 10 μm ($PM_{10}$) and 2.5 μm ($PM_{2.5}$) exceeded WHO's 2021 air quality guidelines (AQG) by up to 12 and 24 times, respectively. The high PM levels across the Region are associated with unsustainable development, ongoing urbanization and industrialization, increasing emissions from mobile sources, open municipal and agricultural waste burning, and natural sources such as sand and dust storms (SDS), which contribute up to 60% of the recorded PM levels.

Air pollution is the greatest environmental risk to human health. Its health burden is now estimated to be competing with other major global health risks, such as unhealthy diets and tobacco smoking. Air pollution is recognized as a risk factor for five main diseases, including ischemic heart disease, stroke, chronic obstructive pulmonary diseases (COPD), lung cancer and acute lower respiratory infections. Growing evidence indicates causal relationships with type II diabetes mellitus, neonatal mortality from low birth weight, and mortality from and incidence of neurological diseases, specifically Alzheimer's disease. According to WHO's Global Health Estimates, the top 10 leading causes of global mortality in 2019 included ischaemic heart disease, stroke, COPD, lower respiratory infections, neonatal conditions, lung cancer, Alzheimer's disease and other dementias, diarrhoeal diseases, diabetes mellitus and kidney diseases. There is a clear correlation between these conditions and exposure to high levels of air pollution. Recent estimates from the Institute for Health Metrics and Evaluation reveal that air pollution now ranks as the second leading cause of natural mortality, following closely behind high blood pressure, and is the foremost risk factor among environmental factors in the Region.

WHO's latest estimates show that the age-standardized mortality rate attributable to air pollution (Sustainable Development Goal indicator 3.9.1) in the Eastern Mediterranean Region is the second highest after the WHO Africa Region. Every year, the Eastern Mediterranean Region experiences more than 570 000 premature deaths due to air pollution, of which 58.5% are due to ischaemic heart disease, 18% due to stroke, 13.4% due to acute lower respiratory infections, 8.4% due to COPD and 1.7% due to lung cancer. There is a strong likelihood that these figures are conservative, as they fail to fully account for the health impacts of dust exposure. Specifically, there is a lack of concentration–response functions to estimate the impact of air pollution in dusty environments accurately. Furthermore, with the looming spectre of climate change, these estimates are expected to increase in the coming years. As temperatures rise and weather patterns become increasingly erratic, the likelihood of greater air pollution and its associated health risks grows ever more pronounced.

SDS represents an environmental challenge faced by various countries of the Region, where most are located within the SDS belt areas and are recognized as source/origin countries for SDS. Recently, the Region has observed a surge not only in the frequency of SDS events but also in their duration and intensity. It is noteworthy that SDS events have coincided with substantial increases in measured concentrations of both the $PM_{10}$ and $PM_{2.5}$ size fractions. The health burden of SDS exposure is still unclear. A growing body of evidence indicates a correlation between SDS events and cardiovascular mortality and respiratory morbidity. Nevertheless, there is a considerable debate regarding the methodology employed in estimating the health burden of dust exposure. Current practice assumes that dust exposure has similar toxicity to anthropogenic PM sources, regardless of its composition. To better understand the shape of the concentration–response relationships between air pollution and health outcomes in dusty environments,

extensive epidemiological studies spanning single and multiple countries are imperative, particularly within the Region.

In this context, and aligned with the WHO AQG good practice statement on SDS, which advocates for the conduct of epidemiological studies, including those addressing the long- and short-term effects of SDS, and research activities aimed at better understanding the toxicity of the different types of PM, the WHO Regional Office for the Eastern Mediterranean held a four-day regional training workshop in Amman, Jordan, on 25–28 February 2024 on building country capacities in estimating the health impacts of air pollution using time series analysis.

The primary objective of the workshop was to empower national representatives with the necessary knowledge and skills to assess the association between short-term exposure to PM and daily mortality using time series regression analysis and RStudio software and to facilitate the implementation of extensive multi-country time series analysis. For this purpose, participants were encouraged to compile datasets for at least three consecutive years for one or two cities within their countries. The datasets comprised the essential data necessary to conduct a comprehensive time series analysis, including daily mortality data for all-natural or specific causes, daily average concentrations of $PM_{10}$ and/or $PM_{2.5}$ from city-specific monitoring stations, daily average temperature readings and additional pertinent environmental variables.

The specific objectives of the regional training workshop were to:

- empower health and environmental professionals with optimal methodologies for conducting time series regression analysis to better understand the health impacts of air pollution in dusty environments; and
- facilitate the conduct of an intercountry time series analysis in the Eastern Mediterranean Region.

The training was attended by 20 air quality and health professionals, representing ministries of health and environment, research centres and universities from seven countries of the Region, namely Egypt, the Islamic Republic of Iran, Jordan, Kuwait, Lebanon, Morocco and Qatar. The workshop was facilitated by experts from the Spanish National Research Council, Lazio Regional Health Service and WHO.

## 2. Summary of discussions

*Current air quality and health research in the Region*

The WHO AQG 2021 represent a significant advancement, drawing upon over 15 years of robust health-based evidence since the last global update in 2005. The guidelines are based on a meticulous review and analysis of all published epidemiological studies on the risks associated with both short- and long-term exposure to air pollution. They recommend levels and interim targets for common air pollutants: PM, $O_3$, $NO_2$, and $SO_2$.

The updating process entailed six systematic reviews of evidence generated from various meta-epidemiological and meta-analysis studies, including cohort studies, case-crossover analyses and time series regression analyses. The available studies have documented adverse health effects not only in countries with high levels of air pollution but also in those with relatively clean air, indicating adverse effects at significantly lower levels than previously studied. It is noteworthy that among the 66 studies included in the systematic reviews, none were conducted in countries of the Eastern Mediterranean Region, highlighting a significant gap in our understanding of the health impacts of air pollution within the Region. The absence of research from countries of the Region underscores the urgency to not only augment the quantity of studies but also enhance their quality.

Recognizing this knowledge gap and aiming to gain deeper understanding of the Region's needs, WHO commissioned a systematic review of published air quality and health research during the period 2000–2022. The review aimed to identify the gaps in the current research. The results indicated a notable scarcity both in terms of the quantity and quality of the available studies. Among 2947 studies, only 353 were relevant to the scope of the systematic review. The review highlighted a stark deficiency in the number of time series analysis studies to assess the short-term health impacts of air pollution, with only 15 identified over the study period. Significantly, none of these studies successfully met the rigorous evaluation criteria for the PECOS (population, exposure, comparator, outcome and study design) appraisal employed in the review or for the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

In addition, the results revealed a highly heterogeneous distribution in the publication of studies on air pollution and health across the countries of the Region. This variability further emphasizes the need for concerted efforts to address the research gaps and enhance collaboration to ensure a more comprehensive understanding of air quality issues and their health implications throughout the Region.

The major challenges in conducting air quality and health research within the Region include: a deficiency in expert capacity and human resources; inadequate studies to estimate the effects of air pollution on health across countries in the Region; the substandard quality of existing research, hindering participation in the formulation of AQG; and a lack of comprehensive multi-country studies aimed at exploring the shape of the concentration–exposure relationships of dust exposure at the regional level.

It is imperative to address these challenges by prioritizing specific areas of research. These areas include: investigating the relationship between long- and short-term exposure to PM, $NO_2$, $O_3$, $SO_2$ and all-cause and

cause-specific mortality in the Region; investigating the relationship between long- and short-term exposure to SDS and all-cause and cause-specific mortality in the Region; and the source-specific health risk assessment of ambient air pollutants. These priorities are critical for guiding future research endeavours and formulating effective policies to safeguard public health in the Region.

*The impact of air pollution in dusty environments*

A WHO-commissioned toxicological review of 67 experimental studies concluded that SDS is a risk factor for inflammatory and allergic lung diseases. These risks are observed not only in the source areas of SDS but also in locations further away, where dust mixes with industrial pollutants and microorganisms.

Another systematic review encompassing 93 epidemiological studies has provided insights into the adverse health effects of SDS. While the evidence indicates a link between desert dust exposure and cardiovascular mortality and respiratory morbidity, inconsistencies arise when considering the various sources of PM across different geographical regions.

Understanding the health effects of anthropogenic and nonanthropogenic PM is particularly challenging due to the complexity of air quality mixture in composite source profiles. Some of the existing studies have predominantly approached dust events as either binary risk exposures, particularly prevalent in eastern Asia, or as effect modifiers for health outcomes associated with specific PM fractions, commonly seen in southern Europe. Discrepancies emerge when comparing the effects of desert dust and anthropogenic PM concentrations independently. For instance, eastern Asia shows a higher association between Asian dust and certain cardiovascular mortality and morbidity

outcomes, whereas southern Europe demonstrates similar health effects for Saharan dust and anthropogenic PM.

Although the Eastern Mediterranean Region has the highest levels of $PM_{10}$ and is affected the most by SDS, the number of studies evaluating the acute health effects of PM exposure is minimal. Thus, the assessment of health impacts associated with ambient air pollution is being done using exposure–response functions derived from non-dusty environments. Unless or until further evidence emerges, this approach relies on the assumption that the health risk per microgram of dust is comparable to other PM constituents (with the exceptions of sulfates and elemental carbon, where evidence suggests greater effects than other constituents). The question of including/excluding the dust fraction of PM in long- and short-term assessments remains unanswered. Time series analysis of reasonable periods of time conducted in dusty environments, such as in the Eastern Mediterranean Region, will partially answer this question.

In summary, while existing research sheds light on the health implications of SDS, there is a pressing need for further investigation, particularly in regions such as the Eastern Mediterranean Region, to comprehensively understand the long- and short-term health impacts and refine assessment methodologies accordingly.

*Building capacities in time series regression analysis*

Time series regression studies have been extensively used in investigating short-term PM-mortality and morbidity associations, providing substantial information to derive and upgrade the WHO AGQ values for acute exposure to $PM_{10}$ and $PM_{2.5}$.

The workshop covered the fundamental principles of conducting time series regression analysis, including defining health effects, distinguishing between short- and long-term impacts, and understanding the underlying objectives of health impact assessments. The facilitators emphasized the necessity of utilizing time series data for multiple years, in order to have adequate power to estimate the short-term effects of dust exposures on daily health outcomes, while adjusting for air temperature, seasonality, days of the week and other potential time-varying confounding factors. These essential elements are very important in exploring the shape of the exposure–response association. The discussion further explored the components of time series data, and the strengths and limitations of the time series design. Additionally, the workshop introduced the case-crossover design as an alternative approach, highlighting its efficiency in controlling for long-term trends and seasonality. Attendees were also briefed on various modelling frameworks, the criteria for model selection and considerations for environmental risk exposures.

Special focus was put on estimating and modelling the short-term effects of desert dust. The facilitators discussed various research questions and hypotheses regarding the impact of desert dust on health outcomes, emphasizing the need for standardized epidemiological studies to facilitate comparisons across regions. Additionally, they outlined methodologies for identifying and quantifying dust events, including the use of aerosol maps, satellite images and air mass back-trajectories.

The facilitators described the process of combining results from multiple locations in environmental epidemiology using a two-stage design, which involves modelling location-specific associations in the first stage and meta-analysis to derive overall summary measures in the second stage. The facilitators discussed methodologies for univariate meta-analysis and meta-regression to explain variability between location-specific effect

estimates, emphasizing the importance of considering factors such as urban characteristics, population demographics and exposure patterns. They highlighted challenges and considerations in combining data across locations, including the need to account for heterogeneity and the potential biases introduced by aggregation and reporting.

Calculation of the burden of disease attributable to environmental exposures was also addressed. The main concepts of the estimation, such as relative risk and attributable risk, were also discussed, emphasizing the importance of absolute measures of risk in understanding the impact at the population level. The facilitators further explained the calculation of attributable risk fractions among both the exposed and total populations, highlighting their role in determining the proportion of cases attributable to a specific exposure. They illustrated these concepts with examples and discussed methods for estimating attributable risk from distributed lag models, emphasizing the relevance of counterfactual scenarios and the practical application of these methods in public health contexts.

The workshop aimed to not only impart theoretical knowledge but also to provide hands-on training, enabling participants to apply their newfound skills effectively using national data. The final day of the workshop provided participating countries with the opportunity to implement time series analysis using their respective national datasets and engage in discussions regarding their initial findings. For instance, the Islamic Republic of Iran and Lebanon focused on estimating the relative risk of natural mortality attributable to $PM_{2.5}$ levels, shedding light on the potential health impacts of PM in their countries. Jordan's analysis centred on assessing the relative risks associated with $PM_{10}$ and $PM_{2.5}$ exposure and cardiovascular hospital admissions, offering valuable insights into the specific health outcomes influenced by air pollution in the Jordanian context.

These preliminary analyses underscored the diverse applications of time series analysis in elucidating the complex relationship between air pollution and public health, highlighting the importance of tailored approaches to address Region-specific challenges and priorities.

As a testament to the workshop's success, participants unanimously agreed to review and refine their national analyses. Furthermore, they committed to disseminating their findings by publishing them in peer-reviewed journals, thereby contributing to the broader scientific discourse and fostering continuous improvement in environmental health research and policy-making.

*The need for multi-country time series analysis in the Eastern Mediterranean Region*

Most of the available evidence on the short-term impacts of PM have been obtained from studies in single cities, countries, or regions, posing significant challenges in comparing results and synthesizing effect estimates due to differences in modelling approaches and potential publication bias. Multi-country time series analysis emerges as a crucial tool to bridge these limitations, offering a unified approach that adopts the same analytic protocol and model specifications to estimate globally representative associations of $PM_{10}$ and $PM_{2.5}$ exposures with daily mortality.

By pooling data from multiple countries, researchers can determine common patterns, identify regional disparities and gain a deeper understanding of the complexity of PM exposure exacerbated by frequent SDS. Moreover, collaborative analysis enables the sharing of expertise, resources and best practices among countries, fostering a collective effort to address common environmental health challenges, such as SDS.

There are numerous examples of multi-location studies in various regions globally, including Europe, the United States of America, Latin America and Asia. However, no collaborative effort has yet been made to conduct a multi-country study in the Eastern Mediterranean Region. Given the transboundary nature of SDS, international collaboration is essential for conducting comprehensive time series studies and addressing the health impacts of PM air pollution in such settings.

Furthermore, multi-country time series analysis holds immense potential to inform evidence-based policy formulation and interventions tailored to the specific needs of the Eastern Mediterranean Region. By elucidating regional variations in air pollution levels and their health impacts, such analyses would enhance policy-makers' understanding of the socioeconomic and cultural factors influencing vulnerability to PM air pollution, thereby enabling more targeted mitigation and adaptation strategies and efficient resource allocation.

Additionally, a collaborative approach facilitates the harmonization of monitoring methodologies and data collection practices across countries, enhancing the comparability and reliability of findings. Ultimately, by embracing multi-country time series analysis, the Eastern Mediterranean Region can enhance its capacity to tackle the pressing issue of air pollution in dusty environments and safeguard the health and well-being of its populations.

## 3. Recommendations

*To Member States*

1. Generate evidence on the short-term health impact of air pollution in dusty environments, adhering to a standardized protocol to ensure the robustness and reliability of findings, enable comparisons and facilitate data- or results-sharing.

2. The Islamic Republic of Iran, Jordan and Lebanon should review and refine their national analyses and disseminate their findings by publishing them in peer-reviewed journals by the fourth quarter (Q4) of 2024.
3. Participate in multi-country time series analysis studies to derive regional estimates and contribute to WHO AQG future updates. The aim is to present the results of the studies at the Second WHO Global Conference on Air Pollution and Health in March 2025.
4. Identify dust indicators and study dust composition to better understand its health burden. Countries of the Region are encouraged to identify national dust indicators during the third quarter (Q3) or Q4 of 2024.
5. Develop better mortality surveillance systems, focusing on daily all natural-cause and cause-specific mortality.
6. Enhance the accessibility of health and environmental data to different national stakeholders.

*To WHO*

7. Provide technical and capacity-building support to countries of the Region to enable them to conduct epidemiological studies, with a specific focus on time series analysis methodologies.
8. Prepare a standardized protocol for conducting time series analysis and disseminate it to countries for use in national studies. The protocol will be disseminated in Q3 of 2024.
9. Assist countries in coordinating and conducting multi-country time series analysis, focusing on PM pollution and its association with natural mortality, fostering collaboration and data sharing among countries.
10. Hold regular training workshops on environmental epidemiology, focusing on air pollution and health in 2025–2026.

World Health Organization
Regional Office for the Eastern Mediterranean
Monazamet El Seha El Alamia Street,
Extension of Abdel Razak El Sanhouri Street
P.O. Box 7608, Nasr City
Cairo 11371, Egypt
www.emro.who.int