Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Archives of Medical Research 53 (2022) 541–542

LETTER TO THE EDITOR

Response to: Regarding the Article: A Multimodal Strategy to Reduce the Risk of Hospitalization/death in Ambulatory Patients with COVID-19

To the editor,

We would like to thank the interesting comments related to our study titled "A Multimodal Strategy to Reduce the Risk of Hospitalization/death in Ambulatory Patients with COVID-19"

We first would like to point out that our study is an objective description and evaluation of an emergency strategy implemented by our institution to deal with the epidemiological emergency poised by the COVID-19 pandemic. In our country, like in other countries around the world, the COVID-19 pandemic has resulted in an unprecedented hospitalization and lethality rate. The information contained in our database was obtained directly from the daily consultation registry of patients diagnosed with COVID-19 as part of the epidemiological surveillance system (SINOLAVE) of the Mexican Institute of Social Security (IMSS) without any external repositories linkage. All personal information was removed to ensure confidentiality; patients were neither localized, nor interviewed. It is important to highlight that, only records from the second epidemic wave (from January 1–August 30, 2021) were analyzed.

From the initial 571,330 data entries identified, 453,663 were excluded due to incomplete information on the delivery of the treatment kit and 17,940 had incomplete data on the COVID-19 notification. We found 8,203 duplicated entries; 8,848 entries without laboratory test results; 46 entries with rejected samples; 50,458 entries with negative laboratory results; 1,171 entries of patients younger than 20 years of age; and 2,953 entries with symptoms onset before January 2021. Thus, we were able to analyze 28,048 records with complete information including treatment kit acceptance and telephone follow-up, as well as the clinical outcomes. Indeed, the information on adherence to treatment and the period of remote monitoring is limited, due variations in patient care.

The family physician was responsible for the remote monitoring as well as for the delivery of the treatment. Both strategies were implemented in the Family Medicine Units to help reduce lethality and reduce operating pressure in IMSS hospitals, given the growing demand for hospitalization beds. The criteria for remote monitoring of patients and referral to hospitalization were established in the Guidelines for quality assurance of care for COVID-19 in the IMSS, in October 2020. The use of the treatment kits was based on evidence published in 2020, when there was still no accurate scientific evidence on treatments for COVID-19. It was not possible to carry out a clinical trial at the peak of the epidemic, due to the growing number of infections, and because a rapid and timely institutional response had to be implemented, to mitigate the number of infections, and reduce the high number of hospitalizations and deaths from COVID-19.

The imbalances among groups were also another limitation of our report. We found that subject with telephonic follow-up showed lower rates of hospitalization, intubation, and death, compared to patients without follow-up; but the first group was also younger and had a lower proportion of medical co-morbidities. Despite these important imbalances, crude association estimates were similar to multivariate model results. We are convinced that our report has a robust enough sample size that supports the statement that the multimodal strategy on primary care implemented in the IMSS, reduced the risk of hospitalization

We agree that new health care programs and changes in medical practice inherently can raise ethical issues (1). Under normal (non-pandemic) conditions, new interventions for the diagnosis, treatment and prevention of diseases must go through a rigorous process to ensure their safety and efficacy before authorization. During the COVID-19 pandemic, like in previous epidemiological emergencies, the imminent need to develop safe and efficient interventions has led to various types of studies. Following the Ebola outbreak in 2014, the WHO formulated the "Monitored Emergency Use of Unregistered and Experimental Interventions" (MEURI), in response to the encountered extraordinary challenges. The MEURI framework identified the criteria for the conditions under which the provision of unproven interventions would be considered ethically appropriate, among them: when immediate initiation of clinical trials is not feasible, in the absence of proven effective and successful treatments, upon the availability of

https://doi.org/10.1016/j.arcmed.2022.05.002

supportive preliminary data on the safety and efficacy of the intervention, and its use outside clinical trials has been proposed by a qualified consultative scientific committee (2) as in the case in our institution.

Although the use of unproven interventions could be ethical during pandemics, they must not compromise efforts needed to conduct clinical trials (3). The high progress rate of pandemics has forced the development of new knowledge acquisition tools other than the standard clinical trial protocols. If the therapy is untested, the only reasonable conclusion is that its efficacy is unknown. However, the situation is rarely as simple as a complete absence of study data. Clinicians are often faced with the dilemma of poor evidence or data from one condition that they are attempting to extrapolate to another (4–6).

In some cases, such as when routinely collected data are obtained and analyzed solely at the group level, the data are truly anonymous, and their use does not confer the individual patient the status of a research participant. Moreover, it is a common practice to publish database analyses such as vaccination results or opportune coverage for the detection of preventable diseases. In the Standardized Guideline for Epidemiological and Laboratory Surveillance of COVID-19 issued by the Ministry of Health (later Standardized Guideline for Epidemiological and Laboratory Surveillance of Viral Respiratory Disease) (7), the follow-up of patients by telephone calls is established for timely detection of complications and contact tracing.

The "Institutional Review Board" (IRB) is not a concept. It is a denomination applicable to a committee made up of individuals who have training in scientific areas, individuals who have expertise and training in nonscientific areas, and members of the community who may represent people who would participate as subjects in research studies. In the USA operates under the United States Food and Drug Administration (FDA) regulations (8). In the European Union there is a wide range of ways of complying with the research ethics appraisal process. The range of ways of conducting research ethics review reflects the variations in the agencies using such a process and the governance arrangements that they must apply: Research Ethics Boards (REBs), Research Ethics Committees (RECs) or IRBs (9). According to Mexican regulations, the use of the term IRB referred to the "IMSS National Scientific Research Committee"

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.arcmed.2022.05.002.

References

1. Sobh Z, El-Banna A. COVID-19 pandemic: Ethical challenges of healthcare and research. Zagazig J Forensic Med 2021;19:1–10. doi:10.21608/zjfm.2020.37901.1061.
2. PAHO. Emergency use of unproven interventions outside of research. Ethics guidance for the COVID-19 pandemic. PAHO. 2020. https://iris.paho.org/handle/10665.2/52429 (Accessed April 5, 2022).
3. PAHO. Considerations for regulatory oversight of clinical trials in the COVID-19 pandemic. PAHO. 2020. https://iris.paho.org/handle/10665.2/52266 (Accessed April 5, 2022).
4. Saleh BM, Aly EM, Hafiz M, et al. Ethical Dimensions of Public Health Actions and Policies With Special Focus on COVID-19. Front Public Health 2021;9:649918. doi:10.3389/fpubh.2021.649918.
5. Antiviral Therapy during the Coronavirus Disease (COVID-19) Pandemic: Is It Appropriate to Treat Patients in the Absence of Significant Evidence? Can J Hosp Pharm 2020;73:167–170.
6. Safety of COVID-19 Patients and Use of Medicines Without Scientific Evidence of Their Benefit - PAHO/WHO Pan American Health Organization. 2020. https://www.paho.org/en/documents/safety-covid-19-patients-and-usemedicines-without-scientific-evidence-their-benefit (Accessed April 5, 2022).
7. Lineamiento estandarizado de vigilancia epidemiológica y por laboratorio de la enfermedad respiratoria viral. Enero 2021. https://coronavirus.gob.mx/wp-content/uploads/2021/02/Lineamiento_VE_y_Lab_Enf_Viral_Ene-2021_290121.pdf (Accessed April 5, 2022).
8. Grady C. Institutional Review Boards: Purpose and Challenges. Chest 2015;148:1148–1155. doi:10.1378/chest.15-0706.
9. The research ethics review process (RECs/IRBs). https://prores-project.eu/the-research-ethics-review-process-recs-irbs/ (Accessed April 5, 2022).

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Received for publication April 27, 2022; accepted May 4, 2022 (ARCMED-D-22-00503).