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Still Unanswered Questions about SARS-CoV-2 Mortality and Future Directions for Occupational Medicine

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Summary

The article discusses a recent study on mortality attributable to COVID-19 in Italy and the need for further analysis. The study used a reliable methodology to estimate excess deaths due to the pandemic. However, there are still questions about the specific effects of COVID-19 compared to other factors, such as delayed or missing access to treatment for other illnesses. Analyzing the time course of excess deaths could reveal such effects. There are also open questions about how COVID-19 deaths are classified and reported, which could lead to over or under-diagnosing cases. The article notes that occupational physicians have played an important role in preventing the spread of COVID-19 among workers. A recent study found that personal protective equipment (PPE), particularly masks, effectively reduced the risk of infection among healthcare workers. However, it is still unclear whether Occupational Medicine should incorporate infectious diseases as a major concern or return to its historically agnostic attitude toward communicable diseases. More data on mortality from specific diseases will be needed for further analysis and understanding of the pandemic's effects on mortality rates in Italy.

In this journal issue, Alicandro et al. [1] publish an article on mortality attributable to the SARS-CoV-2 virus pandemic both in the total population and in the population of potentially working age (25-64 years). The methodology used to estimate expected cases[1], as in their previous works also in this journal [2-4], is the best available to date and certainly more adequate than other approaches based on the average mortality of recent years (e.g., an average of the five-year period 2015-2019). Just because the methodology used makes it possible to provide a reliable estimate of the overall effect of the pandemic event on mortality (excess of cases = observed deaths - expected deaths), it is time to deepen the analysis because it makes sense to ask some more specific questions, which *in fieri* are already highlighted in the discussion of Alicandro and coworkers' article.

The overall estimate of the pandemic effect refers to the joint effect of all factors, other than SARS-CoV-2 infection, that interacted with COVID-19 during the pandemic period, sometimes increasing the death numbers (e.g., the heat wave of summer 2022) other times by decreasing them (e.g., the anticipation of the seasonal effect of the flu) [1]. Is it possible to distinguish the various effects, at least the most significant and recognizable ones, which occurred during the period? Can we try to identify effects directly attributable to the virus? Can the effect of other causes (other risk factors) be estimated? For instance, the delayed or missing access to treatment reported by many professionals in specialties

[1]"*Expected deaths were obtained using over-dispersed Poisson regression models, fitted separately for men and women, including calendar year, age group, and a smoothed function of the day of the year as predictors*" [1] using 2011-2019 mortality data.

such as Cardiology, Oncology, and Diabetes care (and others) could imply consequences on the health status of the patients involved: some early reports suggest that there has been an increase in mortality from cardiovascular diseases, cancer, and diabetes during the COVID-19 pandemic period, which may be related to changes in healthcare delivery and access to care, as well as other factors such as public fear and anxiety [5, 6]. Did the reduction in screening activities already give rise to any consequences on the mortality levels observed? There is debate around all these questions, and answers are eagerly awaited.

The analysis of the time course of the difference between excess total mortality and COVID-19 deaths suggests the existence of these phenomena as an alternative to the virus (or that acted together). For example, when COVID-19 deaths are much higher than total excess deaths, some other disease (or more than one) must be decreased; when COVID-19 deaths are much lower than the total excess deaths, some other pathology (or more than one) must have increased due to some intervening factors other than the SARS-CoV-2 infection.

These and other considerations discount a fundamental question: while the total mortality does not allow for misunderstandings (between alive and dead) and does not appear to be characterized by reporting defects, it remains instead open the great question on what is meant by the term "COVID-19 deaths": to classify the deaths, they have been given definitions, methods, but as with any decision of this type, both conceptual questions (adequacy of the definition) and practical questions (operating methods with which information is collected and reported on the collection tools) remain open. Such decisions can lead to over- or under-diagnosing and certifying COVID-19 cases. Unfortunately, only hypotheses can be formulated to be verified (at least in part) once detailed data on mortality by individual pathologies becomes available.

The excess of deaths of the working age also deserves some reflections and insights about the trend over time. For example, the number of COVID-19 deaths is not available in the working age groups considered. Nor is it available a detailed monthly trend of the observed excesses. Therefore, it is difficult to identify underlying factors. Although small numbers imply a high variability, the ratio between the percentages of excesses among total and working-age populations indicates a drastic change in 2021 compared to 2020 and 2022, which deserves exploration. Just as the share of excess mortality between workers in the 25-64 age group and non-workers in the same group needs to be investigated, considering that weaker subjects could have already been excluded from working activities because of their health conditions and frailty.

Answering these questions will help occupational physicians critically analyze the paradigm shift observed during the COVID-19 pandemic, which has brought them into the context of Public Health as a particular branch of Community Medicine that deals with worker prevention. In other words, we should understand whether the occupational physicians' commitment has been useful and necessary or, rather, only a generous involvement in an inappropriate area, to which Occupational Medicine gave only marginal results. Indeed, the epidemic dynamic among HCWs closely followed that in their living community, arguing against significant occupational transmission. A study also published in this journal issue [7] analyzed the risk factors for SARS-CoV-2 infection among more than 3,700 un-vaccinated healthcare workers (HCWs) identified among more than 38,000 HCWs, making it possible to assess the effectiveness of personal protective equipment (PPE) without the vaccination's concomitant effect. Results showed that HCWs assigned to COVID-19 units were not at higher risk of infection, and that mask use was the most effective personal protective equipment (PPE) in reducing the risk of infection. PPE could play an active role in modulating viral load and boosting the immune response, especially in the pre-vaccinal period, such a mechanism being similar to the so-called "variolation" process, where people susceptible to smallpox were inoculated with a small amount, causing a mild infection and subsequent immunity. Mansour et al. study also found that FFP2/FFP3 masks were more protective than surgical masks during the second wave of the pandemic, whereas using facial shields, disposable gowns, and gloves was associated with an increased risk of infection [7].

Overall, these data provide food for thought on the actual importance of the occupational physician in countering the spread of the virus in the workplace, which only in some situations, such as in slaughterhouses, has proved to be an important factor in the spread of the virus among migrants subjected to overcrowded and precarious housing conditions [8].

The decision to consolidate or abandon the recent choices depends on the outcomes of this assessment, i.e., whether to incorporate infectious diseases into the major concerns of Occupational Health moving toward and consolidating a new role of Occupational Medicine within Public Health, or rather, returning to the substantially agnostic attitude of Occupational Medicine toward communicable diseases, documented by the over a century-old history of our journal accessible in digital format.

Whereas we can consider as achieved with a certain degree of confidence the objective of estimating the total burden of deaths brought about by the pandemic and the other factors that acted simultaneously with it, we are still at the beginning of the knowledge of the specific effects on mortality attributable to the single (or combined) risk factors (virus, heat wave, flu, delayed care) in action over these first three years of SARS-CoV-2 presence in our country. To leap in quality, it will be necessary to wait for further data, particularly the mortality from specific diseases.

Declaration of Interests: The Author declares no conflict of interest.

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