Intensive Care Med (2020) 46:2064–2066
https://doi.org/10.1007/s00134-020-06264-3

EDITORIAL

Intensive care accessibility and outcomes in pandemics

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Limited access to intensive care units (ICU) during pandemics can be a contributor to excessive mortality. While lots of attention is given to individual ICU's performance focusing on staffing, organizational features and adherence to best care management protocols [1, 2], there are few discussions as to how to optimize access to ICU at a regional level taking into account population densities [3]. Such efforts could theoretically result in a more homogeneous distribution of patients and a lower risk of overloading units in a given geographical area. In this issue of Intensive Care Medicine, Bauer and coworkers provide an in-depth study of accessibility to ICU beds in 14 European countries during the coronavirus disease 2019 (COVID-19) pandemic [4]. They demonstrate that great variability exists in geographical access to intensive care in different European countries, and also imply that this may be associated with case fatality ratio (CFR) from COVID-19 (that is, the ratio of deaths due to COVID-19 to the number of COVID-19 cases during a given time). Any attempt to provide clear data on this question is to be commended. There are, however, many challenges to such efforts that are recognized and discussed by the authors.

First, there is currently no uniform definition of what constitutes an ICU bed [5]. Some authors suggest that this requires the immediate availability of mechanical ventilation within the ward in question, but this definition is by no means universally accepted. Second, it is hard to define "accessibility" where multiple models of health care coexist. For example, in countries with mixed public–private models (such as Brazil or Australia), it is commonplace to have an empty private ICU bed a few 100 m from patients in need of ICU care inside a public hospital (or even inside another private hospital with fewer resources). The scarcity of data in low-income countries also precludes similar analysis [6]. In this sense, European countries that have strong public health-care systems and lower social inequalities may represent the best model to evaluate how ease of access is related to outcome.

The authors quite reasonably chose a pragmatic method to address the first issue: using the local definition of an ICU. For the second issue, they measured accessibility in terms of a regional ratio of hospital beds to 100,000 population (accessibility index, AI) and the distance to the closest hospital providing intensive care. While imperfect, this definition captures two important factors influencing access to a resource: how available the resource is, and how far away it is. First, by using detailed geographical information, the authors concluded that there were large differences between the participating countries, with some having a more homogeneous AI and others a lower AI, with poorly covered areas speckled across the country. Germany, Estonia and Austria had the greatest AI, while Sweden and Denmark had the lowest AI values.

Bauer et al. also looked at the association between AI as a marker of ICU access and COVID-19 CFR in countries where data were available. The authors correlated the estimated AI with CRF using the same dataset and concluded that an association exists between AI and CRF for the included countries. If there were a causal relationship, this would be of great importance, but solid conclusions are difficult to make based on an association alone. It is also unclear whether COVID-19 is a highly time-critical condition like cardiac arrest or major trauma where urgent ICU intervention is required [7]. Furthermore, case fatality rate is simply the ratio between the number

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of deaths due to one disease to the number of cases of the disease actually diagnosed. Only under very special circumstances could CFR be considered a perfect proxy of quality of care: for example, in a hypothetical scenario where two almost identical populations (with regards to risk factors) were fully tested for a disease but cared for in different settings. In all other situations, the association between CFR and AI should be considered speculative, since several major factors influence CFR (Fig. 1). The list displayed in Fig. 1 is non-exhaustive, as many other variables, including economical background, race, gender, etc., could also influence access to health care. Finally, case fatality rate can be low simply due to more testing (and greater detection of milder cases) or due to local differences in attributing the cause of death to the disease (for example, unexpected deaths at home may be considered related to the pandemic or not).

Different approaches could have been more informative, but would have required more extensive collection of patient-level data. Ideally, one would aim to estimate the proportion of COVID-19 deaths that are directly *caused* by poor accessibility issues [8, 9]. This would represent the population attributable fraction of mortality [10]. This would require data including, but not restricted to, age, comorbidities and other known risk factors for COVID-19. Another approach would be to simply consider the excess deaths that occurred during the pandemic in the regional areas when compared with previous years and their association with AI [11]. While excess deaths also has shortcomings, it may better reflect the impact of the pandemic on the health-care system and its ability to cope with excess cases. The main advantage of using excess deaths between years for the same country is to indirectly control for other, hard-to-measure confounders which are intrinsically tied to cultural aspects, such as end-of-life care or priorities for ICU admissions.

In brief, the paper by Bauer et al. provides important data on ICU accessibility over several European countries. While the understanding that ICU access is heterogeneous in Europe is not entirely new [12, 13], they are of great importance during the current and possible future

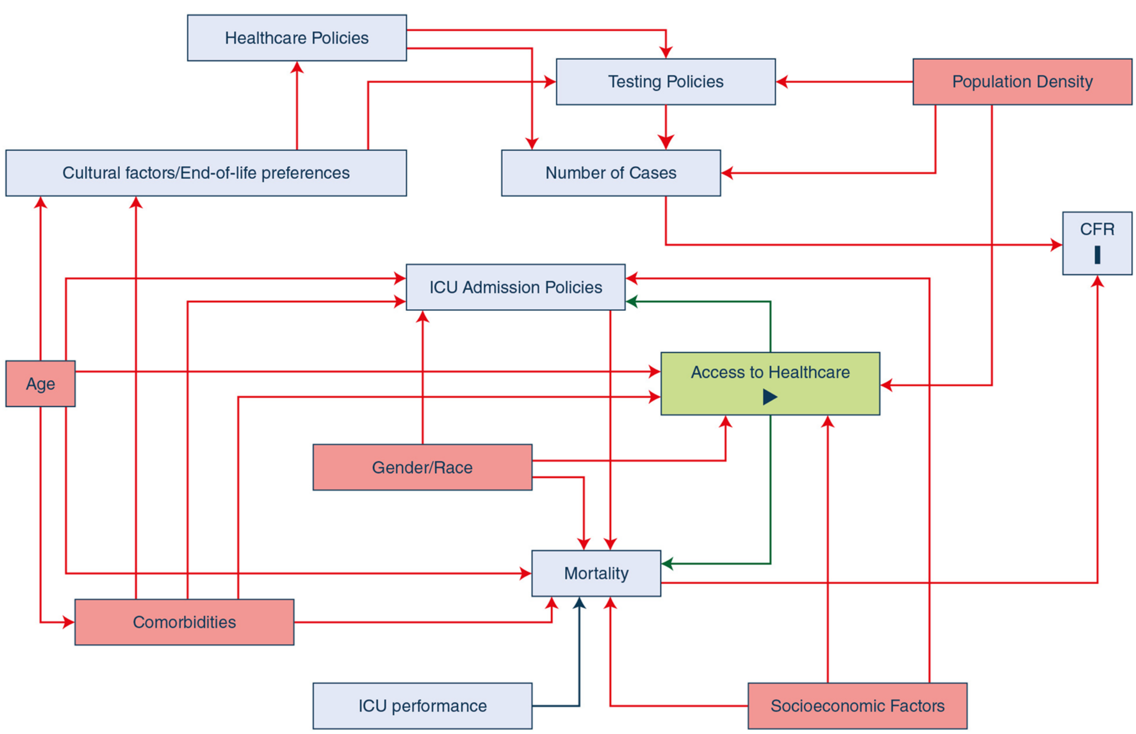

Fig. 1 The complex pathway between access to health care and case report fatality in a directed acyclic graph (DAG). Biasing paths are shown in red and causal paths in green. Minimal sufficient adjustment sets for estimating the total effect of access to health care on CFR include two possible scenarios: (1) adjusted for age, comorbidities, cultural factors/end-of-life preferences, gender/race, number of cases, and socioeconomic factors or (2) age, comorbidities, gender/race, population density, and socioeconomic factors. This DAG was made with *dagitty* R package [15]. Code is provided in the appendix. As all DAGs, items not included are assumed to not be on the causal pathway. For example, socioeconomic factors are not a single value, but a constellation of several other determinants which may be hard to measure. Therefore, the DAG is likely incomplete. *CFR* case fatality rate. The play symbol (Access to Healthcare box) means that is the exposure of interest. The dash (CFR box) is for mentioning which is the outcome of interest

pandemics [14]. If differences in accessibility to ICU care indeed really influence COVID-19-related mortality, this has major ramifications, but this needs to be verified in future studies with more detailed patient-level data.

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s00134-020-06264-3) contains supplementary material, which is available to authorized users.

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Compliance with ethical standards

Conflicts of interest
FGZ has received grants for investigator-initiated clinical trials from Bactiguard, Sweden, and Ionis Pharmaceuticals, USA, in the past 5 years. FGZ has also received grants from the Brazilian Ministry of Health to conduct research, including observational studies, in Brazil through the Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde (PROADI-SUS). FGZ has not received direct compensation, travel support, or holds stock market shares from any pharmaceutical company. Markus B Skrifvars has received travel grants and speaker's fees from BARD Medical (Ireland) and a research grant from GE Healthcare. JA has no conflicts of interest to declare.

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Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 10 September 2020 Accepted: 25 September 2020
Published online: 14 October 2020

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