

Higher COVID-19 outbreak in countries with lower cardiovascular disease mortality, in Europe

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ABSTRACT

The aim of this work was to evaluate, from an epidemiological perspective, whether there is any association between CVD burden and COVID-19 morbidity and mortality, in EU/EEA and UK. A strong, inverse relationship between COVID-19 and CVD death rates in EU/EEA and UK was observed and presented for the first time in the literature. This relationship was independent of various socio-demographic and lifestyle indicators that may acted as potential confounders.

KEY WORDS: *Cardiovascular disease, COVID-19, mortality*

The first pandemic of the 21st century due to the new coronavirus SARS-CoV-2, COVID-19, has caused unprecedented geopolitical, economic and health consequences world-wide¹. Particularly for the European Union/European Economic Area (EU/EEA) and the United Kingdom (UK), as of September 28, 2020, (i.e., end of the first wave, and the beginning of the second COVID-19 wave in most European countries) there have been reported **3,195,947 cases** and 188,780 deaths, with a great variation from country to country, and region to region (Figure 1)². Although previous research has linked viral infections with increased incidence of cardiovascular disease (CVD)³, there are no clear indications regarding the current COVID-19 outbreak. Thus, the aim of this work was to evaluate, from an epidemiological perspective, whether there is any as-

sociation between CVD burden and COVID-19 morbidity and mortality, in EU/EEA and UK.

The information regarding COVID-19 cases and deaths in EU/EEA and UK, as of June 30, 2020, was retrieved from the European Centre for Disease Prevention and Control², information about CVD mortality and diabetes prevalence was retrieved from the 2019 Global Burden of Disease Collaborative Network⁴, information about socio-demographic determinants (i.e., share of older people, share of people who smoke, Gross Domestic Product (GDP) at purchasing power parity, and hospital beds - most recent year available - retrieved from the World Bank, sourced from World Health Organization, Global Health Observatory Data Repository⁵. Counts of COVID-19 cases and CVD deaths used and presented here are standardised per European population (number/per million), and were analyzed using a Poisson regression model, after taking into account the aforementioned socio-demographic indicators. Statistical analyses were

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Submission: 07.05.2021, Acceptance: 19.06.2021

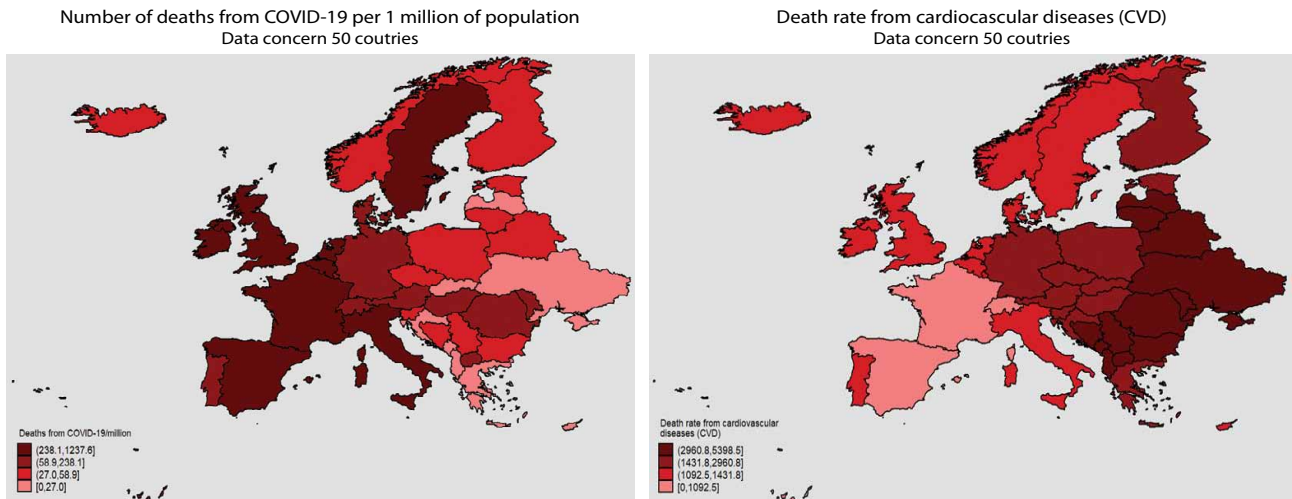


FIGURE 1. Distribution of COVID-19 (as of June 30, 2020) and CVD deaths (as of 2017) per 1,000,000 inhabitants, in EU/EEA and UK.

carried out using Stata 15 (STATA Corp Ltd., Texas, USA).

In Figure 2 a clear inverse relationship between COVID-19 and CVD death rates is illustrated. Overall, data analysis revealed that for every additional 1,000 CVD deaths per 1 M of population, COVID-19 death rate decreased by 88.2 deaths (± 2 , $p < 0.001$) on average at EU/EEA and UK level, after taking into account total population of the country, median age of inhabitants,

share of females and males, share of people older than 70 years, and GDP. The previous relationship remained highly significant ($p < 0.001$) even when the population prevalence of male and female smoking habit, as well as the availability of hospital beds, were taken into account. However, a differential geographical pattern between COVID-19 and CVD death rates was clearly indicated (Figure 2). In particular, when the analysis was focused

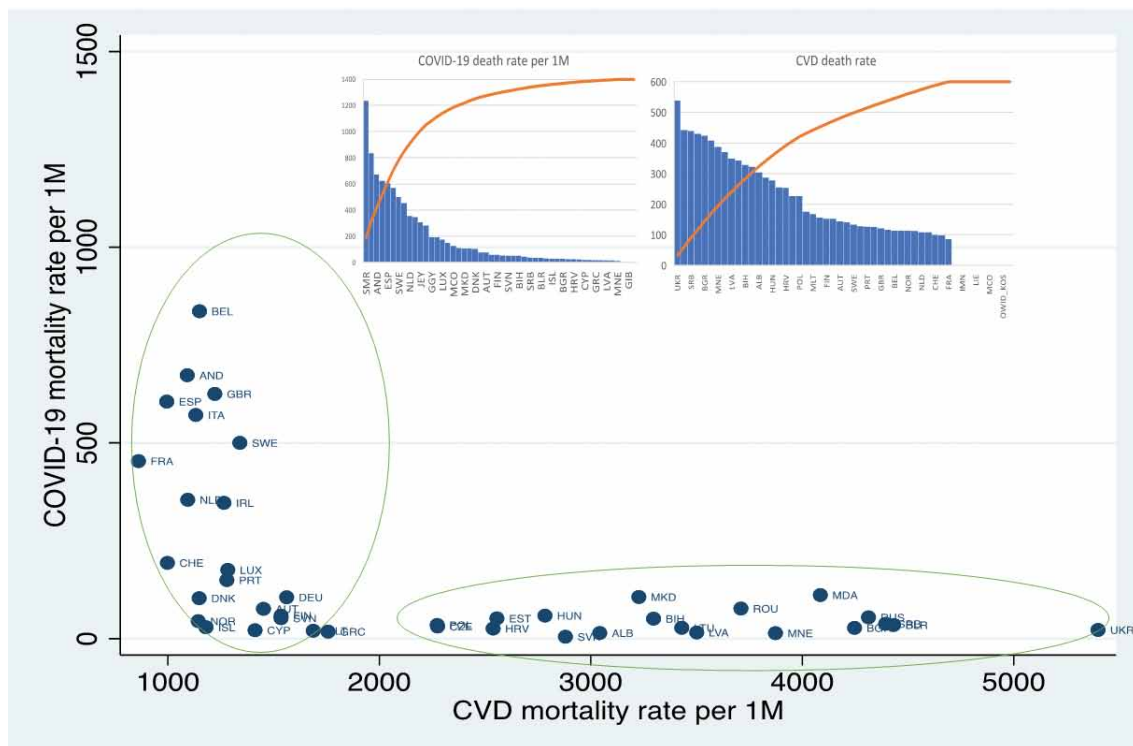


FIGURE 2. Correlation between COVID-19 and CVD mortality rates (per 1 M of population) in Europe (COVID-19 data are until June 30, 2020 and CVD data are until the best available date, in 2017).

by region (i.e., East, West, South and North Europe) it was observed that the inverse relationship between COVID-19 and CVD death rates was significant among West and North European countries (-174.2±6 lower COVID-19 deaths for every 1,000 additional CVD deaths per 1M, $p<0.001$), whereas a modest association was observed in East and South countries (-33.2±2 deaths, $p=0.015$). In addition, a similar trend was observed when the analysis was stratified by median GDP (i.e., 30,000 euro); the aforementioned inverse association was more prominent among countries with higher GDP (-218.3±7 deaths, $p<0.001$), as compared to countries with lower GDP (-13.3±5 deaths, $p=0.026$). It should be noted here that West and North European countries had higher GDP as compared to East and South countries ($p=0.002$). Finally, although an inverse association was observed between life expectancy and CVD death rate (b-coefficient per 1 year in life expectancy -0.13±0.0008, $p<0.001$), suggesting that the lower the CVD mortality the higher the life expectancy of the EU/EEA and UK populations, a positive association was revealed between life expectancy and COVID-19 mortality rate (0.27±0.0004, $p<0.001$).

A strong, inverse relationship between COVID-19 and CVD death rates in EU/EEA and UK was observed and presented for the first time in the literature. This relationship was independent of various socio-demographic and lifestyle indicators that may acted as potential confounders. The association between COVID-19 and CVD has been extensively studied since the beginning of the pandemic, suggesting that people with cardiovascular morbidities are more likely to die due to COVID-19 compared to others. Nishiga et al.,⁶ in a review paper concluded that the interaction between the S protein and Angiotensin-converting enzyme (ACE)-2 may have a central role in COVID-19 pathogenesis, especially in cardiac manifestations of the disease. Early reports

from China found that CVD and its risk factors, such as hypertension and diabetes mellitus, were common co-morbidities in patients with COVID-19⁷. Moreover, the potential CVD related drug-disease synergies in patients with COVID-19 have become a highly studied topic, with inconclusive results. In a recent randomized clinical trial, the BRAVE CORONA study, the investigators studied patients hospitalized with mild-to-moderate COVID-19 and who were taking ACEI or ARB before hospital admission, no difference in the survival was observed between those assigned to discontinue vs. continue their medications⁸.

It is hard to explain the aforementioned finding regarding CVD and subsequent COVID-19 mortality. Moreover, due to the observational design of this study, there could be several limitations that may have influenced the results, like reporting bias of CVD and COVID-19 mortality statistics, delays in reporting COVID-19 deaths, over- or under-reporting COVID-19 mortality, as well as clinical and other factors that were not taken into account, such as prevalence of hypertension, dyslipidemias, obesity, smoking, and other lifestyle habits, including dietary behaviors among the studied populations. Nevertheless, it should be acknowledged that the aforementioned findings have never been reported in the literature, and they were based on an analysis of the entire European population of approximately 750 million inhabitants. Although, clinical, social, behavioural and other cultural characteristics of the studied populations, beyond the pathophysiological mechanisms, may explain the reported relationship, the presented findings may deserve further investigation by future research.

Conflict of interest

None to declare.

ΠΕΡΙΛΗΨΗ

Αυξημένη επίπτωση της COVID-19 σε χώρες με χαμηλότερη θνησιμότητα καρδιαγγειακών παθήσεων, στην Ευρώπη

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Ο στόχος αυτής της εργασίας ήταν να αξιολογήσει εάν υπάρχει κάποια σχέση μεταξύ της επίπτωσης καρδιαγγειακής νόσου και της νοσηρότητας και θνησιμότητας από την COVID-19, στην Ευρώπη. Μια ισχυρή, αντίστροφη

συσχέτιση μεταξύ της θνησιμότητας της COVID-19 και των καρδιαγγειακών παθήσεων παρατηρήθηκε, για πρώτη φορά στη βιβλιογραφία. Αυτή η σχέση ήταν ανεξάρτητη από διάφορους κοινωνικο-δημογραφικούς δείκτες και στοιχεία του τρόπου ζωής των πληθυσμών που εξετάστηκαν.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: Καρδιαγγειακές παθήσεις, COVID-19, θνησιμότητα

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