Burden of COVID-19: Disability-Adjusted Life Years (DALYs) across 16 European countries

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Burden of COVID-19: Disability-Adjusted Life Years (DALYs) across 16 European countries

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Abstract. – OBJECTIVE: The aim of this study is to measure and compare the burden of disease of COVID-19 pandemic in 16 EU/EEA countries through the estimation of Disability-Adjusted Life Years (DALYs) over a long period of time.

MATERIALS AND METHODS: The observational study was based on data from ECDC and WHO databases collected from 27 January 2020 to 15 November 2020. In addition to the absolute number of DALYs, a weekly trend of DALYs/100,000 inhabitants was computed for each country to assess the evolution of the pandemic burden over time. A cluster analysis and Kolmogorov-Smirnov (KS) test were performed to allow for a country-to-country comparison.

RESULTS: The total DALYs amount to 4,354 per 100.000 inhabitants. YLLs were accountable for 98% of total DALYs. Italy, Czechia and Sweden had the highest values of DALYs/100,000 while Finland, Estonia and Slovakia had the lowest. The latter three countries differed significantly from the others – in terms of DALYs trend over time – as shown by KS test. The cluster analysis allowed for the identification of three clusters of countries sharing similar trends of DALYs during the assessed period of time. These results show that notable differences were observed among different countries, with most of the disease burden attributable to YLLs.

CONCLUSIONS: DALYs have proven to be an effective measure of the burden of disease. Public health and policy actions, as well as demographic, epidemiological and cultural features of each country may be responsible for the wide variations in the health impact that were observed among the countries analyzed.

Key Words:
Health policy, Disability-adjusted life years, Years of life lost, Years lost due to disability, COVID-19.

Introduction

The ongoing pandemic coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has leashed an unprecedented global crisis. As of 2 February 2021, more than 103 million of cases were reported across 192 different countries, resulting in more than 2.24 million of deaths[1]. Such a dramatic death toll demonstrates that COVID-19 has rapidly emerged as the world's largest threat to health in recent times. Countries worldwide have adopted different measures in an effort to bend the spread of COVID-19, among which non-pharmaceutical interventions (NPIs) have shown to be the most effective[2,3]. Evidence shows that older individuals who often live with frailty and multiple morbidities such as diabetes, cardiovascular and chronic respiratory diseases, account for most of the deaths due to their higher risk of developing severe health consequences from COVID-19[4]. Europe has been among the most affected areas by COVID-19 pandemic, although with significant differences across its countries.

So far, efforts of comparing the health impacts among European countries brought by the pandemic have been based upon mortal-

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ity-based metrics, such as case fatality rates (CFRs), crude mortality rates (CMRs) and excess all-cause mortality[5-7]. Although these indicators may provide a direct estimate of the impact of a given disease, other measures are necessary to more precisely quantify the overall burden of diseases. A composite measure is the disability-adjusted life year (DALY) whose conceptual framework was originally developed by Murray and Lopez in 1994[8]. DALYs can be calculated by taking the sum of two components: Years of Life Lost (YLLs) due to premature death and Years Lost due to Disability (YLDs)[9]. Therefore, unlike mortality indicators, DALY accounts for both mortality and morbidity associated with diseases giving a more comprehensive picture of the state of health across communities and countries. DALYs were originally used in the first Global Burden of Disease (GBD) study which quantified the health effects of more than 100 diseases for eight regions of the world in 1990. Since then, DALYs have rapidly gained popularity in health policy and health impact assessment (HIA) research. Moreover, the DALY method can be also adopted as an outcome measure in the conduction of cost-effectiveness analysis[10]. The approach of estimating DALYs for COVID-19 has already been made in Italy and Korea, reporting a substantial associated impact on health over a relatively small period of time[11,12].

Up to date, few studies quantified the burden of disease due to COVID-19 in larger contexts, focusing mainly on mortality[13-15]. Here, an estimation of the number of DALYs across 16 EU/EEA countries over a long period of time, ranging from 27 January 2020 up to 15 November 2020, is proposed. The aim of this study is to assess the burden of disease due to the ongoing pandemic in some of the EU/EEA countries throughout the estimation of DALY and to compare the trend of DALYs over time across these countries.

Materials and Methods

In the conduction of this observational study, the methodology developed by Murray and Lopez was tailored to the European context with the aim of estimating the relevant health impact of COVID-19 across the selected countries. Given that, DALYs for COVID-19, calculated for the whole population of each nation, were quantified[16]. DALY is a health gap measure that combines the years of life lost (YLL) with the years lost due to disability (YLD)[17].

Study Data

The comprehensive datasets available from the European Centre for Disease Prevention and Control (ECDC), data from the World Bank Group (WBG) and data from the World Health Organization (WHO)were retrieved to estimate the burden of disease for the following 16 EU/EEA countries: Austria, Croatia, Czechia, Denmark, Estonia, Finland, Germany, Ireland, Italy, Luxemburg, Malta, Netherlands, Poland, Portugal, Slovakia, Sweden[18-20]. The countries were selected for the availability of reliable data. Data has been provided as a data frame of time series ranging over 41 weeks (from week 5 to 46 of 2020).

Model Parameters

In order to estimate the YLLs, number of deaths, average age at death and life expectancy at birth (LE), for each specific country, were retrieved from the selected sources. The average age at death was computed applying the median for grouped data to the cumulative number of deaths in each age class. Regarding the YLDs calculation, total population (at the beginning of 2020), number of incident cases, age at onset of symptoms, duration of disease[21] and disability weights, for each specific country, were obtained from the considered sources. The age at onset of symptoms was estimated applying the median for grouped data to the cumulative number of cases in each age class. Particularly, the ECDC weekly surveillance report at week 46[18] was used to estimate average age at death and average age at onset of symptoms parameters, while incident cases and deaths were retrieved from another ECDC source[20]. Disability weight plays a crucial role in YLDs estimation inasmuch it represents the magnitude of health loss associated with specific health outcomes. The Global Burden of Disease Study 2019 (GBD 2019), coordinated by the Institute for Health Metrics and Evaluation (IHME), derived disability weights for 440 health states used to estimate nonfatal health outcomes[22]. However, at the present time, no disability weight is available for a number of health states including COVID-19. Therefore, the disability weight (i.e. 0.133), attributed to lower respiratory tract infection (LRTI), the health outcome comparable with the case definition of COVID-19, was considered[23].

Method of Estimating YLL and YLD

The following YLL formula was used to estimate the years of life lost associated with the acute respiratory infection:

$$YLL = \frac{KCe^{ra}}{(r+\beta)^2}\left[e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] - e^{-(r+\beta)a}[-(r+\beta)a-1]\right] + \frac{1-K}{r}(1-e^{-rL})$$

where *a* is the age of death; *r* is the social discount rate; β is the age weighting constant; *K* is the age weighting modulation constant; *C* is the adjustment constant for age-weights; and *L* is the standard life expectancy at age of death[9,24].

The following YLD formula was used to estimate the years lost due to disability associated with the acute respiratory infection:

$$YLD = DW\left\{\frac{KCe^{ra}}{(r+\beta)^2}\left[e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] - e^{-(r+\beta)a}[-(r+\beta)a-1]\right] + \frac{1-K}{r}(1-e^{-rL})\right\}$$

where *a* is the age of death; *r* is the social discount rate; β is the age weighting constant; *K* is the age weighting modulation constant; *C* is the adjustment constant for age-weights; and L is the duration of disability; and DW is the disability weight[9,24].

In addition to be endorsed by evidence in the scientific literature[25], the above-described formulas are also adopted in the GBD template provided by the WHO[26], and they are based on specific parameters defined in the template, where *r*, the international standard discount rate, accounts to 0.03; K-values amounts to 0 when no age weights are used and 1 otherwise; the standard age weights use a beta of 0.04 and a constant of 0.1658[16]. In the present study, K-value was set to 1 since age weights were used.

Method of Estimating DALY

Being a composite indicator, disability-adjusted life years were estimated as the sum of YLLs and YLDs. Absolute DALYs were normalized to a common metric (DALYs per 100,000 persons) by dividing the total number of DALYs by the country population and multiplying by one hundred thousand. Results for the following metrics were reported: total YLL; total YLD; total DALY; total DALY per 100,000[11]. Additionally, a weekly trend of DALYs/100,000 inhabitants for each country was calculated.

Statistical Analysis

An R pipeline for preliminary data assessment and analysis was developed. In particular, we took advantage of package *fitdistrplus*[27,28].

In the preliminary assessment step, we resorted to Cullen and Frey graph to summarize the skewness-kurtosis indices to understand the underlying data distribution for each country[29]. Considering that skewness and kurtosis indices are not robust on their own (due to their possible high variance), to properly handle the uncertainty of the estimated values, we enforced the computation by resorting to a large bootstrap procedure without correction for bias[30]. Since the resulting elongated data distributions did not highlight any strong association with reference univariate distributions we then resorted to non-parametric analysis in the next step.

Given the fact that we are dealing with non-univariate data distribution, we resorted to cluster analysis. We first computed a distance matrix using two well-known algorithms (Szymkiewicz-Simpson coefficient and Wasserstein distance) to assess similarity among empirical non-parametric curves, then we performed a hierarchical clustering on top of the distances so far computed[31,32].

Both the algorithms deal with the complexity of computing the similarity between two empirical time-series but they show different sensitivity to curve amplitude. In fact, Szymkiewicz-Simpson is a similarity measure that computes the overlap between two curves considering both amplitude and dynamic, while Wasserstein approach models the time-series as probability distributions and compute their distance, thus implicitly reshaping and normalizing the amplitude of the curves, thus giving much more emphasis to the dynamic. We adopted both the measures to enforce results and better discriminate between dynamic and amplitude similarity. Furthermore Szymkiewicz–Simpson is an asymmetric measure, in other words given two empirical time-series a and b with the same dynamic, SS_*similarity(a,b)* may be different from SS_*similarity(b,a)* due to different amplitude; to cope with this problem and to obtain results better comparable with Wasserstein symmetrical ones, for each country comparison we calculate both the Szymkiewicz–Simpson similarity measures and we considered the maximum similitude score obtaining a symmetrical distance matrix *argmax(*SS_*similarity(a,b),* SS_*similarity(b,a))*. After similarity assessment, we used a *"complete linkage"* hierarchical clustering, which is an agglomerative method able to maximize i) within-cluster homogeneity, thus including countries in a group if they share a really similar behavior, and, ii) between-clusters difference, thus able to guarantee that countries that belong to different clusters show a relatively different behaviors[33].

To further identify possible punctual differences among countries, with a statistical significance score, we eventually computed a two-sided Kolmogorov-Smirnov (KS) test on each country time-line against all the others[34]. The K-S test is a non-parametric test of the equality of discontinuous and continuous probability distribution, able to quantify the distance between the empirical distribution of given two samples. Since KS-test is quite sensitive to the difference of shape and location of the empirical cumulative distribution of the chosen two samples, the two-sample K-S test is efficient to discriminate and identify very different behavior on a country-to-country base.

Results

On 15 November 2020 the estimates of the burden of disease due to COVID-19 in 11 EU/EEA countries were 852,790 DALYs. Stratifying DALYs into its two components, total YLL totaled 835,685 and total YLD equaled 17,105. The highest estimated burden of disease was observed in Italy, with a total of 379,695 DALYs, whereas Estonia had a total of 731 DALYs, the lowest number among the considered countries. When standardized for population size, DALY had a wide range of values with peaks in Italy, Czechia and Sweden. The listed 3 countries had the highest values of DALYs/100,00 inhabitants amounting to 650, 534, and 529, respectively. Other data are reported in Table I.

Figure 1 shows the weekly trend of DALY per 100,000 inhabitants for each country and in comparison with the average of all other countries. The K-S test showed that there is not significant difference among trends of the countries except for Estonia, Finland and Slovakia which, instead, differed significantly ($p < 0.1$) from the other nations especially for a low number of DALYs during all the study-period (**Supplementary Figure 1**).

Despite significant differences among trends were not found, the Szymkiewicz–Simpson algorithm allowed the identification of three clusters, as illustrated in Figure 2. The first cluster included Slovakia, Czechia, Malta, Croatia,

Table I. Years of life lost (YLLs), years lost due to disability (YLDs), disability-adjusted life years (DALYs) and disability-adjusted life years per 100,000 inhabitants (DALYs/100,000) in 16 EU/EEA countries.

Country	YLLs	YLDs	DALYs	DALYs/100,000
Austria	13,853	989	14,842	163
Croatia	9,204	190	9,394	229
Czechia	54,653	2,108	56,761	534
Denmark	6,565	323	6,888	116
Estonia	693	38	731	55
Finland	3,163	99	3,262	59
Germany	102,833	3,700	106,533	132
Ireland	16,895	335	17,230	350
Italy	374,904	4,791	379,695	650
Luxembourg	1,839	72	1,911	311
Malta	839	41	880	178
Netherlands	72,072	2,096	74,168	429
Poland	91,841	244	92,086	239
Portugal	27,916	800	28,716	279
Slovakia	5,204	392	5,596	101
Sweden	53,211	887	54,097	529
Total	835,685	17,105	852,790	4,354

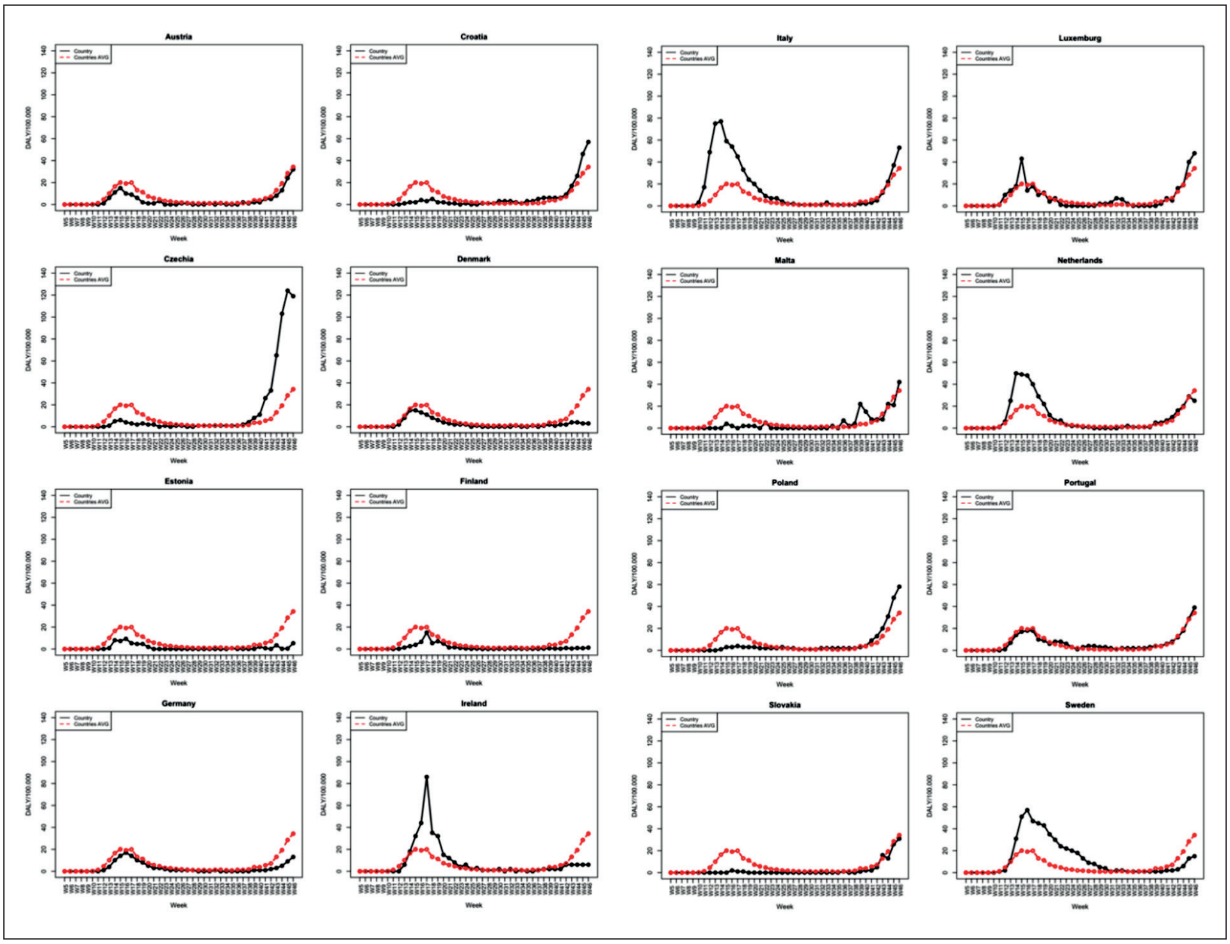

Figure 1. Weekly trend of DALYs per 100,000 inhabitants in 16 EU/EEA countries.

and Poland. The second one contained Austria, Italy, Netherlands, Luxemburg, and Portugal. The third cluster comprised Ireland, Sweden, Estonia, Finland, Denmark, and Germany (Figure 2). Each country, belonging to the respective cluster, shared a similar trend and curve amplitude with other countries in the same cluster. Particularly, those countries in the first cluster (i.e., Slovakia, Czechia, Malta, Croatia and Poland) had none or a low peak during the first wave while they peaked higher in the second period; those in the second cluster (i.e., Austria, Italy, Netherlands, Luxembourg and Portugal) had peaks both in the first and second wave. Lastly, countries in the third cluster (i.e., Ireland, Sweden, Estonia, Finland, Denmark and Germany) shared a similar peak during the first wave and they had none or a low peak during the second wave.

These results were also confirmed by the Wasserstein algorithm, depicted in Figure 3, which is overlapped to the Szymkiewicz-Simpson algorithm.

The heatmaps of Szymkiewicz-Simpson algorithm and Wasserstein algorithm (**Supplementary Figure 2** and **Supplementary Figure 3**).

Discussion

A large and growing body of literature has adopted the DALY metric to estimate the burden of disease due to lower respiratory infections[35,36]. Following the same approach, we estimated the DALYs due to COVID-19 to assess how the pandemic has evolved over time and how it differently hit European countries.

Findings from the present study suggested that, across the analyzed countries, the burden of COVID-19 was owed mainly to mortality while the disability weight associated with the acute phase of the disease was lower. Such finding is

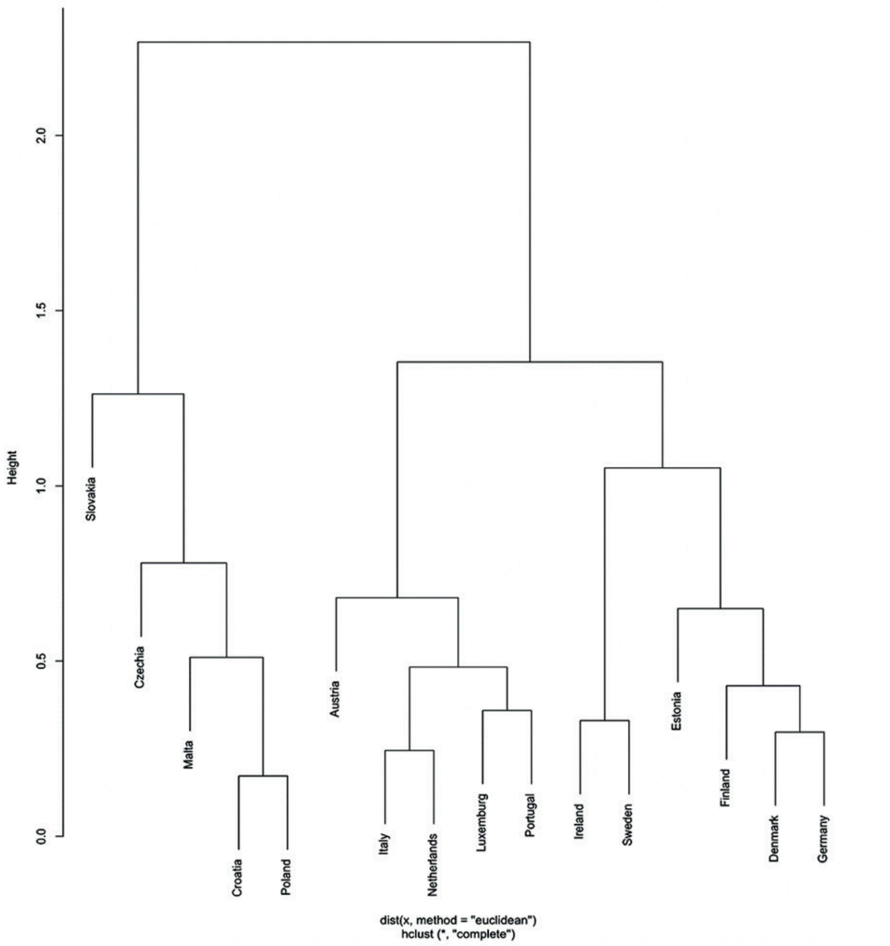

Figure 2. Cluster dendrogram: Szymkiewicz-Simpson algorithm.

even more interesting when looking at the emerging studies which identify post-acute sequelae and reveal that the associated burden of the novel pandemic is evident even among patients whose acute disease was not severe[13].

European studies reported a decline in quality of life in 44.1% of patients, as measured by the EuroQol visual analog scale, and a persistence of symptoms in two-thirds of individuals at 60 days follow-up[37,38]. These studies report that the disability weight could be higher when taking into account DALYs beyond the acute phase of COVID-19 even if the evidence on COVID-19-related disability must be pursued as data and clinical experience accrue over time.

Our estimates of the burden of disease showed that Italy, Czechia and Sweden had the highest value of DALYs per 100,000 inhabitants. Italy is one of the most hit countries by the pandemic, worldwide. The reasons for such results may be multiple. A likely reason may lie in demographics. Indeed, Italy has the second world's oldest population and[39], particularly, almost one in four Italians is over 65 which is at greater risk of dying if diagnosed with COVID-19[40,41]. Another explanation linking the previous one may lie in some shortcomings related to the prevention and management of SARS-CoV-2 infections in long-stay residential care homes. This is confirmed by evidence in the literature showing that an increasing number of elderlies is dying in the above-mentioned structures[42]. Another suggestion, explaining these findings, could be living in multi-generational households that are ubiquitous across Italy. Evidence from Brandén et al[43] highlights that older people living with

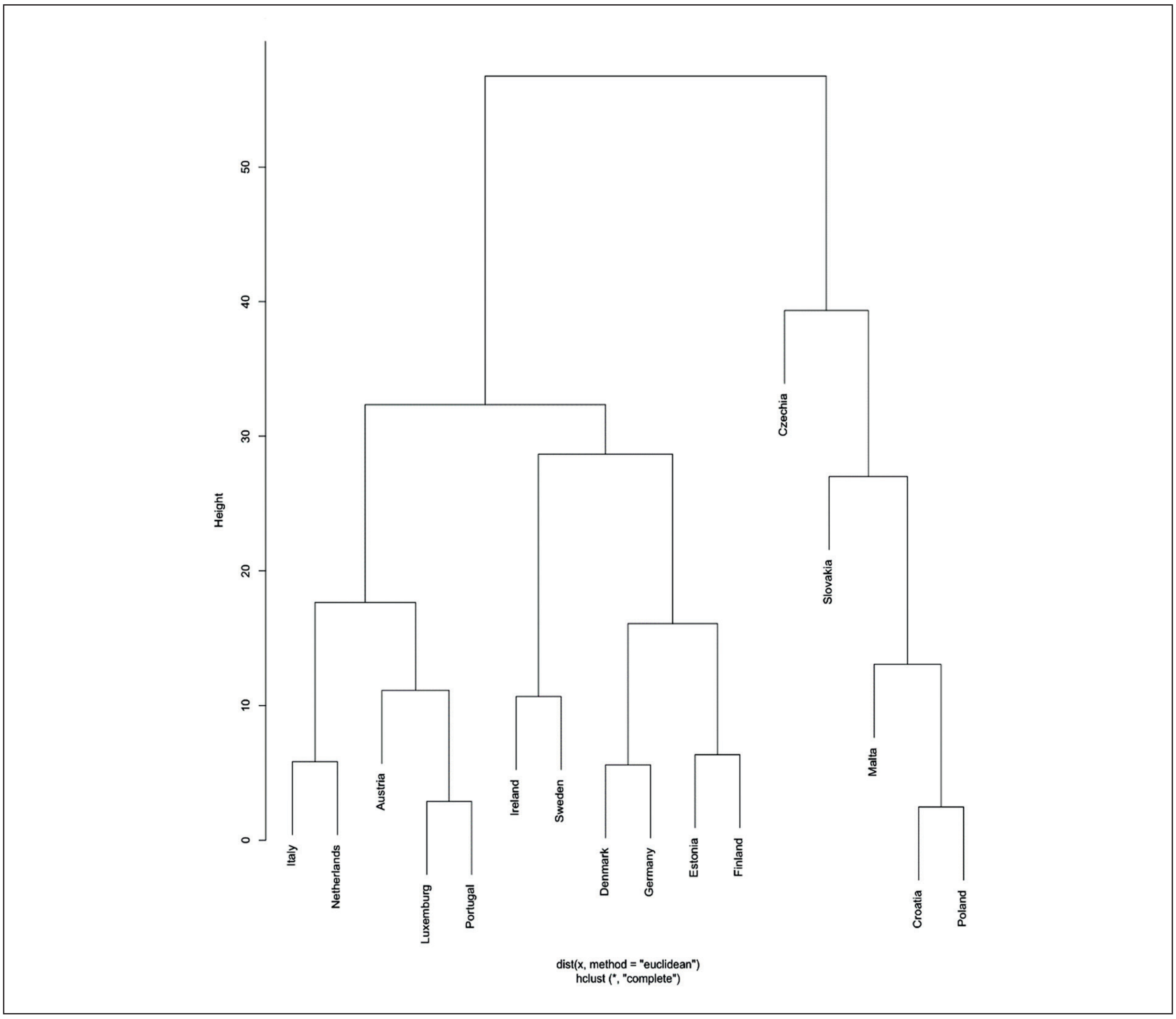

Figure 3. Cluster dendrogram: Wasserstein algorithm.

somebody of working age have a higher significant risk of dying from SARS-CoV-2 related disease. The reasons related to the high impact of the pandemic in Sweden seem to be different. Swedish national response is considered an outlier and the related light-touch COVID-19 strategy was the subject of an international debate. The main reason may largely reside in a de-facto herd immunity approach which allows the community transmission to occur unchecked[44]. As a result, Sweden failed to quickly reduce mortality rates as the pandemic progressed[45]. Further reasons could be associated with flaws in the governance and legal frameworks for health and social services, including a scarce multi-sector coordination, insufficient accountability of the several authorities at macro-, meso-, and micro-level, and an inadequate transparency in policy-making and decision-making processes[44]. The Czech Republic was praised for its quick and effective response to COVID-19 during the first wave but it is now topping global charts of new coronavirus infections and deaths. A reason justifying this sharp change may be the delayed response of its central government in handling the second wave of the virus. Indeed, according to the new Bloomberg's COVID Resilience Ranking, the Czech Republic was ranked the fifth worst country in the world for its COVID-19 coping strategy[46]. In addition to institutional shortcomings, the general attitude throughout the society was characterized by a widespread underestimation of the virus. In fact, an IPSOS survey in October demonstrated that people were noticeably less concerned about the new coronavirus and less compliant with government rules[47].

Although country-disaggregated data for DALYs show a similar trend across countries so far, there seem to be differences in the burden of pandemic by few countries. In support and explanation of this study's result, literature evidence and national reports demonstrated the different and more effective response to COVID-19 by Estonia, Finland and Slovakia. Indeed, as mentioned in the report about the crisis response monitoring in Slovakia by the IZA Institute of Labor Economics, the remarkable performance in terms of containing the pandemic has been due to several key factors: the quick response (i.e., within less than a week since the first case schools and universities in Bratislava had been closed, border controls and mandatory quarantine for people returning from abroad had been introduced and non-essential shops had been closed; within ten days, schools had been closed in the whole country, mandatory face masks had been introduced, and international bus, train, and air passenger services had been banned) and a high level of compliance of the general public[48]. Evidence from Tiirinki et al[49] suggests that the impact of COVID-19 pandemic on the Finnish society has been unpredictable although it has not been as extensive and massive as in many other countries. Particularly, Finland has transferred gradually to a "hybrid strategy", referring to a move from extensive restrictive measures mostly based on policies (e.g., the National preparedness plan for an influenza pandemic), ordinary laws (i.e., Communicable Diseases Act), and legislation on emergency powers (i.e., Emergency Power Act) to enhanced management of the epidemic largely focused on testing, tracing, isolating, and treating[49]. Moreover, the Finnish delegation to the European Union of General Practitioners (UEMO) General Assembly declared that good communications and clear messaging played a paramount role in limiting the spread of the virus[50]. A strong relationship between crowding and COVID-19 has been reported in the literature[51,52]. However, a survey by the Finnish institute for health and welfare (THL) found that 75% of the population only met 2.5 people in one day easing physical distancing measures. As a consequence, instructions to stay apart were likely easier to enforce than in other nations[53]. In relation to the Estonian response to the pandemic, many agree that its successful way of containing the spread of COVID-19 is mainly due to an early and widespread implementation of e-health platforms[54,55], such as the KoroonaKaart online information hub, the self-assessment Koroonatest questionnaire, and the national chatbot SUVE which answers questions about the emergency in Estonian and English[56-58]. Estonia is widely known as one of the most digitally advanced countries in the EU and is internationally recognized for its digitized healthcare system[59]. Hence, alongside common restrictive measures, these digital solutions may have played a pivotal role in strengthening the efforts to control and manage the spread of the virus.

An interesting and complex result of this study is the identification of three clusters internally containing countries with similar temporal DALYs trends. The complexity lies in the difficulty of identifying government policies and public health interventions that have determined the overlap of the DALYs trends in the individual clusters. If we analyze, for instance, the third cluster, the Danish government acted firmly against the virus by closing its borders and declaring a national lockdown, imposing the closure of all schools and universities across the country, providing guidelines to limit the spread of the virus and to respect social distancing. On the contrary, the Swedish government enforced few intervention measures except "social distancing". Italy, which has adopted timelier measures similar to Denmark, belongs to another cluster.

These observations, together with other results of this study, suggest several implications for decision and policy makers. The implications must be considered in light of the study's aim which is to assess the burden of disease due to the ongoing pandemic in some of the EU/EEA countries and not to evaluate the effectiveness of multiple measures.

First, there are many non-replicable factors beyond direct policy actions that may have played a role in how the pandemic unfolded. Specific features of every country, such as demographic and epidemiological characteristics may play a fundamental role in shaping the curves of DALYs. A recent work by Sorci et al[60] has shown that the variability of case fatality rate due to COVID-19 greatly differed among countries and was highly associated with comorbidity risk and demographic, economic and political variables. This suggests to policy makers that the set of measures must be packaged, taking into account the peculiarities of the characteristics of the population to which they apply. Second, the literature shows that a crucial factor in understanding how it was possible for some countries to cope with the coronavirus crisis rests precisely with the combination of rapid response from the government, a high level of confidence in government by citizens and a very high compliance with the various public health measures[61,62]. The capacity to follow established rules and social responsibility for their community are elements of individual behavior and cultural aspects that must be considered by decision makers to be better equipped to tackle pandemic crisis[63,64]. Third, undoubtedly, the patterns of the DALYs curves for each country, with peaks and flattenings over time, reflect COVID-19 mortality for the same countries since the most of DALYs were explained by YLLs. The above-described findings may suggest a twofold weakness of public health systems. The first concerns each national hospital system that has suffered from significant under-investment for many years in several countries[65]. Secondly, the ongoing pandemic highlighted the weakness of primary care organizations which were unable to organize homecare services to avoid patients from moving. A further element of weakness laid in the organization of nursing homes and other residential centers that were not able to contain the infection. The COVID-19 pandemic has reminded everyone of the importance of overcoming day-to-day running a health system in favor of longer-term planning and preparedness. This implies the need to better understand health systems' strengths and vulnerabilities to respond resiliently to the crisis. WHO exhorts to make health systems more resilient in response to crises or shocks, considering that the ability of states to maintain flexible governance and healthcare structures, that can adapt quickly to changing circumstances, becomes even more important "as it is apparent that the threat of the pandemic will have to continuously be balanced against the need to return to normal economic activity"[66]. Lastly, another important implication is related to the importance of DALYs for the decision-making process given its nature of summary metric of population health care status[67]. DALYs are a convenient unit of measurement because decision makers can compare health in one population with health in another population, equate health status in the same population in different times (such as in this study) disaggregating results by countries or regions, sex and/or age. In addition, DALYs also provides information useful on prioritizing and planning healthcare resources[67,68]. Indeed, one overall challenge for public health, and not just in a pandemic period, is to effectively allocate available resources to reduce major causes of disease burden and to decrease health inequalities between and into populations[69]. Furthermore, in order to prioritize health interventions and improve decision making, tracing the population health status in all the health dimensions is needed to avoid making interventions that improve some domains of health but lead to a deterioration in other aspects of health. DALYs link major dimensions of health states: disease, death and disability. Currently, health policies should prioritize issues related to COVID-19 fatality, even if recent evidence shows that SARS-CoV-2 may have long-term effects in affected individuals[70].

Thus, with the increasing aging of the population and the higher prevalence of chronic diseases, disability is an issue of health deterioration. Since the disability refers to the inability to perform expected tasks, it is essential that policy makers adopt a summary measure of population health that also incorporates severity and, especially, weights of severity of disability.

At the best of our knowledge, this study is groundbreaking in investigating the burden of COVID-19 in several EU/EEA countries. The data collected refer to a range of time covering almost one year, allowing us to depict how the health impact of COVID-19 pandemic varied over a long-time frame. The main limitations are related to the database and are common to the largest database studies. Epidemiological data were retrieved from official sources such as the ECDC, the WHO, and the WB. Notwithstanding, data are not comprehensive of the whole European Union and the European Economic Area since some countries do not transmit key information, such as age and gender of COVID-19 cases and deaths, which allows for DALYs computing and potential stratifications. A further limitation is represented by the availability of a most recent WHO protocol[71] for DALY estimation which decided not to include age-weighting and social discounting. Nevertheless, the debate is still ongoing and the scientific literature still presents evidence of the older approach [23,25,72-74]. Even though we acknowledge the importance of stratifying DALYs by age and/or gender, the examined weekly COVID-19 surveillance report at week 46[18] provided only cumulative data on incident cases and deaths, thus not allowing for weekly stratified analyses. Also, since the pandemic is relatively recent, the estimates refer only to the acute phase of the disease without taking into account sequelae and chronicities, potentially correlated to

COVID-19, which are not thoroughly defined so far, although preliminary researches on long-term COVID-19 effects are emerging[70-75]. Consequently, the disability (i.e., YLDs) related to COVID-19 could be higher than expected. Furthermore, in the estimation of YLDs, the value associated with the acute lower respiratory infection value was adopted as a disability weight as long as a specific value for COVID-19 is still not available. Additionally, potential biased estimates might result both from not considering different tiers of disease severity (i.e., mild, moderate, severe and very severe) and asymptomatic individuals. Even taking these weaknesses into account, the applied formulas are best available and endorsed by the WHO and scientific literature. Moreover, the selected sources, despite being the most reliable, did not provide thorough data on asymptomatic individuals since notification of these cases relied on national governments' testing policies.

DALYs have proven to be an effective measure of the burden of the disease. Burden of COVID-19 and its trend is not significantly different among the 16 EU/EEA (except for Estonia, Finland and Slovakia). However, the range of values of DALYs/100,000 is wide and it is probably affected by timing, types of government interventions, public health measures adopted and by the combined effect of demographic, epidemiological and cultural variables of the population into a specific country.

Conclusions

DALYs have proven to be an effective measure of the burden of the disease. Burden of COVID-19 and its trend is not significantly different among the 16 EU/EEA (except for Estonia, Finland and Slovakia). However, the range of values of DALYs/100,000 is wide and it is probably affected by timing, types of government interventions, public health measures adopted and by the combined effect of demographic, epidemiological and cultural variables of the population into a specific country.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Conceptualization, M.M.G. and G.D.; methodology, G.P., M.C.N., A.S., D.P.; software, G.P., M.C.N., A.S., D.P.; validation, M.M.G. and G.D.; formal analysis, G.P., M.C.N., A.S., M.M.G.; investigation, M.C.N., A.S., M.M.G.; resources, A.S., M.C.N., D.P.; data curation, G.P., M.C.N., A.S., D.P.; writing-original draft preparation, M.C.N., A.S., M.M.G., D.P.; writing-review and editing, M.C.N., A.S., M.M.G.; visualization, M.C.N., A.S., M.M.G., D.P., G.P., G.D.; supervision, M.M.G., G.D.; project administration, M.M.G., G.D., A.S., M.C.N.; funding acquisition, none. All authors have read and agreed to the published version of the manuscript.

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