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Original Article

Estimating global burden of COVID-19 with disability-adjusted life years and value of statistical life metrics

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Background: Global burden of COVID-19 has not been well studied, disability-adjusted life years (DALYs) and value of statistical life (VSL) metrics were therefore proposed to quantify its impacts on health and economic loss globally.
Methods: The life expectancy, cases, and death numbers of COVID-19 until 30th April 2021 were retrieved from open data to derive the epidemiological profiles and DALYs (including years of life lost (YLL) and years loss due to disability (YLD)) by four periods. The VSL estimates were estimated by using hedonic wage method (HWM) and contingent valuation method (CVM). The estimate of willingness to pay using CVM was based on the meta-regression mixed model. Machine learning method was used for classification.
Results: Globally, DALYs (in thousands) due to COVID-19 was tallied as 31,930 from Period I to IV. YLL dominated over YLD. The estimates of VSL were US$591 billion and US$5135 billion based on HWM and CVM, respectively. The estimate of VSL increased from US$579 billion in Period I to US$2160 billion in Period IV using CVM. The higher the human development index (HDI), the higher the value of DALYs and VSL. However, there exits the disparity even at the same level of HDI. Machine learning analysis categorized eight patterns of global burden of COVID-19 with a large variation from US$0.001 billion to US$691.4 billion.

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Conclusion: Global burden of COVID-19 pandemic resulted in substantial health and value of life loss particularly in developed economies. Classifications of such health and economic loss is informative to early preparation of adequate resource to reduce impacts.

Introduction

Currently, COVID-19 pandemic still continues globally and represents the greatest global public health crisis since the pandemic influenza outbreak in 1918. According to the World Health Organization (WHO), over 3 million COVID-19 deaths occurred worldwide by the end April 2021.[1] It would be expected that if the epidemic of COVID-19 still persists with high incidence and mortality it would lead to shorten life expectancy.[2] For some countries with long persistent epidemic, such as United States, COVID-19 has become the third leading causes of death behind cancer and cardiovascular diseases in 2020.[3,4] The economic impact of COVID-19 cannot be also overemphasized not only in high-income countries but also in low-income countries. The estimated economic value of life lost from 6429 COVID-19 deaths was US$17.39 billion in Ohio.[5] In order to quantify the global burden of COVID-19 associated with the status in good health and also that in poor health that can be further converted into economic loss, one of complementary summary measures in addition to life expectancy, namely the disability-adjusted life years (DALYs) proposed in the Global Burden of Disease (GBD) Study,[6] is worthy of being estimated across continents and countries as the measurement of DALYs is able to quantify the health loss due to specific diseases and injuries like COVID-19.[7] The DALYs associated with socio-demographic index and global five leading causes of DALYs (including neonatal disorders, ischemic heart disease, stroke, lower respiratory infections, and chronic obstructive pulmonary disease) in 2017 have been reported.[8] One of the leading causes is communicable disease. We should pay our attention to the change of DALYs by COVID-19 as well as the relationship between socio-demographic index and DALYs. Currently, the GBD has not included COVID-19, and only limited periods or specific countries were reported in previous studies.[9—11] To provide health decision-makers for planning and allocating health resources, it is imperative to understand the magnitude of impacts on DALYs caused by COVID-19.

The aim of this study was to elucidate global disease burden with DALYs metric across different regions and also by different periods. The big data analytics with machine learning analysis was further used to classify the patterns of global disease burden by human development index (HDI) to have a better understanding of DALYs caused by COVID-19 given different levels of HDI.

Materials and methods

Data sources for COVID-19

The daily counts of country-based COVID-19 cases and deaths from COVID-19 pandemic between January 2020 and April 2021 were retrieved from public open data, the web-based real-time GitHub repository created by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University.[12] The age distribution of patients who died of COVID-19 was only available in the early phase of epidemic in Italy,[13] France,[14] and South Korea,[15] for which the age distributions were applied to the later epidemic. The age distribution of deaths of COVID-19 in other countries was borrowed by the figures in the US.[16] The entire period was classified evenly into four periods, period I (January—April, 2020), period II (May—August, 2020), period III (September—December, 2020), and period IV (January—April, 2021) in order to quantify the disease burden of COVID-19 with the same interval of time. The countries and the definition of different continents were based on WHO.[1]

In Asia, Taiwan and India have extremely different disease curves from other countries. Therefore, we also investigated these two countries independently.

Disability-adjusted life years

Disability-adjusted life years (DALYs) is composed of years of loss due to disability (YLD) and years of life lost (YLL). YLL represents the life-year lost due to premature death as a result of COVID-19 and YLD captures the time when an affected subject lived in the disabled status due to COVID-19.

Age at death (A), life expectancy at age A (L_A), social discount rate (SDR), age weighting constant (AWC), are needed to derive YLL with the following formula[17]:

$$\begin{aligned}\text{YLL} = {} & \frac{\textit{Age Weight Modulation Constant} \times \textit{Adj. Constant for Age Weights} \times e^{SDR \times A}}{(SDR + AWC)^2} \times \\ & \left\{e^{-(SDR+AWC)\times(L_A+A)} \times [-(SDR + AWC) \times (L_A + A) - 1] - \right. \\ & \left. e^{-(SDR+AWC)\times A} \times [-(SDR + AWC) \times A - 1]\right\} \\ & + \frac{1 - \textit{Age Weight Modulation Constant}}{SDR} \times \left(1 - e^{-SDR \times L_A}\right)\end{aligned} \tag{1}$$

The formula for calculating the YLD is expressed as follows.

$$\text{YLD} = \text{Disability Weight} \times \Big[\!\Big[\frac{\textit{Age Weight Modulation Constant} \times \textit{Adj. Constant for Age Weights} \times e^{SDR \times A}}{(SDR + AWC)^2} \times \{e^{-(SDR+AWC)\times(L_D+A)} \times [-(SDR + AWC) \times (L_D + A) - 1] - e^{-(SDR+AWC)\times A} \times [-(SDR + AWC) \times A - 1]\} + \frac{1 - \textit{Age Weight Modulation Constant}}{SDR} \times (1 - e^{-SDR \times L_D}) \Big]\!\Big], \quad (2)$$

where L_D refers to the duration of disability, and DW is the disability weight. The values of parameters were borrowed from literatures with the age weighting modulation constant as 1, the adjustment constant for age-weights as 0.1658, SDR as 3%, AWC as 0.04, and L_D as 0.038 years (2 weeks).[10] The Disability Weight was designed as 0.133 as applied to the low respiratory diseases.[10] A and L_A depend on the scenario from each country. Details on the parameters used for the derivation of YLL and YLD are listed in Supplementary Table 1. A 14-day (0.038 year) period was used as the disabled duration (L_D) incurred by COVID-19 as a result of isolation and treatment following the general principle applied in most countries and regions.[10] The data on YLL is estimated from the life expectancy data of each country from United Nations (UN)[19] (Supplementary Table 2). For the modified YLL in each country, the age-weighted method was used. The estimated results on DALYs are presented by using a per 100,000 population rate.

Human development index (HDI)

The HDI is an aggregating index that combines life expectancy, education, and per capita income indicators. According to the UN classification, countries with HDI greater than 0.8 are very high developed countries, 0.8—0.7 are high developed, 0.55—0.7 are medium developed, and below 0.55 are low developed countries. The up-to-date human development index (HDI) by country was from public open data.[19]

Value of statistical life (VSL)

VSL is an index to quantify the health life year loss during the pandemic. In order to quantify VSL, we firstly applied the hedonic wage method (HWM) by multiplying the number of DALYs by the Gross Domestic Product (GDP) of each country. We adopted 2017 GDP due to its integrity of database. The economic loss by continents with the summation from the country-specific figures was presented. Information on GDP was based on the estimates of the World Bank, which classified all countries in the world into four income groups (high, upper-middle, lower-middle, and low), accordingly.[20]

Another VSL to reflect individual willingness to pay was based on the contingent valuation method (CVM).[21] The VSL was abstracted from the previous study.[22] As there exists heterogeneity across studies, we adopted the results from a mixed effect meta-regression model. For any given study denoted by j, the regression model can be expressed as

$$VSL_j = \beta_0 + \sum_{k=1}^{p} \beta_k X_{jk} + u_j + e_j$$

where j refers to a given study; β_0 is the common intercept across studies; X_{jk} is the kth covariate of interest, such as income, endogeneity of risk, white-workers sample, for study j; β_k is the corresponding regression coefficient of the fixed effect; u_j is a random effect term for study j; and e_j refers to the estimation errors. The VSL was therefore estimated as $5,863,609 in Bellavance's study. We further considered the impact of COVID-19 and converted it to $521,856 per year based on Mallow's study in Ohio, US.[5] We used the ratio of GDP in each country to that of the US to adjust this estimate of willingness to pay for estimating VSL in different countries.

K-mean clustering analysis for HDI and DALY

The unsupervised machine learning method with k-means clustering was used to classify the patterns of the level of country development indexed with HDI and COVID-19 disease burden indexed with DALYs. The k-means clustering uses iterative refinement to classify countries to any of the k clusters with the nearest mean.[23,24] To determine the optimal number of clusters before k-means clustering algorithm, the aligned box criterion (ABC) method was used to estimate the number of optimal-separated clusters.

All of the statistical analyses were performed with SAS 9.4 and SAS Viya software.

Results

Global incidence, case-fatality, and mortality

Fig. 1 shows different patterns of incidence, mortality, and case-fatality across continents worldwide. High disease burden countries from Europe, North America, South America, Africa, Asia, and India had higher incidence and mortality in both periods III and IV whereas low disease

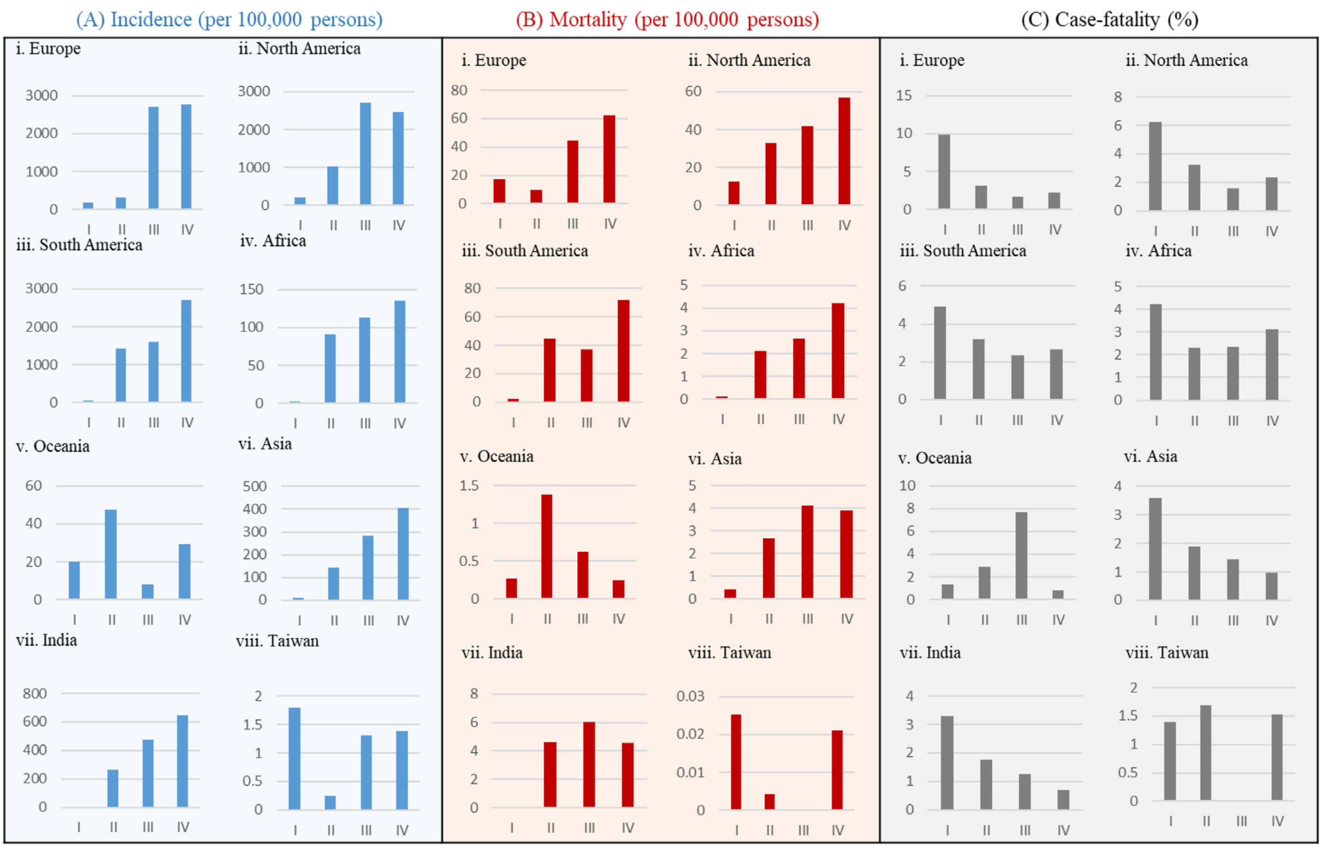

Figure 1 Incidence, mortality and case-fatality of COVID-19 in 8 areas by four periods.

burden countries from Oceania had higher incidence and mortality in the Period II but tended to resurge in the Period IV. Extremely low disease burden countries such as Taiwan often have two unique characteristics, cases mainly derived from importation and these epidemiological profiles are strongly affected by border control and mitigation strategies. Imported cases in Taiwan were much lower in the period II due to strict border control of containing imported cases and domestic non-pharmaceutical interventions for reducing domestic cases. However, imported cases still soared up during the periods of III and IV, which was in parallel with the epidemiological profiles of those high disease burden countries as indicated above. Low incidence profile of COVID-19 also made Taiwan to have a relatively lower case-fatality rate compared with other continents.

It is very interesting to note that the epidemiological profile of mortality was similar to that of incidence except India. The reason is that as the profile of mortality was determined by incidence and case-fatality rate, in high disease burden countries, the contribution of incidence outweighs the improvement of cases-fatality with the accommodation of the optimal allocation of medical capacity of each country as remarkably seen in Europe and North America but moderately in South America and Africa because health care resources may be constrained. A substantially decreasing trend of case-fatality in India was noted and rendered the trend of mortality remain stable. It should be also noted that case-fatality in the period I should be interpreted with great caution as there was a high possibility of underreporting in early period of COVID-19 pandemic.

Table 1 shows the results of incidence and mortality of COVID-19 with the incorporation of independent variables (covariates) including both countries and periods with adjustment for each other using Poisson regression models. Both estimates increased with period, ranging from 7.81-fold in the period II to 23.15-fold in the period IV for incidence and 2.84- fold in the period II to 5.94-fold in the period IV for mortality as compared to the period I. In contrast, the results of case-fatality show the opposite. The magnitudes of risk reduction were 61% in the period II, 76% in the period III, and 72% in the Period IV compare with the period I.

As far as those afflicted countries are concerned, Europe, North America and South America were three high risk continents, being 7.06, 7.56, 6.85, respectively, times likely to get COVID-19 compared with Asia. The risk of getting COVID-19 was reduced to 0.41 and 0.12 for Africa and Oceania, respectively. The similar pattern was also noted for the risk of death, giving 12.11, 13.03 and 14.10 times likely to die from COVID-19 in Europe, North America and South America, respectively. Within Asia, it should be noted that India had unique disease curve. Although COVID-19 case number was stable during Period 3, the case

Table 1 The relative risk of COVID-19 incidence, mortality and case-fatality using Poisson regression models.

Variables	Incidence		Mortality		Case-fatality	
	Relative risk	95% CI	Relative risk	95% CI	Relative risk	95% CI
Continent						
Europe	7.06	7.05–7.06	12.11	12.07–12.15	1.75	1.75–1.76
North America	7.56	7.56–7.57	13.03	12.98–13.07	1.68	1.67–1.68
South America	6.85	6.84–6.85	14.10	14.05–14.15	2.01	2.01–2.02
Africa	0.41	0.4–0.41	0.83	0.82–0.83	1.99	1.98–2.00
Oceania	0.12	0.12–0.13	0.23	0.21–0.24	1.16	1.09–1.23
Asia	1	–	1	–	1	–
Country						
India[a]	1.65	1.64–1.65	1.39	1.38–1.39	0.86	0.86–0.86
Taiwan[a]	0.0056	0.0053–0.0059	0.0046	0.0025–0.0080	0.44	0.25–0.77
Period						
II (May–August, 2020)	7.81	7.80–7.82	2.84	2.83–2.85	0.39	0.39–0.40
III (September–December, 2020)	19.50	19.48–19.52	4.43	4.41–4.45	0.24	0.24–0.24
IV (January–April, 2021)	23.15	23.13–23.18	5.94	5.92–5.97	0.28	0.28–0.28
I (January–April, 2020)	1	–	1	–	1	–

[a] Asia as the reference.

number has increased substantially since January 2021 (see Supplementary Fig. 2). Therefore, India had higher incidence and mortality than other countries. However, there are some countries with extremely low disease burden countries. For example, Taiwan had substantially lower odds of being susceptible to COVID-19 and also dying from COVID-19 as compared to Asia.

Life expectancy (LE) loss

Fig. 2 (a) shows a linear relationship between $\log_{10}$ (GDP) and LE, exhibiting a higher GDP or HDI would lead to a longer LE ($R^2 = 71.8\%$, $P < 0.001$) in 2019 before COVID-19. Fig. 2 (b) show a statistically significantly association between average loss of LE (taking the transformation of cubic power) due to COVID-19 and $\log_{10}$ (GDP), revealing the higher the GDP or the HDI, the larger the average loss of LE ($R^2 = 39.2\%$, $P < 0.001$).

DALYs

The global DALYs (in 100,000) incurred by COVID-19 was estimated as 427.4 from January 2020 to April 2021. The estimated global DALYs increased from 36.1 in the period I (January to April, 2020), 73.4 in the period II (May to August, 2020), 134.7 in the period III (September to December, 2020), and 183.1 in the period IV (January to April, 2021), respectively. Global health loss due to COVID-19 after translating these DALYs estimates per capita into the corresponding DALYs (thousands) based on the actual global population gives 31, 930 from period I to period IV. The corresponding figures were 2699 (thousands) for the period I, 5484 for the period II, 10,065 for the period III, and 13,683 for the period IV (Supplementary Table 3).

Fig. 3 shows the relative contribution of YLL and YLD to DALYs across four periods. The contribution of YLD to DALYs increased from 10% in the period I, 11% in the period II, 16% in the period III, and 14% in the period IV.

Fig. 4 shows the DALYs accumulated through period I–V. In the period I, North America and Europe accounted for the major loss with the order of the DALYs estimated as 127.9 and 223.1, respectively. In the period II, the loss of DALYs in North America still remained relatively high (323.2 DALYs per 100,000) and was 2.53 fold compared with that in the period I. The corresponding figure in Europe was attenuated to 47.5% of period I (105.9 DALYs per 100,000). However, the DALYs of South America, 400.9 per 100,000, surpassed

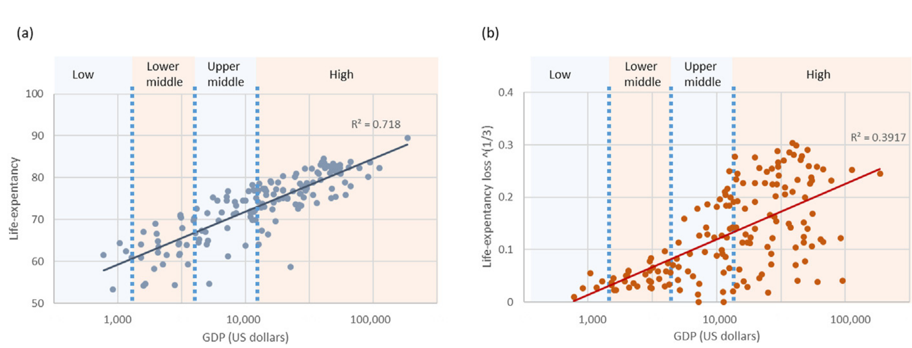

Figure 2 Association between GDP and Life expectancy.

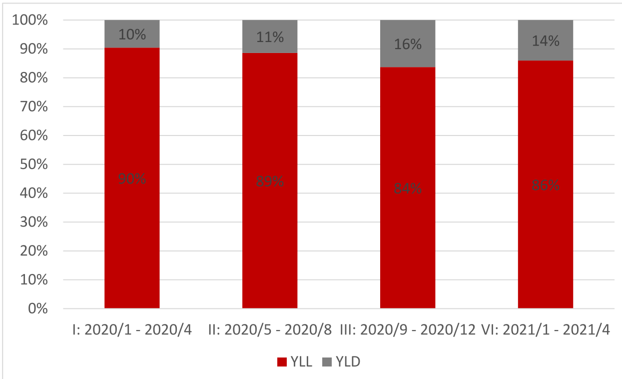

Figure 3 Proportion between YLL and YLD by 4 periods around the world.

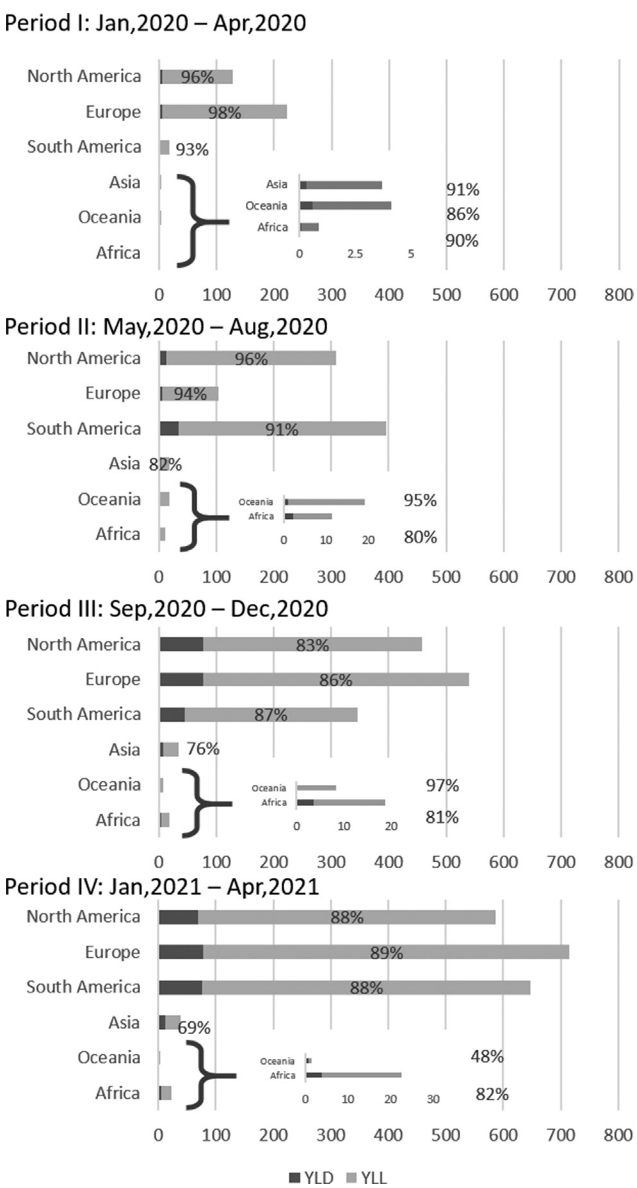

Figure 4 DALYs per 100,000 population by 4 period.

Table 2 The estimated results on both estimates of value of statistical life (VSL) by periods and continents.

Period	Continents	Hedonic wage method (Billion, US$)	Contingent valuation method (Billion, US$)
I	Africa	0.1	0.5
	Asia	1.8	16.0
	Europe	39.5	343.6
	North America	24.5	212.7
	Oceania	0.0	0.3
	South America	0.6	5.6
	overall	66.6	578.8
II	Africa	1.0	8.5
	Asia	8.5	74.0
	Europe	56.6	491.4
	North America	75.0	651.7
	Oceania	0.2	2.0
	South America	15.8	137.1
	overall	157.1	1365.2
III	Africa	2.3	19.9
	Asia	20.5	178.3
	Europe	140.1	1217.3
	North America	149.2	1296.0
	Oceania	0.3	2.8
	South America	29.8	258.7
	overall	342.4	2974.8
IV	Africa	4.1	35.4
	Asia	35.1	305.1
	Europe	252.4	2193.2
	North America	244.2	2121.8
	Oceania	0.3	2.8
	South America	54.5	473.1
	overall	591.0	5135.0

the DALYs of other continents. In the period III, the DALYs of North America, Europe, and South America were top three among all continents (458.4, 539.4, and 345.2 Per 100,000, respectively). There was a substantial increase in Europe during the period III compared to the corresponding figure of the period II. During the period IV, the DALYs of North America, Europe, and South America became extreme high, reaching to 586.8, 715.6, and 647.9. The DALYs in Asia was relatively low compared with other continents from period I to IIII. The DALYs in Oceania fluctuated but remained low (4.1, 19.6, 8.4 and 1.7 from period I to IV, respectively). Although the DALYs in Africa was low but it increased from period I to IV gradually (0.8, 11.9, 18.7, and 23.4 in period I to IV, respectively).

Additionally, the proportions of YLL in DALY were extremely high in Europe and North America in the period I. In the period I, YLLs constituted 96%, 98%, 93%, and 91% of DALYs for North America, Europe, South America and Asia, respectively. The contributions of YLLs to DALYs had a substantial decrease in the period IV (88%, 89%, 88%, and 69% for North America, Europe, South America, and Asia, respectively).

Figure 5 Trend of DALYs and VSL due to COVID-19 with the hedonic wage method.

Value of statistical life (VSL)

Table 2 shows the estimate of VSL increased from US$66.6 billion in the period I to US$591.0 billion in the period IV based on the HWM. The corresponding figures increased from US$579 billion in the period I to US$5135 billion in the period IV using the CVM.

Fig. 5 shows DALYs and VSL using the HWM around the world. At the beginning, the outbreak only showed up in China from December 1 to the end of January. Following the spread of COVID-19 in Asia especially in Japan and South Korea, the DALYs accumulated rapidly. Moreover, Italy became the first European country with an outbreak in the end of February and spread to other European countries afterward. Therefore, the rapid growth of DALYs began with the end of March. Health-life economic losses were worth US$228 million before the large outbreak emerged in Italy. However, financial losses had jumped up to US$11.7 billion on February 29th, 2020. According to the unstoppable spread of COVID-19 the economic losses of health life year grew exponentially till the end of April and reached US$66.6 billion. When the epidemic turned into pandemic, more cases were present in developing areas, including, to a greater extent, such as South America, Africa, and, to a lesser extent, in Asia. Until the end of 2020, the heath loss due to COVID-19 were worth up to US$342.4 billion dollars. In the period IV, the corresponding figure soared up to almost US$591 billion. The slopes of YLD and YLL were stepper in the period I because of emerging pandemic, introducing an overwhelming number of COVID-19 cases and deaths. The trends became stable during the second and third period but re-surged in the period IV.

Europe and North America

The accumulated VSL estimates of Europe and North America are identical and shown in Fig. 6 (a). After February, the figure of loss grew exponentially from US$7.0 million to US$39.5 billion in 2 months in Europe. A similar trend also occurred in North America. Till the end of April, 2020, COVID-19 has resulted in a US$24.5 billion loss in North America. In the period II, the value kept relatively stationary in Europe but continued to increase in North America. However, in the period IV, the slope became steeper to show an increase at increasing rate in both Europe and North America. By the end of April, 2021, the value arrived at US$252.4 billion and US$244.2 billion, respectively.

South America and Asia

Fig. 6 (b) shows the corresponding figures for South America and Asia. The first significant increase occurred in the period II, from US$0.6 billion to US$19.9 billion for South America and US$1.8 billion to US$11.1 billion for Asia. During the next two periods, the outbreak continued to spread. In the end of the period IV, the figures reached US$54.5 billion and US$35.1 billion in South America and Asia, respectively.

Oceania

In the period I, from March to April, the figure of VSL of Oceania rapidly increased to US$39.5 million. (Fig. 6 (c)) And the second wave of the outbreak occurred in the period II, the value was US$234 million. However, it decreased in both periods III and IV because of good containment of epidemic by the Oceania government. In the end of period IV, the health life-year loss of COVID-19 in Oceania was US$321 million.

Africa

Fig. 6 (d) shows the corresponding VSL in Africa. By the end of the period I, the estimate of VSL started to increase dramatically and reached to US$1.0 billion, US$2.3 billion and US$4.1 billion in the next three periods, respectively.

Global burden of COVID-19 by HDI

According to machining learning analysis based on *K*-mean clustering method, the optimal number of clusters was "8", according to the first peak value occurring among the ABC estimates as described in the method section (Supplementary Fig. 2).

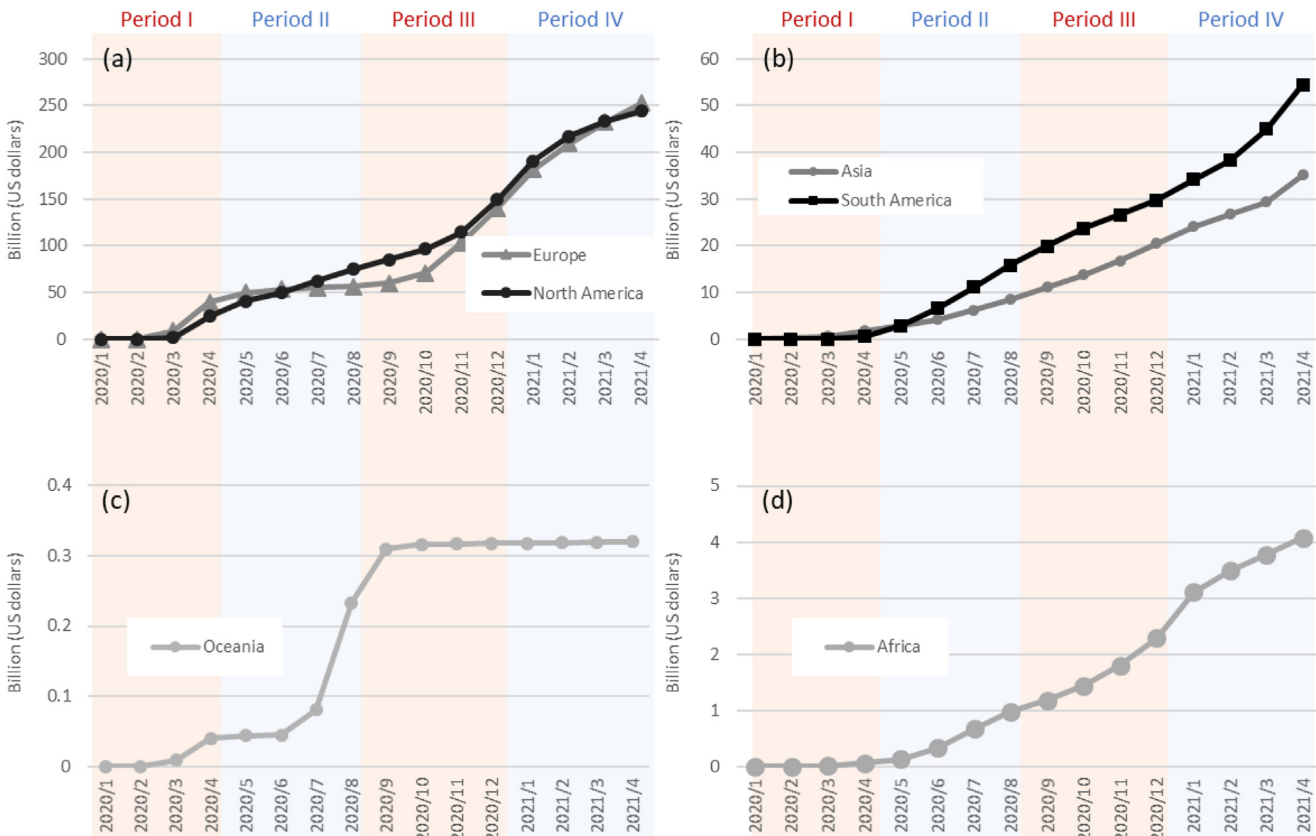

Figure 6 Trend of VSL due to COVID-19 with the hedonic wage method in different continents.

Fig. 7 shows these eight clusters of global disease burden according to the ranking of HDI from low to very high level. It is interesting to see there was still variation even within the same HDI level. In the very high HDI level, there are three categories of DALYs represented by Taiwan for low DALYs and VSL (US$0.49 billion), South Korea and Japan for medium DALYs and VSL (US$27.21 billion), and the USA and the UK for high DALYs and VSL (US$691.36 billion). In both middle and high HDI levels, there were three categories of DALYs as well represented by India, Brazil (period I), Indonesia, and South Africa (II-IV period) for high DALYs and VSL (US$36.75 billion), Vietnam for medium DALYs and VSL (US$0.24 billion), Laos and Fiji for low DALYs and VSL (US$0.001 billion). In the low HDI level, there are two categories represented by Nigeria for medium DALYs and VSL (US$0.40 billion) and Cambodia for low DALYs (US$0.01 billion).

Ranking of DALYs

Twenty countries with the highest DALYs and twenty countries with the lowest DALYs are listed in Supplementary Fig. 3. The top five countries with the highest losses due to COVID-19 consisted of the US, Brazil, Italy, Mexico, and India, all with population size greater than 5 million. Among 20 countries with the lowest DALYS, only five countries had populations greater than 5 million, and Taiwan ranked the fourth, with only 167 DALYs after the top three countries, Tanzania, Laos and Burundi.

Discussion

The current study provides the panorama of global disease burden with DALYs metric due to COVID-19 from January 2020 until April 2021. To make the results of DALYs interpretable and plausible, we begin with the analysis of epidemiological profiles on incidence, mortality, and case-fatality rate across continents and countries in the globe. Time trends of these epidemiological profiles were classified into four periods (I—V) representing the surge of epidemic in various countries during COVID-19 pandemic. It is interesting to note that there was a positive relationship between the average loss of LE and the GDP level. Based on the collection of these real-world epidemiological data and their relevant relationships with LE, we then estimated DALYs by countries and periods. Global health loss due to COVID-19 after translating these DALYs estimates per capita into the corresponding DALYs (thousands) based on the actual global population gives 31,930 from period I to period IV. The estimated DALYs figures increased with time, being 2699 (thousands) for the period I, 5484 for the period II, 10,065 for the period III, and 13,683 for the period IV. The estimate of VSL increased from US$267 billion in the period I to US$996 billion in the period IV using the CVM. Using machine learning analysis, we identified eight clusters of DALYs by three levels of HDI for all the countries worldwide. The tendency is that the higher the HDI the more consequential global disease burden in

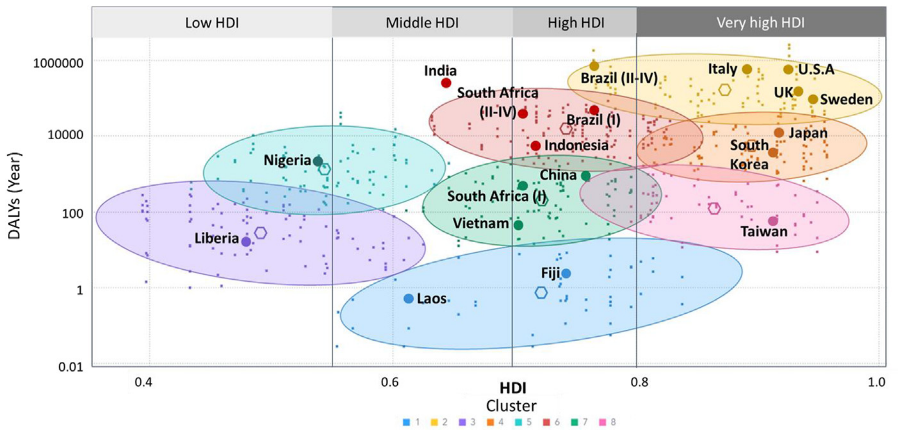

Figure 7 Global disease burden patterns of DALY with HDI by cluster K-means analysis.

terms of DALYs. However, there was still variation across countries even within the same HDI level.

According to the global burden of disease study 2017, the leading causes of DALYs are non-communicable diseases before COVID-19 pandemic. The notable communicable diseases including HIV/AIDS, malaria, and tuberculosis are in the ranking of 13, 14, and 20 for females and 13, 15, and 14 for males, respectively. DALYs attributed to these infectious diseases is often negatively associated with sociodemographic indexes (SDIs). However, the emerging SARS-CoV-2 that is a totally new infectious disease and has led to the loss of many lives and disability loss over past decade led to the reverse phenomenon, the higher SDI, the more DALYs incurred. Even the developed counties, such as the US, Italy, and Spain, are severely afflicted and confirmed cases surpassed the original country, China. Most of those with severe COVID-19 epidemics are developed countries with convenient transportation and in high-income list of the World Bank. However, the variation across countries within the same HDI level also revealed different time series of infection and also public health approaches.

It would be very interesting to compare the estimated DALYs of COVID-19 with that of influenza as both belong to respiratory diseases and also led to pandemic. Cassinni et al.[25] calculated DALYs for 31 selected communicable diseases in the European Union and European Economic Area, influenza had the highest burden (29.8% of the total burden) followed by HIV/AIDS. The main part of the high burden of influenza is the contribution of premature mortality associated with infection (YLL). The estimated mortality rate of influenza varies in different areas and subgroups. The overall average annual mortality rate of influenza is 11.92 (95% CI: 10.1—13.6).[26] It is a high incidence and high mortality infectious disease compared to tuberculosis (low incidence and high mortality), measles (low incidence and low mortality), and Chlamydia infection (high incidence and low mortality). Currently, the final mortality rate of COVID-19 is hardly available due to the still ongoing pandemic. It is intractable to compare data between influenza and COVID-19 as mortality statistics are obtained differently. Faust et al. estimated the case fatality rate with age adjustment from Diamond Princess Cruise ship (13 deaths out of 712 cases) was 0.5%, which was still 5 times than that of influenza.[27] Similar to influenza, the main driver of DALYs of COVID-19 is the contribution of premature death (YLL). Furthermore, the median time from onset to recovery for mild COVID-19 cases is approximately two weeks and three to six weeks for those with severe cases. The coronavirus family has a tropism for the central neural system.[28] If any neurological complications are reported in the future, this will increase the disease burden of YLD. On the other hand, uncomplicated influenza usually improves over two to five days. Although the developing vaccine, novel therapy, and adequate medical resources would mitigate the death burden, COVID-19 is not just another flu and would lead to more disease burden for human society. Will SARS-CoV-2 become seasonal or a major respiratory virus pathogen worldwide? In high-income countries, the incidence of infectious disease has decreased over the last century. SARS-CoV-2 will become a challenge for high-income countries and might lead to an unprecedented level of global morbidity and mortality, especially in resource-poor countries of the tropics and subtropics.[29]

We observed similar trends of health life-year economic loss in Europe and North America. The cluster outbreak of Europe happened in Lombardy, Italy on February 21 after a couple of Chinese tourists arriving in Italy on January 23 and spread to the whole continental Europe and the British Isles. In the period I, Germany has the fifth highest YLD of COVID-19 cases in Europe, but the YLL is relatively low when compared with the first to the fourth ranking of YLD (Russia, United Kingdom, Spain, and Italy, respectively). The first main reasons were Germany conducted many tests (reverse transcription polymerase chain reaction, RT-PCR) at quality-controlled laboratories throughout the country. Many cases of young people were detected actively after they had been on ski holidays in Italy and Austria. The better outcome (lower mortality) in young people compared with the elderly also leads to the low YLL in German. Therefore, the high proportion of total case numbers are relative to the number of death cases. The second reason is that Germany takes the action of social activity restrictions on the national level and the great majority of people are adhering to the contact restriction well and earlier than other European countries.[30] All Nordic countries seem much better than above European countries. However, Sweden's COVID-19 has the worst situation in Scandinavia. Sweden has the highest DALY and YLL (2020.5/1747.0 per 100,000 population) compared with Denmark (604.3/481.0 per 100,000 population), Finland (238.9/194.8 per 100,000 population) and Norway (231.6/171.9 per 100,000 population). Sweden is one of the world's few countries that has not imposed full lockdown when the neighboring countries have closed the schools, public facilities, restaurants, and restricted mass activity. Meanwhile, in the period I the number of hospital beds (2.2 beds per 1000 people) and intensive care unit beds (5.8 per 100,000 people) per capita were lower than most countries in the European Union.[31] Therefore, in addition to the different strategies to the new virus of SARS-CoV-2, it is important to prevent disease burden overwhelming the medical system in consideration of local resources and social environment.

On the other hand, North America also had outbreaks one week later after Europe and the majority of cases are in the United States. The first case was diagnosed on January 20 in an American citizen traveling from Wuhan, China. The outbreaks began to escalate rapidly in the residents, employees, and visitors in the long-term care facilities and residents of the nursing home in King County, State of Washington in late Feb to early March.[32,33] The US Centers for Disease Control (CDC) confirmed community spread on February 26 [34] and issued guidance recommending against social gathering on March 15.[35] Compared with Italy (the first cluster outbreak on February 21) lockdown on February 23, it took more than 50 days for the US government to take the action on social distancing. Therefore, COVID-19 cases number surpassed Italy in a short time on March 26 and became the country with the highest YLL and YLD. The accumulation of healthy life-year economic loss implied the working loss, which is similar to indirect cost. Bartsch et al. simulated a single symptomatic COVID-19 infection would cost a median of US$3045 in direct medical cost. When 20% of the US population becomes infected, it will cost $164.4 billion.[36] This pandemic COVID-19 disease definitely leads to the huge economic impact and recession.

In Asia, the curve of healthy life-year economic loss was different. From January 25 to February 29, the economic loss was mainly contributed from China. Wuhan was first city locked down by China authority on January 23 before Lunar New Year. Areas bordering Wuhan, Hubei provinces also set up a checkpoint on the roads, lockdown, and curfew. Two months later, the new cases there have dropped to practically zero.[37] However, the second epidemic also turned back to Asia, particularly in high population density areas in the countries of Southeast Asia, such as India, Bangladesh, Pakistan, and Indonesia. Although Taiwan are near China, the disease burden of COVID-19 is limited. Taiwan, 81 miles off the coast of mainland China, was expected to have the serious COVID-19 due to close people-to-people exchanges with China. Nevertheless, Taiwan has been on alert to the epidemics arising in China since the SARS epidemic in 2003. The first case was diagnosed on January 21 and entry restriction began with visitors from China's Hubei Province five days later. Taiwan quickly utilized cases identification, tracing, quarantine, and big data analytics to protect public health and achieved low infection and case-fatality rates.[37—39] Similar approaches were also adopted in Singapore and Hong Kong. South Korea also had mass testing, free treatment, compensation for self-isolate, and information technology. Therefore, the UK with a similar population size to South Korea had the same few cases in February but had higher DALY (462.5 vs. 5.5 per 100,000 population) in the end of period I. This is another lesson of the delayed implementation of useful intervention.[40] Furthermore, Asian culture is inherently suited for social distancing, and face mask use can prevent viral spread. All of these reasons protect the countries from the COVID-19 pandemic even in the same geographic region as China.

The epidemic of COVID-19 also hits South America badly with huge life-year economic loss (Fig. 6 (b)). The curve began to soar later than those of Europe, North American, and Asia, there would be a greater disease burden due to the lack of medical resources, low awareness of social distance, cramped and unsanitary dwellings in the big cities of South America. Currently, Oceania and Africa are the least affected regions globally. Although the population in Africa are comparatively young, lower rates of obesity, and familiar with infectious outbreaks, the fragile public health systems and the lack of universal health coverage still exposed them to the high risk of mortality and morbidity.[41] The elderly who is a vulnerable group to SARS-CoV2 in the low- and middle-income Countries (LMICs) faces more challenges, such as poor hygiene environment, poor family support, illiterate, and low accessibility.[42] Furthermore, the poorest are hit hardly. In sub-Saharan Africa, the lockdown and COVID-19 would make more people into absolute poverty (US$1.90 a day). The lockdown also threatens vaccination programs, malaria, interruption of tuberculosis and HIV treatment.

Based on the classification of eight patterns of global disease burden by DALYs cross-tabulated by HDI, there is much variation worldwide. There exits the disparity even at the same level of HDI. Such a finding implies different containment measures, diversified risk perception to COVID-19, heterogeneous response to culture, and time-varying political decision across countries. Some countries have loosened the social restrictions, some planning to ease restrictions, and the others are still in the battlefield to fight SARS-CoV-2. The accelerating epidemic rapidly in many countries indicates the shortfalls in preparedness. The herd immunity is impractical due to the possible high number of people death.[43] Therefore, the early implementation of quarantine and combing other public health actions (keeping social distance, closing big social events, border control measures and contact tracing) are cornerstones to disease control of COVID-19. In early 2021, the development and emergency use authorization of various vaccines provide the large scale of immunization worldwide. However, the capacity and distribution of vaccine will impact the commensuration with effectiveness of worldwide vaccination against COVID-19.[44]

Although great disease burden due to COVID-19 has been seen in high-income countries worldwide it is still possible to see the potential threats to DALYs for LMCs. Currently, the reported cases in low and middle-income countries are still increasing but numbers are relatively small. In fact, there is a high probability the current cases are under-estimated due to the inadequate testing in developing countries as often seen in the period I for the majority of countries in Europe and the USA. Meanwhile, the emerging cases were also noted in South America although the absolute number was still low compared to Europe and North America but there an increasing trend.

There were some limitations in this study. We did not calculate age-standardized DALYs due to the lack of the distribution of age. Although it will be difficult to make comparisons to other disease burdens, this study mainly focused on the disparities of COVID-19 among the areas worldwide. For comparison, the global disease burden from May 2020 to April 2021 was estimated as 29,232 DALYs (thousands), which was only slightly lower than 45,000 (thousands) for TB and Malaria, 4.61-fold of 6340 for upper respiratory disease, and 4% of 696,000 in the broad category of communicable, maternal, and nutritional deficiency. Second, we estimated health-life economic loss using the DALYs multiplying GDPs. This is only a projection of the scale of economic impact, not a real economic loss due to COVID-19. But this method of representation is an understandable representation of the COVID19 impacts. This issue may be tackled by using the value of life approach based on the estimate of willingness to pay (WTP) in the future. Finally, considering the dramatically severe epidemic in India since late April 2021, the retrieved time of data might under-estimate the impact of the rapid spread of COVID-19 in India.

Our study results supported that the effects of timing and contents of the interventions would lead the completely different disease burden of COVID-19. Early preparation (Taiwan) and the adequate resources for testing, isolation, and treatment (South Korea and Germany) would ease the impacts of COVID-19. While some countries are considering the loosening of the coronavirus lockdown, the government should act and prepare sufficiently to ensure that the healthcare system are able to face the repeated surge of COVID-19.

Disclosure statement

The authors have nothing to disclose.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2021.05.019.

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