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Disease burden due to COVID-19 in Taiwan: Disability-adjusted life years (DALYs) with implication of Monte Carlo simulations

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A R T I C L E I N F O

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A B S T R A C T

Background: The novel coronavirus disease 2019 (COVID-19) has affected a large number of countries. Informing the public and decision makers of the COVID-19′s economic burdens is essential for understanding the real pandemic impact.
Methods: COVID-19 premature mortality and disability impact in Taiwan was analyzed using the Taiwan National Infectious Disease Statistics System (TNIDSS) by estimating the sex/age-specific years of life lost through death (YLLs), the number of years lived with disability (YLDs), and the disability-adjusted life years (DALYs) from January 2020 to November 2021.
Results: Taiwan recorded 1004.13 DALYs (95% CI: 1002.75–1005.61) per 100,000 population for COVID-19, with YLLs accounting for 99.5% (95% CI: 99.3%–99.6%) of all DALYs, with males suffering more from the disease than females. For population aged ≥ 70 years, the disease burdens of YLDs and YLLs were 0.1% and 99.9%, respectively. Furthermore, we found that duration of disease in critical state contributed 63.9% of the variance in DALY estimations.
Conclusions: The nationwide estimation of DALYs in Taiwan provides insights into the demographic distributions and key epidemiological parameter for DALYs. The essentiality of enforcing protective precautions when needed is also implicated. The higher YLLs percentage in DALYs also revealed the fact of high confirmed death rates in Taiwan. To reduce infection risks and disease, it is crucial to maintain moderate social distancing, border control, hygiene measures, and increase vaccine coverage levels.

Introduction

As of 11 Jan 2022, a large number of countries have been affected by the novel coronavirus disease 2019 (COVID-19), with 309,997,915 COVID-19 cases and 5494,246 deaths reported worldwide (https://coronavirus.jhu.edu/map.html) [1]. The novel coronavirus was named as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) due to its high homology (~80%) to SARS-CoV [2]. COVID-19 has a broad spectrum of severity. Of serological-confirmed infections, only a fraction will develop symptoms. Among the symptomatic cases, only a fraction of them can be identified via surveillance systems, hospitalization, or confirmed after death [3]. The definition of asymptomatic, mild, moderate, severe and critical is summarized [4].

Taiwan is a country geographically near China and has close contacts with China, making it more susceptible to COVID-19 transmissions. At the early outbreak in 2020, COVID-19 was listed as a notifiable disease by the Taiwan Centers for Disease Control (Taiwan CDC) on January 15, 2020. As of June 18, 2020, a cumulative total 446 cases have been confirmed in Taiwan, among which 355 were imported, 55 community-acquired, and 36 were naval crew members from the Dunmu fleet [5]. As of 13 Jan 2022, Taiwan has been affected by the pandemic with 17,624 COVID-19 cases and 851 deaths reported (https://sites.google.com/cdc.gov.tw/2019ncov/

Abbreviations: DALYs, Disability-adjusted Life Years; YLL, Years of Life Lost; YLD, Years Lived with Disability; DW, Disability Weight; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus-2; Taiwan CDC, Taiwan Centers for Disease Control; CECC, Central Epidemic Command Center; TNIDSS, Taiwan National Infectious Disease Statistics System; MC Simulation, Monte Carlo Simulation; PCR, Polymerase Chain Reaction; ICU, Intensive Care Unit; GBD, Global Burden of Disease; WHO, World Health Organization

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taiwan) [6]. During the pandemic period, the Central Epidemic Command Center (CECC) has rapidly implemented a list of action items including border control, case identification, quarantine of suspicious cases, proactive case finding, resource allocation, and educate the public to manage the disease crisis [7]. However, the evolution of SARS-CoV-2 variant, the Omicron (B.1.1.529), is still interfering with the effectiveness of the current control measures and making cases surging around the world [8].

To inform both the public and decision makers of the COVID-19 impacts in perspectives of society or economic burdens is essential for understanding the real pandemic impacts and implementations of better strategies. The disability-adjusted life years (DALYs) parameter estimates the amount of time, ability, or activity that is lost by an individual as a result of disease-induced disability or death [9]. The DALYs were calculated as the sum of years of life lost through death (YLLs) and number of years lived with disability (YLDs). These health measures incorporate estimates of infection rate, deaths and duration of a particular condition as well as the outcome, whether it is disability or premature death [9]. So far, investigations on disease burdens or direct impacts of COVID-19 on population health have been estimated in various countries, including Germany [10], Korea [11], Denmark [12], India [13], USA [14], Australia [15], Scotland [16], Mexican [17], as long as studies with multiple countries involved [18–20].

Among all the DALY studies exploring COVID-19 disease burdens, there has been a consistent observation that YLLs had more contributions to the overall DALYs than the YLDs in each country investigated [10,12–20]. In the only study conducted in Asia, the total disease burden attributable to COVID-19 during the study period was estimated to be 4.930 DALYs per 100,000 population in Korea, where the YLDs and the YLLs constituted 10.3% and 89.7% of the total DALYs, respectively. Also, subjects who aged > 80 years old were found to have the highest DALYs [11]. Considering the fact that there has been no information regarding the disease burdens of COVID-19 contributed to Taiwan, we thus aimed to quantitatively estimate the overall DALYs to provide more information to regulatory authorities for more soundly control measures being developed. Hence, the purpose of this study was to employ the Taiwan National Infectious Disease Statistics System (TNIDSS) to analyze the premature mortality and disability impact of COVID-19 by calculating amounts of life-years lost stratified by sex and ages in Taiwan from January 2020 to November 2021.

Material and methods

Cases of SARS-CoV-2 in Taiwan

The Taiwan CDC announced COVID-19 as a notifiable disease on January 15, 2020 and the first confirmed case of SARS-CoV-2 infection in Taiwan was imported from China on January 21, 2020 (https://www.cdc.gov.tw/En/Category/Page/0vq8rsAob_9HCi5GQ5jH1Q) [21]. Up to November 30, 2020, a total of 16,609 confirmed cases and 848 deaths of SARS-CoV-2 in Taiwan from January 2020 to November 2021 (Fig. 1). The first peak of confirmed cases occurred in March 2020 and totally 799 cases were accounted in 2020 (Fig. 1A and 1B). However, in the following year, the number of cases increased significantly since May 2021, resulted from the community transmissions of SARS-CoV-2 virus (Fig. 1A). Hence, as of May 19th, the alert level of epidemic prevention was raised to the third level in Taiwan. A total of 15,091 confirmed cases and 830 deaths were accounted from May 1, 2021 to September 30, 2021. In addition, the death number during this period accounted for 97.8% of the total death from 2020 to 2021 (Fig. 1C and 1D).

The number of COVID-19 cases and deaths stratified by age and sex were shown (Appendix Fig. 1), where 64% (546 deaths) and 36% (302 deaths) were accounted in male and female population of Taiwan, respectively. There are no deaths among people under the age of 29. Also, female population aged from 50 to 59 were most susceptible to COVID-19 infections (death case not accounted), while male population with ages from 60 to 69 years had the highest case numbers. In addition, among all age populations, individuals aged over 70 accounted for the largest percentages of deaths from COVID-19 infections (Appendix Fig. 1).

Years of life lost to death (YLLs)

YLLs were calculated by multiplying the number of deaths at a given age group by the standard life expectancy for that age group (Eq. (1)).

$$YLLs = \sum_{x,y} M_{x,y} \times L_{1x,y}, \tag{1}$$

where $M_{x,y}$ represents the age-specific (x) and sex-specific (y) number of deaths of SARS-CoV-2 infection. The age categories (x) were 0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69 and 70 + years. $L_{1x,y}$ is the years of life lost due to premature death at different age groups. We used the life expectancy at the mid-point for each age group, corresponding to available the age-specific death cases. We used the 2020 life-table with a life expectancy varied with the birth year (https://www.moi.gov.tw/cl.aspx?n = 3053) [22]. The life expectancy for 30–39, 40–49, 50–59, 60–69, and 70 + age groups were 44.72/51.02 (M/F), 35.48/41.40 (M/F), 26.99/32.09 (M/F), 19.18/23.17 (M/F), and 10.55/13.00 years (M/F), respectively.

Years lived with disability (YLDs) and overall burden of disease (DALYs)

YLDs were derived as the product of the number of new cases, the average duration of the disability and disability weightings for the disease stages (Eq. (2)).

$$YLDs = \sum_{x,y,z} I_{x,y,z} \times DW_z \times L_{2,z}, \tag{2}$$

where $I_{x,y,z}$ represents age/sex-specific (x,y) confirmed cases at different disease severity (z); DW_z represent the disease severity-specific (z) disability weights (DWs) and $L_{2,z}$ represent disease severity-specific (z) disability duration (year). The disease severities (z) were classified as asymptomatic, mild, moderate, severe, and critical, respectively, based on WHO guideline (https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021–2) [23]. Hence, Table 1 lists the parameter estimations for YLDs in Taiwan. We adopted a published study [24] to estimate distributions for disease severities in first 100 patients with laboratory-confirmed SARS-CoV-2 infections in Taiwan. Furthermore, we used the DWs for COVID-19 that the severity-specific DWs were asymptomatic, 0; mild, 0.006; moderate, 0.051; severe, 0.133; and very severe/critical 0.655 [10,25–27]. The severity-specific durations of illness were 14 days (Asymptomatic, mild, and moderate), 21 days (Severe) and 32 days (Critical) (https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf) [28].

The DALY calculations for confirmed and death cases resulted from COVID-19 in Taiwan from January 2020 to November 2020 were estimated by using the following formula. The YLLs and YLDs are independently calculated and then combined in a single summary measure (Eq. (3)).

$$DALYs = YLLs + YLDs \tag{3}$$

The DALYs for each age-specific category and disease severity were multiplied by the number of cases in each year. These DALYs were then divided by total population in 2020 to derive DALY estimates per 100,000 population per year, which were the units used in the World Bank report [9,29].

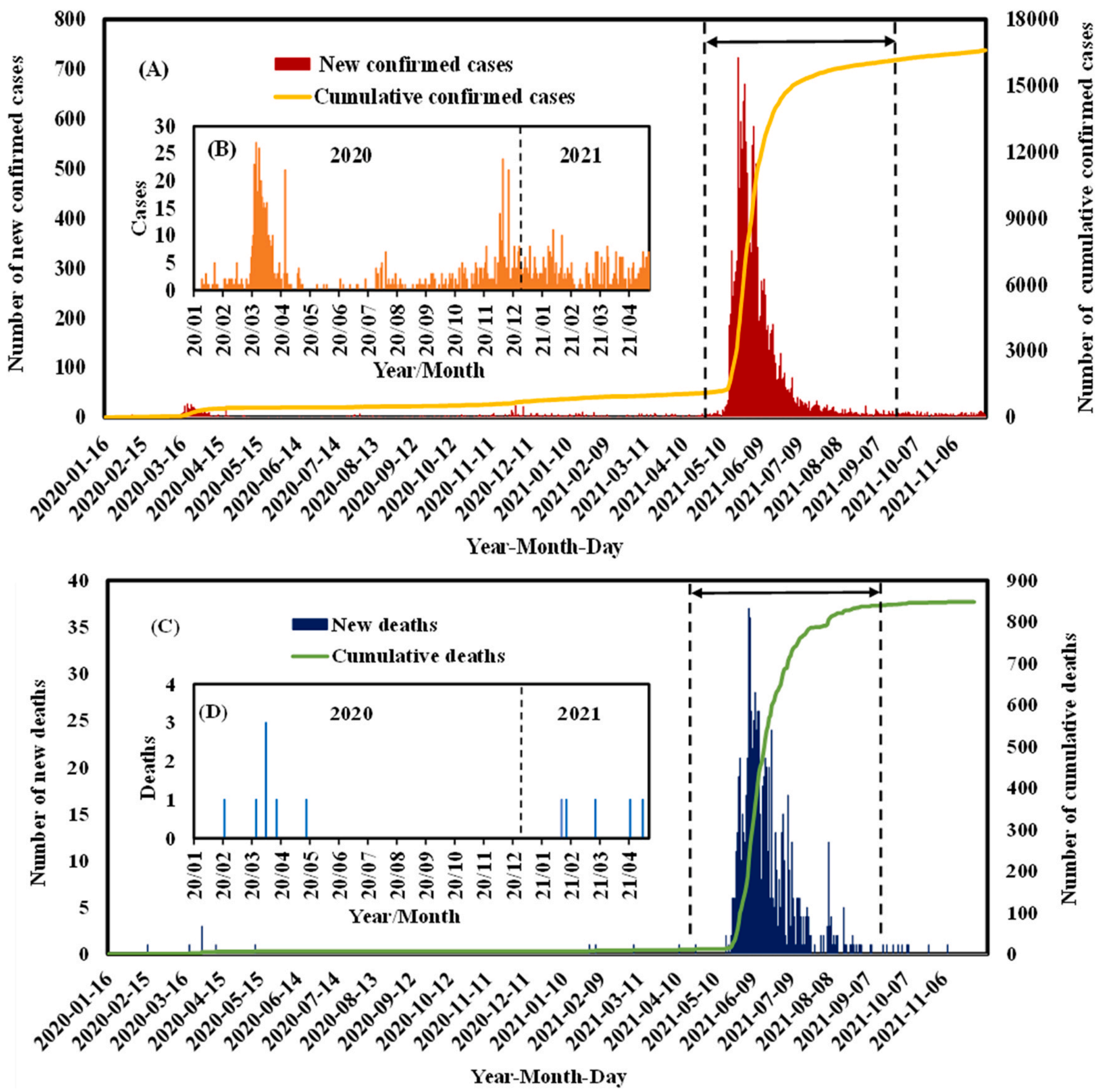

Fig. 1. (A, B) Daily cumulative and reported cases of SARS-CoV-2 from 2020 to 2021 in Taiwan. (C, D) Daily new deaths and cumulative number of deaths in Taiwan from January 2020 to April 2021.

Monte Carlo simulation

Here, a sensitivity analysis was also probabilistically performed with the Monte Carlo (MC) simulation to better understand the impact of severity grade-specific *DW*s and durations of illness. A Monte Carlo (MC) simulation was used to characterize the uncertainties of parameters and exposure scenarios for the YLDs and DALYs among different age or sex groups. Uncertainties of parameters including *DW*s and disease duration (L_2) at different disease severities (mild, moderate, severe, and critical) were measured (Table 1). These data were fitted into the most appropriate or pre-defined probability distributions based on past experiences or historical researches by using the Crystal Ball software (Version 2000.2, Decisioneering Inc., Denver, CO, USA). A log-normal distribution model was assumed to describe the input parameters of *DW* and L_2.

Table 1
Parameters used to calculate the years lived with disability (YLDs) in Taiwan.

Disease severity (Grade)	Distribution[a]	Disability weights[b]	Duration of disease[c]
Asymptomatic	20%	0.000	14 days
Mild	41%	0.006 (0.002–0.012)[d]	14 days
Moderate	20%	0.051 (0.032–0.074)[d]	14 days
Severe	14%	0.133 (0.088–0.190)[d]	21 (21–42)[d] days
Critical	5%	0.655 (0.579–0.727)[d]	32 (21–42)[d] days

[a] The estimation of severity distribution of nonfatal cases of SARS-CoV-2 were based on Taiwan Centers for Disease Control [6] and Tsou et al. [24]
[b] Adopted from Global Burden of Disease study (2019) [25], Haagsma et al. [27], Rommel et al. [10] and Wyper et al. [26].
[c] Adopted from Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)(https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf) [28].
[d] We assumed that the parameters are triangular distribution in Crystal Ball Software. The triangular distribution is continuous. It describes a situation where we know the minimum, maximum, and most likely values to occur.

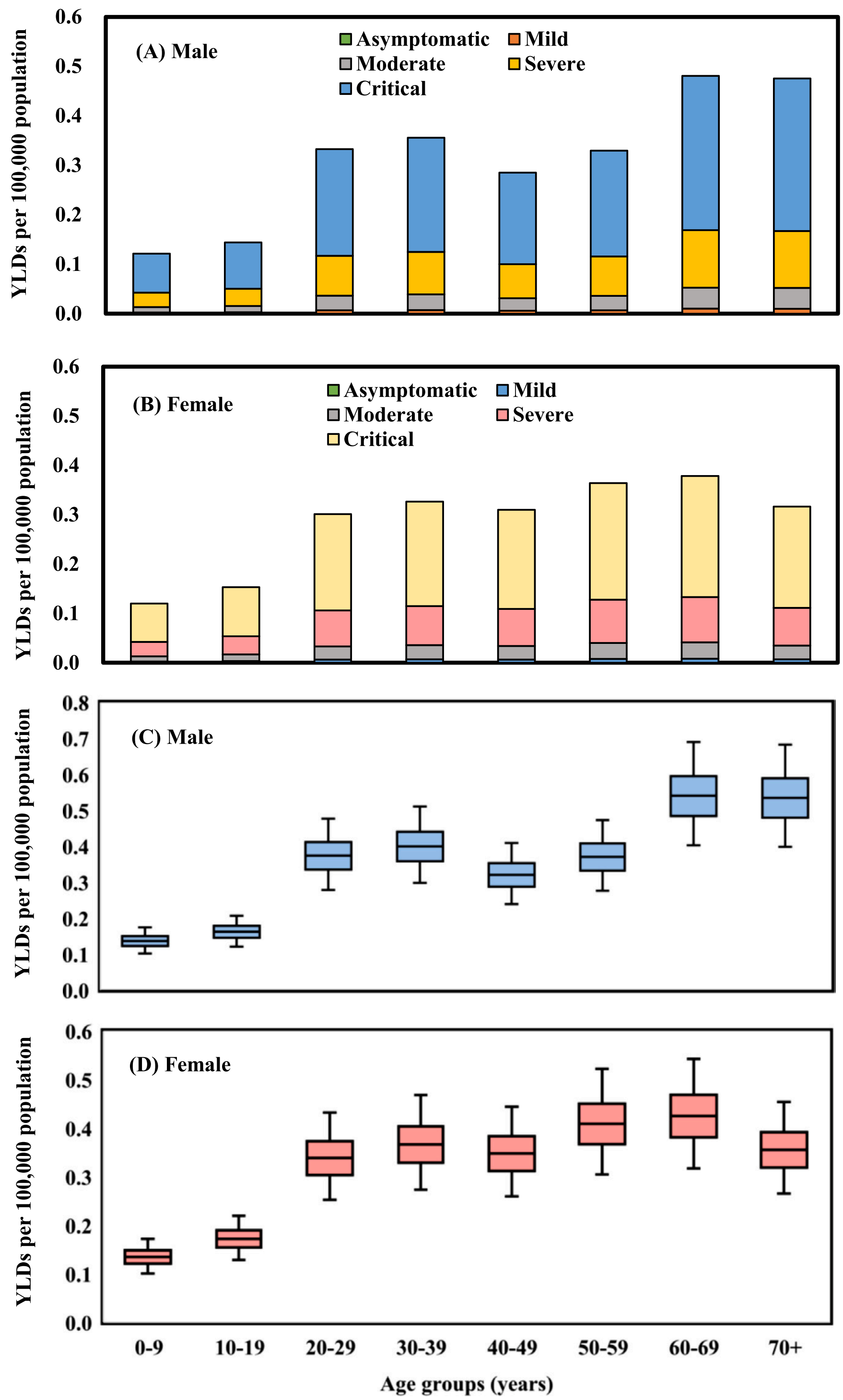

Fig. 2. (A, B) Age- and gender-specific estimations for years lived with disability (YLDs) per 100,000 population for COVID-19 in Taiwan during the study period from January 2020 to November 2021. (C, D) Box-and-whisker plots of estimated YLDs per 100,000 population stratified by different age and gender groups. The whiskers indicate the 5th – 95th percentiles and the box covers the 25th – 75th percentiles of YLDs. The horizontal line that splits the box denotes median (50th percentiles).

Moreover, to explicitly quantify the uncertainty and variability of the DALYs, a MC simulation was performed with 100,000 iterations via the simple random sampling method (stability condition) to obtain the result of robust uncertainty analysis. The sampling data was used to construct its corresponding 95% confidence interval as the uncertainty range. The process of repeatedly sampling from probability distributions derived the distribution of outcomes. We also explore the influences of each parameter on the estimation of target forecast (DALYs).

Results

Years of life lost to death (YLLs)

YLLs for COVID-19 by age-sex groups were shown in Appendix Fig. 2. The total number of YLLs caused by COVID-19 was 13,714 from January 2020 to November 2021. Males and females accounted for 61% and 39%, respectively (Appendix Fig. 2). The YLLs per 100,000 population were 998.74. In addition, the YLLs were greater in males

(639.06 per 100,000 population, 64%) than in females (359.68 per 100,000 population, 36%). Deaths caused by COVID-19 occurred in ages over 30 years old, and proportion of YLLs was the highest in age group over 70 (54%), where males account for 52% (331.95/639.06 YLLs per 100,000 population) and females 57% (203.65/359.68 YLLs per 100,000 population) (Appendix Fig. 2B).

Years of life lived with disability (YLDs)

Fig. 2 shows YLDs for COVID-19 by sex and age group. A total of 4.79 YLDs to health loss per 100,000 population was accounted during the study period. Females (2.27 per 100,000 population (47% of total YLDs)) suffered slightly lower YLDs than those males (2.52 per 100,000 population (53% of total YLDs)). The YLD estimates are mainly affected by the disease severity of COVID-19. For males, the degrees of impact are as follows: critical (1.64 per 100,000 population), severe (0.61), moderate (0.22), and mild (0.05) (Fig. 2A). For females, the degrees of impact are in the order of critical (1.47 per 100,000 population), severe (0.55), moderate (0.20), and mild (0.05) (Fig. 2B). The contribution percentages of disease severities are 65%, 24%, 9%, 2% for critical, severe, moderate, and mild state, respectively (Fig. 2A and 2B).

By assuming the probability distributions of *DW*s and durations of disease, the box and whisker plots of YLDs were then generated. Overall, either male or female population at age from 60 to 69 years were most affected, followed by males over 70 years and females aged 50–59 years. The YLDs in the population aged from 60 to 69 years were 0.54 (0.40–0.69) per 100,000 population (median (95% confidence interval (CI)) and 0.43 (0.32–0.54) per 100,000 population for males and females, respectively (Fig. 2C and 2D, Table 2). The trend of YLDs is consistent with the reported cases in each age section.

Disease burden due to COVID-19 (DALYs)

From January 2020 to November 2021, COVID-19 caused a total of 1003.53 DALYs per 100,000 population in Taiwan, with YLLs accounting for 99.5% of the total DALYs (Fig. 3A and 3B). Furthermore, males (641.58 DALYs per 100,000 population) had larger DALYs than females (361.95 DALYs per 100,000 population). The relative contributions of YLDs and YLLs to DALYs varied by age category, with YLLs increasing with age. In the age group of 0–29 years, the proportions of YLDs and YLLs were 100% and 0%, respectively. The disease burdens of YLDs and YLLs were 0.1% and 99.9%, respectively, among people above the age of 70 (Fig. 3A and 3B).

Table 2
Estimations of YLLs, YLDs, and DALYs for COVID-19 in Taiwan from January 2020 to November 2021. A Monte Carlo (MC) simulation was used to characterize the uncertainties of parameters and exposure scenarios for the YLDs and DALYs among different age or sex groups.

Age group (years)	Sex	YLLs[a]	YLDs[a] Median (2.5th–97.5th percentile)	DALYs[a] Median (2.5th–97.5th percentile)
0–9	Male	–	0.14 (0.10–0.17)	0.14 (0.10–0.17)
	Female	–	0.13 (0.10–0.17)	0.13 (0.10–0.17)
10–19	Male	–	0.16 (0.12–0.21)	0.16 (0.12–0.21)
	Female	–	0.17 (0.13–0.22)	0.17 (0.13–0.22)
20–29	Male	–	0.37 (0.28–0.48)	0.37 (0.28–0.48)
	Female	–	0.34 (0.25–0.43)	0.34 (0.25–0.43)
30–39	Male	17.85	0.40 (0.30–0.51)	18.25 (18.14–18.36)
	Female	2.96	0.37 (0.27–0.47)	3.33 (3.23–3.43)
40–49	Male	17.22	0.32 (0.24–0.41)	17.54 (17.46–17.63)
	Female	30.15	0.35 (0.26–0.44)	30.50 (30.41–30.60)
50–59	Male	77.30	0.37 (0.28–0.47)	77.67 (77.57–77.77)
	Female	26.01	0.41 (0.30–0.52)	26.42 (26.31–26.53)
60–69	Male	194.75	0.54 (0.40–0.69)	195.29 (195.15–195.44)
	Female	96.90	0.43 (0.32–0.54)	97.33 (97.22–97.45)
70 +	Male	331.95	0.53 (0.40–0.68)	332.49 (332.35–332.63)
	Female	203.65	0.36 (0.26–0.45)	204.01 (203.92–204.11)
Total		998.74	5.39 (4.01–6.87)	1004.13 (1002.75–1005.61)

[a] Unit: per 100,000 population

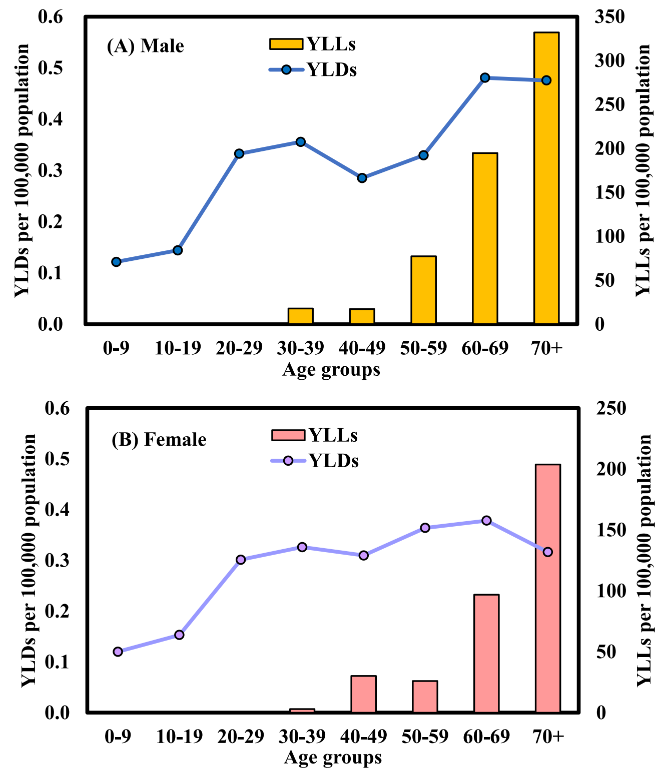

Fig. 3. (A, B) Age- and gender-specific estimations for DALYs per 100,000 population for COVID-19 in Taiwan during the study period from January 2020 to November 2021.

Among all gender and age populations, population with age ≥ 70 years old has the highest DALYs ((332.49 (332.35–332.63) per 100,000 population and 204.01 (203.92–204.11) per 100,000 population) for males and females, respectively) (Table 2). From January 2020 to November 2021, COVID-19 caused a total of 1004.13 DALYs (95% CI: 1002.75–1005.61)) per 100,000 population in Taiwan, with YLLs accounting for 99.5% (95% CI: 99.3%–99.6%) of the total DALYs (Table 3) by using Monte Carlo simulation.

The results of sensitivity analyses for each epidemiological parameter are shown in Appendix Fig. 3. Disease duration (L_2) is the most influential parameter for DALY estimations, with duration of disease in critical state contributing for 63.9% of the variation, followed by duration of disease in severe state accounting for 20.2% of the variance in DALY estimations.

Discussion

Although the prevalence rate of COVID-19 in Taiwan was not relatively high in the world during the study period, this study aims to provide a perspective of the essentiality of prompt and proactive actions of control measures (e.g., border control, mandatory mask wearing, and social distancing) before the disease outbreak. Taiwan has a unique geographic feature that it has close contacts with China due to the geographic location and relations for economic and trades. It is of interests to investigate the underlying factors for the lower prevalence rate of Taiwan compared to other geographic regions by observing the YLL, YLD, and DALY and the policy enforcements during the period of pandemic occurrence in Taiwan.

Table 3
Comparison of DALYs caused by COVID-19 in Taiwan and other countries.

References	Country	Study period	DALYs[a]	YLLs[a]	YLDs[a]	YLLs/DALYs (%)
Asia						
This study	Taiwan	2020/01/21–2021/11/30	1004.13 (1002.75–1005.61)[b]	998.74	5.39 (4.01–6.87)[b]	99.5 (99.3–99.6)[b]
Jo et al. [11]	Korea	2020/01/20–2020/04/24	4.930	4.423	0.507	89.7
Oceania						
Australian Institute of Health and Welfare [15]	Australia	2020 full year	33.1[c]	31.9[c]	1.2[c]	96.5
European						
Cuschieri et al. [20]	Malta	2020/03–2021/03	5478	5229	249	95
Wyper et al. [16]	Scotland	2020 full year	1770–1980	1731–1946	35	98
Pires et al. [12]	Denmark	2020/02/26–2021/02/25	520	514.8	5.2	99
Rommel et al. [10]	Germany	2020 full year	368.2	365.75	2.45	99.3
America						
Salinas-Escudero et al. [17]	Mexico	2020/02/22–2020/12/04	1055	1663.8	30.7	97

[a] Unit: per 100,000 population
[b] Median (2.5th–97.5th percentile)
[c] Calculated based on the reported estimate of 8400 DALY, in population size of 25,364,300 (estimate for mid-2019; Australian Bureau of Statistics)

On the other hand, although the pandemic seemed to be controlled with the practice of vaccination in Taiwan from mid- to late-2021, surprisingly, the case fatality rate (CFR) (ratio between confirmed deaths and confirmed cases) of Taiwan was the highest among countries of Italy, United States, United Kingdom, and South Korea (Appendix Fig. 4). Also, the daily confirmed deaths per million people in Taiwan have been increasingly high until December, 2022 (Appendix Fig. 5). At some timepoints, the death rates in Taiwan were higher than those of United States, United Kingdom, Germany, and France where the prevalence rates were originally much higher than that of Taiwan previously during the pandemic period. Also, the daily confirmed cases have been continuously increasing until September, 2022 (Appendix Fig. 6). Therefore, based on the high CFR, daily new confirmed deaths, and accumulating cases in Taiwan, it would be worthwhile to explore and compare the DALYs of Taiwan with other countries for more deep investigations in the associations of policy enforcements and DALY estimations.

Overall, the total estimated disability-adjusted life years (DALYs) of 1004.13 per 100,000 population were lost to COVID-19 in Taiwan from January 2020 to November 2021, where 998.74 years of life lost through death (YLLs) and 5.39 years lived with disability (YLDs) per 100,000 population were observed in Taiwan (Table 2). We discovered that disease burdens of COVID-19 differ by sex, where male population has higher DALYs (64% (641.58 DALYs per 100,000 population)) than that of female population (36% (361.95 DALYs per 100,000 population)). The reason could be ascribed to more death (546) and confirmed (8526) cases in males than those of females (302 and 8083) in each age category. In accordance with our results, Pifarré I Arolas et al.[19] evidenced that men have lost 45% more life years than that of women.

Higher estimates of YLLs or YLDs in male population compared to those of females were observed in this study. In accordance with the trends in Taiwan, a systematic review and meta-analysis study revealed the higher prevalence of COVID-19 confirmed cases in males (55.00 (51.43 –56.58)) than females (45.00 (41.42 –48.57)) [30]. Peckham et al. [31] also found male patients have almost three times the odds of requiring intensive treatment unit (ITU) admissions and death than female patients. Sex or gender differences in incidences, responses, and outcomes of COVID-19 patients have been prevalently evidenced in numerous literatures. Ya'qoub et al. [32] reported the sex-specific differences in comorbidity profile between males and females that males generally have higher prevalence of smoking, lung or cardiovascular diseases and higher risks in disease progression and intensive care unit (ICU) admissions [32–34]. Sex differences in biological attributes such as hormonal, immune, and inflammatory responses also act as crucial roles in mediating immunology or disease severity in COVID-19 patients. Reasons for less severe symptoms observed in women were ascribed to the existence of estrogens that could promote innate or adaptive responses and robust immune responses to vaccines in hosts. On the contrary, reductions of testosterone levels in aging men has also been found to be associated with increased proinflammatory cytokine levels that might contribute to COVID-19 disease progressions [35]. Takahashi et al. [36] also found females had more robust COVID-19 disease progression-associated CD8 T cell activations. Zeng et al. [37] revealed that females produce larger amounts of neutralizing antibodies in the early phase of COVID-19 than those of males. Moreover, gender differences in social behaviors also have evident impacts on infection risks as long as disease severities. Reported that women were more likely to perceive the COVID-19 pandemic as a serious issue and comply with policy measures subsequently [38]. Also, higher prevalence of high-risk behaviors such as alcohol consumptions or smoking generally happen in males than females, leading to worse symptoms or weaker immune systems in male population [30,39].

Due to the geographical features of Taiwan as an island, most of the confirmed cases in the early stage of the pandemics were contributed from imported cases [40]. From January 2020 to March 2021, the total number of confirmed cases were 1030 (including 77 domestic confirmed cases and 953 imported cases). Among the 953 imported cases, 47% were acquired in Asia, followed by 23.9% in Europe, and 20.0% in America [40]. Moreover, from January 2020 to November 2021, imported cases contributed to 1 death and 2019 confirmed cases, accounted for 0.15 DALYs per 100,000 population and 0.3% of the total DALYs in Taiwan.

To track any occurrences of pandemic-related incidences, less than 1200 total cases were recorded before the pandemic onset (May 2021) (https://sites.google.com/cdc.gov.tw/2019ncov/taiwan) [6]. However, a surge of COVID-19 confirmed cases was observed since May 16, 2021. Based on a daily analysis of imported cases in Taiwan, an evident increase of imported cases occurred from March 12th, 2020, among which most of the them were from middle east, Africa, Europe, and north America [5], suggesting that implementations of border controls in Taiwan may not be adequate enough for long-term disease containments.

Liu et al. [5] also reported that there were 321 imported cases in Taiwan identified from January 21 to April 6, 2020 that half of the cases developed symptoms before arrival, most of the remainder developed symptoms in 14 days after arrival, and 3.4% had no symptoms observed. Most of the cases with symptoms before arrival were identified through airport screening followed by hospital notifications, indicating that the preventive measures at airports had certain effects on preventing the pandemic from evolving into more serious situations in some extents. Taken together, one of the main factors contributing to the case surge since May 16, 2021 is attributed to the sudden increase of confirmed imported cases since Mar, 2020. The geographical characteristics also make Taiwan more susceptible to undertake more symptomatic/asymptomatic cases around the world.

Since May 16, 2021, a level 3 lockdown with mandatory regulations such as mask-wearing in public spaces, limitations in indoor and outdoor gatherings exceeding 5 and 10 persons, respectively, and prohibitions on dining inside restaurants was implemented in Taiwan. It was not until around September, 2021 the overall cases were control in certain extents.

However, for asymptomatic cases on arrival, most of them were identified by home quarantine, hospital notification, or contact tracing/testing [5]. Although it was estimated that there were ~20% asymptomatic cases in first 100 laboratory-confirmed SARS-CoV-2 infection patients in Taiwan [24], more accurate estimates for the total asymptomatic cases during the pandemic period is still pending for investigations due to the lack of real-time detections of asymptomatic patients at that time. Based on clinical observations or retrospective case-control approach, previous studies revealed that there were 48.5%, 52.5%, and 57.8% of SARS-CoV-2 infected cases remained asymptomatic in the country [41–44]. Systematic review and meta-analysis also found approximately 24.2% and 31% asymptomatic cases of infected people [45,46]. Notably, an integrated epidemiological model incorporated with RT-PCR testing provided information that asymptomatic infections together with presymptomatic ones substantially drive community transmission and contribute to at least 50% of the total force of infection [47]. Furthermore, the transmissibility of asymptomatic patients was found to be similar to that of symptomatic patients [48]. Taken together, these findings highlight the great importance of real-time testing and contact tracing especially for imported individuals to prevent further waves of pandemics to come.

As an emerging infectious disease, there are limited information in *DW* for quantifications of COVID-19 DALYs. Jo et al. [11] evaluated disease burdens of COVID-19 in South Korea based on *DW* evaluations of the same symptoms such as the upper respiratory infection (0.088), *Hemophilus influenza* type B pneumonia (0.309), maternal sepsis (0.825), and dysthymia (0.194) [49]. Salinas-Escudero et al. [17] assumed the *DW*s based on the severity of patients' symptoms such as requirements of hospitalization or mechanical ventilation machine, and whether entering into the Intensive Care Unit (ICU). Wyper et al. [26] proposed a systematic method by giving weights according to different severity grades based on studies of European Disability Weights and Global Burden of Disease (GBD) 2019 [25,26]. Similarly, Cuschieri et al. [20] adopted the DWs of Wyper et al. [26] to quantify COVID-19 DALYs on the Malita population from March, 2020 to March, 2021. In this study, we applied the same approach by choosing the European DWs-based World Health Organization (WHO)-defined severity grades for YLD estimations [26].

In the sensitivity analyses, we found duration of disease in critical state with the highest *DW* value has the most significant impact on overall DALYs in Taiwan, followed by duration of disease in severe state, severe disability weight, and critical disability weight. It could be concluded that disease severity, as the factor for *DW* considerations in this study, is not only influential to estimations of DALY in a severity-dependent state, but also sensitive to overall DALYs when more severe cases are applied. Also, durations of disease either in critical or severe state have higher impacts on DALYs than *DW* values, implicating a potential strategy could be proposed to reduce DALYs by controlling the duration of diseases with more advanced medications or personal cares especially on patients at severe or critical state.

A tremendous surge of cases occurred from May 10th, 2021 until October, 2021 when much less cases were observed. A large proportion of COVID-19 DALYs in Taiwan was ascribed to cases occurred during this period. Nevertheless, lower case and mortality rates were observed compared to other members of the Organization for Economic Co-operation and development. The economic growth was also shown positive in the first phase of containment (https://media.nature.com/original/magazine-assets/d41586–022–00649–8/d41586–022–00649–8.pdf) [50]. We found that YLLs contributed more (99.5%) than YLDs (0.5%) to overall DALYs, as in other countries calculating the disease burden of COVID-19 [51] (Table 2). Taiwan Centers for Disease Control (Taiwan CDC) performed imminent reacts in control measures of border control and border quarantine measures, social distancing measures, restriction for foreign migrant workers and business visitors, community precautions, big data analytic tracking system for case identification, and large-scale surveillance. However, there has been no concrete evidence to conclude the association between the governmental control measures and the observed DALYs in Taiwan.

There has been supporting evidence correlated efficient mitigation strategies with lower mortality risks of COVID-19. Liang et al. [52] assessed that one additional COVID-19 screening test per 100 people was associated with an 8% reduction in mortality risk (RR = 0.92; 95% CI 0.87–0.96, P = 0.001). One additional bed per 1000 people led to a 15% reduction of mortality risk (RR = 0.85; 95% CI 0.80–0.90, P < 0.001). A 0.1 increase in government effectiveness score was also associated with a 4% reduction in risk of mortality (RR = 0.96; 95% CI 0.92–0.99, P = 0.017). However, more direct evidence is needed to define the associations between control measure policies and the lower contributing ratio of YLLs in Taiwan. Although there are well-established healthcare system, and younger demographics in Taiwan compared to other severely impacted countries, further investigations are required to be performed to understand the underlying associations among these factors and the DALY estimations [52].

Furthermore, due to the lack of the information of long-term disease sequelae, we didn't take this part into the DALY calculations, which means the actual DALYs could be underestimated without considering this factor. Nevertheless, we have observed that the main contributor to case surges from the time point (May 16, 2021) was ascribed to the imported cases. Liu et al. [5] found that half of the imported cases without fever could not be detected by body temperature screening at the airport. Cases only with neurological symptoms such as loss of smell or taste, gastrointestinal symptoms (e.g., diarrhea), or longer durations of symptom display before arrival because of the prolonged viral shedding can all contribute to the effectiveness of border control. As mentioned before, numerous studies have demonstrated that asymptomatic cases dominated at least half of the infected cases in many countries, the similarities of transmissibility between asymptomatic and symptomatic cases have made disease containments much more challenging [46]. By all means, in addition to vaccination evidence, proactive border controls with strategies such as applications of rapid screenings, quarantining travelers from seriously impacted epidemic areas, and documentations of contact tracing either before arrival or traces after being quarantined should be strictly reinforced to prevent the second wave of outbreaks.

Conclusions

The present study is the first quantification of COVID-19 disease burdens in Taiwan. Estimates of disease burden provide insights into the demographic distributions and key epidemiological parameter for DALYs. The estimated YLLs accounted for 99.5% of the total DALYs during the study period. Although Taiwan has experienced two waves of COVID-19 outbreaks, including community infections and hospital cluster infections, the immediate policy implementation has effectively prevented the further expansion of the epidemic, and the number of deaths has also reduced with an agile automatic tracking system for potential confirmed cases and the well-established healthcare systems. Further investigations are needed to explore the association between governmental control measures and the DALY estimations. In order to prevent occurrences of further epidemic waves or generations of super-spreaders in the future, it is of great importance to continuously maintain moderate social distancing, border control, hygiene measures, and increase vaccine coverages to reduce infection risks and disease burdens.

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Authors' contributions

HCT and PJP conceptualizedthe analysis and YFY and SCC supervised the work. HCT performed the analysesand prepared all Figs and Tables. PJP and SCC gave feedback on methodology andpresentation of results. YFY and SCC reviewed and edited the manuscript. Allco-authors wrote the manuscript, provided feedback on the analyses and themanuscript, and agreed with the final submitted version.

Data Availability

Dataset for this study is open and publicly available at the Taiwan National Infectious Disease Statistics System (TNIDSS) official website (https://sites.google.com/cdc.gov.tw/2019ncov/taiwan). All methods were carried out in accordance with relevant guidelines and regulations.

Declaration of Competing Interest

The authors have declared that no competing interest exists.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2023.03.028.

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