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Research article

Measuring disease burden of dominant variants of COVID-19 in Taiwan

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ABSTRACT

Objectives: The disability-adjusted life years (DALYs) of COVID-19 have been applied as a time-based measurement to estimate years of life lost due to premature mortality or healthy life lost in different countries. Limited information was found for DALYs among different variants of concern (VOC).

Methods: Disease severities based on categories of asymptomatic, mild, moderate, severe, and critical cases were explored among different VOC by analyzing the proportions in confirmed cases. DALY or years of healthy life lost due to disability (YLD)-based annual burdens of COVID-19 on different ages, genders as well as trend analysis were also evaluated for VOC in Taiwan.

Results: Different trends were observed in years of life lost due to premature mortality (YLLs) or YLD for various age or gender categories. Disease severity at critical stage had the highest percentage for overall YLDs encompassed from 2020 to 2022. Also, critical-grade cases were found to be predominantly caused by Wild-type, Alpha, and Omicron variants in 2020, 2021, and 2022, respectively.

Conclusion: Precautionary measures are also suggested for policy makers to take in specific seasons, age or gender groups based on YLL and YLD analyses.

1. Introduction

As of September 7, 2023, Taiwan has been grappling with the pandemic, recording 10,241,523 confirmed COVID-19 cases and 17,668 reported deaths (https://covid-19.nchc.org.tw/) [1]. To address the challenges posed by the COVID-19 pandemic, the Central Epidemic Command Center (CECC) in Taiwan has implemented a range of public health interventions, including non-pharmaceutical measures such as border control, case identification, quarantine of suspected cases, and public education, as well as pharmaceutical measures like vaccines [2]. However, the highly variability of the COVID-19 virus substantially impacted the efficacy of existing pandemic prevention and control strategies. Additionally, the severity of illness among confirmed patients varied significantly across different viral variants [3].

To estimate the impact of the diseases on individual's time, ability, or activities, the disability-adjusted life years (DALYs)

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parameter was used, considering both disability and death [4]. Recent studies across different countries have focused on evaluating the disease burden and direct impacts of COVID-19 on population health [5–7]. The key parameter for assessing DALYs was disability weight (*DW*), reflecting the severity of a disease on scale from 0 (representing good health) to 1 (symbolizing death). Disease severity was categorized into four distinct levels following the guidelines provided by the World Health Organization (WHO) as outlined in the Living Guidance for Clinical Management of COVID-19 (https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2) [8].

Considering the unique challenges posed by this emerging infectious diseases, several studies have explored the quantifications of *DW* for COVID-19. Wyper et al. [9] used a systematic approach by giving weights according to different severity grades based on studies of European Disability Weights and Global Burden of Disease (GBD) 2019 [10]. Similarly, Cuschieri et al. [7] applied the *DWs* of Wyper et al. [9] to assess COVID-19 DALYs in the Malita population from March 2020 to March 2021. Besides, many studies considered the health state of confirmed cases of COVID-19 to different grades of mild/moderate, severe, and critical status. The severity-specific *DWs* were also implicated in Denmark [5], and Scotland [6].

This study lies in the comprehensive assessment of the societal burden of COVID-19 using DALYs, its focus on variant-specific contributions, age/gender-specific outcomes, and its identification of influential epidemiological parameters. These aspects advance our understanding of the pandemic and may inform more targeted and effective public health responses. The benefits to society include (1) more informed policy-making. It empowers authorities to tailor interventions more effectively to the population's needs, potentially reducing the impact of the pandemic on society. (2) variant-specific contributions. It can inform vaccination

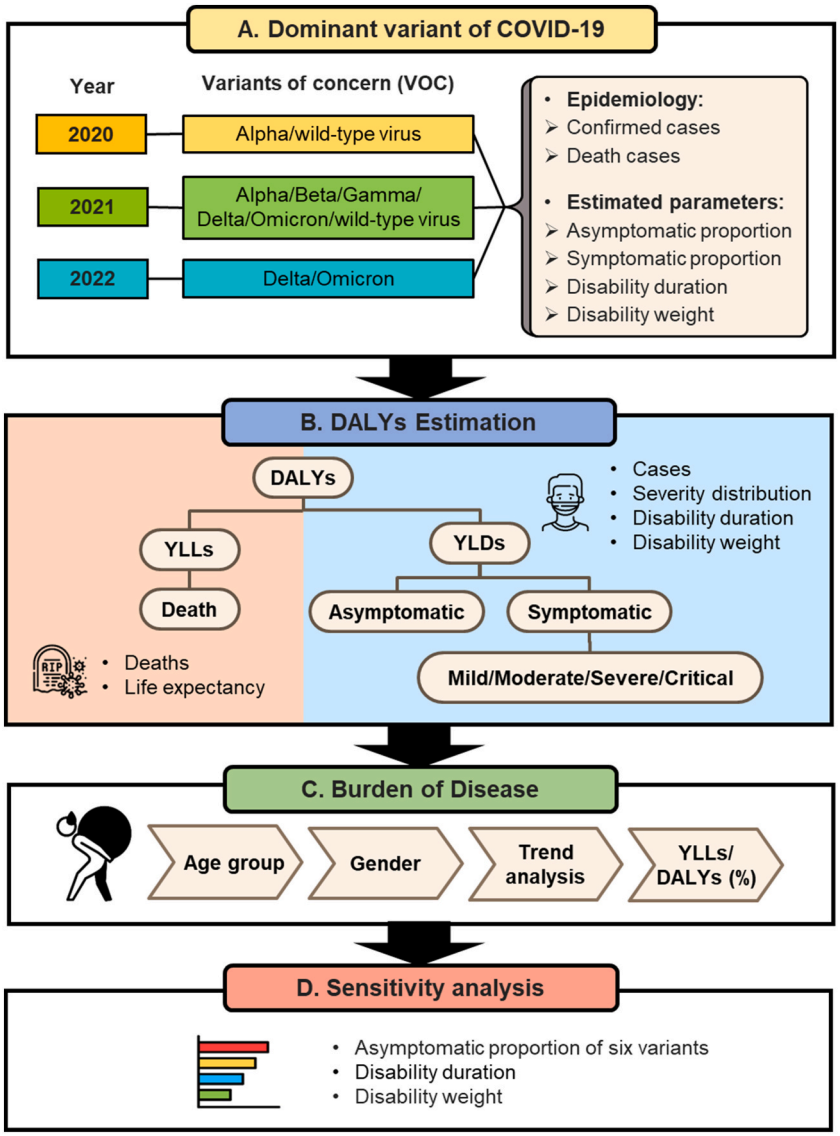

Fig. 1. Research flow chart.

strategies, public health messaging, and resource allocation to target specific variants more effectively. (3) age/gender-specific analysis. This knowledge can guide the allocation of resources and interventions to those most in need, potentially reducing health disparities and improving outcomes for vulnerable groups. In conclusion, all of these contribute to mitigating the impact of the COVID-19 pandemic and promoting the well-being of the population in Taiwan.

Hence, this study used DALYs to assess COVID-19's disease burden across variants, sexes, and ages from January 2020 to December 2022 in Taiwan. It aims to guide governmental agencies in forming effective strategies for future disease control. The objectives of this study are three folds: (i) analyze trends of YLL/YLD from 2020 to 2022, (ii) investigate variant-specific contributions to overall YLDs, (iii) assess age or gender-specific DALYs during COVID-19 pandemic in Taiwan, and (iv) finding the most influential epidemiological parameter contributing to overall DALYs.

2. Materials and methods

2.1. Study framework

Fig. 1 presents the research flowchart illustrating the framework used in this study. Data encompassing confirmed COVID-19 cases and associated fatalities in Taiwan from 2020 to 2022 were collected (Fig. 1A). The proportions of disease severity among distinct circulating variants, including asymptomatic cases, mild and moderate cases, severe cases, as well as critical cases, were determined. This estimation was achieved by combining the confirmed case count with the relevant proportions of disease severity for each dominant variant of COVID-19. Moreover, this study quantified the annual burden of COVID-19 disease in Taiwan under the influence of the different variants using DALYs (Fig. 1B). This approach facilitated exploration of pandemic trends associated with different variants, an examination of years of life lost across age groups and genders, and an assessment of the contribution of premature deaths to the overall disease burden (Fig. 1C). Lastly, a sensitivity analysis was conducted on three key parameters: the proportion of asymptomatic cases, period of disability, and disability weight. This step aimed to clarify the extent of the impact stemming from uncertainties associated with these parameters on the overall disease burden (Fig. 1D).

2.2. Burden of disease (DALYs)

To calculate DALYs for confirmed and death cases of COVID-19 in Taiwan from January 2020 to December 2022, the following formula were employed. The years of life lost due to premature mortality (YLLs) and the years of healthy life lost due to disability (YLDs) were computed independently and then combined in a single summary measure (Eq. (1)).

$$DALYs = YLDs + YLLs, \tag{1}$$

YLDs were calculated by multiplying the number of new cases with the average duration of the disability and disability weightings corresponding to disease stages (Eq. (2)).

$$YLDs = \sum_{x,y,t,v,s} I_{x,y,t} \times P_{v,t} \times S_v \times DW_s \times L_{1,s}, \tag{2}$$

where $I_{x,y,t}$ indicates sex-specific (x) and age-specific (y) number of confirmed cases of SARS-CoV-2 infection in each month (t) from 2020 to 2022. The age categories (y) were defined as 0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, and 70+ years. $P_{v,t}$ indicates the percentage of distinct variants (v) in each month (t), and S_v represent the level of severity associated with different variants (v); v covers six SARS-CoV-2 virus types (Wild-type, Alpha, Beta, Gamma, Delta, Omicron), DW_s represents the disease severity-specific (s) disability weight. $L_{1,s}$ represents the disease severity-specific (s) disability duration (year) and s represents four levels of disease severity (asymptomatic, mild and moderate, severe, critical).

YLLs were computed by multiplying the number of deaths within a specific age group by the standard life expectancy corresponding to that age group (Eq. (3)).

$$YLLs = \sum_{x,y,t} M_{x,y,t} \times L_{2x,y} \tag{3}$$

where $M_{x,y,t}$ represents sex-specific (x) and age-specific (y) number of deaths attributed to SARS-CoV-2 infection per month (t). $L_{2x,y}$ denotes the years of life lost due to premature death across different age groups and sex. These DALYs were then divided by the total population in 2020 and 2021 to calculate DALY estimates per 100,000 population in each year, aligning with the units utilized in the World Bank report [4,11].

2.3. Epidemiological data

This study compiled data on confirmed COVID-19 cases and related deaths from 2020 to 2022. The COVID-19 Global Pandemic Map was developed using epidemiological data released by the Centers for Disease Control (CDC), Ministry of Health and Welfare in Taiwan. Between 2020 and 2022, a cumulative total of 8,867,070 confirmed cases of COVID-19 were reported in Taiwan, comprising 799 cases in 2020, 16,250 cases in 2021, and 8,850,021 cases in 2022.

Fig. 2A shows the monthly progression of COVID-19 cases over three years. In 2020, the outbreak started with 283 cases in March. In 2022, there was another significant increase. Fig. 2B displays COVID-19 cases by age and gender over the same period. Women had

4,722,632 cases compared to men's 4,144,438. Except for younger age groups, women had more cases. Taiwan reported 15,297 COVID-19 deaths between 2020 and 2022. Deaths peaked at 14,440 in 2022. Fig. 2C details monthly COVID-19 deaths. June 2021 had the highest toll with 473 deaths. In April 2022, as cases surged, so did deaths. Fig. 2D presents COVID-19 deaths by age and gender. Male deaths surpassed females (8829 vs. 6468). Deaths increased with age, peaking in the 70+ group.

2.4. Disability weight (DW) and disability duration (L)

The disability weight (*DW*) and disability duration (L_1) by different disease severity of COVID-19 was shown in Appendix Table 1. The definition of asymptomatic cases was assigned a *DW* of 0 due to the absence of symptoms during the diagnostic period. The *DW* for mild/moderate disability and severe disability were adopted from the *DW* attributed to lower respiratory tract infection as defined by the Global Burden of Disease (GBD) 2019 study. Given that COVID-19 is an emerging infectious disease with no established specific *DW*, estimation was conducted using the *DW* of a disease with similar symptoms [10]. The *DW* was determined for critical illness based

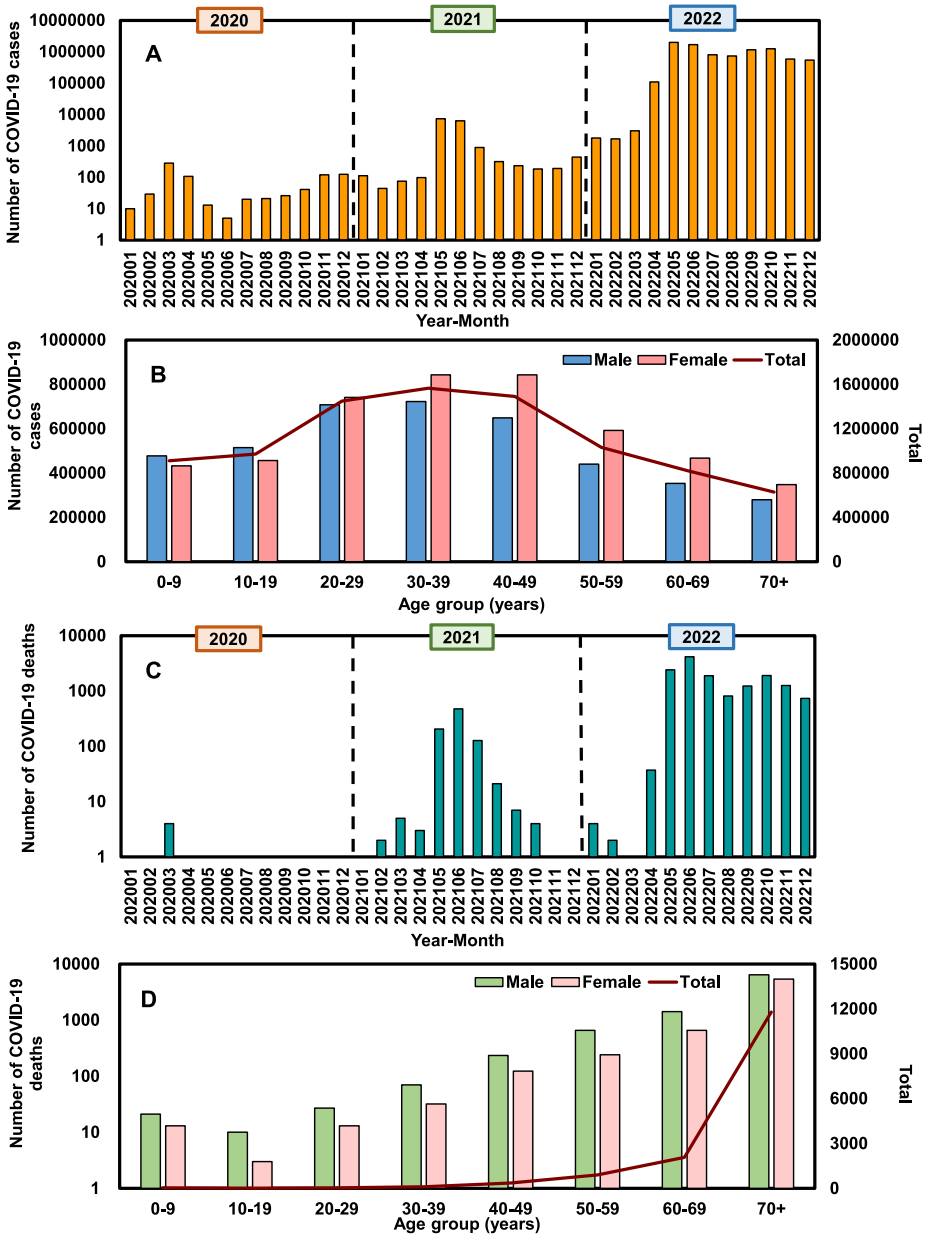

Fig. 2. (A) The number of confirmed COVID-19 cases per month, (B) The number of COVID-19 cases by sex and ages, (C) The number of confirmed death from COVID-19 per month, and (D) The number of confirmed death from COVID-19 by sex and ages from 2020 to 2022 in Taiwan.

Table 1
Distribution of disease severity for wild-type virus and five variants of SARS-CoV-2.

Severity distribution	Wild-type	Alpha	Beta	Gamma	Delta	Omicron
Asymptomatic (95 % CI)	15.6 %[a] (10.1–23 %)	27.6 %[b] (13.6–41.6 %)	27.6 %[b] (13.6–41.6 %)	27.6 %[b] (13.6–41.6 %)	8.4 %[c] (4.4–16.2 %)	25.5 %[c] (17–38.2 %)
Mild/Moderate[h]	42.5 %	39.2 %	50.8 %	50.3 %	58.1 %	45.1 %
Severe	13.6 %[d]	15.8 %[e]	19.3 %[f]	20 %[f]	9.4 %[g]	12.9 %[g]
Critical	28.3 %[d]	17.4 %[e]	2.3 %[f]	2.1 %[f]	24.1 %[g]	16.5 %[g]

[a] Adopted from Ref. [13].
[b] Adopted from Ref. [14].
[c] Adopted from Ref. [15].
[d] Adopted from Ref. [16].
[e] Adopted from Ref. [17].
[f] Adopted from Ref. [18].
[g] Adopted from Ref. [19].
[h] Estimated value.

on Haagsma et al. [12], which assessed the *DW* for 255 health states among 30,660 people from European countries. This evaluation included the estimated disability weight for intensive care unit admissions.

For mild and moderate patients, the L_1 was approximately two weeks. The assumed L_1 for asymptomatic patients was the same as for mild and moderate patients. The disability duration for severe and critical illnesses was 3–6 weeks. In this study, the L_1 was estimated as 21 days for severe disability and 32 days for critical illness (Appendix Table 1). We employed the 2020–2021 life table, where life expectancy varies based on the birth year (https://www.moi.gov.tw/cl.aspx?n=2948) [20]. In 2020, life expectancies for the age groups 30–39, 40–49, 50–59, 60–69, and 70+ were as follows: 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 (Appendix Table 2).

2.5. Dominant variation (P) and variant-based severity (S)

Appendix Fig. 1A illustrates the relative frequency of different variants over time in Taiwan. Data were extracted from the Global Initiative on Sharing All Influenza Data (GISAID) hCoV-19 Variants Dashboard (https://gisaid.org/hcov-19-variants-dashboard/) [21], which compiles genetic sequencing data to present temporal trends in variant frequencies (%). The primary circulating variants in Taiwan from 2020 to 2022 included Alpha, Gamma, Beta, Delta, Omicron, Variants of Interest (VOI), and others. Notably, the category of Omicron variants encompassed all Omicron subtypes (BA.1, BA.2, BA.3, BA.4, BA.5, and other sub-lineages) prevalent at the end of 2021 and throughout 2022 (Appendix Fig. 1B). As Taiwan's Centers for Disease Control and the Ministry of Health and Welfare did not publicly release dominant variant information, this study relied on GISAID data for monthly dominant variants within the country.

In this study, Variants of Interest (VOI) were excluded due to the inability to determine the specific VOI circulating in Taiwan and the challenges in collecting relevant data on severity. Furthermore, the Alpha variant was only detected in Taiwan in November and December of 2020. Therefore, for the remaining months covered in this study, it was assumed that the original SARS-CoV-2 virus strain (Wild-type) was in circulation. Hence, this study focused on six virus types: Wild-type, Beta, Alpha, Gamma, Delta, and Omicron.

Following the above description, we list the distribution of disease severity for the SARS-CoV-2 original virus strain (Wild-type) and five variants (Alpha, Gamma, Beta, Delta, Omicron), as reported in relevant literature (Table 1). Disease severity was classified into asymptomatic, mild/moderate, severe, and critical using the COVID-19 Clinical Progression Scale from the WHO. As local data on variant severity in Taiwan were lacking, percentages for the six variants were sourced internationally, prioritizing local case investigations and high-quality research evidence (Appendix Table 3).

2.6. Monte Carlo simulation

A sensitivity analysis using Monte Carlo (MC) simulations explored the impact of severity grade-specific DWs, illness durations, and asymptomatic case proportions across six virus variants. Two kinds of scenarios were adopted for sensitivity analyses of disease severity, which are based on evaluations from the first 100 laboratory-confirmed SARS-CoV-2 cases in Taiwan (Scenario one) and changes in dominant variants (Scenario two).

Parameters' uncertainties, including *DWs* (Appendix Table 1), disease duration (L_2) (Appendix Table 1) at different severities, and asymptomatic case proportions for the variants (Table 1), were measured and fitted into probability distributions using Crystal Ball software (Version 2000.2, Decisioneering Inc., Denver, CO, USA). To assess DALYs' uncertainty and variability, a Monte Carlo simulation with 100,000 iterations generated robust analysis, constructing a 95 % confidence interval. We employed a triangular distribution model to characterize the input parameters of *DWs* and the proportions of asymptomatic across various variants of SARS-CoV-2. Additionally, a uniform distribution model was assumed to represent the input parameter of L_2. Repeatedly sampling from these distributions illustrated the influence of each parameter on DALY estimation.

3. Results

3.1. Trends of YLLs and YLDs

In the early stages of the epidemic in Taiwan, the YLLs due to COVID-19 amounted to 10.15 per 100,000 population, with March recording the highest at 5.94. Males accounted for 83 % of total YLLs as well as females experienced 53 % of total YLDs (Appendix Fig. 2). With the escalation of the pandemic, the disease burden of YLLs significantly increased to 950 per 100,000 population in 2021, with the peak occurring in June. The elderly (70+ age group) contributed the highest disease burden. Males had 53 % of total YLDs, in comparison, females had 47 % (Appendix Fig. 3). In 2022, Taiwan experienced a severe epidemic outbreak, with YLLs rapidly rising to 15,415 per 100,000 population, peaking in June. Compared to 2021, the contribution by age group remained highest among the elderly, with males contributing a more significant burden than females (Appendix Fig. 4).

3.2. Variant-specific contributed percentage on overall YLDs

Fig. 3A demonstrates that YLDs varied based on COVID-19 severity from 2020 to 2022. Critical cases accounted for 89.5 % in 2020, 83.6 % in 2021, and 83.5 % in 2022. In that, asymptomatic cases were not included in the calculation due to their assigned disability weight of 0, resulting in no contribution to total YLDs. Fig. 3B depicts variant-specific contributions to overall YLDs. Critical cases from Wild-type and Alpha variants had significant impacts in 2020 and 2021. In 2022, the Omicron variant had the most influence, with 83.52 % attributed to critical cases and 8.70 % to severe cases.

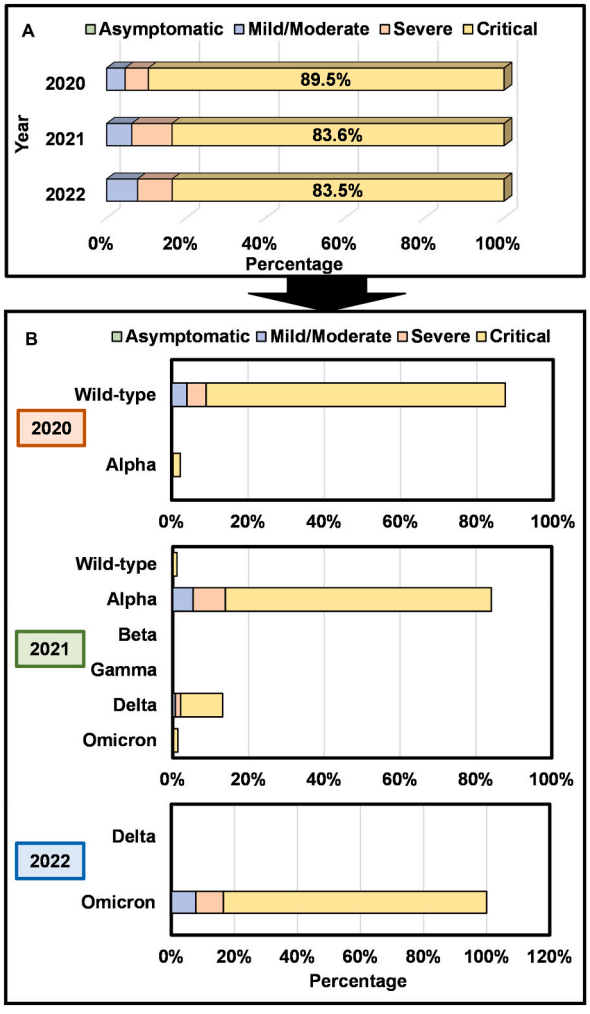

Fig. 3. Variant-specific contributed percentage on overall YLDs. (A) YLDs varied with disease severity across all pandemic variants from 2020 to 2022, and (B) variant-specific contributed percentages on YLDs in each pandemic year.

3.3. DALYs and YLLs/DALYs (%)

Appendix Fig. 5 shows the age/gender-specific total DALYs during the COVID-19 pandemic in Taiwan. COVID-19 resulted in 11.05, 963, and 22,102 DALYs per 100,000 population in 2020, 2021, and 2022, respectively (Appendix Fig. 5A, D, and 5G). The percentage of YLLs/DALYs was 92 %, 99 %, and 70 % each year, which might correspond to the higher transmission rates and lower severity of Omicron variants (Appendix Fig. 5B, E, and 5H). Over the past three years, males experienced a higher burden, totaling 8.84 DALYs per 100,000 population (80 % of total DALYs in 2020), 617 DALYs per 100,000 population (64 % of total DALYs in 2021), and 12,160 DALYs per 100,000 population (55 % of total DALYs in 2022). The age group of 40–49 (in 2020) and the 70+ age group (in 2021 and 2022) had the highest DALYs (Appendix Fig. 5C, F, and 5I).

3.4. Sensitivity analysis

From January 2020 to December 2022, COVID-19 resulted in 23,075 DALYs per 100,000 population in Taiwan, with YLLs constituting 71 % of the total DALYs. Males had 12,786 DALYs compared to females' 10,289 DALYs per 100,000 population. The burden increased with age, notably the 70+ group contributing 50 % of the burden (Appendix Tables 4–6).

By assuming the probability distributions of *DWs*, durations of disease (L_1), and the proportions of asymptomatic in different variants of SARS-CoV-2, the YLLs, YLDs, and DALYs (median (95 % confidence interval (CI)) were then generated (Appendix Tables 4–6). In 2021, YLDs peaked in the 60–69 age group. In 2022, cases surged, with peak YLDs in the 10–19 and 20–29 age groups. The 2022 overall YLDs range was 6922 (5056–8929), resulting in 22,335 DALYs (20,469–24,342) per 100,000 population (Appendix Table 6). Sensitivity analysis revealed that disease duration (L_2) was most influential in DALY estimations across the years, especially in critical states of different virus strains (Appendix Fig. 6).

4. Discussion

This study aims to highlight dominant COVID-19 variants in Taiwan based on disease burden indicators. Since knowledge in variant-specific contributions in DALYs during pandemic is limited, it is worthwhile to investigate the variant-specific contribution by observing the YLLs, YLDs, and DALY and the policy enforcement during the pandemic occurrence in Taiwan. Overall, 23,075 DALYs per 100,000 population were lost from January 2020 to December 2022, with YLLs contributing 71 % of the total DALYs. We observe that the disease burden of COVID-19 differs by sex, where the male population experiencing a higher proportion of DALYs (55 % (12,786 DALYs per 100,000 population) compared to the female population at 45 % (10,289 DALYs per 100,000 population)). The COVID-19 disease burden increased with age, among which the 70+ age group contributed 50 % of the overall COVID-19 disease burden (11,463 DALYs per 100,000 population) (Appendix Tables 4–6).

This study observed higher estimates of YLLs in the male population compared to females. In accordance with the trends in Taiwan, a systematic review and meta-analysis indicated a higher prevalence of confirmed COVID-19 cases in males (55.00 (51.43−56.58)) compared to females (45.00 (41.42−48.57)) [22]. Numerous studies have highlighted sex or gender differences in incidences, responses, and outcomes of COVID-19 patients. Biological factors such as hormonal, immune, and inflammatory responses play critical roles in mediating immunology or disease severity in COVID-19 patients [23]. Takahashi et al. [24] reported that females had more robust COVID-19 disease progression-associated CD8 T cell activations, while Zeng et al. [25] found that females produce more early-phase neutralizing antibodies in COVID-19. Additionally, gender differences in behaviors, such as higher prevalence of high-risk habits like alcohol and smoking among males, impact infection risks and severity [22,26].

The severity of COVID-19 has changed through the worldwide epidemic waves and the variants associated with increased transmissibility have rapidly expanded to become dominant worldwide. In this study, we estimate the disparity burden via the proportion of disease severity. Scenario one used the severity distribution from the first 100 laboratory-confirmed SARS-CoV-2 cases in Taiwan, as reported by Tsou et al. [27]. It assumed a disease severity distribution of 20 % asymptomatic, 41 % mild, 20 % moderate, 14 % severe, and 5 % critical cases without considering the variants at that time. The burden was estimated as 18,988 DALYs per 100,000 population. Conversely, Scenario two considered the effects of variant-based severity (*S*), showing the result of 23,075 DALYs per 100,000 population (Appendix Fig. 7). It became evident that neglecting to consider the varying disease severity among dominant variants may significantly underestimate of the COVID-19 disease burden by at least 4087 DALYs per 100,000 population.

The disability weight (*DW*) was estimated based on the weight of diseases with similar symptoms, utilizing parameters from GBD 2019 for lower respiratory tract infections and the European study conducted by Haagsma et al. [12]. We chose this parameter due to the lack of relevant Taiwan data. Disability duration was assumed from the WHO report on the pandemic's early stage in China. For YLD estimations, we applied the European DWs-based WHO severity grades [9].

Sensitivity analyses showed that disease duration (L_1) in critical state had the most significant impact on overall DALYs in Taiwan. This suggests that controlling disease duration, especially in critical cases, could be a potential strategy to reduce DALYs through advanced medications or personal care. On the other hand, the studies related to the severity of COVID-19 infection in Taiwan had small sample sizes (fewer than 100 confirmed cases), and most of the research was conducted during the early stages of the pandemic. Consequently, estimating disease severity variations among different variants over the three-year pandemic proved challenging. This study conducted a thorough literature review, prioritizing high-quality research evidence, and referenced international literature to determine the proportions of disease severity for the six virus variants.

Moreover, as there is insufficient information on the long-term sequelae of the disease, this factor was not incorporated into the DALY calculations. This implies that the actual DALYs might be underestimated without accounting for this factor. The common

sequelae and disease duration may vary among diagnosed patients of different races, genders, and ages [28]. Instead, three studies assumed that 13.3 % of confirmed cases will have sequelae and still for 28 days [6,7]. Hence, it posed a challenge to predict the effects of sequelae without available information. Supposing comprehensive clinical literature or available data related to the sequelae of confirmed cases in Taiwan would become available in the future. In that case, a better understanding of the impact of sequelae on the burden of COVID-19 in Taiwan can be achieved.

5. Conclusions

In conclusion, this study sheds light on the significant burden of COVID-19 in Taiwan, quantifying it at 23,075 DALYs per 100,000 population over three years. Gender disparities were evident, with men bearing 55 % of the burden. Individuals aged 70 and above were most affected, representing 50 % of the total burden. The study's sensitivity analysis highlighted the critical role of disability duration in severe cases across primary virus variants. Overall, this research underscores the importance of utilizing DALYs to comprehensively assess the impact of COVID-19, considering variant-specific and severity-specific factors.

Ethical approval

No ethical approval was obtained because the data included in this study were publicly available.

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Data availability statement

The datasets used in this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Hsin-Chieh Tsai: Writing – original draft, Validation, Methodology, Data curation. **Ying-Fei Yang:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Cheng-Chieh Hsieh:** Writing – original draft, Methodology, Data curation. **Si-Yu Chen:** Writing – review & editing, Methodology, Data curation. **Szu-Chieh Chen:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e29868.

References

[1] National Center for High-performance Computing, COVID-19 global pandemic map. https://covid-19.nchc.org.tw/dt_005-covidTable_taiwan.php, 2023. (Accessed 1 March 2023).
[2] C.J. Wang, C.Y. Ng, R.H. Brook, Response to COVID-19 in Taiwan: big data analytics, new technology, and proactive testing, JAMA 323 (14) (2020) 1341–1342, https://doi.org/10.1001/jama.2020.3151.
[3] R. Hoteit, H.M. Yassine, Biological properties of SARS-CoV-2 variants: epidemiological impact and clinical consequences, Vaccines 10 (6) (2022) 919, https://doi.org/10.3390/vaccines10060919.
[4] C.J. Murray, Quantifying the burden of disease: the technical basis for disability-adjusted life years, Bull. World Health Organ. 72 (3) (1994) 429–445.
[5] S.M. Pires, H.G. Redondo, L. Espenhain, L.S. Jakobsen, R. Legarth, M. Meaidi, et al., Disability adjusted life years associated with COVID-19 in Denmark in the first year of the pandemic, BMC Publ. Health 22 (1) (2022) 1315, https://doi.org/10.1186/s12889-022-13694-9.
[6] G.M.A. Wyper, E. Fletcher, I. Grant, G. McCartney, C. Fischbacher, O. Harding, et al., Measuring disability-adjusted life years (DALYs) due to COVID-19 in Scotland, 2020, Arch. Publ. Health 80 (1) (2022) 105, https://doi.org/10.1186/s13690-022-00862-x.

[7] S. Cuschieri, N. Calleja, B. Devleesschauwer, G.M.A. Wyper, Estimating the direct Covid-19 disability-adjusted life years impact on the Malta population for the first full year, BMC Publ. Health 21 (1) (2021) 1827, https://doi.org/10.1186/s12889-021-11893-4.
[8] World Health Organization (WHO), Living guidance for clinical management of COVID-19. https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2, 2021. (Accessed 1 March 2023).
[9] G.M.A. Wyper, R.M.A. Assunção, E. Colzani, I. Grant, J.A. Haagsma, G. Lagerweij, et al., Burden of disease methods: a guide to calculate COVID-19 disability-adjusted life years, Int. J. Publ. Health 66 (2021) 619011, https://doi.org/10.3389/ijph.2021.619011.
[10] GBD 2019 Diseases and Injuries Collaborators, Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019, Lancet 396 (10258) (2020) 1204–1222, https://doi.org/10.1016/S0140-6736(20)30925-9.
[11] World Bank, World Development Report, 1993: Investing in Health, Oxford University Press, New York, 1993.
[12] J.A. Haagsma, C. Maertens de Noordhout, S. Polinder, T. Vos, A.H. Havelaar, A. Cassini, et al., Assessing disability weights based on the responses of 30,660 people from four European countries, Popul. Health Metrics 13 (2015) 10, https://doi.org/10.1186/s12963-015-0042-4.
[13] J.J. He, Y.F. Guo, R.C. Mao, J.M. Zhang, Proportion of asymptomatic coronavirus disease 2019: a systematic review and meta-analysis, J. Med. Virol. 93 (2) (2021) 820–830, https://doi.org/10.1002/jmv.26326.
[14] Q. Ma, J. Liu, Q. Liu, L. Kang, R. Liu, W. Jing, et al., Global percentage of asymptomatic SARS-CoV-2 infections among the tested population and individuals with confirmed COVID-19 diagnosis: a systematic review and meta-analysis, JAMA Netw. Open 4 (12) (2021) e2137257, https://doi.org/10.1001/jamanetworkopen.2021.37257.
[15] W.E. Yu, Y.F. Guo, S.Y. Zhang, Y.D. Kong, Z.L. Shen, J.M. Zhang, Proportion of asymptomatic infection and nonsevere disease caused by SARS-CoV-2 omicron variant: a systematic review and analysis, J. Med. Virol. 94 (12) (2022) 5790–5801, https://doi.org/10.1002/jmv.28066.
[16] E. Tan, J. Song, A.M. Deane, M.P. Plummer, Global impact of coronavirus disease 2019 infection requiring admission to the ICU: a systematic review and meta-analysis, Chest 159 (2) (2021) 524–536, https://doi.org/10.1016/j.chest.2020.10.014.
[17] A.C. Huang, S.M. Lin, T.H. Chiu, K.W. Chang, T.H. Huang, T.H. Yang, et al., Comparison of clinical characteristics and outcomes of hospitalized patients infected with the D614G strain or alpha variant of COVID-19 in Taiwan: a multi-center cohort study, Int. J. Med. Sci. 19 (13) (2022) 1912–1919, https://doi.org/10.7150/ijms.76725.
[18] T. Funk, A. Pharris, G. Spiteri, N. Bundle, A. Melidou, M. Carr, et al., Characteristics of SARS-CoV-2 variants of concern B.1.1.7, B.1.351 or P.1: data from seven EU/EEA countries, weeks 38/2020 to 10/2021, Euro Surveill. 26 (16) (2021) 2100348, https://doi.org/10.2807/1560-7917.ES.2021.26.16.2100348.
[19] A.D. Iuliano, J.M. Brunkard, T.K. Boehmer, E. Peterson, S. Adjei, A.M. Binder, et al., Trends in disease severity and health care utilization during the early omicron variant period compared with previous SARS-CoV-2 high transmission periods - United States, December 2020-January 2022, MMWR Morb. Mortal. Wkly. Rep. 71 (4) (2022) 146–152, https://doi.org/10.15585/mmwr.mm7104e4.
[20] Ministry of the Interior Republic of China (Taiwan), Abridged Life Table in Republic of China Area, 2023. https://www.moi.gov.tw/cl.aspx?n=2948. (Accessed 1 March 2023).
[21] Global initiative on sharing all Influenza data (GISAID). hCoV-19 variants dashboard. https://gisaid.org/hcov-19-variants-dashboard/, 2023. (Accessed 1 March 2023).
[22] B.B. Abate, A.M. Kassie, M.W. Kassaw, T.G. Aragie, S.A. Masresha, Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis, BMJ Open 10 (10) (2020) e040129, https://doi.org/10.1136/bmjopen-2020-040129.
[23] T. Hampton, Insight on sex-based immunity differences, with COVID-19 implications, JAMA 324 (13) (2020) 1274, https://doi.org/10.1001/jama.2020.17378.
[24] T. Takahashi, M.K. Ellingson, P. Wong, B. Israelow, C. Lucas, J. Klein, et al., Sex differences in immune responses that underlie COVID-19 disease outcomes, Nature 588 (7837) (2020) 315–320, https://doi.org/10.1038/s41586-020-2700-3.
[25] F. Zeng, C. Dai, P. Cai, J. Wang, L. Xu, J. Li, A comparison study of SARS-CoV-2 IgG antibody between male and female COVID-19 patients: a possible reason underlying different outcome between sex, J. Med. Virol. 92 (10) (2020) 2050–2054, https://doi.org/10.1002/jmv.25989.
[26] T. Takahashi, A. Iwasaki, Sex differences in immune responses, Science 371 (6527) (2021) 347–348, https://doi.org/10.1126/science.abe7199.
[27] T.P. Tsou, W.C. Chen, A.S. Huang, S.C. Chang, Taiwan COVID-19 Outbreak Investigation Team, Epidemiology of the first 100 cases of COVID-19 in Taiwan and its implications on outbreak control, J. Formos. Med. Assoc. 119 (11) (2020) 1601–1607, https://doi.org/10.1016/j.jfma.2020.07.015.
[28] D. Khullar, Y. Zhang, C. Zang, Z. Xu, F. Wang, M.G. Weiner, et al., Racial/ethnic disparities in post-acute sequelae of SARS-CoV-2 infection in New York: an EHR-based cohort study from the RECOVER program, J. Gen. Intern. Med. 38 (5) (2023) 1127–1136, https://doi.org/10.1007/s11606-022-07997-1.