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Estimating the Quality-Adjusted Life-Year Loss due to Fatal and Nonfatal COVID-19 Outcomes across US States and Counties, July 2020 to December 2022

Fatima Mikdashi[1], Rachel E. Murray-Watson[1], Rafael Lopes[2,3], Alyssa Bilinski[4], and Reza Yaesoubi[1]

Abstract

Objective: The population-level quality-of-life impact of nonfatal health outcomes, including prolonged hospitalizations and long COVID, remains poorly understood. In this study, we estimate the cumulative quality-adjusted life-year (QALY) loss attributable to fatal and nonfatal COVID-19 outcomes in the United States and compare that burden with that of other diseases.

Methods: We developed a probabilistic model that accounts for the loss in population health due to COVID-19 symptoms, hospitalizations, long COVID, and deaths. The model was applied to weekly county-level data from July 2020 to December 2022. We used appropriate probability distributions to describe uncertainty in parameter values and used 1,000 repeated samples from these distributions to estimate the expected QALY loss and the 95% uncertainty interval (UI).

Results: We estimate the cumulative QALY loss as 9,242,000 (95% UI: 7,808,000–11,311,000) life-years. Following deaths, long COVID was the second most significant contributor to QALY loss, with an estimated annual QALY loss of approximately 865,000 (95% UI: 355,000–1,591,000). This burden is comparable to the total annual disability-adjusted life-years (DALYs) associated with liver cancer: 581,000 DALYs (95% UI: 549,000–607,000). Although symptomatic infections contributed less to overall QALY loss, their burden was comparable to that of HIV/AIDS (377,000 DALYs, 95% UI: 309,000–465,000).

Conclusion: The quality-of-life burden of nonfatal COVID-19 outcomes, particularly long COVID, is on the same scale as that of major chronic and infectious diseases. As COVID-19 mortality declines and the pandemic transitions to an endemic phase, it is essential to recognize and address the long-term effects of nonfatal outcomes as public health priorities.

Keywords

quality-adjusted life-years (QALYs), long COVID, health burden

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[1]Department of Health Policy and Management, Yale School of Public Health, New Haven, CT, USA
[2]Public Health Modeling Unit, Yale School of Public Health, New Haven, CT, USA
[3]Department of Epidemiology and Microbial Diseases, Yale School of Public Health, New Haven, CT, USA
[4]Department of Health Services, Policy and Practice, Brown University School of Public Health, Providence, RI, USA

Current affiliation: Rachel E. Murray-Watson is now affiliated to Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London, UK. Reza Yaesoubi is now affiliated to Philip R. Lee Institute for Health Policy Studies, University of California San Francisco, San Francisco, CA, USA; Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, USA.

Corresponding Author:
Fatima Mikdashi, Department of Health Policy and Management, Yale School of Public Health, 350 George Street, New Haven, CT 06510, USA.
Email: Fatima.mikdashi@yale.edu

Highlights

- This study provides comprehensive estimates of QALY loss due to COVID-19 in the United States between July 2020 and December 2022, capturing geographic and temporal variation while accounting for a range of fatal and nonfatal health outcomes.
- COVID-19 burden varied substantially across states and counties, with a nearly 3-fold difference in QALY loss per 100,000 population between the highest- and lowest-burden states.
- Long COVID was the second-largest contributor to COVID-19–related QALY loss, generating an annual health burden comparable to that of major diseases such as liver cancer and cardiomyopathy/myocarditis in the United States.

Introduction

The COVID-19 pandemic caused unprecedented health, social, and economic consequences worldwide, with the United States reporting the highest cumulative number of cases and deaths globally.[1] While previous studies have extensively documented the staggering excess mortality and geographic variation in incidence and adverse health outcomes, the population-wide effect of nonfatal health states on quality of life remains poorly understood.[2–5] Many individuals survived infection but experienced prolonged hospitalizations, lingering symptoms associated with long COVID, as well as other nonfatal physical or mental impairments.

Despite growing recognition of the impact of long COVID and other postacute sequelae, the magnitude and distribution of the quality-of-life burdens associated with these nonfatal outcomes remain inadequately characterized.[6–8] Without accounting for morbidity in addition to mortality, estimates of disease burden risk substantially understate the true population-level impact of the pandemic. This gap limits our ability to compare the full spectrum of the pandemic's effect on quality of life across regions and populations or to evaluate the potential benefits of different health interventions.

To address this gap, we use quality-adjusted life-years (QALYs) to estimate the population health loss associated with COVID-19 in the United States. QALY is a composite measure that can synthesize morbidity and mortality to comprehensively estimate population health loss. QALYs enable the comparison of disease burden across different populations and across other diseases and are routinely used in economic evaluations.[9]

As mortality rates decline, it has become increasingly important to assess the relative burden of COVID-19's nonfatal outcomes compared with other endemic diseases, such as seasonal influenza. Furthermore, by quantifying the QALY loss attributable to COVID-19, this study offers a more nuanced understanding of the pandemic's health impact across different regions and time periods in the United States by identifying regional disparities and contextualizing the overall disease burden.

Methods

To estimate the loss in the population QALY, we used data on the number of weekly estimated COVID-19 infections and reported cases, hospital admissions, intensive care unit (ICU) occupancy, and deaths by US counties between July 15, 2020, and December 28, 2022. We limited our analysis to this period because of data availability.[10]

Data Sources

The primary database used in this study was previously compiled, harmonized, and published by Bilinski et al.[11] This database consists of a county-level, weekly panel of reported COVID-19 cases, deaths, hospital admissions, and ICU occupancy in the United States. It integrates multiple public health surveillance data streams, including reported COVID-19 cases and deaths from state and local health agencies, centrally archived by *The New York Times*, and hospital admissions and ICU occupancy reported by hospitals to the US Department of Health and Human Services Unified Hospital Data Surveillance System.[12,13] Bilinski et al harmonized these sources, computed weekly outcomes, and validated internal consistency across data streams prior to publication. In addition to this database, we also use model-based estimates of total SARS-CoV-2 infections, including both detected and undetected infections, generated using the covidestim package. This "Bayesian evidence synthesis model explicitly accounts for reporting delays and secular variation in case ascertainment to generate estimates of incident COVID-19 infections" on the basis of COVID-19 transmission, natural history, and estimated historic exposure and immunity.[14,15] Model outputs were reported as weekly state-level estimates of incident infections represented as posterior probability distributions implied by their reported Bayesian credible intervals (2.5%, 25%, 50%, 75% and 97.5%).

All datasets and analytical code used in this study are publicly available in a GitHub repository, which includes detailed documentation of data sources, preprocessing steps, and model implementation.

Data Definitions

The reported case data include both confirmed and probable cases. Confirmed cases correspond to individuals whose SARS-CoV-2 infection was verified by a laboratory-based test and reported by a federal, state, territorial, or local public health agency. Probable cases are individuals who were evaluated using clinical criteria and using epidemiologic evidence but who did not receive confirmatory testing.[12]

The death data include both confirmed and probable deaths. COVID-19 deaths include individuals with a laboratory-confirmed SARS-CoV-2 infection for whom COVID-19 was listed as a cause of death on the death certificate. State health departments confirmed deaths by cross-referencing laboratory-confirmed COVID-19 case surveillance records with death certificate data and excluding deaths clearly attributable to non–COVID-19 causes (eg, homicide, suicide, accidents, or drug overdose). Deaths in which COVID-19 co-occurred with other medical conditions (eg, stroke or cancer) were included only if COVID-19 was listed as a cause of death. Probable COVID-19 deaths include individuals for whom COVID-19 was listed as the cause of death on the death certificate but for whom no laboratory-confirmed SARS-CoV-2 test result could be linked in disease surveillance records.[12]

Hospital admissions data consisting of patients admitted to inpatient beds with confirmed COVID-19 and ICU occupancy data consisting of the average number of patients currently hospitalized in designated adult ICU beds with confirmed COVID-19 were obtained from US Department of Health and Human Services (Unified Hospital Data Surveillance System) databases.[16] These data were reported by health service area, which consists of 1 or more contiguous counties with self-contained hospital care. To approximate county-level hospitalization, we divided the health service area hospitalization data proportionally by the population size of the included counties.

Estimation of Total Infections

Total infections, unlike reported cases, are not directly observable at the population level. In addition, county-level estimates of incident infections from the covidestim were not available for the full study period. To generate county-level total infection estimates for the entirety of the period considered while avoiding double counting, we relied on both model-based state-level infection estimates and county-level reported case data. Specifically, we drew weekly state-level infections realizations from the posterior distribution of the covidestim model. For each week-state, we computed an infection-to-case scaling factor and applied this factor to the corresponding county-level reported case data within the same state, producing weekly county-level infection estimates.

The weekly number of reported cases, hospital admissions, and deaths and their geographic variation are presented in the Supplementary Materials (Figure S1–3).

Model

To estimate the QALY loss due to COVID-19, we developed a probabilistic model that assume that QALY losses arise from several health states: COVID-19–related symptoms, hospitalizations, deaths, and physical and mental impairments associated with long COVID. The model is structured around 3 key components: 1) the probability that an individual enters the state (eg, an infection becoming symptomatic), 2) the average duration spent in the state, and 3) the average reduction in quality of life while in that state.[17,18] Hence, we used the following formula to estimate the QALY loss during week t:

$$Q_t = C_t p_s l_S q_S + [H_t(1-P)l_{H1} + H_t P l_{H2}]q_H + I_t \Delta t q_I + \Sigma_a D_t \pi_a w_a + \mathscr{L}_t$$

The first term calculates the QALY loss due to symptomatic infections, where C_t is the estimated number of infections during week t (accounting for both detected and undetected infections). We assume that a proportion p_S of the infections became symptomatic and that symptomatic cases experienced, on average, a reduction of q_S in their quality of life for the duration of l_S years.

The second and third terms calculate the QALY loss due to hospital admissions during week t (H_t). We assume that a portion of hospitalized patients (P) required ICU care, while the remaining patients ($1 - P$) received only general ward care. Among patients who received ICU care, we assume that their hospital stay included both time in the ICU and in the general ward, with their average ward length of stay of l_{H2}. In contrast, patients who did not require ICU care spent an average duration l_{H1} in the ward. The reduction in the quality of life in the ICU q_I is assumed to be greater than the reduction in quality of life in the ward q_H. However, we assume that the quality-of-life reduction experienced during ward care q_H is the same for all patients, regardless of whether they also received ICU care.

The fourth term calculates QALY loss due to patients receiving care in the ICU during week t (I_t). We assume that patients who needed ICU care experienced, on average, a reduction of q_I in their quality of life. Since our dataset provided the weekly number of ICU occupancy (as opposed to the weekly number of ICU admissions), we multiplied $I_t q_I$ by $\Delta t = 1/52$ to estimate the loss in QALY due to ICU occupancy during week t.

The fifth term calculates the QALY loss due to deaths during week t (D_t), accounting for age-adjusted life expectancy, with π_a representing the probability that a death belongs to age group a and w_a representing the discounted QALY loss associated with a premature death by age group a.

The last term calculates the QALY loss due to long COVID during week t ($\mathscr{L}_t$). Below, we describe the method used to estimate this term.

Estimating QALY Loss due to Long COVID

Although uncertainty remains regarding how long COVID is defined and diagnosed, we base our definition on the working framework established by the National Academies of Sciences, Engineering, and Medicine (NASEM).[19] Under this definition, long COVID may occur following SARS-CoV-2 infection and does not require laboratory confirmation of the initial infection. It is characterized by a range of symptoms that prior studies have organized into 3 primary clusters (fatigue, cognitive impairment, and respiratory symptoms) and requires symptom persistence for at least 3 mo following acute infection.[20]

Consistent with this definition, we operationalize long COVID incidence as the presence of at least 1 persistent symptom cluster among individuals who survive a symptomatic acute SARS-CoV-2 infection. This definition reflects postacute symptom persistence rather than a formal clinical diagnosis.

The incidence of long COVID is modeled probabilistically among survivors of symptomatic infection. Because emerging evidence suggests that the risk and duration of long COVID may vary by acute disease severity, we developed 2 approaches to estimate QALY loss associated with long COVID (term $\mathscr{L}_t$ in the above formula).[21,22]

In the first simplified approach, we assume that any survivor of an acute symptomatic infection has a probability (s) of developing postacute COVID sequelae or long COVID symptoms and that they experienced an average reduction (q_L) in their quality of life that lasted (l_L) years. Hence, if v is the probability of surviving a symptomatic acute phase of infection, the QALY loss due to long COVID during week t can be estimated as

$$\mathscr{L}_t = C_t p_s s v l_L q_L \quad (1)$$

In the second health state–dependent approach, we allow the risk of developing long COVID and the timeline for the resolution of long COVID symptoms to vary by the severity of the acute phase of disease.[19,20,23–25] To this end, we considered 3 disease states: symptomatic infections that did not lead to hospitalization (denoted by H'), hospitalized cases that did not receive ICU care (denoted by H), and hospitalized cases that lead to admission to ICU (denoted by I). For each of these states, we denote the probability of surviving with $(v_{H'}, v_H, v_I)$, the probability of developing long COVID with $(s_{H'}, s_H, s_I)$, and the average duration of long COVID with $(L_{H'}, L_H, L_I)$. For all states, we assume that the average reduction in the quality of life is the same and equal to q_L. Hence, the loss in QALYs due to long COVID for symptomatic infections that did not lead to hospitalization is on average $v_{H'} s_{H'} L_{H'} q_L$, for hospitalized cases that did not receive ICU care is $v_H s_H L_H q_L$, and for hospitalized cases that lead to admission to ICU is $v_I s_I L_I q_L$.

Therefore, for a week with reported number of symptomatic infections $C_t p_s$ and hospital admissions H_t, the loss in QALYs due to long COVID can be estimated as

$$\mathscr{L}_t = \Big(C_t p_s (1-h) v_{H'} s_{H'} L_{H'} + H_t (1-P) v_H s_H L_H + H_t P v_I s_I L_I \Big) q_L$$

where h is the probability of getting hospitalized for an average symptomatic reported case.

Given the overlap of long COVID symptoms with those of myalgia encephalomyelitis/chronic fatigue syndrome (ME/CFS), we assume that the average reduction in the quality of life while presenting long COVID (ie, q_L) is that of CFS.[19,21,26]

We acknowledge that long COVID exhibits substantial heterogeneity in symptom severity. However, severity-specific utility weights remain poorly characterized. As such, we apply an average disutility parameter, q_L,within a probabilistic modeling framework that incorporates parameter uncertainty rather than relying on a single deterministic estimate.

To calculate Q_t, we used the data on number of infections, hospital admissions, occupied ICU beds, and deaths from the sources described above. The remaining parameters were derived from a variety of sources as described in Tables 1 and 2. The selection of sources was guided by several key principles aimed at ensuring the relevance, quality, and applicability of the data used to inform our model. Priority was given to studies derived from US-based databases, such those from the Centers for Disease Control and Prevention and national clinical databases. Where available, meta-analyses were favored for parameter selection.

To represent uncertainty in estimates used to inform our model parameters, we assumed that each parameter follows a certain probability distribution characterized by the estimate mean and confidence intervals (Table 1 and Table 2). We then used repeated samples from these distributions to estimate the expected QALY loss. All estimates from the model are presented as the average and 95% uncertainty intervals (ie, 2.5th and 97.5th percentiles) of outcomes from 1,000 model replications. The number of

Table 1. Model Parameters for Calculating QALY Loss due to Symptomatic Infection, Hospitalizations, ICU Occupancy, and Deaths.

Symbol	Parameter	Probability Distribution[a]	Notes
Symptomatic infections			
p_S	Probability that an infection was symptomatic	Beta (mean = 0.692, SD = 0.115)	Based on the estimated asymptomatic ratio of 30.8% (95% CI 7.7– 53.8%)[27]
l_S	Average duration of symptoms (y)	Gamma (mean = 7/365, SD = 0.5/365)	Based on the results of a multistate CDC survey of symptomatic COVID-19 patients on the median time to return to their usual state of health (7 d, IQR = 5–12 d) and results of a telesurveillance cohort study on the median time to symptom resolution (7 d, 95% CI: 6–8 d)[28,29]
q_S	Average reduction in the quality of life while presenting symptoms	Beta (mean = 0.102 SD = 0.01)	Based on results of a 2023 study using the EQ-5D-5L to measure health-related quality of life in 676 US adult outpatients who tested positive for SARS-CoV-2, comparing the preinfection utility score adjusted to match the age, sex, diabetes, and hypertension distribution of the US general population (0.922) and the utility score measured after COVID-19 symptoms (0.820)[30]
Hospitalizations			
P	Probability that a hospitalized case requires ICU care	0.174	Based on the proportion of ICU patients among hospitalized patients from the CDC's COVID-NET database for the 2021–2022 season[31]
l_{H1}	Average duration of general ward care among patients who are ultimately admitted to ICU (d)	Gamma (mean = 8.3/365, SD = 0.875/365)	Based on the difference in the mean length of hospital stay among patients admitted to the ICU (19.1 d; 95% CI: 16.3–21.9) and mean length of ICU stay (10.8 d; 95% CI: 9.3–18.4); these values are from a pooled analysis of 45 studies[32]
l_{H2}	Average duration of hospitalization among patients who are not admitted to the ICU (y)	Gamma (mean = 6/365, SD = 3.7/365)	Based on the median length of hospital stay of 6 d (IQR: 3–8 d) among hospitalized patients not admitted to the ICU; these values are from a cohort study using data from a clinical database of academic centers and affiliates across 47 US states[33]
q_H	Average reduction in the quality of life while hospitalized	Beta (mean = 0.5, SD = 0.05)	Based on the quality-of-life utility for a patient hospitalized with COVID-19 (mean = 0.5, 95% CI: 0.4–0.6), interpolated between the utility of a symptomatic patient and a patient in the ICU; this value comes from a modeling study that estimates the QALY loss averted by each COVID infection in the United States[34]
q_I	Average reduction in the quality of life while in the ICU	Beta (mean = 0.70, SD = 0.10)	This value was obtained by averaging the ICU utility of 0.23 (SD = 0.009) from a de novo vignette-based utility study on COVID patients and the ICU utility value of 0.180 (SD = 0.45) from the literature, which was used in the simulation analysis; this average was then converted to disutilities for our analysis[35]
Deaths			
π_a	Probability that a death belongs to an age group	Dirichlet (0–9 y: 1,058.5 deaths, 10–19 y: 1,765 deaths, 20–29 y: 7,711.0 deaths, 30–39 y: 21,254.5 deaths, 40–49 y: 50,478 deaths, 50–59 y: 115,550 deaths, 60–69 y: 208,259 deaths, 70–79 y: 278,484 deaths, 80–90 y: 306,012.5 deaths, 90–100 y: 155,931.5 deaths)	Based on CDC's provisional counts for COVID-19 deaths by age between January 1, 2020, and September 23, 2023[36]

(continued)

Table 1. (continued)

Symbol	Parameter	Probability Distribution[a]	Notes
w_a	Discounted QALY loss associated with premature death by age group	0–9 y: 21,[31] 10–19 y: 19.41, 20–29 y: 17.41, 30–39 y: 15.28, 40–49 y: 12.76, 50–59 y: 10.08, 60–69 y: 7.41, 70–79 y: 4.59, 80–90 y: 2.45, 90–100 y: 1.08	Based on discounted QALY loss from COVID-19 deaths by age group estimated by Briggs et al[37] for the US population, where values account for the difference in life expectancy between men and women; these estimates were obtained using a 3% discount rate, a standardized mortality ratio of 2, and a qCM of 80%[38,39]

CDC, Centers for Disease Control and Prevention; CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; QALY, quality-adjusted life-year; qCM, impact of pre-existing comorbidity on quality of life; SD, standard deviation.
[a]When the SDs were not available in the literature, the SDs for the model parameters were approximated as one-quarter of the difference between the upper and lower bounds of the 95% CIs, based on the assumption that the 95% CI spans approximately 1.96 times the SD in a normal distribution.

Table 2. Model Parameters for Calculating Quality-Adjusted Life-Year Loss due to Long COVID.

Symbol	Parameter	Probability Distribution	Notes
Long COVID approach 1			
v	Probability of surviving an acute phase of infections among all infections	Mean = 0.998 95% UI = 0.9980–0.9981	Computed empirically each simulation iteration as 1 minus the ratio of reported deaths to total estimated infections from covidestim[14]
s	Probability of developing long COVID symptoms among cases that survived and exhibited symptoms during the acute phase of infection	Beta (mean = 0.062, SD = 0.027)	Based on the proportion of individuals who experienced 1 of the 3 long COVID symptom clusters (persistent fatigue, cognitive symptoms, and respiratory symptoms) among individuals who survived a symptomatic acute episode; the value 6.2% (95% UI: 2.4%–13.3%) comes from a pooled analysis of 54 studies and 2 medical record databases of symptomatic SARS-CoV-2 infections between March 2020 and January 2022[20]
l_L	Average duration of long COVID symptoms (y)	Gamma (mean = 4/12, SD = 0.25/12)	Based on a weighted average duration of long COVID recovery for nonhospitalized cases (4.0 mo, 95% UI: 3.6–4.6 mo) and hospitalized patients (9 mo, 95% UI: 7.0–12.0 mo); the duration for the nonhospitalized patients comes from a pooled analysis of 4 studies, and the duration for hospitalized patients comes from a pooled analysis of 6 studies[20]
q_L	Average reduction in the quality of life while presenting long COVID symptoms	Beta (mean = 0.29, SD = 0.027)	Based on the estimated disutility weight for mylagic encephalomyelitic and chronic fatigue syndrome (0.29, 95% CI: 0.21–0.34)[19,40,41]
Long COVID approach 2			
h	Probability that an infection is hospitalized	Mean = 0.0112 95% UI = 0.0111–0.0112	Computed each iteration as total reported hospitalizations divided by total estimated infections from covidestim[14]
$v_{H'}$	Probability of surviving the acute phase of infection if symptomatic and not admitted to the hospital	1	We assume that the mortality rate in the nonhospitalized group was negligible[42]
v_H	Probability of surviving the acute phase of infection among hospitalized patients	Beta (mean = 0.82, SD = 0.02)	Based on the pooled prevalence of mortality among patients hospitalized with COVID-19; the value of 17.62% (95% CI: 14.26%–21.57%) comes from a pooled analysis of 42 international studies[43]
v_I	Probability of surviving an acute phase of infection among patients admitted to the ICU	Beta (mean = 0.61, SD = 0.09)	Based on the mortality rate of patients admitted to the ICU with COVID-19; the value of 39.99% (95% CI: 23.38–59.8) comes from a pooled analysis of 6 North American studies[44]

(continued)

Table 2. (continued)

Symbol	Parameter	Probability Distribution	Notes
$s_{H'}$	Probability of presenting long COVID symptoms among nonhospitalized survivors of a symptomatic acute phase of infection	Beta (mean = 0.057, SD = 0.022)	Based on the proportion of individuals who experienced 1 of the 3 long COVID symptom clusters (persistent fatigue, cognitive symptoms, and respiratory symptoms) among individuals who were not hospitalized during the acute episode; the value 0.057 (95% UI: 0.019–0.131) comes from a pooled analysis of 54 studies and 2 medical record databases of symptomatic SARS-CoV-2 infections between March 2020 and January 2022[20]
s_H	Probability of presenting long COVID symptoms among hospitalized survivors of a symptomatic acute phase of infection	Beta (mean = 0.275, sd = 0.089)	Based on the proportion of individuals who experienced 1 of the 3 Long COVID symptom clusters (persistent fatigue, cognitive symptoms, and respiratory symptoms) among individuals who were admitted to the general ward during the acute episode. The value 0.275 (95% UI: 0.121–0.478) comes from a pooled analysis of 54 studies and two medical record databases of symptomatic SARS-CoV-2 infections between March 2020 and January 2022.[20]
s_I	Probability of presenting long COVID symptoms among survivors of a symptomatic acute phase of infection who received ICU care	Beta (mean = 0.431, SD = 0.107)	Based on the proportion of individuals who experienced 1 of the 3 long COVID symptom clusters (persistent fatigue, cognitive symptoms, and respiratory symptoms) among individuals who were admitted to the ICU during the acute episode; the value 0.431 (95% UI: 0.226–0.652) comes from a pooled analysis of 54 studies and 2 medical record databases of symptomatic SARS-CoV-2 infections between March 2020 and January 2022[20]
$L_{H'}$	Duration of long COVID symptoms (y)	Beta (mean = 4/12, SD = 0.25/12)	Based on the mean duration of long COVID symptoms among individuals who were not hospitalized; the estimated value of 4 mo (95% UI: 3.6–4.6 mo) comes from a pooled analysis of 4 studies[20]
L_H	Duration of long COVID symptoms among hospitalized patients (y)	Beta (mean = 9/12, SD = 1.25/12)	Based on the mean duration of long COVID symptoms among individuals who were hospitalized; the estimated value of 9 mo (95% UI: 7.0–12.0 mo.) comes from a pooled analysis of 6 studies[20]

CI, confidence interval; ICU, intensive care unit; SD, standard deviation; UI, uncertainty interval.

simulations was chosen such that the resulting uncertainty intervals were stable and did not vary appreciably when additional replications were included.

Sensitivity Analyses

We conducted sensitivity analyses focused on parameters with the greatest structural and empirical uncertainty and those most likely to substantially influence QALY estimates. These are presented in the appendix and in Supplementary Table 3.

Results

Between July 15, 2020, and December 28, 2022, an estimated total of nearly 500 million detected and undetected infections occurred in the United States, along with nearly 6 million hospital admissions and 1 million reported deaths. We estimated the QALY loss from COVID-19, accumulated between July 15, 2020, and December 28, 2022, to be 9,242,000 (95% UI: 7,808,000–11,311,000). The QALY loss varied over time, peaking at the end of 2020 and into 2021 and then again in early 2022 (Figure 1). Both approaches we used to estimate the loss in QALYs due to long COVID resulted in similar estimates (comparing purple curves in panels a and b of Figure 1). Hence, we used the estimates provided by our more parsimonious, simplified approach in the analyses presented below.

Deaths were the main contributor to QALY loss, constituting more than 65% of cumulative QALY loss (6,054,000 QALYs, 95% UI: 6,047,000–6,061,000). Notably, long COVID and symptomatic infection also made important contributions to cumulative QALY loss. Long COVID represented more than 22% of total QALY loss (2,146,000 QALYs, 95% UI: 881,000–3,947,000) and symptomatic

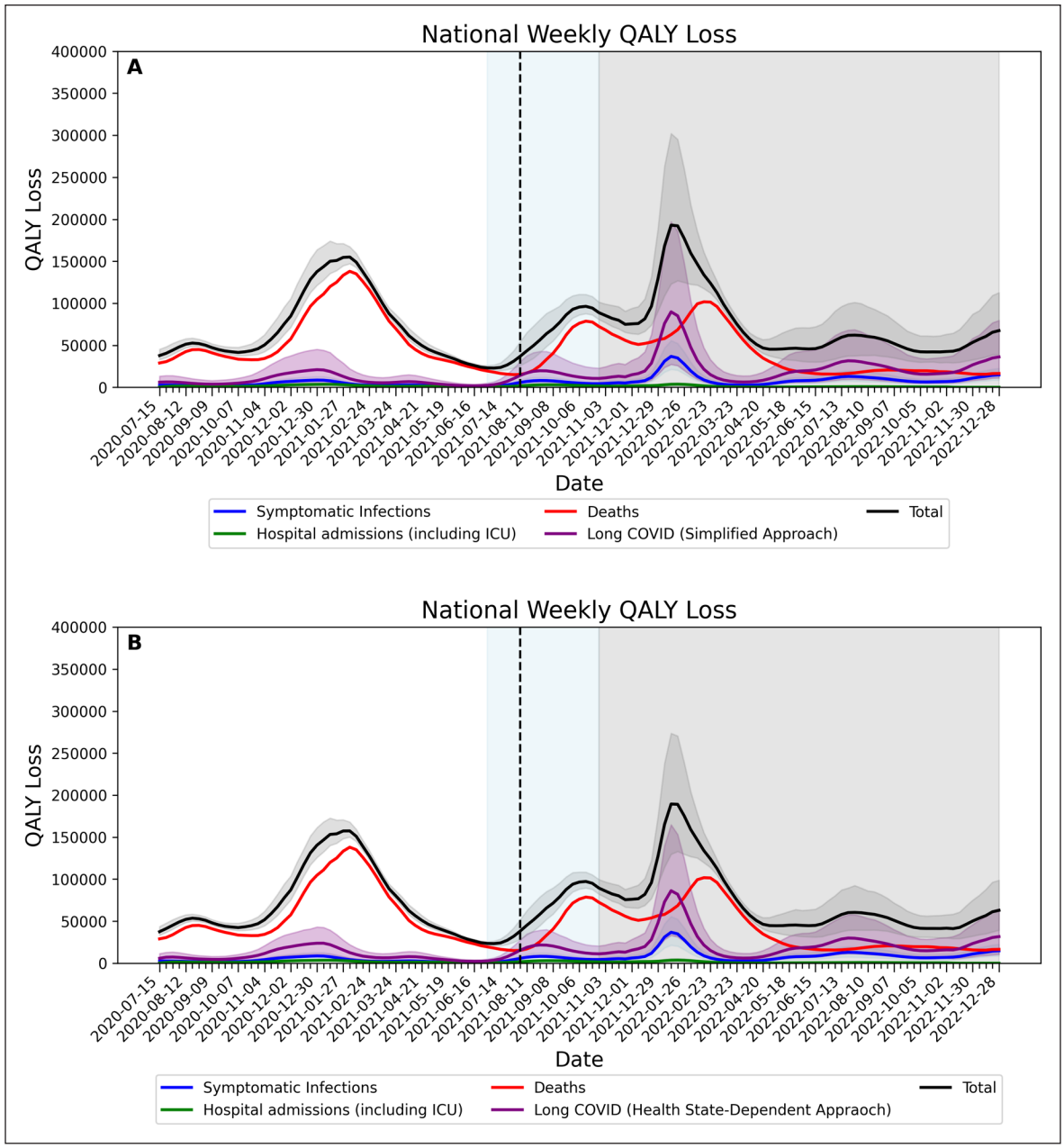

Figure 1. Weekly quality-adjusted life-year (QALY) loss in the United States between July 15, 2020, and December 28, 2022. QALY loss associated with long COVID was estimated using (a) the simplified approach and (b) the health state–dependent approach. The region shaded in blue corresponds to the period when the delta was the predominant circulating strain, and the region shaded in gray corresponds to when the Omicron variant was the dominant circulating strain. The black dotted line corresponds to when 70% of the total population was vaccinated with at least 1 dose.

infections represented 9% (872,000 QALYs, 95% UI: 516,000–1,316,000), whereas hospitalizations represented only 1.5% (132,000 QALYs, 95% UI: 93,000–163,000) of the overall impact.

There was strong geographic heterogeneity in QALY loss across counties (Figure 2a). The most populated counties, urban counties in large metropolitan areas (Los Angeles, New York, Miami Dade), exhibited the highest QALY losses, whereas counties with smaller populations, often in Great Plains and Southwest states, exhibited the lowest QALY losses. However, when accounting for county population, counties in large metropolitan areas were no longer among those with the highest COVID-19 burden but instead exhibited some of the

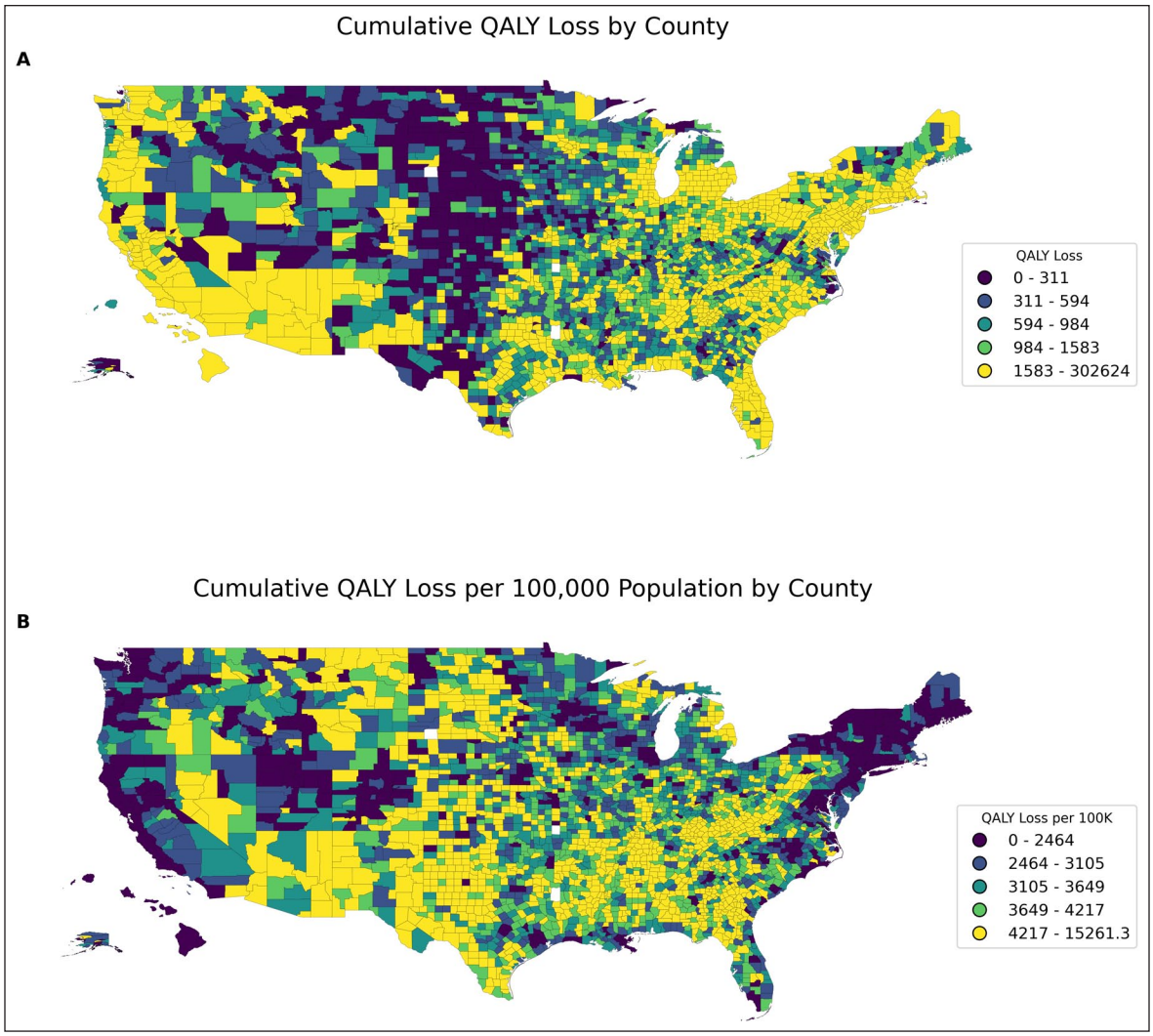

Figure 2. Mean quality-adjusted life-year (QALY) loss (a) and QALY loss per 100,000 population (b) due to COVID-19 between July 15, 2020, and December 28, 2022.

lowest cumulative QALY losses per 100,000 population (Figure 2b). The strong geographic heterogeneity in QALY loss was derived by geographic heterogeneity in the number of cases, hospitalizations, and deaths (Supplemental Figure S2).

Our analysis also revealed strong cross-state differences in QALY loss (Figure 3), with a nearly a 3-fold difference in QALY loss per 100,000 population between Arizona (3,903 QALYs per 100,000 with 95% UI: 3,270–4,904) and Vermont (1,426 QALYs lost per 100,000 population with 95% UI: 1,090–1,954). Despite these cross-state differences, deaths were the primary contributor to QALY loss in every state, underscoring the disproportionate impact of mortality and morbidity on health burden.

Furthermore, our sensitivity analysis on parameters determining the QALY loss from deaths shows that the estimated overall QALYs lost across health states, and the degree to which deaths contributed to QALY loss, was not sensitive to the standardized mortality ratio and the quality of life for the remainder of life (Supplemental Figure S5). Given the outsized contribution of deaths to total QALY loss, varying the extent to which comorbidities increase mortality risk or reduce quality of life in remaining years does not meaningfully alter the overall burden estimates or affect our conclusions. Our sensitivity analysis on parameters determining the QALY loss associated with long COVID shows that regardless of the specific assumptions about the population-level active immunity conferred from the vaccine and subsequent proportion of breakthrough infections, the magnitude of QALY loss due to long COVID remained consistent (Supplemental Figure S6). Under the non–risk-stratified specification, QALY losses attributable to fatal outcomes were higher, reflecting the removal of the downward adjustment for the shorter remaining life

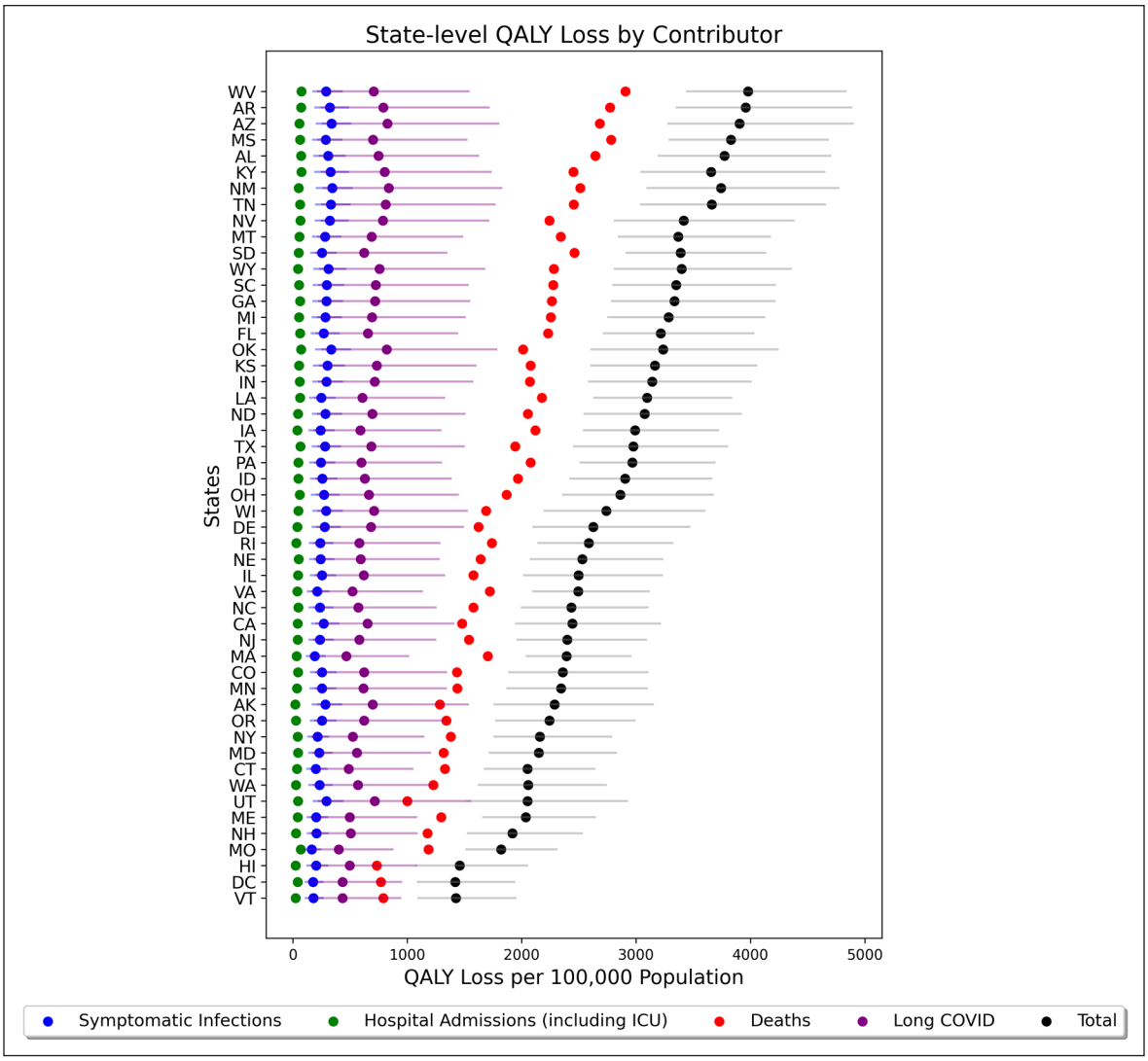

Figure 3. State-level quality-adjusted life-year loss per 100,000 population by contributor.

expectancy and lower baseline quality of life of those who died from COVID-19. This drove a modest increase in total QALY burden estimates compared with a stratified specification. However, the overall magnitude and temporal distribution of QALY losses remained broadly consistent across specifications, supporting the robustness of our primary findings (Supplemental Figure S7).

Discussion

The COVID-19 pandemic was a historic public health crisis that led to unevenly distributed health burdens across different populations and regions. While much attention has focused on the staggering mortality rates, nonfatal health outcomes also contributed to significant disruptions to individuals' quality of life. However, the population-level magnitude of these quality-of-life consequences remains poorly understood. In this study, we used a QALY-based approach that accounts for multiple health states to estimate the cumulative QALY loss attributable to COVID-19 between July 15, 2020, and December 28, 2022. By characterizing the evolution and geographic variation of disease burden, and quantifying the contribution of different health states relative to other diseases, we provide a nuanced depiction of COVID-19 burden in the United States.

QALY loss fluctuated over time, first peaking in late 2020 and early 2021 and again in early 2022, when 70% of the total population was already vaccinated with at least 1 dose. While the first peak was driven primarily by deaths, later peaks showed a more balanced contribution from deaths and nonfatal outcomes, particularly long COVID, highlighting the growing impact of nonfatal health states

as vaccination coverage increased. This shift highlights the changing epidemiology of COVID-19: as vaccination, prior infection, and improved clinical management reduced acute mortality risk, a larger share of the remaining burden became attributable to nonfatal health states.

This pattern is consistent with emerging global evidence. A recent meta-analysis of 429 studies including more than 2 million individuals with confirmed COVID-19 reported that the prevalence of long COVID remains substantial across follow-up periods and geographic regions.[46] Although absolute mortality has declined in the endemic phase of COVID-19, ongoing transmission continues to generate new cohorts of individuals at risk of persistent sequelae. Our findings mirror this broader epidemiologic transition: as mortality decreases, the relative contribution of long-term, nonfatal outcomes to total QALY loss increases.

Geographically, QALY loss was concentrated in large metropolitan areas, but when normalized to population size, more populous counties generally demonstrated a lower burden per 100,000 population compared with many less populous counties in the South and West (Figure 2b). The divergence in regional trends between absolute QALY loss and QALY loss per 100,000 population highlights the value of considering both metrics when analyzing the distribution of disease burden, as each provides complementary insights for strategically directing efforts to reduce disease burden. Absolute QALY loss highlights locations where the aggregate health loss is greatest. For example, large metropolitan areas with high absolute QALY loss may warrant national- or state-level reinforcement through measures such as scaling vaccination campaigns, expanding hospital staffing, or increasing surge capacity, even when per-capita burden is moderate. In contrast, population-standardized QALY loss identifies areas where the burden of COVID-19 is disproportionately high relative to population size, revealing localized vulnerabilities that may be obscured in absolute terms. These metrics are particularly useful for targeted interventions, such as deploying mobile health units or prioritizing outreach in rural or underserved communities experiencing high per-capita QALY loss despite smaller populations.

Stark interstate- and intercounty-level variation in QALY loss, even among counties within the same state, emphasizes the importance of considering local contexts and factors that may influence counties' abilities to respond. These differences may reflect the complex interplay between individual-level factors such as age and preexisting health conditions that influence survival and susceptibility to severe outcomes, as well as community characteristics such as accessibility to health care. This geographic variation may also reflect the diversity of disease management approaches implemented by different states and the flexibility that counties had in determining the stringency of their COVID response relative to state orders.[47,48]

We found that deaths were the primary contributor to QALY loss, aligning with previous research on COVID's severe mortality impact as the third leading cause of deaths in the United States in 2020 and 2021. These findings reinforce the importance of policies focused on preventing deaths to reduce overall health burden, including prioritizing high-risk groups for preventive measures and implementing nonpharmaceutical interventions that effectively reduce disease transmission and, consequently, mortality.[49,50]

Notably, long COVID emerges as the second most significant contributor to QALY loss following deaths, accounting for an average annual QALY loss of approximately 865,000 (95% UI: 355,000–1,591,000). Although QALYs and disability-adjusted life-years (DALYs) are calculated using distinct valuation frameworks, both QALY loss and DALYs capture healthy years lost.[18] They are therefore conceptually aligned, even if they are not interchangeable at the valuation level. In this analysis, we compare QALY loss to DALYs as measures of total population health burden, not as inputs into cost-effectiveness thresholds or resource allocation decisions, where differences in preference weights and disability valuations would be more consequential.

As such, this conceptual overlap allows us to benchmark COVID-19's health burden against DALYs for other diseases: the QALY loss attributable to long COVID alone is comparable to the total annual DALYs associated with liver cancer (581,000 DALYs; 95% UI: 549,000–607,000) or with cardiomyopathy and myocarditis (695,000 DALYs; 95% UI: 610,000–777,000) in the United States in 2021.[51] As ongoing research continues to elucidate the risk factors for long COVID, our findings underscore the importance of preventing new infections to mitigate the burden of long COVID and to address its prolonged effects through comprehensive postinfection care.

Beyond long COVID, other nonfatal health states such as symptomatic infections and hospitalizations, with relatively minor contributions to overall QALY loss, had a nonetheless important health burden relative to other diseases. The annual average QALY losses associated with symptoms (351,000 QALYs, 95% UI: 208,000–530,000) resulted in health losses comparable to those associated with HIV/AIDS (377,000 DALYs, 309,000–465,000) in 2021.[51] Given the elevated burden of nonfatal health outcomes relative to other endemic diseases, it is important to recognize that nonfatal outcomes, including long COVID, warrant attention and intervention as critical public health concerns.

When considering all health states, symptomatic infections, hospitalizations, deaths, and long COVID, the total average annual QALY loss from COVID during the period considered (3,725,000 QALYs, 95% UI:

3,147,000-4,559,000) was more than double the annual DALYs associated with all upper and lower respiratory infections (respectively, 307,000 DALYs, 95% UI: 186,000–452,000, and 959,000 DALYs, 95% UI: 867,000–1,024,000), dispelling the perception that COVID was "like the flu."[51]

There are several limitations to our analysis. First, our analysis was restricted to the period between July 15, 2020, and December 28, 2022, due to the availability of county-level data. The initial wave of COVID-19 infections before this period was not included because county-resolved surveillance data were sparse and inconsistent. Following this period, there was a sharp decline in the number of reported hospital admissions, reflecting a shift in federal reporting guidelines.[10,52] We adjusted for case underascertainment using the described model-based infection estimates. Even with this adjustment, the health burden of the earliest pandemic wave was not captured in our results, so the total QALY loss we present should be interpreted as a lower bound.

Second, we exclusively considered reported deaths, not excess mortality linked to the pandemic.[2] While accounting for excess deaths will increase our estimates of overall disease burden, it is unlikely to meaningfully affect the implications of our findings, instead amplifying previously described conclusions.

Third, we used the approach developed by Briggs to estimate the QALY loss from deaths, and hence our results are subject to limitations of their approach.[37] This approach assumes uniform life expectancy within each age–sex stratum, even though life expectancy varies significantly by racial and ethnic group, location, and over time.[53] While this may bias county-level estimates, it is unlikely to significantly alter national-level aggregates. Furthermore, this approach uses the same hazard ratios across all age groups to capture how, on average, people dying from COVID-19 face lower life expectancies that the average population. Age-specific hazard ratios may yield more accurate estimates of years of life lost, and location- and comorbidity-specific counterfactual life tables could refine our estimate.[54]

Fourth, we did not explicitly model variant-specific differences in disease severity. Although milder variants with higher transmissibility (eg, Omicron) are partially reflected in our data through a higher number of infections without a spike in hospitalizations and deaths (Supplemental Figure S1), we did not stratify key parameters by variant (eg, the probability of developing long COVID). Assuming a uniform risk across variants likely inflates the estimated burden attributable to the comparatively milder strains.

Finally, numerous uncertainties regarding long COVID make characterizing its impact challenging. These uncertainties include how it manifests, with more than 200 potential reported symptoms and whether it is formally diagnosed, complicated by shifts in health care–seeking behaviors and testing practices.[19] For these reasons, we did not rely on clinical records to determine the number of patients with long COVID but instead used modeled estimates of the proportion of individuals exhibiting long COVID symptom clusters among survivors of a symptomatic acute infection, pooled from 54 studies and 2 medical record databases.[20] Another challenge is establishing the duration of long COVID symptoms. A 2024 NASEM report describes long COVID as "present for at least three months in a continuous, relapsing and remitting or progressive state affecting one or more organ system."[19] Given the diversity of temporal patterns and limited data availability, our study relied on disease state–specific durations of symptoms. These uncertainties underscore the need for ongoing research to enhance our understanding of long COVID's impact.

Conclusion

This study provides the first comprehensive estimate of QALY loss due to COVID-19 in the United States, encompassing both geographic and temporal variations while accounting for a range of fatal and nonfatal health outcomes, including long COVID. Our findings demonstrate significant geographic disparities in QALY loss across counties and states, underscoring the need for tailored, context-specific approaches to pandemic management. Our study reveals the substantial quality-of-life burden of nonfatal COVID-19 outcomes, which is comparable to that of major chronic and infectious diseases. As COVID-19 mortality declines, it is crucial to recognize and address the long-term effects of nonfatal outcomes as key public health priorities.

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ORCID iDs

Fatima Mikdashi https://orcid.org/0009-0005-0716-2031

Rachel E. Murray-Watson https://orcid.org/0000-0001-9079-5975

Alyssa Bilinski https://orcid.org/0000-0001-9108-6660

Reza Yaesoubi https://orcid.org/0000-0002-9276-5750

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data Availability

All data used in this study come from publicly available sources. No individual participant data with identifiers were collected or used. The data files, data dictionary, and all code and scripts used to conduct the analysis and generate the figures in the manuscript and supplementary materials are available, and will remain publicly accessible with no approval needed, at the following GitHub repository: https://github.com/tmikdashi/Beyond-Mortality-COVID-19-QALY-Loss.

Supplemental Material

Supplementary material for this article is available online.

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Appendix

Sensitivity Analyses

Deaths

We used the formula provided by Briggs et al.[35] to estimate the discounted QALY loss associated with premature death by age group. We define three different parameters for these calculations: standardized mortality ratio (SMR) which summarizes how a given comorbidity can increase the risk of dying, qCM which adjusts for the impact of a given comorbidity on quality of life for remaining life years, and discount rate which accounts for the value of life years experienced in the future relative to the present. In our base analysis, we used an SMR of 2, a qCM of 80% and a 3% discount rate.[21,22] These parameter values constitute the base analysis and were used to generate the estimates presented in the analyses and in the figures below. In a sensitivity analysis, we varied the level of impact for comorbidities by adjusting the SMR (1.75, 2, 2.25) and qCM (75%, 80%, 85%) parameters, and evaluated the robustness of our estimates against these parameters.

Vaccination Status

We assume that the protective effects of vaccination, such as reduced disease severity and lower risk of infection, hospitalization, and death, are implicitly captured in the data through lower observed counts of infections, hospitalizations, and deaths. To explicitly account for vaccination's effect on the risk of developing long COVID, we allow the risk of developing long COVID to vary by vaccination status.[18, 23, 24, 25] To this end, we assume that vaccinated individuals have a reduced risk of developing post-acute COVID sequelae or long COVID symptoms, captured by a reduction factor r. In this sensitivity analysis, we modified equation (1) to:

$$\mathcal{L}_t = [C_t\gamma_t r + C_t(1-\gamma_t)]p_s s v l_L q_L$$

where γ_t is proportion of infections during week t that are among individuals with vaccine-induced immunity. These infections are referred to as breakthrough infections (BTI). Since there is no accurate estimate for this parameter, we considered scenarios where this proportion increases over time and reaches 50% or 80% by the end of our analysis period (Fig.S4). We do not account for differences in the post-vaccination long COVID trajectories based on vaccine type (mRNA or adenovirus vector) given the limited statistical evidence of differences in post-vaccination long COVID trajectories by vaccine type. Therefore, the reduction factor represents a generalized vaccine against COVID, assuming averaged protection across vaccine product platforms.[55]

Risk Stratification

To evaluate the implications of risk stratification assumptions, we conducted an additional robustness analysis using a non-risk-stratified specification. In this scenario, we removed risk adjustment from fatal QALY losses by setting the standardized mortality ratio (SMR) and mortality-related quality adjustment (qMR) parameters equal to 1. Long COVID was modeled using the simplified population-average approach.

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Supplementary Table 1: Model parameters for sensitivity analysis of impact of vaccination on QALY loss due to long COVID

	Parameters	**Probability Distribution**	**Notes**
γ_t	Proportion of total infections that are breakthrough infections	Sigmoidal function capped at L=0.5 and at L=0.8, with x_0 corresponding to 2021/08/04	Sigmoid variables are based on the rate of vaccine uptake and the estimated time when 70% of the total population was vaccinated with at least one dose.
r	Reduction factor in the probability of presenting long COVID symptoms among breakthrough infections	Beta(mean=0.872, sd = 0.06)	Based on the first vaccine dose being associated with a 12.8% decrease (95% CI: −18.6% to −6.6%) in the odds of developing long Covid. This value comes from a cohort study of participants who received at least one dose of an adenovirus vector or mRNA COVID-19 vaccine after testing positive for SARS-CoV-2 infection. [55]

Supporting Information for

Estimating the Quality-Adjusted Life-Year Loss Due to Non-Fatal COVID-19 Outcomes Across U.S. States and Counties

This PDF file includes:

Figures S1 to S6

S1. Supplementary Figures

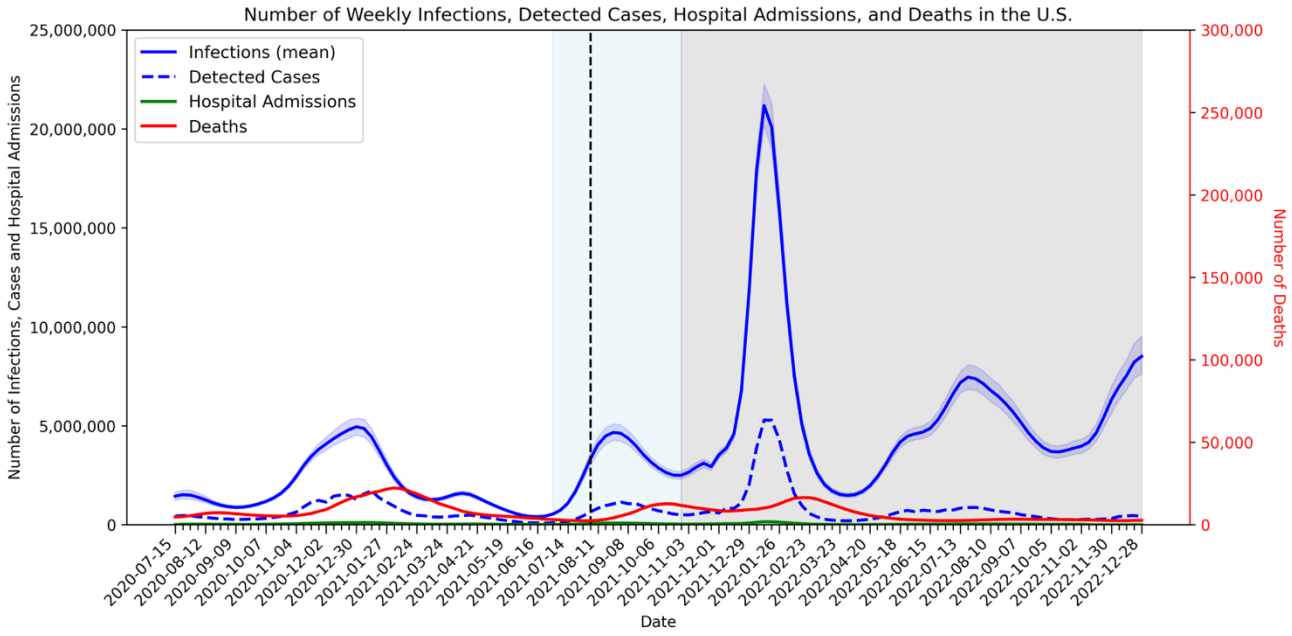

Fig.S1: Weekly COVID-19 infections, detected cases, hospital admissions and deaths in the United States between July 15, 2020 and December 28, 2022 The region shaded in blue corresponds to the period when the delta variant was the predominant circulating strain and the region shaded in grey corresponds to the period during which the omicron variant was the dominant circulating strain. The solid blue line represents the mean infections estimate; shaded regions indicate the 95% uncertainty interval.

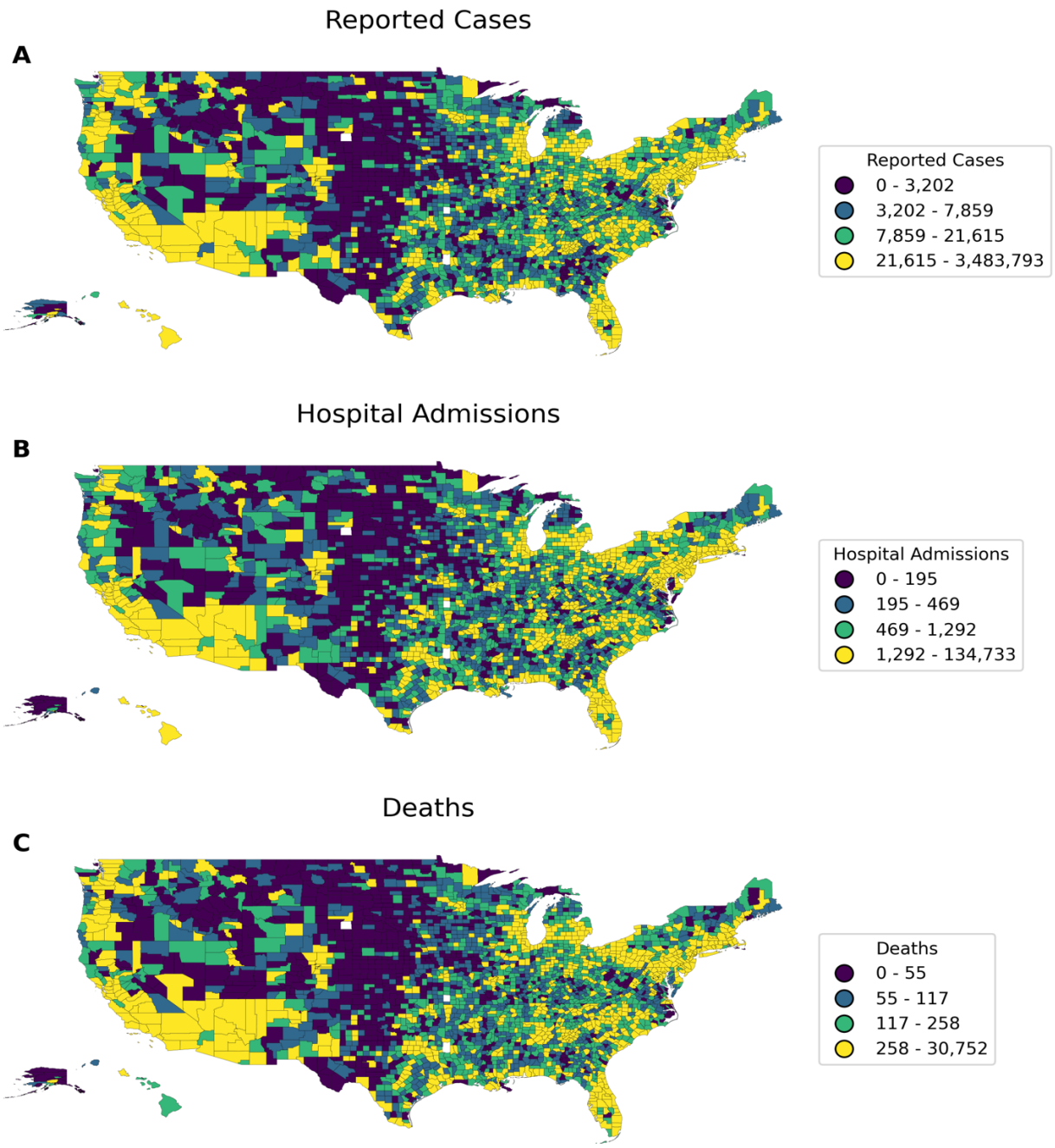

Fig.S2: Map of COVID-19 infections, hospital admissions and deaths, by county, accumulated between July 15, 2020 to December 28, 2022

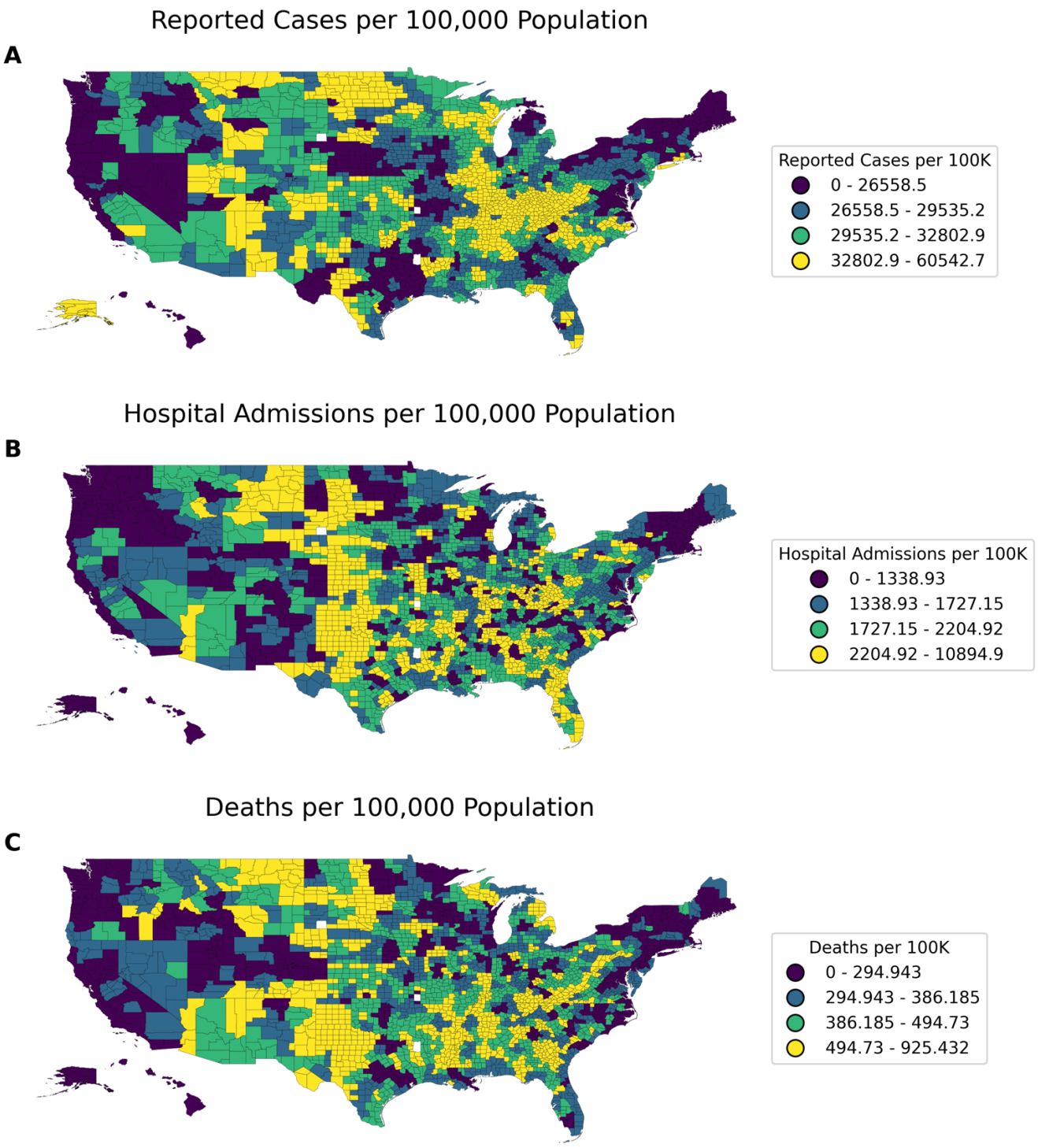

Fig.S3: COVID-19 infections, hospital admissions, and deaths per 100,000 population, by county, accumulated between July 15, 2020 to December 28, 2022. Outcomes per 100,000 population are calculated at an HSA level, but plotted by county.

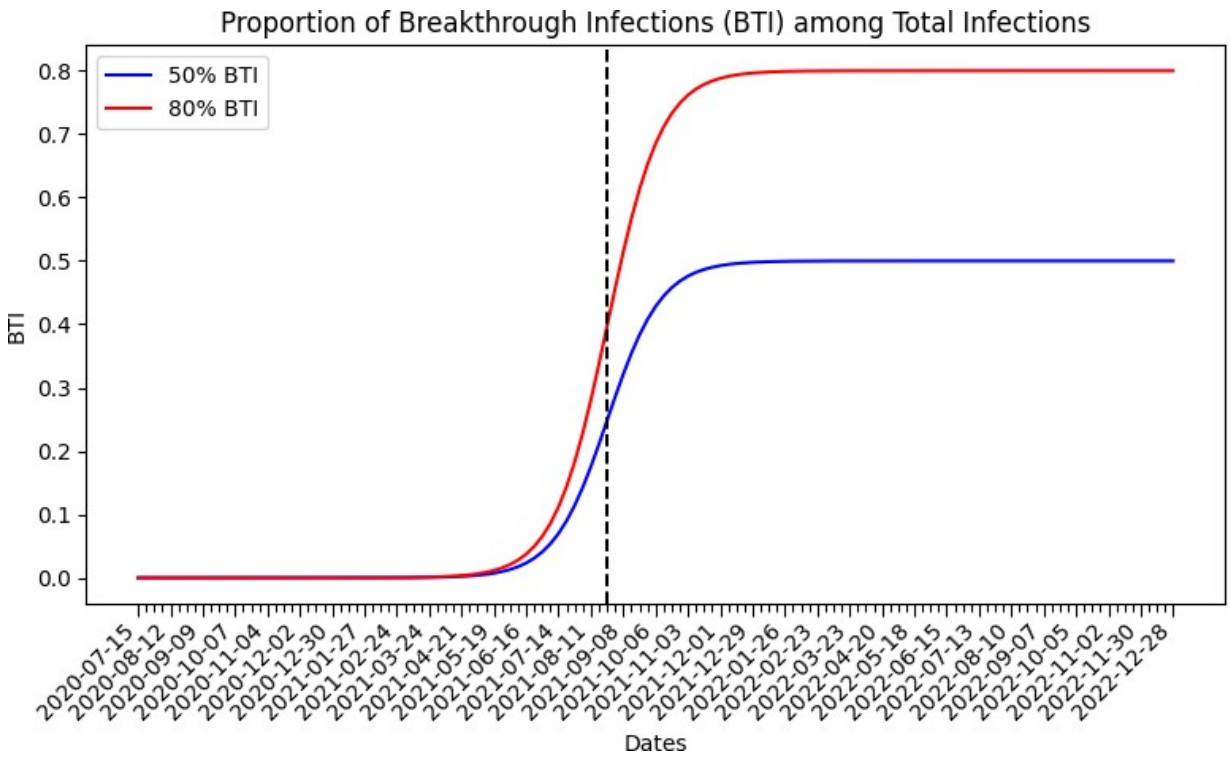

Fig.S4: Sigmoidal Function of Proportion of Breakthrough Infections Among Total Infections Used in Sensitivity Analysis. The black dotted line corresponds to when 70% of the total population was vaccinated with at least one dose.

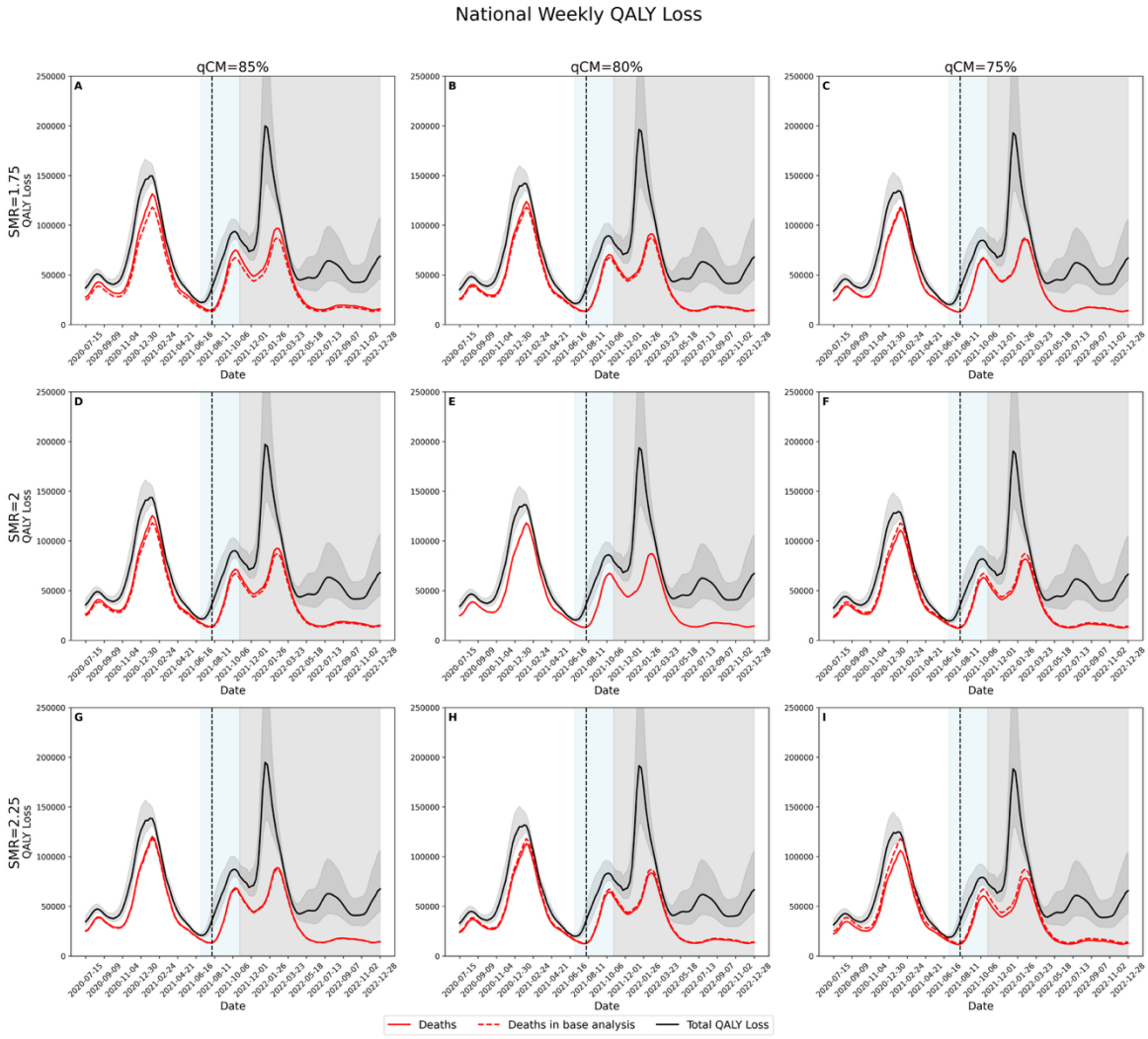

Fig.S5: Weekly QALY loss in the United States between July 15, 2020 and December 28, 2022. QALY loss associated with deaths was estimated by varying standardized mortality ratio (SMR) and comorbidity-induced reductions on population quality of life for remainder of life (qCM). All subplots were generated using a discount rate of 3%. The base analysis, represented by subplot (E) and by a red dotted line in the other subplots, was generated using an SMR of 2 and a qCM of 20%. The region shaded in blue corresponds to the period when the delta variant was the predominant circulating strain and the region shaded in grey corresponds to when the omicron variant was the dominant circulating strain. The vertical black dotted line corresponds to when 70% of the total population was vaccinated with at least one dose.

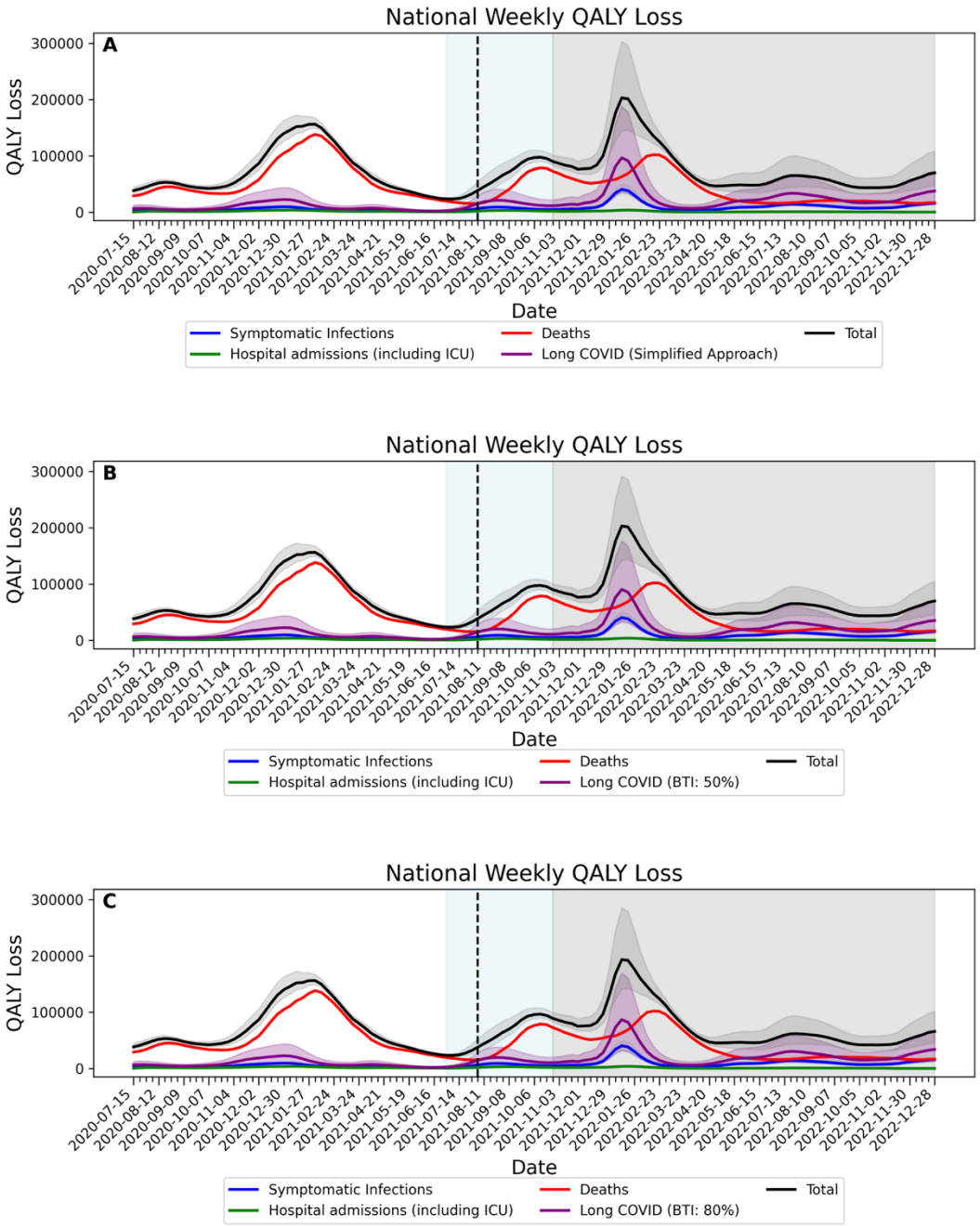

Fig.S6: Weekly QALY loss in the United States between July 15, 2020 and December 28, 2022. QALY loss associated with long COVID accounting for breakthrough infections (BTI) was estimated using the Simplified Approach where up to 50% (Panel B) and 80% (Panel C) of total long COVID cases are among BTIs. The region shaded in blue corresponds to the period when the delta variant was the predominant circulating strain and the region shaded in grey corresponds to when the omicron variant was the dominant circulating strain. The black dotted line corresponds to when 70% of the total population was vaccinated with at least one dose.

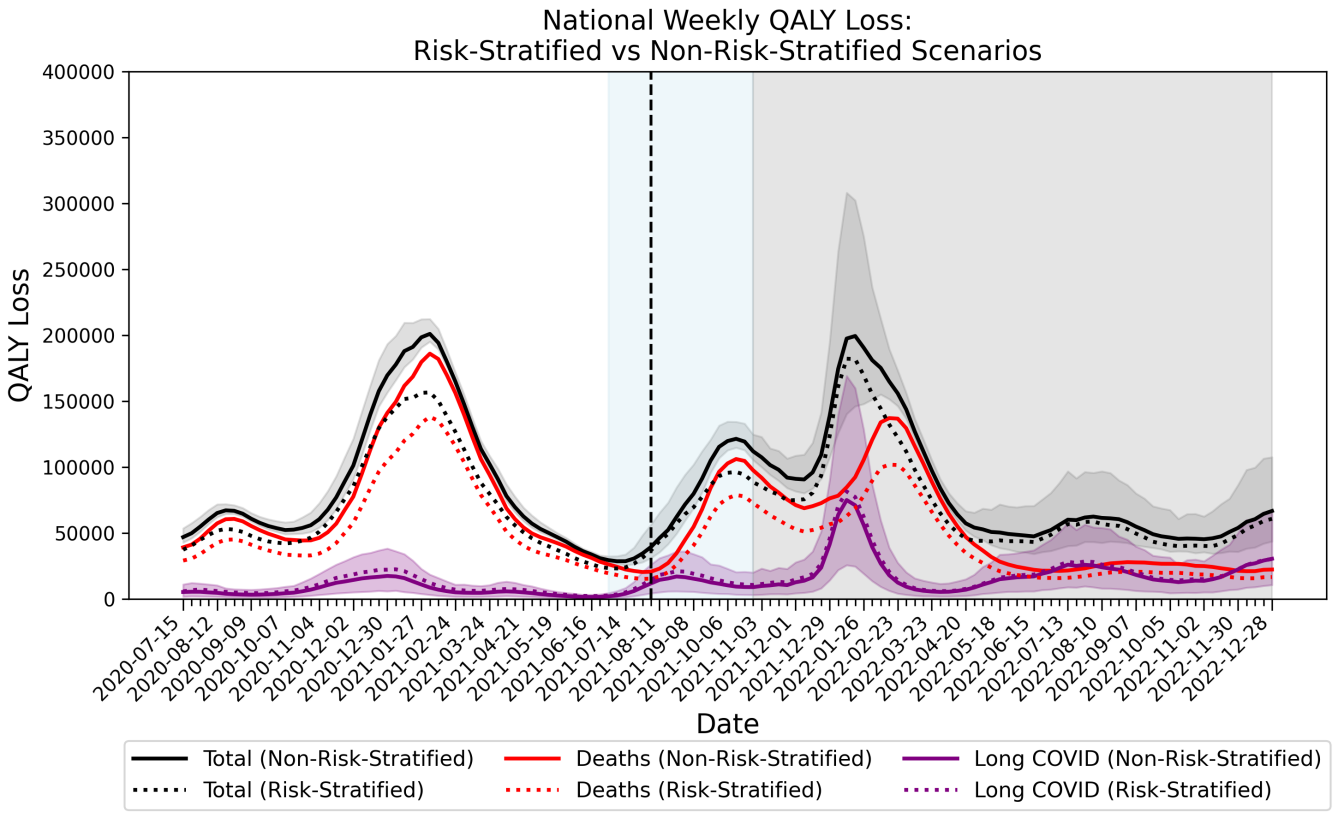

Fig.S7: Comparison of Risk-Stratified and Non-Risk Stratified Weekly QALY loss in the United States between July 15, 2020 and December 28, 2022. National weekly QALY losses are shown for the primary risk-stratified specification (dotted lines) and the non-risk-stratified sensitivity analysis (solid lines). The non-risk-stratified specification sets the SMR and qCM to 1 for fatal outcomes and uses the simplified long COVID approach. The risk-stratified specifications sets the SMR=2, qCM=0.8, and the uses the health-state-dependent long COVID approach.