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REVIEW

Economic Burden of COVID-19: A Systematic Review

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Objective: To review and qualitatively synthesize the evidence related to the economic burden of COVID-19, including healthcare resource utilization and costs.

Methods: A systematic review of studies that assessed the economic burden [eg, direct costs, productivity, macroeconomic impact due to non-pharmaceutical interventions (NPIs) and equity] of COVID-19 was conducted by searches in EMBASE, MEDLINE, MEDLINE-IN-PROCESS, and The Cochrane Library, as well as manual searches of unpublished research for the period between January 2020 to February 2021. Single reviewer data extraction was confirmed independently by a second reviewer.

Results: The screening process resulted in a total of 27 studies: 25 individual publications, and 2 systematic literature reviews, of narrower scopes, that fulfilled the inclusion criteria. The patients diagnosed with more severe COVID-19 were associated with higher costs. The main drivers for higher costs were consistent across countries and included ICU admission, in-hospital resource use such as mechanical ventilation, which lead to increase costs of $2082.65 ± 345.04 to $2990.76 ± 545.98. The most frequently reported indirect costs were due to productivity losses. On average, older COVID-19 patients incurred higher costs when compared to younger age groups. An estimation of a 20% COVID-19 infection rate based on a Monte Carlo simulation in the United States led to a total direct medical cost of $163.4 billion over the course of the pandemic.

Conclusion: The COVID-19 pandemic has generated a considerable economic burden on patients and the general population. Preventative measures such as NPIs only have partial success in lowering the economic costs of the pandemic. Implementing additional preventative measures such as large-scale vaccination is vital in reducing direct and indirect medical costs, decreased productivity, and GDP losses.

Keywords: covid-19, economic Impact, symptom Burden, health Economics, vaccines, costs

Introduction

Since late 2019, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has infected more than 180 million people globally and caused more than 3.9 million deaths worldwide as of June 30th 2021.[1] The virus and the measures taken to control its spread have profoundly impacted people's lives. Since the start of the Coronavirus disease 2019 (COVID-19) pandemic, significant efforts have been made by the industry and academia to discover promising treatments and vaccines that can improve the clinical disease course and patient outcomes or prevent infection, and therefore reduce the burden to public health systems. Quantifying the economic burden of COVID-19 is an essential consideration for evaluating the value of therapeutic and preventive interventions against the COVID-19 disease.

The macroeconomic impact of the COVID-19 pandemic has been overwhelming, with data from Europe showing an average of 7.4% reduction of GDP in 2020, with significant variations across countries.[2,3] The GDP losses were shown to be highly correlated with drops in employment rates, especially in regions that rely on tourism industry. Negative economic growth was just one of the unintended consequences associated with the adoption of non-pharmaceutical interventions (NPIs), such as lockdowns. Governments worldwide have all struggled in balancing the trade-offs between

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controlling the spread of the virus to limit the burden of the disease against the unintended economic, socioeconomic and other health consequences of the imposed NPI measures.[4]

It was estimated that without adequate policy measures, the pandemic would have the most significant economic impact on those of lower income, therefore increasing poverty rates and overall inequality.[2] Similar predictions have been made by the Council of Economic Advisers to the US government, who predicted that without economic support policies, people in the lower-income bracket would have suffered an average reduction of disposable income of more than 10% during Q1 of 2020.[5]

As with any other new disease, initially, the costing data related to the burden of COVID-19 was scarce. Due to the profound economic burden of the disease, several studies related to the medical costs of COVID-19 have recently been published in different regions. Due to this increase in the number of studies, and its profound impact on healthcare budgets as well as global economy, it is essential to understand and synthesize this data to inform policy makers on the overall burden of COVID-19.

The objective of this study is to systematically review and synthesize the evidence on the economic assessment of burden of COVID-19 since the start of the pandemic.

Methods

A systematic literature review based on a protocol was conducted utilizing EMBASE, MEDLINE, MEDLINE-IN-PROCESS, and The Cochrane Library using the search terms presented in Appendix 1. The search was conducted on April 1, 2021. In addition to the searches of electronic database, manual searches were also conducted to capture data from recent studies not yet published. Manual searches included searches of conference proceedings (published from January 2020 onwards) and online information repositories, the MedRxiv preprint server, and health technology agencies from the UK, France, Germany, Canada, US, South Korea, Taiwan, and Australia.

Eligibility Criteria and Study Selection

The study question of this Systematic Literature Review (SLR) was specified using the PICOS (Population, Intervention, Comparison, Outcomes and Study design) framework. The population of interest included patients with COVID-19. People indirectly affected, including populations who suffered from the consequences of COVID-19 prevention measures, caregivers, or carers, were also included. Studies reporting on any population subgroup (for example, patients with a different socioeconomic status, different demographic characteristics) that met the inclusion criteria of being affected by COVID-19 directly or indirectly were included and data from these studies were extracted. All interventions for COVID-19 treatment and strategies for prevention or control of COVID-19 were included.

The study types of interest were observational costing studies and assessments of the economic impact of COVID-19. Systematic reviews were included and extracted separately from the individual studies identified in this review. Individual studies identified from those SLRs were not extracted but are listed in Appendix 2. Randomized controlled trials (RCT), reviews, case reports, and case series were excluded. No date restrictions were placed on the search strategies for the electronic databases. For the manual searches, the date was restricted to the last year.

The titles and abstracts of records identified from the search strategy, where available, were reviewed according to the pre-specified inclusion/exclusion criteria reported in Appendix 3. A second reviewer independently screened the titles and abstracts of the identified studies. Any discrepancy was resolved by discussion. Articles identified as potentially relevant based on screening of titles and abstracts were then reviewed in full and selected according to the list of pre-specified inclusion/exclusion criteria. After the full-text review was completed, a list of the excluded studies was created with the reason for exclusion. The complete list of excluded studies during the full-text review stage is presented in Appendix 4. Meta-analysis synthesis was not conducted due to the broad study heterogeneity.

The outcomes of interest included resource use related to the disease and the associated intervention and measures of equity. These are included but are not limited to hospital admission, length of stay, physician visits, emergency department visits, and pharmacy costs. Indirect costs included, but not limited to, were decreased productivity, lost wages, or caregiver costs. Total costs per health state and patient were also of interest.

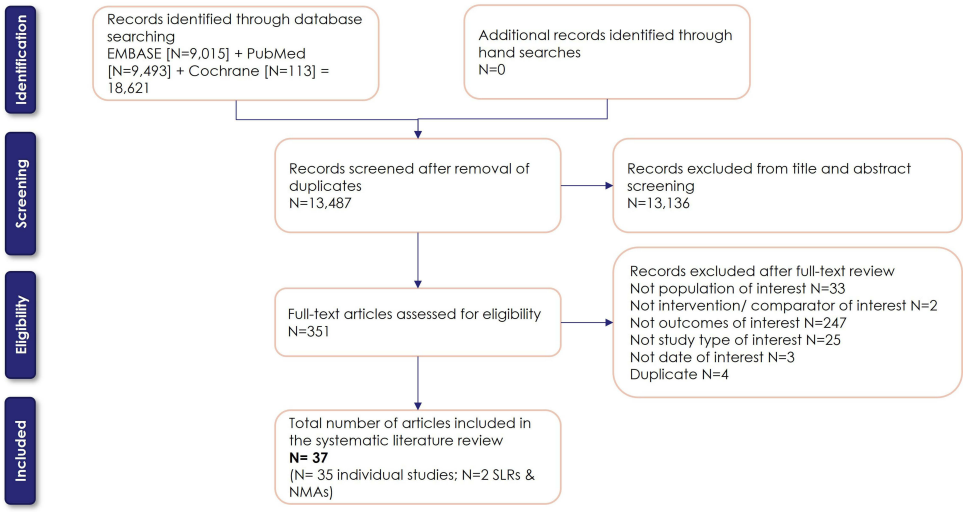

Figure 1 PRISMA diagram.

Results

A total of 18,621 citations were identified through the electronic database search. Duplicates were identified and compared based on an exact match for author, year, title, and abstract. After removal of duplicates, 351 unique citations were obtained and screened.

After application of the pre-specified selection criteria and title, abstract, and full-text stages, a total of 35 individual publications and 2 systemic literature reviews were included in this SLR (Figure 1: PRISMA diagram). Most of the publications (n=247) were excluded because they did not have the outcomes of interest. Furthermore, 25 publications were excluded based on study type, 33 did not include the population of interest, and four were previously missed duplicates. A full list of included studies is presented in Appendix 2.

In exploring the literature, we found an abundance of literature assessing direct and indirect medical costs. The studies included here evaluated some of the following objectives: identifying risk factors for clinical burden and resource use, resource use of hospitalized patients, determining the association of COVID-19 severity with costs as well as assessing the direct impact of COVID-19 on GDP.

Countries analyzed in the individual studies included 12 studies from United States, 5 studies from the UK, 3 from Germany, 3 multinational studies, 2 studies from Turkey and China and one study from the following countries: Italy, France, Greece, Saudi Arabia, Japan, Pakistan, Iran and Brazil.

Objectives and key findings of the included articles are summarized below in Table 1 Economic Burden of Patients and Table 2 Economic burden of the General Population, extraction tables with complete study characteristics and outcomes are in Appendix 5.

Discussion

A total of 37 publications were included in this SLR, 35 individual publications, and 2 SLRs. The SLRs included evaluated age-adjusted risk factors associated with mechanical ventilation and racial and ethnic disparities in hospitalizations and death.[43,44] Consistently reported across all studies were high medical costs and resource use by COVID-19 patients. The increased resource use required for the most severe patients influenced costs substantially.[9,11,12,14–19]

Across multiple countries in the hospital, the costs for COVID-19 patients admitted in an ICU were higher than those not admitted in an ICU. Within the ICU, mechanical ventilation contributed to a further increase in costs $2082.65 ± 345.04 to $2990.76 ± 545.98.[9,15–17,19] Overall, studies from Europe, the US, and Asia showed that more severe COVID-19 patients had higher costs and resource use than milder COVID-19 cases. On a macroeconomic level, the COVID-19 pandemic was a direct cause of GDP losses, mainly due to loss in productivity and implementation of non-pharmaceutical interventions.[1–3]

Table 1 Economic Burden of Patients

Study	Country	Objective	Key Findings
Mackey 2020[6]	US	SLR evaluating racial/ ethnic disparities in COVID-19 infections	• African American/ Black and Hispanic populations have disproportionately higher COVID-19 rates and mortality • African American/ Black and Hispanic populations have an increased risk for hospitalization • Asian populations have similar rates of infections, hospitalizations, and deaths as white Americans
Patel 2020[7]	US, China, Singapore, Australia & South Korea	SLR and Meta-Analysis to evaluate the risk factors associated with poor outcomes of COVID-19 patients	• Pooled prevalence of mechanical ventilation was 23.3% (95% CI: 17.1–30.9%) and Mortality was 13% (9.3–18%) • Male patients (57%) patients with hypertension (28.2%), diabetes (15.4%) cardiovascular disease (12.2%) and cerebrovascular disease (4.4%) had highest infection rates
Bartsch 2020[8]	US	Modeled the infection rate of COVID-19 and estimated the total costs associated with a specific infection rate	• A 20% infection rate, would result in approximately 53.8 million symptomatic COVID-19 cases, resulting in a total direct medical cost of $163.4 billion • The median direct medical cost for a symptomatic patient was $3994 (infection and one-year post-hospital discharge) • Hospitalized COVID-19 patients' costs were higher, which was a median of $18,579 (infection and one-year post-hospital discharge) • The costs for hospitalized COVID-19 patients were similar for all age groups (0–17years old: $11,367; 84 years or older: $11,900)
Price-Haywood 2020[9]	US	Analyzed data from COVID-19 patients at Ochsner Health between March 1-April 11, 2020	• Race was associated with a significantly higher risk of hospitalization • A total of 3481 confirmed COVID-19 patients were included in the study • Of that 76.9% of hospitalized patients, 70.6% of them were Black or African American • Black race, increasing age, a higher score on the Charlson Comorbidity Index (indicating burden of illness), public insurance (Medicare or Medicaid), residence in a low-income area, and obesity were associated with a higher risk of hospital admission • Black race was not independently associated with higher mortality (hazard ratio 0.89, CI 0.68–1.17)

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Table 1 (Continued).

Study	Country	Objective	Key Findings
Di Fusco 2021[10]	US	Evaluated health outcomes and the economic burden of hospitalized COVID-19 patients in the United States	• The average length of stay in a hospital for a COVID-19 patient was 8.3 days, while the proportion of patients who died in a hospital was 13.6% • More than 50% of the patients who were put on mechanical ventilation died in the hospital • Overall, costs were higher for COVID-19 patients treated in an ICU and even higher for patients put on mechanical ventilation
Anderson 2020[11]	US	Investigated the value of remdesivir on the hospital length of stay (LOS) for adult patients with severe COVID-19 between March 9-April 23, 2020	• 1643 patients were admitted with severe COVID-19 with a median age of 67 years • Most of the patients were Hispanic or Black, had ≥1 comorbidity, 12% required mechanical ventilation (MV) within 24 hours • Median LOS was 7 days, and in-hospital 28-day mortality was 26% • Majority of patients with a LOS of 1–4 or 5–8 days were ≥60 years old (67% and 70%), respectively • A 5-day course of remdesivir therapy was found to shorten the hospital stay of patients with severe COVID-19 by 4 days or more
Holy 2020[12]	US	Evaluated healthcare resource utilization changes and costs in patients with inpatient mortality due to COVID-19	• LOS increased from 8.7 days in December 2019 to 10.6 days in May 2020 • Comorbidities did not significantly affect patient costs and were not predictors for higher costs • Older age (84 years or older) was associated with a lower cost than other age groups
Hamer 2020[13]	UK	Analyzed BMI and covariates association with COVID-19 infections	• Independent associations between the following covariates and COVID 19: increased age, male sex, smoking, physical inactivity, non-White ethnicity, and alcohol • Higher likelihood of COVID-19 hospitalization for patients with increasing overall and central adiposity, even in modest weight gain
Karagiannidis 2020[14]	Germany	Provided a detailed account of case characteristics, resource use of patients who were hospitalized with COVID-19 from February 26-April 19, 2020	• Patients with older age and comorbidities were associated with a higher risk of MV • 24% and 25% of patients aged between 60–69 years and 70–79 years, respectively, required MV, while that of for the 18–59 and over 80 years age group were 15% and 12%, respectively • COVID-19 patients with comorbidities were at higher risk of getting ventilated, with 50% of the ventilated COVID-19 patients had a CCI index of 2 or higher • Mortality was higher for elderly patients (≥80 years) and dialysis patients receiving MV

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Table 1 (Continued).

Study	Country	Objective	Key Findings
Athanasakis 2020[15]	Greece	Compared the direct medical healthcare costs for COVID-19 patients	• The hospital's cost per day in the general ward was estimated at 443.1 EUR, while the cost per day in ICU at 2,245.5 EUR • Costs per ICU patient were estimated at 24,167 EUR, which was significantly higher than for non-ICU patients (8852 EUR) • More severe COVID-19 patients and ICU patients were associated with higher healthcare costs compared with milder COVID-19 patients
Gedik 2020[16]	Turkey	Assessed the economic burdens of inpatients with COVID-19	• Mean hospitalization days of clinical patients was 8.97 (1–49 days), and ICU patients was 14.74 (1–61 days) • Mean costs for clinical patients were $ 881.75 ±667.31 (range: $45.07 - $7584.81) • Mean costs for ICU patients were $2924 ± 2347.14 (range: $223.01- $9681.88)
Karahan 2020[17]	Turkey	Calculated the costs of management of COVID-19 patients	• 17.4% of COVID-19 patients require hospitalization, and 7.4% of hospitalized patients required ICU admission • Patients admitted to ICU incurred higher healthcare costs than those in inpatient or outpatient settings
Li 2020[18]	China	Conducted a cost and affordability analysis of 70 COVID-19 patients admitted to a hospital institution in Shandong from January 24-March 16, 2020	• Drug acquisition costs were the main cost driver (45% of the total cost) • Immunomodulators took over 39% of the total drug acquisition costs • Total mean cost was significantly higher in patients with pre-existing diseases compared to those without pre-existing diseases • Advanced disease severity was strongly associated with higher cost • Mild COVID-19: $4552 • Severe COVID-19: $11,058 • Critically ill COVID-19: $16,652
Khan 2020[19]	Saudi Arabia	Conducted a study to report the survival probability across age groups, sex, nationality, MV use, and ICU admission among a sample of hospitalized COVID-19 patients	• Mean direct medical cost of patients with moderate-to-severe symptoms admitted to the general medical ward was much lower than the mean cost per patient per day for patients admitted to the ICU • Mean cost of COVID-19 hospitalization per patient per day was the highest for ICU patients with MV use • The first 14 days of hospitalization are critical for COVID-19 patients

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Table 1 (Continued).

Study	Country	Objective	Key Findings
Dabestani 2020[20]	US	Analyzed the utilization of hydroxychloroquine, chloroquine, and supportive therapy drugs in hospitals in New York during the early weeks of the 2019 pandemic	• There was an increase in utilization of hydroxychloroquine and chloroquine and the number of patients receiving either drug beginning on March 15, with a notable 20% median increase per day through March 31 • Daily utilization of supportive therapy drugs such as midazolam, propofol, ketamine, cisatracurium, and fentanyl also increased during the study period
Ghaffari Darab 2021[21]	Iran	Estimated direct medical and indirect costs of treating the Coronavirus disease 2019 (COVID-19) from a societal perspective in the patients at a referral hospital in Fars province as well as the economic burden of COVID-19 in Iran from March to July 2020	• The overall direct medical costs were estimated to be $1,791,172 • Total hospitalization costs were the highest driver, with a total of $ 735,510 • The average direct medical cost was estimated to be $ 3755 • The study also reported mean costs per patient, per non-severe patient, and per ICU patient • The costs for an ICU COVID-19 patient are highest compared with non-severe and an average patient • The highest indirect costs were lost due to productivity losses after premature death, $10,190 • The lowest were from lost income due to hospitalization, $378
Olusaye 2021[22]	Multinational	Investigated the shortages and burden associated with care for palliative COVID-19 patients	• Being outside the UK was associated with lower odds of staff shortages (OR 0.44, 95% CI 0.26–0.76) • 91% of survey respondents changed how they worked as a result of COVID-19; 77% had staff who had suspected or confirmed cases of COVID-19. 81% of services had cared for patients with suspected or confirmed COVID-19, or both • 48% of survey respondents reported shortages of PPE, 40% shortages of staff, 24% shortages of medicines, and 14% shortages of other equipment • Palliative care services were often overwhelmed. Highest shortages were reported for PPE and staff
Falah 2021[23]	Arab countries	Determined which Arab countries excelled at the detection, containment, and at the treatment stages of COVID-19	• UAE and Bahrain conducted the highest in the number of COVID-19 tests per death which indicated widespread testing and assessment of community transmission • Arab countries show less deaths per million and less doubling time for confirmed deaths compared to most OCED countries such as Italy, Spain, USA, UK, France and Canada • Countries such as Egypt, Sudan, Syria, and Tunisia with a high prevalence of diabetes and cardiovascular disease have higher COVID-19 case fatality rates

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Table 1 (Continued).

Study	Country	Objective	Key Findings
Busch 2020[24]	Brazil	Conducted a retrospective non-interventional study of 41,640 patients using population-based health administrative databases	• Outcomes of this study were the number of prior authorizations to tests and hospitalizations during two periods of 90 days, before (P1) and after (P2) the first registered case of COVID-19 • During the 180-day study period- 21,583 patients underwent to tests, 15,018 in P1 and 6565 in P2, a reduction of 56.3% and 3316 hospitalizations occurred which was a reduction of 39.5%
Hashmi 2020[25]	Pakistan	A single center retrospective study was conducted to quantify losses due to postponement of elective surgeries and extra cost for procurement of PPEs and to quantify the total inpatient costs during COVID	• 625 patients were admitted during study period • During Covid there was a: o 50% reduction in patients' admissions o 43.15% reduction of emergency procedures o 55.7% decrease in revenue due to postponement of elective work
Heppner 2020[26]	US	Conducted a review of all visits in a Louisville, Kentucky level I trauma center from February to May in 2020 in comparison to same time in the previous year	• A total of 34,213 ED visits occurred during the study periods (18,471 in 2019 and 15,742 in 2020) • In 2020, patients were less likely to be female and more likely to arrive by ambulance • The daily mean visits per day in the ED in 2019 was 153.9 (SD = 16.3) which was higher than 2020's daily census average of 129.9 (SD = 25.1) • The mean difference between the two groups of 24 visits per day (95% CI: 18.3–29.7) was statistically significant, $p < 0.001$
Shin 2020[27]	Japan	Aimed to clarify the impact (case volume and claimed hospital charge) of the first wave of the pandemic, from March to May 2020	• A total of 2,739,878 inpatient and 53,479,658 outpatient cases from 195 hospitals were investigated • Total claimed hospital charges decreased in April, May, June 2020 by 7%, 14%, and 5%, respectively, compared to the same months in 2019 • Hospital charges in April and May 2020 decreased by 6.3% for hospitals without COVID-19 patients • Hospitals with COVID-19 patients, there was a median additional decrease of 5.5 million JPY in proportion with the length of hospital stay of COVID-19 patients including suspected cases
Loerinc 2020[29]	US	Conducted a retrospective chart review of all hospitalized COVID-19 patients discharged from an Emory Healthcare Hospital in Atlanta, GA from March 26 to April 21, 2020 to characterize their post-discharge care plans	• A total of 310 patients were included in the study • The most common presenting comorbidities were hypertension (200, 64.5%), obesity (BMI≥30) (138, 44.5%), and diabetes mellitus (112, 36.1%) • The median length of hospitalization was 5 days (range: 0–33) • Seventy-five patients (24.2%) required any home service including home health and home oxygen therapy • Twenty-four patients (7.7%) had one or more visit to an ED after discharge and 16 patients (5.2%) were readmitted

(*Continued*)

Table 1 (Continued).

Study	Country	Objective	Key Findings
Vaughn 2021[30]	US	Analyzed a randomly sampled cohort of 1705 patients hospitalized with COVID-19 in 38 Michigan hospitals between March 13, 2020 and June 18, 2020	• 56.6% of patients were prescribed early empiric antibacterial therapy; 3.5% (59/1705) had a confirmed community-onset bacterial infection • Patients were more likely to receive early empiric antibacterial therapy if they were older, had a lower body mass index, more severe illness, a lobar infiltrate or were admitted to a for-profit hospital
Zhu 2021[33]	UK	Investigated the impact of COVID-19 and national pandemic response on primary care antibiotic prescribing in London between January and November 2020	• 366,059 patients, 730,001 antibiotic items and 848,201 SARS-CoV-2 tests were analyzed • There was a decrease of antibiotic prescribing during March 2020 with a decline of 584 items per month • Prescribing reached its lowest in August 2020

Economic models have assessed the prevention, screening and treatment of COVID-19, In longer-term models, screening tests were considered cost-effective in all economic models. Similarly, social distancing was more cost-effective than quarantine, herd immunity, and having no intervention. Antiviral treatments and curative treatments were considered the most cost-effective option compared with any other measures against COVID-19.[36,45–48]

An economic evaluation conducted in South Africa and the UK evaluated the economic effects of social distancing.[26] The model results showed that if strict lockdown measures were taken in the UK at the beginning of the pandemic, the pandemic would have resolved in 1.5 months with approximately 21,000 deaths. However, the UK decided to implement 4.5 months of semi-lockdown, which resulted in 80,000 deaths. A similar trend was observed in South Africa. Thus, the model results showed that social distancing shortens the pandemic duration and decreases the number of deaths by decreasing the number of infected people.

Another economic evaluation concluded that treatment with remdesivir for non-ventilated patients and dexamethasone for ventilated patients would maximize lives saved and save $11.5 million.[27] The main drivers were the efficacy of the drugs and reduction of ICU-time required.

A stochastic compartment model from the US estimated how hospitalizations and ICU admissions would decrease if the duration of infectious rate was shorter and when symptomatic patients were treated. When high proportions (>50%) of symptomatic patients were treated, the resource use decreased. Similarly, shorter infectious periods were associated with reduced resource use.[28]

One key strategy to prevent the burden associated with COVID-19 is vaccination. Currently, the CDC estimates that available vaccinations such as the yearly influenza vaccine to have prevented 4.4 million illnesses, 2.3 million medical visits, and 58,000 hospitalizations during the 2018–2019 influenza season.[49] A Markov cohort model was used to estimate COVID-19 related direct medical costs and deaths in the United States, With the most optimistic projections, a 60% efficacious COVID-19 vaccine can prevent 31% of expected COVID-19 deaths in the United States versus no vaccines.[50] As COVID-19 vaccines enter the market, more specific cost-effective evaluations will be needed. As of June 2021, there are three COVID-19 vaccines approved by Emergency Use Authorization vaccines in the US—BNT162b2 mRNA (Pfizer-BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Janssen).[51] The European Medicines Agency has approved an additional vaccine ChAdOx1-S by AstraZeneca.[52] Additionally, there are ten other vaccines approved in various countries globally.[53]

Vaccines may also offer additional benefits beyond mitigation case burden alone. Estimates for herd immunity threshold for COVID-19 range from 60–90% of the population. This can be more easily achieved through vaccination supplementing natural immunity from past exposure. There is uncertainty on whether an initial infection leads to long-lasting immunity

Table 2 Economic Burden of the General Population

Study	Country	Objective	Key Findings
Nourazari 2020[35]	US	Assessed the impact of COVID-19 on hospital admissions through the emergency department in Massachusetts, with a specific focus on diagnosis groups, age, gender, and insurance coverage	• COVID-19 was the most common diagnosis group • There was a 32% decrease in non-COVID-19 admissions during weeks 11 through 36 in 2020 compared to the same weeks in 2019 • A substantial reduction in admissions was observed in the pediatric population group, female population group, Medicare patients' group, and various diagnoses related to chronic respiratory conditions and behavioral changes • Lower admissions could also be reduced due to car travel, improved air quality, decreased infectious disease transmission due to social distancing and use of masks • Infants had a significant drop in admissions, while the 55–64 age group had the smallest drop in admissions
Salje 2020[36]	France	Investigated the impact of the lockdown and current population immunity during COVID-19	• There were 95,210 incident hospitalizations due to COVID-19 reported in France and 16,386 deaths in hospitals as of May 7, 2020 • Males were found more likely to be hospitalized, enter an ICU, and die than females across all age groups • Mean age was 68 years for hospitalized patients, and for deceased patients, the mean age was 79 years • 50.0% of hospitalizations occurred in individuals more than 70 years old, and 81.6% of deaths within that age group • For infected patients, 2.9% of them were hospitalized, and 0.5% died, ranging from 0.001% for 20 years old or younger and 8.3% in those 80 years
Davies 2020[37]	UK	Modeled the COVID-19 transmission to data on hospital admission and hospital bed occupancy	• Projections showed that more stringent and longer lockdown measures result in a greater reduction of hospital admissions and deaths • Without additional restrictions, the second wave of COVID-19 was projected to be more severe than the first in terms of hospital admissions and deaths • Lockdown measures consistently outperform the baseline and tiered restrictions in reducing cumulative deaths over the time considered

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Table 2 (Continued).

Study	Country	Objective	Key Findings
Keogh-Brown 2020[38]	UK	Estimated the direct impact (direct disease effects, preventive public actions, and associated policies) on the health-related economic burden on the UK economy	• Assuming a clinical attack rate of 48% and a case fatality ratio of 1.5%, COVID-19 alone would impose a direct health-related economic burden of £39.6 billion (1.73% of GDP) on the UK economy • Under the mitigation strategy (14-day quarantine, social distancing, closing schools and universities for 12 weeks), the direct health-related economic burden increased by a third to £53.1 billion (2.3% of GDP) • Under the suppression scenario (14-day quarantine, social distancing, closing schools and universities indefinitely), the total macroeconomic cost was £668.4 billion, which was almost one-third (29.2%) of the UK GDP of 2020
Birch 2020[39]	UK	Linked a general equilibrium economic model to a simple epidemiological model of the infection using data from Keough Brown 2021	• Suppression is far more 'cost-effective' than mitigation • There is an average increase of 50% for each % reduction in fatalities with 5000 deaths being avoided through mitigation than through suppression
Nurchis 2020[40]	Italy	Assessed the socioeconomic burden of the pandemic by estimating Disability-Adjusted Life Years (DALYs) and productivity loss	• Total lost productivity for the 60–69 age group is £142,347,805, representing 0.08% of the national GDP • The oldest age class has the highest impact, although the number of productive years of life lost is lower than that of the younger age classes • The DALY rate in Italy was 2.01 DALYs per 1000 persons, with the estimated burden of disease being the highest among people aged 80–89 years • The total cost of lost productivity due to absenteeism from work was around £100 million for all the working-age classes • The total cost of lost productivity due to COVID-19 premature mortality for all working-age classes was around £300 million, and its impact on the GDP was estimated to be 0.17% • Temporary productivity loss due to absenteeism from work was lower than the permanent productivity loss due to premature mortality
Wang 2021[41]	China	Investigated the willingness to pay for COVID-19 vaccinations	• The individual's mean willingness to pay for full COVID-19 vaccination was $36.8 with median 78% needed to pay for some or full portions of COVID-19 vaccinations • Regarding the financing mechanism preference, most respondents believe that governments and health insurance both needed to pay some or all portions for COVID-19 vaccination • Some factors affecting the willingness to pay of responders were: o Responders with higher annual family income were willing to pay more for COVID-19 vaccination o Respondents who worked in the workplace with more employees had higher willingness to pay

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Table 2 (Continued).

Study	Country	Objective	Key Findings
Jackson 2020[28]	US	Agent-based model simulated SARS-CoV-2 transmission probabilities for the population of King County, Washington	• The most effective individual strategy was test-and-quarantine, which reduced the total hospitalizations by 12.7% • Removing all existing interventions would result in 42,000 COVID-19 hospitalizations between June 2020 and January 2021
Pham 2021[42]	US	Evaluated the connection between outbreaks of COVID-19 and stock returns over the period January-June 2020	• Daily increases in the number of infected cases, hospitalized cases, and deaths were founded to be negatively associated with next day stock returns of firms headquartered in the same state
Gandjour 2021[34]	Germany	Compared the provision of additional capacity to no intervention from a societal perspective	• Adding a staffed bed to ICU bed capacity yields €21,958 per life-year gained and an ROI of 4.6 • A bed utilization of 1.1% yields a break-even ROI of 1
Viscusi 2020[31]	Multinational	Presents worldwide COVID-19 costs for over 100 countries through July 2, 2020	• The total COVID global mortality cost is $3.5 trillion • The US incurred the highest mortality cost at $1.4 trillion, 41% of total worldwide costs • Five countries had a mortality cost of at least $100 billion: UK at $343 billion, Italy at $246 billion, France at $237 billion, Spain at $189 billion, and Brazil at $175 billion
Pardhan 2021[32]	Europe	Examined the associations between the change in new COVID-19 registered cases per million population and various macroeconomic and well-being indicators in 38 European countries over a 2-month period (April1,-May 31, 2020)	• Luxemburg, with the highest GDP per capita in Europe was found to experience the lowest change in new COVID-19 cases within the period • Countries with lower GDP (Ukraine, Bulgaria, and Romania) experienced a higher level of change in new COVID-19 cases per million population

against COVID-19.[29,54] Furthermore, the emergence of new variants of concern, such as those from the Omicron (B.1.1.529) lineage, would require the demonstration of vaccine effectiveness.

Vaccinations have made an essential contribution to the decreased incidence of infectious diseases and are considered to be a cost-effective public health intervention. Regarding childhood vaccination, it was predicted that for every dollar spent, it saves $3 for the US payer.[55] The eradication of smallpox through vaccines has resulted in a direct medical cost savings of $300 million in the US. The eradication of polio is expected to save the world $1.5 billion yearly.[56] Missed opportunity for the four most common vaccine-preventable diseases in adults over 50 years contributes to an estimated cost of $26.5 billion in the US (medical and indirect).[57] Vaccines demonstrate a considerable return on investment for payers.

Conclusion

The COVID-19 pandemic has an immense impact and current efforts implementing NPIs only have partial success in controlling the humanistic and economic costs of the pandemic. Vaccination is a strategy used to mitigate the evolving landscape of COVID-19, and policymaking bodies will consider their cost-effectiveness in making recommendations for routine use in the future.

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