

Healthcare Resource Utilization (HCRU) and Direct Medical Costs Following Acute SARS-CoV-2 Infection: Findings From a Literature Review

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BACKGROUND

- Long-COVID or post-COVID-19 condition (PCC) can occur after SARS-CoV-2 infection¹
 - Long-COVID can result in a wide range of symptoms that can last weeks, months, or even years after infection; it can also result in disability¹
- Globally, approximately 10% of people diagnosed with COVID-19 developed Long-COVID, with at least 65 million people estimated to be living with Long-COVID²
- In the United States, according to the Centers for Disease Control and Prevention Household Pulse survey, an estimated 7% of patients who had COVID-19 and long-term symptoms are still currently experiencing Long-COVID³
 - An estimated 30% of adults who have ever had COVID-19 have experienced Long-COVID at some point³
- Long-COVID can pose a significant burden on healthcare systems⁴

OBJECTIVE

- To assess the long-term medical costs and healthcare resource utilization (HCRU) following SARS-CoV-2 infection, as well as costs associated with Long-COVID

METHODS

Targeted Literature Search

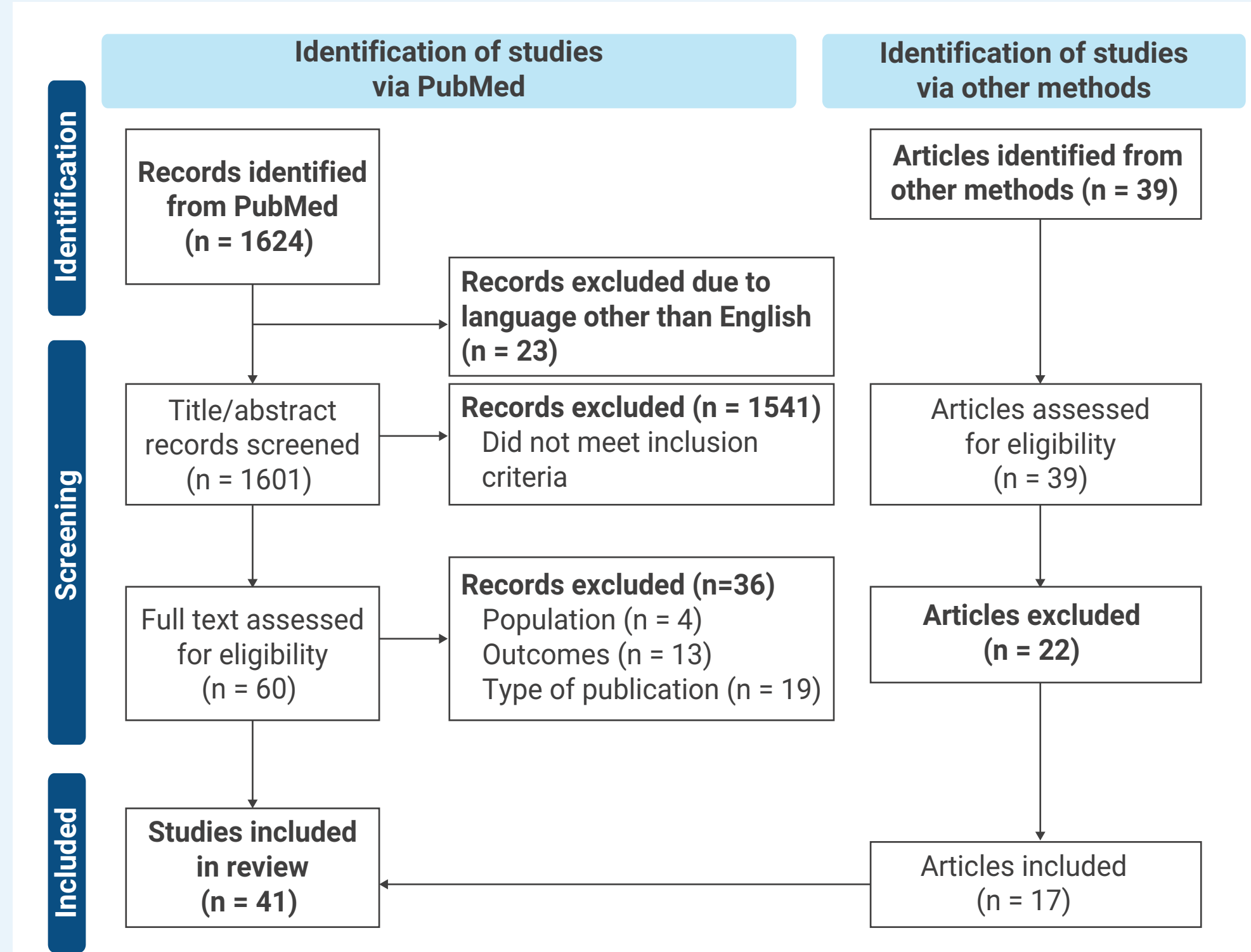
- An advanced PubMed search strategy was conducted in November 2023 and was used to identify English-language studies evaluating the cost and HCRU of Long-COVID or post-acute COVID conditions
- Websites and reports of Health Technology Assessment (HTA) agencies and institutions undertaking HTA activities websites were also searched
- Additional search strategies included a manual search of internet resources using the Google search engine, a review of preprint servers such as *medRxiv* and *Social Science Research Network*, and a review of the reference lists of retrieved publications
- A full list of literature search assumptions is provided in the supplementary materials, which is accessible via the QR code

RESULTS

Characteristics of Studies

- A total of 41 publications were included in the literature review (**Figure 1**)
 - The studies included were conducted in 14 different countries, with most studies conducted in the United States (n = 15 studies), followed by the United Kingdom (n = 7 studies) and Italy (n = 3 studies)
 - Most studies were retrospective in nature (n = 26); there were 29 parallel control and 12 single-arm studies, 5 cross-sectional studies, and 2 studies with pre- and post-diagnosis comparisons
- Long-COVID was explicitly defined in 19 studies (46%), with the definition based on symptoms in 12 studies (57%) and coding in 8 studies (38%) (**Figure 2**)
- In studies that did not explicitly define Long-COVID (9 studies; 22%), the assessment of HCRU and costs of SARS-CoV-2 infection was typically assessed from 1 month after a COVID-19 diagnosis
- Most studies reported either HCRU (29 studies; 71%) or cost (14 studies; 34%), with only 5 studies (12%) providing both HCRU and cost assessments
- Costs/HCRU were reported as absolute differences and relative changes in most studies, with difference-in-difference estimation used in some studies to analyze before and after COVID-19 diagnosis cost/HCRU differences

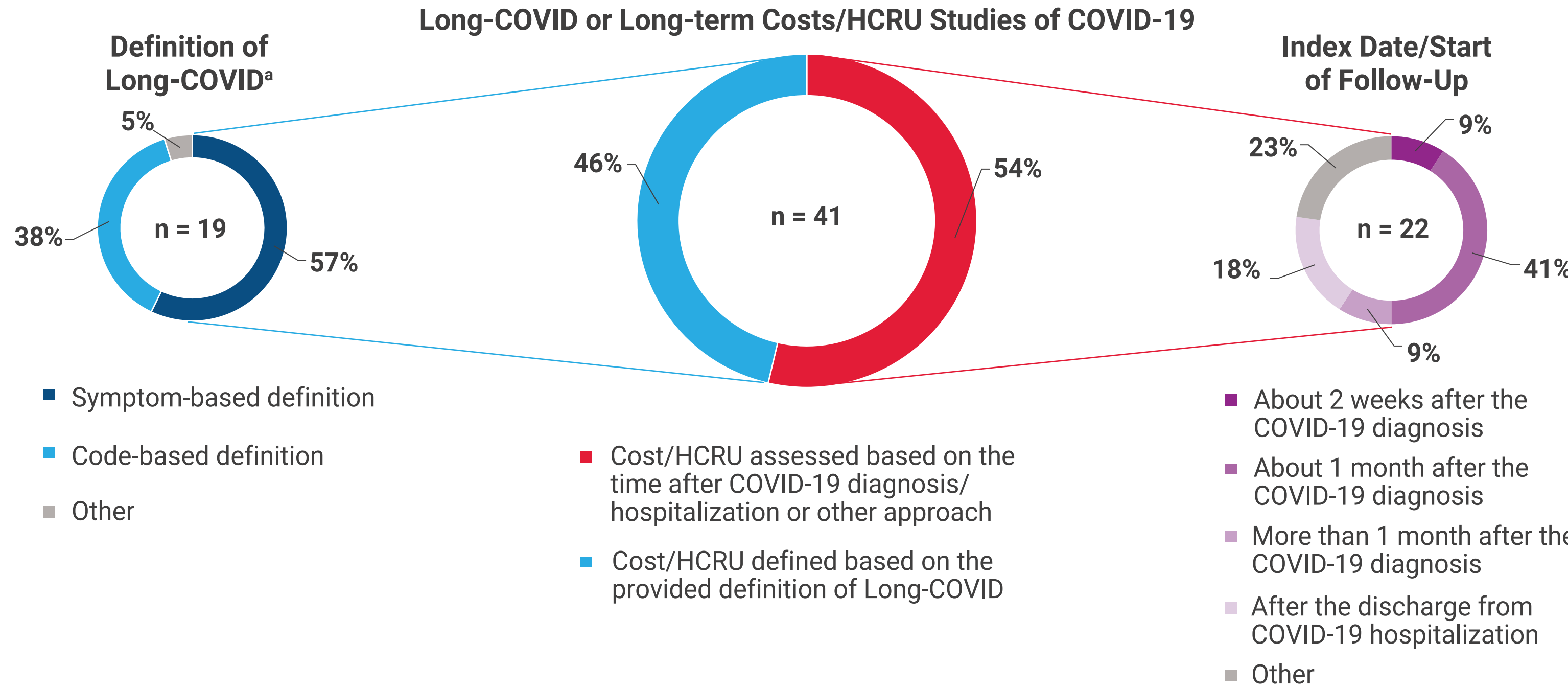
Figure 1. PRISMA Flowchart



Other methods included manual searches of publications on Google Scholar, preprint servers such as *medRxiv* and the *Social Science Research Network*, and reference lists from publications retrieved during the PubMed search.

RESULTS (CONTINUED)

Figure 2. Definition of Long-COVID and Long-Term Costs/HCRU of COVID-19



HCRU, healthcare resource utilization; n, number of studies.

^aTwo studies include 2 types of Long COVID definitions: symptom-based and code-based.

HCRU and Cost in Individuals With Long-COVID

- HCRU and costs were significantly higher in those diagnosed with Long-COVID compared with those without a Long-COVID diagnosis, with an increased burden observed over several months to ≥2 years after diagnosis (**Table 1**)
 - The impact of Long-COVID on HCRU was greater than that of Long Flu (individuals who may fit the diagnostic criteria of Long-COVID after a bout of influenza⁵)

Long-Term HCRU and Cost in Individuals With COVID-19

- A severe course of the disease or risk factors for severe COVID-19 were associated with higher costs and HCRU (**Table 2**)
 - SARS-CoV-2 infection caused up to a 3-fold increase in total follow-up healthcare costs compared with patients without infection
 - Up to a 10-fold increase in burden, or \$17,706, was observed in patients with COVID-19–related hospitalization compared with non-hospitalized individuals
 - Healthcare costs increased nearly 3-fold in older-aged individuals (50-64 years of age vs 18-24 years of age) and in patients with comorbidities (Charlson Comorbidity Index ≥1 vs 0)

Risk Factors for Increased Long-Term HCRU and Costs due to COVID-19 and Long-COVID

- Severe acute COVID-19 was a risk factor for long-term HCRU and costs
 - Increased healthcare demand and costs were observed across different severity levels of the disease in the acute phase in both hospitalized and non-hospitalized patients
- Additional risk factors include older age, presence of 1 or more comorbidities, female sex, and absence of vaccination; these risk factors contributed to the increased need for long-term healthcare, resulting in increased overall costs in these patient groups

Table 1. Impact of Long-COVID on HCRU and Cost

Key Finding	Study(s)
HCRU Associated With Long-COVID	
Overall	
Patients with Long-COVID had significantly elevated HCRU up to 2 years after diagnosis vs patients with COVID-19 without a Long-COVID diagnosis	Debski et al. <i>PLoS Glob Public Health</i> . 2022. Nehme et al. <i>Sci Rep</i> . 2022.
Inpatient Services	
Inconclusive findings on inpatient HCRU in patients with Long-COVID vs patients without Long-COVID	Mu et al. <i>SSRN</i> . 2023. Hedberg et al. <i>J Intern Med</i> . 2022.
COVID-19 outpatients diagnosed with Long-COVID were more likely to have any-cause hospitalization than patients with Long Flu in a study from the United States	Fung et al. <i>PLoS Med</i> . 2023.
Outpatient and Emergency Services	
Trend for significantly increased outpatient service utilization in patients with Long-COVID/PCS, including increase in frequency of ED, primary care, and specialist visits up to 15 months compared with those without Long-COVID or COVID-19	Nehme et al. <i>Sci Rep</i> . 2022.
Cost Associated With Long-COVID	
Total Costs	
Patients with Long-COVID incurred higher total healthcare costs compared with patients without Long-COVID	Mu et al. <i>SSRN</i> . 2023. Tene et al. <i>Int J Infect Dis</i> . 2023. Patterson et al. <i>Value Health</i> . 2022.
Inpatient and Outpatient Costs	
Patients with Long-COVID incurred increased inpatient and outpatient costs due to physician visits, laboratory/imaging procedures, and primary care visit costs compared with patients without Long-COVID	Tene et al. <i>Int J Infect Dis</i> . 2023. Tufts et al. <i>BMC Prim Care</i> . 2023.
Pharmaceutical Costs	
Medication costs trended higher in patients with Long-COVID during the 12-month follow-up compared with patients without Long-COVID	Tene et al. <i>Int J Infect Dis</i> . 2023.

ED, emergency department; HCRU, healthcare resource utilization; PCS, post-COVID syndrome; *SSRN*, Social Science Research Network.

Table 2. Long-Term Impact of COVID-19 on HCRU and Cost

Key Finding	Study(s)
Long-Term HCRU Associated With COVID-19	
Overall	
A significant increase in long-term total HCRU in patients with COVID-19 vs patients without COVID-19 in the United States and Canada	McNaughton et al. <i>CMAJ</i> . 2022. Tartof et al. <i>JAMA Netw Open</i> . 2022.
Inpatient Services	
Individuals with a previous SARS-CoV-2 infection had increased rates of hospitalizations compared with patients that did not have a previous SARS-CoV-2 infection	Castriotta et al. <i>SSRN</i> . 2023. Ayoubkhani et al. <i>BMJ</i> . 2021. Lo et al. <i>CMAJ Open</i> . 2023. Tisler et al. <i>PLoS One</i> . 2022.
Outpatient and Emergency Services	
A significant increase in long-term ED services utilization in patients with COVID-19 compared with controls without COVID-19	Tartof et al. <i>JAMA Netw Open</i> . 2022. McNaughton et al. <i>CMAJ</i> . 2022. Formoso et al. <i>BMJ Open</i> . 2023.
Mixed findings regarding long-term outpatient services utilization in COVID-19 patients vs patients without COVID-19	McNaughton et al. <i>CMAJ</i> . 2022. Tartof et al. <i>JAMA Netw Open</i> . 2022. Formoso et al. <i>BMJ Open</i> . 2023.
Long-term care/home care, virtual care, and pharmaceutical care were higher in COVID-19 patients vs those without COVID-19	McNaughton et al. <i>CMAJ</i> . 2022. Tartof et al. <i>JAMA Netw Open</i> . 2022. Whittaker et al. <i>medRxiv</i> . 2023.
Long-Term Cost Associated With COVID-19	
Total Costs	
Long-term total healthcare costs in patients exposed to SARS-CoV-2 were higher compared with those without prior SARS-CoV-2 infection	Formoso et al. <i>BMJ Open</i> . 2023. Chambers et al. <i>Am J Manag Care</i> . 2023. DeMartino et al. <i>J Manag Care Spec Pharm</i> . 2022. Khan et al. <i>J Am Board Fam Med</i> . 2024. Pike et al. <i>Prev Chronic Dis</i> . 2023. Wolff Sagy et al. <i>BMJ Glob Health</i> . 2023. Koumpias et al. <i>BMC Health Serv Res</i> . 2022.
Inpatient Costs	
Mixed findings on long-term inpatient costs; compared with controls, US commercially insured COVID-19 patients had increase in inpatient healthcare expenditure over 12 months while Medicare Advantage patients had a lesser increase in healthcare spending for inpatient services vs controls	Chambers et al. <i>Am J Manag Care</i> . 2023. Wolff Sagy et al. <i>BMJ Glob Health</i> . 2023.
Outpatient Costs	
Long-term outpatient costs in SARS-CoV-2 infected patients were higher vs those without a prior SARS-CoV-2 infection for commercially insured and Medicare Advantage patients in the United States and hospitalized COVID-19 patients in Sweden	Chambers et al. <i>Am J Manag Care</i> . 2023. Ashman et al. <i>PLoS One</i> . 2023.
Pharmaceutical Costs	
A 6% decrease in medication costs was observed among US commercially insured COVID-19 patients vs controls, while a 19% increase was observed in COVID-19 patients covered by Medicare Advantage vs controls	Chambers et al. <i>Am J Manag Care</i> . 2023. Wolff Sagy et al. <i>BMJ Glob Health</i> . 2023.
Long-term pharmaceutical costs remained relatively constant over 6 months in SARS-CoV-2 infected patients and were comparable to those without prior SARS-CoV-2 infection	Chambers et al. <i>Am J Manag Care</i> . 2023. DeMartino et al. <i>J Manag Care Spec Pharm</i> . 2022. Wolff Sagy et al. <i>BMJ Glob Health</i> . 2023.

ED, emergency department; HCRU, healthcare resource utilization.

Strengths and Limitations

- Limitations common to literature reviews, including publication and language bias
- Heterogeneity in study designs, definition of Long-COVID, populations, and methods applied limit comparability of findings across studies
- Preprint articles and scientific posters included may not be as robust as peer-reviewed publications
- Most studies were conducted during the pandemic period, limiting comparisons with pre-pandemic controls due to disruption in typical care patterns
- Potential underestimation of Long-COVID burden as patients with milder infection and/or those living in remote areas may not have been tested or treated

CONCLUSIONS

- Findings from this literature search suggest that Long-COVID/PCC poses a lasting burden of considerable magnitude on healthcare systems globally
 - Patients diagnosed with Long-COVID, as well as those with COVID-19 who were followed-up long term, incurred higher overall HCRU and costs, in particular in the outpatient setting
- The included studies differed substantially in terms of design and methodologies that were applied, which complicated the ability to draw unambiguous conclusions regarding the healthcare economic impact of Long-COVID
 - Common guidance with regards to definition of Long-COVID and PCC and measurement of associated HCRU/cost could help to strengthen the evidence
- In the absence of effective treatments, prioritizing preventative measures for acute COVID-19, such as vaccination, can be crucial for preventing the development of Long-COVID, thereby mitigating long-term HCRU and medical spending

ADDITIONAL INFORMATION

Please scan the QR code for a PDF copy of the poster and the supplementary material. Copies of the poster and supplementary material obtained through QR codes are for personal use only and may not be reproduced without permission of the authors.



For additional information, please contact Ekkehard Beck(ekkehard.beck@modernatx.com).

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Disclosures

EL, KK, MK, and AM are employees of Assignity and were contracted by Moderna, Inc., to conduct this study. KJ, NV, and EB are employees of Moderna, Inc., and hold stock/stock options in the company. SS is an employee of Moderna, Munich, Germany.