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ORIGINAL RESEARCH

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Real-world healthcare resource utilization and cost burden of COVID-19 in commercially insured adults at high-risk of severe disease in the US: a retrospective database analysis

Tendai Mugwagwa[a], Benjamin A. Abramoff[b], Siddharth Karanth[c], Tram Nham[c], Ravi K. Goyal[c], Elizabeth Esterberg[c], Gurinder S. Sidhu[d], Alon Yehoshua[d] and Ruth Mokgokong[a]

[a]Pfizer Ltd, Tadworth, UK; [b]University of Pennsylvania, Philadelphia, PA, USA; [c]RTI Health Solutions, Durham, NC, USA; [d]Pfizer Inc, New York, NY, USA

ABSTRACT

Background and aim: High-risk patients with COVID-19 remained at elevated risk of severe outcomes in the Omicron era, even after receiving multiple vaccine doses. We report the Omicron-era healthcare resource utilization (HCRU) and cost burden of COVID-19 among commercially insured, oral antiviral therapy-eligible patients at high risk of severe disease.

Methods: This retrospective analysis used the TriNetX Linked US database. Eligible commercially insured patients were aged ≥18 years, had a COVID-19 diagnosis between 1 July 2023 and 30 June 2024, and had ≥1 risk factor for severe COVID-19. All-cause and COVID-19-related HCRU and costs were assessed during acute (0–30 days from diagnosis) and post-acute (31 days until December 31, 2024) follow-up.

Results: Of the 43,487 eligible patients, 56.2% were aged ≥50 years and 85.6% had 1–5 high-risk conditions. Patients were followed for a mean of 11.4 months following COVID-19 diagnosis (acute phase, 1.0 month; post-acute phase, 10.6 months). 13,499 patients (31.0%) received treatment for COVID-19. 9.8% of patients had ≥1 all-cause inpatient general ward admission, with a mean per-patient (PP) total cost of $14,715 (acute phase, $10,833 PP; post-acute phase, $14,403 PP). 1.3% of patients had an all-cause intensive care unit (ICU) admission, with a mean PP total cost of $75,371 (acute phase, $62,882 PP; post-acute phase, $71,666 PP). Among the small number of patients requiring mechanical ventilation in the ICU, mean all-cause PP costs were $135,677 PP overall (acute phase, $106,577 PP; post-acute phase, $130,309 PP). 28.4% of patients had ≥1 all-cause emergency department visit (mean total cost, $1,434 PP; acute phase, $842 PP; post-acute phase, $1,408 PP).

Conclusions: During the Omicron era, HCRU and costs remained substantial and increased with disease severity among commercially insured patients at high risk of severe COVID-19. These findings are crucial to inform economic evaluations and payer decision-making regarding COVID-19 antiviral therapies.

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Introduction

Coronavirus Disease 2019 (COVID-19) placed a significant burden on healthcare systems that persisted beyond the first waves of the pandemic[1–6]. Patients at high risk of severe COVID-19, including older individuals, immunocompromised individuals, and patients with conditions like cancer, diabetes, obesity, cardiovascular disease, and chronic kidney disease, have been disproportionately impacted by COVID-19[7–9]. In these patients, the risk of progression to severe outcomes remained high in the Omicron era, even

CONTACT Tendai Mugwagwa Tendai.Mugwagwa@pfizer.com Director, Value & Evidence, GAV Value & Evidence Strategy, Pfizer Ltd, Walton Oaks, Dorking Road, Walton-on-the-Hill, Tadworth, Surrey KT20 7NS, UK.

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after receiving multiple vaccination doses[10,11], indicating that new infection surges could still result in a substantial disease burden.

A recent systematic literature review demonstrated that, if untreated, this population has a 1–8% risk of hospitalization and a 0%–3% risk of death[12]. In a meta-analysis assessing mortality and hospitalization risk among patients with COVID-19 during the Omicron era, the pooled relative risk for hospitalizations among patients with heart failure was 1.78. Diabetes and obesity were also associated with an increased risk of admission to the intensive care unit (ICU) (relative risk: 1.20 and 1.38, respectively)[13]. During spring 2022, weekly COVID-19-associated hospitalization rates among US adults aged ≥65 years rose threefold from 6.9 to 27.6 per 100,000, whereas rates in adults aged 18–64 years increased only 1.7-fold[6]. More recently, population-based surveillance by COVID-NET reported that, from October 2023 to April 2024, older adults and those with underlying medical conditions remained at higher risk of severe disease, including among vaccinated patients; patients aged ≥65 years accounted for 70% of all adult COVID-19-associated hospitalizations[14].

In December 2021, the first oral antiviral treatment, nirmatrelvir-ritonavir co-administration (Paxlovid), received Emergency Use Authorization from the US Food and Drug Administration for treatment of mild to moderate COVID-19 in patients at high risk for progression to severe disease[15]. The economic evaluation of COVID-19 antiviral therapies requires assessment of healthcare resource utilization (HCRU) and costs among populations at elevated risk for severe COVID-19 for whom these therapies are indicated. Given the continuous evolution of COVID-19, updated estimates of the HCRU and cost burden are needed to ensure evidence remains pertinent. Currently, available evidence on the HCRU and cost burden associated with COVID-19 originates from earlier phases of the pandemic[4,16,17] when antiviral therapies were not yet available[18–20]. In addition, few HCRU and costs analyses have focused on patients at high risk of severe COVID-19[18].

The cost burden of COVID-19 varies across different insurance coverage types[2,21]. An analysis of >1.3 million inpatient stays between 2020 and 2022 across 841 US hospitals[21] showed that hospital costs (in 2022 USD) for treating COVID-19 varied by payer type, with highest adjusted mean direct inpatient costs reported for worker's compensation plans ($13,106), followed by Medicare ($11,609), US military insurance ($11,488), private insurance ($11,274), and Medicaid ($10,629).

The aim of this study was to provide an updated economic evaluation of HCRU and costs during the Omicron era among patients eligible for oral antiviral therapy with nirmatrelvir-ritonavir from a US private/commercial payer perspective. We used real-world data gathered from this population to estimate the all-cause and COVID-19-related HCRU and cost burden of COVID-19, both overall and by care setting, among patients with COVID-19 at high risk of severe disease.

Methods

Study design

This was a retrospective analysis of patient data collected from the TriNetX Linked US database. The overall study period was from 1 July 2022 to 31 December 2024; the detailed study schema is presented in Figure 1. The case selection window for COVID-19 diagnosis was from 1 July 2023 to 30 June 2024. This selection window allowed identification of comorbidities and relevant clinical variables within the 12 months of baseline, which was the period before the index date. It also allowed capture of acute and post-acute consequences of COVID-19 with a minimum of 6 months of potential follow-up for all eligible patients. All patients were followed retrospectively from their index date through the earliest of disenrollment from insurance or the end of the study period (31 December 2024). This study was conducted from the perspective of a US private/commercial healthcare payer.

This study was reviewed by the RTI International IRB (ID: STUDY00023255) and was determined not to be human subjects research, as defined by 45 CFR 46. All methods were performed in accordance with the Declaration of Helsinki. Informed consent was not required as all patient data were deidentified and only aggregate data are reported.

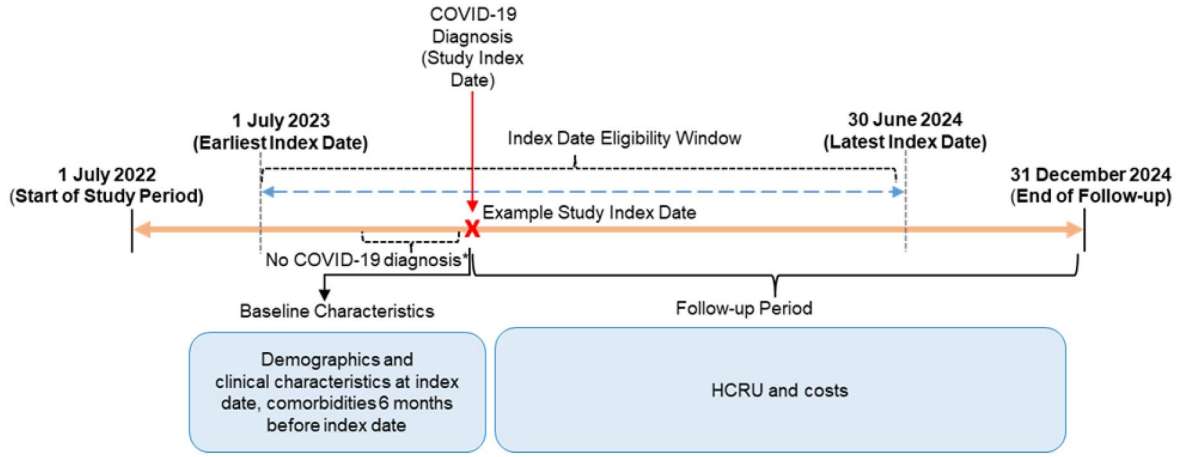

Figure 1. Study schema. Abbreviations. COVID-19, coronavirus disease 2019; HCRU, healthcare resource utilization. *Patients were required to have no COVID-19 diagnosis in the 6 months before study index date.

Data source

The TriNetX Linked database contains deidentified, longitudinal data from approximately 16 million patients in the US, consisting of electronic health record (EHR) data, closed medical claims, prescription claims, a tumor registry, mortality, and laboratory data. EHR data were sourced from over 70 academic and community hospitals and included information on demographics, diagnoses, encounters, laboratory results, and medication orders. The participating healthcare organizations mostly comprise large academic medical institutions with both inpatient and outpatient facilities.

The deidentified EHR data were matched and linked with closed claims data for patients who had private/commercial insurance coverage. The database allows stratification of HCRU and costs by level of care and aligns with previously published economic evaluations[18,22,23]. The TriNetX Linked database contains deidentified patient-level data in compliance with Health Insurance Portability and Accountability Act (HIPAA) de-identification standards. No direct patient identifiers were available to the investigators.

Definitions

The index date was defined as the date of the first COVID-19 diagnosis during the case selection window (Figure 1). The index diagnoses for different settings were defined as follows: for inpatient care, the index COVID-19 diagnosis was the primary or principal International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis code for COVID-19 (Table S1). For other settings, the index COVID-19 diagnosis was the earliest ICD-10-CM diagnosis code in any position or positive test for COVID-19 (e.g. nucleic acid amplification test, COVID-19 antigen test). A gap of at least 6 months between two COVID-19 diagnoses was required for episodes to be considered distinct.

The acute phase of COVID-19 was defined as the 30-day period following the index date, and the post-acute phase was defined as the period following the acute phase, i.e. from 31 days after the index date to the end of the follow-up period. The overall post-index period consisted of both the acute and post-acute phases.

Study population

Eligible patients had a COVID-19 diagnosis in the case selection window and were at high risk of severe disease at the index date. High-risk patients were defined as those aged 50 years or older and those aged 18–49 years with one or more medical conditions that increased the risk of severe illness from COVID-19 (e.g. immunocompromise, cardiovascular disease, diabetes mellitus, obesity, and chronic lung disease identified by respective ICD-10-CM diagnosis codes; Table S2). Eligible patients had continuous health plan enrollment during the baseline period and were required to have private/commercial insurance at the index date.

Patients were excluded if they had chronic liver disease, had a COVID-19 diagnosis within the 6 months before the index date, had been hospitalized for any reason within 7 days before the index date, or were receiving medications that were contraindicated for treatment with nirmatrelvir-ritonavir (Table S3) during the 6 months before the index date. Patients were also excluded if they received a COVID-19 antiviral therapy (molnupiravir, remdesivir, nirmatrelvir-ritonavir) or monoclonal antibody (bamlanivimab, bebtelovimab, casirivimab-imdevimab, cilgavimab-tixagevimab, sotrovimab) during the 6 months before the index date.

Study measures and outcomes

Patients' characteristics at the index date, including demographics, insurance, and clinical characteristics, were summarized for the overall population and for the acute and post-acute phases.

All-cause and COVID-19-related HCRU and costs were assessed from the index date through the end of follow-up and are reported by care setting (e.g. hospitalization and outpatient encounters are reported separately by care setting) and service type assigned at the claim level. COVID-19-related HCRU and costs during inpatient hospital encounters were ascertained based on ICD-10-CM codes for COVID-19 as the primary or principal diagnosis (Table S1). HCRU and costs associated with outpatient care settings were ascertained based on any diagnosis of COVID-19.

Costs were based on allowed amounts (or the proxy cost if allowed amounts were unavailable). All cost measures were adjusted to 2024 US dollars using the medical care component of the US Consumer Price Index[24].

Statistical analysis

Because the sample size available for analysis was dictated by eligible patients available in the study database and the descriptive nature of the study, no formal sample size estimations were performed.

Total and average monthly all-cause and COVID-19-related HCRU and costs from the index date until health plan disenrollment or study completion (31 December 2024) were estimated. All-cause and COVID-19-related HCRU and costs were assessed for the acute and post-acute phases. HCRU, costs, baseline patient demographics, and clinical characteristics were analyzed descriptively.

We report HCRU and allocated costs associated with admissions using two distinct methodologies. The first assigns HCRU and costs for the entire inpatient stay based on the highest level of care received (general ward, ICU without mechanical ventilation (MV), or ICU with MV). This approach facilitates direct comparison with the study by Goswami et al.[18], which utilized the same database over an earlier period of the pandemic (by including individuals who tested positive for COVID-19 between 20 January 2020 and 25 January 2021).

To further differentiate between levels of inpatient care, a supplementary analysis employed an alternative approach that attributes HCRU and costs to specific inpatient admission categories. For example, if a patient is initially admitted to the general ward and subsequently transferred to the ICU without MV, HCRU and costs are reported separately for each admission category.

The first method is referred to as the "highest care-level approach" and the second method as the "split care-level approach." Results from the split care-level approach are included in the supplementary materials and provide an assessment of the robustness of cost allocation.

Analyses were conducted using SAS, version 9.4 or later (SAS Institute; Cary, North Carolina, USA).

Results

Patient characteristics

Overall, 43,487 patients met the eligibility criteria and had continuous private/commercial insurance during the baseline period (Figure S1). The mean (SD) age was 49.3 (13.6) years; more than half of patients (56.2%) were aged 50 years or older. Approximately half of patients (51.0%) were white and almost two-thirds (65.1%) were female (Table 1).

Table 1. Baseline patient characteristics, overall and by COVID-19 phase.

	Overall $N = 43,487$	Acute phase $N = 43,487$	Post-acute phase $N = 42,794$
Age			
Mean years, (SD)	49.3 (13.6)	49.3 (13.6)	49.3 (13.5)
Median years, (IQR)	52 (39, 60)	52 (39, 60)	52 (39, 60)
Age group, n (%)			
18–44 years	14,914 (34.3)	14,914 (34.3)	14,644 (34.2)
45–49 years	4,140 (9.5)	4,140 (9.5)	4,089 (9.6)
50–54 years	6,171 (14.2)	6,171 (14.2)	6,111 (14.3)
55–59 years	6,697 (15.4)	6,697 (15.4)	6,621 (15.5)
60–64 years	7,647 (17.6)	7,647 (17.6)	7,556 (17.7)
≥65 years	3,918 (9.0)	3,918 (9.0)	3,773 (8.8)
Age group, n (%)			
18–49 years	19,054 (43.8)	19,054 (43.8)	18,733 (43.8)
≥50 years	24,433 (56.2)	24,433 (56.2)	24,061 (56.2)
Sex, n (%)			
Female	28,295 (65.1)	28,295 (65.1)	27,845 (65.1)
Male	15,192 (34.9)	15,192 (34.9)	14,949 (34.9)
Race, *n* (%)			
White	22,190 (51.0)	22,190 (51.0)	21,820 (51.0)
Black	3,755 (8.6)	3,755 (8.6)	3,693 (8.6)
Other	4,768 (11.0)	4,768 (11.0)	4,705 (11.0)
Unknown	12,774 (29.4)	12,774 (29.4)	12,576 (29.4)
Health plan type,[a] n (%)			
Private/commercial	43,487 (100)	43,487 (100)	42,794 (100)
Managed Medicaid	2,034 (4.7)	2,034 (4.7)	2,002 (4.7)
Medicare Advantage	110 (0.3)	110 (0.3)	109 (0.3)
Healthcare setting for index visit, n (%)			
Office	22,821 (52.5)	22,821 (52.5)	22,555 (52.7)
Outpatient hospital	3,974 (9.1)	3,974 (9.1)	3,902 (9.1)
Emergency department	3,643 (8.4)	3,643 (8.4)	3,554 (8.3)
Inpatient	226 (0.5)	226 (0.5)	219 (0.5)
Year of COVID-19 index diagnosis, n (%)			
2023	27,309 (62.8)	27,309 (62.8)	26,822 (62.7)
2024	16,178 (37.2)	16,178 (37.2)	15,972 (37.3)
COVID-19 vaccination status, n (%)			
No vaccine received in the 12 months before the index date	30,058 (69.1)	30,058 (69.1)	29,549 (69.0)
Vaccine received in the last 6 months before the index date[b]	7,711 (17.7)	7,711 (17.7)	7,584 (17.7)
Vaccine received 7–12 months before the index date[b]	7,349 (16.9)	7,349 (16.9)	7,268 (17.0)
Vaccine received anytime in the 12 months before the index date	13,429 (30.9)	13,429 (30.9)	13,245 (31.0)
CCI score, at index date			
Mean (SD)	0.8 (1.4)	0.8 (1.4)	0.8 (1.4)
Median (IQR)	0 (0, 1)	0 (0, 1)	0 (0, 1)
CCI score category, at index date			
0	25,103 (57.7)	25,103 (57.7)	24,707 (57.7)
0–1	10,329 (23.8)	10,329 (23.8)	10,171 (23.8)
>1	8,055 (18.5)	8,055 (18.5)	7,916 (18.5)
Number of high-risk medical conditions, n (%)			
0	3,776 (8.7)	3,776 (8.7)	3,726 (8.7)
1	12,941 (29.8)	12,941 (29.8)	12,717 (29.7)
2–5	24,288 (55.9)	24,288 (55.9)	23,913 (55.9)
6–10	2,454 (5.6)	2,454 (5.6)	2,411 (5.6)
>10	28 (0.1)	28 (0.1)	27 (0.1)

Abbreviations. CCI, Charlson Comorbidity Index; COVID-19, coronavirus disease 2019; IQR, interquartile range; SD, standard deviation.
[a]All patients had continuous private/commercial enrolment during baseline, and were required to have private/commercial insurance at index date. The secondary payer categories reflect overlapping coverage and private/commercial insurance were not mutually exclusive.
[b]The response options were not mutually exclusive. An individual patient could have received a COVID-19 vaccine both 7–12 months before the index date and in the last 6 months before the index date.

Most patients were diagnosed in 2023 (62.8%). Overall, 30.9% of patients had received a COVID-19 vaccination within the last 12 months, and 17.7% of patients had received a vaccination within the last 6 months. The majority of patients (85.6%) had between one and five high-risk conditions (Table 1). The most common high-risk comorbidities were obesity/overweight (43.9%), hypertension (39.5%), heart conditions (18.7%), cancer (17.4%), and diabetes (17.0%) (Table S4).

The mean post-index follow-up, including both acute and post-acute phases, was 11.4 months, with a maximum follow-up of 18.1 months. All patients were followed during the acute phase (fixed 30-day window) and nearly all patients (42,794; 98%) were followed into the post-acute phase, with a mean follow-up of 10.6 months (Table 2).

In the post-acute phase, approximately one-third (13,499; 31.0%) of patients received treatment for COVID-19. Of these treated patients, most received nirmatrelvir-ritonavir (11,911; 88.3%), while 12.4%

Table 2. Post-index period clinical characteristics, overall and by COVID-19 phase.

	Overall $N = 43,487$	Acute phase $N = 43,487$	Post-acute phase $N = 42,794$
Length of follow-up (months)			
Mean (SD)	11.4 (4.0)	1.0 (0.1)	10.6 (3.8)
Median (IQR)	11.9 (9–14)	1.0 (1–1)	11.0 (8–13)
Min, Max	0.0, 18.1	0.0, 1.0	0.0, 17.1
Receipt of COVID-19 treatment during post-index period, *n* (%)			
No	29,988 (69.0)	30,185 (69.4)	42,358 (99.0)
Yes	13,499 (31.0)	13,302 (30.6)	436 (1.0)
Type of antiviral treatment during post-index period, *n* (%[a])			
Antiviral treatment	13,496 (100.0)	13,302 (100.0)	431 (100.0)
Nirmatrelvir and ritonavir	11,911 (88.3)	11,750 (88.3)	327 (75.9)
Molnupiravir	1,669 (12.4)	1,586 (11.9)	106 (24.6)
Remdesivir	0 (0.0)	0 (0.0)	0 (0.0)
Monoclonal antibody treatment			
Tocilizumab	5 (100.0)	1 (100.0)	5 (100.0)
Healthcare setting for antiviral treatment during post-index period, *n* (%[a])			
Outpatient pharmacy	13,496 (100.0)	13,302 (100.0)	431 (1.0)
Healthcare setting for monoclonal antibody treatment during post-index period, *n* (%[a])			
Outpatient pharmacy	5 (100.0)	5 (100.0)	5 (100.0)
Number of COVID-19 reinfections, *n* (%)	1,899 (4.4)	0 (0.0)	1,899 (4.4)
Mean (SD)	1 (0.2)		1 (0.2)
Median (IQR)	1 (1,2)		1 (1,2)
Vital status at the end of follow-up, *n* (%)			
Alive	43,044 (99.0)	43,141 (99.2)	42,361 (99.0)
Deceased	102 (0.2)	5 (0.0)	97 (0.2)
Unknown	341 (0.8)	341 (0.8)	336 (0.8)
Respiratory support type, *n* (%)			
Invasive mechanical ventilation	68 (0.2)	68 (0.2)	68 (0.2)
Noninvasive mechanical ventilation	48 (0.1)	48 (0.1)	48 (0.1)
Extracorporeal membrane oxygenation	1 (0.0)	1 (0.0)	1 (0.0)

Abbreviations. COVID-19, coronavirus disease 2019; IQR, interquartile range; SD, standard deviation.
[a]Percentage within the given category (not within the overall population).

received molnupiravir. Five patients received tocilizumab. All antiviral treatments were dispensed through outpatient pharmacies.

Healthcare resource utilization

All-cause

During the overall study period, 4,243 patients (9.8%) had at least one inpatient general ward admission. Among these patients, 1,005 (23.7%) had at least one admission during the acute phase and 3,579 (84.3%) during the post-acute phase; some patients had admissions during both phases (Table 3). Results from the split care-level approach are included in the supplementary materials (Table S5). The mean number of admissions per patient was 1.3 during the acute phase and 1.8 in the post-acute phase. The average length of stay was approximately 3 days per admission in both phases.

Only a small number of patients (570; 1.3%) were admitted to the ICU, with an average of 1.0–1.2 ICU admissions per patient across the two phases and two MV categories (with or without MV) (Table 3). Most ICU admissions did not require MV (503) and occurred during the post-acute phase (431). The length of stay per ICU admission, irrespective of the need for MV, was shorter in the acute phase. Specifically, for ICU admissions without MV, the average length of stay was 6.3 days during the acute phase and 7.3 days during the post-acute phase. Among the 77 ICU admissions requiring MV, the mean length of stay was 9.3 days in the acute phase and 21.2 days during the post-acute phase (Table 3).

Overall, 28.4% of patients had at least one emergency department (ED) visit. Most ED visits occurred in the post-acute phase and did not require hospitalization. The mean per-patient number of ED visits without hospitalization increased from 1.3 during the acute phase to 2.0 in the post-acute phase. However, the mean per-patient number of ED visits requiring hospitalization was similar in the acute and post-acute phases (1.1 and 1.3, respectively) (Table 3).

The mean number of office visits per patient was five times higher in the post-acute phase (11.7) than in the acute phase (2.1) (Table 3). Most patients had at least one outpatient hospital visit, with the

Table 3. Post-index period all-cause and COVID-19-related HCRU, overall and by COVID-19 phase, highest care-level approach[a].

	All-cause			COVID-19-related		
	Overall $N = 43,487$	Acute phase $N = 43,487$	Post-acute phase $N = 42,794$	Overall $N = 43,487$	Acute phase $N = 43,487$	Post-acute phase $N = 42,794$
Inpatient general ward admissions						
≥1 inpatient admission, n (%)	4,243 (9.8)	1,005 (2.3)	3,579 (8.4)	374 (0.9)	353 (0.8)	34 (0.1)
Length of stay per admission, mean days (SD)	3.0 (3.4)	3.5 (3.5)	3.0 (3.5)	4.9 (5.0)	4.6 (3.8)	8.5 (10.1)
Admissions per patient, total, mean (SD)	1.8 (2.3)	1.3 (0.8)	1.8 (2.3)	1.1 (0.4)	1.1 (0.3)	1.2 (0.5)
Admissions per patient, monthly, mean (SD)	0.2 (0.3)	1.3 (0.8)	0.2 (0.3)	0.2 (0.2)	1.1 (0.4)	0.2 (0.2)
ICU admissions, all						
≥1 ICU admission, n (%)	570 (1.3)	192 (0.4)	431 (1.0)	114 (0.3)	108 (0.2)	11 (0.0)
Length of stay per admission, total, mean days (SD)	8.5 (19.8)	6.8 (6.0)	8.9 (20.6)	8.5 (11.0)	7.3 (6.2)	19.1 (17.6)
Admissions per patient, mean (SD)	1.2 (0.7)	1.1 (0.3)	1.2 (0.6)	1.0 (0.2)	1.0 (0.1)	1.0 (0.0)
Admissions per patient, monthly, mean (SD)	0.1 (0.1)	1.1 (0.3)	0.1 (0.1)	0.1 (0.2)	1.0 (0.1)	0.2 (0.1)
ICU admissions, without MV						
≥1 ICU admission, n (%)	503 (1.2)	161 (0.4)	383 (0.9)	97 (0.2)	91 (0.2)	10 (0.0)
Length of stay per admission, total, mean days (SD)	7.1 (9.9)	6.3 (5.5)	7.3 (10.6)	7.7 (8.4)	6.8 (5.7)	15.4 (13.3)
Admissions per patient, mean (SD)	1.2 (0.7)	1.0 (0.2)	1.2 (0.6)	1.0 (0.2)	1.0 (0.1)	1.0 (0.0)
Admissions per patient, monthly, mean (SD)	0.1 (0.1)	1.0 (0.2)	0.1 (0.1)	0.1 (0.1)	1.0 (0.1)	0.2 (0.1)
ICU admissions, with MV						
≥1 ICU admission, n (%)	77 (0.2)	32 (0.1)	54 (0.1)	17 (0.0)	17 (0.0)	1 (0.0)
Length of stay per admission, total, mean days (SD)	18.3 (47)	9.3 (7.6)	21.2 (51.1)	12.9 (19.9)	9.6 (8.2)	56 (NE)
Admissions per patient, mean (SD)	1.1 (0.4)	1.1 (0.3)	1.1 (0.4)	1.0 (0.0)	1.0 (0.0)	1.0 (NE)
Admissions per patient, monthly, mean (SD)	0.2 (0.2)	1.1 (0.3)	0.1 (0.3)	0.2 (0.3)	1.0 (0.0)	0.1 (NE)
ED visits, all						
≥1 ED visit, *n* (%)	12,343 (28.4)	5,633 (13.0)	9,194 (21.5)	4,169 (9.3)	4,077 (9.4)	155 (0.4)
Visits per patient, total, mean (SD)	2.1 (3.6)	1.3 (0.8)	2.1 (3.6)	1.1 (0.4)	1.1 (0.3)	1.1 (0.4)
Visits per patients, monthly, mean (SD)	0.2 (0.3)	1.3 (0.8)	0.2 (0.4)	0.1 (0.2)	1.1 (0.3)	0.1 (0.1)
ED visits, without inpatient hospitalization						
≥1 ED visit, *n* (%)	11,923 (27.4)	5,404 (12.4)	8,857 (20.7)	4,039 (9.3)	3,950 (9.1)	148 (0.3)
Visits per patient, total, mean (SD)	2.1 (3.4)	1.3 (0.7)	2.0 (3.5)	1.1 (0.4)	1.1 (0.3)	1.1 (0.5)
Visits per patients, monthly, mean (SD)	0.2 (0.3)	1.3 (0.7)	0.2 (0.3)	0.1 (0.2)	1.1 (0.3)	0.1 (0.1)
ED visits, with inpatient hospitalization						
≥1 ED visit, *n* (%)	1,357 (3.1)	417 (1.0)	1,040 (2.4)	154 (0.4)	148 (0.3)	7 (0.0)
Visits per patient, total, mean (SD)	1.4 (1.0)	1.1 (0.4)	1.3 (0.9)	1.0 (0.1)	1.0 (0.1)	1.0 (0.0)
Visits per patients, monthly, mean (SD)	0.1 (0.2)	1.1 (0.4)	0.1 (0.1)	0.1 (0.2)	1.0 (0.1)	0.2 (0.1)
Office visits						
≥1 office visit, *n* (%)	40,881 (94.0)	33,369 (76.7)	38,526 (90.0)	24,899 (57.3)	24,602 (56.6)	1,525 (3.6)
Visits per patient, total, mean (SD)	12.7 (13.7)	2.1 (1.6)	11.7 (12.9)	1.1 (0.5)	1.1 (0.3)	1.3 (0.9)
Visits per patients, monthly, mean (SD)	1.1 (1.1)	2.1 (1.6)	1.1 (1.1)	0.1 (0.1)	1.1 (0.3)	0.1 (0.1)
Outpatient hospital visits						
≥1 outpatient hospital visit, *n* (%)	27,845 (64.0)	10,872 (25.0)	25,436 (59.4)	4,507 (10.4)	4,343 (10.0)	262 (0.6)
Visits per patient, total, mean (SD)	4.7 (6.8)	1.5 (1.2)	4.5 (6.6)	1.2 (0.8)	1.1 (0.5)	1.3 (1.4)
Visits per patients, monthly, mean (SD)	0.4 (0.6)	1.5 (1.2)	0.4 (0.6)	0.1 (0.2)	1.1 (0.5)	0.1 (0.4)
Outpatient prescription drugs						
≥1 prescription, *n* (%)	41,096 (94.5)	35,214 (81.0)	38,819 (90.7)	13,504 (31.1)	13,306 (30.6)	416 (1.0)
Prescriptions per patient, total, mean (SD)	25.5 (27.7)	4.0 (3.4)	23.4 (25.6)	1.1 (0.4)	1.1 (0.3)	1.2 (1.0)
Prescriptions per patients, monthly, mean (SD)	2.2 (2.2)	4.0 (3.4)	2.2 (2.2)	0.1 (0.1)	1.1 (0.3)	0.1 (0.1)
Other outpatient visits						
≥1 visit, *n* (%)	32,124 (73.9)	19,473 (44.8)	28,558 (66.7)	13,020 (29.9)	12,603 (29.0)	910 (2.1)
Visits per patient, total, mean (SD)	8.2 (16.6)	1.9 (2.1)	8.0 (16.2)	1.2 (2.2)	1.1 (0.6)	1.8 (6.4)
Visits per patients, monthly, mean (SD)	0.7 (1.4)	1.9 (2.1)	0.8 (1.5)	0.2 (0.3)	1.1 (0.6)	0.2 (0.9)

Abbreviations. COVID-19, coronavirus disease 2019; ED, emergency department; HCRU, healthcare resource utilization; MV, mechanical ventilation; NE. not estimable; SD, standard deviation.
[a]The highest care-level approach allocated HCRU for the entire inpatient admission to the highest of three levels of care provided, which included inpatient general ward, ICU without MV, and ICU with MV[18].

majority occurring in the post-acute phase (59.4%). Patients averaged 4.5 visits during the post-acute phase and 1.5 during the acute phase. Most patients had at least one outpatient prescription in the acute phase (81%) and post-acute phase (90.7%). The mean number of prescriptions was six times higher in the post-acute phase (23.4) than in the acute phase (4.0). Other types of uncategorized outpatient visits were also common, occurring in most patients (73.9%), mainly during the post-acute phase (66.7%); the average number of such visits per patient was four times higher in the post-acute phase (8.0) than in the acute phase (1.9) (Table 3).

COVID-19 related

During the overall study period, 374 patients (0.9%) had a COVID-19 related inpatient general ward admission. Most of these admissions (353) occurred in the acute phase. The mean number of admissions per patient was similar in the acute phase (1.1) and post-acute phase (1.2). The mean length of stay per admission in the post-acute phase (8.5 days) was almost twice as long as in the acute phase (4.6 days) (Table 3 and Figure 2).

A minority of patients (114; 0.3%) required ICU admission due to COVID-19, most commonly during the acute phase (108). Few patients were admitted to the ICU in the post-acute phase (11) and only one required MV. The mean length of stay was much longer in post-acute-phase ICU admissions (19.1 days) than in acute-phase admissions (7.3 days).

Overall, 4,169 patients (9.3%) had at least one COVID-19-related ED visit, with a mean of 1.1 visits per patient. Most ED visits occurred in the acute phase (4,077) and did not require hospitalization (3,950). More than half of patients (57.3%) had an office visit, with most such visits occurring during the acute phase (56.6%). The mean number of office visits per patient was similar in the acute phase (1.1) and post-acute phase (1.3) (Table 3 and Figure 2).

One-tenth (4,507; 10.4%) of patients had at least one outpatient hospital visit; most outpatient hospital visits occurred during the acute phase (4,343). The mean number of outpatient hospital visits per patient was 1.1 in the acute phase and 1.3 in the post-acute phase. At least one outpatient prescription was recorded in about one-third (31.1%) of patients, most commonly during the acute phase. The average number of prescriptions per patient was 1.1.

Costs

All-cause

The overall mean cost of inpatient general ward admissions was $9,016 per admission and $14,715 per patient (acute phase, $10,833 per patient; post-acute phase, $14,403 per patient) (Table 4). Results from the split care-level approach are included in the supplementary materials (Table S6). Mean costs per inpatient general ward admission were similar between the acute and post-acute phases (acute, $9,008; post-acute $8,951). Because the acute phase covered only 30 days whereas the post-acute phase continued through follow-up, phase comparisons are best interpreted using per-patient-per-month or per-admission metrics. The mean per-patient monthly cost of inpatient ward admissions was approximately seven times higher in the acute phase ($10,833) compared with the post-acute phase ($1,486), likely reflecting a higher intensity of care and procedures during the initial severe episode of COVID-19 (Table 4).

Mean costs per ICU admission were high in both the acute ($60,229) and post-acute phases ($61,234). Total mean per-patient costs of ICU admissions were higher in the post-acute phase, and per-patient monthly costs were higher in the acute phase. When MV was required in ICU admissions, costs increased substantially to an overall mean of $124,750 per admission (acute phase, $101,570; post-acute phase, $119,674) (Table 4).

Among patients who had ED visits, the average cost per visit was similar between phases (acute, $633; post-acute $637). For ED visits requiring hospitalization, the mean cost per visit was similarly comparable in the two phases (acute, $2,019; post-acute $1,827) but mean monthly costs per patient were nine times higher in the acute phase ($2,201) than in the post-acute phase ($250).

For office visits, the mean cost per visit was similar between the two phases (acute, $228; post-acute $233), but mean monthly costs per patient were higher during the acute phase ($491) than the

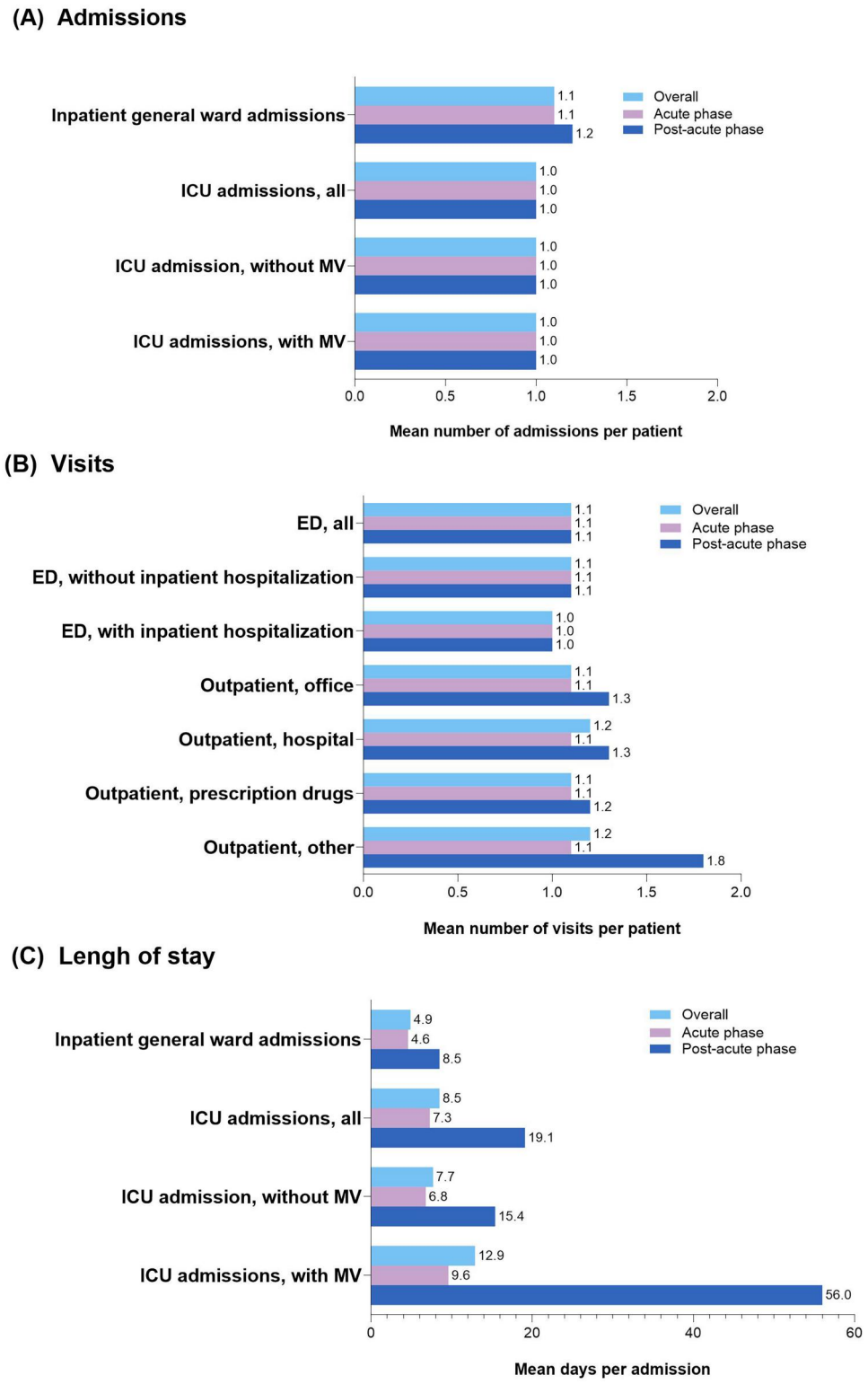

Figure 2. COVID-19-related HCRU per patient, by setting. (A) Admissions, (B) Visits, (C) Length of stay. Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; HCRU, healthcare resource utilization; ICU, intensive care unit; MV, mechanical ventilation.

post-acute phase ($262) (Table 4). Likewise, for outpatient hospital visits, mean costs per visit were similar in the two phases (acute, $1,208; post-acute $1,142), but mean monthly costs per patient were higher in the acute phase ($2,004) than in the post-acute phase ($516).

Table 4. Post-index period all-cause and COVID-19-related healthcare costs, overall and by COVID-19 phase, highest care-level approach[a].

	All-cause			COVID-19-related		
Cost type[b], mean USD (SD)	Overall	Acute phase	Post-acute phase	Overall	Acute phase	Post-acute phase
Inpatient general ward						
per admission	9,016 (19,369)	9,008 (15,843)	8,951 (20,295)	12,614 (23,788)	11,786 (20,545)	21,704 (47,801)
per patient, total	14,715 (33,872)	10,833 (19,595)	14,403 (33,913)	14,646 (39,476)	12,369 (20,802)	32,687 (95,532)
per patient, monthly	1,439 (4,504)	10,833 (19,595)	1,486 (4,975)	2,094 (7,503)	12,369 (20,802)	5,079 (16,015)
ICU admissions, all						
per admission	63,202 (132,275)	60,229 (146,893)	61,234 (113,105)	60,804 (184,291)	60,538 (182,776)	40,138 (29,320)
per patient, total	75,371 (161,326)	62,882 (147,396)	71,666 (150,992)	61,701 (184,264)	61,041 (182,722)	40,138 (29,320)
per patient, monthly	8,237 (21,196)	62,882 (147,396)	7,571 (16,670)	9,460 (34,092)	61,041 (182,722)	5,652 (4,460)
ICU admissions, without MV						
per admission	54,590 (115,401)	51,812 (143,738)	53,878 (97,898)	50,240 (176,950)	50,205 (179,111)	35,253 (25,758)
per patient, total	64,641 (144,272)	53,807 (144,275)	62,275 (134,584)	51,294 (176,980)	50,802 (179,080)	35,253 (25,758)
per patient, monthly	6,455 (14,704)	53,807 (144,275)	6,541 (15,259)	5,610 (16,776)	50,802 (179,080)	5,604 (4,699)
ICU admissions, with MV						
per admission	124,750 (219,452)	101,570 (155,599)	119,674 (210,237)	121,085 (217,853)	115,850 (197,730)	88,990 (NE)
per patient, total	135,677 (227,401)	106,577 (155,075)	130,309 (222,600)	121,085 (217,853)	115,850 (197,730)	88,990 (NE)
per patient, monthly	18,807 (41,194)	106,577 (155,075)	14,037 (22,551)	31,425 (76,926)	115,850 (197,730)	6,139 (NE)
ED visits, all						
per visit	636 (950)	633 (1,094)	637 (861)	301 (340)	300 (343)	336 (405)
per patient, total	1,434 (4,276)	843 (1,591)	1,408 (4,264)	329 (398)	322 (381)	382 (469)
per patient, monthly	146 (464)	843 (1,591)	139 (447)	46 (121)	322 (381)	38 (59)
ED visits, without inpatient hospitalization						
per visit	548 (851)	547 (980)	549 (760)	296 (333)	295 (335)	329 (411)
per patient, total	1,199 (4,075)	709 (1,442)	1,182 (4,067)	323 (391)	316 (373)	377 (477)
per patient, monthly	121 (414)	709 (1,442)	114 (416)	45 (117)	316 (373)	36 (55)
ED visits, with inpatient hospitalization						
per visit	1,884 (1,676)	2,019 (1,834)	1,827 (1,593)	427 (484)	423 (491)	473 (253)
per patient, total	2,507 (2,595)	2,201 (2,052)	2,389 (2,449)	434 (495)	429 (504)	473 (253)
per patient, monthly	265 (560)	2,201 (2,052)	250 (396)	65 (148)	429 (504)	90 (99)
Office visits						
per visit	232 (740)	228 (1,208)	233 (737)	103 (888)	103 (921)	114 (838)
per patient, total	3,103 (9,746)	491 (2,341)	2,867 (9,062)	120 (1,234)	113 (1,223)	139 (845)
per patient, monthly	269 (923)	491 (2,341)	262 (849)	17 (467)	113 (1,223)	17 (211)
Outpatient hospital visits						
per visit	1,159 (2,367)	1,208 (3,136)	1,142 (2,408)	238 (469)	239 (474)	214 (365)
per patient, total	5,867 (22,802)	2,004 (5,837)	5,566 (21,926)	291 (672)	283 (601)	314 (913)
per patient, monthly	512 (2,043)	2,004 (5,837)	516 (2,150)	35 (128)	283 (601)	41 (263)

(*continued*)

Table 4. Continued.

Cost type[b], mean USD (SD)	All-cause			COVID-19-related		
	Overall	Acute phase	Post-acute phase	Overall	Acute phase	Post-acute phase
Outpatient prescription drugs						
per patient, total	4,169 (17,147)	446 (2,030)	4,009 (16,247)	10 (605)	0 (31)	308 (3,311)
per patient, monthly	360 (1,383)	446 (2,030)	373 (1,410)	1 (42)	0 (31)	24 (246)
Other outpatient visits						
per visit	380 (1,596)	320 (2,371)	404 (2,268)	136 (1,432)	139 (1,517)	151 (1,280)
per patient, total	3,432 (29,081)	684 (4,600)	3,394 (28,939)	189 (2,201)	165 (1,868)	418 (3,654)
per patient, monthly	304 (2,326)	684 (4,600)	315 (2,425)	24 (384)	165 (1,868)	44 (357)
Post-MV costs	$N = 19$	$N = 19$	$N = 18$	$N = 19$	$N = 19$	$N = 18$
per patient, total	47,858 (81,485)	7,946 (21,983)	42,129 (74,460)	547 (1,375)	523 (1,380)	25 (92)
per patient, monthly	4,002 (5,699)	7,946 (21,983)	3,896 (5,322)	37 (81)	523 (1,380)	2 (6)
Total cost per patient						
per patient, total	15,914 (48,709)	2,165 (12,729)	13,972 (44,218)	477 (10,911)	422 (9,963)	56 (2,996)
per patient, monthly	1,429 (4,850)	2,165 (12,729)	1,315 (4,345)	68 (2,140)	422 (9,963)	8 (488)

Abbreviations. COVID-19, coronavirus disease 2019; ED, emergency department; ICU, intensive care unit; MV, mechanical ventilation; NE, not estimable; SD, standard deviation.
[a]The highest care-level approach allocated HCRU for the entire inpatient admission to the highest of three levels of care provided, which included inpatient general ward, ICU without MV, and ICU with MV [18].
[b]Costs were measured over all available follow-up periods. The denominator for mean costs includes all patients. The denominator for mean costs by care setting (e.g. ED visit costs) includes only those with $\geq$1 service use (e.g. patients with $\geq$1 ED visit). All cost measures were adjusted to 2024 US dollars using the medical component of the Consumer Price Index.

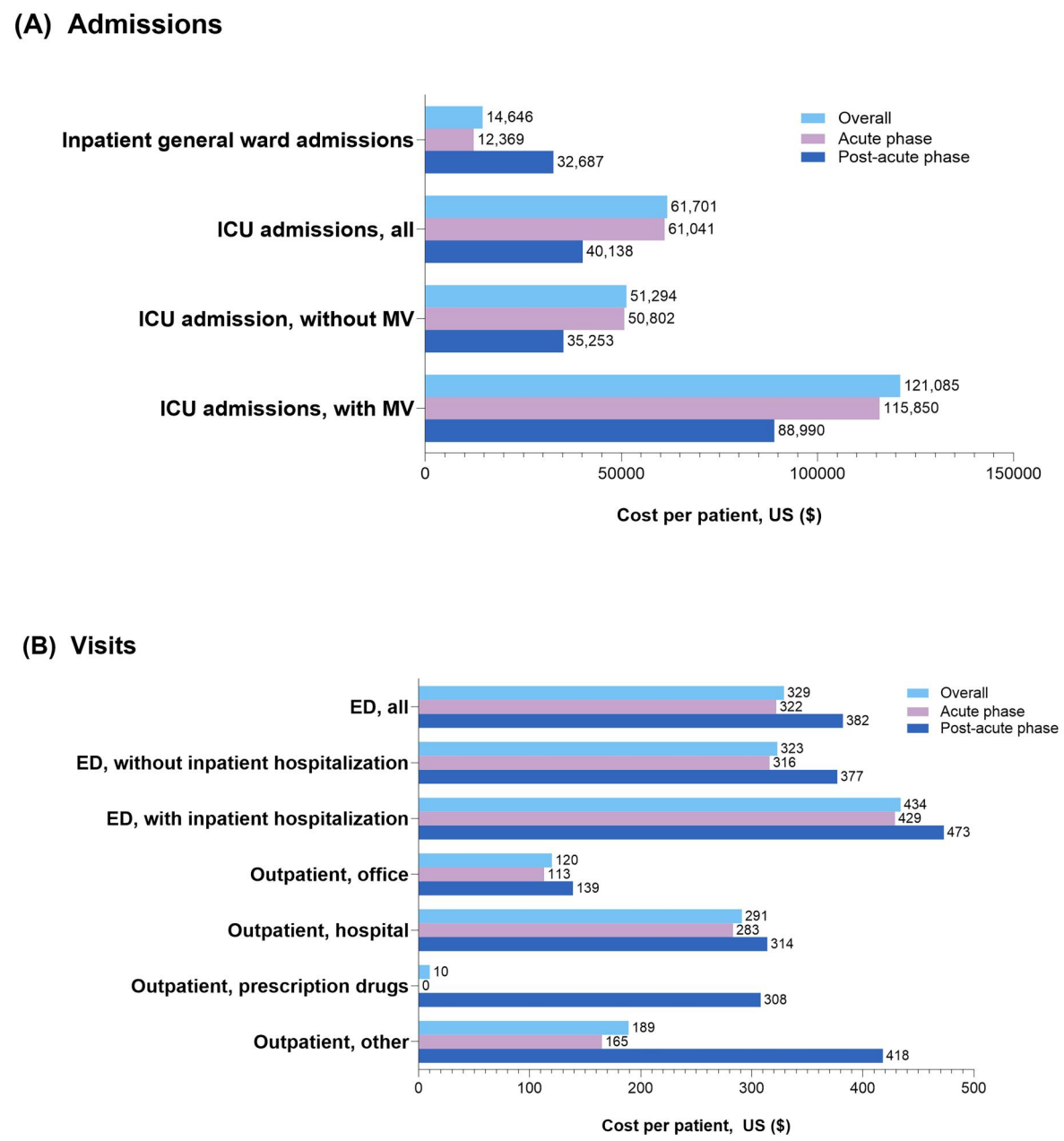

Figure 3. COVID-19-related cost per patient, by setting. (A) Admissions, (B) Visits. Abbreviations. COVID-19, coronavirus disease 2019; ED, emergency department; HCRU, healthcare resource utilization; ICU, intensive care unit; MV, mechanical ventilation.

Among patients with outpatient prescriptions, the mean monthly cost per patient was $446 in the acute phase and $373 in the post-acute phase. Following the same pattern of post-acute phase monthly cost decreases, the mean monthly cost per patient of other outpatient visits was $684 in the acute phase and about half that in the post-acute phase ($315). Mean post-MV monthly costs per patient were two times higher in the acute phase ($7,946) than in the post-acute phase ($3,896).

COVID-19-related

For COVID-19-related inpatient general ward admissions, the mean overall cost was $12,614 per admission and $14,646 per patient (Table 4). The mean monthly per-patient cost of inpatient general ward admissions was $12,369 in the acute phase and $5,079 in the post-acute phase (Table 4 and Figure 3). The mean cost per admission increased from $11,786 in acute phase to $21,704 in the post-acute phase.

For COVID-19-related ICU admissions, the mean cost per admission was higher during the acute phase ($60,538) than the post-acute phase ($40,138). For ICU admissions with and without MV, mean per-admission and per-patient costs were higher in the acute phase compared to the post-acute phase, likely reflecting a higher intensity of care and procedures during the initial severe episode of COVID-19. In both phases, per-admission and per-patient costs of ICU admissions more than doubled when MV was required (Table 4).

For COVID-19-related ED visits, the mean cost per visit was similar between phases (acute, $300; post-acute, $336), but mean monthly costs per patient were higher in the acute phase ($322) than in the post-acute phase ($38). Mean per-visit and per-patient costs of ED visits increased when hospitalization was required (Figure 3 and Table 4). Similarly, for office visits, mean costs per visit were comparable between phases (acute, $103; post-acute, $114), but the mean monthly cost per patient was $113 in acute phase and only $17 in the post-acute phase.

For outpatient hospital visits, the mean cost per visit was comparable between phases (acute, $239; post-acute, $214), but the mean monthly per-patient cost was seven times higher in the acute phase ($283) than the in post-acute phase ($41). For outpatient prescriptions, the mean monthly cost per patient was $0 in the acute phase and $24 in the post-acute phase. Mean post-MV monthly costs per patient were $523 during the acute phase and $2 during the post-acute phase.

Discussion

Using a large US administrative claims database, we evaluated HCRU and costs among adults at high risk of severe COVID-19 with up to 18 months of follow-up after COVID-19 diagnosis during the Omicron era. All patients were eligible for treatment with nirmatrelvir-ritonavir and were enrolled in private/commercial insurance plans. We found that HCRU and costs remained substantial and increased with disease severity. These findings were consistent across cost allocation approaches, supporting robustness of estimated HCRU and costs.

While outpatient encounters accounted for most HCRU (drug prescriptions, office visits, and other outpatient visits), inpatient care represented the largest component of overall costs. ICU admissions and admissions requiring MV were infrequent, as reported previously[4], but were associated with disproportionately high costs in both the acute and post-acute phases. COVID-19-related HCRU and costs remained high throughout the study period, remaining substantial even in the long-term post-acute phase.

The acute and post-acute phases of COVID-19 showed distinct HCRU and cost patterns. The acute phase was characterized by infrequent but high-severity events associated with high per-patient costs. In contrast, the post-acute phase accounted for the most cumulative HCRU and costs through sustained all-cause inpatient, outpatient, and ED care, and prescription drug use, indicating the broader economic burden high-risk patients accrue beyond the acute infection period. Our findings are consistent with a previous study showing that healthcare needs often persist after recovery from acute COVID-19, particularly in outpatient settings[19]. Because the highest care-level approach was used to estimate costs, COVID-19-related costs per patient in the acute phase were higher than in the post-acute phase when patients required intensive care (ICU admissions with MV and without MV). In contrast, among patients admitted to the general ward, COVID-19-related costs per patient during the acute phase were lower than during the post-acute phase. The monthly per-patient costs of admission were always higher in the acute phase. These results show that the intensity of care in the acute phase led to higher costs per patient.

A previous economic assessment of patients at high risk for severe COVID-19 using the TriNetX Linked database was conducted by Goswami et al.[18] among patients diagnosed during 2020–2021, before the emergence of the Omicron variant. They reported that direct medical costs–including visit costs, oxygen support costs, and pharmacy costs–amounted to $32,543 for general ward admissions, $54,867 for ICU admissions, and $101,401 for admissions requiring MV[18]. However, their analysis did not consider the type of insurance coverage. Liu et al.[4] estimated all-cause HCRU and costs within 28 days from COVID-19 diagnosis during the first four months of the Omicron era. Although they did not strictly focus on high-risk patients, results were stratified by the presence of severe comorbidities. Using the

HealthVerity database, they found that 19% of patients had an admission to the ICU, with mean length of stay (8 days) similar to the findings from the current analysis (8 days). They also found that the mean cost was $15,905 for inpatient hospital admissions, $35,577 for ICU admissions without MV, and $77,790 for ICU admissions with MV. Total costs were higher for older patients (≥65 years) and those with risk factors for severe COVID-19 outcomes. Costs increased with each additional comorbidity, both in patients who were never admitted and in those who required hospitalization. However, their analysis included all insurance types.

Other recent studies on HCRU and costs among high-risk COVID-19 patients have focused on specific subpopulations rather than the broader high-risk population. The EPOCH-US study[8] and the EON-US study[25] included only immunocompromised patients with COVID-19 from the Healthcare Integrated Research Database. Both studies showed that COVID-19-related HCRU and costs were higher in immunocompromised patients. In the EPOCH-US study[8], total all-cause (health plan + patient paid) costs associated with a first COVID-19 hospitalization were $31,976–$95,011, depending on the severity of immunocompromise. The corresponding cost range among the general population of patients with COVID-19 was $23,365–$54,587. In the EON-US study[25], compared to the general population, the immunocompromised population had ten times higher all-cause costs ($91,703 vs $9,476; $p < 0.01$) and COVID-19-related costs ($21,226 vs $2,102; $p < 0.001$). HCRU were also significantly higher in the high-risk population.

Strengths and limitations

Using real-world evidence, this study provides insights into the healthcare system and economic burden of COVID-19, assessing both all-cause and COVID-19-related HCRU and costs during the Omicron era. As new SARS-CoV-2 variants emerge, real-world evidence is required to provide contemporaneous patterns of HCRU and costs among patients with COVID-19 who are eligible for antivirals. The present data provide contemporary evidence to inform clinical decision-making and improve patient outcomes. Moreover, this research emphasizes the necessity of continued access and optimal antiviral treatment among patients at risk of progressing to severe disease. The results reported here are consistent between the two care-level approaches used in this analysis.

This study has several limitations. First, due to its retrospective design, internal validity is subject to the accuracy and completeness of coding within the underlying database. Second, COVID-19-related costs may be overestimated because costs incurred in inpatient facilities were rolled up into a single cost for the entire claim, which may have included procedures not related to COVID-19. Third, vaccinations were missing if administered outside a claim/EHR feed. Fourth, the study was limited to patients with commercial insurance; therefore, the results might not be generalizable to the overall population at risk for severe COVID-19 outcomes in the US. Finally, estimates for MV should be interpreted cautiously due to the small number of events.

Conclusions

All-cause and COVID-19-related HCRU and costs for patients at risk of severe disease were substantial in the Omicron era during both acute (short-term) and post-acute (long-term) follow-up. Vaccinations and appropriate antiviral treatment management may prevent escalation to severe disease among high-risk patients, reduce severe infections, and thus decrease COVID-19-related the acute and longer-term HCRU and cost burden.

Transparency

Declaration of funding

This study was sponsored by Pfizer as part of a research contract with RTI Health Solutions.

Declaration of financial/other interests

TM, GSS, AY, and RM are employees of Pfizer Ltd and hold shares in Pfizer.

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Authors contributions

All authors adhere to the ICMJE authorship guidelines, have approved the final version, and agree to be accountable for all aspects of the work. During the proofs stage of this publication, the journal editors used AI to generate the descriptive text for the figures. The authors reviewed, edited, and verified all AI-generated output and accept full responsibility for the content of this publication.

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Data availability statement

All data relevant to the study are included in the article or uploaded as supplementary information.

ORCID

Tendai Mugwagwa http://orcid.org/0000-0001-7515-8548
Benjamin A. Abramoff http://orcid.org/0000-0002-6005-3505
Siddharth Karanth http://orcid.org/0000-0002-4923-2692
Tram Nham http://orcid.org/0009-0009-3389-2782
Ravi K. Goyal http://orcid.org/0000-0003-1632-036X
Elizabeth Esterberg http://orcid.org/0000-0003-0780-4776
Gurinder S. Sidhu http://orcid.org/0009-0000-8726-8648
Alon Yehoshua http://orcid.org/0009-0009-2920-916X
Ruth Mokgokong http://orcid.org/0000-0002-6278-4969

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