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Keywords: COVID-19; influenza; vaccination; hospitalization; real-world evidence; mRNA vaccines



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Article

# Incidence of COVID-19 and Influenza-Related Outcomes and Vaccinations in the United States, October 2022 Through December 2024

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## Abstract

**Background/Objectives:** We still do not clearly know whether COVID-19 continues to impose a greater clinical burden than influenza in the “post-pandemic” era. Our study quantified and compared monthly COVID-19 and influenza hospitalization incidence among adult subgroups from October 2022 through December 2024. We assessed vaccine coverage trends and examined vaccination status among those hospitalized. **Methods:** Using the Veradigm linked claims and electronic health record dataset, we conducted a non-interventional, retrospective cohort study; three monthly cohorts included individuals aged 65+, high-risk (HR) adults (defined as adults 18+ with HR conditions and/or aged 65+), and adults aged 50–64 years who were enrolled with both medical and pharmacy coverage. We estimated monthly cumulative incidence of COVID-19 and influenza-related hospitalizations, vaccination coverage rates, and the proportion of hospitalized individuals who had received seasonal vaccines. **Results:** COVID-19 hospitalizations consistently exceeded those of influenza across months and populations. Among adults aged 65+, COVID-19 hospitalization rates were 2–3 times higher than influenza in winter and 20–30 times higher during off-season months, with similar trends observed in high risk adults. COVID-19 incidence surged in summer, while influenza remained seasonally confined. Vaccination coverage for influenza peaked near 50% annually; COVID-19 coverage was lower, peaking at ~26% by December each year. Most hospitalizations occurred among unvaccinated individuals, particularly for COVID-19. **Conclusions:** COVID-19 continues to impose a substantial, year-round burden, particularly in older and high-risk adults, exceeding that of influenza. The high proportion of unvaccinated hospitalizations highlight a critical gap in prevention efforts and underscore the need for improved public health messaging and vaccine adoption.

**Keywords:** COVID-19; influenza; vaccination; hospitalization; real-world evidence; mRNA vaccines

## 1. Introduction

Respiratory viruses such as influenza and SARS-CoV-2 (the virus which causes COVID-19) continue to drive significant morbidity and mortality worldwide. Historically, influenza has been a perennial concern, causing an estimated 3–5 million cases of severe illness and 290,000–650,000 respiratory deaths annually, often clustering during the winter months in temperate climates, where indoor activities result in higher transmission [1]. Influenza epidemiological trends have shaped what we consider the “respiratory season”, typically defined as October to May in the US, with peak activity from December to February [1,2]. However, when SARS-CoV-2 emerged in 2019, it quickly eclipsed previous respiratory threats, disrupting normal seasonal patterns and placing unprecedented strain on healthcare systems globally [3–5]. Notably, SARS-CoV-2 has not remained clustered during the ‘respiratory season’, resulting in summer surges and persistent healthcare

demand [5,6]. As such, surveillance systems which rely on influenza seasonality to define the “respiratory season” do not reflect COVID-19 transmission patterns and will not accurately reflect the true burden of disease [7,8].

In the post-pandemic period, there continues to be discussion around whether COVID-19 or Influenza provides the highest burden of disease. Some epidemiological and clinical studies suggest convergence in severity between the two infections under certain conditions—such as Omicron-predominance and high population immunity—while others indicate that COVID-19 still leads to higher rates of hospitalization, ICU admission, mechanical ventilation, and death. For example, a recent study in the Veterans Affairs Health System, covering the 2023–2024 winter season, found that patients hospitalized with COVID-19 had a 35% higher adjusted 30-day mortality compared to those with influenza (5.7% vs. 4.2%) [9]. Similarly, an 8-hospital cohort in Michigan reported that COVID-19 was associated with a 30% greater risk of a composite endpoint of ICU admission, mechanical ventilation, or in-hospital death compared to influenza between January 1, 2021, and July 20, 2024 [10]. However, some surveillance network analyses have observed narrowing gaps between severe COVID-19 and influenza outcomes since mid-2022, possibly due to improved treatment, vaccination, and natural immunity [11,12].

Beyond potential differences in clinical severity, vaccine availability and uptake also present additional challenges in comparing disease burden between respiratory infectious diseases. Each year, the majority of seasonal influenza vaccines are FDA approved, and become available in the US in August. Since the advent of yearly updates, COVID-19 vaccines have had a less predictable timeline, specifically with adult vaccines being available in August–October 2022 (2022–23 season), September–November 2023 (2023–24 season) and August 2024 (2024–25 season). This fluctuation leads to confusion, missed opportunities, and subsequent lower vaccine uptake [13]. It is worth noting that in early 2024 the FDA released a proposed timeline for yearly COVID-19 vaccines to align to the process for influenza vaccines, and this was adhered to in the 2024–25 season, resulting in August approvals for both COVID and the majority of influenza vaccines [14]. Vaccine uptake has also had its challenges in recent years. Looking at the last decade, self-reported influenza vaccination coverage among US adults 18 and older peaked in the 2020–21 season at 50%, though it has declined to 45% for 2023–24 [15]. In contrast, self-reported updated COVID-19 booster coverage has remained substantially lower—approximately 20%, among all adults for the 2024 season, and as low as ~43% among those aged 65 and older. This discrepancy in vaccination rates hints at the growing variety of concerns patients have regarding COVID vaccines, including safety, effectiveness, risk perception, lack of trust in the government and others, and the need for targeted campaigns focused on increasing rates [16].

Emerging vaccine technologies may help simplify immunization programs, reduce system inefficiency and mitigate missed vaccination opportunities. For instance, several influenza/COVID-19 combination vaccines are under development [17], including an investigational multicomponent influenza/COVID-19 mRNA vaccine which recently met noninferiority criteria compared with co-administered standard vaccines in adults  $\geq 50$  years in a large phase 3 trial [18]. Such innovations have the potential to result in increased COVID vaccination rates.

Despite these advances, uncertainties remain and diverging hypotheses persist: are COVID-19 and influenza now clinically comparable in severity due to evolving immunity, preventative strategies and treatment, or does COVID-19 still pose a disproportionate threat? Specifically, it is still unclear what impact seasonal behavioral factors, viral evolution, and waning immunity may have on hospitalization patterns.

To address these questions, our study quantified and compared monthly COVID-19 and influenza hospitalization incidence among adults aged 50–64 years, aged  $\geq 65$  years, and high-risk (HR) adults (defined as adults 18+ with HR conditions and/or aged 65+). We assessed vaccine coverage trends and examined vaccination status among those hospitalized.

## 2. Methods

We conducted a series of retrospective monthly cohort analyses to assess the incidence of hospitalization with COVID-19 or influenza burden from October 1st, 2022, through December 31, 2024, in an integrated Dataset of real-world data originating from the Veradigm EHR dataset integrated with pharmacy and medical claims data, based on data availability at the time of study onset.

We assessed 3 subgroups each month: adults aged 65+, HR adults, and adults aged 50-64. For each of the 27 monthly cohorts during the study period, patients were included if they met the age criteria on the first day of the indicated month in the linked dataset who are enrolled with both pharmacy and medical for the indicated month. To assess HR conditions, patients were required to have evidence of at least one of the HR conditions documented at any point during the 365 days prior to the start of the indicated month. HR conditions were defined as conditions associated with increased risk of severe COVID-19 outcomes, as defined by the Centers for Disease Control and Prevention (CDC) [19]. These included asthma, cancer, cerebrovascular disease, chronic kidney disease, chronic liver disease, chronic lung disease, cystic fibrosis, dementia, diabetes mellitus, disability, heart conditions, HIV, mental health conditions, obesity (body mass index > 30), pregnancy, primary immunodeficiencies, respiratory tuberculosis, smoking, and solid organ or stem cell transplant, and use of select immunosuppressive medications, as recorded in the database.

In each monthly cohort, we assessed the monthly cumulative incidence of hospitalizations, vaccination coverage, and vaccination rates among hospitalized patients independently for both COVID-19 and influenza. Hospitalizations were defined as a hospitalization with COVID-19 or influenza diagnosis in any position, respectively. Patients were considered up to date on their vaccination if they received a COVID-19 vaccine updated for the respiratory season after the date the seasonal vaccination update was approved (August 31, 2022; September 11, 2023; August 22, 2024) and before the next seasonal approval. For influenza, all vaccinations after July 15th of the given year were assumed to be updated vaccinations.

All results were reported descriptively. Incidence and corresponding 95% confidence intervals (CIs) were calculated per 100,000 individuals for all outcomes for each month. Incidence ratios were calculated by dividing the incidence of COVID-19 by the incidence of influenza for each month. All baseline categorical characteristics were reported as counts and percentages. No statistical testing was performed. Analyses were conducted using SAS V9.4 (SAS, Cary, NC).

This study was designed and implemented and reported in accordance with Good Pharmacoepidemiology Practice (GPP), with applicable local regulations and with the ethical principles laid down in the Declaration of Helsinki. Given this is a retrospective database study using de-identified data, adverse event reporting was not applicable. As a noninterventional, retrospective database study using a certified Health Insurance Portability and Accountability Act-compliant deidentified research database, approval by an institutional review board was not required.

## 3. Results

A total of 47,778,112 patients were aged 18 and over, including 8,559,461 (17.9%) aged 65 or older, and 13,602,755 aged 50-64. Over 25 million patients (54.3%) of the study population had an underlying medical condition, making them high-risk for severe outcomes with COVID-19. The most common underlying conditions were hypertension (30.9%), endocrine disorders, including Type 1 and Type 2 diabetes (25.6%), and obesity (24.2%). More than half (57.2%) of the study population was female. Demographics and clinical characteristics of the full adult population are available in Table 1. Demographic and clinical characteristics by monthly cohort are presented in Supplementary Table S1.

**Table 1.** Demographic and clinical characteristics.

	<b>All Patients <sup>1</sup></b>	
	<b>N = 47,778,112</b>	
<b>Female (N, %)</b>	27,344,682	57.2%
<b>Age, in years, at start of month (Mean, SD)</b>	47.5	17.6
18-49 years old (N, %)	25,615,896	53.6%
50-64 years old (N, %)	13,602,755	28.5%
65+ years old (N, %)	8,559,461	17.9%
<b>High-risk conditions during 12-months prior to the first day of the month (N, %)</b>		
<b>Any</b>	25,953,000	54.3%
Asthma	3,579,446	7.5%
Cancer	2,129,443	4.5%
Cerebrovascular disease	1,663,027	3.5%
Chronic kidney disease	2,394,086	5.0%
Chronic lung disease	2,558,477	5.4%
Chronic liver disease	418,744	0.9%
Diabetes type 1 or 2	6,751,500	14.1%
Heart conditions	4,015,532	8.4%
HIV	189,540	0.4%
Hypertension	14,740,708	30.9%
Mental health disorders	7,006,016	14.7%
Musculoskeletal Conditions	8,108,114	17.0%
Neurologic and neurodevelopment conditions	1,461,079	3.1%
Dementia	725,131	1.5%
Obesity (BMI >30 kg/m <sup>2</sup> )	11,543,480	24.2%
Pregnancy	1,164,440	2.4%
Primary immunodeficiencies	366,211	0.8%
Smoking, current and former	6,441,303	13.5%
Solid organ or hematopoietic stem cell transplant	115,746	0.2%
Stroke	993,238	2.1%
Use of immunosuppressants	1,664,269	3.5%
<b>Other comorbid conditions during 12-months prior to the first day of the month (N, %)</b>		
Blood disorders	6,599,115	13.8%
Cystic fibrosis	9,164	0.0%
Down's syndrome	20,017	0.0%
Endocrine disorders	12,242,571	25.6%
Disabilities	3,145,460	6.6%
Metabolic disorders	16,625,637	34.8%
Morbid obesity/class III obesity (BMI >40 kg/m <sup>2</sup> )	4,064,420	8.5%
Tuberculosis	14,916	0.0%

1. Based on first month of inclusion in the analyses

### 3.1. Incidence of Hospitalizations

In the 65+ population, incidence of hospitalization with COVID-19 was substantially higher than incidence of hospitalization with influenza for each of the 27 months of the study period. In the 2023 and 2024 calendar years, the lowest observed incidence of COVID-19 in June (0.089%) and May (0.050%), respectively, were similar to the highest observed incidence of hospitalization with influenza those same years (0.073% in Dec 2023 and 0.076% in Jan 2024). Similar trends in incidence were observed in the HR population and in the 50-64 population. See Figure 1.

In the population aged 65+, The incidence ratio between COVID-19 and influenza hospitalizations ranged from a low of 1.3 in the last month of the study period (Dec 2024) to a high of 26.5 in August 2024. Of the 27 months in the study period, more than half (n=14) had an incidence ratio of at least 10x more hospitalizations with COVID-19 than influenza, and 26 out of the 27 months

(96.2%) had more than 2x more hospitalizations with COVID-19 than influenza. Similar trends were seen in the HR population and in the 50-64 population (See Figure 2).

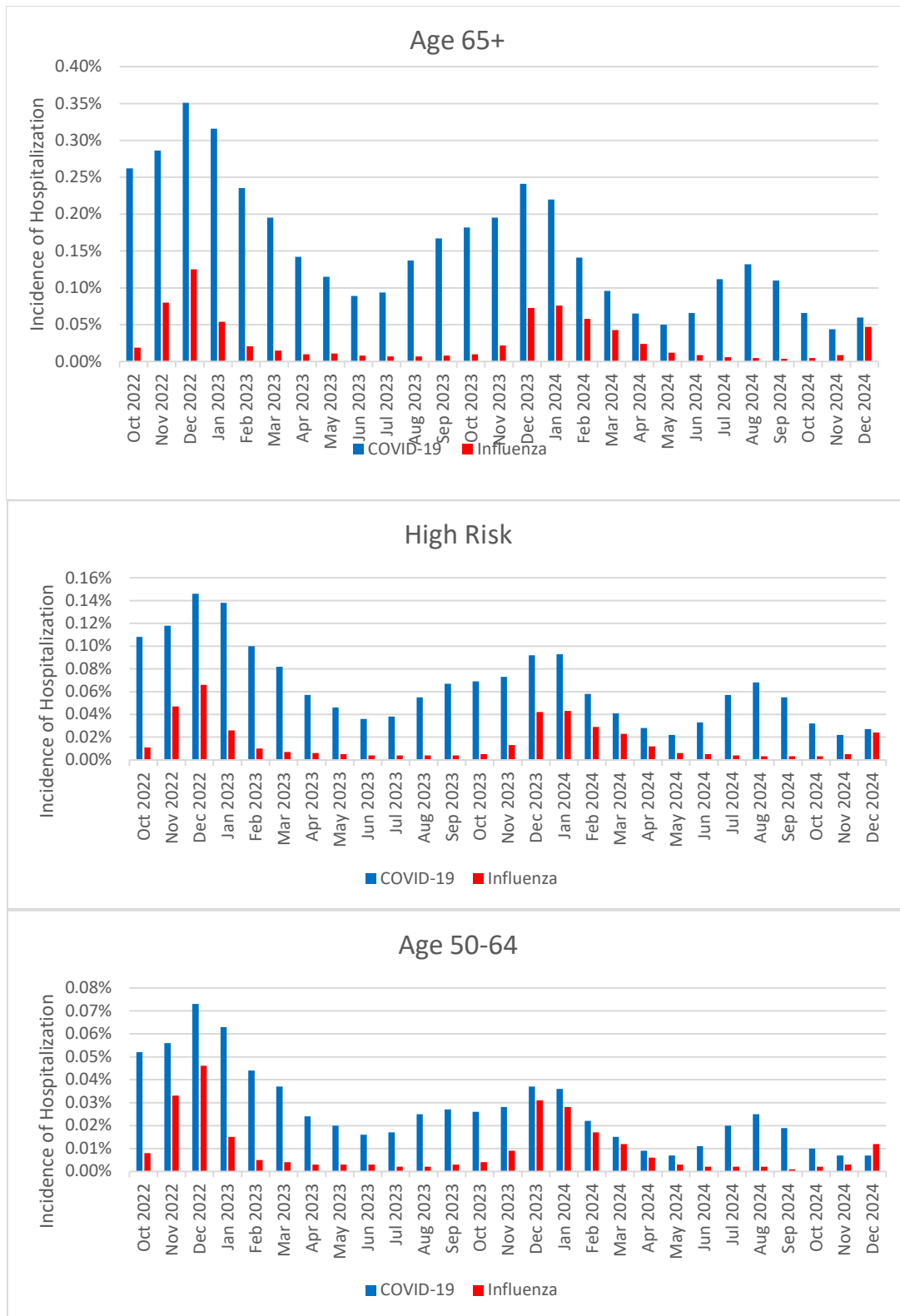
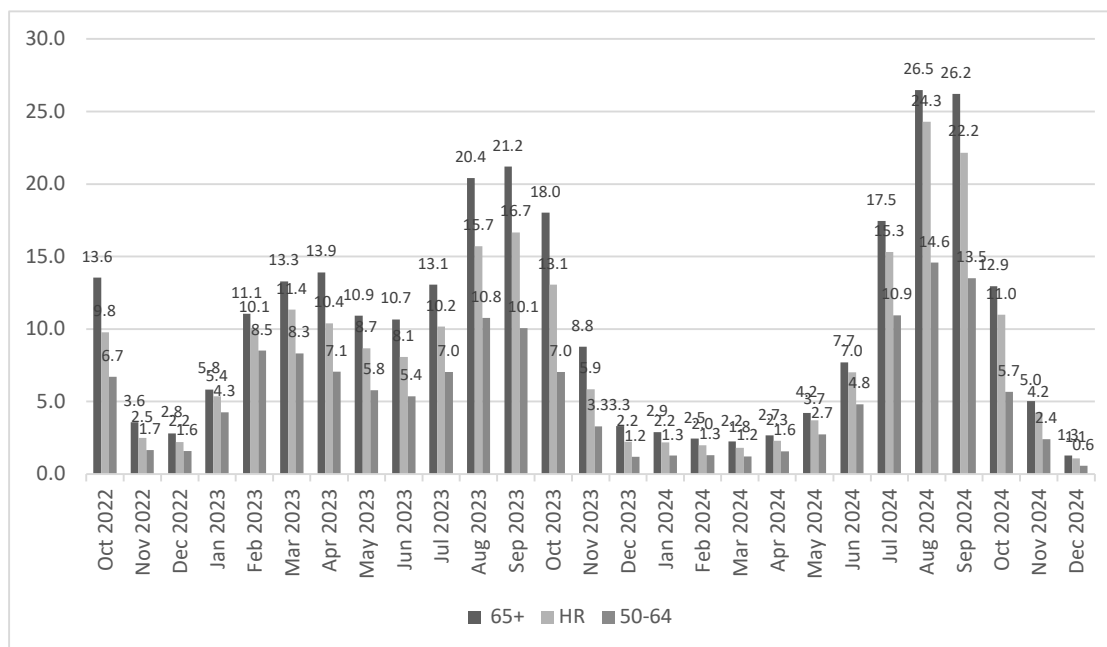


Figure 1. Monthly Incidence of Hospitalizations with COVID-19 and Influenza.

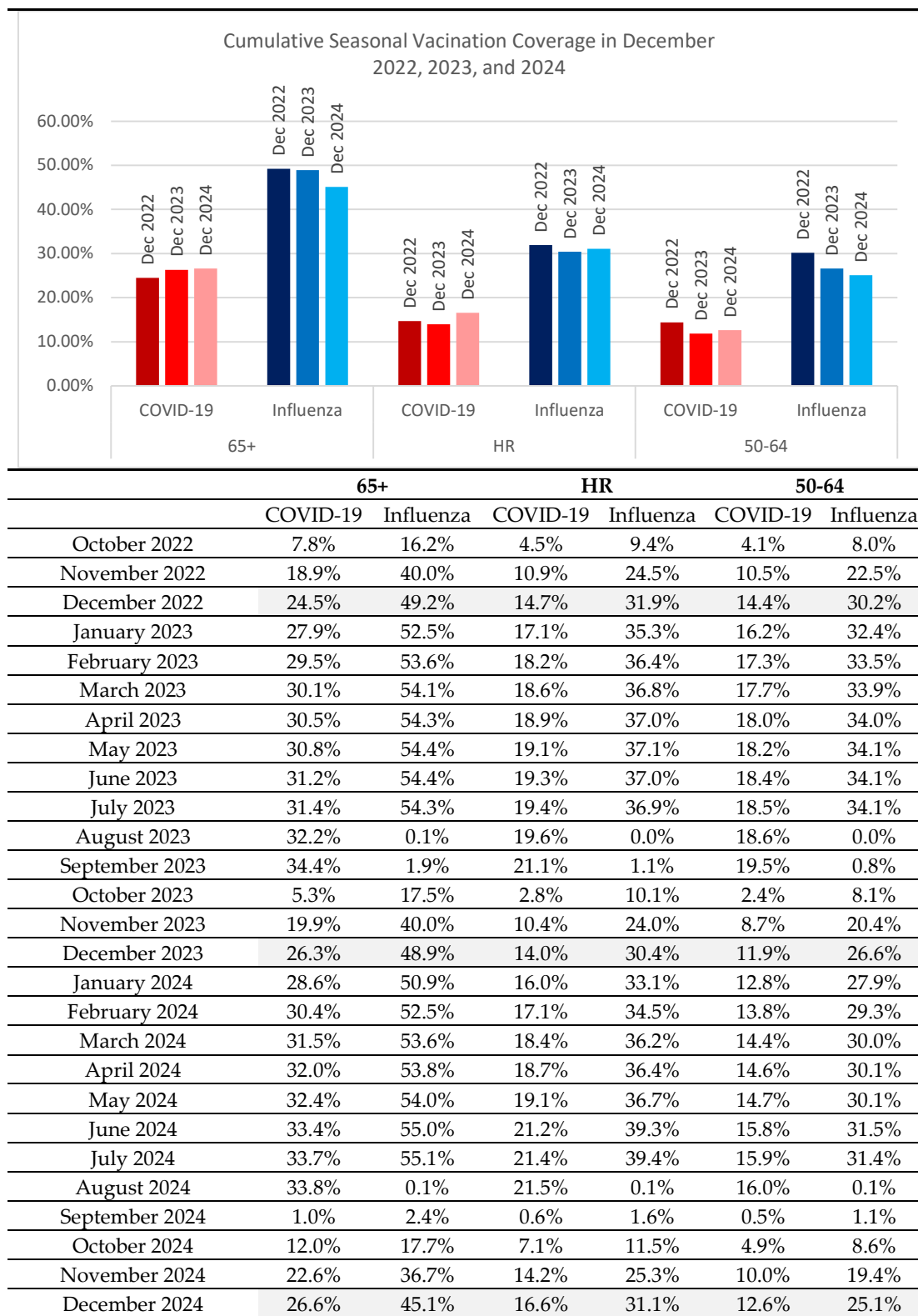




**Figure 2.** Incidence Ratio of Hospitalizations with COVID-19 to Influenza, by Age Group and Month.

### 3.2. Vaccine Coverage Trends

Vaccine coverage rates (VCR) were consistently higher for influenza vaccination as compared with COVID-19 vaccination during the course of the study. Notably, in each season, COVID-19 vaccine availability trailed influenza vaccine availability except for the 2024-25 season, which may have resulted in lower uptake of COVID-19 vaccines regardless of other factors. In the 65+ population, influenza VCR was similar across the 3 seasons, with 49.2% by the end of December 2022 (peaking to 54.3%), 48.9% by the end of December 2023 (peaking to 55.1%) and 45.1% by the end of December 2024. COVID-19 VCR was lower, 24.5%, 26.3%, and 26.6% by the end of each December, rising to 34.4% and 33.8% by the Summer of 2023 and 2024, respectively. In the HR population, we see the same trends. In the population aged 50-64, overall vaccination rates were lower, with 14.4% vaccinated by December 2022, 11.9% by December 2023, and 12.6% by December 2025 vaccinated for COVID-19, and 30.2%, 26.6%, and 25.1%, respectively, at the same months for influenza. (See Table 2).

**Table 2.** Cumulative Vaccination Coverage, by Month and Age Group.

### 3.3. Vaccinations Status Among those Hospitalized

Among those hospitalized with COVID-19 or influenza, the percentage who received an updated annual vaccination was consistently higher among those hospitalized with influenza than COVID-19, reflecting the lower vaccination coverage for COVID-19. With the earlier roll-out of the

influenza vaccine in the years of the study period, we also see the earlier vaccinations reflected in the data. By December 2024, approximately 80-90% of hospitalizations with COVID-19 were not up to date on their vaccinations across the age groups assessed. See Figure 3.



**Figure 3.** Proportion of Hospitalizations Who Did Not Receive Current Seasonal Vaccination.

#### 4. Discussion

In this large, retrospective analysis of over 47 million adults in the United States, we found that COVID-19 hospitalizations consistently exceeded those of influenza across all age and risk groups between October 2022 and December 2024. Among adults  $\geq 65$  years, COVID-19 hospitalization incidence was 2–3 times higher than influenza during winter respiratory seasons and up to 20–30 times higher during summer months. Similar patterns were observed in adults aged 50–64, though at lower absolute rates. These findings suggest a persistent, year-round COVID-19 burden that frequently surpasses seasonal influenza, particularly in older adults.

This study aligns with recent national and international reports showing that COVID-19 continues to impose a disproportionately greater clinical burden compared with influenza. A Veterans Affairs study reported 35% higher adjusted mortality for COVID-19 than influenza hospitalizations during the 2023–2024 winter season [9]. Likewise, CDC RESP-NET surveillance has documented age-adjusted COVID-19 hospitalization rates nearly double those of influenza in adults

[6]. European data similarly indicate that SARS-CoV-2 activity persists across longer seasonal windows than influenza, often with bimodal peaks [5] Taken together, this reinforces that COVID-19 is not fully seasonalized and remains a major driver of hospital demand outside of traditional influenza months.

A key secondary finding of our study was the persistent gap in vaccine coverage between influenza and COVID-19. Seasonal influenza vaccine uptake approached 50% among adults  $\geq 65$  years each winter, while COVID-19 coverage plateaued at ~25–27% by December. This discrepancy was even greater among adults aged 50–64. Importantly, most hospitalizations for both COVID-19 and influenza occurred among individuals who had not received a seasonal updated vaccine, though the gap was more pronounced for COVID-19. These results highlight missed opportunities for prevention and echo CDC survey reports of low updated vaccine uptake (15–40% by age group) among US adults in 2023–2024 [20].

The lower uptake of COVID-19 vaccines in the US relative to influenza likely reflects several factors, including vaccine misinformation, evolving perceptions of COVID-19 severity, and barriers to access [16,21,22]. Public health strategies emphasizing the comparable—or greater—burden of COVID-19 relative to influenza may help address these challenges. Innovations such as combined influenza/COVID-19 vaccines may also improve convenience and acceptance, thereby narrowing coverage gaps [23,24].

#### *Strengths and Limitations*

This study has several strengths, including the use of a large, linked claims–EHR dataset spanning multiple seasons, and the consistent methodology applied to both COVID-19 and influenza outcomes. However, limitations should be noted. First, the dataset used in this analysis is limited to insured individuals, mainly commercial insurance. Uninsured individuals and those with certain types of insurance, such as those who receive their healthcare through the Veterans Health Administration, are not captured in this dataset. Nevertheless, this integrated dataset has been shown to be generally representative of the US and has also been used in our previous analysis to evaluate the Covid-19 burden, which were highly aligned with CDC data highlighting the volume and robustness of the dataset [25–27]. Second, we used a diagnosis of Influenza or COVID-19 at any diagnostic position, which captures patients who are hospitalized for any reason and then test positive for influenza or COVID-19, respectively. This could inflate the incidence of both outcomes if they are heavily tested, especially among patients with non-severe disease who would not otherwise have been hospitalized. If patients are tested at different frequencies for influenza and COVID-19, the incidence of the under-tested condition will be lower due to the testing practices. Finally, the cumulative incidence was estimated each month independently, so a single episode of disease (either COVID-19 or influenza) could show up in the data as an event in subsequent months if the patient is re-admitted. This methodology allows for interpretation of burden on the healthcare system by month, but may over-estimate total incidence of disease if months are pooled together.

## 5. Conclusions

Our findings provide timely, real-world evidence of the sustained burden of COVID-19 relative to influenza and the persistent gaps in seasonal vaccination coverage. These data support continued public health messaging on the importance of updated yearly COVID-19 vaccination, particularly among older and high-risk adults, in an era where apathy has grown and the public underestimates the risk, particularly versus that of influenza. Furthermore, we continue to see COVID-19 hospitalizations outside of the traditional respiratory season and year-to-year variation in burden due to the pathogenicity of circulating strains. For these reasons, vaccination remains the best way to be prepared for unpredictable COVID-19 epidemiology.

**Supplementary Materials:** The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Table S1: Part 1. Demographic and clinical characteristics by monthly cohort; Part

2. Demographic and clinical characteristics by monthly cohort; Part 3. Demographic and clinical characteristics by monthly cohort.

**Author Contributions:** Conceptualization, A.W., M.B. and I.W.; Methodology, A.W., M.B. and I.W.; Formal Analysis, I.W., C.A. and T.L.; Investigation, A.W., M.B. and I.W.; Data Curation, I.W., C.A. and T.L.; Interpretation of Data, H.H., Y.P. and K.J.; Writing—Original Draft Preparation, A.W., M.B. and I.W.; Writing—Review and Editing, H.H., Y.P., K.J., T.L., C.A., I.W., M.B. and A.W.; Supervision, A.W., M.B. and I.W. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** This study was conducted in accordance with the Declaration of Helsinki and relevant guidelines for observational research. Ethical review and approval were not applicable for this study because it used de-identified administrative and clinical data and did not involve direct patient contact or intervention.

**Informed Consent:** The research involved de-identified administrative and clinical data and did not require direct patient involvement. Patient consent was not applicable because the study used anonymized, de-identified data and did not involve direct patient participation; the data were anonymized and complied with patient privacy regulations.

**Data Availability Statement:** The data that support the findings of this study were used under license from Veradigm and Komodo Health. Due to data use agreements and its proprietary nature, restrictions apply regarding the availability of the data. Further information is available from the corresponding author.

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**Conflicts of Interest:** Authors A.W., K.J., T.L., Y.P., and H.H. are employees and stockholders of Moderna, Inc. Authors M.B., I.W., C.A. are employees of Veradigm, which was contracted by Moderna and received fees for data management and statistical analyses. The sponsor participated in the design of the study, data analysis, interpretation of the data, review of the manuscript, and the decision to submit the manuscript for publication.

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