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Original Article

Impact of universal masking in reducing the risk of nosocomial respiratory viruses among people with cancer

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Abstract

Background: Universal masking within healthcare settings was adopted to combat the spread of coronavirus disease 2019 (COVID-19). In addition to mitigating the risk for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, it also had an added benefit of preventing the nosocomial transmission of other respiratory viral diseases.

Objective: This study examines the impact of the masking intervention on nosocomial respiratory viral infections (RVI) in vulnerable sub-populations of people with cancer at a tertiary care hospital.

Design: Interrupted time series analysis.

Methods: We reviewed non-SARS-CoV-2 nosocomial RVI between January 1, 2017 and December 31, 2023 and compared its quarterly trends before (January 2017 to March 2020) and after (April 2020 to December 2023) the universal masking intervention was implemented.

Results: Prior to the masking policy, there was no significant change in the quarterly rate of non-SARS-CoV-2 nosocomial RVI (baseline trend: $P = 0.662$). Crude infection rates decreased from 5.6% preintervention to 4.3% after the masking policy was implemented ($P < 0.001$). Quarterly trends continued to steadily decline post-intervention ($\beta = -0.10$, SE = 0.04, $P < 0.007$).

Conclusions: Our results suggest that universal face masking is associated with reduced non-SARS-CoV-2 nosocomial RVI, providing further evidence to support the continued use of face masks in healthcare settings to protect the health of immunocompromised patients.

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Introduction

During the initial phase of the coronavirus disease 2019 (COVID-19) pandemic, universal masking was implemented in many healthcare settings to reduce the nosocomial spread of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Subsequently, in addition to COVID-19 reduction, many hospitals observed a concurrent and rapid decline in the incidence of other healthcare-associated respiratory viral infections (RVI).[1–3] With the end of the public health emergency, the Centers for Disease Control and Prevention (CDC) have allowed institutions to relax masking requirements. High population-level immunity and more widely available effective treatments have led many healthcare facilities in the United States to update their universal masking policies and revert to masking as part of standard precaution measures and in only limited circumstances, such as when healthcare professionals are caring for patients with respiratory symptoms.[4] Emerging studies suggest the benefits of masking extend to prevention of several respiratory viral pathogens.[5,6]

Respiratory infections are the leading cause of high mortality, morbidity, and therapy failure of primary diseases for immunocompromised patients. Among critically ill patients with influenza, 12.5% were immunocompromised and had a mortality that was 2.5 times as high as those who were non-immunocompromised.[7] Furthermore, it has been shown that many of these infections are acquired in a healthcare setting.[8–10] For example, in a study performed among 67 adult bone marrow transplant patients, 48% of RVI were associated with nosocomial transmission.[11] Given the frequency of nosocomial acquisition of these viruses and the high morbidity and mortality associated with them, infection control measures that include masking can be an essential tool to mitigate nosocomial spread to severely immunocompromised patients.

In the present study, we assess the impact of universal masking in reducing the nosocomial spread of common RVI. We hypothesize that the intervention of masking for source control which was implemented to reduce nosocomial spread of SARS Cov-2 resulted in a decrease in the number of non-SARS-CoV-2 hospital-acquired RVI among people with cancer.

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Methods

Memorial Sloan Kettering Cancer Center (MSKCC) is a 514-bed tertiary cancer care center in New York that treats more than 400 different subtypes of cancer and is devoted to the prevention, treatment, and care of patients with cancer and associated diseases. The MSKCC Institutional Review Board (IRB) reviewed the study and granted a Health Insurance Portability and Accountability Act (HIPAA) waiver of authorization. To assess the impact of the universal masking policy on non-SARS-CoV-2 nosocomial RVI, we conducted a quasi-experimental interrupted time series analysis pre- and post-intervention. Retrospective data of hospitalized patients at MSKCC diagnosed as having nosocomial RVI between January 1, 2017 and December 31, 2023 were collected. The primary outcome of interest was the quarterly non-SARS-CoV-2 nosocomial RVI rate of patients with incident positive human rhinovirus/enterovirus, coronavirus, metapneumovirus, influenzas A and B, parainfluenza viruses (types 1–4), and respiratory syncytial virus. To normalize the data for community transmission, infection rate was calculated as the proportion of non-SARS-CoV-2 nosocomial RVI divided by the overall number of non-SARS-CoV-2 respiratory infections in the same period. Sensitivity analyses were then performed to assess whether possible biases could have affected our findings.

Masking policy in the pre- and post-period

In April 2020, following the CDC's recommendations on masking for hospitals and other healthcare settings, MSKCC implemented a masking policy that required all individuals with direct patient contact, including caregivers, visitors, and healthcare personnel (HCP) to wear a mask regardless of suspicion of RVI. The main intention of this recommendation was to reduce the nosocomial spread of COVID-19 by source control, especially from asymptomatic or minimally symptomatic individuals. However, we hypothesize the intervention also resulted in a decrease in the number of non-SARS-CoV-2 hospital-acquired RVI. Of note, before the study commenced, masking during direct patient care was only performed as part of transmission-based or standard precautions, or as part of protective isolation for transplant recipients. No patient-specific masking policy was implemented. There have been no changes to universal masking during direct patient care since this policy was implemented.

Definitions for nosocomial and community-acquired

Infections were considered nosocomial when symptoms developed three or more days after hospital admission or if the patient was readmitted within three days of discharge with a positive respiratory viral test on admission. If symptom onset was not available, laboratory onset date was used to characterize the nosocomial infection incident. Community-onset cases were classified as infections diagnosed at the time of admission or detected within the first two days of hospitalization. The pre-COVID-19 masking period was defined as January 2017 to March 2020; and the post-COVID-19 period was defined as April 2020 to December 2023. All data were collected from institutional electronic medical records.

Testing for respiratory virus infections (RVI)

Testing for RVI in both the pre- and post-intervention periods was performed only for symptomatic patients using a multiplex polymerase chain reaction (PCR) method.

Statistical approach

The crude relative risk was calculated by dividing the cumulative incidence of nosocomial respiratory virus infection cases in the post-COVID masking intervention period by that of in the pre-intervention period; 95% confidence intervals were calculated by the Wald method. We then used interrupted time series estimation with segmented regression methods to assess the change in quarterly rates (expressed as percentages) of respiratory virus infections before and after the intervention period. Using the PROC GENMOD procedure, the quarterly rates were modeled using a quasi-Poisson distribution with a log-link function to allow for over-dispersion. Incidence rate ratios (IRR) were calculated by taking the exponent of the coefficient estimate.

The baseline period for the interrupted time series analysis comprised 13 annual quarters (January 2017–March 2020) before the intervention and 15 annual quarters (April 2020–December 2023) after the intervention. In this study, lag effects were not characterized because we aimed to explore the total rate of nosocomial respiratory infections across the full period after the intervention.

Results from the segmented regression model were analyzed for time (representing the pre-intervention trend), intervention (representing the change in level of the outcome immediately prior to and immediately after the intervention), and time after the intervention (representing the difference in time trend between the pre- and post-intervention periods). To test for the presence of autocorrelation in the time series analyses, we performed a visual inspection of residual plots. Using the Durbin–Watson (DW) statistic, we tested up to fourth-order autocorrelation and found no evidence of autocorrelation within the model (DW = 1.98). A two-sided $P < 0.05$ was considered statistically significant. The segmented regression analysis is as follows:

$$Rate_t = \beta_0 + \beta_1 * time_t + \beta_2 * intervention_t + \beta_3 * time\ after\ intervention_t + e_t$$

$Rate_t$ *is* the nosocomial respiratory infection rate where t is the annual quarter. β_0 estimates the baseline level of the nosocomial respiratory infection rate at the beginning of the study. β_1 estimates the pre-intervention trend where $time_t$ is a continuous variable starting from January 2017 indicating the number of annual quarters from the start of the study period. β_2 estimates the change in level in the first quarter following the implementation of the intervention. Finally, β_3 estimates the change in trend after the intervention where $time\ after\ intervention_t$ is a continuous variable starting from April 2020, indicating the number of annual quarters that have passed since the intervention was implemented.

All statistical analyses were performed with SAS (version 9.4; Cary, NC).

Results

During the pre- and post-universal masking intervention period, 760 (5.6%) and 434 (4.3%) cases of nosocomial respiratory virus infections were diagnosed, respectively. For community-acquired infections, there were 12,894 cases pre- and 9,740 cases post-intervention. Compared to the pre-intervention period, the overall relative risk of nosocomial RVI was 23% lower during the postperiod (RR = 0.77, 95% CI = 0.68–0.86). Overall crude infection rates decreased from 5.6% before to 4.3% after the masking policy was implemented ($P < 0.001$). For most non-SARS-CoV-2 nosocomial

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Table 1. Frequency of respiratory viruses pre- and post-masking intervention

	Pre-period[a]		Post-period[a]		
Respiratory viruses	**Total respiratory infections[b]**	% Nosocomial	**Total respiratory infections[b]**	% Nosocomial	***P***
Coronavirus[c]	2,223	5.7%	1,395	5.1%	0.456
Human rhinovirus/enterovirus	5,758	4.9%	5,434	4.1%	0.038
Influenza					
Influenza A	1,432	5.5%	659	3.2%	0.020
Influenza B	530	2.6%	37	2.7%	0.982
Metapneumovirus	873	5.7%	546	2.9%	0.015
Parainfluenza					
Type 1	296	7.8%	140	7.1%	0.817
Type 2	91	8.8%	131	6.1%	0.447
Type 3	904	8.4%	713	5.3%	0.016
Type 4	217	5.5%	191	5.2%	0.896
Respiratory syncytial virus	1,330	6.8%	928	4.0%	0.005
Total	**13,654**	**5.6%**	**10,174**	**4.3%**	**<0.001**

[a]Pre-period: 2017 Q1 through 2020 Q1; post-period: 2020 Q2 though 2023 Q4.
[b]Total respiratory infections include community-acquired and nosocomial cases of human rhinovirus/enterovirus, non-SARS-CoV-2 coronavirus, metapneumovirus, influenzas A and B, parainfluenza viruses (types 1–4), and respiratory syncytial virus.
[c]Coronavirus excludes SARS-CoV-2.

Table 2. Quasi-Poisson segmented regression analysis of the impact of masking on quarterly rates of non-SARS-CoV-2 nosocomial respiratory viruses

Parameter	Beta coefficient [95% CI]	Standard error	Incidence rate ratio [95% CI]	***P*-value**
Baseline trend $\beta 1$	0.01 [−0.04, 0.07]	0.03	1.01 [0.96–1.07]	0.662
Level change after Intervention $\beta 2$	1.92 [0.84, 2.99]	0.55	6.82 [2.31–19.88]	<.0001
Trend change after intervention $\beta 3$	−0.10 [−0.18, −0.03]	0.04	0.90 [0.83–0.97]	<.007

respiratory viruses, the percentage of nosocomial infections decreased from the pre-intervention period. The breakdown of infections by pathogen is shown in Table 1.

Table 2 summarizes the results of the segmented regression analyses of the study outcomes. Figure 1 illustrates the magnitude, time course, and direction of the changes in the non-SARS-CoV-2 nosocomial RVI rates during the pre- and post-intervention periods. Findings show that prior to the universal masking intervention, there was no significant quarter-to-quarter change in this rate (IRR = 1.01; 95% confidence interval (CI): 0.96–1.07). A significant rate increase was observed in April 2020 (IRR = 6.82; 95% CI: 2.31–19.88) when universal masking was implemented as a response to the rise in SARS-CoV-2 infections. After the intervention was initiated, rates of non-SARS-CoV-2 nosocomial RVI dropped, decreasing from 14.5% at the onset of the intervention to 13.2% in the subsequent quarter. Quarterly trends continued to steadily decline post-intervention (IRR = 0.90; 95% CI: 0.83–0.97).

To further investigate the trends in non-SARS-CoV-2 nosocomial respiratory viruses during the study period, we conducted two sensitivity analyses. First, we examined the effect on viruses associated with high morbidity and mortality by excluding rhinovirus infections from the analysis and found that it did not change the significance of the trend. Second, we separately measured the impact of year-round masking in the transplant units pre- and post-intervention and found the risk of non-SARS-CoV-2 nosocomial RVI was comparable in the two transplant units (RR = 1.03).

Discussion

In the present study, we demonstrate a significant and sustained decline in the proportion of nosocomial non-SARS-CoV-2 respiratory infections with universal masking during direct care of hospitalized high-risk patients with cancer. We attribute this decrease to universal source control via masking, thereby mitigating the risk of spread from healthcare workers and visitors.

Nosocomial respiratory viruses are a significant cause of morbidity and mortality among people undergoing cancer treatment, especially those with hematologic malignancy and hematopoietic stem cell transplant recipients,[12] in whom progression to severe respiratory disease is common and attributable mortality can be up to 10%.[13] Furthermore, a fifth of all cases of hospital-acquired pneumonias are due to RVI.[14] Small and large particle respiratory droplets spread respiratory viruses. Hence, HCP and visitors who may be asymptomatic or mildly symptomatic and have prolonged close contact with hospitalized patients are an important source of unrecognized transmission.

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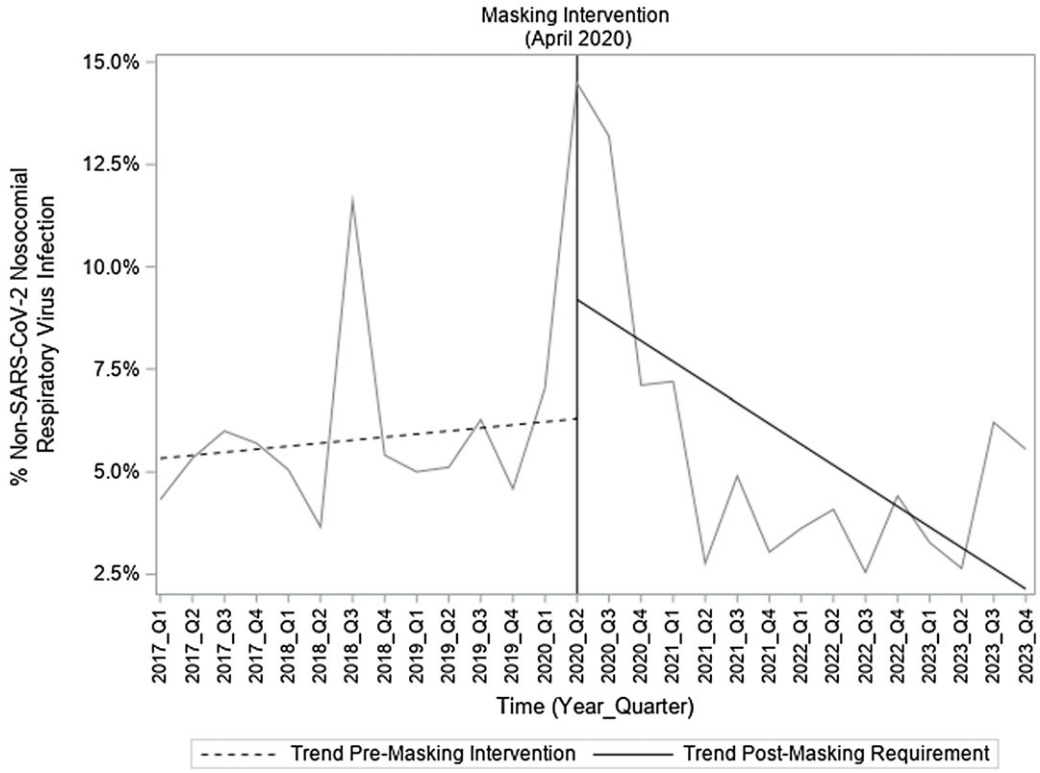

Figure 1. Interrupted time series analysis of the impact of the masking intervention on non-SARS-CoV-2 nosocomial respiratory viral infections. Respiratory viruses include human rhinovirus/enterovirus, coronavirus, metapneumovirus, influenzas A and B, parainfluenza viruses (types 1–4), and respiratory syncytial virus.

Several studies describe the role of HCP as a source of outbreaks in high-risk cancer patients[15] and the role of universal masking in combating respiratory virus outbreaks.[16]

Strategies to protect vulnerable patients in non-outbreak settings include addressing presenteeism, masking on high-risk units during the respiratory season, and prescribing seasonal antiviral prophylaxis, where feasible. There is wide variability in current and past practices and no clear consensus on the best and most practical approach. Notably, a study conducted at Duke University[17] in the pre-COVID-19 era implemented universal masking between 2010 and 2014 on a stem cell transplant unit. A 60% reduction in RVI was observed, with the most notable decrease in parainfluenza infection type 3 during the non-winter months. Allogenic transplant recipients who are at a higher risk of severe infection compared to autologous recipients had a larger significant reduction in RVI incidence with universal mask use. RVI-related deaths also decreased. In the Duke study, compliance with masking was high and other high-risk units did not see a simultaneous decline, strengthening the conclusion that mask use led to a decline in RVI among high-risk cancer patients who have undergone stem cell transplants. Similar studies from other transplant centers have also arrived at the same conclusions.[18] More recently, Ehrenzeller et al.[5] demonstrated a 44% and 53% reduction in hospital-onset influenza and respiratory syncytial virus, respectively, with precautions implemented since the COVID-19 pandemic at a large academic center in Boston.

When interpreted in concert with the current understanding of the direct and indirect health risks posed by nosocomial RVI and the effect of masking in RVI prevention in outbreak and non-outbreak settings, our study adds to the existing evidence by demonstrating the benefits of universal masking during care delivery as an effective RVI prevention strategy. We propose the broad adoption of masking as the standard-of-care for hospitalized cancer patients. Although the enhanced infection control measures in hospitals during the COVID-19 pandemic are potential confounders, universal masking in conjunction with other infection prevention measures are key approaches to control the nosocomial transmission of respiratory viruses. Results from this study support the continued use of masks in the clinical setting as an integral component of standard precautions for immunocompromised people.

Our study had several limitations. First, misclassification of nosocomial and community-acquired cases may have occurred; however, this would have affected the rates in a nondifferential manner. Second, we observed unusually high peaks in non-SARS-CoV-2 nosocomial RVI rates in 2020 Q2 and Q3 in the segmented regression analysis. This may be due to several factors: testing for RVI in 2020 Q2 and Q3 was aberrant compared to other periods due to the challenges to clinical and public health laboratories posed by the COVID-19 pandemic. These included shortfalls in testing supplies such as reagent solutions and test swabs which hindered testing capacity and decreased RVI detection. Additionally, to reduce public density and mitigate the transmission of COVID-19, New York State issued a statewide lockdown during this time where social distancing and stay-at-home restrictions markedly reduced the risk of community-acquired and nosocomial RVI commonly encountered during these months. These combined factors resulted in an unusually small number of RVI in 2020 Q2 and Q3 compared to other study quarters leading to what we consider to be spuriously inflated non-SARS-CoV-2 nosocomial respiratory rates during these periods. Third, while pre-post studies can be affected by regression toward

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the mean effects, our study differs from this phenomenon for two reasons. Due to its ability to conduct multiple measurements across time, interrupted time series are among the strongest observational research designs and can address threats to internal validity including regression to the mean.[19–21] Moreover, non-SARS-CoV-2 nosocomial respiratory infections were repeatedly higher before the masking intervention, decreased shortly after the intervention, and remained repeatedly lower in comparison to the pre-period thereafter. Finally, adherence to the mask-wearing policy was also not evaluated.

Despite these limitations, our study also has several unique strengths. First, we measured the incidence of nosocomial infections as rate proportions to account for the low community rates and less testing of all non-SARS Cov-2 infections in the early part of the COVID-19 pandemic—a major gap in previously published studies.[22,23] Second, the sample size, representing a high-risk patient population who are at a greater risk for adverse complications from nosocomial RVI, was large. Third, although there may have been underlying secular trends that were occurring simultaneously as the study period, a lengthy follow-up period when other short-term non-pharmacologic measures and social precautions had largely ceased highlights the observed sustained reduction was likely due to masking rather than unrecognized confounders. Finally, the exclusive focus on RVI and the degree and timing of the effect suggest a strong association between masking and infection transmission.

In conclusion, although mask utilization is becoming less ubiquitous in the current phase of the COVID-19 pandemic, the results of this present study support continued mask use during patient interaction in healthcare settings as a measure to help prevent and control nosocomial transmissions of all respiratory viruses, not just SARS-CoV-2, in immunocompromised populations.

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Competing interests. N.E.B. has received research grants from GenMark Diagnostics and ArcBio/Canta and is on the advisory board at Bio-Rad Molecular, Agena Diagnostics, and ArcBio/Canta; M.K. has acted as a consultant for Regeneron and has received speaker fees for WebMD/Medscape.

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