Assessing the Impact of Comorbidities on Respiratory Virus Prevalence Across Age Groups in Washington State

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ABSTRACT

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Background. Respiratory viruses, such as respiratory syncytial virus (RSV), human metapneumovirus (hMPV), and parainfluenza viruses (PIV) 1-4 cause significant disease burden. Vaccines against RSV are now in use in the United States to protect specific populations, including older adults and young infants, and hMPV and PIV vaccines are in development. There are few data on community-based estimates of RSV, hMPV and PIV in individuals with comorbidities, particularly in younger adults. These data are needed to identify additional at-risk groups who would benefit particularly from vaccination.

Methods. We conducted active surveillance for ambulatory care visits for acute respiratory illness (ARI) among members of a health care provider network, Kaiser Permanente Washington (KPWA), a site in the US Flu Vaccine Efficacy Network. Enrolled participants provided respiratory specimens which were tested for 12 respiratory viruses via polymerase chain reaction. We estimated the prevalence of infection due to each virus by age group and comorbidity.

Results. The KPWA population who presented for ARI and received swab tests consisted of 4,335 unique individuals tested from 2018 to 2023. After rhinovirus (106 per 1000), RSV (93 per 1000), hMPV (63 per 1000), and PIV (50 per 1000) were the most detected viruses. Prevalence

of RSV was highest in the youngest (0-5) and oldest (60+) age groups. However, cases followed a more heterogenous distribution among individuals with comorbidities, where individuals under 60 with cancer, chronic liver disease, pulmonary disease, diabetes, or a history of organ transplant had higher prevalences than adults above 60 without comorbidities. RSV prevalence also differed by racial/ethnic groups, with higher prevalences of RSV among individuals who self-identified as Black, American Indian/Alaska Native, or Native Hawaiian/Pacific Islander.

Conclusions. Among individuals with ARI symptoms under 60, we found that individuals with comorbidities such as cancer, chronic liver disease, and a history of organ transplants, as well as individuals of Black, Native Hawaiian, or American Indian/Alaska Native race/ethnicity had a higher prevalence of RSV infection. Clinical recommendations for vaccination and prevention should consider the impact of comorbidities to minimize morbidity related to respiratory viruses among high-risk populations.

Keywords: respiratory syncytial virus, parainfluenza, human metapneumovirus, prevalence, viruses

Introduction

Respiratory syncytial virus (RSV), human metapneumovirus (hMPV), and parainfluenza virus (PIV) cause severe respiratory illness in infants and young children as well as older adults[1,2].[3]. Recent studies have shown that patients hospitalized with RSV are more likely to receive standard flow oxygen therapy and be admitted to the ICU compared to people hospitalized with COVID-19 or influenza; and more likely to receive intensive mechanical ventilation or die compared to people with influenza[5]. Further, preliminary studies have shown that patients above 50 are the most likely age group to be hospitalized for RSV, and that above 90% of RSV cases in this age group have at least one comorbidity[6]. More recent data has also shown that American Indian/Alaska Native, Black, Native Hawaiian, and Hispanic patients account for a larger proportion of respiratory virus-related hospitalizations, likely driven by racial and ethnic disparities in underlying health conditions, socioeconomic factors including living and working environments, and access to medical care[7],[8]. However, while the burden of disease in hospitalized adults is increasingly recognized, the recognized burden of disease in the community is still very limited. This could partly be due to the lack of routine testing for these viruses in older children and adults in the outpatient setting. Further, the impact of different comorbidities on infection prevalence among different age groups, particularly in larger populations, is unexplored.

More detailed information on the outpatient epidemiology of respiratory viruses is necessary to better understand their impact among various populations, especially considering recent developments in prevention. For the first time, the potential exists for widespread RSV prevention, given the 2023 release of the two first publicly available RSV vaccines, Arexvy and Abrysvo; and the first monoclonal antibody treatment for RSV in infants, nirsevimab, in 2022[9][10][11]. The Centers for Disease Control and Prevention recently added nirsevimab to the standard child immunization schedule[12]. In the US, vaccine approval was granted by the Food

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and Drug Administration (FDA) to adults aged 60 and over (May 2023) and to pregnant individuals at 32 to 36 weeks gestational age (August 2023), with the intended effect of preventing RSV infection in infants[13][14]. Further, the FDA recently granted GlaxoSmithKline priority review for use of Arexvy among adults aged 50 to 59[15]. No vaccine or treatment currently exists for hMPV or PIV, though Icosavax recently completed a Phase II Trial for a combined hMPV/RSV VLP-based vaccine showing robust immune induction against both viruses one month after vaccination[16].

The release of the vaccines and monoclonal antibody comes at a unique time in the context of RSV, as rates reached a historic low during the Covid-19 pandemic (2020-2022) but soared in the latter half of 2022 after pandemic restrictions were relaxed[17]. This surge was particularly pronounced in Washington State, where multiple new viral strains with higher fitness were first detected[18]. RSV rates have been elevated in the 2023-2024 season compared to pre-pandemic, and as of February 2024, there have been 67 RSV deaths in Washington, compared to 98 by this point in the 2022-2023 season, and 16 in the 2021-2022 season[19].

Nevertheless, a substantial portion of the population remains without access to RSV vaccines. A particular area of need is among people with comorbidities, particularly those known to exacerbate symptoms associated with other acute respiratory infections (ARIs) such as Influenza and Covid-19: comorbidities known to contribute to severe illness in combination with ARIs include heart failure, chronic obstructive pulmonary disorder (COPD), asthma, and type II diabetes mellitus[20]. The risk of mortality is also sharply elevated in cases of ARI among people with one or more of these comorbidities[21]. Covid-19 is a case example of the excess risk associated with these comorbidities: people with Covid-19 who had been previously diagnosed with obesity were 1.3 times more likely to die of Covid-19; and, alarmingly, people

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with Covid-19 who had more than one of the above comorbidities were between 1.5 and 3.8 times as likely to die of Covid-19[22].

The objectives of this study are to 1) identify the prevalences of respiratory syncytial viruses, human metapneumovirus, and parainfluenza virus stratified by comorbidity status, age group, and race/ethnicity; and 2) to use these results to make recommendations about future vaccine distribution among adults under 60 years old.

Methods

1. *Study Design*

This analysis of RSV and other respiratory viruses among patients in a large healthcare network followed a test-negative design[23]. The dataset used was a subset of the US Influenza Vaccine Efficacy Network, described previously (from here on described as the US Flu VE Network)[24]. The primary exposures evaluated include comorbidities related to medically attended acute respiratory illnesses: namely pulmonary conditions (Asthma, COPD), cardiac conditions (congestive heart failure, general cardiovascular disease), cancer, type II diabetes mellitus, chronic liver disease (CLD), and organ or stem cell transplant status[26]. Comorbidity status was ascertained through EHR review using ICD-10 codes (see Appendix 1 for all included codes). The main outcome assessed in this analysis was non-influenza respiratory viral infection status, which was previously ascertained as described in Jackson et al.[27]. Briefly, viral infection status was determined by collecting nasal and oropharyngeal swabs from patients. Then, a multiplex RT-PCR assay was performed to detect any of 20 respiratory viruses[28].

2. *Study Setting*

The clinical data and biospecimens for this analysis were collected as part of the Washington State site of the US Flu VE Network, details of which have been previously published[29]. Active surveillance for acute respiratory events was conducted in ambulatory care settings at Kaiser Permanente Washington (KPWA), a large non-profit health care system.

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3. *Study Subjects*

The source population of this study is based on membership in KPWA's integrated group practice: members have healthcare coverage through KPWA, receive care at KPWA medical centers, and have a primary care provider at a medical center where US Flu VE Network was occurring. Study participants were all patients at Kaiser Permanente Washington ambulatory clinics from November 2018 to March 2020 and February to September 2023. (note: due to cessation of data gathering during the Covid-19 pandemic, 2021 data was not included). For this study, patients whose 1) primary care provider was at an active surveillance recruitment site and 2) sought outpatient medical care at a KPWA site for ARI were included. ARI was defined as having a cough illness within the last 8 days. Patients in the US Flu VE Network were not included if their home medical center was not part of the KPWA or if they sought care at a site not receiving active surveillance.

4. *Data Collection*

Key study data was derived from the Kaiser Permanente Washington cohort of the overall US Flu VE Network. Briefly, the U.S. Flu VE Network started in 2003 consisting of seven study sites spread across the United States and is designed to provide estimates of clinical effectiveness of yearly flu vaccines by age group and flu virus subtype[30]. Data items from the US Flu VE Network were summarized for the purposes of this analysis and will include age, race, ethnicity, receipt of the current season's influenza vaccine, respiratory virus PCR test results, census tract of residence, and ICD-10 codes pertaining to patient comorbidities.

5. *Data Analysis*

We calculated descriptive statistics for the following variables across each comorbidity group of interest: median age, age group (0-4, 5-17, 30-39, 40-49, 50-59, 60-74, 75+ years), sex, race, ethnicity, seasonal flu vaccine status, Covid-19 vaccine status, and year of hospital visit for ARI. Age groups were defined according to the age groups used on the CDC Respiratory Virus Hospitalization Surveillance Network, RESP-NET[31]. Racial and ethnic categories were determined using two different methods. The first method classified individuals into one of five racial groups based on self-reporting: Asian American/Native Hawaiian or Pacific Islander (AA/NHPI), American Indian/Alaska Native (AI/AN), Black, White, or Multiracial. Individuals were also asked about Hispanic/Non-Hispanic status. For the purposes of data analysis, we also classified individuals by hypodescent, in which multiracial people are categorized as members of their socially subordinated racial group (e.g. classifying individuals who reported being multiracial and Native American as Native American, see *Albuja et al., 2024)*[32]. A 'non-Hispanic White' category was also created and used as the reference group for analyses involving race/ethnicity.

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We then calculated the period prevalence of non-influenza respiratory viral infections for the whole data collection period, from November 2018 to February 2023. Viruses examined included respiratory syncytial virus (RSV), human metapneumovirus (hMPV), parainfluenza virus (PIV), adenovirus, enterovirus, enterovirus-D68 (EV-D68), and rhinovirus. We performed stratified prevalence analyses according to patient groups of interest, namely age group, comorbidity, and race/ethnicity, and calculated prevalence estimates, prevalence ratios, and confidence intervals. All analyses were performed using R 4.3.1. Prevalence estimates were calculated using the *epiR* package (Version 2.0.74). Our analyses on RSV, hMPV, and PIV only will be included in this report.

IRB statement?

Results

The source cohort consisted of 4,335 unique individuals who visited a KPWA primary care center and tested positive for ARI from November 2018 to March 2020 and February to September 2023 (Table 1). A total of 1,425 (32.9%) individuals tested positive for at least one of the selected non-influenza respiratory viruses (RSV, hMPV, PIV). The cohort had a median age of 41 (SD: 23.6), and the three most represented age groups were 5-17 (n = 611), 30-39 (n=600) and 50-59 (n=586). 60.8% of the cohort were female, and 72.6% were non-Hispanic White. 12.5% were Asian American or Native Hawaiian/Pacific Islander; 5.5% were Black; 1.4% were American Indian or Alaska Native; and 8.0% were Multiracial. When the multiracial category was disaggregated by hypodescent, the percentage of Black individuals increased to 7.8%; the percentage of AI/AN individuals increased to 3.2%; and the percentage of Native Hawaiian/Pacific Islander individuals was 3.0%. 9.1% identified as Hispanic. A subset of 1,016 (23.3%) individuals had at least one of the specified comorbidities, with pulmonary conditions (Asthma, COPD, 15.6%) and diabetes (5.7%) being the most represented. Rhinovirus was the most frequently detected virus in our cohort, with 10.6% testing positive, followed by RSV at 9.3%, hMPV at 6.3%, and PIV at 5.0%.

Prevalence of viral infection was heterogenous across age, comorbidity, and racial/ethnic groups. This section will focus on RSV, hMPV, and PIV.

RSV prevalences were not uniformly higher among patients with comorbidities compared to patients without comorbidities across age groups (Table 2; Figure 1). Among individuals aged 50-59, the prevalence of RSV was 0.105 in individuals with no comorbidities, and 0.099 in those with any comorbidity. However, we observed higher prevalences in some comorbidity groups. For example, the point prevalence in the 50-59 age group was 0.125 in those with cancer, corresponding to a prevalence ratio of 1.4 [95% CI: 0.51, 3.83] when compared to individuals without cancer. Further, the prevalence was 0.2 in those with chronic liver disease (CLD, PR = 2.5 [0.61, 10.23]), and 0.143 in those with organ/stem cell transplants (PR = 1.87 [0.43, 8.08]). This compares to the 60-74 age group, in which the prevalence among individuals with cancer was 0.036 (PR = 0.92 [0.39, 2.14]), 0.091 in those with CLD (PR = 1.72 [0.38, 7.85]), and 0.429 in those with organ/stem cell transplants (PR = 6.28 [2.75, 14.34]). We also observed higher prevalence of RSV among individuals with any of these three comorbidities in younger age groups (5-17, 30-39). Notably, the prevalences among individuals 50-59 with comorbidities typically indicated for vaccine distribution were lower than the prevalences for individuals with no comorbidities: individuals 50-59 with pulmonary conditions had a prevalence of 0.097 (PR = 0.98 [0.51, 1.9]), and those with cardiac conditions had a prevalence of 0.053 (PR = 0.73 [0.15,

3.48]). Further, individuals with pulmonary conditions in the 18-29 age group had the highest prevalence of RSV (0.127; PR = 3.02 [1.41, 6.45]); chronic liver disease among those in the 30-39 age group (0.5; PR = 8.33 [2.56, 27.06]).; and diabetes in the 40-49 age group (0.16, PR = 2.86 [1.15, 7.11]).

RSV prevalence also differed among racial and ethnic groups (Figure 4). Except for Hispanic/Latino individuals (0.184), non-Hispanic White individuals had the lowest prevalence of RSV in the 0-4 age group (0.27), compared to 0.34 among AA/NHPI, 0.375 among AI/AN, and 0.5 among Black and Native Hawaiian/Pacific Islander individuals. Black children aged 0-4 years had 1.47 [95% CI: 0.93, 2.31] times the prevalence of RSV as Non-Hispanic White children; AI/AN individuals had 1.41 [0.56, 3.57] times the prevalence; and NH/PI individuals had 1.88 [1.06, 3.36] times the prevalence in this age group. Non-Hispanic White and AI/AN individuals had the lowest prevalence in the 5-17 age group (0.083), compared to a maximum of 0.125 among NHPI individuals (PR = 1.57 [0.59, 4.22]).

Prevalences of RSV were lower among all other groups in the 50-59 age group category compared to non-Hispanic White individuals, except for Hispanic/Latino individuals (0.118 compared to 0.108, PR = 1.12). In contrast, a pronounced difference in prevalence was observed in the 40-49 age group, where Black (0.088, PR = 1.24 [0.39, 3.99]) and AI/AN (0.100, PR = 1.43 [0.36, 5.74]) individuals showed higher prevalence. A similar trend was observed in the 30-39 age group, where Black individuals had the highest prevalence of any group (0.109, PR = 1.69 [0.66, 4.31]).

Similar trends were observed among individuals with hMPV (Figure 2). Among patients without comorbidities, we observed increases in hMPV prevalence with increasing age (except for the 0-4 age group). However, no such trend was observed among patients with comorbidities. Patients with pulmonary conditions in the 0-4 age group had higher prevalence compared to all older patients without comorbidities (0.148; PR = 2.0 [0.79, 5.05]); patients with pulmonary conditions in the 50-59 age group had similarly higher prevalence (hMPV prevalence of 0.117; PR = 1.83 [0.96, 3.49]). Prevalences were likewise higher among patients with cancer, particularly in the 40-49 (0.071; PR = 1.69 [0.36, 8.03]) and 50-59 (0.083; PR = 1.34 [0.4, 4.52]) age groups; however, the prevalence of hMPV among cancer patients aged 60-74 and 75+ was lower than among patients without cancer. Prevalence was again higher among individuals 50-59 who had an organ/stem cell transplant (0.143; PR = 8.41 [1.15, 61.52]) and individuals who have chronic liver disease (0.2; PR = 1.67 [0.12, 23.67]).

PIV prevalence showed different associations with comorbidities (Figure 3). PIV prevalence among individuals in the 40-49 age group with pulmonary illness was more than twice that of individuals without pulmonary illness (0.067 compared to 0.031). Further, while data on individuals with diabetes was not available for every age group, all age groups represented but for the 50-59 age group had higher PIV prevalence than individuals without comorbidities. We also observed higher prevalence among individuals who had an organ/stem cell transplant in the 50-59 age group: 0.286 compared to 0.051 among individuals who had never had a transplant.

Discussion

In this study, we estimate the burden of non-influenza respiratory viruses in an outpatient population of 4,335 individuals receiving care for acute respiratory illness at Kaiser Permanente

Washington Healthcare centers from 2018-2020 and in 2023. Compared to the state of Washington, our cohort was more Female; had more White, Black, Asian, American Indian/Alaska Native, Asian American, and Native Hawaiian/Pacific Islander individuals; and had fewer Hispanic individuals[33]We found that the prevalences of RSV, hMPV, and PIV were generally elevated in the presence of certain comorbidities (pulmonary, cardiac, cancer, chronic liver disease, and organ/stem cell transplant status). We further observed that the age distribution of individuals with a respiratory virus infection varied by the presence of a comorbidity. Among individuals without a comorbidity, the youngest and oldest age groups display the highest prevalence, in agreement with previous studies.[1,2,4] However, we find that other age groups were at higher risk if they had cancer, chronic liver disease, or an organ/stem cell transplant, pulmonary disease, or diabetes; or if they are Black, Native Hawaiian/Pacific Islander, or American Indian/Alaska Native.

Our study expands on the understanding of how specific factors, including comorbidities and race/ethnicity, impact respiratory virus prevalence among different age groups. Previous studies have found that RSV prevalence and hospitalizations were elevated among individuals with comorbidities: Havers et al. (2023) found that of 1,634 patients above 60 years old hospitalized for RSV, 95.5% had at least one underlying comorbidity, the most common being cardiovascular disease and pulmonary conditions[7]. Malosh et al. (2018) assessed comorbidities among 1,308 individuals hospitalized for ARI and found that 98% of individuals in the 50-64 age group had at least one comorbidity; and that individuals with RSV admitted to the hospital had a higher Charlson Comorbidity Index[6]. Our study extends on these findings by examining the impact of comorbidities among individuals under 60 years old in those in the outpatient setting and examining a larger set of comorbidities. Following, our results among these typically healthier adult age groups suggest that comorbidities may be a driver of risk independent of age.

We similarly observed that individuals with certain comorbidities had increased prevalence of hMPV and PIV across age groups, though the prevalence of hMPV was generally lower among individuals with comorbidities, including those with cancer, chronic liver disease, and organ/stem cell transplant. To our knowledge, these are the first results observed on a population level including both pediatric and adult populations. Individuals with cancer had high prevalence of hMPV in the 5-17, 40-49, and 50-59 age groups. Individuals with chronic liver disease and organ/stem cell transplants also had high hMPV prevalence. Further, while changes in PIV prevalence among individuals with comorbidities were limited, we did observe a large increase in prevalence in the 18-29 and 40-49 age groups. While the prevalence ratios we calculated were inconclusive, our estimates suggest that comorbidities may also be drivers of risk independent of age for hMPV and PIV as well.

Our analysis of RSV among different racial/ethnic populations corroborate results from previous studies[7]. Black, NHPI, and AIAN individuals had higher prevalences of RSV among the youngest (0-4) and oldest (75+) groups; and Black and AIAN individuals also showed higher prevalences in the middle age groups. While this finding may be driven by different age distributions within the catchment population, it likely also reflects disparities in underlying medical and environmental conditions and socioeconomic status. Further, the use of

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hypodescent to analyze race and ethnicity provided more granular data on community-level disparities than the aggregated multiracial approach.

The CDC currently recommends RSV vaccination for adults ≥60 years using shared clinical decision-making, which may consider a patient's risk for severe disease[35]. Our results suggest that age-based criteria are not sufficient, and that special attention be given to underlying medical conditions in RSV vaccination. Focus must also be placed on equitable access for AI/AN, Black, and NH/PI communities, who faced higher burdens of illness in different age groups compared to non-Hispanic White individuals. Future vaccine development and distribution efforts for respiratory viruses must also consider these factors: while Arexvy is currently in priority review for use among individuals aged 50-59, no efforts have been made thus far to distribute vaccines to other adult age groups based on underlying comorbidities.

This study does have several limitations. Our surveillance definition required that all enrollees have ARI with cough, thus excluding individuals who presented without a cough and likely underestimating the burden of infection given the frequently mild symptoms of RSV, hMPV, and PIV. Similarly, this study measured prevalence among people who sought ambulatory medical care at a large healthcare provider and may differ compared to the prevalence of illness in community or inpatient settings, as well as among those without insurance coverage. Further, respiratory illness rates in Washington State have been elevated since the Covid-19 pandemic, and it is possible that patterns of illness have changed since this data was collected, which primarily contains observations from 2018-2020. Moreover, sample size in many comorbidity and demographic groups was limited, likely increasing the error of our estimates.

Regardless, our study provides one of the first assessments of the prevalence of multiple respiratory viruses among individuals of different comorbidity and age groups. We show that comorbidities disrupt age-based patterns of respiratory virus spread and recommend that future prevention efforts focus on individuals facing underlying comorbidities and health disparities, who are not included in the current age criteria.

[35] Melgar, M., Britton, A., Roper, L. E., Talbot, H. K., Long, S. S., Kotton, C. N., & Havers, F. P. (2023). Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023. MMWR. Morbidity and Mortality Weekly Report, 72(29), 793–801. https://doi.org/10.15585/mmwr.mm7229a4

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Table 1. Demographic Characteristics and Diagnoses of the KPWA Cohort.

		Overall (n = 4335)
Age		
	Median (SD)	41 (23.6)
Age Group (n, %)		
	0-4	347 (8.0)
	5-17	611 (14.1)
	18-29	536 (12.4)
	30-39	600 (13.8)
	40-49	544 (12.5)
	50-59	586 (13.5)
	60-64	320 (7.4)
	65-69	277 (6.4)
	70-74	239 (5.5)
	75+	265 (6.1)
Sex (n, %)		
	Female	2635 (60.8)
	Male	1700 (39.2)
Hispanic		393 (9.1)
Race (CDC)		
	AA/NHPI	494 (12.5)
	AI/AN	55 (1.4)
	Black	218 (5.5)
	White, Non-Hispanic	2871 (72.6)
	Multiracial	318 (8.0)
Race (Hypodescent)		
	Any NH/PI	130 (3.0)
	Any AI/AN	138 (3.2)
	Any Black	338 (7.8)
Flu Shot		2747 (63.4)

Covid Shot[1]	***2023 Only***	623 (87.3)
Comorbidity		
	Pulmonary (Asthma/COPD)	677 (15.6)
	Cardiac (CHF/CVD)	120 (2.8)
	Cancer	171 (3.9)
	Diabetes	247 (5.7)
	Chronic Liver Disease	22 (0.5)
	Transplant	18 (0.4)
Viral Infection		
	RSV	378 (9.3)
	hMPV	255 (6.3)
	PIV	203 (5.0)
	Adenovirus	95 (2.3)
	Rhinovirus	429 (10.6)
	Enterovirus	59 (1.5)
	Enterovirus-D68	6 (0.1)

SD = Standard Deviation. AA/NHPI = Asian American/Native Hawaiian/Pacific Islander; AI/AN = American Indian/Alaska Native; NH/PI = Native Hawaiian/Pacific Islander. COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; CVD = Cardiovascular disease. RSV = Respiratory syncytial virus; hMPV = Human Metapneumovirus; PIV = Parainfluenza virus.

Table 2. Prevalence of RSV by Age Group and Comorbidity Status (estimate [95% CI]).

	Age Group							
	0-4	*5-17*	*18-29*	*30-39*	*40-49*	*50-59*	*60-74*	*75+*
Number of Cases	94	51	27	34	33	54	57	28
Any Comorbidity (n, %)	7 (7.4)	9 (17.6)	8 (29.6)	3 (8.8)	9 (27.3)	16 (29.6)	31 (54.3)	18 (64.3)
Dx								
No Comorbidities	0.278 [0.229 , 0.331]	0.087 [0.063 , 0.116]	0.047 [0.028 , 0.072]	0.069 [0.047 , 0.096]	0.067 [0.043 , 0.098]	0.105 [0.075 , 0.141]	0.095 [0.065, 0.132]	0.096 [0.047 , 0.17]
Any Comorbidities	0.269 [0.116 , 0.478]	0.094 [0.044 , 0.171]	0.127 [0.056 , 0.235]	0.041 [0.008 , 0.114]	0.071 [0.033 , 0.13]	0.099 [0.058 , 0.155]	0.056 [0.037, 0.082]	0.155 [0.095 , 0.234]
Any Pulmonary Illness (Asthma/COPD)	0.269 [0.116 , 0.478]	0.075 [0.031 , 0.149]	0.133 [0.059 , 0.246]	0.035 [0.004 , 0.121]	0.087 [0.041 , 0.159]	0.097 [0.045 , 0.176]	0.085 [0.047, 0.139]	0.088 [0.029 , 0.193]
Any Cardiac Illness (CHF/CVD)	0 [0 , 0.975]	0 [0 , 1]	0 [0 , 1]	0 [0 , 0.975]	0 [0 , 0.842]	0.053 [0.001 , 0.26]	0.083 [0.023, 0.2]	0.102 [0.034 , 0.222]
Cancer	0 [0 , 0.975]	0.5 [0.013 , 0.987]	0 [0 , 1]	0 [0 , 0.41]	0 [0 , 0.232]	0.125 [0.027 , 0.324]	0.062 [0.021, 0.14]	0.209 [0.1 , 0.36]
CLD	0 [0 , 1]	0 [0 , 1]	0 [0 , 1]	0.5 [0.013 , 0.987]	0 [0 , 0.602]	0.2 [0.005 , 0.716]	0.091 [0.002, 0.413]	0 [0 , 1]
Diabetes	0 [0 , 1]	0.5 [0.013 , 0.987]	0 [0 , 0.602]	0 [0 , 0.308]	0.16 [0.045 , 0.361]	0.091 [0.03 , 0.2]	0.134 [0.079, 0.209]	0.226 [0.096 , 0.411]
Organ/Stem Cell Transplant	0 [0 , 1]	0 [0 , 1]	0 [0 , 1]	0 [0 , 0.842]	0 [0 , 1]	0.143 [0.004 , 0.579]	0.429 [0.099, 0.816]	0.5 [0.013 , 0.987]

Table 3. Prevalence ratios associated with RSV in the presence of comorbidities compared to the reference group of individuals without comorbidities (per age group).

	Age Group							
Dx	*0-4 (npos = 94)*	*5-17 (npos = 51)*	*18-29 (npos = 27)*	*30-39 (npos = 34)*	*40-49 (npos = 33)*	*50-59 (npos = 54)*	*60-74 (npos = 57)*	*75+ (npos = 28)*
Any Comorbidities	0.97 [0.51 , 1.84]	1.13 [0.58 , 2.21]	2.86 [1.33 , 6.12]	0.72 [0.25 , 2.11]	1.15 [0.56 , 2.36]	0.99 [0.57 , 1.7]	1.67 [1.02 , 2.75]	1.73 [0.85 , 3.53]
Any Pulmonary Illness (Asthma/COPD)	0.97 [0.51 , 1.84]	0.88 [0.42 , 1.86]	3.02 [1.41 , 6.45]	0.67 [0.19 , 2.35]	1.49 [0.73 , 3.06]	0.98 [0.51 , 1.9]	1.26 [0.71 , 2.23]	0.69 [0.28 , 1.66]
Any Cardiac Illness (CHF/CVD)	NA	NA	NA	NA	NA	0.73 [0.15 , 3.48]	1.27 [0.51 , 3.18]	0.87 [0.36 , 2.09]
Cancer	NA	5.91 [1.85 , 18.89]	NA	NA	NA	1.4 [0.51 , 3.83]	0.92 [0.39 , 2.14]	2.13 [1.05 , 4.29]
CLD	NA	NA	NA	8.33 [2.56 , 27.06]	NA	2.5 [0.61 , 10.23]	1.72 [0.38 , 7.85]	NA
Diabetes	NA	5.91 [1.85 , 18.89]	NA	NA	2.86 [1.15 , 7.11]	0.96 [0.42 , 2.22]	2.22 [1.3 , 3.8]	2.22 [1.06 , 4.67]
Organ/Stem Cell Transplant	NA	NA	NA	NA	NA	1.87 [0.43 , 8.08]	6.28 [2.75 , 14.34]	4.24 [1.3 , 13.85]

Prevalence ratios were calculated using individuals with no comorbidities as a reference group. NAs are indicated where there were no individuals in at least one exposure:outcome group.

Table 4. Prevalence of RSV by Age Group and Race/Ethnicity (estimate [95% CI]).

	Age Group							
Race/Ethnicity	*0-4 (npos = 94)*	*5-17 (npos = 51)*	*18-29 (npos = 27)*	*30-39 (npos = 34)*	*40-49 (npos = 33)*	*50-59 (npos = 54)*	*60-74 (npos = 57)*	*75+ (npos = 28)*
Asian American or Native Hawaiian/Pacific Islander	0.34 [0.209 , 0.493]	0.095 [0.039 , 0.185]	0 [0 , 0.066]	0.072 [0.024 , 0.161]	0.032 [0.004 , 0.11]	0.096 [0.032 , 0.21]	0.25 [0.006 , 0.806]	0.154 [0.019 , 0.454]
American Indian/Alaska Native	0.375 [0.085 , 0.755]	0.083 [0.01 , 0.27]	0 [0 , 0.247]	0 [0 , 0.285]	0.1 [0.012 , 0.317]	0.1 [0.012 , 0.317]	0.111 [0.014 , 0.347]	0.5 [0.013 , 0.987]
Black (Any)	0.39 [0.242 , 0.555]	0.113 [0.05 , 0.21]	0.054 [0.007 , 0.182]	0.109 [0.036 , 0.236]	0.088 [0.019 , 0.237]	0.061 [0.007 , 0.202]	0.125 [0.035 , 0.29]	0.4 [0.053 , 0.853]
Multiracial	0.312 [0.202 , 0.441]	0.072 [0.03 , 0.143]	0.053 [0.006 , 0.177]	0 [0 , 0.116]	0.05 [0.001 , 0.249]	0.053 [0.001 , 0.26]	0.12 [0.025 , 0.312]	0 [0 , 0.975]
Native Hawaiian/Pacific Islander (Any)	0.5 [0.23 , 0.77]	0.125 [0.035 , 0.29]	0 [0 , 0.232]	0.071 [0.002 , 0.339]	0 [0 , 0.218]	0 [0 , 0.265]	0.125 [0.016 , 0.383]	0.5 [0.013 , 0.987]
Non-Hispanic White	0.27 [0.206 , 0.343]	0.083 [0.055 , 0.118]	0.068 [0.042 , 0.104]	0.062 [0.038 , 0.093]	0.066 [0.041 , 0.1]	0.108 [0.079 , 0.143]	0.072 [0.053 , 0.095]	0.115 [0.073 , 0.168]
White (Any)	0.255 [0.195 , 0.323]	0.092 [0.064 , 0.127]	0.064 [0.04 , 0.096]	0.059 [0.037 , 0.089]	0.079 [0.052 , 0.113]	0.107 [0.078 , 0.141]	0.07 [0.051 , 0.093]	0.112 [0.072 , 0.165]
Hispanic/Latino	0.184 [0.077 , 0.343]	0.1 [0.038 , 0.205]	0.045 [0.009 , 0.125]	0.047 [0.01 , 0.131]	0.094 [0.031 , 0.207]	0.118 [0.033 , 0.275]	0.071 [0.009 , 0.235]	0 [0 , 0.522]

Table 5. Prevalence Ratios associated with RSV per different racial/ethnic groups and age group (estimate [95% CI]).

	Age Group							
Race/Ethnicity	*0-4 (npos = 94)*	*5-17 (npos = 51)*	*18-29 (npos = 27)*	*30-39 (npos = 34)*	*40-49 (npos = 33)*	*50-59 (npos = 54)*	*60-74 (npos = 57)*	*75+ (npos = 28)*
Asian American or Native Hawaiian/Pacific Islander	0.94 [0.17 , 5.23]	1.05 [0.67 , 1.66]	NaN [NaN , NaN]	1.02 [0.59 , 1.76]	1.09 [0.64 , 1.87]	0.96 [0.65 , 1.42]	1 [0.68 , 1.48]	1.07 [0.63 , 1.82]
American Indian/Alaska Native	1.41 [0.56 , 3.57]	1.01 [0.25 , 4]	NaN [NaN , NaN]	NaN [NaN , NaN]	1.43 [0.36 , 5.74]	0.87 [0.22 , 3.35]	1.55 [0.41 , 5.91]	4.57 [1.08 , 19.3]
Black (Any)	1.47 [0.93 , 2.31]	1.42 [0.67 , 2.99]	0.77 [0.19 , 3.16]	1.69 [0.66 , 4.31]	1.24 [0.39 , 3.99]	0.56 [0.14 , 2.22]	1.74 [0.67 , 4.56]	3.05 [0.92 , 10.09]
Multiracial	1.16 [0.75 , 1.8]	0.91 [0.41 , 2.02]	0.77 [0.19 , 3.16]	NaN [NaN , NaN]	0.75 [0.11 , 5.32]	0.48 [0.07 , 3.29]	1.67 [0.56 , 5.03]	NaN [NaN , NaN]
Native Hawaiian/Pacific Islander (Any)	1.88 [1.06 , 3.36]	1.57 [0.59 , 4.22]	NaN [NaN , NaN]	1.08 [0.15 , 7.54]	NaN [NaN , NaN]	NaN [NaN , NaN]	1.74 [0.46 , 6.58]	4.57 [1.08 , 19.3]
Non-Hispanic White	1.06 [0.75 , 1.5]	1.13 [0.66 , 1.93]	0.55 [0.24 , 1.28]	1.13 [0.59 , 2.2]	0.97 [0.48 , 1.94]	0.84 [0.45 , 1.54]	1.05 [0.58 , 1.91]	1.71 [0.75 , 3.9]
White (Any)	1.15 [0.81 , 1.62]	1.01 [0.57 , 1.79]	0.58 [0.24 , 1.42]	1.23 [0.63 , 2.42]	0.66 [0.28 , 1.52]	0.85 [0.45 , 1.59]	1.13 [0.63 , 2.05]	2.11 [0.94 , 4.72]
Hispanic/Latino	0.68 [0.33 , 1.38]	1.2 [0.52 , 2.79]	0.63 [0.19 , 2.07]	0.72 [0.22 , 2.35]	1.43 [0.56 , 3.66]	1.12 [0.43 , 2.95]	1 [0.25 , 3.9]	NaN [NaN , NaN]

Prevalence ratios were calculated using non-White Hispanic individuals as the reference group. For non-White Hispanic individuals, all other individuals were used as the reference group. NAs are indicated where there were no individuals in at least one exposure:outcome group.

Table 6. Prevalence of hMPV by Age Group and Comorbidity Status (estimate [95% CI]).

	Age Group							
	0-4 (npos = 29)	*5-17 (npos = 16)*	*18-29 (npos = 25)*	*30-39 (npos = 33)*	*40-49 (npos = 30)*	*50-59 (npos = 40)*	*60-74 (npos = 59)*	*75+ (npos = 23)*
Number of Cases	29	16	25	33	30	40	59	23
Any Comorbidity (n, %)	7 (7.4)	9 (17.6)	8 (29.6)	3 (8.8)	9 (27.3)	16 (29.6)	31 (54.3)	18 (64.3)
Dx								
No Comorbidities	0.079 [0.052 , 0.114]	0.026 [0.014 , 0.044]	0.052 [0.033 , 0.077]	0.06 [0.04 , 0.085]	0.063 [0.041 , 0.092]	0.069 [0.046 , 0.1]	0.1 [0.073 , 0.133]	0.138 [0.081 , 0.214]
Any Comorbidities	0.148 [0.042 , 0.337]	0.031 [0.006 , 0.087]	0.047 [0.01 , 0.131]	0.054 [0.015 , 0.133]	0.047 [0.017 , 0.098]	0.086 [0.048 , 0.14]	0.055 [0.032 , 0.086]	0.059 [0.024 , 0.118]
Any Pulmonary Illness (Asthma/COPD)	0.148 [0.042 , 0.337]	0.032 [0.007 , 0.09]	0.049 [0.01 , 0.137]	0.07 [0.019 , 0.17]	0.048 [0.016 , 0.108]	0.117 [0.06 , 0.2]	0.038 [0.014 , 0.081]	0.051 [0.011 , 0.141]
Any Cardiac Illness (CHF/CVD)	0 [0 , 0.975]	NA [0 , 1]	NA [0 , 1]	0 [0 , 0.975]	0 [0 , 0.842]	0.053 [0.001 , 0.26]	0.091 [0.025 , 0.217]	0.082 [0.023 , 0.196]
Cancer	0 [0 , 0.975]	0.5 [0.013 , 0.987]	NA [0 , 1]	0 [0 , 0.41]	0.071 [0.002 , 0.339]	0.083 [0.01 , 0.27]	0.067 [0.022 , 0.149]	0.07 [0.015 , 0.191]
CLD	NA [0 , 1]	NA [0 , 1]	NA [0 , 1]	0 [0 , 0.842]	0 [0 , 0.602]	0.2 [0.005 , 0.716]	0 [0 , 0.285]	NA [0 , 1]
Diabetes	NA [0 , 1]	0 [0 , 0.842]	0 [0 , 0.602]	0 [0 , 0.308]	0 [0 , 0.137]	0.036 [0.004 , 0.125]	0.053 [0.02 , 0.112]	0 [0 , 0.112]
Organ/Stem Cell Transplant	NA [0 , 1]	NA [0 , 1]	NA [0 , 1]	0 [0 , 0.842]	NA [0 , 1]	0.143 [0.004 , 0.579]	0 [0 , 0.41]	0 [0 , 0.842]

Table 7. Prevalence ratios associated with hMPV in the presence of comorbidities compared to the reference group of individuals without comorbidities (per age group).

	Age Group							
Dx	*0-4 (npos = 29)*	*5-17 (npos = 16)*	*18-29 (npos = 25)*	*30-39 (npos = 33)*	*40-49 (npos = 30)*	*50-59 (npos = 40)*	*60-74 (npos = 59)*	*75+ (npos = 23)*
Any Comorbidities	2 [0.79 , 5.05]	1.31 [0.41 , 4.17]	1.02 [0.34 , 3.05]	0.99 [0.38 , 2.59]	0.78 [0.34 , 1.82]	1.26 [0.68 , 2.32]	0.58 [0.34 , 0.99]	0.45 [0.2 , 1.02]
Any Pulmonary Illness (Asthma/COPD)	2 [0.79 , 5.05]	1.36 [0.43 , 4.32]	1.08 [0.36 , 3.21]	1.32 [0.51 , 3.43]	0.83 [0.34 , 2.03]	1.83 [0.96 , 3.49]	0.46 [0.21 , 1.02]	0.5 [0.17 , 1.5]
Any Cardiac Illness (CHF/CVD)	NA	NA	NA	NA	2.79 [0.22 , 35.89]	0.99 [0.21 , 4.75]	1.23 [0.49 , 3.06]	0.86 [0.32 , 2.28]
Cancer	NA	19.26 [5.61 , 66.13]	NA	NA	1.69 [0.36 , 8.03]	1.34 [0.4 , 4.52]	0.88 [0.38 , 2.06]	0.75 [0.25 , 2.21]
CLD	NA	NA	NA	NA	NA	3.39 [0.82 , 13.98]	NA	NA
Diabetes	NA	NA	NA	NA	NA	0.56 [0.16 , 1.96]	0.68 [0.31 , 1.5]	NA
Organ/Stem Cell Transplant	NA	NA	NA	NA	NA	2.53 [0.58 , 11.04]	NA	NA

Prevalence ratios were calculated using individuals with no comorbidities as a reference group. NAs are indicated where there were no individuals in at least one exposure:outcome group.

Table 8. Prevalence of PIV by Age Group and Comorbidity Status (estimate [95% CI]).

	Age Group							
	0-4	*5-17*	*18-29*	*30-39*	*40-49*	*50-59*	*60-74*	*75+*
Number of Cases	43	36	16	19	20	26	30	13
Any Comorbidity	3 (7.0)	3 (8.3)	4 (25.0)	1 (5.3)	8 (40.0)	7 (26.9)	11 (36.7)	5 (38.5)
Dx								
No Comorbidities	0.126 [0.092 , 0.168]	0.066 [0.046 , 0.091]	0.028 [0.015 , 0.049]	0.037 [0.022 , 0.058]	0.031 [0.016 , 0.054]	0.051 [0.031 , 0.078]	0.041 [0.025 , 0.064]	0.069 [0.03 , 0.131]
Any Comorbidities	0.111 [0.024 , 0.292]	0.031 [0.006 , 0.087]	0.062 [0.017 , 0.152]	0.014 [0 , 0.073]	0.062 [0.027 , 0.119]	0.043 [0.017 , 0.086]	0.034 [0.017 , 0.059]	0.042 [0.014 , 0.096]
Any Pulmonary Illness (Asthma/COPD)	0.111 [0.024 , 0.292]	0.032 [0.007 , 0.09]	0.049 [0.01 , 0.137]	0.018 [0 , 0.094]	0.067 [0.027 , 0.133]	0.032 [0.007 , 0.09]	0.037 [0.014 , 0.078]	0.034 [0.004 , 0.117]
Any Cardiac Illness (CHF/CVD)	1 [0.025 , 1]	NA [0 , 1]	NA [0 , 1]	0 [0 , 0.975]	0 [0 , 0.842]	0 [0 , 0.176]	0.062 [0.013 , 0.172]	0.02 [0.001 , 0.109]
Cancer	1 [0.025 , 1]	0 [0 , 0.842]	NA [0 , 1]	0 [0 , 0.41]	0 [0 , 0.232]	0.042 [0.001 , 0.211]	0.038 [0.008 , 0.106]	0.07 [0.015 , 0.191]
Diabetes	NA [0 , 1]	0 [0 , 0.842]	0.25 [0.006 , 0.806]	0 [0 , 0.308]	0.04 [0.001 , 0.204]	0.036 [0.004 , 0.125]	0.034 [0.009 , 0.084]	0.097 [0.02 , 0.258]
CLD	NA [0 , 1]	NA [0 , 1]	NA [0 , 1]	0 [0 , 0.842]	0 [0 , 0.602]	0 [0 , 0.522]	0 [0 , 0.285]	NA [0 , 1]
Organ/Stem Cell Transplant	NA [0 , 1]	NA [0 , 1]	NA [0 , 1]	0 [0 , 0.842]	NA [0 , 1]	0.286 [0.037 , 0.71]	0 [0 , 0.41]	0 [0 , 0.842]

Table 9. Prevalence ratios associated with PIV in the presence of comorbidities compared to the reference group of individuals without comorbidities (per age group).

	Age Group							
Dx	*0-4 (npos = 43)*	*5-17 (npos = 36)*	*18-29 (npos = 16)*	*30-39 (npos = 19)*	*40-49 (npos = 20)*	*50-59 (npos = 26)*	*60-74 (npos = 30)*	*75+ (npos = 13)*
Any Comorbidities	0.98 [0.35 , 2.73]	0.53 [0.18 , 1.56]	2.36 [0.83 , 6.71]	0.53 [0.1 , 2.73]	2.01 [0.86 , 4.69]	0.88 [0.39 , 2.01]	0.83 [0.41 , 1.7]	0.64 [0.22 , 1.8]
Any Pulmonary Illness (Asthma/COPD)	0.98 [0.35 , 2.73]	0.55 [0.19 , 1.61]	1.79 [0.57 , 5.64]	0.7 [0.14 , 3.63]	2.14 [0.9 , 5.09]	0.7 [0.23 , 2.1]	1 [0.43 , 2.35]	0.64 [0.17 , 2.43]
Any Cardiac Illness (CHF/CVD)	6.07 [2.6 , 14.18]	NA	NA	NA	NA	NA	1.92 [0.66 , 5.63]	0.45 [0.08 , 2.36]
Cancer	6.07 [2.6 , 14.18]	NA	NA	NA	NA	1.21 [0.25 , 6]	1.11 [0.38 , 3.31]	1.45 [0.45 , 4.66]
CLD	NA	NA	NA	NA	NA	NA	NA	NA
Diabetes	NA	NA	9.41 [2.26 , 39.14]	NA	1.44 [0.29 , 7.25]	0.88 [0.25 , 3.15]	0.95 [0.36 , 2.53]	2.12 [0.67 , 6.72]
Organ/Stem Cell Transplant	NA	NA	NA	NA	NA	6.8 [2.27 , 20.39]	NA	NA

Prevalence ratios were calculated using individuals with no comorbidities as a reference group. NAs are indicated where there were no individuals in at least one exposure:outcome group.

Figure 1. Prevalence of RSV Stratified by Comorbidity and Age, 2018-2023

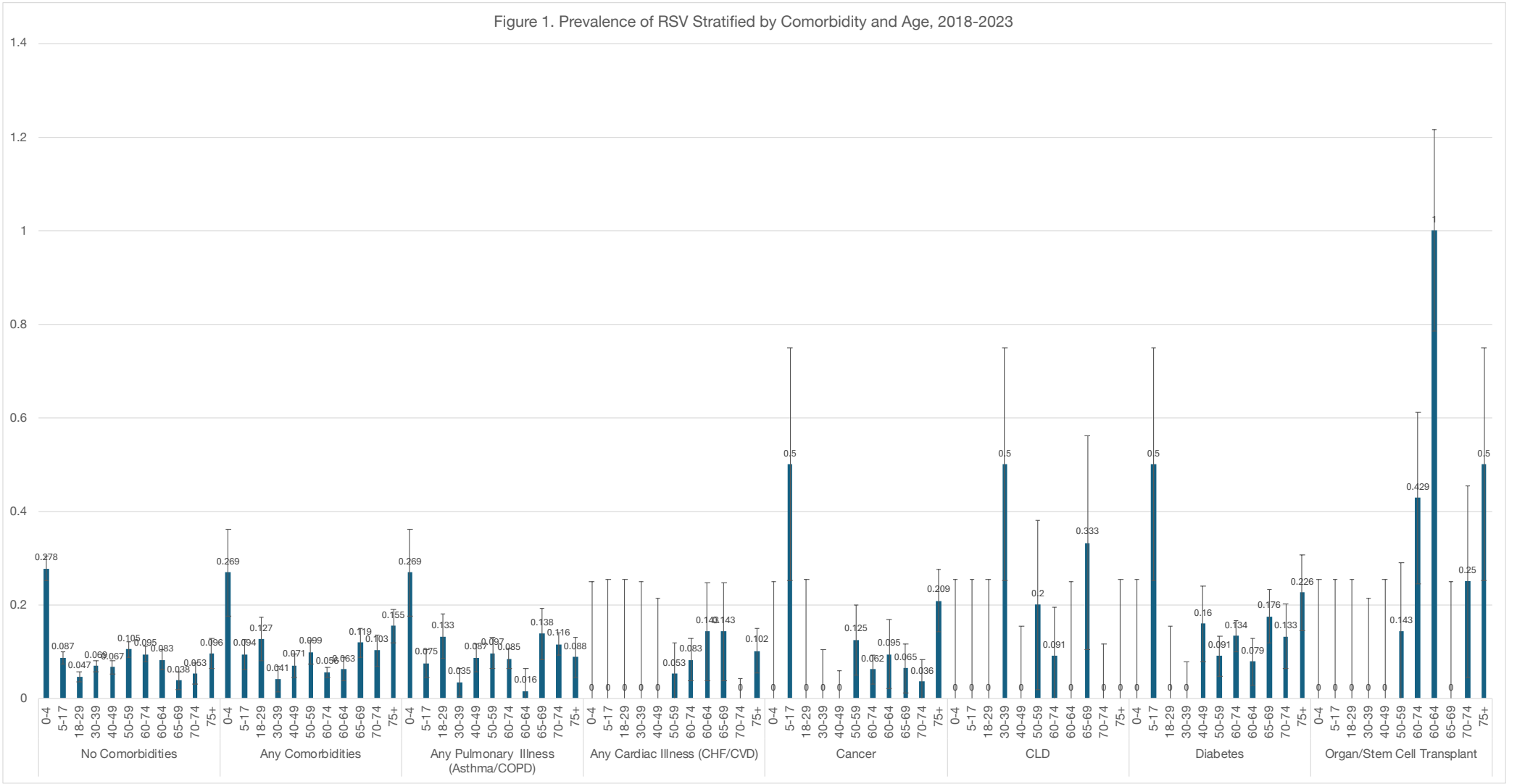

Figure 2. Prevalence of RSV Stratified by Age Group and Race/Ethnicity

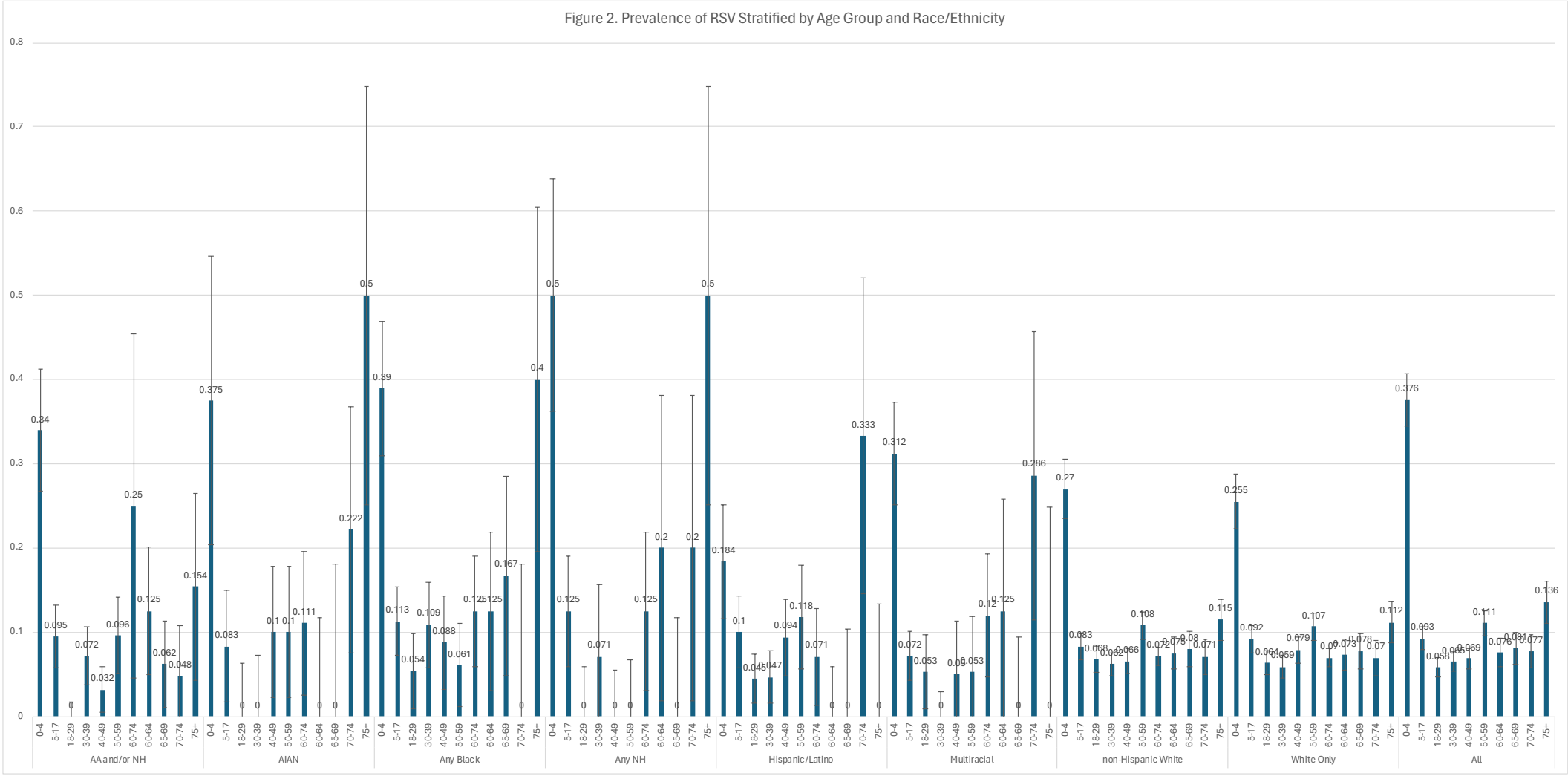

Figure 3. Prevalence of hMPV Stratified by Comorbidity and Age, 2018-2023

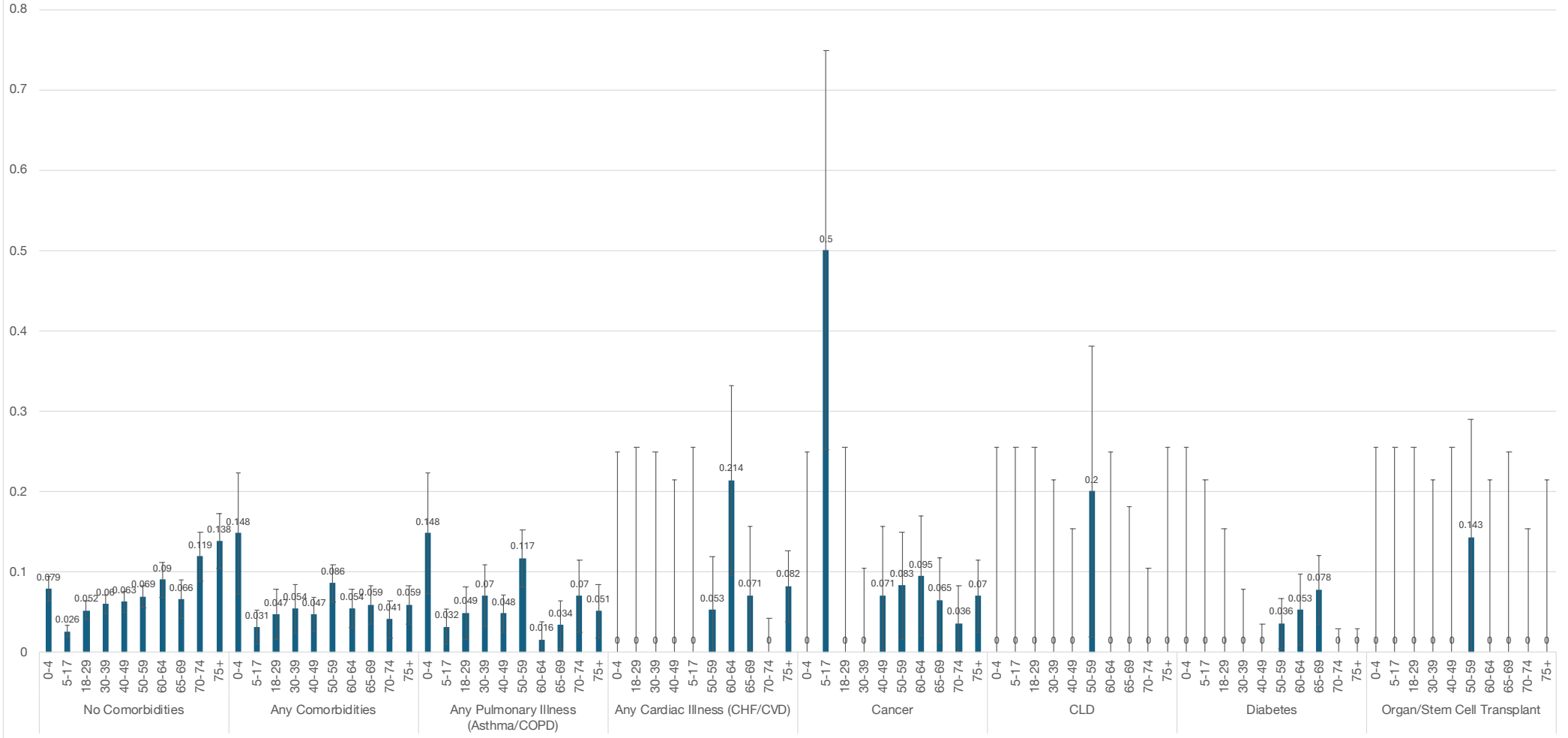

Figure 4. Prevalence of hPIV Stratified by Comorbidity and Age, 2018-2023