Cumulative Incidence of RSV from 2015-16 Through 2019-20 in a High-Risk Adult Population in a Rural US Community

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Background

- Adults with certain **underlying health conditions** may experience substantial incidence of outpatient respiratory syncytial virus (RSV)
- However, existing data on incidence of RSV outpatient illness in adults at increased risk for severe outcomes after respiratory illness ("high-risk adults") are **sparse** and **heterogeneous**
- We assessed the seasonal **cumulative incidence proportion of medically-attended RSV** in adults ≥18 years of age with high-risk conditions seeking care for an acute respiratory illness (ARI) in an outpatient setting in a rural US community (Marshfield, Wisconsin)

Methods

Setting, participants, and samples

- Retrospective study using existing data and respiratory samples from adult participants in an influenza vaccine effectiveness (VE) test-negative design study, from 2015-16 through 2019-20 seasons
- This analysis includes adults ≥18 years old at the time of original study enrollment, with ≥1 underlying high-risk condition:
  - Cardiac disorders [including arrhythmias, heart failure, and coronary artery disease (CAD)]
  - Chronic respiratory disease [including asthma, cystic fibrosis, and chronic obstructive pulmonary disease (COPD)]
  - Chronic liver disease
  - Chronic kidney disease
  - Immunocompromised status (including individuals with malignancy, transplant, and other immunosuppressive conditions)
- Residual respiratory specimens tested for RSV and other pathogens using a multiplex panel (GenMark RPP)

Statistical analysis

- Inverse population (IP) weighting to extrapolate cases of RSV during winter seasons among individuals in the study to the total population of high-risk adults in the community who would have been eligible to participate in the study
- IP weights applied on age, sex, and number of health system visits for respiratory illness, and adjusted for length of season
- Seasonal cumulative incidence proportion (cases per 10,000 high-risk individuals) was calculated using Poisson regression with analytic weights, follow-up time offsets, and robust variance estimation

Results

- There were 3601 study enrollments included in this analysis among high-risk adults, across 5 seasons
- Median (IQR) age was 55 (38 – 67) years, with 30% of enrollments in high-risk individuals 65 years of age or older
- 52% had ≥2 high-risk conditions
- We identified a total of **303 cases of RSV** (40% RSV A)
- Cumulative incidence of RSV was **94.1 (95% CI: 79.5 – 111.5) RSV cases per 10,000 high-risk adults** across 5 winter seasons

Table 1. Selected demographic and illness characteristics of enrollments with and without RSV.

	RSV: n=303	Non-RSV: n=3,298	Total: N=3,601
Age group: n (%)			
18-49 years	90 (29.7)	1,367 (41.4)	1,457 (40.5)
50-59 years	58 (19.1)	639 (19.4)	697 (19.4)
60-64 years	35 (11.6)	332 (10.1)	367 (10.2)
≥65 years	120 (39.6)	960 (29.1)	1,080 (30.0)
Female sex: n (%)	199 (65.7)	2,159 (65.5)	2,358 (65.5)
Self-reported general health before illness: mean (SD)	2.6 (0.9)	2.5 (0.9)	2.5 (0.9)
Charlson score: mean (SD)	1.5 (2.0)	1.1 (1.6)	1.2 (1.6)
Number of high-risk conditions in separate condition categories: n (%)			
1	128 (42.2)	1,588 (48.2)	1,716 (47.7)
≥2	175 (57.8)	1,710 (51.8)	1,885 (52.3)
Days from symptom onset to specimen collection: median (IQR)	4.0 (3.0 – 5.0)	3.0 (2.0 – 5.0)	3.0 (2.0 – 5.0)
Illness signs and symptoms: n (%)			
Fever/feverishness	168 (55.4)	2,135 (64.7)	2,303 (64.0)
Fatigue/feeling run down	283 (93.4)	3,082 (93.5)	3,365 (93.4)
Nasal congestion	278 (91.7)	2,684 (81.4)	2,962 (82.3)
Wheezing	227 (74.9)	1,980 (60.0)	2,207 (61.3)
Shortness of breath/trouble breathing	222 (73.3)	2,170 (65.8)	2,392 (66.4)
Sore throat	195 (64.4)	2,223 (67.4)	2,418 (67.1)

Figure 1. Estimated incidence of RSV A and B by season (blue and red bars) and 95% CIs (gray lines).

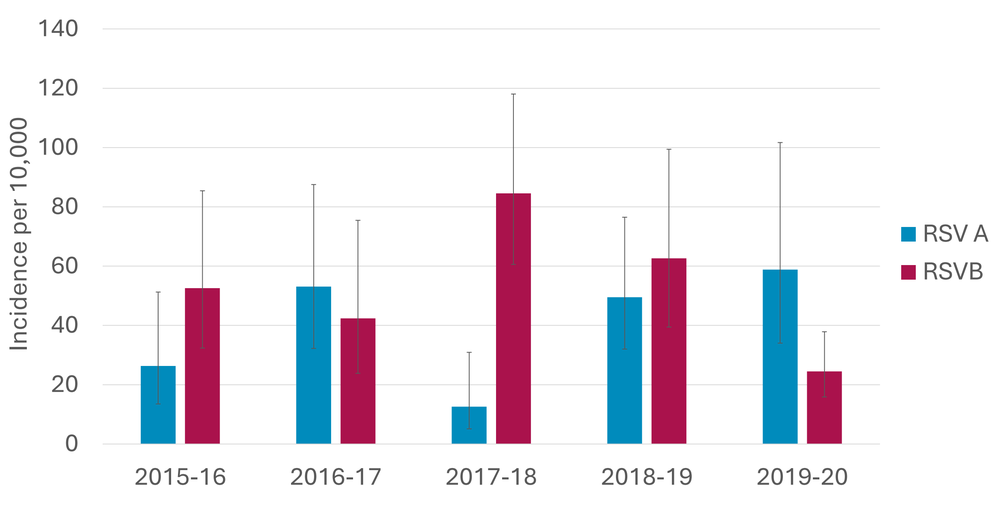


Figure 2. Forest plot of RSV incidence estimates (black diamonds) and 95% CIs (gray bars) by season, sex, and age.

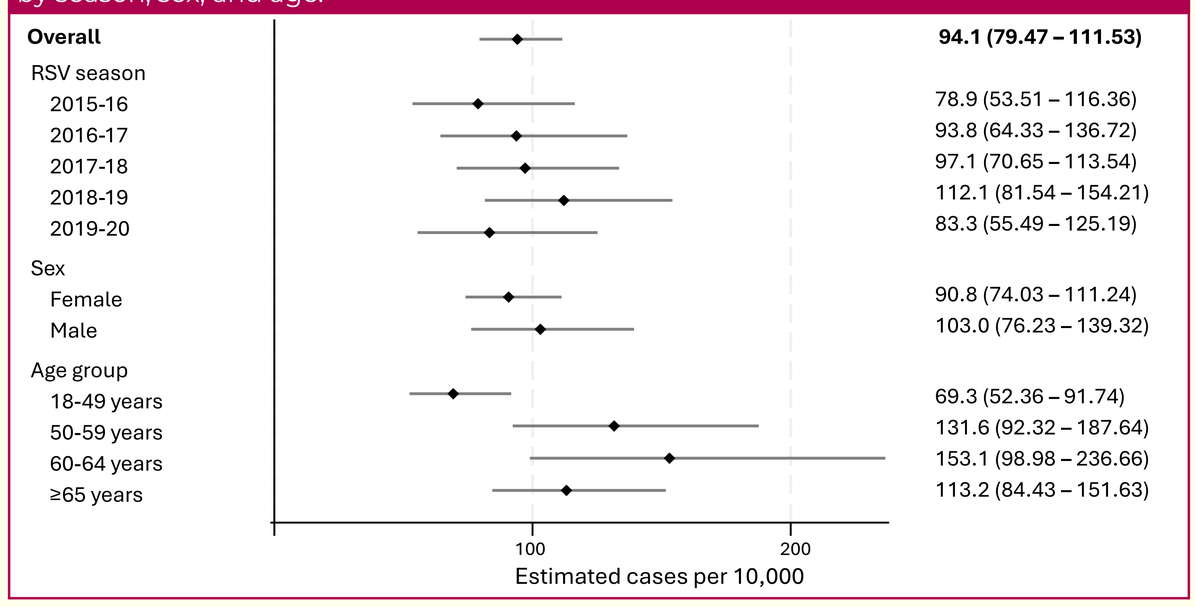
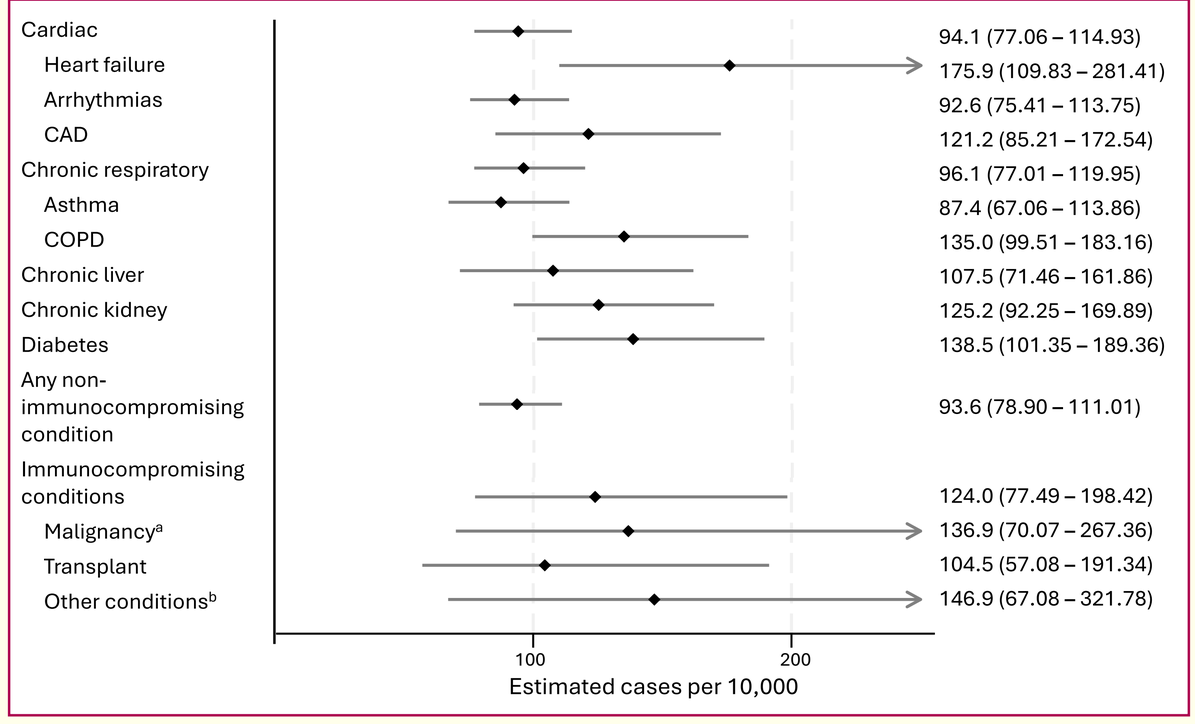


Figure 3. Forest plot of RSV incidence estimates (black diamonds) and 95% CIs (gray bars) by high-risk conditions.



Discussion and Limitations

- These findings suggest an incidence of approximately 100 outpatient RSV cases per 10,000 high-risk adults
- Incidence estimates were variable based on age, high-risk conditions, and winter season, sometimes with wide 95% CIs
- Study estimates are similar to those published previously (Falsey et al. 2005, Jackson et al. 2021 JID/CID)
- Future work should consider epidemiological variability in RSV over age, high-risk conditions, and season, and assess impact of vaccines
- Findings are based on identification of respiratory illness in **outpatient setting**; study design might potentially underestimate the overall incidence of medically-attended RSV by missing RSV illness occurring in hospital
- Study ascertained RSV based on upper respiratory samples; additional true RSV cases may have been identified using additional methods such as sputum or serology

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Definitions

[a] Malignancy includes lymphomas (ICD-10 codes C81*-C86*, C88*), multiple myeloma and malignant plasma cell neoplasms (C90*), leukemias (C91*-C95*), and other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue (C96*).

[b] Other immunodeficiencies include functional disorders of polymorphonuclear neutrophils (D71*), immunodeficiency with predominantly antibody defects (D80*), combined immunodeficiencies (D81*), immunodeficiency associated with other major defects (D82*), common variable immunodeficiency (D83*), and other immunodeficiencies (D84*).