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Estimating the burden of adult hospitalized RSV infection using local and state data - methodology

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ABSTRACT

Respiratory syncytial virus (RSV) is becoming increasingly recognized as a serious threat to vulnerable population subgroups. This study describes the statistical analysis plan for a retrospective cohort study of adults hospitalized for acute respiratory infection (ARI) to estimate the population burden of RSV especially for groups such as the elderly, pregnant women and solid organ transplant patients. Disease burden estimates are essential for setting vaccine policy, e.g., should RSV vaccine become available, burden estimates may inform recommendations to prioritize certain high-risk groups. The study population is residents of Allegheny County, Pennsylvania ≥18 years of age who were hospitalized in Pennsylvania during the period September 1, 2015–August 31, 2018. Data sources will include U.S. Census, Pennsylvania Health Care Cost Containment Council (PHC4) and the electronic medical record for the health system to which the hospitals belong. The algorithm involves: 1) ARI-associated hospitalizations in PHC4 data; 2) adjustment for ARI hospitalizations among county residents but admitted to hospitals outside the county; and 3) RSV detections from respiratory viral panels. Key sensitivity analyses will adjust for undertesting for viruses in the fall and spring quarters. The results will be population-based estimates, stratified by age and risk groups. Adjusting hospitalization data using a multiplier method is a simple means to estimate the impact of RSV in a given area. This algorithm can be applied to other health systems and localities to estimate RSV and other respiratory pathogen burden in adults, to estimate burden following introduction of RSV vaccine and to make cost-effectiveness estimates.

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Introduction

Respiratory syncytial virus (RSV) is a highly contagious respiratory virus that can result in bronchiolitis, otitis media, upper respiratory tract infections, and pneumonia.[1] The virus was first isolated in young children over 60 years ago and much is known about its epidemiology and burden among the very young. Some decades later, documentation of the impact of RSV on morbidity and mortality of adults, especially older adults began. Advanced age and presence of high-risk medical conditions, especially cardiopulmonary disease, are known risk factors for severe RSV outcomes.[2] RSV is estimated to cause 12% of acute respiratory illness (ARI) visits[3] and 7% of influenza like illness (ILI)-ARI in the U.S. in adults over age 50 years.[4] An estimated 3–7% of older adults and 4–10% of high risk adults contract RSV infections each year in the U.S.,[5] numbers which rise with increasing age.[3] Moreover, detections of RSV in hospitalized patients have increased steadily between 1997 and 2012, especially among those ≥60 years of age.[6] CDC estimates that there are 177,000 adult RSV-associated hospitalizations in the U.S. annually. RSV has been estimated to account for 11% percent of hospitalizations for pneumonia and chronic obstructive pulmonary disease exacerbations among elderly and high-risk adults during the RSV season.[5] Hospitalized adults with RSV typically stay 3–6 days and frequently require mechanical ventilation and intensive care admission.[3] The majority of RSV-associated deaths occur in adults >65 years (estimated at 14,000/year);[7] RSV mortality also increases with increasing age,[6] and particularly, among those who are compromised by chronic respiratory and cardiovascular diseases, such as COPD, those with transplants and other immunocompromising conditions,[8] and adults requiring chronic immunosuppressive treatments for rheumatological conditions and solid tumors.[9]

To date, there is no RSV vaccine available for use in either children or adults, although there are many in development.[10] Except for use of monoclonal antibodies in premature infants, there is also no method of attenuating its severity through antiviral or other medication.

Accurate estimates of RSV burden are essential for healthcare planning, resource allocation and vaccine policy. RSV burden studies have primarily focused on children and, while similar studies of adults are becoming more common, there are still relatively few from the U.S.[11] Of those included in reviews and meta-analyses,[4,12,13] only a subset includes younger adults or those with specific high-risk conditions. Surveillance-based studies with laboratory confirmation of RSV infection to calculate RSV burden can be resource intensive. Alternatively, statistical modeling strategies and multiple-regression time-series to assess the burden of disease have

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the advantages of being able to control for influenza, which presents with similar symptoms and co-circulates with RSV, and add a secular polynomial component of time to estimate the burden of RSV infection in adults.[14–17] A simple approach that will provide more generalizable, more accurate, and more precise estimates is possible if population-wide data are available.

Herein, we describe the statistical analysis plan that will be used to produce population-based estimates of RSV burden using data from a large health system supplemented by statewide hospitalization data. This method was developed to facilitate burden estimates in situations where individual data are not available. This proposed multiplier method has the advantages of being simple, straightforward, able to account for adjustment factors, and can be used to estimate burden for an array of risk groups. Furthermore, should a RSV vaccine become available, this method may be used to compare RSV burden following introduction of the vaccine.

Methods

The University of Pittsburgh IRB has determined that the calculation of burden estimates is not human research, therefore approval is not necessary. The methods described herein will be used for a retrospective aggregate cohort study to evaluate the epidemiology and burden of RSV infection in adults (≥18 years of age) over three seasons in Allegheny County, Pennsylvania. The methods allow estimates to be calculated overall and for subtypes of RSV infection and population subgroups.

Data

The cohort will be defined as adult (≥18 years old) residents of Allegheny County Pennsylvania (PA) who were hospitalized in PA between September 1, 2015 and August 31, 2018. All data will be requested and reported across a series of cohort subgroups for which we will request either total counts or average values. Each hospital admission for a given individual will be included.

We will obtain retrospective data from three sources: 1) U.S. Census; 2) Pennsylvania Healthcare Cost Containment Council (PHC4); and 3) University of Pittsburgh Clinical Translational Science Institute (CTSI)'s Health Record Research Request (R3) system that draws data from the health system's electronic medical record (EMR). U.S. Census estimates for Allegheny County, PA as of July 1, 2017 will be used to obtain the number of adult county residents as the denominator for overall burden estimate, where the numerator will be the adjusted number of RSV cases from county residents of the surveillance area. Residency will be established through the individual's home zip code, using those codes listed online for Allegheny County.

Statewide hospitalization data on adult Allegheny County residents from PHC4 will be used. A hospitalization is defined generally, as an encounter for which admission orders are written. For this study, a hospital admission is defined specifically by criteria of the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NSHN; see Appendix Table A1). Admissions to specialty hospitals such as psychiatric or rehabilitation institutions will be excluded from the analysis.

PHC4 will provide data in aggregate for 3-month periods. The 3-month historical segments were selected to best reflect the active RSV season of September through May. The first segment will be September-November 2015, followed by successive segments from December-February, March-May, and June-August through August 2018. These aggregated data contain variables that will allow subgroup analyses, such as age, residency, high-risk conditions, etc. Admitting diagnoses and respiratory viral panel (RVP) findings on any adult Allegheny County resident who was hospitalized in the health system will be obtained through R3. Findings from repeat RVPs during a single admission will be collapsed into a single variable coded as a positive finding of RSV on any RVP performed (RSV = yes/no).

Sample size

A sample size calculation was performed to ensure that the selected health system and county datasets were sufficiently large to provide adequate power to achieve the desired outcome. We used a two-sided exact proportion test with a significance level of set at $\alpha = 0.05$, RSV positivity rate ranging from 0.06 to 0.09, and RVP positive sample size n = 500 to achieve adequate power.[18–20] Table 1 shows the power for various values of the proportion of RSV cases under the alternative hypothesis and for different population sizes using the normal approximation method. Assuming a population size (i.e., the number of patients who had an RVP) of 1500 and a 7% RSV positivity rate, the study would be adequately powered with 105 RSV cases. A sample size of 1500 achieves 90% power to detect a difference of 0.02 using a two-sided Z-test with a significance level of 0.05. These results assume that the population proportion of RSV cases under the null hypothesis is 0.05.

Statistical tests and confidence intervals will be two-sided. Estimates will be presented with 95% confidence intervals, not testing the significance of the estimates.

Calculating RSV population burden

RSV hospitalization burden = RSV hospitalized cases per 100,000 adult residents. The calculation of burden has five steps. Table 2 lists the variables used in the equations and their definitions.

Step 1: Obtain from PHC4 the number of annual acute respiratory illness (ARI) hospitalizations for Allegheny County residents in Allegheny County hospitals (ARI_{ACYear}).

Step 2: Create an adjustment for out-of-county hospitalizations in the state using PHC4 data by calculating the proportion of ARI hospitalizations of Allegheny County residents in

Table 1. Estimated power for a given proportion of RSV positive RVP tests.

	Proportion of RSV positive RVPs			
Number of RVP tests	0.06	0.07	0.08	0.09
1000	0.35	0.83	0.98	0.99
1500	0.42	0.90	0.99	0.99
2000	0.49	0.95	0.99	0.99
2500	0.74	0.95	1	1

Table 2. Variables used in RSV hospitalization burden estimate calculations.

Variable	Definition	Source
Base analyses		
ARI_{ACYear}	Number of ARI hospitalizations of Allegheny County residents admitted to Allegheny County hospitals during the year	PHC4
ARI_{PAYear}	Number of ARI hospitalizations of Allegheny County residents admitted to all Pennsylvania hospitals during the year	PHC4
P_rARI_{AC}	Proportion of ARI hospitalizations of Allegheny County residents in Allegheny County, PA, compared to all Pennsylvania hospitals.	Calculated
$aARI_{ACYear}$	Adjusted number of ARI hospitalizations of Allegheny County residents admitted to Allegheny County hospitals during the year	Calculated
RVP_{RSV}	Number of RSV detections among all RVPs performed in health system, after accounting for duplicate tests in a time period, such as 2 weeks	R3
RVP_{All}	Number of RVPs performed in health system, after accounting for duplicate tests within a time period, such as 2 weeks	R3
P_rRSV_{RVP}	Proportion of RVP tests that are positive for RSV	Calculated
RSV_{ACYear}	Number RSV cases in Allegheny County hospitals during the year	Calculated
Pop_{AC}	Total population of Allegheny County	U.S. Census
$RSV_{ACBurdenYear}$	RSV hospitalization burden per 100,000 adults in all hospitals in Allegheny County during the entire year	Calculated
Sensitivity analyses		
ARI_Q	Number of ARI hospitalizations of Allegheny County residents admitted to health system Allegheny County hospitals during a given quarter	PHC4
RVP_Q	Number RVP tests in the health system in Allegheny County in a quarter	R3
RSV_Q	Number RSV positive RVP tests in the health system in Allegheny County in a quarter	R3
$RVPFract_Q$	Fraction of RVPs performed in a given quarter	Calculated

Allegheny County hospitals, compared to all Pennsylvania hospitals for a given time period, in this case, one year. The outcome is used in the adjustment variable in Equation (2).

$$PrARI_{AC} = \frac{ARI_{ACYear}}{ARI_{PAYear}} \quad (1)$$

Calculate adjusted ARI_{ACYear}:

$$aARI_{ACYear} = \frac{ARI_{ACYear}}{PrARI_{AC}} \quad (2)$$

In settings where this variable is directly available, the adjustment simplifies to ARI_{PAYear}.

Step 3: Calculate the proportion of respiratory viral panel (RVP) tests from R3 for health system hospitals in Allegheny County that are positive for RSV. Repeat tests within a timeframe such as 2 weeks need to be removed so as not to inappropriately estimate viral burden.

$$PrRVP_{RSV} = \frac{RVP_{RSV}}{RVP_{All}} \quad (3)$$

Step 4: Estimate the crude number of RSV hospitalizations in Allegheny County by multiplying the number of ARI hospitalizations by the proportion of RSV positive RVP tests from R3 for health system hospitals in Allegheny County.

$$RSV_{ACYear} = aARI_{ACYear} * PrRVP_{RSV} \quad (4)$$

Step 5: Calculate the RSV burden in Allegheny County during the year by dividing the adjusted RSV burden by the adult population of Allegheny County and multiplying by 100,000.

$$RSV_{ACBurdenYear} = \frac{RSV_{ACYear}}{Pop_{AC}} \text{x} 100,000 \quad (5)$$

U.S. Census estimate for Allegheny County was 1,222,344 for 2017 of whom 974,362 (80%) were adults aged ≥18 years.

ARI hospitalizations include pneumonia and similar respiratory diseases. RSV and other respiratory viruses can also cause exacerbations of asthma, chronic obstructive pulmonary disease and heart failure; these are termed "ARI-related hospitalizations." Because the fraction associated with RSV may differ between ARI hospitalizations and ARI-related hospitalizations and because the overall incidence of ARI hospitalizations and ARI-related hospitalizations is likely to differ, data should be stratified by ARI and ARI-related before being inputted into Equations (1)–(5). These individual results should be combined to estimate the true RSV burden. For simplicity, in this example, ARI hospitalizations and ARI-related hospitalizations were not separated.

The same general approach can be used in 3-month increments to make quarterly burden determinations, using the same equations but substituting quarterly data from R3 and PHC4.

Variance and 95% confidence estimates

Variance and 95% confidence intervals (CIs) were calculated by the following formulas:

$VAR(aRSV_{ACYear}) = aRSV_{ACYear}{}^2 \text{x} Var\left(\frac{1}{X}\right)$,
where $X = PrARI_{AC} \text{x} PrRSV_{PAYear}$

$$95\%CI = aRSV_{ACYear} \pm 1.96 * \sqrt{Variance(aRSV_{ACYear})}$$

Using the Taylor expansion of first order that $Var\left(\frac{1}{X}\right)$ be approximated to $\frac{Var(X)}{\mu^4}$ and μ equals the mean of the random variable X. Under certain conditions and with assumptions of mean and variance values, the approximation of $Var\left(\frac{1}{X}\right)$ $\approx 1\text{x}10^{-6}$. In general, the mean and variance of inverse normal distributions do not exist based on the law of total expectations.[21]

Subgroup or special population analyses

Equations (4) and (5) give the burden estimates for Allegheny County that can be used to estimate burden for each of the age groups and other stratifications. A subgroup or special population of interest can be defined by ICD criteria and data from PHC4 and R3 can be obtained for this special population. For instance, immunocompromised persons may be preferentially tested by RVP and RSV cases might be higher in this population. To calculate the

Table 3. Example of a RSV burden calculation.

Hypothetical inputted or calculated variable values	Equation		Outcome
$ARI_{ACYear} = 24{,}437$ $ARI_{PAYear} = 25{,}000$	$PrARI_{AC} = \frac{ARI_{ACYear}}{ARI_{PAYear}}$	(1)	0.9775
$ARI_{ACYear} = 24{,}437$ $PrARI_{AC} = 0.9775$	$aARI_{ACYear} = \frac{ARI_{ACYear}}{PrARI_{AC}}$	(2)	24,999.5
$RVP_{RSV} = 291$ $RVP_{All} = 2{,}425$	$PrRVP_{RSV} = \frac{RVP_{RSV}}{RVP_{All}}$	(3)	0.12
$aARI_{ACYear} = 24{,}999.5$ $PrRVP_{RSV} = 0.12$	$RSV_{ACYear} = aARI_{ACYear} * PrRVP_{RSV}$	(4)	2,999.94
$RSV_{ACYear} = 2999.94$ $Pop_{AC} = 974{,}362$	$RSV_{ACBurdenYear} = \frac{RSV_{ACYear}}{Pop_{AC}} \text{x} 100{,}000$	(5)	$307.8 \approx$ 308 per 100,000

Table 4. Simulated RSV hospitalization burden (RSV/100,000 adult population) for Allegheny County in a season with 75,000 ARI cases in Pennsylvania.

Proportion of RVPs positive for RSV in health system ($PrRVP_{RSV}$)	Adjusted ARI hospitalizations in Allegheny County ($aARI_{ACYear}$)		
	20,000	25,000	30,000
0.05	103	128	154
0.07	144	180	215
0.12*	246	308	369

*Based on estimate from Colosia AD *PloS one* 2017, 12(8):e0182321.

population burden, data from PHC4 would be used for Equations (1) and (2). Using the proportion of RSV for this population from R3 for Equation (4), the number of RSV cases in immunocompromised persons can be calculated. To determine RSV burden in this group, (Equation (5)), the number of immunocompromised Allegheny County residents would need to be estimated, using a data source such as the National Health Interview Survey.

Sensitivity analyses (SA) for undertesting respiratory infections in the health system in the fall and spring quarters

SA-Step 1: Create an adjustment to estimate effects of undertesting outside of the winter respiratory season, which is when most RVP testing occurs. Compute the UPMC Allegheny County RVP testing fraction for each quarter (Q), shown in Equation (6).

$$RVPFract_Q = \frac{RVP_Q}{ARI_Q} \tag{6}$$

SA-Step 2: Determine if this fraction is approximately equal across the fall (F), winter (W) and spring (S) quarters. If so, then sensitivity analyses are moot. If the testing fractions are not the same, then SA-Step 3 is needed. The definition of approximately equal is open to debate; we propose ≤5% difference as the criterion.

SA-Step 3: Determine if the proportion of RSV detected by RVP varies by season.

$$PrRSV_Q = \frac{RSV_Q}{RVPFrac_Q} \tag{7}$$

If *PrRSV* does not vary across seasons, then sensitivity analyses are unnecessary. If the proportion of RSV varies (we propose by ≥5%) by season, then SA is needed.

SA-Step 4: Adjust fall and spring quarter numbers of RVPs for testing fraction. If we assume that RVP testing in the fall and spring is weighted more heavily to those with immunosuppressive conditions than in the winter, then we can adjust for this situation. If RSV occurred in summer, then it could be added as well but this is not the case in our locale.

$$aRVP_F = RVP_F * \left(\frac{RVP_w}{RVP_F}\right) \tag{8}$$

$$aRVP_S = RVP_S * \left(\frac{RVP_W}{RVP_S}\right) \tag{9}$$

Then addition across the 3 seasons of RSV yields:

$$aRVP_{Year} = aRVP_F + RVP_W + aRVP_S \tag{10}$$

In a similar manner, the number of RSV cases can be adjusted for fall and for spring to create a total across the quarters:

$$aRSV_{Year} = aRSV_F + RSV_W + aRSV_S \tag{11}$$

Finally, an adjusted proportion of RSV can be estimated:

$$aPrRSV_{Year} = \frac{aRSV_{Year}}{aRVP_{Year}} \tag{12}$$

Simulated results

The above equations were used to create simulated results for Allegheny County using U.S. Census population data for Allegheny County and a range of values for *PrRSV* and proportion of state ARI hospitalizations in the county shown in Tables 3 and 4. For example, when we assume that there are 75,000 ARI hospitalizations across the Commonwealth and 25% are in Allegheny County hospitals, and we assume that RSV cases represent 12% of all RVP tests, we calculate the RSV hospitalization burden for Allegheny County per 100,000 adult population would be 308/100,000 adult population.

Discussion

We have developed a simple, adaptable method for estimating RSV burden that can be generalized to other diseases and other locales, provided that adequate viral testing has been done. Equations (1)–(5) can be used to calculate RSV burden for an entire geographical region or for a specific hospital or hospital system within that region. This proposed method can also be used to calculate the burden estimates for any respiratory infection on which data are collected at the hospital or health system and state levels. Alternatively, it can be adapted for use in international settings where local and regional or provincial data are accessible. It can also be used for high-risk sub-populations, provided that the appropriate data are available. RSV burden estimates may be quite different in the season or two following the current coronavirus pandemic, in which RSV infections were radically reduced,[22] thereby offering further insight into its epidemiology.

There is no generalized method currently in use to estimate disease burden across an array of data structures. A recent review of studies to estimate RSV burden across the globe concluded that the significant heterogeneity of methodologies was reflected in widely differing RSV burden estimates. Differences included the methods for case ascertainment; quality of and protocols for laboratory testing; reliance on influenza surveillance to estimate RSV burden and a relatively low number of studies of adults, especially older adults.[4] Our method has the advantage of using population data that are not constrained by the weaknesses of surveillance samples,[23,24] such as lack of representativeness.

Several burden estimation methods have been developed that attempt to adjust surveillance data for under-detection of the burden estimate for seasonal influenza in the Netherlands, pandemic A/H1N1 influenza and novel influenza A/H3N2 in the United States, and influenza A/H7N9 in China.[25–28] The methods developed for those studies ranged from simple multipliers to more complex mathematical and statistical models, depending on setting and data availability. Our method does not require such adjustments because it depends on RSV-specific hospitalization data.

Strengths and limitations

Our method is subject to some limitations. It assumes that viruses causing hospital admission are the same for health system and non-health system hospitals in the county. Given that the health system has 60% of the market share in the county and includes both community and subspecialty hospitals, this is not unreasonable but the viral burden in other hospitals is an extrapolation. Given the higher burden of some viruses in immunocompromised and transplant patients, care is needed to make sure that both community hospitals and subspecialty hospitals are included so as not to bias estimates one way or another. As mentioned in the methods, the mean and variance of the inverse of the random variables do not exist. Through the Taylor series of expansion, we get the approximations of these values that limit the width of the confidence bounds of the estimate. Study of the behavior of the density function of the normal random variable is beyond the scope this manuscript. If the magnitude of ARI data is underreported in PHC4, then we may overestimate RSV burden. Given that Allegheny County is an hour from the state border and that strong hospital systems exist within the county, the likelihood that substantive numbers of out-of-state hospitalizations that would be missed is low, except for those persons who split the year as residents of two different states. Viral detections may not always represent symptomatic infection but could represent asymptomatic infections or perhaps colonization; this topic is beyond the scope of the current paper to address and is an area for further research. Similarly, co-detections of multiple viruses may not represent symptomatic infection from all of those viruses but co-detections in adults are uncommon (5%-10%).[29,30] Bacterial co-infections have been reported to account for 12% of RSV ARIs among hospitalized patients,[31] and 9.3%[32] to 19.7%[33] of RSV-associated pneumonias among hospitalized patients. These severe outcomes would need to be factored into any analysis of severity and consequential economic burden.

The association between grouped ICD codes in PHC4 and individual ICD codes from the EMR that are associated with RVP tests is unknown and cannot be adjusted for in this analysis. If the association between data sources were high (close to 1), actual RSV burden would be similar to calculated estimates; whereas, if the association were low, actual RSV burden would be higher than calculated estimates.

To reduce the complexity, we made estimates using the number of cases and RSV hospitalizations by quarter. There may be variations across seasons and age-specific subgroups, thus our expected burden estimates may not fully reflect the level of uncertainty. Burden may be underestimated or overestimated if careful consideration of the correction multipliers is not made. The multiplier components should be recalculated for each season because the detection probabilities may vary by season.

The strength of this method is that it is not specific to the US healthcare system and can be applied in a variety of settings in which the number of ARI hospitalizations and the RSV positives within the boundaries of the area are available.

Conclusions

The proposed method is relatively a simple method for adjusting and generalizing data to estimate RSV disease burden and may be used in other population-based settings and for other respiratory diseases. When RSV vaccines become available, accurate and timely estimates of RSV burden in various population subgroups will be important factors to consider for RSV vaccination recommendations.

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Authors' contribution

GKB contributed to the study design and was responsible for statistical analysis, drafting and editing the manuscript. MPN contributed to the study design, obtained grant funding, revised the manuscript and is the lead investigator. HE contributed to the study design, acquired data for this study from PHC4 and UPMC health plan and revised the manuscript. RZ contributed to the study design and revised the manuscript. All authors read and approved the final version.

Abbreviations

ARI	Acute Respiratory Infection
CDC	Centers for Disease Control and Prevention
CTSI	Clinical Translational Science Institute

EMR	Electronic medical record
NHSN	National Healthcare Safety Network
PHC4	Pennsylvania Health Care Cost Containment Council
R3	Health Record Research Request
RSV	Respiratory Syncytial Virus
RVP	Respiratory Viral Panel

Disclosure of potential conflicts of interest

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Appendix A

Table A1. List of ARI-specific and ARI-related (i.e. COPD, asthma, CHF) ICD-9/10 codes adapted from CDC's HAIVEN study.

Category	ICD10	Description	ICD9	Description
ARI-specific	A37.01	Whooping cough due to Bordetella pertussis with pneumonia	484.3	Pneumonia in whooping cough
ARI-specific	A37.11	Whooping cough due to Bordetella parapertussis w pneumonia		
ARI-specific	A37.81	Whooping cough due to oth Bordetella species with pneumonia		
ARI-specific	A37.91	Whooping cough, unspecified species with pneumonia		
ARI-specific	B25.0	Cytomegaloviral pneumonitis	484.1	Pneumonia in cytomegalic inclusion disease
ARI-specific	B97.4	Respiratory syncytial virus causing diseases classd elswhr	796	Respiratory Syncytial Virus (Rsv)
ARI-specific	J00	Acute nasopharyngitis [common cold]	460	Acute nasopharyngitis [common cold]
ARI-specific	J01.00	Acute maxillary sinusitis, unspecified	461.0	Acute Maxillary Sinusitis
ARI-specific	J01.01	Acute recurrent maxillary sinusitis		
ARI-specific	J01.10	Acute frontal sinusitis, unspecified	461.1	Acute frontal sinusitis
ARI-specific	J01.11	Acute recurrent frontal sinusitis		
ARI-specific	J01.20	Acute ethmoidal sinusitis, unspecified	461.2	Acute ethmoidal sinusitis
ARI-specific	J01.21	Acute recurrent ethmoidal sinusitis		
ARI-specific	J01.30	Acute sphenoidal sinusitis, unspecified	461.3	Acute sphenoidal sinusitis
ARI-specific	J01.31	Acute recurrent sphenoidal sinusitis		
ARI-specific	J01.40	Acute pansinusitis, unspecified		
ARI-specific	J01.41	Acute recurrent pansinusitis		
ARI-specific	J01.80	Other acute sinusitis	461.8	Other acute sinusitis
ARI-specific	J01.81	Other acute recurrent sinusitis		
ARI-specific	J01.90	Acute sinusitis, unspecified	461.9	Acute sinusitis, unspecified
ARI-specific	J01.91	Acute recurrent sinusitis, unspecified		
ARI-specific	J02.0	Streptococcal pharyngitis	340	Streptococcal pharyngitis
ARI-specific	J02.8	Acute pharyngitis due to other specified organisms	462	Acute pharyngitis
ARI-specific	J02.9	Acute pharyngitis, unspecified		
ARI-specific	J03.00	Acute streptococcal tonsillitis, unspecified	463	Acute tonsillitis
ARI-specific	J03.01	Acute recurrent streptococcal tonsillitis		
ARI-specific	J03.80	Acute tonsillitis due to other specified organisms		
ARI-specific	J03.81	Acute recurrent tonsillitis due to other specified organisms		
ARI-specific	J03.90	Acute tonsillitis, unspecified		
ARI-specific	J03.91	Acute recurrent tonsillitis, unspecified		
ARI-specific	J04.0	Acute laryngitis	464.*	Acute laryngitis and tracheitis
ARI-specific	J04.10	Acute tracheitis without obstruction		
ARI-specific	J04.11	Acute tracheitis with obstruction		
ARI-specific	J04.2	Acute laryngotracheitis		
ARI-specific	J04.30	Supraglottitis, unspecified, without obstruction		
ARI-specific	J04.31	Supraglottitis, unspecified, with obstruction		
ARI-specific	J05.0	Acute obstructive laryngitis [croup]		
ARI-specific	J05.10	Acute epiglottitis without obstruction		
ARI-specific	J05.11	Acute epiglottitis with obstruction		
ARI-specific	J06.0	Acute laryngopharyngitis	465.0	Acute laryngopharyngitis
ARI-specific	J06.9	Acute upper respiratory infection, unspecified	465.8	Acute upper respiratory infections of multiple sites
ARI-specific			465.9	Acute upper respiratory infection of unspecified site

(*Continued*)

Table A1. (Continued).

Category	ICD10	Description	ICD9	Description
ARI-specific	J09.X1	Influenza due to ident novel influenza A virus w pneumonia	487.*	Influenza
			488.*	Influenza due to identified avian influenza virus
ARI-specific	J09.X2	Flu due to ident novel influenza A virus w oth resp manifest		
ARI-specific	J09.X3	Influenza due to ident novel influenza A virus w GI manifest		
ARI-specific	J09.X9	Flu due to ident novel influenza A virus w oth manifest		
ARI-specific	J10.00	Flu due to oth ident flu virus w unsp type of pneumonia		
ARI-specific	J10.01	Flu due to oth ident flu virus w same oth ident flu virus pn		
ARI-specific	J10.08	Influenza due to oth ident influenza virus w oth pneumonia		
ARI-specific	J10.1	Flu due to oth ident influenza virus w oth resp manifest		
ARI-specific	J10.2	Influenza due to oth ident influenza virus w GI manifest		
ARI-specific	J10.81	Influenza due to oth ident influenza virus w encephalopathy		
ARI-specific	J10.82	Influenza due to oth ident influenza virus w myocarditis		
ARI-specific	J10.83	Influenza due to oth ident influenza virus w otitis media		
ARI-specific	J10.89	Influenza due to oth ident influenza virus w oth manifest		
ARI-specific	J11.00	Flu due to unidentified flu virus w unsp type of pneumonia		
ARI-specific	J11.08	Flu due to unidentified flu virus w specified pneumonia		
ARI-specific	J11.1	Flu due to unidentified influenza virus w oth resp manifest		
ARI-specific	J11.2	Influenza due to unidentified influenza virus w GI manifest		
ARI-specific	J11.81	Flu due to unidentified influenza virus w encephalopathy		
ARI-specific	J11.82	Influenza due to unidentified influenza virus w myocarditis		
ARI-specific	J11.83	Influenza due to unidentified influenza virus w otitis media		
ARI-specific	J11.89	Influenza due to unidentified influenza virus w oth manifest		
ARI-specific	J12.0	Adenoviral pneumonia	480.0	Adenoviral pneumonia
ARI-specific	J12.1	Respiratory syncytial virus pneumonia	480.1	Respiratory syncytial virus pneumonia
ARI-specific	J12.2	Parainfluenza virus pneumonia	480.2	Parainfluenza virus pneumonia
ARI-specific	J12.3	Human metapneumovirus pneumonia		
ARI-specific	J12.81	Pneumonia due to SARS-associated coronavirus	480.3	Pneumonia due to SARS-associated coronavirus
ARI-specific	J12.89	Other viral pneumonia	480.8	Other viral pneumonia
ARI-specific	J12.9	Viral pneumonia, unspecified	480.9	Viral pneumonia, unspecified
ARI-specific	J13	Pneumonia due to Streptococcus pneumoniae	481	Pneumonia due to Streptococcus pneumoniae
ARI-specific	J14	Pneumonia due to Hemophilus influenzae	482.2	Pneumonia due to Hemophilus influenzae [H. influenzae]
ARI-specific	J15.0	Pneumonia due to Klebsiella pneumoniae	482.0	Pneumonia due to Klebsiella pneumoniae
ARI-specific	J15.1	Pneumonia due to Pseudomonas	482.1	Pneumonia due to Pseudomonas
ARI-specific	J15.20	Pneumonia due to staphylococcus, unspecified	482.4	Pneumonia due to staphylococcus, unspecified
ARI-specific	J15.211	Pneumonia due to methicillin suscep staph	482.4	Pneumonia due to methicillin suscep staph
ARI-specific	J15.212	Pneumonia due to Methicillin resistant Staphylococcus aureus	482.4	Methicillin resistant pneumonia due to Staphylococcus aureus
ARI-specific	J15.29	Pneumonia due to other staphylococcus	482.4	Pneumonia due to other staphylococcus
ARI-specific	J15.3	Pneumonia due to streptococcus, group B	482.3	Pneumonia due to Streptococcus, group B

(*Continued*)

Table A1. (Continued).

Category	ICD10	Description	ICD9	Description
ARI-specific	J15.4	Pneumonia due to other streptococci	482.3	Pneumonia Due To Unspecified Streptococcus
ARI-specific			482.3	Pneumonia Due to Streptococcus, group A
ARI-specific			482.3	Pneumonia Due to Other Streptococcus
ARI-specific	J15.5	Pneumonia due to Escherichia coli	482.8	Pneumonia due to Escherichia coli
ARI-specific	J15.6	Pneumonia due to other aerobic Gram-negative bacteria	482.8	Pneumonia due to other gram-negative bacteria
ARI-specific	J15.7	Pneumonia due to Mycoplasma pneumoniae	483.0	Pneumonia due to Mycoplasma pneumoniae
ARI-specific	J15.8	Pneumonia due to other specified bacteria	482.8	Pneumonia due to other specified bacteria
ARI-specific			482.8	Pneumonia due to anaerbes
ARI-specific	J15.9	Unspecified bacterial pneumonia	482.9	Bacterial pneumonia, unspecified
ARI-specific	J16.0	Chlamydial pneumonia	483.1	Pneumonia due to chlamydia
ARI-specific	J16.8	Pneumonia due to other specified infectious organisms	483.8	Pneumonia due to other specified organism
ARI-specific	J17	Pneumonia in diseases classified elsewhere	484.8	Pneumoina in other infectious diseases classified elsewhere
ARI-specific			484.7	Pneumonia in other systemic mycoses
ARI-specific	J18.0	Bronchopneumonia, unspecified organism	485	Bronchopneumonia, unspecified organism
ARI-specific	J18.1	Lobar pneumonia, unspecified organism		
ARI-specific	J18.2	Hypostatic pneumonia, unspecified organism		
ARI-specific	J18.8	Other pneumonia, unspecified organism	486	Other pneumonia, unspecified organism
ARI-specific	J18.9	Pneumonia, unspecified organism		
ARI-specific			482.8	Pneumonia due to Legionella
ARI-specific			484.5	Pneumonia in anthrax
ARI-specific			484.6	Pneumonia in aspergillus
ARI-specific	J20.0	Acute bronchitis due to Mycoplasma pneumoniae	466.0	Acute Bronchitis
ARI-specific	J20.1	Acute bronchitis due to Hemophilus influenzae		
ARI-specific	J20.2	Acute bronchitis due to streptococcus		
ARI-specific	J20.3	Acute bronchitis due to coxsackievirus		
ARI-specific	J20.4	Acute bronchitis due to parainfluenza virus		
ARI-specific	J20.5	Acute bronchitis due to respiratory syncytial virus		
ARI-specific	J20.6	Acute bronchitis due to rhinovirus		
ARI-specific	J20.7	Acute bronchitis due to echovirus		
ARI-specific	J20.8	Acute bronchitis due to other specified organisms		
ARI-specific	J20.9	Acute bronchitis, unspecified		
ARI-specific	J21.0	Acute bronchiolitis due to respiratory syncytial virus	466.1	Acute bronchiolitis due to respiratory syncytial virus
ARI-specific	J21.1	Acute bronchiolitis due to human metapneumovirus	466.1	Acute bronchiolitis due to other specified organisms
ARI-specific	J21.8	Acute bronchiolitis due to other specified organisms		
ARI-specific	J21.9	Acute bronchiolitis, unspecified		
ARI-specific	J22	Unspecified acute lower respiratory infection	519.8 519.9	Other diseases of respiratory system, not elsewhere classified
ARI-specific	J39.8	Other specified diseases of upper respiratory tract		Unspecified disease of respiratory system
ARI-specific	J39.9	Disease of upper respiratory tract, unspecified		
ARI-specific	J40	Bronchitis, not specified as acute or chronic	490	Bronchitis, not specified as acute or chronic
ARI-specific	R05	Cough	786.2	Cough
ARI-specific	R06.00	Dyspnea, unspecified	786.0	Shortness of breath
ARI-specific	R06.02	Shortness of breath		
ARI-specific	R06.1	Stridor	786.1	Stridor
ARI-specific	R06.2	Wheezing	786.0	Wheezing
ARI-specific	R06.82	Tachypnea, not elsewhere classified	786.0	Tachypnea

(*Continued*)

Table A1. (Continued).

Category	ICD10	Description	ICD9	Description
ARI-specific	R09.02	Hypoxemia	799.0	Hypoxemia
ARI-specific	R09.2	Respiratory arrest	799.1	Respiratory arrest
ARI-specific			786.0	Other dyspnea and respiratory abnormality
ARI-related	J45.20	Mild intermittent asthma, uncomplicated	493.*	Asthma
ARI-related	J45.21	Mild intermittent asthma with (acute) exacerbation		
ARI-related	J45.22	Mild intermittent asthma with status asthmaticus		
ARI-related	J45.30	Mild persistent asthma, uncomplicated		
ARI-related	J45.31	Mild persistent asthma with (acute) exacerbation		
ARI-related	J45.32	Mild persistent asthma with status asthmaticus		
ARI-related	J45.40	Moderate persistent asthma, uncomplicated		
ARI-related	J45.41	Moderate persistent asthma with (acute) exacerbation		
ARI-related	J45.42	Moderate persistent asthma with status asthmaticus		
ARI-related	J45.50	Severe persistent asthma, uncomplicated		
ARI-related	J45.51	Severe persistent asthma with (acute) exacerbation		
ARI-related	J45.52	Severe persistent asthma with status asthmaticus		
ARI-related	J45.901	Unspecified asthma with (acute) exacerbation		
ARI-related	J45.902	Unspecified asthma with status asthmaticus		
ARI-related	J45.909	Unspecified asthma, uncomplicated		
ARI-related	J45.990	Exercise induced bronchospasm		
ARI-related	J45.991	Cough variant asthma		
ARI-related	J45.998	Other asthma		
ARI-related	I50.1	Left ventricular failure	428.*	Congestive heart failure
ARI-related	I50.20	Unspecified systolic (congestive) heart failure		
ARI-related	I50.21	Acute systolic (congestive) heart failure		
ARI-related	I50.22	Chronic systolic (congestive) heart failure		
ARI-related	I50.23	Acute on chronic systolic (congestive) heart failure		
ARI-related	I50.30	Unspecified diastolic (congestive) heart failure		
ARI-related	I50.31	Acute diastolic (congestive) heart failure		
ARI-related	I50.32	Chronic diastolic (congestive) heart failure		
ARI-related	I50.33	Acute on chronic diastolic (congestive) heart failure		
ARI-related	I50.40	Unsp combined systolic and diastolic (congestive) hrt fail		
ARI-related	I50.41	Acute combined systolic and diastolic (congestive) hrt fail		
ARI-related	I50.42	Chronic combined systolic and diastolic hrt fail		
ARI-related	I50.43	Acute on chronic combined systolic and diastolic hrt fail		
ARI-related	I50.810	Right heart failure, unspecified		
ARI-related	I50.811	Acute right heart failure		
ARI-related	I50.812	Chronic right heart failure		
ARI-related	I50.813	Acute on chronic right heart failure		
ARI-related	I50.814	Right heart failure due to left heart failure		
ARI-related	I50.82	Biventricular heart failure		
ARI-related	I50.83	High output heart failure		
ARI-related	I50.84	End stage heart failure		
ARI-related	I50.89	Other heart failure		
ARI-related	I50.9	Heart failure, unspecified		
ARI-related	J41.0	Simple chronic bronchitis	491.0	Simple chronic bronchitis
ARI-related	J41.1	Mucopurulent chronic bronchitis	491.1	Mucopurulent chronic bronchitis
ARI-related	J41.8	Mixed simple and mucopurulent chronic bronchitis	491.8	

(*Continued*)

Table A1. (Continued).

Category	ICD10	Description	ICD9	Description
ARI-related	J42	Unspecified chronic bronchitis	491.9	Unspecified chronic bronchitis
ARI-related	J43.0	Unilateral pulmonary emphysema [MacLeod's syndrome]	492.8	Other emphysema
ARI-related	J43.1	Panlobular emphysema		
ARI-related	J43.2	Centrilobular emphysema		
ARI-related	J43.8	Other emphysema		
ARI-related	J43.9	Emphysema, unspecified		
ARI-related	J44.0	Chronic obstructive pulmon disease w acute lower resp infct	491.2	Obstructive chronic bronchitis, without exacerbation
ARI-related	J44.1	Chronic obstructive pulmonary disease w (acute) exacerbation		Obstructive chronic bronchitis, with (acute) exacerbation
ARI-related	J44.9	Chronic obstructive pulmonary disease, unspecified		Obstructive chronic bronchitis with acute bronchitisChronic airway obstruction, not elsewhere classified (includes COPD NOS)

*Take ALL codes under the root number.