

Mortality Associated With Respiratory Syncytial Virus, Bronchiolitis, and Influenza Among Infants in the United States: A Birth Cohort Study From 1999 to 2018

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Background. Infant mortality due to respiratory syncytial virus (RSV) in the United States is not well understood.

Methods. From 1999 to 2018, RSV, bronchiolitis, and influenza deaths were described for infants <1 year using linked birth/death datasets from the National Vital Statistics System. Mortality was described overall and by infant birth and death characteristics. Bronchiolitis was included as the plausible upper limit of RSV, while influenza served as a comparator.

Results. Total infant deaths were 561 RSV, 1603 bronchiolitis, and 504 influenza, and rates were 6.9 (95% confidence interval [CI], 6.4–7.5), 19.8 (95% CI, 18.9–20.8), and 6.2 (95% CI, 5.7–6.8) per 1 000 000 live births, respectively. The highest RSV rates were observed among <29 weeks' gestational age infants (103.5; 95% CI, 81.8–129.1), American Indian/Alaskan Native (20.3; 95% CI, 11.6–33.0), and Medicaid-insured (7.3; 95% CI, 5.9–8.9). However, RSV mortality burden was greatest in full-term (53.7%), white (44.9%), and Medicaid-insured (61.7%) infants. Deaths outside the inpatient setting were 21% and 54% for RSV and bronchiolitis; more Medicaid- (58%) and other/unknown-insured (69%) infants with bronchiolitis died outside of the inpatient setting, compared to privately insured infants (48%) ($P = .0327$).

Conclusions. These national estimates emphasize the importance of considering all infants across all healthcare settings when describing RSV mortality.

Keywords. bronchiolitis; infants; mortality; influenza; respiratory syncytial virus; RSV.

Respiratory syncytial virus (RSV) is the leading cause of hospitalization for infants aged <1 year in the United States [1, 2]. RSV is also a major viral cause of death from acute respiratory tract infections in young children globally [3]. Seasonal influenza epidemics usually coincide with those of RSV [4]. As annual vaccination for influenza has been recommended for all US infants ≥ 6 months of age since 2003 [5, 6], influenza mortality results are useful for comparison. In fact, a recent study reported that among US infants aged <1 year, excess mortality due to RSV was 5 times that of influenza from 1999 to 2018 [7]. While many influenza vaccines are available [8], palivizumab is the only immunoprophylaxis for RSV, recommended only for a subset of infants based on gestational age and comorbidity status [9].

RSV mortality varies by sociodemographic and clinical characteristics, including prematurity, comorbid conditions, and insurance payer status [1, 10–17], although contemporary, nationally representative estimates of RSV mortality among US infants stratified by infant birth characteristics other than sex and race have yet to be published [17]. A few recent studies have examined the total number of infant deaths due to RSV in the United States. Prill et al (2016) [18] used the National Center for Health Statistics (NCHS) multiple cause of death data from 2004 to 2007 and reported a mean of 36 infant RSV deaths per year. Prill et al (2021) [19] used an updated version of the multiple cause of death data and found a total of 315 RSV deaths among infants from 2005 to 2016. However, these studies only report disease burden and did not report mortality rates. Recently, Hansen et al [7] modeled excess RSV and influenza mortality rates for age groups including infants <1 year, using death certificate and surveillance data from 1999 to 2018. In another study, Hansen et al. [20] reported death counts and population-based rates for age and race categories using NCHS death certificate data for 1999–2018, for purposes of comparing to prior excess mortality estimates of RSV, bronchiolitis, and influenza. Neither of these studies provided rates by infant birth characteristics, which was acknowledged as a study limitation [7, 20]. Estimating both RSV mortality rates and burden allows policy makers to not only identify those infants most at risk,

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but also those populations which drive healthcare utilization during the relatively rapid onset and short RSV season [21].

Using the linked birth and death dataset from the National Vital Statistics System (NVSS) of the NCHS, the objective of this study was to address the identified gaps and describe infant RSV, bronchiolitis, and influenza mortality rates and burden among US infants aged <1 year, by infant characteristics at birth and death.

METHODS

The NVSS of the NCHS is the only source of comprehensive data for all US infant births and deaths by year from all 50 states and the District of Columbia. From the state birth and death certificate data and the NCHS natality and mortality files, birth and death records for unique infants are linked via a validated process that yields >99% successful record linkage [22]. While the linked data are available as early as 1983, cause of death codes using International Classification of Disease, Tenth Revision (ICD-10) were implemented starting in 1999. Altogether, the NCHS/NVSS datasets have inventoried more than 3.7 million state-reported births per year and more than 21 000 infant deaths per year since 1999. These data report infant characteristics at birth, including birth year, birth month, weeks' gestational age (wGA), birth weight, insurance payer, maternal race/ethnicity, and neonatal intensive care unit (NICU) admission at birth. Importantly, these data also capture setting at death, including those that occurred outside of the hospital setting [22].

Study Population

For this cohort study, the population comprised all infants born to residents of the United States and those who died at age <1 year with RSV, bronchiolitis, or influenza as the cause of death using ICD-10 codes in any position on the death certificate (up to 20 ICD-10 codes can be listed on the death certificate for the cause of death; ICD-10 cause of death codes were used starting in 1999).

RSV was defined by at least one ICD-10 cause of death code: B97.4 (RSV); J12.1 (RSV influenza); J20.5 (acute bronchitis due to RSV); and J21.0 (acute bronchiolitis due to RSV). The ICD-10 codes for bronchiolitis included all RSV codes as well as J21.8 (acute bronchiolitis due to other specified organisms) and J21.9 (acute bronchiolitis, unspecified). Influenza included at least 1 of the following ICD-10 codes: J09 (influenza, identified), J10.0 (influenza with pneumonia, influenza virus identified); J10.1 (influenza identified, with other respiratory manifestations), J10.2 (influenza identified, with gastrointestinal manifestations), J10.8 (influenza identified, with other manifestations), J11.0 (influenza with pneumonia, virus not identified); J11.1 (influenza unidentified, with other respiratory manifestations), J11.2 (influenza unidentified, with gastrointestinal manifestations), and J11.8 (influenza unidentified, with other manifestations).

Because routine laboratory testing for RSV is not recommended [23], bronchiolitis was included as a potential upper estimate of RSV mortality, which is consistent with the methodology used in other RSV studies [1, 12, 17]. RSV is typically in circulation at the same time as influenza and prior RSV mortality studies have also assessed influenza mortality [7, 20, 24]; thus, influenza mortality was also evaluated. Infants born outside of the United States were excluded from this study. This study was exempt from institutional review board review due to the deidentified nature of the datasets. Additionally, the data use agreement procedures and reporting guidelines from the NVSS were followed to safeguard subject confidentiality.

Infant Characteristics at Birth and Death

Infant characteristics from the linked birth certificate included birth year, birth month, wGA, birth weight, insurance payer, maternal race/ethnicity, and NICU admission at birth. NICU admission at birth and insurance payer data were available for only a subset of years: 2014–2018 for NICU admission and 2011–2018 for insurance payer. NICU admission at birth was evaluated as a dichotomous variable. wGA was described as <29, 29–34, 35–36, and ≥ 37 (full-term). Birth weight was categorized as <1500, 1500–2499, or ≥ 2500 g. Insurance payer was described as Medicaid, private, or other/unknown, which included self-pay, other insurance, and unknown. Infant race/ethnicity, based on maternal race/ethnicity, was classified as non-Hispanic white, non-Hispanic black, American Indian/Alaskan Native (AI/AN), Asian/Pacific Islander, or Hispanic.

Infant characteristics from the linked death certificate included calendar month of death, calendar year of death, chronological age at death, and setting of death. Setting of death was categorized as inpatient (IP), emergency department (ED)/outpatient (OP), home, and other/unknown (including IP dead-on-arrival, nursing home/long-term care, hospice, other, and setting unknown). In addition, comorbidity conditions at death including higher-risk congenital heart disease (CHD), chronic lung disease (CLD), Down syndrome without higher-risk CHD, and other conditions evaluated in prior RSV studies [11, 25] were assessed.

Statistical Analysis

Two mortality outcomes were described in this study: (1) infant mortality burden reported as counts and percent of total infant deaths; and (2) infant mortality rates described as per 1 000 000 live births and corresponding 95% confidence intervals (95% CIs). Mortality burden (ie, the number of infants who have died from RSV, bronchiolitis, and influenza) was used to describe the absolute representation of each subgroup among all deaths and to identify subgroups that bear the greatest burden of death due to disease. In contrast, mortality rates were used to describe the risk of mortality for each subgroup and to identify those subgroups that bear the greatest risk of death due to the disease.

Mortality burden—the number of infant deaths due to RSV, bronchiolitis, or influenza and their proportions of total infant deaths—was described overall and by infant characteristics at birth and death. The denominator used to calculate burden was the total number of infant deaths for RSV, bronchiolitis, or influenza for the entire study period or for the subset of years for which data were available.

Mortality rates—the number of infant RSV, bronchiolitis, and influenza deaths per 1 000 000 live births—were described overall and by infant characteristics at birth. The denominator for rate calculations was the total number of live births overall or the total number of live births in each stratum (eg, non-Hispanic white live births). The nonparametric Mann-Kendall test was used to assess trends in mortality rates and the Fisher exact test was used to compare mortality burden by setting at death and insurance payer.

While the main analyses considered deaths coded with RSV, bronchiolitis, or influenza in any position on the death certificate, a sensitivity analysis was conducted including only deaths with these outcomes as the underlying cause of death (ie, ICD-10 code in the primary position).

Analyses were conducted using SAS/STAT software, version 9.4 of SAS System for Windows (SAS Institute). Data visualization was done using GraphPad Prism for Mac, version 9.2.

RESULTS

Overall Rates and Burden of Infant RSV, Bronchiolitis, and Influenza Mortality

From 1999 to 2018, there were 80 764 705 total live births in the United States and 510 502 total infant deaths from all causes (Supplementary Table 1); annually, infant deaths from all causes ranged from 21 346 to 28 725 per year. There were 561, 1603, and 504 infant deaths associated with RSV, bronchiolitis, and influenza, respectively, from 1999 to 2018, corresponding to the following annual average number of deaths: 28 (SD 7.9) for RSV; 80 (SD 17.0) for bronchiolitis; and 25 (SD 11.1) for influenza. In this period, the overall infant RSV, bronchiolitis, and influenza mortality rates were 6.9 (95% CI, 6.4–7.5), 19.8 (95% CI, 18.9–20.8), and 6.2 (95% CI, 5.7–6.8) per 1 000 000 live births, respectively.

Rates by Infant Characteristics at Birth

RSV Mortality Rates

Over the entire study period, infant RSV mortality rates by birth year showed a statistically significant downward trend over time ($P = 0.0035$); from 2008 to 2018, the mortality rates ranged from 8.1 (95% CI, 5.5–11.4) to 3.4 (95% CI, 1.9–5.7) per 1 000 000 live births (Figure 1). Mortality rates by birth month were highest in those born August through January, ranging from 6.5 (95% CI, 4.8–8.7) for births in August to 9.4 (95% CI, 7.2–12.1) for births in January, with a peak of 11.9 (95% CI, 9.4–14.8) for births in December (Figure 2). Infant RSV mortality rates were highest among <29 wGA infants (103.5; 95% CI, 81.8–129.1; Figure 3A)

and among AI/AN (20.3; 95% CI, 11.6–33.0; Supplementary Figure 1A). Medicaid-insured infants had the highest RSV mortality rates (7.3; 95% CI, 5.9–8.9) compared with those who were privately insured (3.6; 95% CI, 2.7–4.7) and other/unknown insured infants (2.5; 95% CI, 1.0–5.2) (Figure 4A).

Bronchiolitis and Influenza Mortality Rates

While the bronchiolitis mortality rates were more than 2.5 times that of RSV and more than 3 times higher than influenza rates, the patterns in infant mortality rates and burden for bronchiolitis and influenza were similar to those of RSV. Significant downward trends by year were found for both diseases (bronchiolitis, $P = .0103$; influenza, $P = .0162$; Figure 1).

Burden by Infant Characteristics at Birth and Death

RSV Mortality Burden

Infant RSV burden was greatest in full-term infants, with 53.7% of RSV deaths occurring in those born ≥ 37 wGA (Figure 3A). By race/ethnicity, infant RSV mortality burden was greatest in non-Hispanic white (44.9% of infant RSV deaths), non-Hispanic black (25.8%), and Hispanic (21.7%) infants (Supplementary Figure 1A). Medicaid-insured infants had the highest RSV burden, with 61.7% of RSV deaths compared with 33.6% among privately insured infants and 4.7% among other/unknown insured infants (Figure 4A).

When evaluated by wGA and comorbidity conditions (the criteria of palivizumab eligibility), RSV mortality burden was highest in full-term infants without any comorbidities (group A, 37.8% of infant RSV deaths) (Figure 5). Of the infant RSV deaths, 36.7% occurred in preterm infants without CLD/higher-risk CHD, and full-term infants with other comorbidities (group C), while 24.1% occurred in palivizumab-eligible infants (group B). The majority of RSV deaths occurred in infants without NICU admission at birth, and those ≥ 2500 g birth weight. (Complete results by NICU admission at birth and birth weight are reported in Supplementary Text 1.)

Evaluation of the RSV mortality burden by setting showed that 79.1% of infant RSV deaths occurred in the IP hospital setting and 20.8% were outside (ED/OP, 14.4%; home, 3.9%; other/unknown, 2.5%) (Figure 6). Setting at death did not vary by payer type when comparing the inpatient setting versus all other settings ($P = .6714$). When RSV deaths were stratified by chronological age, infants aged 1–4 months comprised the majority of RSV deaths (63.8%) (Supplementary Figure 2A). More than 80% percent of all RSV deaths occurred during the winter/early spring months (November–March), with the greatest proportion of RSV deaths observed in January (23.4% of RSV deaths) (Supplementary Figure 2B).

Bronchiolitis and Influenza Mortality Burden

Of the bronchiolitis deaths, 64.3% were among full-term infants (Figure 3B), as were 63.3% of influenza deaths (Figure 3C).

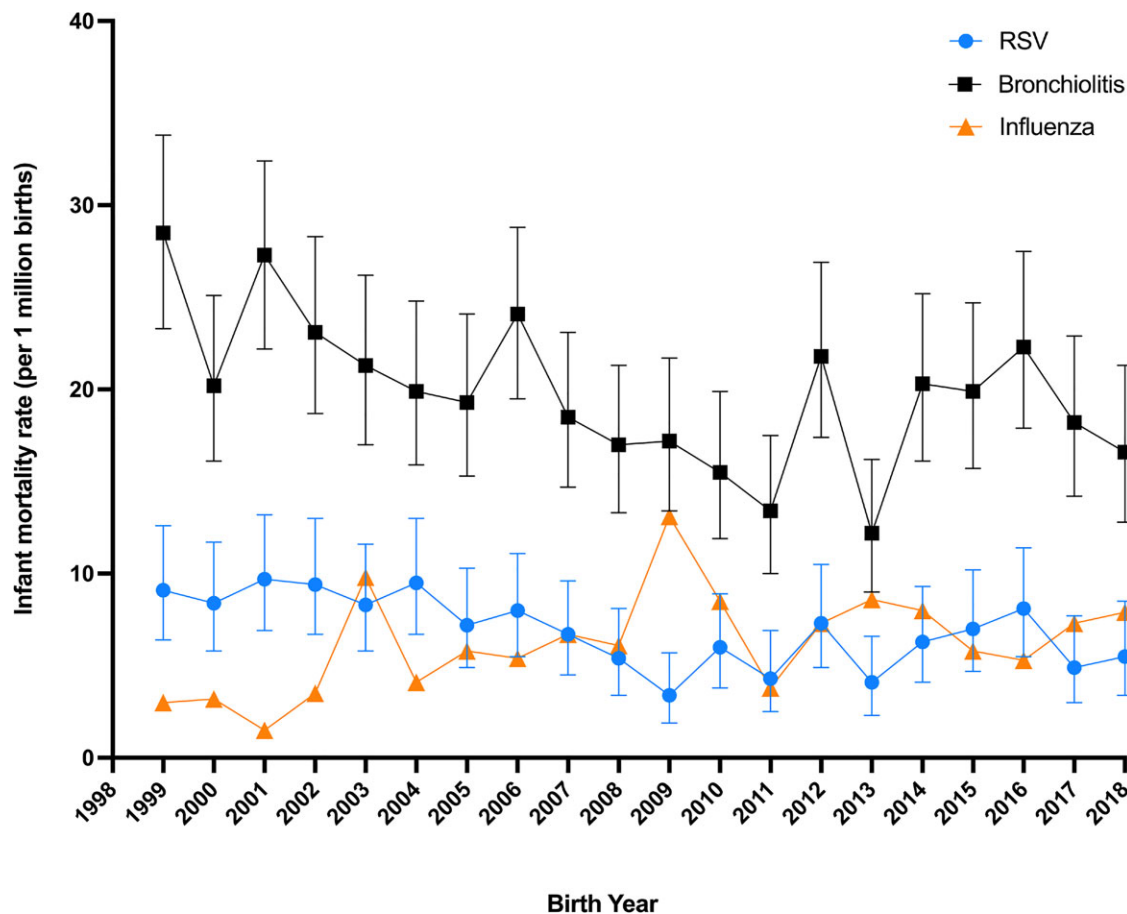


Figure 1. Infant respiratory syncytial virus (RSV), bronchiolitis, and influenza mortality rates per 1 000 000 live births by birth year, US infants aged <1 year, National Center for Health Statistics/National Vital Statistics System 1999–2018. RSV, bronchiolitis, and influenza were defined by ICD-10 cause of death code in any position: RSV, B97.4, J12.1, J20.5, J21.0; bronchiolitis, all RSV codes and J21.8, J21.9; and influenza, J09, J10.0, J10.1, J10.2, J10.8, J11.0, J11.1, J11.2, J11.8.

For bronchiolitis, 45.8% of deaths were non-Hispanic white, 27.1% non-Hispanic black, and 19.4% Hispanic (Supplementary Figure 1B). Among influenza deaths, 38.1% were non-Hispanic white, 21.1% non-Hispanic black, and 29.7% Hispanic (Supplementary Figure 1C). Of bronchiolitis and influenza deaths, 63.9% and 67.7% were among infants covered by Medicaid at birth, respectively, and 26.4% and 20.7% were privately insured (Figure 4B and 4C).

When assessed by wGA and other comorbidity conditions, bronchiolitis and influenza deaths were predominantly among full-term infants without any comorbid conditions (group A, 52.2% for bronchiolitis; 51.2% for influenza; Figure 5).

By death characteristics, bronchiolitis and influenza mortality were similar to that of RSV, except the mortality burden by setting. For infant bronchiolitis deaths, the majority (53.8%) occurred outside of the IP hospital setting (ED/OP, 32.6%; home, 14.9%; other/unknown, 6.3%; Figure 6). When evaluating insurance type, a greater proportion of Medicaid-insured and other/unknown insured infants at birth died outside of

the inpatient setting compared to privately insured infants at birth (58.4%, 68.9%, and 48.0%, respectively, $P = .0327$). For influenza, 40.9% occurred outside of the IP setting (ED/OP, 27.4%; home, 7.3%; other/unknown, 6.2%; Figure 6); however, the proportion of deaths by setting did not vary significantly across the different payer groups ($P = .5485$). Younger infants aged 1–4 months accounted for 59.5% and 46.8% of bronchiolitis and influenza deaths, respectively (Supplementary Figure 2A), and 69.3% of deaths associated with bronchiolitis and 71.7% of deaths associated with influenza occurred during the months of November–March; deaths occurred most frequently in January (bronchiolitis, 18.8%; influenza, 18.7%; Supplementary Figure 2B).

Sensitivity Analysis Using Underlying Cause of Death

When only the underlying cause of death on the death certificate was considered, there were 344 RSV, 802 bronchiolitis, and 361 influenza deaths from 1999 to 2018. Patterns of mortality rates and burden (data not shown) among this subset were similar to the main study findings for all 3 diseases. Yearly

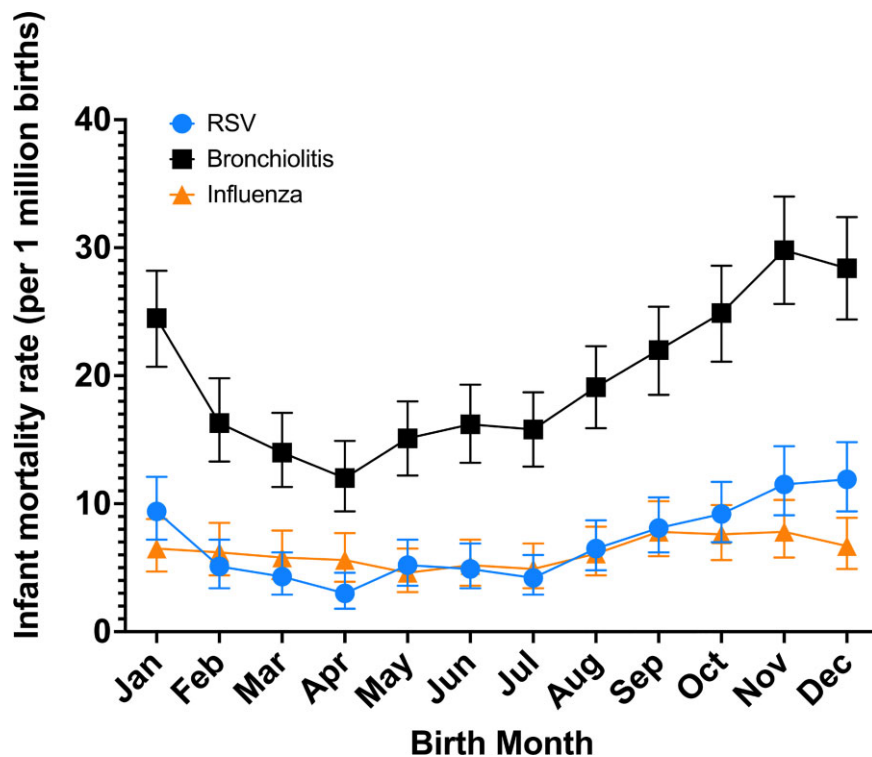


Figure 2. Infant respiratory syncytial virus (RSV), bronchiolitis, and influenza mortality rates per 1 000 000 live births by birth month, US infants aged <1 year, National Center for Health Statistics/National Vital Statistics System 1999–2018. RSV, bronchiolitis, and influenza were defined by ICD-10 cause of death code in any position: RSV, B97.4, J12.1, J20.5, J21.0; bronchiolitis, all RSV codes and J21.8, J21.9; and influenza, J09, J10.0, J10.1, J10.2, J10.8, J11.0, J11.1, J11.2, J11.8.

mortality counts by underlying cause of death code are presented in [Supplementary Table 2](#).

DISCUSSION

This study reports contemporary, nationally representative estimates of RSV, bronchiolitis, and influenza mortality rates and burden among US infants aged <1 year, by infant characteristics at birth and death. To our knowledge, this is the first study to provide mortality rates and burden stratified by infant characteristics at birth, including results for late preterm to full-term infants and those without comorbidities.

By wGA, there was an inverse relationship between the mortality rate and burden. Premature infants had substantially higher RSV or bronchiolitis mortality risk compared with full-term infants, while a substantially higher burden of deaths occurred among full-term infants without comorbidities. By race/ethnicity, rates were highest among AI/AN infants, while the burden was greatest among white, black, and Hispanic infants. Consistent with these findings, Prill et al (2021) [19], using the NCHS 2005–2016 dataset, reported greater RSV mortality burden among younger infants and white, black, and Hispanic infants. Additionally, this study found that the greatest burden of RSV deaths remains in Medicaid-insured infants. These findings illustrate that both

rate and burden estimates need to be considered together to reduce the impact of RSV.

As RSV laboratory testing is not recommended in the United States, the mortality rates and burden reported in this study are likely an underestimation. A recent systematic literature review by N. Movva et al (submitted) reported variation in RSV testing frequency by setting, location, and infant population and noted not all infants were being tested for RSV. Hence, bronchiolitis represents a plausible upper bound for RSV mortality. Notably, Hansen et al [7] reported model-based underlying respiratory mortality due to RSV for 1999–2018 using both death certificate and laboratory surveillance data. They estimated the average annual number of respiratory deaths due to RSV was 96 [7], roughly 3.4 times greater than the RSV deaths and 1.2 times greater than the bronchiolitis deaths reported in the current study, which was not an excess mortality analysis.

Our findings also showed that RSV mortality in infants often exceeded influenza mortality, which is consistent with Hansen et al who reported RSV mortality to be 5 times greater than influenza mortality for the same time period of 1999–2018 [7]. Since 1998, palivizumab is the only available RSV immunoprophylaxis, but it is not broadly recommended for all infants [9, 26]. In contrast, since 2003, annual influenza vaccination is recommended for all infants starting at 6 months of age [5, 6]. Development of new immunization strategies for RSV

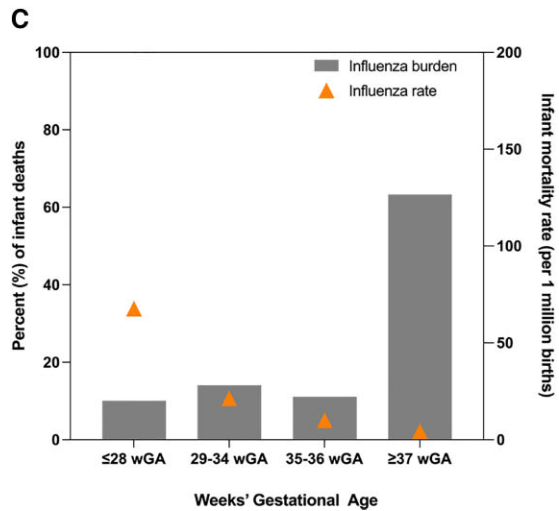
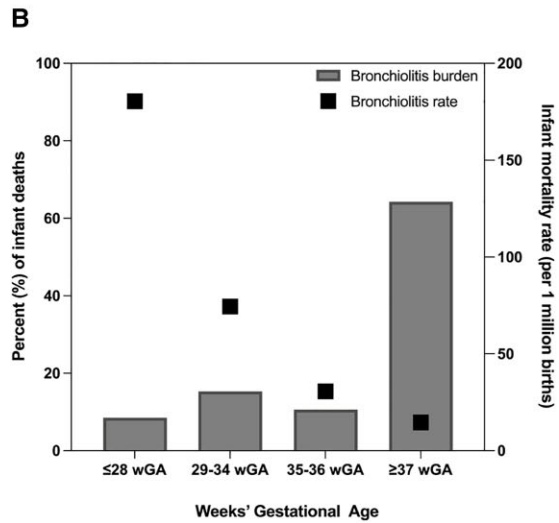
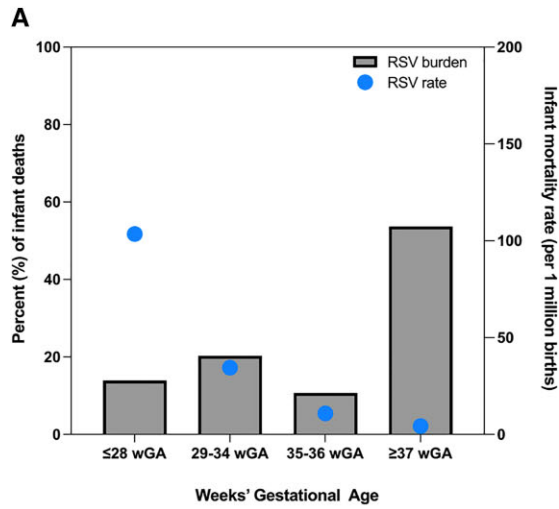


Figure 3. Percent of infant deaths (burden) and infant mortality rate per 1 000 000 live births by weeks' gestational age (wGA), US infants aged <1 year, National Center for Health Statistics/National Vital Statistics System 1999–2018: (A) respiratory syncytial virus (RSV); (B) bronchiolitis; and (C) influenza. RSV, bronchiolitis, and influenza were defined by ICD-10 cause of death code in any position: RSV, B97.4, J12.1, J20.5, J21.0; bronchiolitis, all RSV codes and J21.8, J21.9; and influenza, J09, J10.0, J10.1, J10.2, J10.8, J11.0, J11.1, J11.2, J11.8.

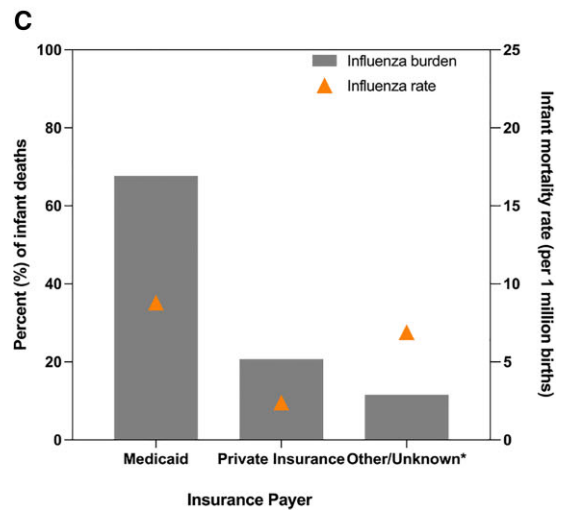
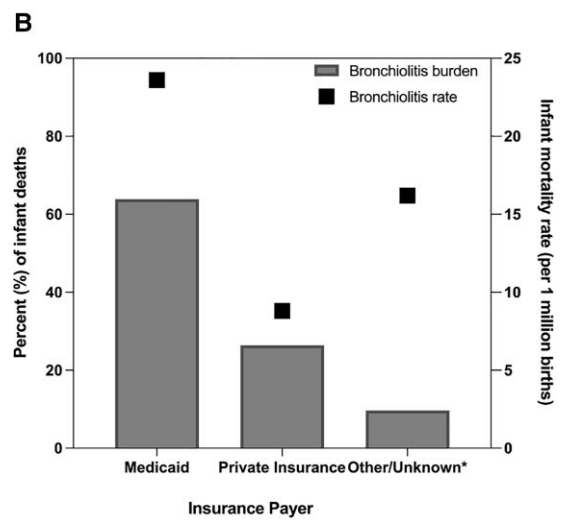
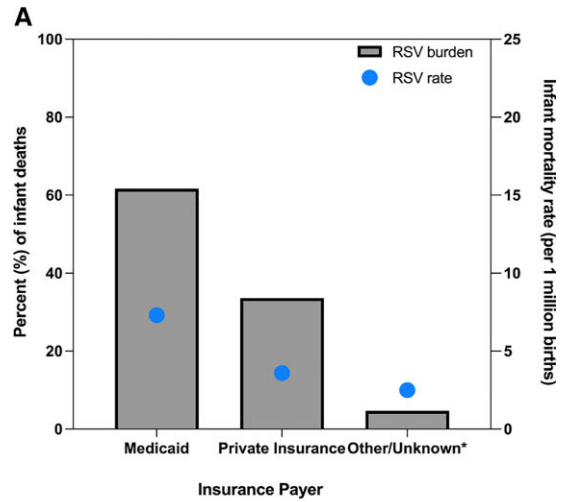


Figure 4. Percent of infant deaths (burden) and infant mortality rate per 1 000 000 live births by insurance payer, US infants aged <1 year, National Center for Health Statistics/National Vital Statistics System 1999–2018: (A) respiratory syncytial virus (RSV); (B) bronchiolitis; and (C) influenza. RSV, bronchiolitis, and influenza were defined by ICD-10 cause of death code in any position: RSV, B97.4, J12.1, J20.5, J21.0; bronchiolitis, all RSV codes and J21.8, J21.9; and influenza, J09, J10.0, J10.1, J10.2, J10.8, J11.0, J11.1, J11.2, J11.8.

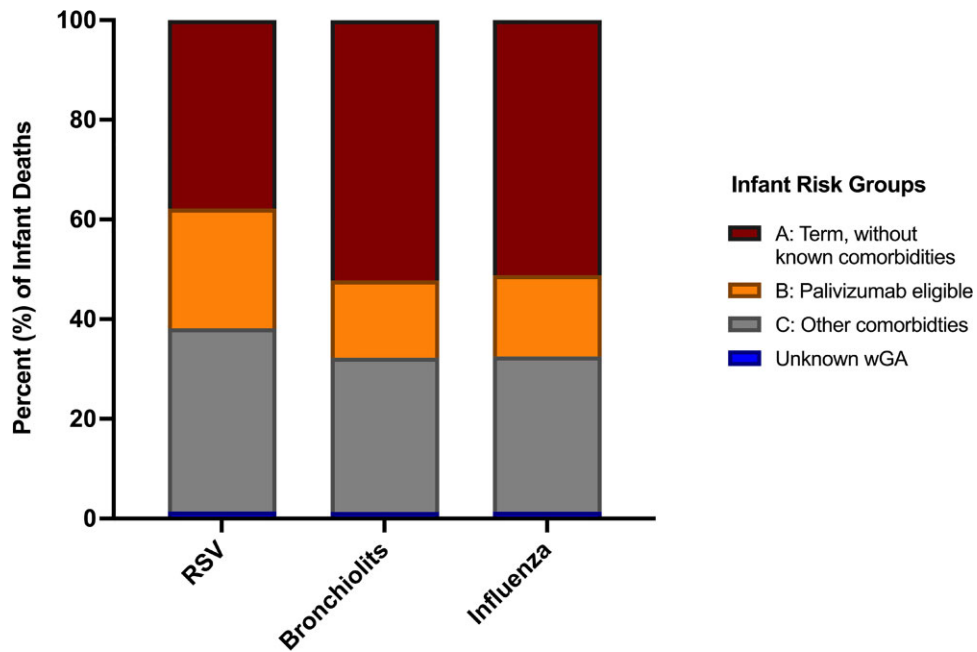


Figure 5. Percent of infant deaths associated with respiratory syncytial virus (RSV), bronchiolitis, and influenza by risk group, US infants aged <1 year, National Center for Health Statistics/National Vital Statistics System 1999–2018. Infant risk groups were defined as (A) full term (37+ wGA) infants without comorbidities; (B) palivizumab eligible, preterm <29 wGA, preterm 29–31 wGA with CLD, or preterm 29+ wGA with higher-risk CHD; and (C) preterm 29–31 weeks without CLD or higher-risk CHD, preterm 32–36 wGA without higher-risk CHD, or full term with other comorbidities. RSV, bronchiolitis, and influenza were defined by ICD-10 cause of death code in any position: RSV, B97.4, J12.1, J20.5, J21.0; bronchiolitis, all RSV codes and J21.8, J21.9; and influenza, J09, J10.0, J10.1, J10.2, J10.8, J11.0, J11.1, J11.2, J11.8. Abbreviations: CHD, congenital heart disease; CLD, chronic lung disease of prematurity; wGA, weeks' gestational age.

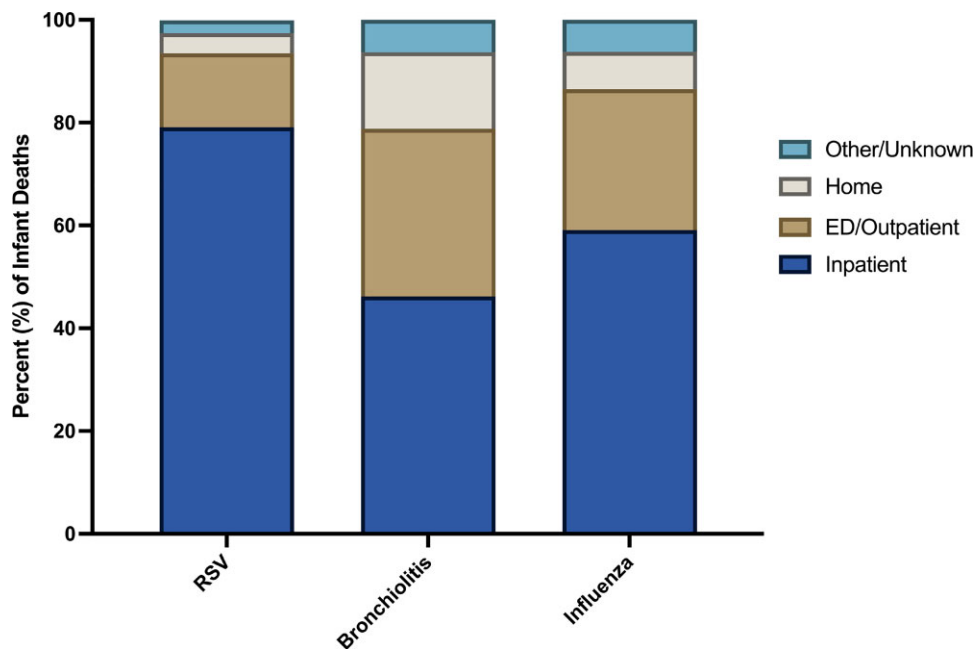


Figure 6. Percent of infant deaths associated with respiratory syncytial virus (RSV), bronchiolitis, and influenza by setting of death, US infants aged <1 year, National Center for Health Statistics/National Vital Statistics System 1999–2018. RSV, bronchiolitis, and influenza were defined by ICD-10 cause of death code in any position: RSV, B97.4, J12.1, J20.5, J21.0; bronchiolitis, all RSV codes and J21.8, J21.9; and influenza, J09, J10.0, J10.1, J10.2, J10.8, J11.0, J11.1, J11.2, J11.8. Abbreviations: ED, emergency department.

offer hope to prevent RSV illnesses and thus RSV mortality burden [27, 28]; however, these strategies depend on timely and accurate data. Considering that infant mortality from RSV greatly exceeds that of influenza and full-term infants and those without comorbidities comprise the majority of RSV and bronchiolitis deaths, adoption of a similar RSV immunoprophylaxis program for all infants may be warranted to protect at-risk infants and also alleviate the mortality burden due to this disease.

Another important finding is the setting at time of death. Leader and Kohlhasse [1] reported approximately 52% of RSV deaths occurred outside of the IP setting in 1999. C. L. Hansen et al. [20] reported 27% of RSV deaths and 75% of bronchiolitis deaths occurred outside of the IP setting; the study authors used unspecified bronchiolitis (J21.9) to define bronchiolitis deaths. Our study, which used a broader definition of bronchiolitis (6 codes), found that 21%–54% of RSV, bronchiolitis, and influenza deaths occurred outside of the IP hospital, with a greater proportion of bronchiolitis deaths occurring outside of the IP setting for Medicaid-insured infants, compared to infants with private insurance. One study evaluated trends in overall infant mortality from all causes in the United States from 1915 to 2017 and concluded that social inequalities continue to persist among disadvantaged populations [29]. In this study, RSV deaths outside of the IP setting may be due to barriers in healthcare utilization, including lack of information (eg, education disparities), limited facility access, or financial limitations. As Medicaid-insured infants experienced the highest RSV mortality rate and burden including greater proportion of out-of-hospital deaths, this study highlights the need to focus on early detection of disease, immunoprophylaxis, and access to medical care in these populations. Moreover, evaluating deaths in the IP setting alone does not provide a comprehensive perspective of RSV mortality in infants.

Limitations of this study include the reliance on ICD-10 coding for cause of death, which is subject to error and may result in misclassification. In addition, comorbidity coding of CLD and higher-risk CHD relied on ICD-10 codes on the death certificate, which may result in underreporting of these conditions. Additional misclassification may have occurred with the characterization of infant race/ethnicity based on maternal race/ethnicity. Furthermore, given the presence of multiple cause-of-death codes, infant deaths could have been counted in multiple disease categories. Due to small cell counts in some cases, multivariate analyses are not presented. Despite these limitations, this study has many strengths, including the representativeness of the data by utilizing the sole source of national linked birth and death data in the United States capturing all mortality regardless of setting; data for full-term infants and those without comorbidities; and the stratification of RSV, bronchiolitis, and influenza mortality by infant birth and death variables including setting at death.

These recent, national data indicate that mortality estimates based solely on IP hospital deaths or infants with comorbidity

conditions may severely underestimate the burden of RSV and bronchiolitis among US infants. Implementation of prevention and mitigation strategies, including early detection, immunoprophylaxis, and access to care, is dependent on accurate and representative estimates of both the risk and burden. Therefore, the contribution of all infants across all healthcare settings needs to be accounted for when describing the true incidence and resulting mortality associated with RSV.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (<http://jid.oxfordjournals.org/>). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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