

# Pediatric Population Size Is Associated With Geographic Patterns of Acute Respiratory Infections Among Adults

**John S. Brownstein, PhD**  
**Kenneth D. Mandl, MD, MPH**

From the Division of Emergency Medicine, Children's Hospital Boston; Children's Hospital Informatics Program at the Harvard-MIT Division of Health Sciences and Technology; and the Department of Pediatrics, Harvard Medical School, Boston, MA.

**Study objectives:** We measure the association between proportion of children and specific pediatric age groups in a local population with the timing and rate of adult emergency department (ED) utilization for influenza and other acute respiratory infections.

**Methods:** We performed an ecologic study on a time-series of adult patients presenting to Massachusetts EDs and residing in the greater Boston area from October 1, 2001, to September 30, 2005. Patients presenting with acute respiratory infection, used as a marker for influenza, were aggregated by home address ZIP code. We measured geographic patterns of timing and rate of adult respiratory infection-related ED utilization. We performed correlation analysis of rates and peaks identified in this analysis with pediatric population data from the US census (including specific pediatric age groups) by Poisson regression.

**Results:** One hundred fifty seven thousand five hundred forty two adult respiratory infection-related ED visits (30 visits per 1,000 adults per year) were analyzed. Visits were distributed across 55 of ZIP codes, in which proportions of children (aged 0 to 18 years) ranged from 2.7% to 34.9% in these communities. Proportion of children in a ZIP code was directly associated with timing of seasonal onset of acute respiratory infections among adults (univariate Poisson regression rate ratio [RR] 0.985; 95% confidence interval [CI] 0.977 to 0.993). The proportion of children also explained the patterns of adult acute respiratory infection-related ED utilization rates (RR 1.035; 95% CI 1.024 to 1.047). Three- to 4-year-olds were found to be the most significant predictors of adult illness rate (RR 1.380; 95% CI 1.238 to 1.539) and timing of onset (RR 0.881; 95% CI 0.816 to 0.952).

**Conclusion:** We demonstrate a positive correlation between the timing and rate of ED utilization by adults and the proportion of children in the population. These findings add to a growing body of evidence supporting a critical role played by children in community-wide transmission of acute respiratory infections. [Ann Emerg Med. 2008;52:63-68.]

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## INTRODUCTION

Influenza epidemics occur each year during the winter in temperate areas of the world, causing tens of thousands of deaths<sup>1-2</sup> and hundreds of thousands of hospitalizations<sup>3,4</sup> and having enormous economic influence.<sup>5</sup> Other respiratory virus epidemics, including respiratory syncytial virus and parainfluenza virus, co-occur with influenza epidemics, contributing to morbidity and mortality.<sup>6</sup> The ready spread of acute respiratory infections among children in daycare, preschool, and schools and household transmission to family members appear to be important modes of transmission.<sup>7-12</sup>

There is empirical confirmation of a relationship between geography and respiratory infection risk and timing across spatial scales.<sup>13</sup> However, spatial patterns for health care use and the contribution of population age structure are not well characterized, usually because of the paucity of health care data sets with high geographic resolution. In this study, we seek to measure the role of children as vectors for spread of influenza and other acute respiratory infections among adults. Specifically, we measure the association, per administrative geographic area, of the proportion of children on the rate and timing of adult emergency department (ED) utilization for acute respiratory

**Editor's Capsule Summary***What is already known on this topic*

Acute respiratory infections account for a large number of emergency department (ED) visits during influenza season.

*What question this study addressed*

Does the proportion of children in the population correlate with the incidence of adult respiratory infections?

*What this study adds to our knowledge*

Records of Boston-area ED visits throughout a 4-year period were matched with census data to demonstrate that a higher local population density of children is associated with more adult respiratory infection visits and an earlier seasonal onset.

*How this might change clinical practice*

Targeting children for influenza vaccination might improve influenza control in the adult population.

infections. We then break down the association by specific policy-relevant pediatric age groups.

**MATERIALS AND METHODS****Study Design, Setting, and Data Collection and Processing**

We performed an ecologic study based on time-series analyses of influenza and other acute respiratory infection–related adult ED visits in eastern Massachusetts to define spatial and temporal patterns of disease in areas surrounding Boston and association with the pediatric population. These data are from the Massachusetts Division of Health Care Finance and Policy.<sup>14</sup> This database, which began in fiscal year 2002, captures data for outpatient visits to all Massachusetts acute care hospitals EDs and satellite emergency facilities (89 facilities included in total). Data elements include patient demographics, clinical characteristics, services provided, charges, and hospitals and practitioner information, as well as mode of transport. The study had institutional review board approval (protocol No. X05-09-069R).

**Selection of Participants**

Inclusion criteria were adults aged 18 years or older, presentation to one of 89 medical institutions in Massachusetts with an acute respiratory infection–related ED diagnostic code, and home address 5-digit ZIP code in the greater Boston area. Diagnostic codes were based on the *International Classification of Diseases, Ninth Revision (ICD-9)* and included 079.99, 382.9, 460, 461.9, 465.8, 465.9, 466.0, 486, 487.0, 487.1, 487.8, 490, 780.6, and 786.2. These *ICD-9* codes have been used as markers of influenza-like illness in the absence of laboratory-confirmed infection data.<sup>9</sup> The time series of these syndromes corresponds especially tightly with time series for virologic

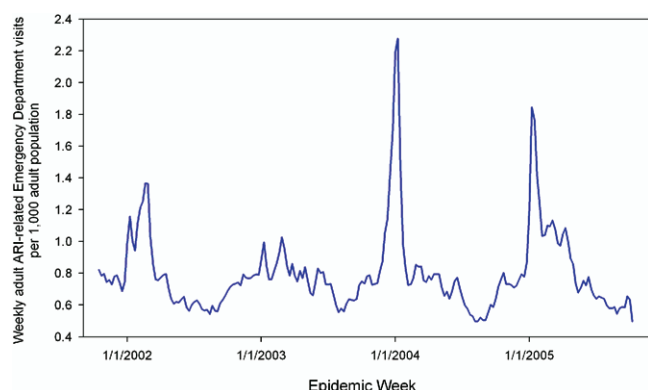
isolates of influenza. The sample spanned October 1, 2001, to September 30, 2005, inclusive of 4 winter seasons. Acute respiratory infection visits were aggregated by the 5-digit ZIP code of the patient's home address.

**Primary Data Analysis**

The primary outcome is rate of ED utilization for acute respiratory infections among adults in each ZIP code. We calculated this rate of visits among adults (18 years and older) attributed to acute respiratory infections per year, using all adults living in those selected ZIP codes from the 2000 US census as the denominator. The secondary outcome was the timing or onset of the winter acute respiratory infections among these adults. To construct this outcome, we created a weekly time series of adult acute respiratory infection–related ED utilization in each ZIP code. We identified the timing of winter acute respiratory infections in a given ZIP code by calculating peak week of acute respiratory infection visits. We estimated phase shifts (ie, lead time) between the underlying yearly components of the acute respiratory infection time series in each ZIP code by calculating the mean peak week of activity; these estimates are measures of the extent to which one series leads the other, yielding the second outcome of relative timing of activity in each ZIP code. This approach allowed determination of the relative timing of spread across different areas.

First, our 2 outcomes were analyzed against the proportion of pediatric patients in each ZIP code to measure the association of the proportion of children with the rate and timing of adult ED utilization because of acute respiratory infections. The 2000 US census provided estimates for the proportion of all children (younger than 18 years) in each ZIP code. We assessed the association between the proportion of all children and the timing and rate of acute respiratory infection–related utilization by fitting generalized linear models to respiratory presenting complaints.<sup>15</sup> Poisson distribution was assumed because it is appropriate for modeling counts of independent events. To account for this overdispersion in the count data, extra-Poisson variability was modeled and incorporated into estimates of standard errors.<sup>16</sup> Specifically, standard errors were multiplied by a dispersion (scale) parameter, a ratio of the deviance to its associated degrees of freedom. We built log-linear regression models of ZIP-code-based counts of adult-related acute respiratory infection, using the log-transform of the underlying census-estimated population as the offset.

Because other demographic factors may influence both the rate and timing of adult acute respiratory infections and the population of children, we adjusted for potential confounding of the effect of age by population density, race, and socioeconomic status. For each of the study ZIP codes, we calculated the number of individuals per square mile and proportion of the population below the poverty line per ZIP code, as provided by the US census. We also examined confounding by race by including the proportion of nonwhite residents by ZIP code. Each of these factors was included as



**Figure 1.** Weekly rate of adult acute respiratory infection-related ED visits per 1,000 adult population, eastern Massachusetts, 2001 to 2005.

additional covariates in the model. Their interaction with the proportion of children per ZIP was also examined.

Second, we assessed association between our 2 outcomes and specific pediatric age groups to measure which pediatric age groups are most associated with the rate and timing of adult ED utilization because of acute respiratory infections. We obtained US census population estimates for 5 policy-relevant pediatric age groups: 0 to 2, 3 to 4, 5 to 9, 10 to 14, and 15 to 17 years. For each ZIP code, we calculated the proportion of each pediatric age group relative to the estimated total population in the ZIP. We applied the same regression strategy as above but this time including each age group as a covariate. Individual age groups were included in the model separately and in aggregate.

Overall model fit for each of the Poisson regression models was calculated by comparing deviance statistics with their asymptotic  $\chi^2$ .<sup>17</sup> Parameter estimates were transformed to rate ratios (RRs) so that they could be expressed as percentage change in respiratory presenting complaints. A significant contribution of each effect to model fit was assessed by using 2-tailed  $\chi^2$  tests and  $\alpha \leq 0.05$  for rejecting the null hypothesis of no effect. All analyses were carried out using the SAS statistical software (version 9.0; SAS Institute, Inc., Cary, NC).

## RESULTS

Our data set included 18,710,970 visits during the 4 influenza seasons (October 1, 2001, to September 30, 2004) across 89 health care institutions (Figure 1). Of those, 247,843 were classified as acute respiratory infection in the 55 ZIP codes comprising the greater Boston area; 157,542 of the visits (63.7%) were by adults (aged 18 years and older), which composed our study sample. The rate of visits attributed to acute respiratory infection ranged from 2.94 to 87.67 per 1,000 adult population per year, with a median of 31.93 per 1,000 adults (Figure 2B). Each ZIP code population had a highly seasonal cycle in which onset of illness occurred from the beginning of December to the end of April (Figure 2C). The majority of ZIP codes had onset within a much narrower period, at the end of January/beginning of February; the 95% confidence interval (CI) ranged 3.2 weeks.

We found wide variation in population age structure across our study area in eastern Massachusetts. According to the Census 2000 data, the proportion of children younger than 18 years ranged from 2.69% to 34.91% in the study ZIP codes (Figure 2A). ZIP codes with relatively higher numbers of children were identified in outlying areas primarily south and north of Boston.

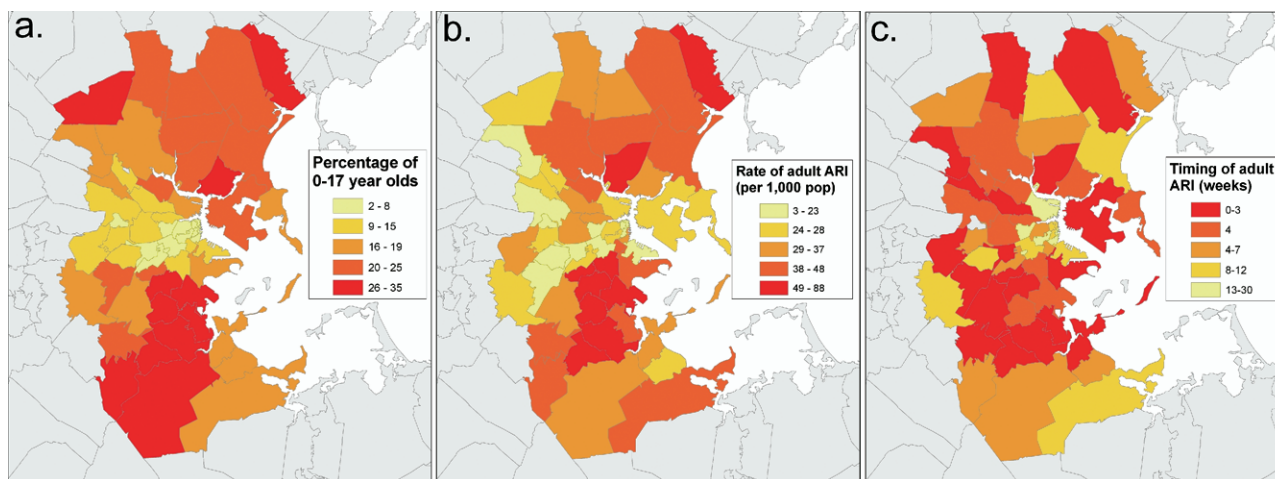
Onset of the winter acute respiratory infection season among the adult population was associated with the proportion of children in each ZIP code (Table 1). Univariate Poisson regression revealed that increase in the proportion of children in a ZIP code was significantly associated with an earlier than average onset of acute respiratory infections (RR 0.985; 95% CI 0.977 to 0.993) (Figure 3B). Further Poisson regression analyses were conducted to examine the influence of specific pediatric age groups (Table 1). All pediatric age groups were predictors of acute respiratory infection timing among adults, with the 3- to 4-year-olds having the strongest association (RR 0.881; 95% CI 0.816 to 0.952).

The pediatric population also significantly explained patterns of adult acute respiratory infection-related ED utilization, with increases in the proportion of children in a ZIP code significantly associated with higher utilization rates (RR 1.035; 95% CI 1.024 to 1.047) (Figure 3A). Although all proportions of each of the pediatric age groups were significant predictors of acute respiratory infection utilization rate, the preschool-age children (3 to 4 years) were the best predictors of utilization among adults (RR 1.380; 95% CI 1.238 to 1.539).

We examined potential confounding of the effect of age on timing and rate of ED utilization by population density, race/ethnicity, and poverty. We did not find a significant effect, nor did inclusion in the model including interaction terms influence prediction by age (Table 2). However, in the geographic region studied, the population was relatively homogeneous with respect to these factors.

## LIMITATIONS

Our study is based on a number of assumptions. The indirect approach to defining the association between ED visits and census-level characteristics may result in ecologic fallacy. Although we identified a strong correlation, the study design prevented us from making inference about causation. We did not measure the contact network between individual pediatric acute respiratory infection cases and infection in adults. Furthermore, our use of patient residence address ZIP code may incorrectly imply that infection took place in the home. Other unmeasured variables related to changes in the pediatric population may explain the geographic differences in adult acute respiratory infection. For instance, the Boston city center, with the smallest pediatric populations, is populated by college students who may not receive care from the ED or may report a home address outside of the state. This confounder would tend to artificially diminish the rates of adult acute respiratory infection illness. Furthermore, given our relatively small RR values, we expect that other unmeasured individual factors may play an important role in the observed spatial patterns of utilization.



**Figure 2.** Comparison of spatial distribution of children and overall population-wide timing and incidence of acute respiratory infection-related ED visits, eastern Massachusetts, 2001 to 2005. A, Proportion of children younger than 18 years in the population across according to the 2000 US census in 55 ZIP codes surrounding Boston, MA. B, Rate of adult visits related to acute respiratory infection per 1,000 adult population per year by ZIP code. C, Timing of influenza activity as determined by peak analysis performed on each ZIP code time series data. The phase shift (in weeks) between each data stream represents the timeliness of the data stream, in which lower values indicate earlier activity and week 1 represents the first week of the year.

**Table 1.** Timing and rate of acute respiratory infection-related ED utilization among adults per percentage increase in the proportion of pediatric age groups in eastern Massachusetts, 2001 to 2005.

Population	Regression Models*	
	Effect of Percentage Increase in Pediatric Population on Timing of Adult ARI Visits (by Week of Year), RR (95% CI)	Effect of Percentage Increase in Pediatric Population on Rate of Adult ARI Visits (per 1,000 Population), RR (95% CI)
All children	0.98 (0.98–0.99)	1.04 (1.02–1.05)
Age, y		
0–2	0.98 (0.92–1.05)	1.24 (1.14–1.37)
3–4	0.88 (0.81–0.96)	1.38 (1.24–1.54)
5–9	0.95 (0.92–0.97)	1.12 (1.08–1.16)
10–14	0.999 (0.9998–1.0)	1.0002 (1.0001–1.0003)
15–17	0.91 (0.87–0.95)	1.23 (1.15–1.32)

ARI, Acute respiratory infection.

\*Results are based on univariate Poisson regression analyses.

The study may be also limited by the broad case definition for acute respiratory infection and the lack of viral confirmation of cases, though this method of identifying cases of influenza has been validated in multiple previous studies.<sup>18,19</sup> Children in particular have different clinical presentations that may lead to misclassification. Thus, influenza-like illness surveillance is not entirely specific to influenza. Nonetheless, previous studies have shown that this subset of ICD-9 codes data is an accurate measure of acute respiratory infection burden in the absence of viral data and that ED data do track closely with viral isolates and with traditional Centers for Disease Control and Prevention

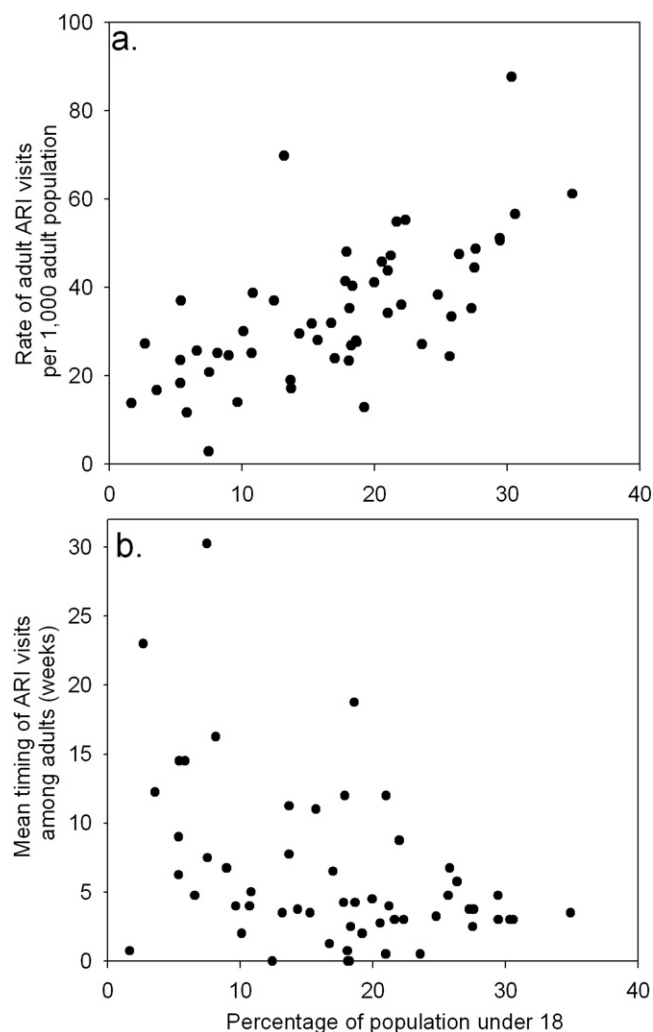
influenza surveillance data.<sup>7,20</sup> Because primary uses of these data are for nonresearch purposes and health care utilization encompasses a complex behavioral component, caution should be applied to any conclusions drawn from these primarily administrative data sets. Finally, because our analysis was based on population data from the 2000 US census and the study is from 2001 to 2004, potential population shifts in the pediatric population could not be accounted for.

## DISCUSSION

To our knowledge, we found for the first time that spatial patterns of ED utilization for respiratory viruses among adults are associated with the population age structure. We demonstrated a positive correlation between the rate of acute respiratory infection-related ED utilization by adults and the proportion of children in the population. Further, the proportion of children in a local population was significantly associated with the timing of the winter respiratory viral season among adults. Areas with high proportion of children tended to have early and greater adult presentations for influenza and other acute respiratory infections. These findings add to a growing body of evidence supporting a critical role played by children in community-wide transmission of acute respiratory infections.<sup>9–12</sup>

Our findings are consistent with previous research showing preschool-age children to be the early sentinels of activity and significantly associated with population-wide morbidity and mortality caused by influenza.<sup>7</sup> The US Advisory Committee on Immunization Practices recently recommended vaccinating 3- and 4-year-olds, extending the 2004 recommendation for vaccination of 6- to 24-month-olds.<sup>21</sup> Our findings lend support to the 2006 committee's recommendation to expanded





**Figure 3.** Association between pediatric populations and timing and rate of acute respiratory infection-related ED utilization among adults, eastern Massachusetts, 2001 to 2005. Influence of the proportion of all children living in each of 55 ZIP codes on (A) rate (per 1,000 adult population/year) and (B) timing of visits because of acute respiratory infection by adults (>18 years of age), in which week 1 is the first week of the year.

universal vaccination to include preschool children but further suggest that expansion of these recommendations to include all children may yield substantial benefit. Although preschool children may be the earliest sentinels of infection, schoolchildren represent a larger segment of the population and thus may contribute more substantially to overall transmission intensity.<sup>20,22</sup> Our findings suggest that there may be community-wide benefits from routinely vaccinating older children against influenza as well. Whereas previous recommendations were based on protecting vulnerable individuals from severe complications of influenza, such a policy would shift toward a public health orientation; vaccinating

**Table 2.** Timing and rate of acute respiratory infection-related ED utilization among adults per percentage increase in the proportion of children after accounting for potential confounders in eastern Massachusetts, 2001 to 2005.

Variables*	Regression Models	
	Effect of Percentage Increase in Pediatric Population on Timing of Adult ARI Visits (by Week of Year), RR (95% CI)	Effect of Percentage Increase in Pediatric Population on Rate of Adult ARI Visits (per 1,000 Population), RR (95% CI)
Children alone (univariate)	0.98 (0.98–0.99)	1.04 (1.02–1.05)
+Poverty	0.98 (0.98–0.99)	1.03 (1.02–1.05)
+Density	0.98 (0.97–0.99)	1.04 (1.02–1.05)
+Race/ethnicity	0.99 (0.98–1.00)	1.03 (1.01–1.04)
+Poverty, density, race/ethnicity	0.98 (0.97–0.99)	1.02 (1.00–1.04)

\*Poverty was defined as percentage of population per ZIP code below poverty level. Population density was defined as total population per square mile by ZIP code. Race was defined as proportion of nonwhite residents by ZIP code.

children in part may protect others by reducing the overall community burden of influenza.<sup>23</sup>

Our findings may also have application for the control and prevention of other acute respiratory infections. Development of vaccines for respiratory syncytial virus and parainfluenza virus is under way. Understanding the impact of different pediatric age groups on community-wide acute respiratory infection transmission can help define control strategies including priority groups for targeted disease control and prevention.<sup>24,25</sup>

Although we cannot make claims about causality, this spatial analysis adds to a growing body of literature on the importance of the pediatric population in community-wide respiratory infection. Because this study is based on patient populations in the Boston area only, a larger US sample would more accurately reflect the variability of population characteristics, including age distribution, ethnicity, race, and socioeconomic status, and serve to bolster this relationship.

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**Address for correspondence:** John Brownstein, PhD, Division of Emergency Medicine, Children's Hospital Boston, Harvard Medical School, 1 Autumn Street, Room 542, Boston, MA 02215; 617-355-6998, fax 617-730-0267; E-mail: [john\\_brownstein@harvard.edu](mailto:john_brownstein@harvard.edu).

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