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Influenza And Asthma Hospitalizations In Nyc From 2002-2012

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Abstract

INTRODUCTION: The literature has focused primarily on rhinoviruses as the major determinant of asthma exacerbations. The association between other respiratory viruses such as influenza and asthma exacerbations is not well characterized and further understanding can better inform prevention strategies to reduce influenza-related asthma.

OBJECTIVES: The primary objective of this study is to determine whether asthma hospitalizations of children and adults in the five boroughs of New York City is correlated with influenza hospitalizations temporally and spatially and whether these correlations differ by county or age.

METHODS: A times series regression analysis was performed using influenza hospitalizations as the explanatory series and and asthma hospitalizations as the outcome series. A cross correlation function was computed to determine the temporal correlations between the two time series. A measure similar to traditional attributable risks was calculated across age groups and boroughs to assess differences in influenza-related asthma hospitalizations. Additionally, times series analysis was stratified by age and boroughs to examine the significance of influenza and asthma correlations across strata.

RESULTS: A seasonal ARIMA $(1,0,0)x(0,1,1)_{12}$ model was the final model for our data and yielded a significant positive correlation between asthma and influenza hospitalizations. After stratification by age, individuals 18 and older had significant correlations between influenza and asthma whereas there was no significant temporal correlation found in children 17 years or younger. Attributable risk percentages for adults (18-44, 45-64, 65+) increased with increasing age (2.9%, 3.4%, 4%, respectively). Positive significant correlations between asthma and influenza were found in the Bronx, Brooklyn, and Manhattan. Attributable risk percentages by borough identified the Bronx and Manhattan as the highest risk areas (2.6% and 2.5%).

CONCLUSION: Significant positive correlations between influenza and asthma hospitalizations were identified in this study. Influenza prevention strategies should emphasize older age groups. Environmental pollutants may interact with influenza to exacerbate asthma. Further research needs to be performed to understand the nature of interaction between environmental pollutants and respiratory viruses in effecting asthma and other respiratory-related outcomes.

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Table of Contents

Background

Asthma is a chronic lung disease that inflames and narrows the airways of the lungs, resulting in wheezing, coughing, shortness of breath, and chest tightness symptoms. The cause of asthma is believed to be an interaction of environmental and genetic factors (NIH). Irritants that trigger asthma are multi-factorial and include pollens, air pollutants, stress, and respiratory infections (Jackson et al. 2011, Johnston et al. 2002). Although a large body of research has demonstrated the positive association between viral respiratory infections and asthma exacerbations in children and adults, the reasons behind the increasing rates of asthma remain largely unknown (D'amato 2002). A growing body of evidence suggests that urbanization is linked to the rising rates of respiratory allergic diseases (D'Amato 2002, Brauer et al. 2002). The prevalence and severity of allergic diseases such as rhinitis and bronchial asthma are increasing, with individuals living in urban areas experiencing higher rates of asthma than those living in rural areas (D'Amato 2002). Reasons behind this urban trend have pointed to increasing concentrations of traffic related air pollutants in urban areas that parallel increasing frequencies of asthma (D'Amato 2002, Heinrich and Wichmann 2004). The influence of environmental factors, such as air pollutants, on asthma exacerbations in urban areas, therefore, warrants consideration alongside the effects of viral respiratory infections.

Research has tried to understand the link between asthma and viral infections. Upper respiratory tract viral infections by rhinoviruses, influenza, and respiratory syncytial virus (RSV) have been extensively reported as triggers for exacerbation of asthma in children and adults (Jackson et al. 2011). In an attempt to identify the major determinant of asthma exacerbation, further studies have examined the importance of certain

respiratory viral infections in asthma exacerbation and demonstrated that rhinoviruses in particular account for 50-80% of asthma exacerbations (Johnston et al. 1996, Nicholson et al. 1993, Khetsuriani et al. 2007). Though rhinoviruses have been identified as the most prevalent viruses amongst adults and children exhibiting acute asthma exacerbations, the seasonality of rhinoviruses does not match the seasonality exhibited in adult populations. Rhinoviruses are the most frequently isolated virus during most of the year aside from winter and comprise more than three-quarters of the viruses circulating in early autumn (Monto 2002). Peaks in asthma hospitalizations would therefore be expected to occur during the fall, however, this has only been observed in children (D'Amato 2002). On the other hand, influenza viruses predominate during the winter when the peak asthma hospitalizations rates occur in adults, suggesting the potential for influenza as one potential determinant of asthma hospitalizations in adult populations that has been overlooked by a literature that has emphasized rhinoviruses.

The objective of this research was to determine whether the incidence of asthma hospitalizations of children and adults in the five boroughs of New York City was associated with influenza hospitalizations, temporally, spatially. We expected that influenza and asthma hospitalizations would be correlated significantly in adult populations and less so with children due to the differences in peak asthma seasons. In addition, we suspected that areas with environmental stressors such as pollution or allergens would display higher proportions of influenza-related asthma hospitalizations. In order to assess the temporal relationship between influenza and asthma, a time series regression analysis was performed on influenza and asthma hospitalizations over a 10-year period (January 2002-December 2011). Data for the year 2012 was not included in time series analysis in order

to be used for model validation. Validation of the final model was done by creating a 2012 forecast of the model with and without influenza as a predictor of asthma. The results were then compared to the actual asthma hospitalizations that occurred in 2012 and examined for the best predictive capability. To determine the proportion of influenza-related asthma hospitalizations spatially, a measure similar to an attributable risk percentage was calculated for each borough using the complete 11-year period (January 2002-December 2012). By examining the patterns of influenza-related asthma hospitalizations within an urban environment, more targeted intervention measures can be employed to reduce influenza transmission and abate asthma exacerbations.

Methods

Data Collection

Data was extracted from the Statewide Planning and Research Cooperative System (SPARCS), a comprehensive, all-payer data reporting system that was established in 1979 in order to collect information on hospital discharges. The SPARCS database currently collects patient-level data of patient characteristics, diagnoses and treatments, services, and charges for all inpatient and outpatient hospitalizations in the state of New York. This study was approved by the institutional review boards of Yale University and Columbia University. It was deemed eligible for expedited review at Columbia University, and classified as non-human subjects research at Yale University due to the de-identified nature of the data.

Study Population

The SPARCS data used in this study spanned the period from January 2002 to December 2012, and was geographically restricted to the five New York City boroughs: Manhattan, Brooklyn, Queens, the Bronx, and Staten Island. First, all hospitalizations with a primary diagnosis of either asthma or influenza were identified using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes. Observations that had primary/principal ICD-9-CM codes of 493.0, 493.1, 493.2, 493.8, or 493.9 were classified as asthma-related hospitalizations. Observations that had primary/principal ICD-9-CM codes of 487, 487.0, 487.1, or 487.8 were classified as influenza-related hospitalizations. Additional variables extracted from the SPARCS database as control variables were age, sex, race, and ethnicity, which were based on medical records and were patient self-reported.

Descriptive Statistics

Descriptive statistics of asthma and influenza by age, sex, race, and ethnicity were performed to provide a basic outline of the sample from January 2002 to December 2012. Age was categorized into five groups (0-4, 5-17, 18-44, 45-64, 65+), based on clinical diagnosis ages and sample distribution. Plots were generated to examine the seasonality of asthma and influenza hospitalizations by each year, with seasons defined as three-month intervals ranging from December-February (Winter), March-May (Spring), June-August (Summer), and September-November (Fall). ZIP codes were aggregated to the borough level for analysis. Intra-class correlation coefficients (ICC) were calculated to explore how much of the outcome variation was explained by county and ZIP code.

Seasonal Auto-regressive Integrated Moving Average Modeling

Data from January 2002 to December 2011 was used for performing time series analysis, with the year 2012 used to validate the predictive capabilities of the final model. Before performing times series analysis, the Durbin-Watson test for autocorrelation was conducted on both flu and asthma hospitalization counts to determine whether time series analysis was applicable (Ali 1987). Once time series analysis was deemed appropriate for the data, the first step in creating a time series model was to determine whether the variables for asthma and flu hospitalizations met the assumption of stationarity (Dahlhaus 1997). Non-stationary variables require appropriate levels of differencing in order to stationarize the series. To assess stationarity, the augmented Dickey-Fuller test for stationarity was performed on both flu and asthma counts of hospitalizations, and plots of the autocorrelation function and time series were visually inspected (Dickey Fuller 1979, Dickey 1984). Based on these plots and statistics, the asthma and influenza series were log transformed and seasonally differenced.

In order to measure the similarity between the flu and asthma time series, a cross correlation function (CCF) was computed between the two series. Cross-correlation functions measure the degree of similarity between two time series by using the lags of both series (Box and Jenkins 2008). If the input series is auto-correlated, cross-correlation functions can result in misleading indications of the relationship between an input and response series. To solve this issue, pre-whitening was performed in our analysis. Pre-whitening of the model involved identification of a time series model for flu hospitalizations and filtering the asthma hospitalizations series with the flu time series

(Box and Jenkins 2008). Using results from the cross-correlation function plot, we fit a transfer function to the model and examined the residuals before proceeding to determine the auto-regressive and moving average orders.

A seasonal auto-regressive integrated moving average (SARIMA) model was used for this study, with asthma serving as the response series and influenza serving as the explanatory series. The auto-regressive and moving average orders for the SARIMA model were selected through evaluation of the autocorrelation function and partial autocorrelation residuals graphs (Liu 1987). Once the best-fit model was selected, the forecasted values for the model with and without flu over the 2002-2012 time period was plotted against the original data. Validation of the model was performed by utilizing the final model with and without influenza as the explanatory series to generate predicted values of asthma hospitalizations for 2012. The resulting predictions with and without influenza for 2012 were compared to the actual 2012 data to determine whether inclusion of influenza as an explanatory variable improved the predictive capability of the model.

To examine the associations between flu and asthma in the different age groups and boroughs, we applied our final model onto the complete data from January 2002 to December 2012 stratifying by age group (0-4, 5-18, 19-59, 60+) and borough (Bronx, Brooklyn, Manhattan, Queens, Staten Island).

Calculation of Excess Risk

A measure similar to an attributable risk percentage (ARP) was calculated for all age groups and boroughs in order to assess the excess risk of asthma hospitalizations due to influenza. This measure was formed by first identifying the peak month of influenza

between January and December of each year, from 2002 to 2012. Once the peak month was identified, the average counts of asthma hospitalizations were calculated for the 11 non-peak months and the complete 12 months, including the peak. The difference between the non-peak average and the average including the peak was defined as the excess risk. Attributable risk percentages were defined as the ratio between the excess risk and the total 12-month average of asthma hospitalizations. The final ARP shown represents the average ARP over the 11-year period.

All statistical analysis was performed using Statistical Analysis Software (SAS), version 8.4.

Results

Descriptive statistics of asthma and influenza hospitalizations from January 2002 to December 2012 are displayed in Table 1. There were a total of 6,342 counts of flu hospitalizations compared to 273,664 counts of asthma hospitalizations. The striking difference in hospitalization counts highlights the larger relative burden of asthma on hospital use and thereby hospital costs than influenza. Compared with influenza hospitalizations, there were more hospitalizations for asthma among non-Hispanic black individuals (29% vs. 42%, respectively). Females were disproportionately affected by asthma, as females comprised 58.5% of asthma hospitalizations. Analysis of sex by child and adult asthma hospitalizations revealed that amongst children (<18 years old), males were admitted nearly twice as often as females. Among adults between 18 and 45 years of age, the female-to-male ratio was 2:1. Adults 45 years of age and older had a female-to-male ratio of 2.5:1. Therefore, adult females and male children appeared to be

disproportionately affected by asthma. 26.3% of asthma hospitalizations were individuals between the ages of 45-64. Influenza hospitalizations by age group followed a bimodal distribution, where the youngest and oldest age groups comprised the majority of cases. Individuals 0-4 years of age made up the largest portion of influenza hospitalizations (40.5%). Examination of influenza and asthma hospitalizations between race and ethnicity were also performed and highlighted the potential classification issues with our race and ethnicity variables. Individuals who were Hispanic were found in all race categories with the largest proportion of Hispanics classified mostly as White or Other (Appendix A.1). The meaningfulness of our race and ethnicity variables is therefore questionable and raises concerns with regard to the reliability of hospital reporting of race and ethnicity.

Intra-class correlation coefficients (ICC) for seasonal asthma and influenza hospitalization counts were calculated across boroughs and ZIP codes to assess how strongly counts in their spatial clusters resembled each other. For influenza hospitalizations, 73.9% of the seasonal variability was explained by the clustering of boroughs, whereas only 37.9% of the variability was explained by ZIP code clustering (Appendix). For asthma hospitalizations, 66.9% of the seasonal variability was explained by the clustering of boroughs, and only 32.2% of the variability was explained by ZIP code clustering (Appendix). Examination of the correlation between influenza and asthma hospitalizations at the borough level is therefore more meaningful than at the ZIP code level.

Plots of the asthma and influenza hospitalization series by each year from 2002 to 2012 are displayed in Figure 1. Visual examination of the plots revealed a seasonal pattern for asthma and influenza, with peaks occurring in the winter months for influenza and

fall/winter for asthma. Asthma hospitalizations also appeared to be decreasing gradually over time (Figure 1a). In 2009, the United States experienced an outbreak of the H1N1 influenza strain, which resulted in an uncharacteristic peak of influenza activity in June (CDC). The plot for influenza in Figure 1d reflects this irregular summer peak, with the year 2009 plotted in pink. Figure 2 features seasonal plots of influenza and asthma hospitalizations for children (<18 years old) and adults (≥18 years old). Asthma hospitalizations in children presented a strong peak in fall that did not coincide with the winter peak of child influenza hospitalizations. Adult asthma hospitalizations, however, displayed a winter peak in asthma hospitalizations that matched the winter peak in influenza hospitalizations.

Time series analysis was performed on the January 2002—December 2011 time frame and the resulting SARIMA model was used to forecast asthma hospitalizations for 2012. The Durbin-Watson test for autocorrelation for both flu and asthma series was significant ($p<0.001$), confirming that positive autocorrelation existed in both series and that ARIMA modeling was appropriate. Before generating model parameters, the flu and asthma series were log transformed and seasonally differenced to normalize and stationarize the series. Based on the cross-correlation coefficient plot generated in the pre-whitening process, both variables appeared to evolve concurrently, with no variable leading or lagging the other (Appendix A.2). The final SARIMA model parameters are shown in Table 2. The final model consisted of an auto-regressive component of order 1 (AR(1)) and a seasonal moving average of order 1 (SMA(1)). The best-fit SARIMA model was therefore an ARIMA $(1,0,0)x(0,1,1)_{12}$ model. Also included in Table 2 is the flu estimate of 0.036 ($p=0.001$). The incidence of flu is therefore significantly correlated with asthma in a positive direction.

Additionally, the Akaike Information Criterion (AIC) for the model decreased from -153.8 to -161.9 when flu was incorporated into the model. The lower AIC value when including flu as a predictor of asthma suggested that the model with flu is a better fit for the data.

To further assess the fit of the model, the predicted values of asthma hospitalizations with flu as an explanatory variable were plotted with the actual asthma hospitalizations for the study period, as shown in Figure 3a. Visual inspection of the predicted series including flu with the actual asthma hospitalizations showed the model's close adherence to the actual hospitalizations. The model with and without influenza hospitalizations as an explanatory variable was then used to generate forecasted counts of asthma hospitalizations for 2012. Figure 3b displays the forecasted asthma counts with and without influenza hospitalizations, along with the actual 2012 asthma counts. The model including influenza appeared to yield similar predictions as the model without influenza. However, based on the findings from Figure 2, the differences in peak coincidence of asthma and influenza between adults and children raised questions regarding differences in forecasting by varying age groups, particularly with adults. Figure 3c and 3d present the 2012 forecasting plots of the model with and without influenza as an explanatory variable for individuals 18-44 years of age and individuals 45 years and older. The predicted asthma counts of the flu-inclusive model best matched the actual counts of asthma hospitalizations in those 45 years and older. These results, therefore, suggest that the influence of the temporal patterns of influenza hospitalizations on asthma hospitalization increases with increasing age.

Attributable risk percentages were calculated to examine excess risk of asthma hospitalizations that were associated with the flu. Figure 4 displays ARPs calculated by age

and borough. The ARPs represent the percentage of asthma hospitalizations that would be reduced if influenza hospitalizations during the peak month were controlled to the yearly average of influenza hospitalizations. Analyzing ARPs by age group revealed an increase in ARPs with increasing age (Figure 4a). When examining ARPs by borough, Manhattan and the Bronx had the highest ARPs (Figure 4b).

Time series analysis by age and borough was conducted to assess the significance of the correlation between flu and asthma by each stratum. Influenza estimates by age and borough are found in Table 3. Age groups under 18 years old did not have significant correlation between flu and asthma hospitalizations. Relating this significance to the attributable risk percentages would suggest that influenza and asthma are significantly correlated in age groups greater than 18 years old, and that at increasing age, temporal patterns in influenza hospitalizations increasingly accounted for asthma risk. Furthermore, controlling influenza hospitalizations to the monthly average could result in a reduction of as many as 4% of asthma hospitalizations amongst 65+ year olds. Examination of the Z-values, which reflect the size of the standardized effect, revealed the increasing magnitude of the effect of the temporal patterns of influenza hospitalizations on asthma hospitalizations with increasing age.

Flu hospitalizations were significantly correlated to asthma hospitalizations in the Bronx, Manhattan, and Brooklyn (Table 3). The Bronx and Manhattan had the highest percentage of asthma hospitalizations due to peak influenza activity, with roughly 2.5% of asthma hospitalizations in each area that could be avoided if influenza activity in the peak month were controlled to the yearly average (Figure 4b). The z-values for the boroughs in Table 3 were consistent with these ARP findings, as the magnitude of the z-values and,

thereby, the temporal effect of influenza hospitalizations on asthma hospitalizations was highest in the Bronx and Manhattan.

Discussion

The results from time series analysis indicate that flu and asthma hospitalizations are significantly correlated. In addition to the positive temporal associations between influenza and asthma hospitalizations, there is a spatial difference in attributable risk of asthma related to influenza across the five boroughs with the Bronx and Manhattan displaying the highest attributable risk percentages. The 2:1 ratio of black to white asthma hospitalizations supports previous research establishing the widening gap between white and black populations in asthma hospitalizations (Gupta et al. 2005). Differences in asthma hospitalizations between sexes at different ages in our findings were consistent with previous studies where male children and adult females had higher rates of hospital admissions for asthma (Skobeloff et al. 1992). Potential reasons for the higher rates of asthma admissions in adult females have pointed to hormonal or biochemical differences between sexes (Skobeloff et al. 1992). The results from the study also support previous research suggesting that improvement of surveillance, prevention, and transmission of influenza may lead to reduction of asthma hospitalizations (Gerke et al. 2014). However, more specific details as to who and where the preventative services should be targeting is necessary.

The combination of time series analysis by age group and calculation of ARPs revealed a directly proportional relationship between increasing asthma risk due to influenza and increasing age. However, the correlation between influenza and asthma was

only significant amongst age groups 18 and older. Individuals less than 18 years of age displayed low or even negative ARPs and non-significant influenza to asthma correlations. Such findings suggest that the temporal patterns of influenza hospitalizations are not correlated with asthma hospitalization and that influenza may not be a significant contributor to asthma hospitalizations in pediatric patients despite what previous research has concluded (Miller et al. 2008, Kramarz et al. 2001). These results are less surprising as asthma exacerbations in children lacked peak seasonal coincidence between asthma and flu as seen in Figure 2. Although, there does exist the potential for children to have high enough rates of influenza vaccination that would thereby reduce counts of influenza-related asthma hospitalizations. However, even with high vaccination rates, several studies examining the effectiveness of flu vaccination in reducing asthma exacerbations in children have presented null findings or even an inversely proportional relationship (Christy et al. 2004, Bueving et al. 2004, Cates et al. 2008). Other respiratory viruses such as rhinoviruses are more likely to be the major contributors to asthma exacerbations in children as they have accounted for two thirds of viruses detected in upper respiratory viral infections (Johnston et al. 1995). The lack of significant correlation between temporal patterns of flu hospitalizations and asthma hospitalizations in our findings advocates for additional analysis of the temporal correlations between rhinoviruses and asthma hospitalizations, particularly amongst children.

Asthma exacerbations in adults, however, would appear to benefit from influenza prevention strategies targeted particularly at older age groups. The temporal correlation between asthma and influenza hospitalizations in adults is further supported when considering that peak asthma hospital admissions rates for adults occur in the winter

months of December and January and peak hospitalization rates for children occur in the autumn months of September and October (Sears 2008). Interpretation of the cross correlation function plot suggested that associations between asthma and influenza occur concurrently with no variable leading or lagging. The peak months of asthma hospital admissions in adults would therefore coincide with the seasonal winter peaks observed in our time series plot of influenza and interactions between asthma and flu would arise concurrently (Figure 2). The fact that older populations have higher attributable risk percentages provides support for findings from studies that have examined the impact of influenza on hospitalizations. Influenza-related hospitalizations have been known to disproportionately affect elderly populations compared to those <65 years of age (Simonsen et al. 2000).

When influenza and asthma associations were examined by borough, correlations between both variables were significantly correlated in only the Bronx, Brooklyn, and Manhattan. The Bronx and Manhattan were identified as areas with the highest attributable risk percentages. Investigation of the three-way associations between asthma or flu, borough and sex, age, race, or ethnicity did not reveal any patterns of distribution that matched borough ARPs. The Bronx consistently ranks the highest out of the five boroughs in terms of negative health outcomes due to a mixture of poverty, crime, and environmental stressors (Maantay 2007, Garg et al. 2003). Based on data collected by the New York Department of Health, the highest asthma hospitalization rates exist in the Bronx, followed by Manhattan, Brooklyn, Queens, and Staten Island (Maantay 2007, Garg et al. 2003).

Aside from low socioeconomic status related factors, the spatial distribution of asthma hospitalization rates have been linked to air quality and pollutants as potential

causes (NYC DOH). A study conducted by the New York City Department of Health and Hygiene identified areas with the highest ozone attributable rates of ER visits for asthma among children and adults. The highest risk areas were concentrated in northern Manhattan, the Bronx, Central Brooklyn, and parts of eastern Queens (NYC DOH 2012). Additionally, air pollutant data on particulate matter, nitrogen dioxide, nitric oxide, and sulfur dioxide concentrations from the New York City Community Air Survey 2008-2010 identified Manhattan and the Bronx as the areas with the highest densities of pollutants due to the traffic density in those boroughs (NYC DOH 2012). The overlap of air pollutant spatial data with the borough stratified attributable risk percentages from our study suggests the potential for interaction between influenza and air pollution in determining asthma outcomes. Recent studies examining the potential effect modification of influenza on air pollution and health outcomes have yet to understand the association between the two factors (Wong et al. 2009, Thach et al. 2010). A 2002 study conducted by Green et al. examined the importance of exposure to allergens and viral infection on precipitating acute asthma and found that allergens and viruses may interact synergistically to increase asthma hospitalization risk. Further research is necessary to understand whether the relationship between influenza and air pollutants is synergistic or competitive and thereafter inform future research examining air pollutants and health outcomes such as asthma.

The large difference between the counts of asthma and influenza hospitalizations raises concern regarding the hospital use and the healthcare burden due to asthma. Each year asthma accounts for 479,000 hospitalizations (CDC). The incremental costs of asthma between 2002—2007 has been estimated at $3,259 per person per year with hospital costs

comprising the second largest percentage (~20%) of the incremental direct cost of asthma. Efforts to reduce asthma hospitalizations by controlling influenza activity in the peak month to the yearly average and/or reducing environmental pollutants that may synergistically interact with influenza to exacerbate asthma would therefore help in alleviating some of these asthma-related healthcare costs.

Our study had several limitations. First, the data do not provide asthma severity information, which is an issue as cases of asthma hospitalizations could be the more severe asthma cases. Individuals who have more severe asthma may already be vaccinated against flu in which case our results would not reflect the full potential effect of influenza on asthma. Secondly, we were not able to control for socioeconomic status due to the unavailability of an income variable in the SPARCS database. Socioeconomic status may reflect issues between poverty and health outcomes that we were not able to account for in our analysis. A proxy variable could potentially be set up for future improvement of our study. We also lacked environmental data such as humidity and temperature, which are known environmental factors that influence influenza transmission (He et al. 2013, Lowen et al. 2007, Shaman et al. 2010). Furthermore, we were not able to utilize a traditional method of calculating attributable risk due to the fact that we do not know the total number of people who had asthma and influenza and were at risk for hospitalization. Our study is also an ecological study so the findings of this hypothesis-generating study cannot be used to draw causal inferences at the individual level. Finally, issues with misdiagnosis of asthma in pediatric and adult populations could potentially under or over estimate the association between influenza and asthma hospitalizations. Likewise, changing definitions

over the 11-year period of influenza classification and diagnosis accuracy would affect the true association between influenza and asthma.

To conclude, our study findings indicate that influenza hospitalizations are significantly correlated with asthma hospitalizations. Based on our results, influenza prevention strategies to reduce asthma exacerbation should focus more heavily on older populations while further assessment of the effectiveness of influenza vaccination recommendations on childhood asthma hospitalizations needs to be conducted. Additionally, further research examining the relationship between influenza and environmental pollutants on asthma outcomes is necessary to improve upon our understanding of the risk factors behind asthma exacerbations. The relationship between influenza and environmental risk factors on health outcomes such as asthma is not well understood and warrants more investigation to understand pathways of manifestation.

Tables & Figures

Table 1. Percentage of Influenza and Asthma Hospitalizations January 2002—December 2012

	Diagnosis [a]			
	Influenza		**Asthma**	
Characteristic	(N = 6342)[b]	p[c]	(N =273664)[b]	p[c]
Age (years)		<0.001		<0.001
0-4	40.5		19.3	
5-17	9.0		17.2	
18-44	13.5		18.4	
45-64	15.1		26.3	
65+	22.0		18.8	
Sex		<0.001		<0.001
Female	49.7		58.5	
Male	50.3		41.5	
Ethnicity		<0.001		<0.001
Hispanic	32.5		35.1	
Non-Hispanic	67.6		64.9	
Race		<0.001		<0.001
White	32.7		21.2	
Black	28.9		41.9	
Asian	4.9		2.5	
Other	33.5		34.4	
Boroughs		<0.001		<0.001
Bronx	27.0		31.0	
Brooklyn	23.0		33.0	
Manhattan	21.8		16.0	
Queens	24.6		16.7	
Staten Island	3.7		3.4	

[a] Table values are column % for categorical variables.
[b] Percentages may not sum to 100% due to rounding.
[c] P-value is for t-test (continuous variables) or χ^2 test (categorical variables).

Table 2. Summary of the parameter estimates from the final time series model

Component	Estimate	SE	P-value
AR(1)	0.330	0.067	<0.001
SMA(1)	-0.763	0.094	<0.001
Flu	0.036	0.011	0.001

AR(1)—Autoregressive component of order 1
SMA(1)—Seasonal moving average component of order 1

Note: The final time series model was a seasonal ARIMA $(1,0,0)x(0,1,1)_{12}$ model.

Table 3. Flu estimates and effects of influenza on asthma hospitalizations by age and borough

Variable	Flu Estimate	SE	Z-value	P-value
Age (years)				
0-4	-0.025	0.017	-1.471	0.159
5-17	-0.014	0.024	-0.583	0.560
18-44	0.060	0.013	4.615	<0.001
45-64	0.070	0.011	6.363	<0.001
65+	0.063	0.009	7.000	<0.001
Borough				
Bronx	0.037	0.011	3.219	<0.001
Brooklyn	0.028	0.011	2.509	0.015
Manhattan	0.048	0.013	3.692	0.002
Queens	0.022	0.013	1.692	0.098
Staten Is.	0.037	0.025	1.480	0.13

The final time series model (seasonal ARIMA $(1,0,0)x(0,1,1)_{12}$ model) was applied to stratified age groups and boroughs to determine correlation between influenza and asthma by each stratum. Z-values were calculated by dividing flu estimates by standard errors to reflect the size of the standardized effect.

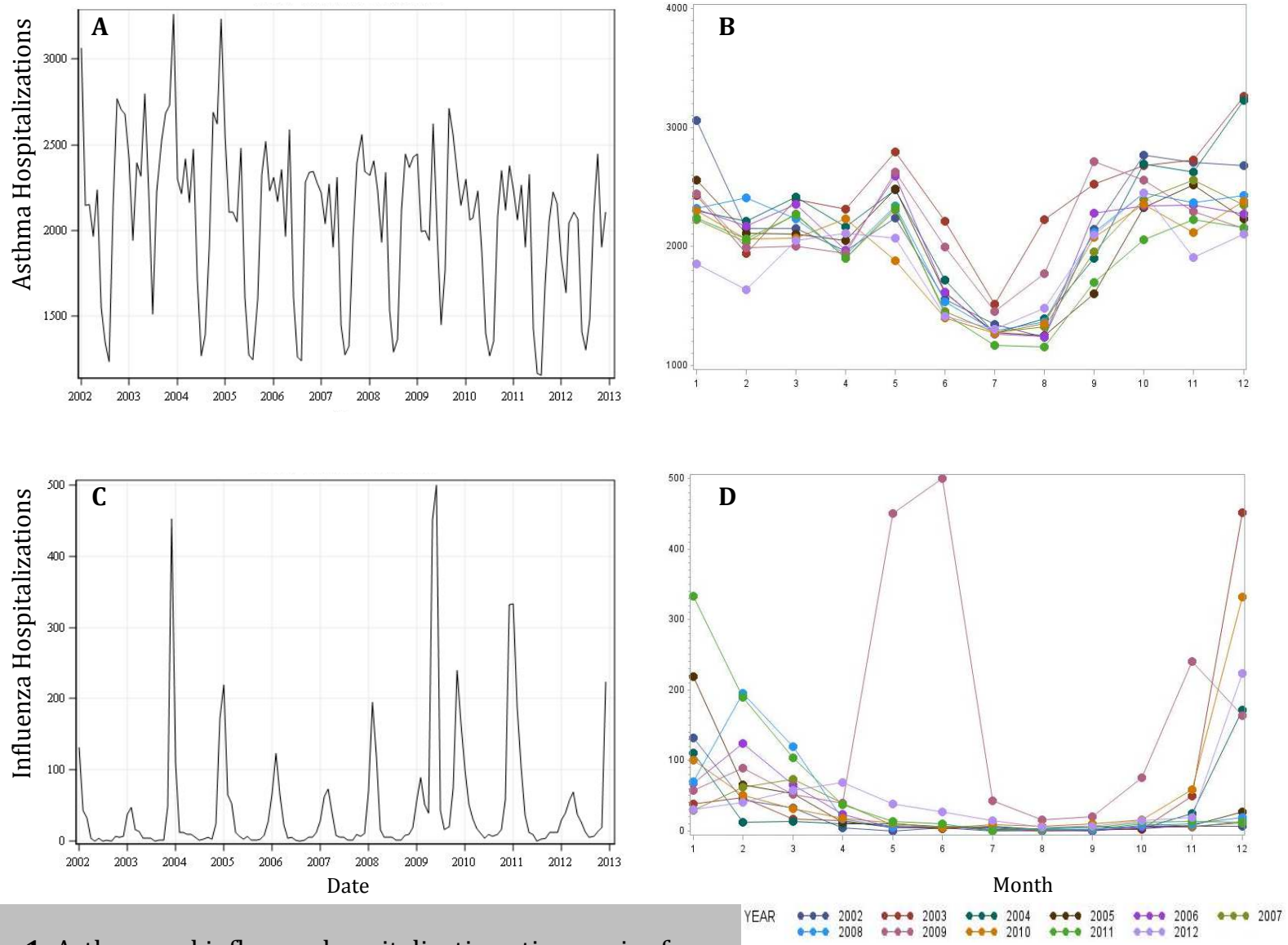


Figure 1. Asthma and influenza hospitalizations time series from January 2002-December 2012 (a and c) and monthly plots (b and d) with years color-coded. The pink series (d) identifies the 2009 H1N1 pandemic that peaked during the summer.

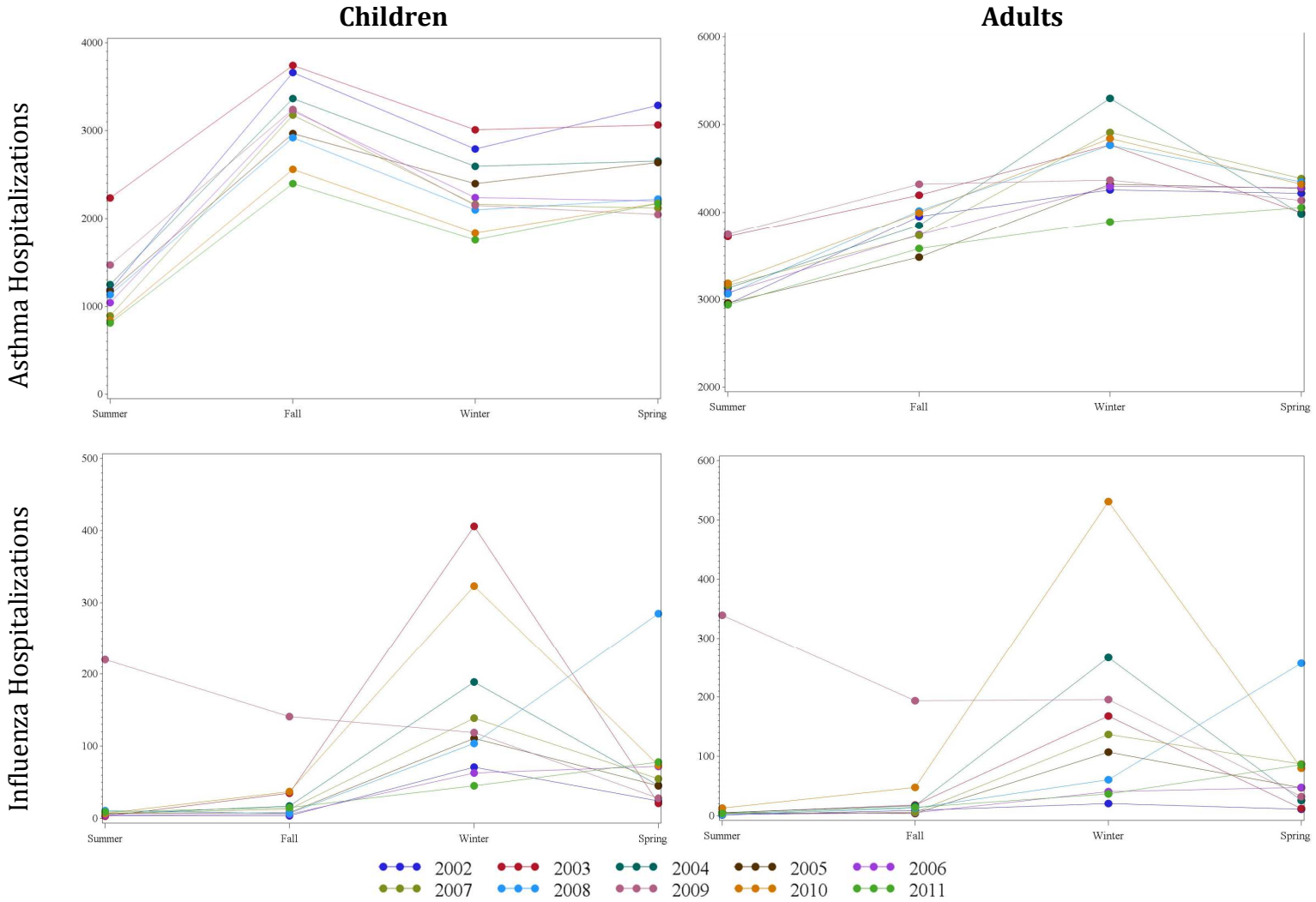


Figure 2. Seasonal plots of asthma and influenza hospitalizations for children and adults. Seasonal plots of (A) adult asthma hospitalizations, (B) child asthma hospitalizations, (C) adult flu hospitalizations, and (D) child influenza hospitalizations. Adults were defined as ≥18 years old and children were <18. Peak seasons for influenza hospitalizations occur during the winter for both children and adults. Peak seasons for asthma hospitalizations occur during the fall for children and during the winter for adults. Seasonal plots reveal the coinciding peak seasons between influenza and asthma hospitalizations in adults. Years are labeled based on the summer, fall, and winter seasons of that year with spring belonging to the following year (i.e. the blue 2002 plot represents Summer 2002—Spring 2003).

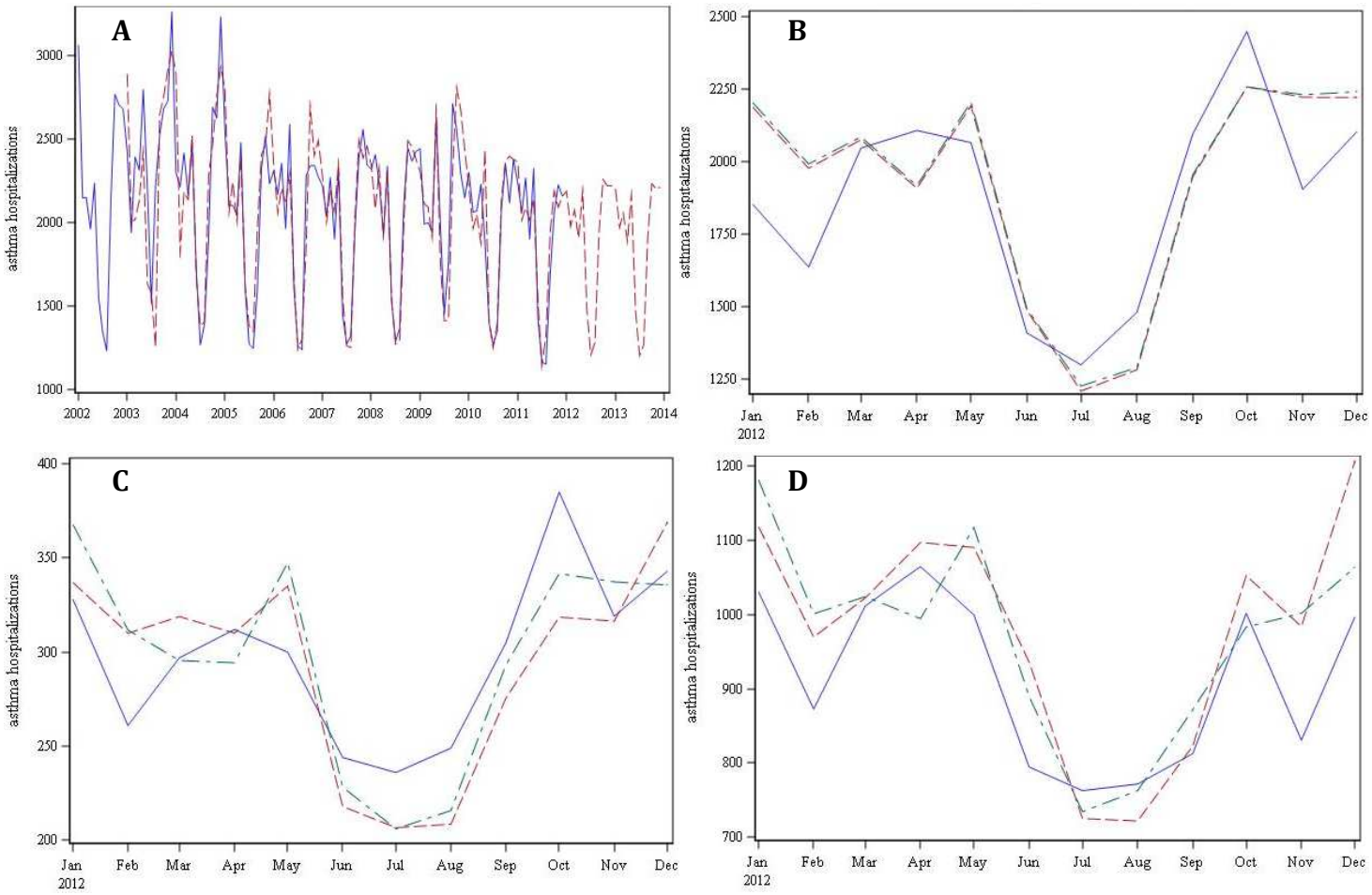
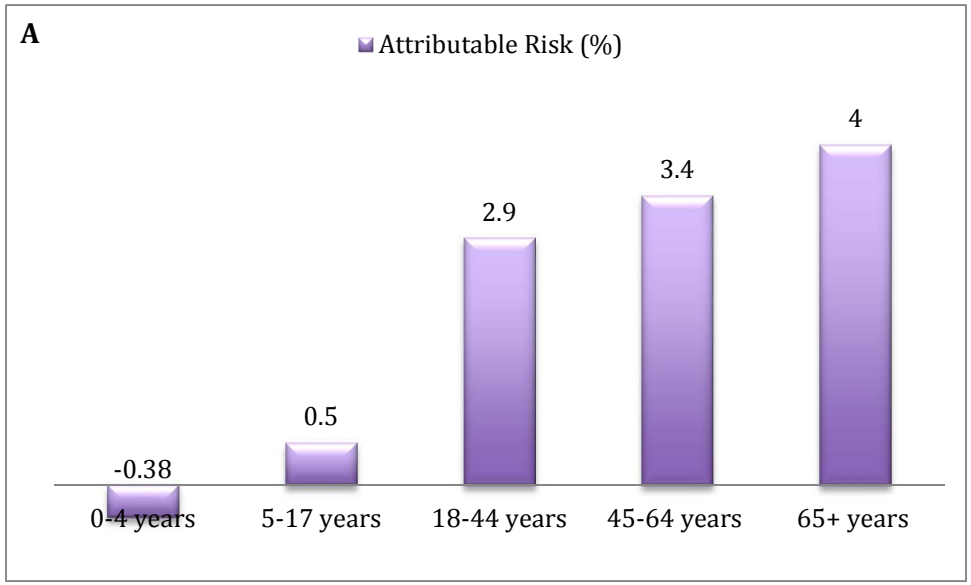


Figure 3. Asthma admissions (A) from 2002-2011 with forecasted estimates of asthma hospitalizations from 2012-2014. The red dotted line represents the forecasted values fitted based on the time series model with concurrent influenza as an explanatory variable. (B) The predicted asthma hospitalizations for 2012 with and without influenza as an explanatory variable show no definitively better model. Performing time series analysis on (C) adults 18- 44 years old and (D) adults 45 and older reveal a better fitting model when influenza is included in the model for older age groups.



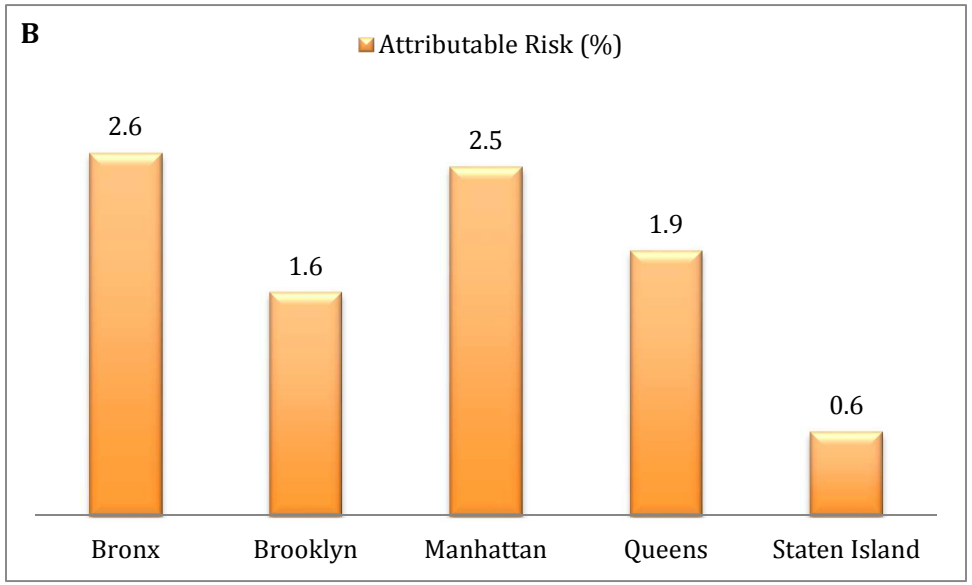


Figure 4. Percentage of asthma hospitalizations attributable to excess peak Influenza activity**.** Attributable risk percentages (ARP) were calculated by age and borough. The ARPs represent the percentage of asthma hospitalizations that would be reduced if influenza hospitalizations during the peak month were controlled to the yearly average of influenza hospitalizations. Analyzing ARPs by age group reveal an increase in ARPs with increasing age (A). Analysis by borough exposes the highest ARPs to be in Bronx and Manhattan followed by Queens, Brooklyn, and Staten Island (B).

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Appendix: Supplemental Figures

A.1

Ethnicity	Race				
	Asian (N=6980)	Black (N=110769)	Other (N=68186)	White (N=58049)	Total (N=243984)
Hispanic	64	6277	54023	23878	84242
Non-Hispanic	6916	104492	14163	34171	159742

[a]Values represent N counts

A.2