

# Relationship between community prevalence of obesity and associated behavioral factors and community rates of influenza-related hospitalizations in the United States

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**Background** Findings from studies examining the association between obesity and acute respiratory infection are inconsistent. Few studies have assessed the relationship between obesity-related behavioral factors, such as diet and exercise, and risk of acute respiratory infection.

**Objective** To determine whether community prevalence of obesity, low fruit/vegetable consumption, and physical inactivity are associated with influenza-related hospitalization rates.

**Methods** Using data from 274 US counties, from 2002 to 2008, we regressed county influenza-related hospitalization rates on county prevalence of obesity (BMI  $\geq 30$ ), low fruit/vegetable consumption ( $<5$  servings/day), and physical inactivity ( $<30$  minutes/month recreational exercise), while adjusting for community-level confounders such as insurance coverage and the number of primary care physicians per 100 000 population.

**Results** A 5% increase in obesity prevalence was associated with a 12% increase in influenza-related hospitalization rates [adjusted

rate ratio (ARR) 1.12, 95% confidence interval (CI) 1.07, 1.17]. Similarly, a 5% increase in the prevalence of low fruit/vegetable consumption and physical inactivity was associated with an increase of 12% (ARR 1.12, 95% CI 1.08, 1.17) and 11% (ARR 1.11, 95% CI 1.07, 1.16), respectively. When all three variables were included in the same model, a 5% increase in prevalence of obesity, low fruit/vegetable consumption, and physical inactivity was associated with 6%, 8%, and 7% increases in influenza-related hospitalization rates, respectively.

**Conclusions** Communities with a greater prevalence of obesity were more likely to have high influenza-related hospitalization rates. Similarly, less physically active populations, with lower fruit/vegetable consumption, tended to have higher influenza-related hospitalization rates, even after accounting for obesity.

**Key words** Diet, exercise, influenza, influenza-like illness, obesity.

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## Introduction

In the United States, direct medical costs associated with seasonal influenza were estimated at over \$10 billion dollars in 2003, and hospitalizations contributed heavily to the economic burden.<sup>1,2</sup> Influenza is considered ambulatory care sensitive as risk of influenza-related hospitalizations,

and severe outcomes may be mitigated through appropriate primary care.<sup>3</sup> Preventative efforts in the form of vaccination and the detection and control of chronic diseases, such as type II diabetes, can reduce rates of influenza-related hospitalizations.<sup>4,5</sup> Despite these effective clinical interventions, the public health and economic impact of influenza epidemics remains high and motivates the need to identify

additional individual- and community-level risk factors that may respond to public health interventions.

Though studies report conflicting findings, some studies suggest that obesity and related chronic conditions increase the risk of influenza and other acute respiratory infections.<sup>6–9</sup> Behavioral factors associated with obesity, such as a low consumption of fruits and vegetables and physical inactivity, may independently increase rates of infection but there is limited empirical evidence of an association between acute respiratory infections and diet/exercise after accounting for obesity. Any observed association between diet/exercise and risk of infection could primarily be attributed to their correlation with body mass index (BMI). The relationship between obesity/diet/exercise and risk of influenza-related infections may be further complicated by community-level factors such as climate, which can influence both lifestyle and influenza virus transmission rates.<sup>10,11</sup> Also, barriers of access to primary care, such as limited health insurance coverage, may also confound the relationship between risk of influenza-related infections and obesity/diet/exercise.<sup>3</sup>

In this study, using county-level data from 19 states of the United States, we assessed the association between community prevalence of obesity and community rates of influenza-related hospitalizations, after adjusting for several county-level confounders. We determined whether influenza-related hospitalization rates were also associated with community prevalence of low consumption of fruits and vegetables and prevalence of physical inactivity after accounting for community prevalence of obesity. As a secondary objective, with respect to their effect on influenza-related hospitalization rates, we examined the interaction between the obesity, diet and exercise variables, and barriers to primary care access, using county measures of insurance coverage as a marker of access.

## Materials and methods

### Data

The number of counties/states for which hospitalization and survey data were available increased throughout the years. Consequently, limiting the study period to the most recent years would improve geographic representation. However, given the substantial year-to-year variability in vaccine match, vaccine uptake, and influenza epidemic intensity, a longer period of study would provide more generalizable results. In an attempt to balance geographic representation with length of study period, we obtained survey, census, and hospitalization data for 274 counties in 19 states from 2002 to 2008. The 19 states that were included in the study are listed in Table A1.

For each county in our study, we compiled the total number of influenza hospitalizations over the study period

and summaries of several county-level variables. From a non-exhaustive review of the literature, we identified potential confounders: insurance coverage,<sup>12,13</sup> number of primary care physicians per 100 000 population,<sup>14,15</sup> environmental humidity,<sup>11,16</sup> chronic disease and pregnancy rates,<sup>17–20</sup> percentage of the county population living below the poverty level,<sup>12,21,22</sup> vaccination uptake,<sup>23–25</sup> racial composition,<sup>26–29</sup> population density,<sup>30,31</sup> and prevalence of smoking.<sup>32–34</sup> A concise description of data sources and variable definitions for all covariates is provided in Table 1.

### Hospitalizations

Hospitalization records were compiled from the State Inpatient Databases (SID) of the Healthcare Cost and Utilization Project (HCUP).<sup>35</sup> Records were aggregated from 2002 to 2008 by county, age group, diagnoses, and sex. Age standardization of rates was carried out using age groups: 0–4, 5–9, 10–18, 19–39, 40–64, 65–79, 80+ years. To best capture influenza hospitalizations, we only included hospitalizations with admission dates between the last week of October and the third week of May. This date range was informed by the Centers for Disease Control and Prevention (CDC)'s epidemic curves of lab-confirmed influenza (<http://www.cdc.gov/flu/weekly/weeklyarchives2007-2008/07-08summary.htm>).

Accurately capturing influenza-related hospitalizations can be challenging as the influenza case definition based only on influenza diagnostic codes (i.e., International Classification of Diseases (ICD-9) codes starting with 487) is known to be highly specific but not sensitive.<sup>36</sup> For this reason, as a sensitivity analysis, we compared findings from the analyses of data based on two definitions of an influenza-related hospitalization: (i) a hospitalization with a primary or secondary diagnosis of influenza or pneumonia (i.e., Influenza ICD-9 code 487 or Pneumonia, organism unspecified code 486) and (ii) a hospitalization with an ICD-9 code belonging to the set of ICD-9 codes listed in the Centers for Disease Control and Prevention (CDC)'s Influenza-like Illness definition.<sup>36</sup>

### Primary independent variables

County prevalence of obesity (BMI  $\geq$  30), low fruit/vegetable consumption (<5 servings of fruits/vegetables per day), and physical inactivity (<30 minutes recreational exercise per month) were obtained from the United States Department of Health and Human Services/Community Health Status Indicators (CHSI) (<http://www.communityhealth.hhs.gov/homepage.aspx?j=1>). These data were compiled from the CDC's Behavioral Risk Factor Surveillance System surveys (<http://www.cdc.gov/brfss>). Though only adults were surveyed, obesity and obesity-related factors tend to cluster within families and communities so

**Table 1.** Description of data sources

Variable	Data source	Description	Median (1st quartile, 3rd quartile)
Influenza-related hospitalizations	HCUP State Inpatient Databases (SID)	Inpatient stays with ICD-9 487 and/or 486 from 2002 to 2008*	1046 (331, 2984)
Obesity	CHSI**/BRFSS*** Aggregation of surveys from 2000 to 2006	Percentage adults in the population with BMI $\geq 30.0$	22.0 (19.3, 24.6)
Low fruit/vegetable consumption	CHSI/BRFSS Aggregation of surveys from 2000, 2002, 2003, and 2005	Percentage adults reporting consumption of fewer than 5 servings of fruits and vegetables	75.6 (72.7, 78.3)
Physical inactivity	CHSI/BRFSS Aggregation of surveys from 2000, 2001, 2003, and 2005	Percentage adults reporting less than 30-minute recreational exercise in past month	23.1 (19.6, 26.0)
Chronic condition rate	HCUP 2002–2008	Number of diagnoses of specific conditions (Table A1) in hospitalized patients divided by county person-years.	1.87 (1.56, 2.31)
Smokers	CHSI/BRFSS Aggregation of surveys from 2000 to 2006	Percentage adult population that reported that they smoke at the time of the survey	20.6 (18.2, 23.2)
Vaccine uptake	CHSI/BRFSS Aggregation of surveys from 2001–2003 and 2005–2006	Percentage population aged 65 years and older, vaccinated against influenza within the previous year	70.0 (65.4, 74.4)
Primary Care Physician (PCP) rate	CHSI/Health Resources and Services Administration, AMA	Rate active, non-federal physicians per 100 000 population in 2007	85.1 (58.8, 110.8)
Uninsured	CHSI/US Census Bureau	Percentage population aged 64 years or younger that were uninsured in 2006	16.7 (12.6, 21.1)
Poverty	US Census Bureau	Percentage population living below the poverty level in 2000	12.0 (9.2, 14.3)
Environmental Humidity (VPD)	Terrestrial Observation and Prediction System	VPD averaged from November 1 to March 31 (over 2002 to 2008) (Pascal)	355.7 (252.6, 493.2)
Population density	US Census Bureau	Estimated population size divided by land area (square miles) in 2000	281.0 (55.5, 745.0)
Caucasian or Asian	US Census Bureau	Percentage population that are Caucasian or Asian	92.1 (85.5, 95.7)

AMA, American Medical Association; VPD, vapor pressure deficit.

\*Influenza-like illness definition<sup>36</sup> was used in the sensitivity analysis.

\*\*Community Health Status Indicators.

\*\*\*The Behavioral Risk Factor Surveillance System.

prevalence of adult obesity should correlate strongly with prevalence of obesity in children.<sup>29,37</sup>

#### Survey and census data

Data on the prevalence of smoking in adults ( $\geq 18$  years), percent of the population without health insurance ( $< 65$  years) ('% uninsured'), vaccination uptake ( $\geq 65$  years), and the number of primary care physicians per 100 000 ('PCP rate') were compiled from the CHSI. The percentage of the county population living below poverty level ('poverty'), the percentage of the county population identifying themselves as Caucasian or Asian, and population sizes by age–sex strata were obtained from the United States Census 2000 (<http://www.census.gov/main/www/cen2000.html>). We did not have data on county vaccine uptake in the general population, but had vaccination data for the population  $\geq 65$  years. Though not necessarily repre-

sentative of vaccine coverage in the whole population, the greatest proportion of influenza hospitalizations is in individuals  $\geq 65$  years.<sup>38</sup> Nevertheless, we conducted additional analyses to assess the sensitivity of the results to vaccine coverage in the general population.

#### Chronic conditions

Using the State Inpatient Databases (HCUP), we identified the incidence of hospitalizations with ICD-9 codes corresponding to several chronic diseases and predisposing conditions (i.e., pregnancy). These conditions (Table A2), hereafter referred to as 'chronic conditions', are risk factors for influenza-related hospitalizations.<sup>19</sup> For all ages combined and separately for the pediatric population ( $\leq 18$  years), we obtained the total number of diagnoses of each condition in hospitalized patients for each county, from 2002 to 2008.

### Environmental humidity

Experimental studies have demonstrated that influenza transmission rates depend on absolute humidity.<sup>11</sup> Vapor pressure deficit (VPD) is a measure of humidity with high VPD indicating low humidity. We obtained daily estimates of average saturation vapor pressure deficit (VPD) from spatially continuous surfaces for the US from the Terrestrial Observation and Prediction System (TOPS).<sup>39</sup> These daily meteorological surfaces were averaged from November to March (over 2002–2008) to have a representative humidity value for each county during the time period preceding and during weeks with elevated influenza activity (<http://www.cdc.gov/flu/about/season/flu-season.htm>).

### Statistical analyses

Assuming the number of hospitalizations in a county is Poisson distributed, we regressed the log-transformed age-sex standardized hospitalization rates on each of the primary independent variables and potential confounders separately ('univariable' analyses) and then each primary independent variable while adjusting for covariates ('multivariable' analyses). Covariates were percentage uninsured, poverty, VPD, PCP rate, percentage smokers, vaccine uptake, percentage Caucasian or Asian, population density, and chronic condition rate. The covariates included in the multivariable analyses of the pediatric population were the same as those included in the analyses of the general population with the exception of vaccine uptake, which was measured in the population aged 65 years or older. We used a quasi-Poisson regression model as we expected the variation in the hospitalization rates to exceed that assumed by the Poisson model. Also, influenza-related hospitalization rates from counties belonging to the same state could be correlated; so, all univariable and multivariable regression models included indicator variables to represent the state to which the county belongs.

Studies that have sufficient statistical power to assess main effects may have insufficient power for interactions.<sup>40</sup> Therefore, we limited the covariates to those variables that were not highly correlated ( $\geq 0.5$ )<sup>41</sup> with percentage uninsured. We expected to gain little by including highly correlated variables because they would reduce the precision of the regression coefficient estimates and would make the interpretation of the results more challenging. To assess the interaction between each independent variable and percentage uninsured, we added the interaction term to the model with the independent variable and the covariates. We did not assess interactions in the general population because in the United States, nearly all persons aged 65 years and older have access to health insurance through Medicare (<http://www.medicare.gov>).

In addition to a sensitivity analysis of the influenza-related hospitalization definition, we conducted a sensitivity analysis

to estimate the impact of vaccine coverage (in the population <65 years) on the association between the three primary independent variables and influenza-related hospitalization rates. This was accomplished by restricting the data to years in which there was a poor vaccine match (2003–2004 and 2007–2008). If associations from the restricted analysis were weaker than those from the full analysis, then vaccine coverage in the population <65 years may be driving the associations between obesity, low fruit/vegetable consumption, physical inactivity, and influenza-related hospitalizations. In this case, failing to account for vaccine coverage in the population <65 years could bias the results.

## Results

From 2002 to 2008, from a combined population of 116 146 020 in 274 counties, there were 3 076 699 hospitalizations using the case definition based on ICD-9 codes 486 and 487, and 4 254 939 hospitalizations using the CDC's influenza-like illness definition. Since the two influenza case definitions produced similar findings (Tables A3 and A4) (the influenza-like illness definition resulted in weaker associations for some variables), we present only the results based on the first case definition, that is, using ICD-9 codes 486 and 487. There was also little difference in the adjusted rate ratios from the analysis of hospitalizations from 2002 to 2008 and the analysis restricted to data from 2003 to 2004 and 2007 to 2008 (Table A4).

### General population

In univariable analyses, a 5% increase in prevalence of obesity, low fruit/vegetable consumption, and physical inactivity was associated with an increase in influenza-related hospitalization rates of 17% [rate ratio (RR) 1.17, 95% confidence interval (CI) 1.13, 1.21], 16% (RR 1.16, 95% CI 1.11, 1.22), and 15% (RR 1.15, 95% CI 1.13, 1.18) (Table 2). After adjusting for potential confounders, there remained a 12% [adjusted rate ratio (ARR) 1.12, 95% CI 1.07, 1.17], 12% (ARR 1.12, 95% CI 1.08, 1.17), and 11% (ARR 1.11, 95% CI 1.07, 1.16) increase in hospitalization rates associated with prevalence of obesity, low fruit/vegetable consumption, and physical inactivity, respectively (Table 3, Models 1–3). Including all three independent variables in a single model while adjusting for confounders, the increase in rates was lower at 6% (ARR 1.06, 95% CI 1.01, 1.11), 8% (ARR 1.08, 95% CI 1.04, 1.13), and 7% (ARR 1.07, 95% CI 1.03, 1.11) for obesity, low fruit/vegetable consumption, and physical inactivity, respectively (Table 3, Model 4).

### Pediatric population

In univariable analyses of the pediatric population ( $\leq 18$  years), a 5% increase in obesity, low fruit/vegetable consumption, and physical inactivity was associated with a

**Table 2.** Rate ratios and confidence intervals for influenza-related hospitalizations from univariable analyses

Covariate	All ages RR*,**	All ages 95% CI	Children RR	Children 95% CI
Obesity (%)	1.17	1.13, 1.21	1.25	1.18, 1.32
Low fruit/vegetable consumption (%)	1.16	1.11, 1.22	1.16	1.07, 1.26
Physical inactivity (%)	1.15	1.13, 1.18	1.26	1.21, 1.32
PCP rate	0.93	0.90, 0.97	0.91	0.85, 0.97
Uninsured (%)	1.14	1.10, 1.18	1.52	1.35, 1.71
Poverty (%)	1.10	1.07, 1.14	1.21	1.16, 1.26
Population density	1.001	0.998, 1.003	1.003	1.000, 1.007
Caucasian or Asian	0.94	0.91, 0.98	0.98	0.92, 1.05
Respiratory	1.20	1.15, 1.26	–	–
Cardiac	1.10	1.06, 1.16	–	–
Neurologic-Central	1.19	1.13, 1.26	–	–
Neurologic-peripheral	1.17	1.12, 1.21	–	–
Endocrine	1.28	1.23, 1.34	–	–
Diabetes	1.12	1.08, 1.16	–	–
Renal	1.14	1.10, 1.18	–	–
Immune	1.05	1.03, 1.08	–	–
Hematologic	1.20	1.13, 1.28	–	–
Pregnancy	1.18	1.13, 1.24	–	–
chronic condition rate	1.21	1.16, 1.26	1.19	1.10, 1.30
Smokers (%)	1.14	1.09, 1.18	1.07	0.99, 1.15
Vaccine uptake (%)	0.87	0.84, 0.91	–	–
VPD	1.05	1.00, 1.10	1.14	1.06, 1.23

PCP, Primary Care Physician; VPD, vapor pressure deficit.

\*Rate ratio for 5% change in obesity, low fruit/vegetable consumption, and physical inactivity; for all other variables, rate ratio is for change corresponding to inter-quartile range.

\*\*Adjusting for the state to which a county belongs.

25% (RR 1.25, 95% CI 1.18, 1.32), 16% (RR 1.16, 95% CI 1.07, 1.26), and 26% (RR 1.26, 95% CI 1.21, 1.32) increase in influenza-related hospitalization rates, respectively. We found that the relative increase in hospitalization rates associated with obesity, low fruit/vegetable consumption, and physical inactivity was 21% (ARR 1.21, 95% CI 1.12, 1.31), 14% (ARR 1.14, 95% CI 1.06, 1.23), and 19% (RR 1.19, 95% CI 1.12, 1.26), respectively (Table 3). When all three independent variables were included in the same model, the increase in hospitalization rates associated with a 5% increase in obesity, low fruit/vegetable consumption, and physical inactivity was 13%, 6%, and 13% (ARR 1.13, 95% CI 1.05, 1.23; ARR 1.06, 95% CI 0.98, 1.14; ARR 1.13, 95% CI 1.06, 1.21), respectively.

### Interaction of insurance coverage and obesity-related variables in children

Only the correlation between VPD and percentage uninsured was high at 0.73, exceeding our threshold of 0.5, so in the model used to assess interactions we adjusted for the same covariates as in the multivariable analysis of the pediatric population with the exception of VPD. We found an interaction between percentage uninsured and both obesity

(regression coefficient: 0.0016, 95% CI 0.00025, 0.0029) and physical inactivity (regression coefficient: 0.0012, 95% CI 0.000051, 0.0023). Evidence of an interaction with low fruit/vegetable consumption was inconclusive (regression coefficient: 0.0010, 95% CI –0.00083, 0.0027). This suggests that low insurance coverage (i.e., high percentage uninsured) is associated with increased rates of influenza-related hospitalizations, and the size of the increase in hospitalization rates depends on the county's prevalence of obesity and physical inactivity. For example, increasing percentage uninsured from 15% to 25%, the estimated increase in influenza-related hospitalization rates is 13% in counties with physical inactivity prevalence equal to 25%, but the increase in influenza-related hospitalization rates is only 7% for counties with physical inactivity prevalence equal to 20%.

## Discussion

Increasing county prevalence of obesity was associated with increasing county rates of influenza-related hospitalizations. Prevalence of low consumption of fruits and vegetables and physical inactivity was also associated with influenza

**Table 3.** Adjusted rate ratios and confidence intervals

	Covariates	All ages RR*	All ages 95% CI	Children RR	Children 95% CI
Model 1	Obesity (%)	1.12	1.07, 1.17	1.21	1.12, 1.31
	Uninsured (%)	1.05	1.02, 1.09	1.40	1.23, 1.59
	Chronic condition rate	1.09	1.04, 1.14	1.13	1.05, 1.22
	Vaccine uptake (%)	0.93	0.90, 0.97	–	–
	PCP rate	1.03	0.99, 1.08	1.00	0.94, 1.07
	Poverty (%)	0.95	0.91, 0.99	1.08	1.03, 1.14
	Smokers (%)	1.04	0.99, 1.08	0.94	0.87, 1.01
	VPD	0.98	0.94, 1.02	0.95	0.89, 1.02
	Population density	0.997	0.998, 1.002	1.002	0.999, 1.006
	Caucasian or Asian	0.97	0.94, 1.01	1.03	0.98, 1.09
Model 2	Low fruit/vegetable consumption (%)	1.12	1.08, 1.17	1.14	1.06, 1.23
	Uninsured (%)	1.06	1.02, 1.09	1.32	1.17, 1.51
	Chronic condition rate	1.12	1.07, 1.17	1.15	1.06, 1.24
	Vaccine uptake (%)	0.95	0.92, 0.99	–	–
	PCP rate	1.03	0.99, 1.07	0.97	0.91, 1.03
	Poverty (%)	0.97	0.93, 1.01	1.14	1.09, 1.19
	Smokers (%)	1.04	1.00, 1.09	0.97	0.90, 1.04
	VPD	1.00	0.96, 1.04	0.99	0.93, 1.06
	Population density	0.998	0.996, 1.00	1.00	0.997, 1.004
	Caucasian or Asian	0.95	0.93, 0.98	1.00	0.95, 1.06
Model 3	Physical inactivity (%)	1.11	1.07, 1.16	1.19	1.12, 1.26
	Uninsured (%)	1.02	0.99, 1.06	1.20	1.05, 1.36
	Chronic condition rate	1.09	1.04, 1.14	1.10	1.02, 1.19
	Vaccine uptake (%)	0.97	0.93, 1.01	–	–
	PCP rate	1.04	1.00, 1.08	1.01	0.95, 1.07
	Poverty (%)	0.97	0.93, 1.01	1.07	1.01, 1.12
	Smokers (%)	1.06	1.02, 1.10	0.96	0.89, 1.03
	VPD	1.00	0.96, 1.04	1.02	0.95, 1.09
	Population density	1.000	0.997, 1.001	1.003	1.000, 1.007
	Caucasian or Asian	0.97	0.94, 1.00	0.98	0.92, 1.05
Model 4	Obesity (%)	1.06	1.01, 1.11	1.13	1.05, 1.23
	Low fruit/vegetable consumption (%)	1.08	1.04, 1.13	1.06	0.98, 1.14
	Physical inactivity (%)	1.07	1.03, 1.11	1.13	1.06, 1.21
	Uninsured (%)	1.04	1.01, 1.08	1.29	1.13, 1.47
	Chronic condition rate	1.10	1.05, 1.15	1.14	1.05, 1.23
	Vaccine uptake (%)	0.97	0.93, 1.01	–	–
	PCP rate	1.06	1.02, 1.10	1.04	0.97, 1.11
	Poverty (%)	0.94	0.90, 0.98	1.04	0.98, 1.10
	Smokers (%)	1.03	0.99, 1.08	0.93	0.86, 1.00
	VPD	1.00	0.96, 1.03	0.99	0.92, 1.06
Population density	1.000	0.997, 1.001	1.003	1.000, 1.007	
Caucasian or Asian	0.97	0.94, 1.00	0.98	0.92, 1.05	

PCP, Primary Care Physician; VPD, vapor pressure deficit.

\*Rate ratio for 5% change in obesity, low fruit/vegetable consumption, and physical inactivity; for all other variables, rate ratio is for change corresponding to inter-quartile range.

hospitalization rates, even after adjusting for prevalence of obesity and other county-level covariates. In addition to these associations, we found that low insurance coverage was strongly associated with higher rates of influenza-related hospitalizations in the pediatric population. Fur-

thermore, the interaction between insurance coverage and obesity/physical activity suggests that the increase in hospitalization rates associated with low insurance coverage was greater when there was also a high prevalence of obesity/physical inactivity.

Findings from studies of the association between body mass index and acute respiratory infection are inconsistent,<sup>6</sup> but in general, studies powered to assess the effect of obesity on hospitalizations and/or mortality found increased risk associated with obesity<sup>8,9,42,43</sup> while studies examining the effect of obesity on healthcare service utilization for influenza-like illness found no association or increased utilization associated with low BMI.<sup>4,44–46</sup> Thus, obesity may not be related to increased utilization of outpatient healthcare services for influenza-like illness, but there is some evidence that obesity is related to increased rates of influenza-related hospitalizations.

Several biological mechanisms have been proposed to explain the relationship between obesity and severe influenza infection. Studies have shown that obesity leads to impaired immune and lung function.<sup>47–49</sup> Obesity is also a risk factor for conditions that, in turn, increase risk of severe respiratory infection or severe outcomes, for example, hyperglycemia, obstructive sleep apnea, and aspiration associated with gastroesophageal reflux disease.<sup>50–52</sup> An association between obesity and influenza-related hospitalizations may also be attributed to the increased risk of cardiovascular events following influenza infection.<sup>53</sup> Furthermore, given that obesity is a risk factor for a number of chronic conditions, such as cardiovascular disease and obstructive sleep apnea, physicians may be more inclined to admit an obese patient than a non-obese patient with similar influenza symptom severity.

Coleman *et al.*,<sup>54</sup> in their study of the effect of obesity on risk of influenza, pointed to the need to examine the effects of diet and exercise on risk of influenza infection. Previous research, mainly focusing on populations in developing nations, linked malnutrition and micronutrient deficiency with respiratory infection.<sup>55–58</sup> Several studies also demonstrated benefits of chronic moderate exercise in stimulating immune function and increasing serum concentrations of vitamin D (25 (OH) D).<sup>59–61</sup> Due to limitations in data availability, we only considered specific definitions of poor diet and physical inactivity but other forms of malnutrition and physical inactivity may also play a role. For example, protein-energy malnutrition has been associated with decreases in immune function,<sup>62</sup> and non-recreational forms of physical activity may also be protective. Though the observed associations appeared robust to adjustment for a number of potential confounders, we could not account for all aspects of self-care and material deprivation; thus, it is conceivable that other factors that are correlated with fruit and vegetable consumption and physical activity underlie the observed associations with influenza-related hospitalizations.

A limitation of our study was our reliance on survey data for county-level prevalence estimates of obesity, low fruit/vegetable consumption, and physical inactivity. How-

ever, the BRFSS survey measures from which our prevalence estimates are derived, that is, height, weight, fruit/vegetable intake, and leisure-time physical activity, have moderate to high reliability and validity.<sup>63</sup> In addition, though only adults were surveyed, Agras *et al.*<sup>64</sup> reported that having obese parents was the strongest independent predictor of childhood obesity. For this reason, we saw value in assessing the effect of prevalence of obesity, low fruit/vegetable consumption, and physical inactivity in adults on rates of influenza-related hospitalizations in children. Another limitation of our study is that our findings, which are observed at the county level, do not necessarily imply causation at the individual level. However, the diversity of the county environments and populations in our study permitted us to demonstrate generalizability of the association between the obesity variables and influenza-related hospitalizations. For example, we had counties representing each of the climate zones, states at the extremes with respect to insurance coverage rates (<http://www.census.gov/hhes/www/hlthins/>), obesity prevalence (<http://www.cdc.gov/obesity/data/adult.html/>), and primary care physician rates (<https://www.aamc.org/download/55436/data/statephysdec2007.pdf>). In addition, we were able to assess and adjust for the impact of a variety of community-level factors.

Our study findings suggest that county prevalence of obesity, low consumption of fruits/vegetables, and physical inactivity is each associated with county rates of influenza-related hospitalizations, even after accounting for neighborhood and environmental confounders. In addition to these associations, we found that low insurance coverage was associated with higher rates of hospitalizations in children and the increase in hospitalization rates was more pronounced in counties that also had a high prevalence of physical inactivity and obesity. Though we can only extrapolate these findings to the individual with caution, we have preliminary evidence that regardless of body mass index, a low dietary intake of fruits and vegetables and insufficient recreational exercise are associated with increased risk of severe influenza.

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## Appendix

**Table A1.**

States with counties that were included in the study

State
California
Colorado
Florida
Illinois
Kansas
Maryland
Massachusetts
Minnesota
New Jersey
New York
Ohio
Oregon
South Carolina
South Dakota
Texas
Utah
Vermont
Washington
Wisconsin

**Table A2.**

continued

Condition	Coding system	Code numbers
Cardiac dysthymia	CCS	106
Conduction disorders	CCS	105
Congestive heart failure	CCS	108
Coronary heart disease	CCS	101
Other heart disease	CCS	104
Pulmonary heart disease	CCS	103
Hematologic		
Sickle Cell Disease	CCS	61
Coagulation and hemorrhage disorders	CCS	62
Endocrine		
Diabetes Mellitus	CCS	49, 50
Renal		
Acute or chronic renal failure	CCS	157, 158
Immune		
Chemotherapy	CCS	224
HIV	CCS	5
Transplant	CCS	64, 105, 176
Pregnancy	CCS	MDC 14 and 15*

**Table A2.**

Clinical conditions potentially impacting influenza disease course and the need for inpatient care

Condition	Coding system	Code numbers
Respiratory		
Asthma	CCS	128
Apnea	Dx	3722
COPD	CCS	127
Cystic fibrosis	CCS	56
Neurologic – central		
Cerebral palsy	Dx	3430, 3431, 3432, 3433, 3434, 3438, 3439
Dementia	CCS	653
Epilepsy	CCS	83
Stroke	CCS	109
Neurologic – peripheral		
Muscular dystrophy	Dx	3590, 3591, 3592, 3593, 3594, 3595, 3596, 3598, 35981, 35989, 3599
Multiple Sclerosis	CCS	80
Paralysis	CCS	82
Cardiac		
Acute myocardial infarction	CCS	100

CCS, HCUP Clinical Classification Software categories (<http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp>).

\*[http://www.hcup-us.ahrq.gov/reports/factsandfigures/2008/sources\\_methods.jsp](http://www.hcup-us.ahrq.gov/reports/factsandfigures/2008/sources_methods.jsp)

**Table A3.**

Rate ratios and confidence intervals for univariable analyses for the pneumonia and influenza (P&I) and influenza-like illness (ILI) definitions

Covariate	P&I RR**,**	P&I 95% CI	ILI RR	ILI 95% CI
Obesity (%)	1.17	1.13, 1.21	1.16	1.12, 1.19
Low fruit/vegetable consumption (%)	1.16	1.11, 1.22	1.15	1.11, 1.20
Physical inactivity (%)	1.15	1.13, 1.18	1.15	1.12, 1.18
PCP rate	0.93	0.90, 0.97	0.94	0.91, 0.97
Uninsured (%)	1.14	1.10, 1.18	1.14	1.10, 1.18
Poverty (%)	1.10	1.07, 1.14	1.12	1.09, 1.15
VPD	1.05	1.00, 1.10	1.06	1.01, 1.11
Population density	1.000	0.998, 1.002	1.001	0.999, 1.004
Caucasian or Asian	0.94	0.90, 0.97	0.94	0.91, 0.97
Respiratory	1.20	1.15, 1.26	1.20	1.16, 1.25
Cardiac	1.10	1.06, 1.16	1.12	1.07, 1.16

**Table A3.**  
continued

Covariate	P&I RR <sup>*,**</sup>	P&I 95% CI	ILI RR	ILI 95% CI
Neurologic	1·19	1·13, 1·26	1·22	1·16, 1·27
– Central				
Neurologic	1·17	1·12, 1·21	1·09	1·07, 1·11
– Peripheral				
Endocrine	1·28	1·23, 1·34	1·30	1·26, 1·35
Diabetes (%)	1·12	1·08, 1·16	1·10	1·07, 1·14
Renal	1·14	1·10, 1·18	1·16	1·12, 1·20
Immune	1·05	1·03, 1·08	1·06	1·04, 1·08
Hematologic	1·20	1·13, 1·28	1·25	1·18, 1·32
Chronic condition rate	1·21	1·16, 1·26	1·23	1·18, 1·28
Smokers (%)	1·14	1·09, 1·18	1·11	1·07, 1·15
Vaccine uptake (%)	0·87	0·84, 0·91	0·85	0·82, 0·89

PCP, Primary Care Physician; VPD, vapor pressure deficit.

\*Rate ratio for 5% change in obesity, low fruit/vegetable consumption, and physical inactivity; for all other variables, rate ratio is for change corresponding to inter-quartile range.

\*\*With adjustment for the state to which a county belongs.

**Table A4.**

Adjusted rate ratios and 95% confidence intervals for the multivariable analysis using data from all years (2002–2008), the analysis restricted to 2003–2004 and 2007–2008, and the analysis using the influenza-like illness (ILI) definition

All ages	Variable	ARR <sup>*,**</sup> 2002–2008	ARR <sup>*,***</sup> 2003–2004 and 2007–2008	ARR <sup>*,**</sup> ILI case definition
Model 1	Low fruit/veg consumption	1·12(1·08, 1·17)	1·13(1·09, 1·18)	1·11(1·07, 1·15)
Model 2	Obesity	1·12(1·07, 1·17)	1·12(1·07, 1·17)	1·08(1·04, 1·13)
Model 3	Physical inactivity	1·11(1·07, 1·16)	1·11(1·07, 1·16)	1·08(1·04, 1·12)
Model 4	Low fruit/veg consumption	1·08(1·04, 1·13)	1·09(1·05, 1·14)	1·09(1·05, 1·13)
	Obesity	1·06(1·01, 1·11)	1·05(1·00, 1·10)	1·05(1·01, 1·08)
	Physical inactivity	1·07(1·03, 1·11)	1·07(1·03, 1·12)	1·03 (0·99, 1·07)

\*ARR = adjusted rate ratio, adjusting for uninsured (%), chronic condition rate, PCP rate, poverty (%), smokers (%), VPD, population density, Caucasian or Asian race, and vaccine uptake (for analysis of all years).

\*\*Rate ratio for 5% change in obesity, low fruit/vegetable consumption, and physical inactivity.

\*\*\*No adjustment for county vaccination rates.