Int J Obes (Lond). Author manuscript; available in PMC 2016 September 15.

Published in final edited form as:
Int J Obes (Lond). 2014 January ; 38(1): 113–119. doi:10.1038/ijo.2013.57.

The association between obesity and outpatient visits for acute respiratory infections in Ontario, Canada

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Abstract

Objectives—Recent evidence suggests that obesity increases the risk of severe outcomes following respiratory infection. It is less clear whether obesity is associated with the risk of being infected with influenza or other respiratory pathogens. Therefore, we examined the association between obesity and outpatient visits for acute respiratory infections.

Design—We conducted a retrospective cohort study over 13 years on 104,665 individuals in Ontario, Canada who responded to population health surveys and agreed to linkage with health administrative data. Individuals aged 18–64 years who responded to a survey within 5 years prior to the start of an influenza season were included. Poisson regression, with adjustment for relevant confounders, was used to measure the association between self-reported BMI and outpatient visits coded as acute respiratory infection. We conducted numerous sensitivity analyses to assess the robustness of our findings.

Results—We observed higher rates of outpatient visits for ARI during influenza season periods compared with normal weight individuals for those who were overweight (BMI 25–29.9) (Rate Ratio [RR] 1.10; 95% Confidence Interval [95% CI] 1.07–1.13), obese class I (BMI 30–34.9) (RR 1.17; 95% CI 1.13–1.22), and obese class II or III (BMI ≥35) (RR 1.19; 95% CI 1.12–1.25)

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Conflicts of Interest
All authors report no conflicts of interest.

Disclaimer: The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Author contributions
Dr. Kwong and Mr. Campitelli had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Kwong, Campitelli, Rosella.
Analysis and interpretation of the data: Kwong, Campitelli, Rosella.
Drafting of the manuscript: Kwong, Campitelli.
Critical revision of the manuscript for important intellectual content: Kwong, Campitelli, Rosella.
Statistical analysis: Campitelli, Rosella.
Administrative, technical, or material support: Campitelli.
Obtained funding: Kwong.
Study supervision: Kwong.

Associations of a similar magnitude were observed during non-influenza season periods. Obesity was a greater risk factor for acute respiratory infections managed in emergency departments than physician offices.

Conclusions—Obese individuals are at an increased risk of outpatient visits for acute respiratory infection during both influenza and non-influenza season periods, suggesting that the effect of obesity on the risk of respiratory infections is not limited to influenza. Interventions designed to reduce the prevalence of obesity may have the added benefit reducing the population burden of respiratory infections.

Keywords

Obesity; infection; influenza; human; respiratory tract infections

Introduction

Obesity is a global health concern with the World Health Organization estimating 500 million adults to be obese (Body Mass Index [BMI] >30) in 2008.(1) In Canada, approximately 23% of adults are obese,(2) and the prevalence is increasing, particularly among the severe (BMI 35–39.9) and morbid (BMI ≥40) obesity categories.(3) Obesity has previously been identified as a risk factor for many chronic conditions, including diabetes, cardiovascular disease, hypertension, osteoarthritis, asthma, and chronic obstructive pulmonary disease.(4–6)

Less clear is the impact of obesity on the immune response to infection, although several *ex vivo* studies on obese human and animal cellular functionality have demonstrated immune function deficiencies, including decreased cytokine production, reduced macrophage and dendritic cell function, and natural killer cell impairment.(7) Recent evidence suggests proper energy balance is essential for robust immune responses to respiratory pathogens.(8)

Epidemiological data has begun to emerge that indicates obesity is a risk factor for infectious diseases.(9) Prior to the 2009 influenza A/H1N1 pandemic, obesity had not been considered a risk factor for influenza morbidity and mortality.(10;11) However, several studies revealed that obesity was associated with hospitalization, intensive care unit admission, and mortality following infection with pandemic influenza A/H1N1.(12–19) Additionally, severely obese individuals (BMI ≥35) are at an increased risk for respiratory hospitalizations during seasonal influenza epidemics.(20) This increased risk is present for both individuals without previously identified risk factors for severe influenza complications (e.g. chronic pulmonary disorders, cancer, diabetes mellitus, and immunosuppressive conditions) and for individuals with one of these risk factors. Obesity is also associated with poorer outcomes for those hospitalized with lower respiratory tract infections.(21)

While there is evidence that obesity increases the risk of severe outcomes following respiratory infection, it remains less clear whether obesity is associated with the risk of being infected with influenza or other respiratory pathogens. The relationship between obesity and the risk of acquiring respiratory infection is difficult to assess since many patients with respiratory infection do not seek medical care and BMI is not routinely recorded in patients' medical records or health administrative datasets. Therefore, we sought to examine the association between obesity and outpatient visits coded as acute respiratory infections (ARIs), a proxy for actual respiratory infection in the community, using population-based survey data to capture BMI as an exposure.

Subjects and Methods

Study population and design

We conducted a retrospective cohort study of Ontario respondents to the 1996/97 cycle of the National Population Health Survey (NPHS), or cycle 1.1 (2000/01), cycle 2.1 (2003), cycle 3.1 (2005), or cycle 4.1 (2007/08) of the Canadian Community Health Survey (CCHS). Statistics Canada conducts these nationally representative cross-sectional surveys using a combination of telephone and in-person interviews to capture health information on the household population aged ≥12 years (response rates ranged from 75 to 82%).(22–24) Institutionalized residents, full-time members of the Canadian military forces, on-reserve residents, and certain remote regions were excluded from the sampling frame. Additionally, for the purposes of our analysis, we excluded respondents with a height of <3 feet or ≥7 feet and women who were pregnant or breastfeeding when surveyed, as Canadian guidelines do not recommend the calculation of BMI for these populations.(25) We further restricted our analysis to respondents who agreed to be linked to health administrative datasets and were linked successfully (84% of all respondents). We used encrypted health card numbers as unique identifiers to achieve linkage across the datasets.

We examined rates of outpatient visits for ARIs during 13 influenza seasons (1996–97 to 2008–09) and control periods when influenza was not circulating. To assemble our cohort, at the start of each influenza season (index date) we included all individuals who were alive, were between the ages of 18 and 64 years, and completed a survey in the previous five years. Since respondents were included in this manner, an individual could have appeared in the cohort five separate times. For the small proportion (~0.5%) of individuals who completed more than one survey, their earliest five appearances were kept for analysis. All subjects had free access to physician and hospital services during the study period, and to influenza vaccines starting in September 2000.

Ethics approval for this analysis was obtained from the Research Ethics Board of Sunnybrook Health Sciences Centre, Toronto, Canada.

Data sources and definitions

Influenza season and non-influenza season periods—Influenza viral surveillance data collected by sentinel laboratories (using mainly viral culture and direct antigen detection methods) in Ontario and submitted to the Public Health Agency of Canada were used to define influenza seasons. The start and end dates for each influenza season were defined as the first and last occurrences of two consecutive weeks where 5% of respiratory specimens sent to the sentinel laboratories tested positive for influenza. Non-influenza season periods were defined as July 1 to September 30 following an influenza season as there is extremely little influenza virus circulation during these months. Individuals dying before the start of non-influenza season periods were excluded from these periods.

Body mass index—We used self-reported height and weight in the NPHS or CCHS to capture BMI in kg/m^2 and created the following BMI categories consistent with Health Canada's guidelines for Body Weight Classification in adults: <18.5 (Underweight); 18.5–24.9 (Normal weight); 25.0–29.9 (Overweight); 30.0–34.9 (Obese class I); 35.0–39.9 (Obese class II); ≥40 (Obese class III).(25) We aggregated those in the obese class II and III categories since there were relatively fewer people in these extreme weight categories. Previous research has shown that people tend to underestimate weight and overestimate height when self-reporting, causing them to underestimate their BMI compared with direct measurement.(26–28) However, in an analysis of 3 895 respondents to a sub-section of CCHS 3.1, where both measured and self-reported BMI were calculated, there was a high correlation between the two methods (r = 0.93).(29)

Main outcome measure—The primary outcome of interest was the number of outpatient visits (physician office or emergency department (ED) visits) with a diagnosis of ARI during influenza season and non-influenza season periods. The Ontario Health Insurance Plan (OHIP) physician billing claims database, which contains service and diagnostic information for outpatient visits made to approximately 94% of physicians in the province,(30) was used to determine the number of ARI-coded visits made by each cohort member. Our definition of ARI included: acute nasopharyngitis, acute sinusitis, acute tonsillitis, acute laryngitis, acute bronchitis, pneumonia, influenza, and other viral diseases (OHIP diagnostic codes 460, 461, 463, 464, 466, 486, 487, and 079). A validation study of physician billing claims from a comparable setting found that a similar group of diagnostic codes had excellent specificity (99%) and positive predictive value (PPV) (93%), but only modest sensitivity (49%) for ARI when using medical chart review as the reference standard.(31) To avoid capturing multiple outcomes for the same episode of infection, we only included outpatient visits if they were separated by at least seven days from a previous visit.

Covariates—Since an individual could appear in the cohort up to five times, we updated the information regarding covariates obtained from the administrative data (e.g., comorbidities) at each index date. Information on covariates measured using the survey data (e.g., smoking status) was obtained only at survey completion.

We obtained age, sex, rural residence (living in a community with <10 000 residents), and neighborhood income quintile from the Ontario Registered Persons database, which contains demographic information on individuals with a valid Ontario health card.(32) Neighborhood income quintile was determined by linking respondent postal code to census data.(33)

The OHIP database was used to determine the number of outpatient visits in the year previous to the index date. The OHIP database was also used to determine influenza vaccination status by looking for service codes specific to immunization in the months prior to the start of the influenza season (index date). Individuals vaccinated after the start of an influenza season were considered unvaccinated; only 5% of vaccines are given after the onset of influenza seasons.(34) Additionally, the Canadian Institute of Health Information's

Discharge Abstract Database (CIHI-DAD), which contains information on hospital stays to all acute-care facilities in Ontario,(35) was used to determine the number of inpatient hospitalizations in the three years previous to the index date. We defined comorbidities for patients if there was evidence of a diagnosis in outpatient or hospitalization records during the prior three years using an adaption of the ambulatory care group (ACG) classification which has been previously described.(36) We considered the following comorbidities: chronic cardiovascular disease (e.g., previous myocardial infarction, congenital heart diseases, cardiomyopathies), chronic respiratory disease (e.g., asthma, chronic obstructive pulmonary disease, cystic fibrosis), diabetes, cancer, anemia, renal disease, immunodeficiency (due to disease and/or therapy), and history of aspiration.

Responses to the health surveys were used to determine the number of individuals living in the respondent's household and whether the respondent was a current daily smoker.

Statistical analyses

Poisson regression models were used to estimate the association between BMI category and the number of ARI-coded outpatient visits during influenza season and non-influenza season periods. The offset term was the log of follow-up time (in days) for each of these periods. We also conducted separate analyses to evaluate the association between BMI and both physician office and ED visits. In all analyses, the 'normal' BMI category was the referent and both unadjusted models and models adjusting for all covariates were considered. Furthermore, generalized estimating equation (GEE) models were employed to adjust for the correlated nature of the data as a result of repeated measures within individuals since they may have been included in analyses up to five times.

Since self-reported BMI has been shown to underestimate measured BMI, we conducted a sensitivity analysis in which we applied correction equations that were developed using measured values and validated on a subsample of our data,(29) to adjust self-reported BMI values for this potential underestimation. Additionally, we conducted subgroup analyses to examine the association in those with and without chronic conditions and restricted the cohort to their first appearance in the dataset to determine if bias was introduced by including individuals multiple times.

Statistical analyses were conducted using SAS 9.1 (SAS Institute INC., Cary, NC) and STATA 9.2 (Statacorp LP, College Station, TX). All tests were two-tailed and we used $p<0.05$ as the level of statistical significance.

Results

There were a total of 104 665 survey respondents who contributed 404 892 person-seasons of observation (124 710.6 total person-years) during influenza season periods and 404 368 person-seasons of observation (100 782.1 total person-years) during non-influenza season periods. A total of 50 346 physician office visits and 5 341 ED visits coded as ARI occurred during influenza season periods, while 20 726 physician office visits and 2 340 ED visits were observed during non-influenza season periods.

Among cohort members, approximately 45.5% reported a normal body weight (BMI 18.5–29.9), 2.4% reported being underweight (BMI <18.5), 32.9% reported being overweight (BMI 25.0–29.9), 12.2% reported being obese (BMI 30.0–34.9), and 4.9% reported being severely obese (BMI ≥35) (Table 1). After applying correction equations to adjust self-reported BMI values for potential underestimation, 1.3% were estimated to be underweight, 38.1% were estimated to be normal body weight, 35.6% were estimated to be overweight, 16.0% were estimated to be obese, and 7.0% were estimated to be severely obese. There was a gradient of increasing prevalence of chronic conditions with increasing BMI category (44% had at least one chronic condition in the highest BMI category compared to 23% for those in the normal BMI category). Additionally, those in the highest BMI category had lower socioeconomic status, were more likely to live in rural areas, and had more physician visits in the previous year and hospitalizations in the previous three years. However, those in the highest BMI category also had the lowest rate of current daily smoking and the highest level of influenza vaccine coverage.

After adjusting for covariates, we observed moderate but statistically significantly higher rates of outpatient visits for ARI during influenza season periods compared with normal weight individuals for those who were overweight (Rate Ratio [RR] 1.10; 95% Confidence Interval [95% CI] 1.07–1.13), obese class I (RR 1.17; 95% CI 1.13–1.22), and obese class II or III (RR 1.19; 95% CI 1.12–1.25) (Table 2). Similar increases in outcome rates during non-influenza season periods were observed among obese class I (RR 1.11; 95% CI 1.05–1.17) and obese class II or III (RR 1.13; 95% CI 1.04–1.23) individuals, but not among overweight individuals, compared with normal weight individuals. When analyzing physician office and ED visits separately, the RRs comparing the obese groups to the normal weight group were higher for ED visits than for physician office visits.

Using validated correction equations to adjust self-reported BMI values for potential underestimation yielded similar associations to the primary analysis (Table 3). The associations between BMI category and ARI-coded outpatient visit rates were higher among individuals without chronic conditions compared with those who had at least one chronic condition (p=0.0013). The results of the primary analysis were consistent when the cohort was restricted to an individual's first appearance in the dataset

Discussion

Increasing BMI was associated with ARI-coded outpatient visits during influenza seasons, with severely obese individuals having rates nearly 20% higher than normal weight individuals. However, comparable (but slightly attenuated) increases were found during non-influenza season periods, suggesting that the effect of obesity is not specific to influenza infection and that increased BMI may enhance susceptibility to other viral and bacterial respiratory pathogens that cause ARI. After applying validated correction equations to adjust self-reported BMI values for potential underestimation, which yielded obesity prevalence estimates that were closer to the Canadian average,(2;27) the associations between BMI category and ARI-coded outpatient visits remained consistent.

Previous studies have demonstrated that obesity is a risk factor for severe outcomes following infection with influenza and other respiratory pathogens.(12–21) However, evidence of obesity increasing susceptibility to respiratory infection is scarcer. Baik *et al.* found that obesity (BMI ≥30) was associated with an increased risk of community-acquired pneumonia (CAP) in women but not among men, although their referent BMI category was different from what was used in our study.(37) In two other studies, obese individuals were not at increased risk for CAP compared to normal weight individuals.(38;39) A null finding between obesity and infection was also reported in a recent test-negative case-control study analyzing laboratory-confirmed influenza infections.(40) Since our study evaluated the effect of obesity on outpatient visit rates for all ARIs, it may not be directly comparable to previous studies that examined only CAP or influenza infection as the outcome.

Although we detected an association between obesity and ARI-coded outpatient visits, the obesity effect was not as pronounced as what we observed in a similar cohort of individuals using hospitalization for respiratory conditions as the outcome. In our previous study, obese class I (Odds Ratio [OR] 1.45; 95% CI 1.03–2.05) and obese class II or III individuals (OR 2.12; 95% CI 1.45–3.10) were at an increased risk of respiratory hospitalizations during periods of seasonal influenza activity.(20) Those associations are much larger than the increases in ARI-coded outpatient visits among obese individuals observed in this study. However, the stronger association between obesity and ARI-coded ED visits compared with physician office visits suggests that obesity is a stronger risk factor for respiratory infections of greater severity.

Increased rates of ARI-coded outpatient visits were found among the obese and severely obese weight groups despite higher influenza vaccination coverage within these BMI categories, suggesting the vaccine did not adequately protect obese individuals. This finding is consistent with a recent study by Sheridan *et al.* that found impaired immune responses to the influenza vaccine among obese participants.(10) However, it should be noted that ARI can be caused by many other pathogens besides influenza and our study did not capture influenza vaccinations administered outside of a physician office setting. Therefore, while our results support the theory that the influenza vaccine inadequately protects obese individuals from infection, future studies with more appropriate methods and data sources are required to confirm this hypothesis.

Underweight individuals were found to have higher rates of ARI-coded outpatient visits compared with normal weight individuals during non-influenza season periods but not during influenza season periods. It was expected that underweight individuals would be at greater risk to respiratory infection since poor energy balance due to caloric restriction has been shown to diminish immune responses to respiratory pathogens.(8) It is unknown why this effect was not observed during influenza season periods, although having only self-reported BMI rather than measured BMI available in the data might be a reason.

Linking survey responses to health administrative data gave us the ability to assess this association in a large, population-based sample of individuals, enabling the detection of small but clinically relevant differences between BMI categories. However, there were several limitations to this study that merit emphasis. We did not have access to laboratory test results for respiratory pathogens to confirm ARI diagnoses. We used a slightly modified definition of ARI-coded outpatient visits that was found to have excellent specificity (99%) and PPV (93%) with modest sensitivity (49%) in a similar setting;(31) however, that study used medical chart review instead of laboratory confirmation as the reference standard which is not ideal to determine the accuracy of outpatient diagnostic codes for detecting actual infections. Another validation study of these outpatient codes that used laboratory confirmation as the reference standard only considered viral pathogens and reported PPV without providing sensitivity and sensitivity estimates.(41) Furthermore, without laboratory confirmation, we were unable to assign ARI-coded visits to particular respiratory pathogens to determine if the effect of obesity varied by pathogen. Additionally, our study used self-reported BMI, which tends to underestimate BMI compared to direct measurement,(26–28) although a high correlation (r = 0.93) between these measures has been observed when analyzing a sub-sample of CCHS data in which self-reported BMI was compared to measured BMI,(29) and a sensitivity analysis using corrected values of self-reported BMI yielded similar results to the primary analysis. Another concern was using BMI measurements from survey responses that may have been five years in the past, although similar results to the primary analysis were observed when only the individual's first appearance was used. In the context of this study, the limitations in the measurement of either ARI outpatient visits or BMI category would have biased our effect estimates toward the null and yielded conservative estimates of the effect of obesity on outpatient visits for ARI. Finally, although we considered a number of important potential confounders, as with all observational studies, we cannot rule out the possibility of residual confounding.

Since we used outpatient visits as a proxy for laboratory-confirmed ARI, our results could have been biased if the propensity to seek medical care was differential between BMI categories. To minimize this potential bias, we included measures of previous outpatient and hospital care use, which are extremely strong predictors of future utilization, into our statistical models to directly control for any health care utilization bias.

This is one of the first studies to evaluate the association between obesity and ARI, and we found that overweight, obesity, and severe obesity are associated with an increased risk for respiratory infection. However, the strength of this conclusion depends on the adequacy of ARI-coded outpatient visits as a proxy for respiratory infection in the community. The ability for outpatient visits for ARI to serve as a proxy could not be investigated using our data and has not been firmly established in other studies from the literature. Prospective studies using laboratory methods to confirm the presence and type of respiratory infection between BMI groups are needed to confirm the results from our study and to indicate if observed differences are specific to certain pathogens. Obesity is emphasized as a public health concern in relation to its contribution to the burden of chronic diseases; however, this study suggests that the impact on infectious diseases may also be important. Interventions designed to reduce the prevalence of obesity and subsequent chronic diseases may have the added benefit reducing the burden of respiratory infections in the population.

Acknowledgments

We would like to thank the sentinel laboratories participating in the Respiratory Virus Detection Surveillance System and the FluWatch team at the Public Health Agency of Canada for providing the viral surveillance data used in this study who received no financial compensation for their contributions.

Financial Support: This study was supported by an operating grant from the Canadian Institutes of Health Research (XIN 82408). JCK was supported by a Clinician Scientist Award from the University of Toronto Department of Family and Community Medicine. JCK and MAC receive salary support from the Institute for Clinical Evaluative Sciences (ICES). This study was supported by the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The study sponsors did not participate in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; or the decision to submit the manuscript for publication.

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Table 1

Patient characteristics by Body Mass Index (BMI) group

Characteristic	No. (%) of person-seasons[1] Underweight BMI < 18.5 (n = 9,849)	Normal weight BMI 18.5–24.9 (n = 184,165)	Overweight BMI 25.0–25.9 (n = 133,378)	Obese class I BMI 30.0–34.9 (n = 49,519)	Obese class II/III BMI ≥ 35 (n = 19,670)
Age, years, mean (SD)	35.07 ± 12.26	40.71 ± 12.52	45.30 ± 11.80	46.23 ± 11.65	46.28 ± 12.55
Age group, years					
18–29	4 231 (43.0%)	45 052 (24.5%)	15 983 (12.0%)	5 040 (10.2%)	1 931 (9.8%)
30–49	4 210 (42.7%)	90 646 (49.2%)	65 665 (49.2%)	23 628 (47.7%)	9 420 (47.9%)
50–64	1 408 (14.3%)	48 467 (26.3%)	51 730 (38.8%)	20 850 (42.1%)	8 319 (42.3%)
Male	1 891 (19.2%)	76 094 (41.3%)	80 345 (60.2%)	27 542 (55.6%)	8 128 (41.3%)
Rural residence[2]					
No	8 199 (83.2%)	147 425 (80.1%)	102 928 (77.2%)	37 288 (75.3%)	14 706 (74.8%)
Yes	1 540 (15.6%)	34 779 (18.9%)	29 341 (22.0%)	11 952 (24.1%)	4 877 (24.8%)
No data	110 (1.1%)	1 961 (1.1%)	1 109 (0.8%)	278 (0.6%)	87 (0.4%)
Income quintile					
1 (lowest)	2 364 (24.0%)	33 942 (18.4%)	24 125 (18.1%)	9 950 (20.1%)	4 737 (24.1%)
2	1 874 (19.0%)	36 056 (19.6%)	26 530 (19.9%)	9 941 (20.1%)	4 468 (22.7%)
3	1 881 (19.1%)	36 592 (19.9%)	27 232 (20.4%)	10 483 (21.2%)	3 987 (20.3%)
4	1 781 (18.1%)	37 433 (20.3%)	27 600 (20.7%)	9 963 (20.1%)	3 437 (17.5%)
5 (highest)	1 818 (18.5%)	37 803 (20.5%)	26 431 (19.8%)	8 782 (17.7%)	2 893 (14.7%)
No data	131 (1.3%)	2 339 (1.3%)	1 460 (1.1%)	399 (0.8%)	148 (0.8%)
No. admissions, past 3 years, mean (SD)	0.24 ± 0.79	0.18 ± 0.62	0.18 ± 0.62	0.22 ± 0.72	0.31 ± 0.90
No. outpatient visits, past year, mean (SD)	7.76 ± 10.17	6.74 ± 9.11	6.99 ± 9.23	8.34 ± 10.45	10.46 ± 12.55
No. living in household, mean (SD)	2.93 ± 1.47	2.83 ± 1.39	2.76 ± 1.37	2.71 ± 1.35	2.56 ± 1.36
Current daily smoker	3 589 (36.4%)	50 086 (27.2%)	32 012 (24.0%)	11 227 (22.7%)	4 257 (21.6%)
Vaccinated against influenza	1 096 (11.1%)	21 867 (11.9%)	19 090 (14.3%)	8 478 (17.1%)	4 180 (21.3%)
At least one chronic condition	2 279 (23.1%)	41 993 (22.8%)	35 948 (27.0%)	16 860 (34.0%)	8 660 (44.0%)
Chronic cardiovascular disease	451 (4.6%)	9 192 (5.0%)	10 244 (7.7%)	4 834 (9.8%)	2 358 (12.0%)
Chronic respiratory disease	1 140 (11.6%)	18 079 (9.8%)	13 616 (10.2%)	6 153 (12.4%)	3 305 (16.8%)
Cancer	360 (3.7%)	9 008 (4.9%)	7 481 (5.6%)	2 954 (6.0%)	1 119 (5.7%)

Characteristic	No. (%) of person-seasons[1]				
	Underweight BMI < 18.5 (n = 9,849)	**Normal weight BMI 18.5–24.9 (n = 184,165)**	**Overweight BMI 25.0–25.9 (n = 133,378)**	**Obese class I BMI 30.0–34.9 (n = 49,519)**	**Obese class II/III BMI ≥ 35 (n = 19,670)**
Diabetes	150 (1.5%)	4 523 (2.5%)	7 822 (5.9%)	5 868 (11.9%)	4 219 (21.4%)
Anemia	599 (6.1%)	7 562 (4.1%)	4 158 (3.1%)	1 754 (3.5%)	958 (4.9%)
Renal	86 (093%)	1 518 (0.8%)	1 494 (1.1%)	725 (1.5%)	389 (2.0%)
Immunodeficiency[3]	127 (1.3%)	1 993 (1.1%)	1 378 (1.0%)	583 (1.2%)	239 (1.2%)
Aspiration history	23 (0.2%)	436 (0.2%)	454 (0.3%)	176 (0.4%)	94 (0.5%)

[1] Data are presented as Number (%) unless otherwise noted.

[2] Communities with <10,000 inhabitants were defined as rural.

[3] Due to disease and/or therapy.

Table 2

Associations between BMI category and outpatient visits for acute respiratory infections during influenza season and non-influenza season periods

BMI Category	Influenza Season Periods			Non-Influenza Season Periods		
	Event rate per 1,000 person-years	Unadjusted RR (95% CI)	Adjusted[1] RR (95% CI)	Event rate per 1,000 person-years	Unadjusted RR (95% CI)	Adjusted[1] RR (95% CI)
All outpatient visits						
< 18.5 (underweight)	513.1	1.20 (1.12–1.29)	1.03 (0.96–1.10)	321.8	1.38 (1.27–1.51)	1.13 (1.03–1.23)
18.5–24.9 (normal weight)	430.2	1.00	1.00	231.7	1.00	1.00
25–29.9 (overweight)	425.3	0.99 (0.97–1.02)	1.10 (1.07–1.13)	206.5	0.89 (0.86–0.93)	1.02 (0.98–1.06)
30–34.9 (obese class I)	476.5	1.11 (1.07–1.15)	1.17 (1.13–1.22)	236.2	1.02 (0.97–1.07)	1.11 (1.05–1.17)
35+ (obese class II and III)	557.2	1.29 (1.22–1.36)	1.19 (1.12–1.25)	286.1	1.23 (1.14–1.33)	1.13 (1.04–1.23)
Physician office visits						
< 18.5 (underweight)	464.8	1.19 (1.10–1.28)	1.02 (0.95–1.10)	286.7	1.36 (1.24–1.50)	1.11 (1.01–1.22)
18.5–24.9 (normal weight)	394.1	1.00	1.00	209.4	1.00	1.00
25–29.9 (overweight)	385.6	0.98 (0.95–1.01)	1.09 (1.06–1.12)	184.5	0.88 (0.84–0.92)	1.01 (0.97–1.05)
30–34.9 (obese class I)	426.0	1.08 (1.04–1.23)	1.15 (1.11–1.20)	208.6	0.99 (0.94–1.05)	1.09 (1.03–1.15)
35+ (obese class II and III)	484.9	1.22 (1.16–1.29)	1.14 (1.07–1.21)	247.0	1.18 (1.08–1.28)	1.09 (1.00–1.19)
Emergency department visits						
< 18.5 (underweight)	52.9	1.44 (1.21–1.72)	1.16 (0.97–1.38)	32.2	1.52 (1.20–1.93)	1.19 (0.93–1.51)
18.5–24.9 (normal weight)	36.8	1.00	1.00	21.2	1.00	1.00
25–29.9 (overweight)	41.9	1.14 (1.06–1.22)	1.28 (1.19–1.38)	21.4	1.00 (0.90–1.11)	1.14 (1.03–1.27)
30–34.9 (obese class I)	53.1	1.45 (1.32–1.59)	1.50 (1.36–1.64)	27.3	1.29 (1.12–1.47)	1.35 (1.18–1.55)
35+ (obese class II and III)	72.1	1.96 (1.75–2.21)	1.69 (1.50–1.91)	37.4	1.76 (1.48–2.09)	1.56 (1.30–1.87)

RR = Rate Ratio; CI = Confidence Interval

[1] All models adjusted for age, sex, calendar year, influenza vaccination status, rural residence, income quintile, number of individuals living in the household, smoking status, previous hospitalizations in past 3 years, previous outpatient visits in past year, and diagnosis of chronic cardiovascular disease, chronic respiratory disease, diabetes, cancer, anemia, renal disease, immunodeficiency and aspiration history

Table 3

Supplementary analyses

	Influenza Season Periods		Non-Influenza Season Periods	
BMI Category	**Event rate per 1,000 person-years**	**Adjusted[1] RR (95% CI)**	**Event rate per 1,000 person-years**	**Adjusted[1] RR (95% CI)**
Primary analysis				
< 18.5 (underweight)	513.1	1.03 (0.96–1.10)	321.8	1.13 (1.03–1.23)
18.5–24.9 (normal weight)	430.2	1.00	231.7	1.00
25–29.9 (overweight)	425.3	1.10 (1.07–1.13)	206.5	1.02 (0.98–1.06)
30–34.9 (obese class I)	476.5	1.17 (1.13–1.22)	236.2	1.11 (1.05–1.17)
35+ (obese class II and III)	557.2	1.19 (1.12–1.25)	286.1	1.13 (1.04–1.23)
Self-reported BMI adjusted for potential underestimation				
< 18.5 (underweight)	498.2	1.04 (0.94–1.14)	329.4	1.17 (1.03–1.32)
18.5–24.9 (normal weight)	429.7	1.00	236.7	1.00
25–29.9 (overweight)	425.3	1.11 (1.08–1.14)	205.6	1.00 (0.96–1.04)
30–34.9 (obese class I)	463.0	1.17 (1.13–1.21)	229.5	1.09 (1.03–1.14)
35+ (obese class II and III)	544.1	1.21 (1.15–1.26)	281.6	1.15 (1.07–1.23)
Individuals with chronic conditions				
< 18.5 (underweight)	718.7	1.00 (0.88–1.12)	460.1	1.10 (0.94–1.29)
18.5–24.9 (normal weight)	571.6	1.00	328.4	1.00
25–29.9 (overweight)	548.4	1.08 (1.03–1.13)	269.0	1.00 (0.94–1.07)
30–34.9 (obese class I)	561.1	1.14 (1.08–1.20)	289.5	1.04 (0.96–1.13)
35+ (obese class II and III)	598.5	1.12 (1.04–1.20)	311.1	1.08 (0.98–1.20)
Individuals without chronic conditions				
< 18.5 (underweight)	501.6	1.04 (0.96–1.13)	314.3	1.14 (1.03–1.26)
18.5–24.9 (normal weight)	421.3	1.00	225.7	1.00
25–29.9 (overweight)	411.3	1.11 (1.07–1.14)	199.6	1.02 (0.97–1.07)
30–34.9 (obese class I)	459.9	1.17 (1.12–1.23)	226.0	1.14 (1.06–1.21)
35+ (obese class II and III)	542.2	1.28 (1.20–1.37)	277.2	1.22 (1.10–1.35)
Cohort restricted to first appearance of individual in the dataset				
< 18.5 (underweight)	557.1	1.08 (0.98–1.20)	355.0	1.19 (1.04–1.37)
18.5–24.9 (normal weight)	439.9	1.00	240.4	1.00
25–29.9 (overweight)	429.2	1.07 (1.02–1.11)	219.7	1.04 (0.98–1.10)
30–34.9 (obese class I)	468.0	1.10 (1.05–1.17)	250.4	1.13 (1.04–1.22)
35+ (obese class II and III)	566.5	1.14 (1.06–1.23)	302.4	1.13 (1.02–1.26)

RR = Rate Ratio; CI = Confidence Interval

[1]All models adjusted for age, sex, calendar year, influenza vaccination status, rural residence, income quintile, number of individuals living in the household, smoking status, previous hospitalizations in past 3 years, previous outpatient visits in past year, and diagnosis of chronic cardiovascular disease, chronic respiratory disease, diabetes, cancer, anemia, renal disease, immunodeficiency and aspiration history (with the exception of the analyses stratified by the presence of chronic conditions which excluded chronic conditions from the model).