Obesity and Respiratory Hospitalizations During Influenza Seasons in Ontario, Canada: A Cohort Study

Jeffrey C. Kwong,1,2,3,4 Michael A. Campitelli,1 and Laura C. Rosella1,2,4

1Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada; 2Surveillance and Epidemiology, Public Health Ontario, Toronto, Ontario, Canada; 3Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada; and 4Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada

(See the Editorial Commentary by Jain and Chaves, on pages 422–424.)

Background. Previous studies suggest that obesity may be a risk factor for complications from pandemic influenza A(H1N1) infection. We aimed to examine the association between obesity and respiratory hospitalizations during seasonal influenza epidemics and to determine the extent of this association among individuals without established risk factors for serious complications due to influenza infection.

Methods. We conducted a cohort study over 12 influenza seasons (1996–1997 through 2007–2008) of 82 545 respondents to population health surveys in Ontario, Canada. We included individuals aged 18–64 years who had responded to a survey within 5 years prior to the start of an influenza season. We used logistic regression to examine the association between self-reported body mass index (BMI) and hospitalization for selected respiratory diseases (pneumonia and influenza, acute respiratory diseases, and chronic lung diseases), both in the entire cohort and stratified by chronic condition status.

Results. Obese class I (BMI, 30–34.9) (odds ratio [OR], 1.45 [95% confidence interval {CI}, 1.03–2.05]) and obese class II or III (BMI, ≥35) individuals (OR, 2.12 [95% CI, 1.45–3.10]) were more likely than normal weight individuals to have a respiratory hospitalization during influenza seasons. Among obese class II or III individuals, the association was present both for those without previously identified risk factors (OR, 5.10 [95% CI, 2.53–10.24]) and for those with 1 risk factor (OR, 2.11 [95% CI, 1.10–4.06]).

Conclusions. Severely obese individuals with and without chronic conditions are at increased risk for respiratory hospitalizations during influenza seasons. They should be considered a priority group for preventive influenza measures, such as vaccination and treatment with antiviral medications.

Influenza causes substantial mortality and serious morbidity each year [1, 2]. Cardiac and pulmonary disorders, diabetes mellitus and other metabolic diseases, cancer, immunosuppression, renal disease, and anemias are recognized risk factors for serious complications from influenza infection [3].

Prior to the 2009 influenza A(H1N1) pandemic, obesity had not previously been considered a risk factor for severe influenza infection [4]. However, animal studies suggest that obesity may increase the risk of influenza complications; compared with lean controls, diet-induced obese mice have decreased and delayed expression of proinflammatory cytokines, decreased natural killer cell cytotoxicity, and impaired dendritic cell function during influenza infection, resulting in higher morbidity and mortality from influenza viruses [5, 6]. In humans, greater than expected prevalence of obesity (body mass index [BMI], ≥30) and morbidity...
obesity (BMI, ≥40) were recently reported among individuals hospitalized for pandemic H1N1 infection [4, 7–9]. Individuals with high BMIs are more likely to have conditions that increase the risk of influenza complications, including diabetes mellitus and cardiovascular conditions [10–12], but it is unclear whether elevated BMI is an independent risk factor.

The prevalence of obesity is 23.1% in Canada and 33.8% in the United States [13, 14], and obesity rates are increasing, especially in the higher obesity categories [15]. Although obesity seems to be a risk factor for severe pandemic H1N1 infection, the association between obesity and seasonal influenza has, to our knowledge, never been studied. Therefore, we sought to examine the association between obesity and respiratory hospitalizations during seasonal influenza epidemics (as a proxy for severe outcomes related to influenza) and to determine the extent of this association among individuals without established risk factors for serious complications due to influenza. Obese individuals without other comorbidities have previously not been considered a priority group for influenza immunization; therefore, an association in this group would be relevant for the determination of public health policy.

METHODS

Population, Setting, and Study Design
We conducted a cohort study of individuals who responded to one of Canada’s nationally representative cross-sectional population health surveys conducted by Statistics Canada: the 1996/1997 cycle of the National Population Health Survey (NPHS), or cycle 1.1 (2000–2001), cycle 2.1 (2003), or cycle 3.1 (2005) of the Canadian Community Health Survey (CCHS) [16, 17]. Targeting the household population aged ≥12 years, these surveys exclude full-time military, institutionalized, and on-reserve populations. The surveys were conducted using a combination of telephone and in-person interviews and had response rates ranging from 75% to 82% for Ontario. This study was restricted to those who agreed to linkage of their responses to health administrative data sets and whose data were linked successfully (linkage rate, 84%); linkage was achieved using encrypted health card numbers that served as unique identifiers.

We examined outcomes for study subjects over 12 influenza seasons (1996–1997 through 2007–2008). Setting the start of each influenza season as the index date, we included Ontario residents aged 18–64 years on the index date who had responded to a survey up to 5 years prior to that date. Therefore, an individual could be included in the cohort up to 5 times. Sensitivity analyses were conducted excluding repeated cohort entries. Women who were pregnant or breastfeeding at the time of survey (n = 2115) and individuals with a height of <3 feet or ≥7 feet (n = 39) were excluded, because Canadian guidelines do not recommend BMI calculation in such individuals [18].

We also identified women who became pregnant during subsequent influenza seasons by extracting hospital admission dates for births for all women in the cohort and excluding for the relevant influenza seasons women who had a birth record during an influenza season or within 40 weeks following the end of an influenza season (4785 influenza seasons of observation), because the prepregnancy BMI measured at the time of survey may not have been reflective of BMI during pregnancy.

All cohort members had free access to hospital care and physician services, and starting in fall 2000, with the introduction of universal influenza immunization in Ontario, all were able to receive the influenza vaccine free of charge regardless of risk status. Ethics approval was obtained from the Research Ethics Board of Sunnybrook Health Sciences Centre, Toronto, Canada.

Data Sources and Definitions

Influenza Seasons and Control Periods
We obtained laboratory test results for influenza (mainly viral culture and direct antigen detection) submitted by a network of sentinel laboratories to the Public Health Agency of Canada. Two study periods were defined: (1) influenza seasons, defined as the period between the first and last occurrences of 2 consecutive weeks with ≥5% of influenza tests yielding positive results, corresponding to the start and end dates of the influenza season; and (2) post–influenza season periods (control periods), defined as July 1–September 30 annually. In a sensitivity analysis, we defined influenza seasons using a 10% threshold.

Body Mass Index
BMI was calculated using self-reported height and weight from the NPHS or CCHS. In general, there is high correlation between self-reported and measured height and weight [19]; however, people tend to underestimate weight and overestimate height, causing reported BMI to be generally lower than measured BMI [19–21]. Measured BMI is not available from these surveys but was available in CCHS cycle 2.2. That cycle was not included in this study, because it has not been linked to health administrative data sets. In that sample (N = 1131), self-reported BMI reliably predicted measured BMI for individuals aged 20–64 years (r = 0.93). BMI categories were defined using 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), and ≥40 (obese class III) [18]. Because of the small number of individuals in the obese class II and III categories, these were collapsed.

Main Outcome Measure
The primary outcome was hospitalization for the following respiratory diseases: pneumonia and influenza (International Classification of Diseases, Ninth Revision, Clinical Modification
Covariates

Demographic information (age, sex, neighborhood income quintile, and rural residence) was obtained from Ontario’s Registered Persons Database, which contains key demographic data about anyone with an Ontario health card [26]. Neighborhood income quintiles were defined by using patients’ postal codes to assign them to geographic regions where the average annual income could be determined through linkage to census data [27]. Responses from the health surveys were used to determine an individual’s smoking status (current daily smoker or not) and the number of individuals residing in the respondent’s household. Previous health care utilization was assessed using the Ontario Health Insurance Plan (OHIP) physician billing claims database (outpatient clinic visits during the past year), which contains claims for outpatient clinic visits from approximately 98% of Ontario physicians [28], and the CIHI discharge abstract database (hospital visits during the previous 3 years).

Influenza vaccination status was assessed using the OHIP database. Individuals vaccinated after the start of an influenza season were considered unvaccinated, although only 5% of vaccines were administered after the onset of influenza seasons.

Comorbidities were defined on the basis of an adaptation of the adjusted clinical group classification as any mention of the diagnosis in the outpatient or hospitalization data sets during the 3 years prior to an index date [29]. The comorbidities of interest were the chronic health conditions identified by Canada’s National Advisory Committee on Immunizations (NACI) as increasing the risk of complications from influenza (heart diseases, respiratory diseases, diabetes mellitus, cancers, immunodeficiency due to underlying disease and/or therapy, renal diseases, anemias, and aspiration history) [3]. Because individuals could have been included multiple times, we updated covariate information at each index date.

Statistical Analyses

We fitted logistic regression models to estimate the risk of hospitalization during influenza seasons among BMI categories, with normal weight individuals as the referent. In an adjusted analysis, covariates were added to the models. Because individuals with comorbidities were already recommended to receive influenza vaccines regardless of BMI, we also conducted a stratified analysis in which we divided the cohort into individuals without any NACI-recognized comorbidities associated with increased risk of influenza complications, individuals with 1 NACI-recognized risk factor, and individuals with ≥2 risk factors.

To test the robustness of our findings, we conducted multiple sensitivity analyses. To determine the underlying propensity for individuals in different weight categories to be hospitalized, we assessed the association between BMI and hospitalization for any cause during influenza seasons. To test for the lack of an association where none was expected (ie, specificity), we examined the association between BMI category and hospitalization for external causes of injury (ICD-9-CM codes, E800–E999; ICD-10-CM codes, V01–Y98) during influenza seasons, and we assessed the association between the main outcome conditions (ie, respiratory conditions) during control periods when influenza was not circulating.

Because an individual could have been included in the analysis up to 5 times, we used generalized estimating equations to adjust for the correlated nature of the data. Statistical analyses were conducted using SAS, version 9.1 (SAS Institute), and STATA, version 9.2 (StataCorp). All tests were 2-tailed, and a P value of <.05 was considered to reveal a statistically significant difference.

RESULTS

The cohort comprised 82,545 unique survey responders who were included for a total of 348,350 person-seasons and who contributed 105,035.6 person-years of observation during influenza seasons. A total of 372 hospitalizations occurred during influenza seasons, and 288 hospitalizations occurred during control periods. Weekly outcome rates during the study period revealed seasonality, with spikes coinciding with periods of influenza activity (Figure 1). The prevalence of having ≥1 high-risk comorbidity for influenza was 27%.

Approximately 46% of the cohort self-reported a normal body weight, 2.4% reported a BMI <18.5, 33% reported a BMI of 25–29.9, 12% reported a BMI of 30–34.9, and 5% reported...
a BMI $\geq 35$ (Table 1). Individuals in the highest BMI category were older, had lower socioeconomic status, were more likely to live in rural areas, were less likely to smoke daily, had more outpatient visits, and were more likely to receive influenza vaccination. They also had more risk factors for influenza complications, particularly for chronic cardiovascular diseases, chronic respiratory diseases, and diabetes mellitus; 44% in the highest BMI category had $\geq 1$ risk factor, compared with 23% in the normal BMI category.

Increased BMI was associated with greater odds of respiratory hospitalizations during influenza seasons (Table 2). In the adjusted analysis, individuals who were obese class I (odds ratio [OR], 1.45 [95% confidence interval {CI}, 1.03–2.05]) and individuals who were obese class II or III (OR, 2.12 [95% CI, 1.45–3.10]) had significantly higher odds of the outcome during influenza seasons. Adjustment for confounders attenuated the observed ORs for the higher BMI categories. Similar results were seen when stratifying the cohort by the presence of comorbidities known to increase risk for serious influenza outcomes. The point estimate for the odds ratio among obese class II or III individuals was larger for those without risk factors (OR, 5.10 [95% CI, 2.53–10.24]), compared with those with only 1 risk factor (OR, 2.11 [95% CI, 1.10–4.06]) and those with $\geq 2$ risk factors (OR, 1.66 [95% CI, 0.97–2.84]), but the confidence intervals overlapped. The event rate for obese class II or III individuals without risk factors was similar to the event rate for normal weight individuals with 1 risk factor (3.97 events per 1000 person-years vs 4.07 events per 1000 person-years).

Obese class II or III individuals also had greater odds of respiratory hospitalizations resulting in admission to an ICU during the 2002–2003 through 2007–2008 influenza seasons (OR, 3.23 [95% CI, 1.24–8.45]) (Table 3). Obese individuals were more likely to be hospitalized for any cause during influenza seasons. There was no association between BMI and hospitalization for external causes of injury during influenza seasons. Also, we observed no association between BMI and hospitalization for selected respiratory conditions during control periods, except for the underweight category. When the cohort was restricted to the first appearance of each individual, and when influenza seasons were defined using a 10% threshold, the results were generally consistent with those of the primary analysis.

**DISCUSSION**

We found obesity (BMI, $\geq 30$) to be independently associated with an increased risk of respiratory hospitalizations during periods of seasonal influenza activity. The association between severe obesity (BMI, $\geq 35$) and respiratory hospitalizations was present both for those without previously recognized risk factors for serious influenza complications and for those with 1 risk factor. In addition, severely obese individuals without risk factors had an event rate similar to that of normal weight individuals with only 1 risk factor, indicating that severe obesity may be as important a predictor of influenza complications as are other identified chronic conditions. We also observed a similar association using ICU admissions as an outcome.
Although obese individuals are at increased risk of hospitalization from any cause during influenza season, the association was greater for respiratory conditions than for other conditions. Additional sensitivity analyses revealed specificity and consistency of the association.

This study examines the relationship between obesity and respiratory hospitalizations during seasonal influenza epidemics. Previous studies have revealed a high prevalence of obesity among individuals with complications of pandemic H1N1 infection [4, 7–9]. Furthermore, a recent case-cohort study reported that morbidly obese individuals (BMI, $\geq 40$) had a 4–5 times greater risk of hospitalization for H1N1 than did normal weight individuals [30]. Our study found a smaller association between severe obesity (BMI, $\geq 35$) and hospitalization, and we detected an increase in risk for obese individuals in addition to morbidly obese individuals. Differences in the study

Table 1. Baseline Characteristics by Body Mass Index (BMI) Group

| Characteristic | No. (%) of person-seasons |
|---------------|--------------------------|
|                | Underweight | Normal | Overweight | Obese class I | Obese class II and III |
| BMI < 18.5    | (n = 8400) | (n = 158 987) | (n = 115 342) | (n = 42 268) | (n = 16 366) |
|               | [2.4%] | [45.6%] | [33.1%] | [12.1%] | [4.7%] |
| Age, mean years (SD) | 35.2 (12.3) | 40.9 (12.5) | 45.3 (11.7) | 46.2 (11.6) | 46.4 (11.3) |
| Age group, years | 18–29 | 3559 (42.4) | 37 722 (23.7) | 13 435 (11.7) | 4181 (9.9) | 1514 (9.3) |
|                | 30–49 | 3632 (43.2) | 79 369 (50.0) | 57 300 (49.7) | 20 398 (48.3) | 7867 (48.1) |
|                | 50–64 | 1209 (14.4) | 41 806 (26.3) | 44 607 (38.7) | 17 689 (41.9) | 6985 (42.7) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |
| Age, mean years (SD) | 35.2 (12.3) | 40.9 (12.5) | 45.3 (11.7) | 46.2 (11.6) | 46.4 (11.3) |
| Age group, years | 18–29 | 3559 (42.4) | 37 722 (23.7) | 13 435 (11.7) | 4181 (9.9) | 1514 (9.3) |
|                | 30–49 | 3632 (43.2) | 79 369 (50.0) | 57 300 (49.7) | 20 398 (48.3) | 7867 (48.1) |
|                | 50–64 | 1209 (14.4) | 41 806 (26.3) | 44 607 (38.7) | 17 689 (41.9) | 6985 (42.7) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |
| Income quintile | 1 (lowest) | 2053 (24.4) | 29 014 (18.3) | 20 648 (17.9) | 8639 (20.4) | 3952 (24.2) |
|                | 2 | 1564 (18.6) | 31 322 (19.7) | 22 855 (19.8) | 8487 (20.1) | 3630 (22.2) |
|                | 3 | 1616 (19.2) | 31 551 (19.9) | 23 779 (20.6) | 8922 (21.1) | 3347 (20.5) |
|                | 4 | 1552 (18.5) | 32 196 (20.3) | 23 779 (20.6) | 8524 (20.2) | 2863 (17.5) |
|                | 5 (highest) | 1507 (17.9) | 32 746 (20.6) | 23 025 (20.0) | 7363 (17.4) | 2461 (15.0) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |
| Rural residence | Yes | 1306 (15.6) | 30 514 (19.2) | 25 474 (22.1) | 10 288 (24.3) | 4064 (24.8) |
|                | No | 6996 (83.3) | 126 592 (79.7) | 88 874 (77.1) | 31 741 (75.1) | 12 225 (74.7) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |
| No data | 98 (1.2) | 1791 (1.1) | 994 (0.9) | 239 (0.6) | 77 (0.5) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |
| Male sex | 1651 (19.7) | 67 020 (42.2) | 70 294 (60.9) | 23 749 (56.2) | 6855 (41.9) |

NOTE. Data are no. (%) of patients unless otherwise specified.

* Chronic conditions identified by Canada’s National Advisory Committee on Immunizations as increasing the risk of complications from influenza.
populations, influenza strains, BMI categories, outcome measures, and study designs may explain some of the discrepancies. This study had several limitations. BMI was based on self-reported height and weight, rather than direct measurement. Nevertheless, we showed that self-reported BMI reliably predicted measured BMI for this population. Any misclassification would be minor and, if present, would tend to underestimate our associations. Another limitation is that because individuals were included if they had completed a survey within 5 years of an influenza season, it is possible that their BMI may have changed over the study period. Data from the longitudinal NPHS suggests that BMI increases on average only 0.5 units over a 6-year period [31]. Such a small increase would have resulted in minimal misclassification of individuals to BMI categories in the years following survey response in this study. The selected respiratory hospitalizations during periods of influenza circulation used as the outcome measure in this study were non-specific and may have been due to causes other than influenza. However, they correlate well with influenza circulation and have been used in previous studies [22, 23]. We lacked sufficient event counts to adequately examine risk of outcomes in individuals without chronic conditions, as evidenced by the wider confidence intervals. Ontario’s universal influenza immunization program facilitates access to influenza vaccines through workplaces and community settings; thus, not all vaccination is captured by physician billing data [32]. This may lead to misclassification of vaccination status. However, using self-reported vaccination as the gold standard, a physician billing claim for influenza vaccination had a positive predictive value of 0.89 and a negative predictive value of 0.81 for the age group in this study. Another limitation is that covariates derived from responses to the health surveys (smoking status and number of individuals living in household) may have changed over the study period and could not be updated at each index date. Finally, we were unable to distinguish whether obesity was associated with increased risk of influenza infection.

### Table 2. Associations Between BMI Category and Hospitalization for Selected Respiratory Conditions (Adjusted and Stratified Analyses)

| BMI category                     | Event rate per 1000 person-years | Unadjusted | Adjusteda |
|----------------------------------|----------------------------------|------------|-----------|
| Entire cohort                    | 3.54                             |            |           |
| <18.5 (underweight)              | 5.54                             | 2.27 (1.21–4.23) | 1.65 (0.88–3.08) |
| 18.5–24.9 (normal weight)        | 2.49                             | 1.00       | 1.00      |
| 25–29.9 (overweight)             | 2.88                             | 1.16 (0.87–1.55) | 1.02 (0.75–1.37) |
| 30–34.9 (obese class I)          | 5.43                             | 2.15 (1.54–3.01) | 1.45 (1.03–2.05) |
| ≥35 (obese class II or III)      | 11.60                            | 4.73 (3.28–6.82) | 2.12 (1.45–3.10) |
| Without risk factors             | 0.93                             |            |           |
| <18.5 (underweight)              | 0.51                             | 0.73 (0.10–5.38) | 0.89 (0.12–6.72) |
| 18.5–24.9 (normal weight)        | 0.71                             | 1.00       | 1.00      |
| 25–29.9 (overweight)             | 0.79                             | 1.12 (0.63–2.01) | 0.98 (0.55–1.77) |
| 30–34.9 (obese class I)          | 1.43                             | 2.03 (1.02–4.02) | 1.73 (0.86–3.46) |
| ≥35 (obese class II or III)      | 3.97                             | 5.68 (2.81–11.50) | 5.10 (2.53–10.24) |
| With 1 risk factorb              | 4.89                             |            |           |
| <18.5 (underweight)              | 8.63                             | 2.10 (0.75–5.92) | 1.62 (0.54–4.83) |
| 18.5–24.9 (normal weight)        | 4.07                             | 1.00       | 1.00      |
| 25–29.9 (overweight)             | 4.14                             | 1.02 (0.63–1.67) | 1.04 (0.63–1.72) |
| 30–34.9 (obese class I)          | 5.98                             | 1.51 (0.85–2.70) | 1.48 (0.83–2.65) |
| ≥35 (obese class II or III)      | 9.49                             | 2.40 (1.25–4.60) | 2.11 (1.10–4.06) |
| With ≥2 risk factorsb            | 29.10                            |            |           |
| <18.5 (underweight)              | 73.15                            | 2.96 (1.28–6.86) | 2.15 (0.92–5.07) |
| 18.5–24.9 (normal weight)        | 25.98                            | 1.00       | 1.00      |
| 25–29.9 (overweight)             | 22.50                            | 0.86 (0.56–1.33) | 0.94 (0.59–1.48) |
| 30–34.9 (obese class I)          | 30.20                            | 1.16 (0.72–1.88) | 1.18 (0.72–1.94) |
| ≥35 (obese class II or III)      | 43.58                            | 1.83 (1.09–3.09) | 1.66 (0.97–2.84) |

**NOTE.** CI, confidence interval; OR, odds ratio.

a All models were adjusted for age group, sex, influenza vaccination status, rural residence, income quintile, number of individuals living in the household, smoking status, previous hospitalizations during past 3 years, and previous outpatient visits during past year. In the nonstratified analysis, models were also adjusted for chronic cardiovascular disease, chronic respiratory disease, diabetes mellitus, cancer, anemia, renal disease, immunodeficiency, and aspiration history.

b Chronic conditions identified by Canada’s National Advisory Committee on Immunizations as increasing the risk of complications from influenza.
or an increased risk of serious complications arising from influenza infection.

Among the strengths of this study, the most notable was our ability to link population-based BMI data for a large number of individuals to health administrative data sets to determine outcomes, vaccination status, and comorbidities. This afforded a unique opportunity to study this association. Furthermore, we studied multiple influenza seasons, and we used influenza viral surveillance data to define periods of influenza activity. Future research should use laboratory-confirmed influenza outcomes and objective measures of height and weight, although it may not be feasible to collect such data on a sufficiently large population to examine serious complications from influenza.

Obesity is recognized as an important and growing public health problem because of its association with many serious chronic conditions. This study offers a new perspective on the

| Table 3. Sensitivity Analyses |
|-----------------------------|
| Outcome | Event rate per 1000 person-years | OR* (95% CI) |
| Respiratory hospitalizations resulting in admission to an Intensive care unit (2002/2003 through 2007/2008 influenza seasons only) | 0.67 |  |
| <18.5 (underweight) | 1.64 | 3.27 (0.76–14.15) |
| 18.5–24.9 (normal weight) | 0.29 | 1.00 |
| 25–29.9 (overweight) | 0.75 | 2.21 (0.98–4.96) |
| 30–34.9 (obese class I) | 0.83 | 1.88 (0.72–4.94) |
| ≥35 (obese class II or III) | 2.78 | 3.23 (1.24–8.45) |
| All hospitalizations during influenza seasons | 47.89 |  |
| <18.5 (underweight) | 40.34 | 0.96 (0.77–1.20) |
| 18.5–24.9 (normal weight) | 39.54 | 1.00 |
| 25–29.9 (overweight) | 48.46 | 1.09 (1.02–1.17) |
| 30–34.9 (obese class I) | 63.14 | 1.20 (1.09–1.31) |
| ≥35 (obese class II or III) | 88.77 | 1.42 (1.26–1.60) |
| Hospitalizations for external causes of injury during influenza seasons | 9.64 |  |
| <18.5 (underweight) | 8.70 | 0.90 (0.58–1.41) |
| 18.5–24.9 (normal weight) | 8.39 | 1.00 |
| 25–29.9 (overweight) | 9.72 | 1.08 (0.92–1.26) |
| 30–34.9 (obese class I) | 11.99 | 1.12 (0.91–1.38) |
| ≥35 (obese class II or III) | 15.59 | 1.22 (0.93–1.59) |
| Respiratory hospitalizations during control periods | 3.41 |  |
| <18.5 (underweight) | 7.86 | 2.18 (1.24–3.84) |
| 18.5–24.9 (normal weight) | 2.73 | 1.00 |
| 25–29.9 (overweight) | 3.18 | 1.06 (0.76–1.47) |
| 30–34.9 (obese class I) | 4.28 | 1.07 (0.71–1.60) |
| ≥35 (obese class II or III) | 6.28 | 0.99 (0.60–1.65) |
| Respiratory hospitalizations during influenza seasons, cohort restricted to first appearance of individual in data set | 3.60 |  |
| <18.5 (underweight) | 5.60 | 1.53 (0.41–5.81) |
| 18.5–24.9 (normal weight) | 2.21 | 1.00 |
| 25–29.9 (overweight) | 2.88 | 1.10 (0.59–2.03) |
| 30–34.9 (obese class I) | 4.47 | 1.33 (0.64–2.77) |
| ≥35 (obese class II or III) | 16.13 | 2.97 (1.48–5.94) |
| Respiratory hospitalizations during influenza seasons, using 10% of influenza tests yielding positive results as the threshold | 4.06 |  |
| <18.5 (underweight) | 6.15 | 1.53 (0.73–3.21) |
| 18.5–24.9 (normal weight) | 2.99 | 1.00 |
| 25–29.9 (overweight) | 3.35 | 0.96 (0.68–1.35) |
| 30–34.9 (obese class I) | 5.46 | 1.20 (0.81–1.78) |
| ≥35 (obese class II or III) | 13.68 | 1.98 (1.29–3.04) |

NOTE. CI, confidence interval; OR, odds ratio.

* All models were adjusted for age group, sex, influenza vaccination status, rural residence, income quintile, number of individuals living in the household, smoking status, previous hospitalizations during past 3 years, previous outpatient visits during past year, and the presence of chronic cardiovascular disease, chronic respiratory disease, diabetes mellitus, cancer, anemia, renal disease, immunodeficiency, and aspiration history.
dangers of obesity and its relationship to severe influenza infection. The results of this study suggest that severe obesity is associated with an increased risk of respiratory hospitalizations during influenza season, although this relationship may vary (ie, be stronger or weaker) in future years, with new influenza strains and different circumstances. To minimize this risk, severely obese individuals should be recommended to receive annual influenza vaccination and be considered for treatment with antiviral medications if they present with influenza-like illness during periods of influenza circulation. In the presence of universal influenza immunization, obese individuals should be prioritized to receive vaccine. Public health and clinical interventions to reduce the prevalence of obesity in the population may also reduce the annual health and economic burden of influenza.

Acknowledgments

Nick Daneman, MD, Sunnybrook Health Sciences Centre, and Donald Redelmeier, MD, Institute for Clinical Evaluative Sciences (ICES), provided helpful comments on an earlier version of the manuscript and received no financial compensation for their contributions. The sentinel laboratories participating in the Respiratory Virus Detection Surveillance System and the FluWatch team at the Public Health Agency of Canada provided the viral surveillance data used in this study and received no financial compensation for their contributions.

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 Ministry of Health and Long-Term Care (MOHLTC) is intended or should be inferred.

J. C. K. and M. A. C. 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: J. C. K., M. A. C., and L. C. R.

Analysis and interpretation of the data: J. C. K., M. A. C., and L. C. R.

Drafting of the manuscript: J. C. K. and M. A. C.

Critical revision of the manuscript for important intellectual content: J. C. K. and L. C. R.

Statistical analysis: M. A. C. and L. C. R.

Administrative, technical, or material support: M. A. C.

Obtained funding: J. C. K.

Study supervision: J. C. K.

Financial support. This study was supported by an operating grant from the Canadian Institutes of Health Research (XIN 82408). J. C. K. was supported by a Career Scientist Award from the Ontario MOHLTC and a Research Scholar Award from the University of Toronto Department of Family and Community Medicine. J. C. K. and M. A. C. receive salary support from the ICES. This study was supported by the ICES, which is funded by an annual grant from the Ontario 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.

Potential conflicts of interest. All authors: No reported conflicts.

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

References

1. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. JAMA 2003; 289:179–86.

2. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. JAMA 2004; 292:1333–40.

3. National Advisory Committee on Immunization (NACI). Statement on influenza vaccination for the 2008–2009 season: an Advisory Committee Statement (ACS). Can Commun Dis Rep 2008; 34:1–46.

4. Napolitano LM, Park PK, Siiber KC, et al. Intensive-care patients with severe novel influenza A (H1N1) virus infection—Michigan, June 2009. Morb Mortal Wkly Rep 2009; 58:749–52.

5. Smith AG, Sheridan PA, Harp JB, Beck MA. Diet-induced obese mice have increased mortality and altered immune responses when infected with influenza virus. J Nutr 2007; 137:1236–43.

6. Smith AG, Sheridan PA, Tseng RJ, Sheridan JB, Beck MA. Selective impairment in dendritic cell function and altered antigen-specific CD8+ T-cell responses in diet-induced obese mice infected with influenza virus. Immunology 2009; 126:268–79.

7. Jain S, Kamimoto L, Bramley AM, et al. Hospitalized patients with 2009 H1N1 influenza in the United States, April–June 2009. N Engl J Med 2009; 361:1935–44.

8. Kumar A, Zarychanski R, Pinto R, et al. Critically ill patients with 2009 influenza A(H1N1) infection in Canada. JAMA 2009; 302:1872–9.

9. Louie JK, Acosta M, Winter K, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza A(H1N1) infection in California. JAMA 2009; 302:1896–902.

10. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health 2009; 9:88.

11. Murugan AT, Sharma G. Obesity and respiratory diseases. Chron Respir Dis 2008; 5:233–42.

12. Poulain M, Doucet M, Major GC, et al. The effect of obesity on chronic respiratory diseases: pathophysiology and therapeutic strategies. CMAJ 2006; 174:1293–9.

13. Tjepkema M. Measured obesity. Adult obesity in Canada: measured height and weight. Ottawa, ON, Canada: Statistics Canada, 2005.

14. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. JAMA 2010; 303:235–41.

15. Katzmarzyk PT, Mason C. Prevalence of class I, II and III obesity in Canada. CMAJ 2006; 174:156–7.

16. Tambay JL, Catlin G. Sample design of the national population health survey. Health Rep 1995; 7:29–42.

17. Beland Y. Canadian community health survey—methodological overview. Health Rep 2002; 139–14.

18. Canadian guidelines for body weight classification in adults. Ottawa, ON, Canada: Health Canada, 2003.

19. Nawaz H, Chan W, Abdulrahman M, Larson D, Katz DL. Self-reported weight and height: implications for obesity research. Am J Prev Med 2001; 20:294–8.

20. Rowland ML. Self-reported weight and height. Am J Clin Nutr 1990; 52:1125–33.

21. Shields M, Gorber SC, Tremblay MS. Estimates of obesity based on self-report versus direct measures. Health Rep 2008; 19:61–76.

22. Izurieta HS, Thompson WW, Kramarz P, et al. Influenza and the rates of hospitalization for respiratory disease among infants and young children. N Engl J Med 2000; 342:232–9.

23. Neuzil KM, Reed GW, Mitchell EF Jr, Griffin MR. Influenza-associated morbidity and mortality in young and middle-aged women. JAMA 1999; 281:901–7.

24. Naylor CD, Slaughter P. Cardiovascular health and services in Ontario: an ICES atlas. Toronto, ON, Canada: Institute for Clinical Evaluative Sciences, 1999.

25. Scales DC, Guan J, Martin CM, Redelmeier DA. Administrative data accurately identified intensive care unit admissions in Ontario. J Clin Epidemio 2006; 59:802–7.

26. Iron K, Zagoski BM, Sykora K, Manuel DG. Living and dying in Ontario: an opportunity for improved health information. ICES investigative report. Toronto, ON, Canada: Institute for Clinical Evaluative Sciences, 2008.
27. Wilkins R. Automated geographic coding based on the statistics Canada postal code conversion files, including postal codes to December 2003. Ottawa, ON, Canada: Health Analysis and Measurement Group, Statistics Canada, 2004.

28. Chan B. Supply of physicians’ services in Ontario. Toronto, ON, Canada: Institute for Clinical Evaluative Sciences, 1999.

29. Starfield B, Weiner J, Mumford L, Steinwachs D. Ambulatory care groups: a categorization of diagnoses for research and management. Health Serv Res 1991; 26:53–74.

30. Morgan OW, Bramley A, Fowlkes A, et al. Morbid obesity as a risk factor for hospitalization and death due to 2009 pandemic influenza A(H1N1) disease. PLoS One 2010; 5:e9694.

31. Rosella LC. A population based approach to diabetes mellitus risk prediction: methodological advances and practical applications. Toronto, ON, Canada: University of Toronto, 2009.

32. Kwong JC, Manuel DG. Using OHIP physician billing claims to ascertain individual influenza vaccination status. Vaccine 2007; 25: 1270–4.