



Severe Obesity in Children May Not Pose Independent Risk for Influenza Complications☆



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ABSTRACT

Purpose: Subsets of children are targeted for influenza vaccination due to known conditions that increase the risk of influenza complications. The purpose of this study was to determine if severe obesity in children suggests targeted vaccination.

Design and methods: A retrospective chart review of a large Midwestern pediatric hospital identified 188 cases of influenza complications (defined as requiring hospitalization or death) aged 2 to <20 years old from August 1, 2010 through June 30, 2013. Severe obesity was defined as body mass index (BMI) $\geq 99\%$ for age and gender, with patients grouped by severe obesity status (yes vs. no). Cases were reviewed for previously identified risk conditions for influenza complications (e.g., asthma, pneumonia, diabetes), and were classified as having or not having a known high risk condition.

Results: Of 188 cases, 174 (93%) had a high-risk condition, while only 14 (7%) had no known condition. All 14 (100%) with no known high-risk condition had a BMI <99%. All 15 (100%) with BMI $\geq 99\%$ had a known high-risk condition. The association between severe obesity status and influenza complications was not statistically significant ($p = 0.61$).

Conclusions: This suggests that severe obesity in children is not an independent high-risk condition for influenza complications defined as requiring hospitalization or resulting in death, once other known influenza risk factors are considered.

Implications: Based on this data, clinicians should not target children for influenza vaccination based on weight status. We cannot comment about whether severe obesity represents increased risk for less severe cases of influenza.

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Introduction

Every year otherwise healthy children die from influenza (American Academy of Pediatrics [APA], 2016; Centers for Disease Control and Prevention [CDC], 2017). The Centers for Disease Control and Prevention (2015) reported 146 pediatric influenza related deaths during 2014–2015 influenza season. Overall, the annual total economic burden of influenza is estimated at \$87.1 billion, including projected lost earnings from illness and loss of life (Molinari et al., 2007). Children

are at an increased risk of hospitalization and death because of influenza complications, compared with adults (Centers for Disease Control and Prevention, 2017). In 2010 the Advisory Committee on Immunization Practice (ACIP) first recommended universal influenza vaccination for all children at least 6 months of age without contraindications (Centers for Disease Control and Prevention, 2011). Despite the availability of a safe and effective influenza vaccination (American Academy of Pediatrics, 2017; Centers for Disease Control and Prevention, 2017; World Health Organization [WHO], 2012) and universal recommendations for influenza vaccination of children and adolescents, many children and adolescents remain unvaccinated each year (Molinari et al., 2007).

In addition to universal vaccination, experts recommend targeted vaccination of high-risk populations, such as children and adolescents with asthma and diabetes to decrease morbidity and mortality related to influenza infection (American Academy of Pediatrics, 2017; Centers for Disease Control and Prevention, 2017; World Health Organization, 2012). Identification of target populations for vaccination is also recommended by World Health Organization (2012) in relation to pandemic

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preparation and response. Targeting vaccinations to accurately identified, high-risk groups also allows for effective allocation of resources in situations where vaccine supplies do not meet demand.

Starting in 2010 and reconfirmed in 2018 (Centers for Disease Control and Prevention, 2010; Centers for Disease Control and Prevention, 2018b), the CDC indicated that “people who are morbidly obese [Body Mass Index, or BMI, of 40 or greater]” were at increased risk of severe influenza complications, and should be targeted for vaccination. Additional research highlights morbid obesity as a high-risk condition for influenza complications in adults (The Australian and New Zealand Intensive Care (ANZIC) Influenza Investigators, 2009; Barrau et al., 2012; Bergman, Livornese, Sambhara, Santoro, & Dessain, 2011; Gilca et al., 2011; Karlsson, Marcelin, Webby, & Schultz-Cherry, 2012; Kwong, Campitelli, & Rosella, 2011; Louie et al., 2009; Morgan et al., 2010). The CDC does not clearly define what age groups are included in their recommendation. Thus is it unclear whether children and adolescents age 2 to 19 years old, where severe obesity is defined using age- and gender-specific BMI percentiles rather than static BMI values (Ogden, Carroll, Curtin, Lamb, & Flegal, 2010), are at increased risk for complications and should therefore be a targeted vaccination group. Considering the universal vaccination guidelines and subgroup targeting strategies already in place for children and adolescents, it remains unclear if severe obesity represents an increased risk in children.

The objective of this study was to address two questions: First, is severe obesity a risk factor for severe influenza complications (defined as requiring hospitalization or resulting in death) in children and adolescents, beyond already-targeted conditions? Second, should clinicians be targeting children and adolescents with severe obesity for influenza vaccination beyond universal vaccination recommendations?

Methods

Study Design

The current study utilized a quantitative observational research design to assess the association between severe obesity in children and adolescents and high risk vaccination criteria in a cohort of complicated influenza cases (hospitalization or death in the hospital or Emergency Department). A retrospective chart review of children with severe influenza complications from a 598 bed Midwestern, urban pediatric hospital was used to evaluate data from three consecutive influenza seasons. All subjects in this study experienced severe influenza complications that resulted in hospitalization or death. The Institutional Review Boards (IRB) of the study site and the corresponding author's university granted this study a waiver of informed consent.

Population

The Informatics for Integrating Biology and the Bedside (i2b2) is a de-identified research data warehouse. Researchers identified 313 unique cases using the i2b2 warehouse, selecting on specific patient criteria. The i2b2 Research Data Warehouse and the electronic medical record were used to complete data collection. Influenza seasons 2010–2011; 2011–2012 and 2012–2013 were included. August 2010 represents the beginning of the first influenza season following the implementation of the inpatient electronic medical record at the study site. This study aimed to include all individuals who were diagnosed with influenza and experienced an influenza complication (e.g., were either admitted to the hospital or died in the hospital). To ensure complete case ascertainment, subjects included in the initial data extraction met the following inclusion criteria:

1. Influenza (ICD-9 codes 487.0–487.8),
2. Admission or death,
3. Hospitalization dates August 1, 2010 to June 30, 2013
4. Any age at diagnosis.

Data extracted from the i2b2 data warehouse included medical record number, age, sex, ethnicity, weight, height, BMI, BMI percentile for age and gender, and all ICD-9 codes for the influenza admission. The electronic medical record was then used to collect missing data, validate data, and to confirm no known high risk conditions.

Three hundred thirty-nine (339) cases were reviewed. After reviewing the electronic charts for all cases with missing data, 19 (6%) were excluded for incomplete data consisting of missing height measurements which are necessary to calculate BMI. In addition, six (2%) cases were found to be duplicate encounters and one (0.03%) case was found to contain non-normative data. The number of all unique cases with complete data was 313.

Of the 313 patients with complete data, additional data trimming was conducted to test the study's hypothesis regarding childhood severe obesity. For this study, children and adolescent are subjects 2 to 19 years old, where severe obesity is defined using age- and gender-specific BMI percentiles (Ogden et al., 2010). Subjects <2 years of age and ≥20 years of age were excluded from these analyses. The CDC growth charts and percentile-based weight status categories, are applicable for those 2 years of age up to 20 years of age. Severe obesity is not defined below age 2. Those age 20 and above exceeded the childhood age range for this study and adult BMI thresholds apply. The age criteria excluded 125 cases; 115 cases <2 years old, and 10 cases ≥20 years old. Severe obesity in this study was defined as BMI ≥99th percentile for age and gender according to the CDC 2000 growth charts, with patients grouped by severe obesity status (yes vs. no). The final sample for analysis consisted of 188 cases 2 to <20 years of age, herein after referred to as childhood.

Identification of High-risk Conditions

High-risk conditions (Centers for Disease Control and Prevention, 2018b) and the ICD-9 manual were reviewed to identify ICD-9 codes that capture the conditions reported by the CDC to be high-risk, and therefore already officially targeted for influenza vaccination (Appendix). Although the CDC does not have an official ICD-9 set to capture all chronic conditions known to put people at high-risk for influenza complications (cdc.info@cdc.gov, personal communication, April 23, 2014), previous studies have developed such lists, which were employed in this study (Daley et al., 2004; Irwin et al., 2001; Neuzil, Wright, Mitchell, & Griffin, 2000).

The i2b2 code was designed to identify the presence of the ICD-9 codes for the following known high-risk conditions for influenza complications:

- a. Chronic pulmonary disease including asthma. Asthma includes a medical diagnosis of asthma or reactive airway disease. Chronic lung diseases include conditions such as bronchiolitis obliterans, chronic aspiration pneumonia, and interstitial lung disease.
- b. Cardiovascular diseases include conditions such as coronary heart disease, cardiac valve disorder, congestive heart failure, pulmonary hypertension, and aortic stenosis.
- c. Renal diseases include conditions such as acute or chronic renal failure, nephrotic syndrome, glomerulonephritis, and impaired creatinine clearance.
- d. Hepatic diseases.
- e. Hematological diseases including sickle cell disease
- f. Metabolic disorders include conditions such as diabetes mellitus, thyroid dysfunction, adrenal insufficiency, and liver disease.
- g. Neurologic and neurodevelopment conditions include conditions such as seizure disorders, cerebral palsy, muscular dystrophy, and cognitive dysfunction.
- h. Immunosuppression including that caused by medications or by HIV infection.
 - i. People <19 years of age on long-term aspirin therapy.
 - j. Children 24–59 months of age.

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