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Multimorbidity is associated with uptake of influenza vaccination

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ABSTRACT

Objective: Patients with chronic conditions have higher rates of severe influenza-related illness and mortality. However, influenza vaccination coverage in high-risk populations continues to be suboptimal. We describe the association between cumulative disease morbidity, measured by a previously validated multimorbidity index, and influenza vaccination among community-dwelling adults.

Methods: We obtained interview and medical record data for participants ≥18 years who sought outpatient care for influenza-like illness between 2011 and 2016 as part of an outpatient-based study of influenza vaccine effectiveness. We defined cumulative disease morbidity by using medical diagnosis codes to calculate a multimorbidity-weighted index (MWI) for each participant. MWI and influenza vaccination status was evaluated by logistic regression. Akaike information criterion was calculated for all models.

Results: Overall, 1458 (48%) of participants out of a total of 3033 received influenza vaccination. The median MWI was 0.9 (IQR 0.00–3.5) and was higher among vaccinated participants (median 1.6 versus 0.0; $p < 0.001$). We found a positive linear association between MWI and vaccination, and vaccination percentages were compared between categories of MWI. Compared to patients with no multimorbidity (MWI = 0), odds of vaccination were 17% higher in the second category (MWI 0.01–1.50; [OR: 1.17, 95% CI: 0.92–1.50]), 58% higher in the third category (MWI 1.51–3.00; [OR: 1.58, 95% CI: 1.26–1.99]), 130% higher in the fourth category (MWI 3.01–6.00; [OR: 2.30, 95% CI: 1.78–2.98]) and 214% higher in the fifth category (MWI 6.01–45.00;[OR: 3.14, 95% CI: 2.41–4.10]). Participants defined as high-risk had 86% greater odds of being vaccinated than non-high-risk individuals (OR: 1.86, 95% CI: 1.56–2.21). The AIC was lowest for MWI compared with high-risk conditions.

Conclusions: Our results suggest a dose response relationship between level of multimorbidity and likelihood of influenza vaccination. Compared with high-risk condition designations, MWI provided improved precision and a better model fit for the measurement of chronic disease and influenza vaccination.

1. Introduction

Rates of severe influenza-related illness and mortality among those with chronic diseases, such as asthma and heart disease, are high compared to those with no underlying conditions [1]. In the 2014–2015 influenza season, 97% of patients hospitalized with laboratory-confirmed influenza suffered from at least one high-risk medical condition [2]. Between 2005 and 2008, adults with illnesses such as chronic lung disease, cardiovascular disease, and immunosuppression were both more likely to be hospitalized with influenza-related pneumonia and to experience ICU admission, mechanical ventilation, and death [3]. Despite this established morbidity, influenza vaccine coverage among U.S. adults with high-risk chronic medical conditions continues to be suboptimal [1,4–7]. Although vaccination is prioritized in this group and recommended as the primary defense against influenza illness [1], over 50% remained unvaccinated as of the 2015–2016 season [4]. To reduce the burden of influenza-related complications and death, increased vaccine coverage among high-risk individuals is necessary [1,8].

Imprecise characterization of influenza high-risk status has limited clarification of its relationship with influenza vaccination. Individual high-risk status, based on diagnosis with any single high-risk condition as recommended by the Advisory Committee on Immunization Practices (ACIP) [1,4,9], has previously been used to assess the relationship between underlying conditions

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and vaccine uptake or effectiveness [10–12]. However, this classification method does not account for individual variation in number, type, or severity of chronic diseases. For example, Lu et al. found a 10% increase in influenza vaccine coverage for those with two or more high-risk conditions when compared to those with one or more high-risk conditions [5].

Multimorbidity, the presence of multiple medical conditions in a single individual, is increasingly common in developed countries [5,13,14]. Estimates for burden of multimorbidity in the U.S. adult population vary by definition and disease classification method [15–19], but prevalence is between 25 and 45% when most commonly defined as ≥2 conditions in the same patient [5,13,14]. The cumulative effect of multiple diseases is associated with worse clinical outcomes than those resulting from one condition alone [20].

Wei et al. developed and validated a multimorbidity-weighted index (MWI) appropriate for disease severity and burden assessment in U.S. ambulatory adult populations [21,22]. Unlike prior indices weighted to outcomes such as mortality, healthcare cost or utilization, MWI weights diseases to concurrent physical functioning, a patient-centered outcome of value to community-dwelling adults. MWI has a convenient twofold interpretation: each unit provides an estimate of both an individual's cumulative disease burden and associated decline in physical functioning. Compared to the ACIP definition of high-risk, MWI may offer improved precision for identification of clinical subgroups at greatest risk for influenza-associated complications arising from low vaccination rates. We used MWI to measure the number and severity of medical conditions among participants enrolled in an outpatient-based study of influenza vaccine effectiveness over five influenza seasons from 2011 to 2016. The association between MWI and influenza vaccination was estimated and compared to the association between ACIP-defined influenza high-risk status and vaccination uptake.

2. Methods

2.1. Study population

The study population included adults enrolled in case-test negative study conducted in southeast Michigan at participating University of Michigan Health System and Henry Ford Health System outpatient clinics in partnership with the U.S. Influenza Vaccine Effectiveness Network [12,23–27]. For influenza seasons between 2011 and 2016, patients ≥6 months old seeking medical care at a participating ambulatory care clinic for an acute respiratory illness of ≤7 days duration including cough were eligible for study inclusion. Study staff obtained informed consent, completed an enrollment interview, and collected nasal and oropharyngeal swabs for laboratory confirmation of influenza by reverse transcription-PCR. Clinical characteristics including medical conditions were extracted from the electronic medical record. Institutional Review Board approval was obtained prior to the initiation of all patient recruitment and data collection activities.

2.2. Multimorbidity and high risk measurement and assessment

MWI was evaluated both as a continuous measure and as a categorical measure. MWI was categorized as participants who scored zero (no multimorbidity) and approximate quartiles of those with non-zero MWI (0.01–1.50, 1.51–3.00, 3.01–6.00, 6.01–45.00). Alternate strategies for categorization (deciles) had no effect on overall results. The MWI contains regression coefficients approximating typical influence of each of 81 chronic diseases on physical health-related quality of life, with a range from 0 to 100 (lowest to highest) Short Form-36 physical functioning units. MWI is calculated by summing the regression coefficients corresponding to all diagnoses for a given individual and is described in detail by Wei et al. [22]. We also categorized patients as high-risk or not based on presence of 1 or more conditions defined by the ACIP as increasing the risk of complicated influenza illness [28].

We used International Classification of Diseases, 9th edition, Clinical Modification (ICD-9) diagnosis codes associated with health care encounters in the year prior to the start of each year's vaccination season (September 1st through August 31st) to identify diseases included in the MWI as well as ACIP-defined high-risk conditions.

2.3. Influenza vaccination status and assessment

We assessed documented influenza vaccination as the primary outcome. Vaccination status was determined by medical record review, and review of state registry records.

2.4. Covariate measurement and assessment

We included age, sex, socioeconomic status, race, smoking status, study year and health system as covariates in our analysis due to potential confounding effects. Age in years and sex (male or female) were determined by medical record review. Measures of socioeconomic status varied across study years. In the 2011–2012 and 2012–2013 study years, subjects reported subjective social status on a scale from 1 (lowest) to 9 (highest), as described by Singh-Manoux et al. [29]; from the 2013–2014 through 2015–2016 study years subjects reported highest level of education achieved. These 2 measures were dichotomized (subjective social status >5 in years 2011–2013; bachelor's degree or higher in years 2013–2016) to create a consistent, binary approximation of socioeconomic status across all study years. Self-reported race was categorized as white, black, Asian, or other. Self-reported ethnicity was categorized as Hispanic or non-Hispanic. Self-reported smoking status was defined as a categorical variable indicating whether the participant was a current smoker (every day or some days) or non-smoker.

2.5. Statistical analysis

We conducted logistic regression analysis of unadjusted and adjusted associations between MWI and influenza vaccination, along with unadjusted and adjusted associations between ACIP-defined high-risk status and influenza vaccination for comparison. Fully adjusted models included MWI or ACIP high-risk status as predictors of vaccination as well as the following variables hypothesized *a priori* to be associated with vaccination and multimorbidity: age, sex, ethnicity, race, socioeconomic status, smoking status, health system, and influenza season. The Akaike information criterion (AIC) model fit statistic was used to select the optimal form of each variable and to assess fit of final models. Associations were assessed using odds ratios and 95% confidence intervals. All analyses were completed using SAS 9.4 (SAS Institute, Cary, NC, 2013).

3. Results

We obtained interview and medical record data for the 3168 patients ≥18 years old enrolled in the vaccine effectiveness study between 2011 and 2016. A total of 3033 participants were included in the analysis (Table 1); 135 participants were excluded due to missing values of important variables. The number of enrolled subjects ranged from 497 in 2011–2012 to 845 in the 2014–2015

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