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Incidence of medically attended influenza infection and cases averted by vaccination, 2011/2012 and 2012/2013 influenza seasons

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ABSTRACT

Background: We estimated the burden of outpatient influenza and cases prevented by vaccination during the 2011/2012 and 2012/2013 influenza seasons using data from the United States Influenza Vaccine Effectiveness (US Flu VE) Network.

Methods: We defined source populations of persons who could seek care for acute respiratory illness (ARI) at each of the five US Flu VE Network sites. We identified all members of the source population who were tested for influenza during US Flu VE influenza surveillance. Each influenza-positive subject received a sampling weight based on the proportion of source population members who were tested for influenza, stratified by site, age, and other factors. We used the sampling weights to estimate the cumulative incidence of medically attended influenza in the source populations. We estimated cases averted by vaccination using estimates of cumulative incidence, vaccine coverage, and vaccine effectiveness.

Results: Cumulative incidence of medically attended influenza ranged from 0.8% to 2.8% across sites during 2011/2012 and from 2.6% to 6.5% during the 2012/2013 season. Stratified by age, incidence ranged from 1.2% among adults 50 years of age and older in 2011/2012 to 10.9% among children 6 months to 8 years of age in 2012/2013. Cases averted by vaccination ranged from 4 to 41 per 1000 vaccinees, depending on the study site and year.

Conclusions: The incidence of medically attended influenza varies greatly by year and even by geographic region within the same year. The number of cases averted by vaccination varies greatly based on overall incidence and on vaccine coverage.

1. Introduction

Seasonal influenza epidemics cause considerable morbidity and mortality worldwide [1–3]. Many countries have implemented annual influenza vaccination programs to reduce the burden of illness caused by influenza, which involve considerable public health investments (e.g. [4–6]). To evaluate vaccine program impact, policy makers need annual data on vaccine effectiveness (VE), on the burden of influenza disease, and on cases averted by vaccination. Several countries have systems in place to annually estimate influenza VE [7–10]. Estimates of the burden of influenza are more difficult to obtain, due to under-diagnosis of influenza in clinical settings [11]. Influenza-related hospitalizations or deaths are typically estimated retrospectively using ecologic trend studies [12]. A few household studies have estimated influenza incidence (e.g [13]), but geographically diverse estimates of the incidence of outpatient influenza are generally lacking. Estimates of outpatient cases averted by vaccination currently come from models that infer outpatient burden from influenza hospitalization surveillance data and that combine surveillance and VE estimates from separate populations [14,15].

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The United States Influenza Vaccine Effectiveness (US Flu VE) Network provides yearly estimates of influenza VE against medically attended influenza illness [8,16,17]. The network sites conduct active influenza surveillance among persons seeking outpatient care for acute respiratory illness (ARI) and estimate influenza VE using a test-negative design [18]. Several of the US Flu VE sites conduct this surveillance in populations that can be fully enumerated, and for whom demographic and health care utilization data are available, based on enrollment in health care payer and/or provider networks. In this study, we estimate the incidence of outpatient influenza and the cases prevented by vaccination in the US Flu VE Network over the 2011/2012 and 2012/2013 influenza seasons.

2. Methods

The US Flu VE Network consists of five geographically separated sites in the United States: Group Health Cooperative in western Washington State (GH); the Marshfield Clinic in Marshfield Wisconsin (MC); Scott and White Healthcare in Temple Texas (SW); the University of Michigan and the Henry Ford healthcare systems in Michigan (UM); and the University of Pittsburgh partnered with the UPMC healthcare system in Pittsburgh Pennsylvania (UP). For the present study, the University of Michigan subjects were restricted to the Henry Ford population, as an enumerated cohort could not be defined from the UM population. Data were available from UP for 2012/2013 only.

2.1. Source populations

The GH source population consists of enrollees in the GH integrated group practice, who have healthcare coverage through GH and receive medical care from GH providers at GH medical centers. We restricted the population to GH enrollees whose primary healthcare provider was at one of three GH medical centers where active surveillance for influenza occurred. The MC population were members with at least 12 months of residency (or since birth for those less than 12 months old) in the central Marshfield Epidemiology Area Study, a 14 zip code region centered around Marshfield, Wisconsin [19]. The SW population consists of persons who had seen a SW primary care provider for any reason within the 3 prior years and lived in the Temple Population Research Area of East Bell County defined by zip codes (765xx, excluding 7654x). The UM population consists of all Health Alliance Plan insurance members who have identified a primary care provider within the Henry Ford Health System. The UP population consists of patients seen between July 1, 2011 and July 20, 2013 in selected UPMC primary care centers or in an after-hours care site located physically in a primary care site. Many of these practices are part of practice-based research networks (Pediatric PittNet and Family Medicine PittNet); all of these UP sites use a common electronic health record.

The ages of subjects in the source populations were defined as of September 1st of each study year. Because influenza vaccination is not recommended before 6 months of age, subjects <6 months of age as of September 1st were not eligible for enrollment in the US Flu VE Network study and were excluded from study cohorts.

2.2. Influenza testing

Active surveillance for medically attended influenza in the US Flu VE Network has been described previously [8]. In brief, study staff (GH, MF, SW; UM in 2012/2013) or clinical staff (UP, UM in 2011/2012) identified patients seeking care for ARI, defined as illness with cough or fever/feverishness (2011/2012 season) or illness with cough (2012/2013 season) of less than eight days duration. Eligible patients provided informed consent, after which study staff collected nasal swabs (children <24 months of age) or both nasal and oropharyngeal swabs for testing. Specimens were tested for influenza A or B using real-time reverse transcriptase polymerase chain reaction (rRT-PCR), with probes and primers provided by the Centers for Disease Control and Prevention (CDC). Specimens positive for influenza A were further tested for subtype. US Flu VE Network enrollees who were not part of one of the defined source populations were excluded from the present study.

2.3. Covariate data

We used administrative data from healthcare payers and providers to define covariates for all subjects in the source population. We used enrollment data to define subjects' age, grouped as 6 months–8 years; 9–17 years; 18–49 years; and ≥50 years. We used vaccination databases to classify all subjects as vaccinated (defined as having received at least one dose of seasonal influenza vaccination) or unvaccinated in each influenza season. We used International Classification of Diseases, Version 9, Clinical Modification (ICD-9) codes (available from the authors) to identify all outpatient visits for presumptive medically attended ARI (MAARI) during study periods, classified as 0, 1, or ≥2 MAARI visits.

2.4. Analyses

We extrapolated the number of medically attended influenza infections in our Flu VE enrollees to the entire source population. For this, we first stratified the source populations into mutually exclusive groups based on age, influenza vaccination, and number of MAARI visits during the study period. We stratified by number of MAARI visits because subjects with more MAARI visits may be more likely to seek care if they develop influenza. We then calculated a sampling weight for each Flu VE enrollee. The sampling weight for an enrollee of age group a, vaccine status v, MAARI visits m, and study site s was the ratio of the number of people in the source population in the (a, v, m, s) stratum to the number of Flu VE enrollees in that stratum. Rarely, some Flu VE enrollees had zero MAARI visits during the study period. These subjects were enrolled based on symptoms but were not assigned a MAARI ICD-9 code for the visit at which they were enrolled. We assumed that the only influenza illnesses among persons with zero MAARI visits were those detected by our surveillance, and assigned these Flu VE enrollees a sampling weight of 1.0. Using the sampling weights, we estimated the total number of medically attended influenza illnesses in each (a, v, m, s) stratum, with confidence limits calculated by bootstrap sampling from the source populations and Flu VE enrollees.

During the study period, influenza surveillance at the Flu VE Network sites did not always cover the full influenza season at all five sites. We adjusted the estimated case counts to account for cases occurring outside Flu VE surveillance. From state influenza surveillance data for Michigan, Pennsylvania, Texas, Washington, and Wisconsin, we determined the proportion of cases state-wide that occurred during Flu VE surveillance at each site [20–25]. We divided the estimated number of cases by these proportions for our final estimate of the number of persons with medically attended influenza in each (a, v, m, s) stratum. We then calculated the cumulative incidence of medically attended influenza in each stratum by dividing the estimated number of persons with medically attended influenza by the population size of each stratum.

We used age-specific estimates of influenza VE from the US Flu VE Network [8,26] (Supplemental Table 1) to estimate the number of cases of medically attended influenza averted at each site. For these calculations, we assumed VE for a given age group was