Vaccine 34 (2016) 486–494

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Trends in U.S. hospitalizations and inpatient deaths from pneumonia and influenza, 1996–2011

D.H. Chang[a,*], Robert A. Bednarczyk[b], Edmund R. Becker[c], Jason M. Hockenberry[c], Paul S. Weiss[d], Walter A. Orenstein[b,e,f], Saad B. Omer[b,g,**]

[a] Department of Health Policy and Management, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[b] Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA
[c] Department of Health Policy and Management, Rollins School of Public Health, Emory University, Atlanta, GA, USA
[d] Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, GA, USA
[e] Department of Medicine, Division of Infectious Diseases, Emory University School of Medicine, Atlanta, GA, USA
[f] Influenza Pathogenesis & Immunology Research Center (PIRC), Emory University School of Medicine, Atlanta, GA, USA
[g] Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

ARTICLE INFO

Article history:
Received 22 July 2015
Received in revised form
25 November 2015
Accepted 1 December 2015
Available online 17 December 2015

Keywords:
Pneumonia and influenza
Influenza vaccine
Pneumococcal conjugate vaccine
Vaccination policy

ABSTRACT

Background: To reduce excess morbidity and mortality of pneumonia and influenza (PI), the Advisory Committee on Immunization Practices has recommended the use of 7-valent pneumococcal conjugate vaccine (PCV7), and incrementally expanded the target group for annual influenza vaccination of healthy persons, to ultimately include all persons ≥6 months of age without contraindications as of the 2010–2011 influenza season. We aimed to capture broader epidemiologic changes by looking at PI collectively.
Methods: Using interrupted time series, we evaluated the changes in the rates of PI hospitalization and inpatient death across three periods defined according to the changes in vaccination policy. We assessed linear trends adjusting for seasonality, sex, and age group, allowing for differential impact across age groups. PI hospitalizations were defined as a principal diagnosis of PI, or a principal diagnosis of sepsis or respiratory failure, accompanied by a secondary diagnosis of PI.
Results: Overall annual rates of PI hospitalizations and inpatient deaths declined by 95 per 100,000 (95% CI: 45–145) and by 4.4 per 100,000 (95% CI: 0.9–7.8), respectively. This translates to 295,000 fewer PI hospitalizations and 13,600 fewer PI inpatient deaths than expected based on the average rates from 1996 through 1999. PI hospitalizations dropped the most among seniors aged 65+ by 487 per 100,000, followed by children aged <2, by 228 per 100,000. PI inpatient deaths declined most among seniors aged 65+, by 25.3 per 100,000.
Conclusions: In this nationally representative study, PI hospitalizations and inpatient deaths decreased in U.S. between 1996 and 2011. There is a temporal association with the introduction and widespread use of pneumococcal conjugate vaccines, and the expansion of the target group for annual influenza vaccination to include all persons ≥6 months of age, while it is difficult to attribute these changes directly to specific vaccines used in this era.

1. Introduction

Pneumonia and influenza (PI) are a source of substantial morbidity and mortality in the United States (U.S.) and worldwide [1–3]. Annually, around 1 million patients are hospitalized for 5.2 days on average, and about 70,000 deaths occur, due to PI [4–7]. The average rate of PI deaths from 1999 to 2006 was 21.5 per 100,000 (range: 17.8–23.7) [8], and seniors aged 65+ accounted for 90% of all PI deaths [9] with an average death rate of 218 per 100,000 (range: 189–237) [8].

To reduce the burden of PI, the Advisory Committee on Immunization Practices (ACIP) recommended the use of 7-valent pneumococcal conjugate vaccine (PCV7) for children aged 2–23 months and children aged 24–59 months at increased risk in 2000 [10], and 13-valent pneumococcal conjugate vaccine (PCV13) for children aged 2–59 months and children aged 60–71 months

* Corresponding author at: 42 Church St, Boston, MA 02138, USA. Tel.: +1 281 928 9438; fax: +1 404 727 4590.
** Corresponding author at: Hubert Department of Global Health, 1518 Clifton Road NE, Room 7017, Atlanta, GA 30322, USA. Tel.: +1 404 727 9814; fax: +1 404 727 4590.
E-mail addresses: dchang@hsph.harvard.edu (D.H. Chang), somer@emory.edu (S.B. Omer).

http://dx.doi.org/10.1016/j.vaccine.2015.12.003
0264-410X/

with underlying medical conditions in 2010 [11], as well as incrementally expanded the target group for annual influenza vaccination of healthy persons, from all persons aged 65+ years to ultimately include all persons ≥6 months of age without contraindications [12–16]. Adults aged 50–64 were introduced into the target group during the 2000–2001 season [12], and children aged 6–23 months were included during the 2004–2005 season [13]. Universal influenza vaccination policy began from the 2010–11 season, after the age groups of 2–4, 5–18, and 19–49 years were consecutively added to the target group at two-year intervals [14–16].

Previous studies focused on evaluating the impact of individual vaccines, either pneumococcal or influenza vaccine [9,17–22]. The effectiveness of pneumococcal vaccines was measured by examining the trends in incidences of invasive pneumococcal disease, or pneumonia-related hospitalizations [17–19], and the effectiveness of influenza vaccines was estimated in terms of prevented cases, hospitalizations, and deaths, or by analyzing the trends in influenza-associated hospitalizations and deaths, calculated based on viral surveillance data [9,20–22]. In this study, we aimed to capture broader epidemiologic changes in health burden by looking at PI collectively, given substantial evidence of predisposition to pneumococcal infection with preceding influenza infection [23,24].

2. Methods

2.1. Study population

The National Inpatient Sample (NIS) is the largest all-payer publicly available database of hospital discharge records, funded by the Agency for Healthcare Research and Quality (AHRQ) [25]. The NIS is comprised of approximately 8 million hospitalizations annually from about 1000 hospitals. Time trend analysis is recommended from 1993, when the coverage of the sampling frame exceeded 50% [26]. We analyzed the NIS from 1996 to 2011, during which the sampling coverage steadily increased from about 60% [27]. As of 2011, the NIS represented over 97% of all U.S. hospitalizations involving 46 states [27]. The NIS has a complex sampling design, employing a community hospital as a primary sampling unit, and sampling probabilities are proportional to the size of each cluster with an approximate 20% sampling rate [27,28].

2.2. Definition of hospitalizations for pneumonia and influenza

Patients with a primary diagnosis of pneumonia or influenza (*International Classification of Disease, 9th Revision, Clinical Modification*, ICD-9-CM; 480.xx-488.xx) at the time of discharge were included in the study. To account for alternative coding options, and temporal trends in diagnostic coding practices, patients with a principal diagnosis of sepsis (038.xx, 995.91, 995.92, 785.52), or respiratory failure (518.81, 518.82, 518.84, 799.1), followed by a secondary diagnosis of PI were also included [29].

2.3. Data analysis methods

We estimated monthly U.S. nationwide PI hospitalizations and inpatient deaths for six pre-determined age groups (<2, 2–4, 5–17, 18–49, 50–64, 65+) stratified by sex, and converted these estimates into crude rates dividing the counts by the annual national population estimates of each year from the U.S. Census Bureau.

Using interrupted time series, we evaluated the changes in rates across the three periods defined as follows: (i) when only seniors aged 65+ were recommended for annual influenza vaccination among healthy individuals (Period 1, January 1996–January 2000); (ii) when PCV7 was introduced, and age groups of pre-school children (<2, and 2–4) were included in the recommendation (Period 2, February 2000–September 2008); and (iii) when universal vaccination policy was reached with the inclusion of children aged 5–18 and adults aged 19–49 (Period 3, October 2008–December 2011).

We assessed linear trends over time adjusting for seasonality, sex, and age group, allowing for differential base rates (intercept), time trend (slope), seasonality, and gender gap across age groups and across periods. Terms assessing differential time trend, seasonality, and gender gap across periods were dropped from the initial full model using backward elimination strategy. Seasonality was addressed treating months as one of fixed effects. The PI inpatient death rates of children (<2, 2–4, 5–17) were not modeled because the rates did not demonstrate seasonality. We estimated overall rates comprising all age groups, standardized to the U.S. population in 2011. All analyses were performed using SAS 9.4 (Cary, NC, USA).

2.4. Disclosures

This study was exempt for review, not meeting the criteria of research involving human subjects nor clinical investigation, determined by the Emory University institutional review board.

3. Results

Between 1996 and 2011, there was a total of 23,858,402 PI hospitalizations, and 1,782,794 PI inpatient deaths in the U.S., which accounted for 4.0% and 13.6% of all hospitalizations and inpatient deaths in the U.S., respectively. The proportions of PI hospitalizations among all hospitalizations were on average 4.6% among males (range: 4.3%-5.1%) and 3.5% among females (range: 3.2%-3.9%) throughout the study period.

Overall, monthly rates of PI hospitalizations and inpatient deaths decreased from 41 to 33 per 100,000, and 3.2 to 2.8 per 100,000, respectively (Fig. 1A and B). PI hospitalization rates decreased from 95 to 76 per 100,000 among children aged <2 (Fig. 2A), while the rates of other children age groups (2–4, and 5–17) did not change from the initial rates of 29 and 7 per 100,000, respectively (Fig. 2B and C).

The changes in the rates of PI hospitalization and inpatient death showed similar trend among adults. Average monthly rates of PI hospitalization and inpatient death among seniors aged 65+ decreased from 185 to 144, and from 20.2 to 18.1, respectively (Figs. 3C and 4C). The rates among adults aged 50–64 slightly dropped from 37 to 30, and 2.2 to 1.8, respectively (Figs. 3B and 4B), and the rates among adults aged 18–49 had little change, fluctuating around the average rates of 11 and 0.3, respectively (Figs. 3A and 4A).

In Period 3 (October 2008–December 2011), there was a total of 295,000 (95% CI: 139,000–451,000) fewer PI hospitalizations and 13,600 (95% CI: 2700–24,400) fewer PI inpatient deaths than expected based on the rates in Period 1 (January 1996–January 2000) (Table 1). The reductions in PI hospitalization rates were biggest among seniors aged 65+ by 487 per 100,000 (95% CI: 370–604), followed by children aged <2 by 228 per 100,000 (95% CI: 111–345). The rates of PI inpatient death significantly declined among seniors aged 65+ by 25.3 per 100,000 (95% CI: 16.0–34.7).

Seasonal peaks were observed both in PI hospitalizations and inpatient deaths, mostly in winter months (December, January, or February), and sometimes in March (Figs. 1–4). All age groups demonstrated seasonality in PI hospitalizations (Figs. 2 and 3), while the seasonality of PI inpatient deaths were observable among adult age groups only (18–49, 50–64, 65+) (Fig. 4). The rates of PI inpatient death among children heavily fluctuated with low rates of <0.7 per 100,000 among children aged <2, and below <0.2 per 100,000 for children aged 2–4 and 5–17 (Fig. S1).