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Research Article

Effectiveness of the 23-Valent Pneumococcal Polysaccharide Vaccine in Patients with Chronic Lung Diseases: A Self-Controlled Case Series Study

Masahiro Aoshima[1]* Kei Nakashima[1] and Satoko Ohfuji[2]

[1]Department of Pulmonology, Kameda Medical Center, 929 Higashi-cho, Kamogawa-City, Chiba 296-8602, Japan

[2]Department of Public Health, Osaka City University Faculty of Medicine, 1-4-3 Asahi-machi, Abeno-ku, Osaka 545-8585, Japan

Abstract

Background/purpose: Studies on the effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) in patients with chronic lung comorbidities are limited. To evaluate the effectiveness of PPSV23 in these patients, including immunosuppressed individuals, we conducted a retrospective study using the self-controlled case series method.

Methods: Patients with lung comorbidities who were immunized with PPSV23 in a hospital setting between April 2011 and March 2015 were included. The primary and secondary outcomes were all-cause pneumonia and pneumococcal pneumonia, respectively, the incidences of which were compared before and after immunization. To calculate the post-immunization rate ratio (RR) of pneumonia compared to that before immunization, the Mantel-Haenszel method was used. Vaccine effectiveness (VE) was estimated as follows: (1-RR) × 100%.

Results: Data of 110 patients (80% men; median age, 68.06 years) were analyzed. Chronic lung comorbidities included lung cancer (n: 56, 50.9%), interstitial pneumonia (n: 27, 24.5%), chronic obstructive pulmonary disease (n: 22, 20%), and other chronic lung diseases (n: 5, 4.5%). More than 80% of the patients with lung cancer were immunized during the initial course of anticancer chemotherapy; 92% of the patients with interstitial pneumonia were immunized at the beginning of immunosuppressive therapy. The rates of pre- and post-immunization all-cause pneumonia were 334.34 and 185.06 per 1,000 person-years, respectively. Further, the RR and VE were 0.643 (95% confidence interval [CI] 0.449-0.922) and 35.7% (95% CI 7.6-55.1%), respectively. The rates of pre- and post-immunization pneumococcal pneumonia were 38.33 and 23.36 per 1,000 person-years, respectively. Further, the RR and VE were 0.441 (95% confidence interval [CI] 0.210-0.926) and 55.9% (95% CI 7.4-79.0%), respectively.

Conclusion: PPSV23 immunization significantly reduced the incidence of both all-cause pneumonia and pneumococcal pneumonia. In patients with chronic lung comorbidities, immunization should be scheduled during the early clinical period.

Keywords: 23-Valent Pneumococcal Polysaccharide Vaccine; Lung Comorbidities; Pneumonia; Self-Controlled Case Series; Vaccine Effectiveness

***Corresponding author:** Masahiro Aoshima, Department of Pulmonology, Kameda Medical Center, 929 Higashi-cho, Kamogawa-City, Chiba 296-8602, Japan, Tel: +81-4-7092-2211; E-mail: aoshima.masahiro@kameda.jp

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Introduction

Vaccination guidelines in many industrialized countries recommend immunization with pneumococcal vaccines for elderly individuals, and national immunization programs have been widely implemented [1-4]. Although many systematic reviews and meta-analyses have evaluated the preventative effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for pneumococcal diseases, its effectiveness in individuals with chronic lung comorbidities, including those in an immunosuppressive state, remains unclear [5-9]. Most studies to date have been randomized controlled trials, cohort studies, and case-control studies, all of which require significant effort and are costly. The test-negative design has been increasingly used to monitor the annual vaccine effectiveness (VE) in several countries [10-13]. Using this study design, Suzuki et al. reported PPSV23 effectiveness of 27.4% for all types of pneumococcal pneumonia and 33.5% for the PPSV23 serotype [14]. The self-controlled case series (SCCS) method is self-matched, thus eliminating the effects of fixed confounders [15]. Pneumonia due to pneumococci as well as many other kinds of pathogens influences the clinical course of patients with lung comorbidities, such as declining lung function, triggering exacerbation of chronic obstructive pulmonary disease (COPD), or interstitial pneumonia, or interfering ongoing anticancer chemotherapies. Therefore, the prevention of all-cause pneumonia is essential for disease management. To the best of our knowledge, no study has evaluated the VE of PPSV23 against all-cause pneumonia by using the SCCS method. Therefore, we aimed to evaluate the effectiveness of PPSV23 in patients with lung comorbidities, including those in an immunosuppressive state, by using the SCCS method.

Methods

Study design and subjects

We conducted a single-center retrospective study with the SCCS method to eliminate the effects of confounders [15]. Patients hospitalized for chronic lung diseases and who were immunized with the

initial PPSV23 vaccine between April 2011 and March 2015 in a hospital setting were recruited. The study protocol was approved by the Ethical Committee of the Kameda Medical Center (No. 18-029), and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Data collection

The onset of pneumonia was evaluated retrospectively. The diagnosis of pneumonia was based on the presence of the following clinical and laboratory findings: newly formed consolidation on chest imaging and leukocytosis in peripheral blood or elevated serum C-reactive protein level. Additionally, at least two of the following four criteria had to be met: a body temperature of>37.0°C; chest symptoms such as cough, sputum, chest pain, or dyspnea; coarse crackles on chest auscultation; and causative bacteria in the specimen obtained from patients with respiratory tract infections [16]. Pneumococcal pneumonia was defined as a certified positive culture of pneumococci in a specimen obtained from the respiratory tract or blood or positive pneumococcal urinary antigen, based on recommendations of the Centers for Disease Control and Prevention [17]. The primary outcome was the onset of all-cause pneumonia; the incidence rate per 1,000 person-years was compared before and after PPSV23 immunization. The secondary outcome was the onset of pneumococcal pneumonia; again, the incidence rate per 1,000 person-years was compared before and after PPSV23 immunization.

Sample size

We assumed that the pneumonia incident rates were 263 per 1000 person-years before PPSV23 vaccination and 96 per 1000 person-years after PPSV23 vaccination. Based on a previous study [18], subjects were observed for 1.5 years. A sample size of 100 was required to detect a possible 50% VE (RR: 0.5, 95% confidence interval [CI]: 0.27-0.92); owing to the SCCS design, the number of cases was the same as that of the controls.

Statistical Analysis

To calculate the number of person-days before PPSV23 immunization, we followed patients from the beginning of the follow-up period until the date of pneumonia onset or the date of PPSV23 immunization. The follow-up period started on April 1, 2011, or the date of the first visit if the first visit was later than April 1, 2011. We calculated the number of person-days after PPSV23 immunization by following up patients from the date of PPSV23 immunization until the date of pneumonia onset or the end of the follow-up period, whichever was first. The follow-up period ended on March 31, 2015, or the date of the last visit if the last visit was earlier than March 31, 2015. To estimate the incidence rates and RRs, only the first onset of pneumonia during the relevant time period was considered, and the observation period was ended at the time of the first onset of pneumonia. To compare the incidence rate before and after PPSV23 immunization for a study subject, Mantel-Haenszel RRs (RRMH) and 95% CIs were calculated [19,20]. The RRMH was calculated using the following equation: (pneumonia onset after immunization (*ai*) × observation period before immunization (*y0i*)/total observation period (*yi*))/(pneumonia onset before immunization (*bi*) × observation period after immunization (*y1i*)/total observation period (*yi*)). Analyses were conducted using person-days, but the results were translated to person-years for ease of interpretation. VE was estimated as (1-RR) × 100%. To compare categorical variables, Fisher's exact test was used, while comparisons for >3 different continuous variables were made using the Kruskal-Wallis test. P-values <0.05 were considered statistically significant. All statistical analyses were performed using R, version 3.22 (The R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org/).

Results

A total of 110 patients (88 men, 80%) were included in this study. The total follow-up periods were 38,321 and 47,601 person-days before and after immunization, respectively. Of the lung comorbidities, lung cancer was most frequent (n=56, 50.9%), followed by interstitial pneumonia (n=27, 24.5%) and COPD (n=22, 20.0%). Of all patients, 4.5% had other chronic lung diseases such as bronchiectasis (n=2), Goodpasture syndrome (n=1), eosinophilic granulomatosis with polyangiitis (n=1), and diffuse pan-bronchiolitis (n=1) (Table 1). The various lung comorbidities significantly varied according to patient age, for example, patients with lung cancer were younger than those with COPD (p<0.001).

Table 1: Clinical and demographic characteristics of the study subjects.

Age, median (Q1; Q3)	68.06 (62; 74)	
Sex, M/F	88/22	
Observation period		
Before immunization, person-days	38,321	
After immunization, person-days	47,601	
Lung comorbidities	N (%)	Age, median (Q1; Q3)
Lung cancer	56 (50.9)	66 (62.0; 70.0)
Interstitial pneumonia	27 (24.5)	74 (60.0; 77.5)
COPD	22 (20.0)	73.5 (69.3; 79.8)
Other chronic lung diseases[a]	5 (4.5)	60 (56.0; 65.0)

Note: Variables are expressed as numbers (percentages) unless otherwise specified; [a]chronic lung diseases other than lung cancer, interstitial pneumonia, and COPD; COPD: Chronic obstructive pulmonary disease; Q: Quartile

Table 2 shows the timing of PPSV23 immunization. Most patients with chronic lung diseases were immunized with PPSV23 during the early period of their clinical course. More than 80% of the patients with lung cancer were immunized before the end of first-line chemotherapy. Additionally, more than 92% of the patients with interstitial pneumonia were immunized at the initiation of long-term steroid therapy or during the first immunosuppressant cycle. Among the patients with COPD, more than 90% were immunized after disease exacerbation, at which point sustained inhaled corticosteroid (ICS) therapy was usually administered because it is recommended by global guidelines [21].

The rates of all-cause pneumonia were 334.34 and 185.06 per 1,000 person-years before and after immunization, respectively. Recurrent all-cause pneumonia was observed in five cases before immunization and in seven cases after immunization. PPSV23 immunization was significantly associated with a reduced rate of all-cause pneumonia onset in those with chronic lung diseases (RR: 0.643, 95% CI: 0.449-0.922). The subgroup analysis also showed a significant reduction in the onset of all-cause pneumonia in patients with COPD (Table 3).

Table 2: Timing of immunization with the 23-valent pneumococcal polysaccharide vaccine.

Lung comorbidities and immunization timing	N (%)
Lung cancer	56
At diagnosis	1 (1.8)
Before first-line chemotherapy	28 (50.0)
During first-line chemotherapy	16 (28.6)
After second-line chemotherapy or later	4 (7.1)
Others	7 (12.5)
Interstitial pneumonia	27
At initiation of long-term steroid therapy	24 (88.9)
During the first cycle of intravenous cyclophosphamide	1 (3.7)
After a later cycle of intravenous cyclophosphamide	1 (3.7)
Others	1 (3.7)
COPD	22
After exacerbation	20 (90.9)
Others	2 (9.1)
Other chronic lung diseases	5
At initiation of long-term steroid therapy	2 (40.0)
Others	3 (60.0)

Note: Values in parentheses show the proportions of timing of immunization for each comorbidity; COPD, chronic obstructive pulmonary disease.

We identified four and three cases with episodes of pneumococcal pneumonia onset before and after immunization with PPSV23, respectively. Before immunization, pneumococcal pneumonia was diagnosed based on only certified positive sputum culture in three patients and based on both positivity of sputum culture and urinary antigen in one patient. After immunization, pneumococcal pneumonia was diagnosed based on only certified positive sputum culture in two patients and based on both positivity of sputum culture and urinary antigen in one patient. No pneumococcal pneumonia episode was diagnosed based on only positive urinary antigen before or after immunization. The rates of pneumococcal pneumonia were 38.33 and 23.36 per 1,000 person-years before and after immunization, respectively. No case of recurrent pneumococcal pneumonia was observed before or after immunization. PPSV23 immunization was significantly associated with a reduced rate of pneumococcal pneumonia onset (RR: 0.441, 95% CI: 0.210-0.926). However, the episodes of pneumococcal pneumonia onset were very few, and a significant reduction in the rate of pneumococcal pneumonia was not noted in cases with comorbidities (Table 4). The VE rates for all-cause pneumonia and pneumococcal pneumonia were 35.7% (95% CI: 7.8-55.1%) and 55.9% (95% CI: 7.4-79.0%), respectively.

Discussion

In this study, we assessed the effectiveness of PPSV23 immunization by using the SCCS method. Because we think all-cause pneumonia is an important factor to be considered in the clinical outcomes of the patients with lung comorbidities, we chose the onset of all-cause pneumonia as the primary outcome. Our data showed that PPSV23 immunization significantly reduced the incidence of all-cause pneumonia (RR: 0.643) and pneumococcal pneumonia (RR: 0.441) in patients with lung comorbidities.

Although several systematic reviews and meta-analyses have evaluated the preventative effectiveness of PPSV23 for pneumococcal diseases, VE remains unclear [5-9]. As these systematic reviews and meta-analyses included heterogeneous studies with different populations, case definitions, outcome measures, medical practices, and serotype distributions, the results varied widely.

Table 3: All-cause pneumonia incidence rates and rate ratios before and after immunization.

	Before immunization			After immunization			RR	95% CI
	Pneumonia onset, N[a]	Observation period[a] (pd)	Rate[a] (per 1,000 py)	Pneumonia onset, N	Observation period[a] (pd)	Rate[a] (per 1,000 py)		
All patients	32	34,928	334.34	22	43,424	185.06	0.643[b]	0.449–0.922
Lung cancer	3	17,529	62.42	8	23,894	122.28	2.679[b]	0.969–7.408
Interstitial pneumonia	9	9,514	345.29	8	9,449	309.16	1.375[b]	0.861–2.195
COPD	18	7,161	917.61	6	8,456	259.15	0.107[b]	0.041–0.285
Other chronic lung diseases	2	724	1008.13	0	1,625	0	ND[c]	ND[c]

Note: [a]To estimate the incidence rates and rate ratios, only the first pneumonia onset during the relevant time period was counted, and the observation period ended at the time of the first pneumonia onset. [b]The rate ratio was calculated with the Mantel-Haenszel method; [c]not determined because the rate before or after immunization was zero; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; ND: Not determined; PY: person-years; RR: Rate ratio.

Table 4: Pneumococcal pneumonia incidence rates and rate ratios before and after immunization.

	Before immunization			After immunization			RR	95% CI
	Pneumonia onset, N[a]	Observation period[a] (pd)	Rate[a] (per 1,000 py)	Pneumonia onset, N	Observation period[a] (pd)	Rate[a] (per 1,000 py)		
All patients	4	38,199	38.33	3	46,947	23.36	0.441[a]	0.210-0.926
Lung cancer	0	17,717	0	1	24,472	14.97	ND[b]	ND[b]
Interstitial pneumonia	2	11,528	63.15	1	10,642	34.31	0.797[a]	0.325-1.954
COPD	2	7,373	98.92	1	10,208	35.77	0.254[a]	0.054-1.177

Note: [a]The rate ratio was calculated with the Mantel-Haenszel method; [b]not determined because the rate before or after immunization was zero; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; ND: Not determined; py: person-years; RR: Rate ratio

Few studies on VE in immunocompromised patients with chronic lung diseases have been reported. Nichol et al. conducted a 2-year retrospective cohort study and found that among elderly persons with chronic lung diseases, PPSV23 significantly reduced pneumonia hospitalization and death by 47% and 29%, respectively [5]. In a case-control study, Vila-Corcoles et al. reported that pneumococcal vaccination did not alter the risk of overall pneumococcal pneumonia occurrence in patients with chronic lung diseases. They reported VE of 29%; however, the finding was not statistically significant [7]. In conclusion, the VE of PPSV23 in immunocompromised hosts and patients with chronic lung diseases remains controversial.

In our study, most patients with lung cancer and interstitial pneumonia were expected to be in a potentially immunosuppressive state because of ongoing anticancer chemotherapy or immunosuppressive therapies. Vila-Corcoles et al. reported VE of 48% against all-cause pneumococcal pneumonia in a case-control study [6]. Their study included immunocompromised participants such as individuals with cancer (7.9%), undergoing corticosteroid therapy (6.6%), or with chronic lung diseases (37.2%). Some studies showed that the antigenicity of vaccines was preserved despite an immunosuppressive state. We previously reported that patients with lung cancer undergoing anticancer chemotherapy showed acceptable immune responses to a trivalent influenza vaccine [22]. Another study showed that ongoing treatment with corticosteroids and/or immunosuppressive agents did not affect the antibody response to pneumococcal vaccination in patients with interstitial pneumonia [23]. These results suggest that immunization during the early period of patients' clinical course is important.

During our study period, ICS treatment was recommended for COPD patients with a history of prior exacerbation based on the global guidelines for COPD, GOLD2011 [21]. Ishifuji et al. conducted a prospective observational study and showed that the use of ICS was one of the risk factors for recurrent pneumonia, with an adjusted hazard ratio of 1.78 [24]. Several other studies showed an elevated risk of pneumonia in COPD patients undergoing ICS [25,26]. In our study, ICS was administered in COPD patients with a history of disease exacerbation; immunization with PPSV23 occurred after exacerbation. We found that PPSV23 immunization was significantly associated with a reduced rate of all-cause pneumonia (RR: 0.11, 95% CI: 0.04-0.29); however, this was not significant for pneumococcal pneumonia (RR: 0.25, 95% CI: 0.05-1.18).

A previous 7-year retrospective observational cohort study using two large healthcare claims databases with more than 1 million subjects reported that adults aged ≥ 50 years with chronic lung diseases or cancer had a higher risk of pneumococcal pneumonia than did healthy adults [27]. The authors suggested that because the risk of pneumococcal diseases in adults aged 50–64 years was the highest among those with chronic lung disease and cancer, extending pneumococcal vaccination to adults aged<65 years with such lung comorbidities may be desirable. At our institution, patients with chronic lung comorbidities are immunized with PPSV23 irrespective of their age (i.e., aged>65 years or less). Because only vaccine-naïve patients were enrolled in this study, the number of patients in each subgroup was small, and the 95% CIs were widely distributed. Thus, we avoided subgroup analyses and used the overall RR instead.

We found higher VE for pneumococcal pneumonia than that reported in previous studies. This difference may be explained by differences in patient population and study design. We enrolled patients with chronic lung comorbidities including those in the immunosuppressive state. Our study was performed using the SCCS method, which is self-matched and thus minimizes the effects of fixed confounders [15,28]. Due to chronic lung comorbidities, all patients included in this study were carefully followed up under our supervision. Thus, the data regarding pneumonia onset were deemed highly reliable. Hence, we showed the effectiveness of PPSV23 with consideration of the effects of potential confounders. A few studies have investigated VE by using the SCCS method for influenza, mumps, measles, and rubella [29-32]. To the best of our knowledge, our study was the first to investigate the VE of PPSV23 against all-cause pneumonia and pneumococcal pneumonia by using the SCCS method.

This study has several limitations. First, the current study was a single-center retrospective study with a small sample size. As we only enrolled vaccine-naïve patients, the number of patients in each subgroup was small; thus, subgroup analysis was avoided. Second, the probability that the event of pneumonia increased the chance of immunization of PPSV23 caused the relative incidence to be biased towards null. Third, serotype specificity was not assessed. Concerning serotype distribution, three different surveillance studies were conducted in Japan at the same time as the current study [33-35]. These three studies showed almost identical serotype distribution of pneumococcal pneumonia. PPV23 accounted for more than 60% of all serotypes. We participated in one of these surveillance studies [33]. Although the serotype of pneumococcal pneumonia cases included in the current study was not specified, our pneumococcal pneumonia patients were expected not to differ from the general pneumococcal pneumonia population in Japan. Fourth, the indirect effect of pediatric pneumococcal conjugate vaccine immunization, the so-called "herd protection," was not excluded. In Japan, a public vaccination subsidy system of pneumococcal conjugate vaccine for children aged 2-60 months was implemented in 2011, and a national immunization program was implemented in April 2013. As a result of these programs, the vaccination rate increased and the frequency of pediatric invasive pneumococcal diseases significantly decreased [36]. Fifth, a selection bias might exist; the patients included in this study might not be representative of the general population with chronic lung diseases in Japan. Sixth, the effect of health-conscious behaviors after immunization, which might reduce the incidence rate, was not excluded [37]. Seventh, as we used the Mantel-Haenszel method, the onset of repetitive pneumonia was difficult to assess [19,20]. However, very few cases showed the onset of repetitive pneumonia; thus, its effect on the incidence rate was considered negligible. Finally, there might have been other unmeasured confounders.

Using the SCCS method, we found that immunization with PPSV23 in patients with lung comorbidities reduced the incidence of both all-cause pneumonia and pneumococcal pneumonia. Most patients received PPSV23 immunization shortly after the initiation of anticancer chemotherapy, long-term corticosteroid therapy, or ICS therapy. Despite the above limitations, our results suggest that immunization with PPSV23 was effective. Thus, immunization should be scheduled during the early clinical period in patients with lung comorbidities, including those in a potentially immunosuppressive state. We believe that our results provide evidence for recommending pneumococcal vaccination in persons with pulmonary comorbidities.

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References

1. Bridges CB, Coyne-Beasley T (2014) Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older: United States, 2014*. Ann Intern Med 160: 190-197.

2. https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2004-30/recommendations-use-pneumococcal-23-valent-polysaccharide-vaccine-shortage.html

3. 3.https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/224765/JCVI_statement_on_pneumococcal_vaccination_for_clinical_risk_groups_Final.pdf

4. https://www.rki.de/EN/Content/infections/Vaccination/recommandations/recommendations_node.html

5. Nichol KL, Baken L, Wuorenma J, Nelson A (1999) The health and economic benefits associated with pneumococcal vaccination of elderly persons with chronic lung disease. Arch Intern Med 159: 2437-2442.

6. Vila-Corcoles A, Salsench E, Rodriguez-Blanco T, Ochoa-Gondar O, de Diego C, et al. (2009) Clinical effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumonia in middle-aged and older adults: A matched case-control study. Vaccine 27: 1504-1510.

7. Vila-Corcoles A, Ochoa-Gondar O, Rodriguez-Blanco T, Gutierrez-Perez A, Vila-Rovira A, et al. (2012) Clinical effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumonia in patients with chronic pulmonary diseases: A matched case-control study. Hum Vaccin Immunother 8: 639-644.

8. Diao W, Shen N, Yu PX, Liu BB, He B (2016) Efficacy of 23-valent pneumococcal polysaccharide vaccine in preventing community-acquired pneumonia among immunocompetent adults: A systematic review and meta-analysis of randomized trials. Vaccine34: 1496-1503.

9. Tin Htar M, Stuurman AL, Ferreira G, Alicino C, Bollaerts K, et al. (2017) Effectiveness of pneumococcal vaccines in preventing pneumonia in adults, a systematic review and meta-analyses of observational studies. PLoS One 12: e0177985.

10. Treanor JJ, Talbot HK, Ohmit SE, Coleman LA, Thompson MG, et al. (2012) Effectiveness of seasonal influenza vaccines in the United States during a season with circulation of all three vaccine strains. Clin Infect Dis 55: 951-959.

11. Skowronski DM, Janjua NZ, De Serres G, Dickinson JA, Winter AL, et al. (2013) Interim estimates of influenza vaccine effectiveness in 2012/13 from Canada's sentinel surveillance network, January 2013. Euro Surveill 18.

12. Kissling E, Valenciano M, Falcao J, Larrauri A, Widgren K, et al. (2009) "I-MOVE" towards monitoring seasonal and pandemic influenza vaccine effectiveness: lessons learnt from a pilot multi-centric case-control study in Europe, 2008-9. Euro Surveill 5: 14.

13. Carville KS, Grant KA, Sullivan SG, Fielding JE, Lane CR, et al. (2015) Understanding influenza vaccine protection in the community: An assessment of the 2013 influenza season in Victoria Australia. Vaccine 33: 341-345.

14. Suzuki M, Dhoubhadel BG, Ishifuji T, Yasunami M, Yaegashi M, et al. (2017) Serotype-specific effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumococcal pneumonia in adults aged 65 years or older: A multicentre, prospective, test-negative design study. Lancet Infect Dis 17: 313-321.

15. Petersen I, Douglas I, Whitaker H (2016) Self-controlled case series methods: An alternative to standard epidemiological study designs. BMJ 354: i4515.

16. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, et al. (2007) Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Management of community-acquired pneumonia in adults. Clin Infect Dis 44: 27-72.

17. https://www.cdc.gov/pneumococcal/about/diagnosis-treatment.html

18. Kawakami K, Ohkusa Y, Kuroki R, Tanaka T, Koyama K, et al. (2010) Effectiveness of pneumococcal polysaccharide vaccine against pneumonia and cost analysis for the elderly who receive seasonal influenza vaccine in Japan. Vaccine 28: 7063-7069.

19. IARC (1999) Mantel-Haenszel rate ratio. In: Dos S Silva I (ed). Cancer epidemiology: Principles and methods. IARC Press France p.311-313.

20. IARC (1999) Confidence interval for Mantel-Haenszel rate ratio. In: Dos S Silva I, (ed) Cancer epidemiology: Principles and methods. IARC Press France p.330.

21. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, et al. (2013) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 187: 347-365.

22. Nakashima K, Aoshima M, Ohfuji S, Suzuki K, Katsurada M, et al. (2017) Immunogenicity of trivalent influenza vaccine in patients with lung cancer undergoing anticancer chemotherapy. Hum Vaccin Immunother 13: 543-550.

23. Kuronuma K, Honda H, Mikami T, Saito A, Ikeda K, et al. (2018) Response to pneumococcal vaccine in interstitial lung disease patients: Influence of systemic immunosuppressive treatment. Vaccine 36: 4968-4972.

24. Ishifuji T, Sando E, Kaneko N, Suzuki M, Kilgore PE, et al. (2017) Recurrent pneumonia among Japanese adults: Disease burden and risk factors. BMC Pulm Med 17: 12.

25. Crim C, Calverley PM, Anderson JA, Celli B, Ferguson GT, et al. (2009) Pneumonia risk in COPD patients receiving inhaled corticosteroids alone or in combination: TORCH study results. Eur Respir J 34: 641-647.

26. Wedzicha JA, Banerji D, Chapman KR, Vestbo J, Roche N, et al. (2016) Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. N Engl J Med 374: 2222-2234.

27. Imai K, Petigara T, Kohn MA, Nakashima K, Aoshima M, et al. (2018) Risk of pneumococcal diseases in adults with underlying medical conditions: A retrospective, cohort study using two Japanese healthcare databases. BMJ Open 8: e018553.

28. http://www.med.monash.edu.au/assets/docs/creps/2016/2016registrysigmay_stellagwini.pdf

29. Hardelid P, Ghebremichael-Weldeselassie Y, Whitaker H, Rait G, Gilbert R, et al. (2018) Effectiveness of live attenuated influenza vaccine in preventing amoxicillin prescribing in preschool children: A self-controlled case series study. J Antimicrob Chemother 73: 779-786.

30. Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C (2012) Vaccines for measles, mumps and rubella in children. Cochrane Database Syst Rev 15: CD004407.

31. Pan JR, He HQ, Yan R, Fu J (2013) Self-controlled case-series (SCCS) method as a tool for the evaluation on the safety of vaccine. Zhonghua Liu Xing Bing Xue Za Zhi 34: 836-839.

32. Huang WT, Yang HW, Liao TL, Wu WJ, Yang SE, et al. (2013) Safety of pandemic (H1N1) 2009 monovalent vaccines in taiwan: A self-controlled case series study. PLoS One 8: e58827.

33. Morimoto K, Suzuki M, Ishifuji T, Yaegashi M, Asoh N, et al. (2015) The burden and etiology of community-onset pneumonia in the aging Japanese population: A multicenter prospective study. PLoS One 10: e0122247.

34. Akata K, Chang B, Yatera K, Kwanami T, Yamasaki K, et al. (2015) Distribution and annual changes in Streptococcus pneumoniae serotypes in adult Japanese patients with pneumonia. J Infect Chemother 21: 723-728.

35. Shoji H, Maeda M, Takuma T, Niki Y (2017) Serotype distribution of Streptococcus pneumoniae isolated from adult respiratory tract infections in nationwide Japanese surveillances from 2006 to 2014. J Infect Chemother 23: 538-544.

36. Suga S, Chang B, Asada K, Akeda H, Nishi J, et al. (2015) Nationwide population-based surveillance of invasive pneumococcal disease in Japanese children: Effects of the seven-valent pneumococcal conjugate vaccine. Vaccine 33: 6054-6060.

37. Ohfuji S, Deguchi M, Tachibana D, Koyama M, Takagi T, et al. (2017) Estimating influenza disease burden among pregnant women: Application of self-control method. Vaccine 35: 4811-4816.

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