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＜ Brief Report ＞

Medical expenditures for community-acquired pneumococcal disease in Japan

FUKUDA Haruhisa[1)], ONIZUKA Hiroaki[2)], MURATA Fumiko[1)]

[1)] Department of Health Care Administration and Management, Kyushu University Graduate School of Medical Sciences
[2)] Department of Interdisciplinary Science and Innovation, Kyushu University School of Interdisciplinary Science and Innovation

Abstract

Objectives: The decision-making process for vaccination programs must be informed by cost-effectiveness analyses. This study was performed to quantify the medical expenditures for pneumococcal disease (PD) in Japan.

Methods: Surveillance data from the Japan Nosocomial Infections Surveillance program and insurance claims data were collected from community-acquired PD patients admitted to 29 hospitals in Japan. Patients with positive blood specimens were designated as having invasive PD (IPD). We estimated the medical expenditures incurred during the PD hospitalization episodes.

Results: The study sample comprised 1,358 PD patients from 28 hospitals between April 2015 and September 2017. Of these, 69 were IPD patients and 1,289 were non-IPD patients. The mean medical expenditures (standard deviation) for all PD patients, IPD patients, and non-IPD patients were estimated to be $6,610 ($13,133), $13,975 ($16,415), and $6,216 ($12,823), respectively.

Conclusion: This study is the first to quantify the medical expenditures for community-acquired PD in Japan.

keywords: *Streptococcus pneumoniae*; invasive pneumococcal disease; medical expenditures; community-acquired infection

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I. Introduction

Streptococcus pneumoniae is a gram-positive diplococcal bacterium that is the causative agent of various vaccine-preventable pneumococcal diseases (PDs) such as pneumonia, bacteremia, and meningitis. In 2018, there were 39,194 patients from whom *S. pneumoniae* isolates were obtained during hospitalization in Japan [1]. Children aged below five years in Japan have undergone routine vaccinations with the 13-valent pneumococcal conjugate vaccine (PCV13) since November 2013, and this vaccine was approved for adults aged 65 years or older in June 2014. The 23-valent pneumococcal polysaccharide vaccine (PPSV23) was subsequently included in the National Immunization Program in October 2014 for use in adults aged 65 years or older, and is routinely administered to younger adults aged 60–64 years with cardiac, renal, pulmonary, or immune (due to human immunodeficiency virus infection) functional impairment. However, these vaccines offer no protection against infections caused by pneumococcal serotypes not included in their formulations.

The prevalence of community-acquired PD may be systematically reduced through various strategies. One such strategy is the expansion of vaccination coverage to include age groups that are not yet approved for these vaccines under Japan's insurance system. Another approach is to provide clinicians with multiple options for pneumococcal vaccines under the routine vaccination schedule, and allow the administration of PCV13 to individuals with an increased risk of PD. Furthermore, the routine vaccination schedule could be modified to allow sequential vaccination of PCV13 and PPSV23 to high-risk adults aged 65 years or older. The

Corresponding Author: FUKUDA Haruhisa
3-1-1 Maidashi Higashi-ku Fukuoka 812-8582, Japan.
Phone: +81-92-642-6956
Fax: +81-92-642-6961
E-mail: h_fukuda@hcam.med.kyushu-u.ac.jp

decision-making process for shifts in vaccination policy must be informed by cost-effectiveness analyses, but these are precluded by the paucity of relevant cost data in Japan.

Previous studies from the US [2-6], Spain [7], and New Zealand [8] have reported on the costs associated with PD. Among these, five studies had identified target PD cases using International Classification of Diseases codes [2,5,6,8,9]. In contrast, only three studies utilized *S. pneumoniae* isolates from clinical specimens to definitively identify PD patients [3,4,7]. Although a previous Japanese study had produced cost estimates that approximated the economic burden of PD, their study sample consisted of all-cause pneumonia cases (including non-pneumococcal infections) identified using International Classification of Diseases codes [9]. There is therefore a lack of information on the medical expenditures of PD patients in Japan. Moreover, previous reports have generally focused on invasive PD (IPD) patients [3,5-8], and there is a dearth of studies that provide separate estimates for IPD and non-IPD patients in the existing literature.

To address these gaps in the evidence, this study aimed to identify patients in Japanese hospitals with community-acquired PD that was clinically diagnosed using *S. pneumoniae* isolates, and to estimate the medical expenditures for all PD patients, IPD patients, and non-IPD patients.

II. Materials and Methods

1. Database

The study was conducted using surveillance data from the Japan Nosocomial Infections Surveillance (JANIS) program's Clinical Laboratory Division and insurance claims data under the Diagnosis Procedure Combination (DPC) system. Data from April 2015 to September 2017 were obtained from 145 hospitals throughout Japan. The JANIS data included information on the types of collected specimens and bacterial isolates, which allowed the identification of hospitalization episodes with PD. The DPC data contained information on patient sex, age, comorbidities, medical expenditures, and length of stay for each hospitalization episode. However, there were no common patient identifiers that enabled the complete integration of the two datasets. Therefore, a deterministic record linkage was performed to identify the same patients in both datasets using specimen test dates, admission dates, birthdates, and sex.

2. Participants

The study participants comprised patients who were hospitalized for community-acquired PD. PD was first identified as cases in which *S. pneumoniae* isolates were recovered from clinical specimens. Patients with isolates from blood cultures were designated IPD patients, and patients with isolates from any other specimen were designated non-IPD patients. Next, patients in which isolates were obtained from specimens taken within two days of admission were identified as community-acquired PD patients [10], and patients in which isolates were obtained from specimens taken on the third day or later were identified as hospital-acquired PD patients. We also excluded patients who had been transferred from other hospitals or long-term care facilities. Only community-acquired PD patients were included in the analysis.

3. Statistical Analysis

As the analysis focused on community-acquired infections, the medical expenditures incurred during the PD hospitalization episodes directly represented the expenditures for these infections. The descriptive statistics of the medical expenditures (mean, standard deviation, median, and interquartile range) incurred by the PD patients were calculated from the linked JANIS data and DPC data. In addition, these descriptive statistics were also generated according to the presence/absence of IPD, age groups, and presence/absence of comorbidities. The 2019 purchasing power parity rate ($1.00 = 101.5 yen) was used to convert Japanese yen to US dollars. Statistical analyses were performed using Stata/MP version 15.1 (StataCorp, Texas, US). The study was approved by the Kyushu University Institutional Review Board for Clinical Research (Approval No. 2019-406).

III. Result

The study sample comprised 1,358 PD patients from 28 hospitals during the study period. Of these, 69 were IPD patients and 1,289 were non-IPD patients. The mean patient age was 27.5 years, women accounted for 40.8% of patients, and the in-hospital mortality rate was 3.3% (Table 1). The

Table 1 Patient characteristics

	All patients (n = 1358)	IPD (n = 69)	Non-IPD (n = 1289)
Age, mean years [SD]	27.5 [34.6]	49.9 [31.3]	26.3 [34.3]
0–4 years, n (%)	762 (56.1)	16 (23.2)	746 (57.9)
5–59 years, n (%)	173 (12.7)	14 (20.3)	159 (12.3)
60–64 years, n (%)	49 (3.6)	10 (14.5)	39 (3.0)
≥65 years, n (%)	374 (27.5)	29 (42.0)	345 (26.8)
Female, n (%)	554 (40.8)	26 (37.7)	528 (41.0)
CCI, mean [SD]	0.49 [1.00]	1.01 [1.70]	0.46 [0.94]
In-hospital mortality, n (%)	45 (3.3)	10 (14.5)	35 (2.7)
Year			
2015, n (%)	418 (30.8)	21 (30.4)	397 (30.8)
2016, n (%)	564 (41.5)	26 (37.7)	538 (41.7)
2017, n (%)	376 (27.7)	22 (31.9)	354 (27.5)

CCI, Charlson comorbidity index; IPD, invasive pneumococcal disease; SD, standard deviation.

Table 2 Medical expenditures for community-acquired pneumococcal disease

		Medical expenditures			Length of stay		
		All patients	IPD	Non-IPD	All patients	IPD	Non-IPD
All Ages	Mean [SD]	6,610 [13,133]	13,975 [16,415]	6,216 [12,823]	11.5 [6.0]	24.7 [25.5]	10.8 [17.1]
	Median (IQR)	3,199 (2,154-5,620)	9,724 (4,434-16,062)	3,082 (2,115-5,173)	17.8 (4-11)	16 (8-34)	6 (4-10)
0–4 years	Mean [SD]	3,255 [5,945]	8,135 [10,237]	3,150 [5,785]	6.2 [9.6]	13.6 [13.7]	6.07 [9.48]
	Median (IQR)	2,554 (1,950-3,464)	4,275 (2,804-5,464)	2,540 (1,935-3,394)	5 (4-7)	8 (7-10.5)	5 (4-7)
5–59 years	Mean [SD]	9,952 [25,037]	18,449 [24,148]	9,204 [25,049]	13.4 [24.7]	27.6 [34.3]	12.1 [23.5]
	Median (IQR)	3,803 (2,243-6,772)	11,215 (6,249-20,235)	3,589 (2,169-5,849)	7 (5-11)	20 (8.25-24)	7 (5-10)
60–64 years	Mean [SD]	11,024 [14,236]	17,411 [23,418]	9,386 [10,612]	17.2 [19.2]	27.3 [30.6]	14.6 [14.5]
	Median (IQR)	6,596 (3,486-12,360)	10,552 (6,694-15,943)	5,678 (3,188-11,680)	13 (7-20)	16 (10-33.5)	12(6.5-18.5)
≥65 years	Mean [SD]	11,321 [13,685]	13,852 [10,840]	11,108 [13,889]	20.7 [22.2]	28.7 [23.1]	20.1 [22.0]
	Median (IQR)	6,656 (3,912-12,821)	11,301 (6,577-14,023)	6,385 (3,781-12,199)	15 (8-26)	25 (14-37)	14 (8-25)

IPD, invasive pneumococcal disease; IQR, interquartile range; SD, standard deviation.

descriptive statistics of the medical expenditures for PD are presented in Table 2. The mean medical expenditures (standard deviation) for all PD patients, IPD patients, and non-IPD patients were estimated to be $6,610 ($13,133), $13,975 ($16,415), and $6,216 ($12,823), respectively.

Among the patients, there were 762 aged 0–4 years, 173 aged 5–59 years, 49 aged 60–64 years, and 374 aged 65 years or older; their respective medical expenditures (standard deviation) were $3,255 ($5,945), $9,952 ($25,037), $11,024 ($14,236), and $11,321 ($13,685).

IV. Discussion

In this study, we calculated the medical expenditures for PD using a database that linked JANIS data containing bacteriological test results and DPC data containing information on treatments and expenditures at the patient level. To our knowledge, this is the first report that quantifies the medical expenditures for PD in Japan.

Here, the mean medical expenditures were estimated to be $6,610 for all PD patients, $13,975 for IPD patients, and $6,216 for non-IPD patients. For patients aged 60 years or older (who are eligible for the PPSV23 vaccine), these expenditures (standard deviations) were $14,765 ($25,805) for IPD patients and $10,933 ($1,7479) for non-IPD patients (data not shown). These estimates were considerably lower than those reported by studies from the US [5], which may be due to inherent differences in healthcare insurance systems. These differences highlight the problems in using cost estimates from one country to inform economic assessments of pneumococcal vaccines in another. Konomura et al. estimated the median hospitalization expenditure for community-acquired pneumonia patients aged 65 years or older to be $5,321 [9], whereas this study produced an estimate that was slightly higher at $6,656. This disparity is likely to be the result of a difference in target subject patients, as the present study focused on *S. pneumoniae* infections. The estimates of medical expenditures for PD in Japan are vital to the decision-making process for national vaccination policies.

A study limitation is that the record linkage between the JANIS data and DPC data was not complete. Although there were 10,544 patients with *S. pneumoniae* isolates during the study period, only 1,689 patients (16.0%) could be linked with the DPC data. This was due to the lack of shared patient identifiers between the two datasets, and the linkage was limited to information that is available in JANIS data (e.g., birthdates and admission dates). However, the possibility of linkage is dependent on each hospital's record policy, and the inclusion or non-inclusion of these records is unaffected by disease severity. As a consequence, the bias toward the patients included in this study would be limited, and is unlikely to have a substantial effect on the expenditure estimates. Next, our analysis aimed to estimate the medical expenditures of PD patients, but did not consider the influence of concurrent infections from other pathogens. There is therefore a need to construct a database with a larger study population to focus on patients with only PD.

In conclusion, this study is the first to quantify the medical expenditures for community-acquired PD in Japan. The estimates produced here can be applied to cost-effectiveness analyses of preventive measures for *S. pneumoniae* infections, thereby informing and guiding national vaccination policies.

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Conflict of Interest

Haruhisa Fukuda received an Investigator Sponsored Research grant from Pfizer Japan Inc.

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＜短報＞

日本における市中肺炎球菌感染症による医療費

福田治久[1)]，鬼塚浩明[2)]，村田典子[1)]

[1)] 九州大学大学院医学研究院医療経営・管理学講座
[2)] 九州大学共創学部

抄録

目的：ワクチン接種プログラムの意思決定プロセスには，費用対効果評価が必要である．本研究の目的は，市中肺炎球菌感染症（PD）による医療費を推定することである．

方法：日本の29のDPC対象病院に入院した市中肺炎球菌感染症患者について，厚生労働省院内感染対策サーベイランス事業（JANIS）の検査部門データとDPCデータを突合した．JANISデータにおいて血液検体が陽性の患者を侵襲性肺炎球菌感染症（IPD）と定めた．市中肺炎球菌感染症症例の医療費を推定した．

結果：解析対象症例は28病院における1,358症例である．IPD症例は69症例，非IPD症例は1,289症例であった．全PD症例，IPD症例，非IPD症例における平均医療費（標準偏差）は，それぞれ6,610ドル（13,133ドル），13,975ドル（16,415ドル），6,216ドル（12,823ドル）と推定された．

結論：本研究は日本において市中肺炎球菌感染症による医療費を初めて定量化することができた．

キーワード：肺炎球菌感染症，侵襲性肺炎球菌感染症，医療費，市中感染