












Effectiveness of a Program to Raise Awareness About Pneumococcal Vaccination Among Physicians and Patients with Chronic Respiratory Diseases: A Multicenter Cohort Study

Zühal Karakurt¹ , Enver Yalnız² , Sedat Altın³ , Özlem Oruç¹ , Özgür Uslu² , Nurdan Şimşek Veske³ , Oğuz Kılınc⁴ , Seval Kul⁵ , Abdullah Sayiner⁶ 

¹Department of Pulmonology and Critical Care, University of Health Sciences, İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Research and Training Hospital, İstanbul, Turkey

²Department of Pulmonology University of Health Sciences, İzmir Suat Seren Chest Diseases and Thoracic Surgery Research and Training Hospital, İzmir, Turkey

³Department of Pulmonology, University of Health Sciences, İstanbul Yedikule Chest Diseases and Thoracic Surgery Research and Training Hospital, İstanbul, Turkey

⁴Department of Pulmonology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey

⁵Department of Biostatistics, Gaziantep University Faculty of Medicine, Gaziantep, Turkey

⁶Department of Pulmonology, İzmir University of Economics Faculty of Medicine, İzmir, Turkey

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Abstract

OBJECTIVE: There is a need to increase patient and clinician awareness on the effectiveness of pneumococcal vaccination in at-risk groups. The aim of the study was to evaluate the effect of reminders for physicians and patients using the vaccination tracking system created in the hospital information management system (HIMS) on the vaccination rate, and the effect of pneumococcal vaccination on pneumonia-related hospitalization and mortality over a 12-month period.

MATERIAL AND METHODS: This prospective observational cohort study was undertaken during a 2-year period in 3 tertiary care centers. Patients were followed up for 12 months following vaccination, and hospital admissions and mortality were recorded via HIMS. During the campaign, HIMS transmitted pneumococcal immunization reminder messages in accordance with guideline recommendations to physicians' computers and patients' mobile phones. Educational posters on pneumococcal vaccination were posted in outpatient clinics. Regular seminars on the evidence for pneumococcal vaccination were organized. All patients who were hospitalized during the follow-up period for chronic obstructive pulmonary disease (COPD), asthma, lung cancer, or pneumonia were analyzed in relation to their vaccination history regarding clinical outcomes.

RESULTS: A total of 29 530 patients were included in the study. During the study period, the annual vaccination rate increased by 74.4% and reached 4.8% in 3 hospitals ($P = .001$). The rates were 3.9% in patients older than 65 years without comorbidities and 5.2% in those with COPD and asthma ($P = .002$). In pneumococcal vaccine recipients, pneumonia-related hospital mortality was lower (relative risk (RR) = 0.19, CI 0.09-0.35, $P < .001$).

CONCLUSION: It is possible to raise the rate of pneumococcal vaccination through awareness campaigns. Individuals with COPD and asthma are more willing to receive pneumococcal vaccination. Among patients hospitalized for pneumonia, prior pneumococcal vaccination is associated with lower mortality.

KEYWORDS: 65-year-old, chronic obstructive pulmonary disease, mortality, pneumonia, pneumococcal vaccination

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INTRODUCTION

Streptococcus pneumoniae is the leading bacterial cause of community-acquired pneumonia (CAP) worldwide and in Turkey.¹⁻⁵ Advanced age, chronic disorders (diabetes, chronic lung, heart, liver, kidney, and nervous system diseases), malignancies, and immunosuppressive conditions are associated with an increased incidence of pneumococcal infection and a worse prognosis.²⁻⁶ For these reasons, national and international guidelines advocate vaccination against pneumococcal infections for the at-risk groups. Comprehensive studies on pneumococcal vaccination rates in Turkey are lacking, but estimates remain well below the targets. The coverage rate in risk categories was around 1% until recently when the Ministry of Health adopted policies encouraging adult vaccination and initiated the free rollout of conjugate vaccines to family physicians.⁷ In Western nations, this rate ranges from 13% to 69%.⁸ The main obstacles to adult vaccination are that health authorities and professional organizations do not make clear recommendations on this subject, physicians do not have enough knowledge about the efficacy and safety of vaccines, and this issue is not a primary concern during the limited time they spend with the patient because of their heavy workload, whereas patients expect clear guidance from their

Corresponding author: Zühal Karakurt, e-mail: zuhalkarakurt@hotmail.com



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physicians and health authorities regarding vaccination.⁹⁻¹² In Turkey, the Ministry of Health and professional organizations such as the Turkish Thoracic Society and the Infectious Diseases and Clinical Microbiology Society have developed guidelines recommending pneumococcal immunization for those in at-risk groups. However, these recommendations hardly reach any physician-patient encounter because of the time constraint imposed by the adopted health policies. In such brief patient contacts, simple reminders may be of help to the physicians in recommending vaccination to their at-risk patients. Besides, physician training programs and goal setting for vaccination coverage can boost the adult immunization rate, as shown in a study from Denizli, Turkey.¹³ Another questionnaire-based study showed that patients had knowledge gaps and misperceptions regarding adult vaccination.¹⁴

This study was planned and implemented in 3 large tertiary chest disease training and research hospitals to improve the pneumococcal conjugate vaccination (PCV-13) rates of adults in high-risk groups. The project included reminder mechanisms for both patients and physicians, and training programs to raise physicians' awareness of the impacts of pneumococcal vaccine on adult health and health economy. This study aimed to assess whether these interventions had any effect on adult vaccination rates and any impact on pneumonia-related hospital mortality during a 12-month period.

MATERIAL AND METHODS

This was a prospective observational cohort study and included all patients who presented to the outpatient clinics of 3 tertiary care centers for respiratory diseases in 2 major cities of the country.

Patients

During the study period, all patients with pneumococcal vaccine indications were retrieved from the hospital information management system (HIMS) and included in the study. Thus, patients who were older than 65 years and those previously diagnosed and/or followed up with chronic conditions were included in the study (Figure 1).

The diagnosis of patients was based on the International Classification of Diseases, Tenth Revision (ICD-10), which was used for the eligible study population, and all study-related diseases and their ICD-10 coding were obtained from

the hospital electronic system. International Classification of Diseases, Tenth Revision coding J44.0-J44.9 were accepted as COPD, J45.0-J45.9 were accepted as asthma, and C00.0-C97.0 were accepted as malignancy. However, patient-specific age, gender, and comorbidities were not obtained from the hospital electronic system. In this study, total numbers of patients were recorded and given for COPD, asthma, and malignancy. The region and the type of malignancy were not classified. Pneumonia (J13.0-J18.9) cases were recorded. Besides, pneumonia-related in-hospital mortality was derived from patients whose diagnosis of hospitalization was pneumonia (J13.0-J18.9). However, we were not able to obtain the data on these patients' characteristics.

Individuals with contraindications to the pneumococcal vaccine, patients who had previously (within 1 year) received the pneumococcal vaccine, pregnant or breastfeeding patients, and those lost to follow-up were excluded from the study.² Patients who received a 13-valent pneumococcal conjugate vaccine (PCV13 [Prevenar 13, Pfizer, Inc.]) but who moved to another location during the 1-year follow-up period were also not included (see Figure 1) The intervention period was between November 15, 2018 and November 15, 2019. All participants were followed up for at least 1 year until November 15, 2020.

Clinical Endpoints

The primary endpoint was the rate of vaccination during the 1-year follow-up period. The study population was divided into 2 groups, namely those who were vaccinated and those who were not vaccinated, despite the interventions. The secondary endpoint was in-hospital mortality in hospitalized patients with pneumonia.

Patients who were and who were not administered the 13-valent pneumococcal conjugate vaccine were identified from the data registry. The patients were monitored for a duration of 1 year, regardless of whether they were admitted to the hospitals in the study centers. If these individuals were admitted to the hospital because of pneumonia (ICD-10 J13.0-J18.9), any deaths that occurred during their hospital stay (including in the emergency department or intensive care unit) were recorded as "mortality with pneumonia."

Interventions

Mobile phone messages were sent to patients who had made an appointment at the hospital to raise their awareness about pneumococcal vaccination. These messages were sent 1 hour prior to the hospital appointment time to all patients for whom the 13-valent conjugate vaccine was indicated.²⁻⁴ The message read: "If you have not been vaccinated against pneumonia, please ask your doctor whether you could benefit from one such vaccine. Best wishes." In addition, pneumococcal vaccine reminder pop-ups were also prepared for physicians when the patient's electronic records were opened on the doctor's computer. These messages only appeared for patients 65 years and older and/or with a previous diagnosis of a disease listed as an indication for pneumococcal vaccination. The pop-up message read: "This patient may be at increased risk for pneumococcal infections. If you think he/she qualifies for pneumococcal vaccination, please refer him/her to the vaccination unit".

Main Points

- This study found that programs aimed at raising awareness of pneumococcal vaccination through messages and reminder posters to physicians and patients could produce a nearly 75% increase in the annual pneumococcal vaccination rate.
- The study also discovered that adults over the age of 65 with COPD and asthma have greater rates of pneumococcal vaccination than those in the same age group who do not have such comorbidities.
- The pneumonia vaccinations have shown protective effect in-hospital mortality for pneumonia patients with risky comorbid diseases.

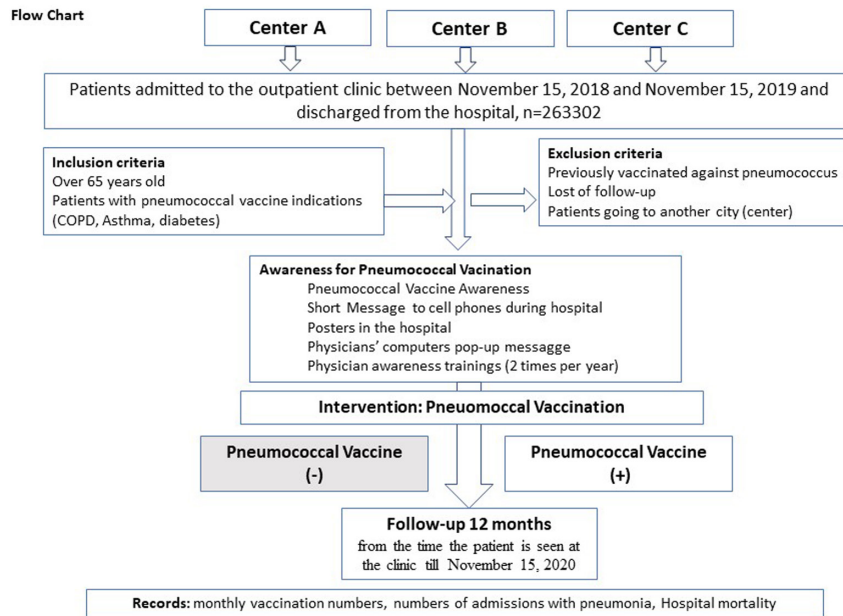


Figure 1. Flow chart of patients' enrollment.

Posters were posted on outpatient clinic doors for patient and physician awareness. For patients, a 50 × 70 cm poster with the following information was displayed on the outer side of the clinic door facing the waiting hall. The poster read, “Dear Patients, if you are 65 or older or if you have respiratory conditions such as COPD, asthma, bronchiectasis, or other chronic conditions like diabetes, please consult your physician about pneumococcal vaccine. We wish you well.” For physicians, a 50 × 70 cm poster containing the following information was posted on the inner side of the clinic door facing the doctor's table. The poster contained information about the pneumococcal vaccination indications and schedule.

Modifications to the Program Serving as the HIMS: A large room was designed for and dedicated to adult vaccination (according to standards set by the Ministry of Health). Nurses were appointed to serve during work hours. A HIMS-programmed computer was installed in the vaccination room. This enabled the nurses in charge of the vaccination to see online the list of patients referred by the physicians and to make sure they were all called and immunized. The vaccine section on the HIMS page was updated with the vaccine's name, type, and vaccination date/time. This allowed all physicians taking care of the patient to be informed about his/her vaccination status. This study was approved by the Ethics Committee of the University of Health Sciences Süreyyapaşa Chest Diseases and Thoracic Surgery Teaching and Research Hospital (032-01.11.2018), and it was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. Signed informed consent was obtained from all participants.

Statistical Analysis

The statistical analysis was done by the Statistical Package for Social Sciences version 20.0 package program (IBM Corp.; Armonk, NY, USA). The age and gender of the patients were determined through descriptive analysis of additional disorders. Dichotomous values are shown as numbers and percentages. For continuous variables with a normal distribution,

the mean values and standard deviation (SD) are used. For variables with nonnormal distribution, the median values and interquartile ratio (IQR) are used. The vaccinated and nonvaccinated groups were compared using Student's *t*-test for continuous numerical data, with a normal distribution, or Mann–Whitney *U*-test when there was a nonnormal distribution, and with chi-square test for dichotomous. The significant *P* value was accepted if below .05.

RESULTS

In the study period, a total of 263 302 patients were evaluated. Table 1 shows the summary of monthly vaccination data for all and individual hospitals during the study period. Between November 2018 and October 2019, the administration of the 13-valent conjugate vaccine increased by 74.4% compared to the previous year at the 3 chest disease hospitals ($P < .001$).

The numbers of inpatients and outpatients classified according to their vaccination status are shown in Table 2. In the follow-up period, unvaccinated patients with COPD or asthma who were 65 years and older had 18.3-fold (8077/442); patients without COPD and asthma who were 65 years and older had 24.9-fold (3506/141); patients with COPD irrespective of age had 16.4-fold (9005/549); patients with asthma irrespective of age had 12.5-fold (2044/163); patients with pneumonia had 21.7-fold (8751/404); and patients with malignancy had 28.4-fold (4798/169) increased risk of hospitalization (Table 2).

Among the risk groups, the rate of hospitalization in the vaccinated individuals compared with the unvaccinated ones (Table 3).

Pneumonia-related hospital mortality rates in vaccinated and unvaccinated groups were 2.5% and 13.6%, respectively (relative risk (RR) = 0.19, CI 0.09-0.35, $P < .001$), pointing to a 81% decrease in the risk of pneumonia-related mortality.

Table 1. Monthly Pneumococcal Vaccination Numbers and Percent Changes in the 3 Centers

Months	All Centers*				Center A				Center B				Center C			
	Preintervention	Postintervention	Change %	Preintervention	Post-intervention	Change %	Preintervention	Postintervention	Change %	Preintervention	Postintervention	Change %	Preintervention	Postintervention	Change %	
November	481	680	141	140	166	119	162	186	115	179	328	183	179	328	183	
December	421	591	140	161	131	81	162	180	111	98	280	286	98	280	286	
January	281	534	190	92	137	149	98	137	140	91	260	286	91	260	286	
February	198	526	266	61	127	208	73	198	271	64	201	314	64	201	314	
March	225	475	211	59	115	195	112	192	171	54	168	311	54	168	311	
April	344	524	152	158	112	71	108	271	251	78	141	181	78	141	181	
May	671	883	132	460	441	96	118	312	264	93	130	140	93	130	140	
June	240	519	216	55	103	187	116	314	271	69	102	148	69	102	148	
July	264	535	203	72	99	138	78	336	431	114	100	88	114	100	88	
August	149	409	274	45	67	149	56	260	464	48	82	171	48	82	171	
September	458	867	189	142	226	159	133	527	396	183	114	62	183	114	62	
October	709	1203	170	220	263	120	160	832	520	329	108	33	329	108	33	
Total	4441	7746	174	1665	1987	119	1214	3559	293	1400	2014	144	1400	2014	144	

Pre-awareness period: November 15, 2017-November 14, 2018; Awareness period: November 15, 2018-November 14, 2019.

*All center difference.

Table 2. Vaccination Numbers Among Outpatients and Hospitalized Patients During the Study Follow-Up Period

3 Centers	Vaccinated			Unvaccinated			General Total (Row, n)
	Hospitalized	Outpatients	Total (Row%)	Hospitalized	Outpatients	Total (Row%)	
65-year older people with COPD or asthma, n (%)	442 (16.5)	2235 (83.5)	2677 (100)	8072 (6.3)	120625 (93.7)	128697 (100)	131374
65-year older people without COPD and asthma, n (%)	141 (10.9)	1149 (89.1)	1290 (100)	3506 (4.1)	81571 (95.9)	85077 (100)	86367*
COPD, n (%)	549 (21.2)	2022 (78.8)	2571 (100)	9005 (12.7)	61788 (87.3)	70793 (100)	73364*
Asthma, n (%)	163 (8.7)	1700 (91.3)	1863 (100)	2044 (2.5)	78878 (97.5)	80922 (100)	82785*
Pneumonia, n (%)	404 (30.1)	940 (69.9)	1344 (100)	8751 (16)	45954 (84)	54705 (100)	56049
Malignancy, n (%)	169 (22.7)	576 (77.3)	745 (100)	4798 (23.9)	15243 (76.1)	20041 (100)	20786*

(%) Row. Total of these cases 263302.
 COPD, chronic obstructive pulmonary disease. *Total number of cases in vaccinated and unvaccinated group in row.

The group over 65 with COPD and asthma received 3 times more vaccinations than the group over 65 without COPD or asthma. Among the individuals older than 65 years without comorbidities, the pneumococcal vaccination rate was 3.9%, as compared to 5.2% among individuals with COPD and asthma in the same age group (RR =1.34, P = .002).

DISCUSSION

This study shows that a nearly 75% increase in the annual pneumococcal vaccination rate can be achieved with programs aiming to raise awareness through messages and reminder posters to physicians and patients. The study also reveals that adults older than 65 years with COPD and asthma have higher rates of pneumococcal vaccination than individuals without such comorbidities in the same age group. Finally, vaccination with pneumococcal conjugate vaccine is associated with an 81% decrease in hospital mortality.

Awareness of Pneumococcal Vaccination

Stoffel et al¹⁵ examined Swiss general practitioners’ (GPs) knowledge of pneumococcal vaccination guidelines for adult risk categories. In this study, 4607 GPs were invited to complete a survey by email, and 300 GPs responded. They indicated that they prescribed pneumococcal vaccine for at-risk people, they concluded that GP awareness could increase immunization rates and protect at-risk people.¹⁵ A randomized controlled trial was conducted in Brazil to investigate

whether contacting diabetes patients via phone (intervention group) to update their vaccinations would be an effective method of intervention.¹⁶ Significant improvements in vaccination rates were found among the intervention group subjects following a phone call, showing it to be an easy and successful method. The authors indicated that a professional was required for the phone calls.¹⁶ The present study aimed to improve both the physicians’ and patients’ awareness about pneumococcal vaccination.

Artificial intelligence can be used to raise awareness about vaccination. Hospital information management systems are easily adaptable to inform physicians about the possibility of pneumococcal vaccination when it is indicated. In this study, HIMS of the 3 centers followed similar algorithms to draw the attention of physicians and patients on pneumococcal vaccination. This was an easy and cost-effective method both to raise awareness and for follow-up of the vaccinated patients. Monthly pneumococcal vaccination reports showed significant increases.

Pneumococcal Vaccination in 65-Year-Old and Older

Ates Bulut et al¹⁷ aimed to evaluate whether specialists know about older people’s vaccination schedules and how often the defined vaccines are recommended to patients in daily practice. In 2021, they used a questionnaire and sent a link to the doctors via email, social media, and text message. In

Table 3. Number and Percentages of Hospitalized Patients in the Vaccinated and Unvaccinated Groups

	Vaccinated (n = 1426)	Unvaccinated (n = 28104)	% Difference (95% CI)	P
COPD, n (%)	549 (38)	9005 (32)	5.6 [3.06-8.21]	0.001*
Asthma, n (%)	163 (11)	2044 (7)	4.16 [2.58-5.94]	0.001*
Pneumonia, n (%)	404 (28)	8751 (31)	2.8 [0.39-5.18]	0.024*
Malignancy, n (%)	169 (12)	4798 (17)	5.22 [3.39-6.86]	0,001*
65-year older people without COPD and asthma, n (%)	141 (%10)	3506 (%13)	2.59 [0.89-4.08]	0.004*

COPD, chronic obstructive pulmonary disease.
 *Significant value P = .05; chi-square test.

that study, it was emphasized that vaccines, including inactivated or recombinant influenza, PPSV23, PCV13, and other vaccines, were recommended for older people in the guidelines. There were a total of 435 physicians who took part, and 94.5% (411) of the doctors said they had told their patients to get vaccinated. However, 20% of the physicians chose the correct vaccination and 33.8% had not asked the patients about their vaccination background. Doctors who had not looked at the “National Adult Vaccination Scheme,” were younger and had less experience, and had not asked patients about their vaccination history. They concluded that physicians should be more aware of routine vaccination regimens, periodic reminders for immunization should be given in each health-care environment and novel methods should be put into practice to improve physicians’ attitudes on immunization.¹⁷

In this study, older patients without comorbidities were less frequently vaccinated than the same age group with COPD and asthma. The tendency to receive pneumococcal vaccination was lower in healthy elderly individuals than in those with pulmonary comorbidities. PCV-13 vaccine has been recommended for persons aged ≥ 65 years who do not have an immunocompromising condition, CSF leak, or cochlear implant and who have not previously received PCV13.^{18,19} Very recently, in 2022, PCV-20 was developed, and pneumococcal vaccination programs have been revised.²⁰ In the CAPITA study, PCV-13 was found to lower the incidence of invasive pneumococcal illness by 75% and the need for hospital care owing to vaccine-type strains of CAP by 45.6% in the 84496 senior participants.²¹ This study showed that an easy and pragmatic multidimensional awareness approach significantly contributed to the vaccine uptake in the elderly patients with chronic lung diseases. There will hopefully be further increases in the percentage of healthy adults over 65 who receive vaccinations as publications and awareness of the benefits increase. Physician and individual awareness-raising efforts should keep growing in this regard.

Pneumococcal Vaccination and Mortality in Patients Hospitalized due to Pneumonia

This study showed that the mortality was lower in PCV-13 vaccinated patients if they were hospitalized for pneumonia. Similar observations were made in other studies. Kolditz et al²² identified a significant reduction in 30-day all-cause mortality after pneumonia. They found that the number needed to vaccinate was 1722 to prevent one death due to pneumonia. In that population-based cohort of people over 60 years of age, PPV13 immunization was linked to a slight decrease in all-cause pneumonia, which was only found in women, and a decrease in all-cause mortality after pneumonia, which was only seen in patients between the ages of 60 and 79. This effect on mortality following pneumonia may be explained by either a shortened course of pneumococcal pneumonia or a switch to less virulent pneumococci.²² Beatty et al²³ conducted a prospective, population-based clinical registry of 1636 hospitalized adult patients (18 years and above) with bacteremic pneumococcal pneumonia between 2000 and 2010. The study showed that the pneumococcal vaccination rate was less than 5% and all-cause hospital mortality was 14% (226/1636).²³ The pneumococcal vaccination

was associated with reduced in-hospital mortality (adjusted odds ratio, 0.2; 95% CI, 0.05-0.9, $P = .033$). Vaccination was not associated with any decrease in the rate of major complications ($P = .2$).²³ In a recent retrospective study from Japan, Naito and colleagues aimed to evaluate whether prior pneumococcal vaccination (with 23-valent polysaccharide vaccine) contributed to better clinical outcomes, as well as the cost related to all-cause hospital admissions in people 65 years old and above.²⁴ In this study, a total of 1355 patients were enrolled, including 310 (22.9%) patients who had received pneumococcal vaccine.²⁴ The percentages of patients with pneumonia were similar in vaccinated and unvaccinated groups ($n = 35$, 11.3% and $n = 119$, 11.4%, respectively, $P > .99$), but vaccinated patients had lower all-cause in-hospital mortality rate than unvaccinated patients (3.9% vs 8.2%, $P = .008$).²⁴

The main strengths of the study were that it was a multicenter, prospective study which included a big population, that several interventions directed to both physicians and patients were used and that all vaccinated and unvaccinated participants were followed up for 1 year.

This study had some limitations that should be noted. First, the number of hospital admissions due to pneumonia during the study period may have been higher than that observed in the study. Because the follow-up period partly coincided with the pandemic’s first year (November 2019–November 2020), curfews, mask wearing, and precautions to keep distance from others may have prevented pneumonia, especially in people 65 and older. However, the lower mortality in patients hospitalized for pneumonia is a relevant finding, independent from the prevalence of serious pneumonia in the general population. Secondly, mortality risk analysis could not be carried out by comparing the comorbidities of people who had and had not been vaccinated. We did not have access to the individual data (age, gender, and comorbid diseases) of the patients followed by the 3 tertiary care centers. We were only able to report the total number of patients with age over 65, COPD, asthma, and malignancy. Thirdly, the fact that this study was performed in 3 large teaching institutions for chest diseases possibly prevents generalizability of the findings to other hospitals. These referral centers mostly deal with more severe and complicated cases, and the outcomes may be different in health-care centers dealing with less severe patients. Finally, mortality that was reported was crude mortality and the causes of death were not precisely determined.

In summary, activities to improve awareness of pneumococcal vaccination, including delivering messages to physicians and patients and placing reminder posters in hospitals, can increase vaccination rates. The presence of comorbidities appears to influence the physicians’ attitudes more than older age. Pneumococcal vaccination is associated with lower mortality in patients hospitalized for CAP. Continued efforts are needed to further improve awareness among physicians and patients.

Ethics Committee Approval: This study was approved by Ethics Committee of University of Health Sciences Süreyyapaşa Chest Diseases and Thoracic Surgery Teaching and Research Hospital (032-01.11.2018), and it was conducted in accordance with the ethical principles stated in the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Z.K., A.S., O.K., S.A., E.Y., Ö.O.; Design – Z.K., S.K., S.A., A.S., E.Y., Ö.O., O.K.; Supervision – A.S., O.K., Z.K., S.A.; Resources – Z.K., S.A., E.Y.; Materials – Z.K., S.A., E.Y.; Data Collection and/or Processing – Ö.O., N.Ş.V., Ö.U.; Analysis and/or Interpretation – S.K., Z.K.; Literature Search – A.S., O.K., Ö.O., N.Ş.V., Ö.U.; Writing – Z.K., A.S.; Critical Review – O.K., S.A., E.Y.

Declaration of Interests: The authors have no conflicts of interest to declare.

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