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Individual and health system variation in rehospitalizations the year after pneumonia

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Abstract

Little is known about variation in patterns of recovery among patients discharged alive from hospitalizations for pneumonia.

The aim of the is observational cohort study was to characterize the variation in patterns of hospital readmission and survival in the year after discharge for pneumonia in 3 different health systems.

The 3 cohorts consisted of (1) the Health and Retirement Study participants enrolled in Fee-for-service Medicare (FFS), (2) Veterans Administration (VA) Healthcare system, and (3) Kaiser Permanente of Northern California (KPNC). The 365-day survival and re-hospitalizations were determined for each cohort. Multinomial logistic regression was used to identify potential contributors to the different patterns.

We identified 2731, 23,536, and 39,147 hospitalizations for pneumonia in FFS Medicare, VA, and KPNC, respectively, of whom 88.1%, 92.8%, and 89.7% survived to hospital discharge. The median patient survived to 1 year and was rehospitalized twice in FFS (9.0%), once in VA (14.1%) and KPNC (9.1%). Of the patients who survived the hospitalization, 33.3% (FFS), 30.2% (VA), and 26.8% (KPNC) died during the subsequent year. Of those who survived, 29.8% (FFS), 35.9% (VA), and 46.1% (KPNC) were never rehospitalized. 11.9% (FFS), 11.9% (VA), and 11.7% (KPNC) had greater than 3 hospitalizations. Age, race, gender, comorbidity, ICU use, and hospital length stay collectively explained little (5–7%) of the variation in the recovery pattern.

There is significant variation in the year after the hospitalization for pneumonia across individuals, but less so across health systems. There may be important opportunities to better classify these heterogeneous individual-level pathways.

Abbreviations: FFS = Fee for Service, HRS = Health and Retirement Study, ICD-9-CM = International Classification of Diseases, 9th Edition, clinical modification, IQR = interquartile range, IRB = Institutional Review Board, KPNC = Kaiser Permanente Northern California, RRR = relative risk ratio, SD = standard deviation, VA = Veterans Administration.

Keywords: hospitalization, patient outcomes, patient readmission, pneumonia

1. Introduction

Despite health systems' increasing focus on chronic conditions, pneumonia remains an important disease in the developed world —currently the 8th leading cause of death in the United States.[1]

The incidence of pneumonia is estimated at 47.4 per 1000 patients in Medicare beneficiaries, resulting in approximately 1.3 million hospitalizations each year.[2,3] Readmission rates within 30 days for patients hospitalized for pneumonia have been reported to be 12% to 20%[4–6] with 1 study reporting a median of 2 readmissions in 3280 patients over a median follow-up of 3.8 years.[7] Furthermore, patients who survive pneumonia have higher mortality rates relative to matched controls for up to 10 years, with older age and co-morbidities contributing to the higher level of mortality.[8–11]

Yet, there is very little published empirical evidence characterizing the various health care utilization trajectories after pneumonia hospitalization.[8,12] Although we know new-onset cognitive impairment occurs in some patients, we know relatively little about to what extent patients have differing courses of recurrent hospitalizations in the subsequent year.[4] Further, despite the growing attention to short-term readmissions (less than 30 days) under the Hospital Readmission Reduction Program in 2013, we have little information about the extent to which recurrent hospitalization in the year after pneumonia is influenced by health care delivery systems, as opposed to the patients' own biology and support systems.

In light of this gap, we sought to characterize the variation in patterns of re-hospitalization over 1 year among patients discharged alive from a hospitalization for pneumonia. We considered 3 patterns: uncomplicated recovery (surviving 1 year without re-hospitalization); a more typical recovery (survival with 1 hospitalization in the year); and complex or failed recovery

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(dying within 1 year of discharge or surviving with multiple hospitalizations). We asked: what is the frequency of each of these patterns? To what extent are these influenced by the healthcare system in which the hospitalization occur? We conducted parallel analyses in 3 different patient populations and health care systems: the uncoordinated system of fee-for-service Medicare (FFS) beneficiaries participating in the Health and Retirement Study (HRS); Veterans receiving care from the integrated Veterans Administration (VA) hospitals and health systems; and patients receiving care from the highly integrated Kaiser Permanente of Northern California (KPNC) delivery system.

2. Methods

2.1. Study populations

We obtained data from 3 separate hospitalization cohorts from the above-mentioned populations.

Data for FFS Medicare beneficiaries were drawn from the HRS, an ongoing, nationally representative, prospective cohort study of older Americans aged 50 and above.[13] Started in 1992, the HRS has enrolled over 35,000 participants; of those aged 65 and above, most have agreed to link their data with Medicare.[13] Participants with a hospitalization for pneumonia during 1998–2009 were included with a follow-up period until the end 2010 representing 908 hospitals. Additionally, the participants were required to have greater than 12 consecutive months of FFS Medicare coverage prior to their index hospitalization.

Data on Veterans in the VA health system were identified from the Corporate Data Warehouse files for 2013–2014 and represented over 100 hospitals. The Corporate Data Warehouse includes direct transaction records from the entire VA system; diagnostic codes are now audited and used for internal funds allocation processes.[14] It is one of the largest integrated health care systems in the world incorporating both outpatient and inpatient care. [15]

In contrast to both the FFS and the VA health system, KPNC is a community-based, geographically focused, integrated healthcare delivery system. Under a mutual exclusivity agreement, the 9000 physicians of The Permanente Medical Group, Inc., care for members of Kaiser Foundation Health Plan, Inc., at facilities operated by Kaiser Foundation Hospitals, Inc., using information systems operated by KP Information Technology. These information systems, which we have described previously, include a common electronic medical record known as KP HealthConnect.[16,17] KPNC currently serves 3.9 million members at 21 hospital-based medical centers and more than 200 medical offices.

Patients provided informed consent on enrollment in the HRS and again for linkage to Medicare. The University of Michigan institutional review board (IRB) approved the use of the HRS data for research. Analyses from the VA were approved by the IRB of the VA Ann Arbor Health System. Analyses from KPNC were approved by the KPNC IRB. Analyses were done separately for each cohort; no data transfer between institutions occurred.

2.2. Identification of pneumonia

We identified patients hospitalized for pneumonia by using a commonly employed validated method that requires International Classification of Diseases, 9th Edition, clinical modification (ICD-9-CM) coding for a principal diagnosis of pneumonia (480*x*, 481, 482*xx*, 483*x*, 485, 486, 487.0, where *x* indicates any value) or a principal diagnosis of septicemia (038.*x*, 785.52, 995.92, 995.91) or respiratory failure (518.81, 518.82, 518.84, 799.1) and a secondary diagnosis of pneumonia.[18–20] For patients who were transferred, the claims were merged to 1 hospitalization retaining the ICD9s from the first hospitalization.

2.3. Data abstraction

Hospital outcomes and rehospitalizations were abstracted from the same data sources as the index hospitalization for pneumonia. Demographics and comorbidities were abstracted from the index hospitalization for pneumonia as well as evaluation of inpatient and outpatient claims for the year prior to admission. Mortality data in the HRS were obtained from the National Death Index, in the VA from the Vital Status File, and in KPNC from KPNC hospitalization and membership databases, linked California death certificates, and the United States Social Security administration death master file. Charlson comorbidities were tabulated using the method of Deyo.[21,22]

2.4. Analysis plan

For descriptive statistics, we computed baseline characteristics from the index hospitalization. We present patient characteristics as counts (percentages), means (standard deviation [SD]), or medians (interquartile ranges [IQR]) as appropriate. An additional analysis was performed to compare the FFS cohort from 1998–2009 as compared to 2005–2009 (supplemental Table 1, http://links.lww.com/MD/B820). Because of the large sample sizes, we present differences between cohorts in Table 1 without testing for differences between the cohorts, as *P*-values may confuse statistically significant differences with clinically significant differences.[23]

We conducted all analysis with Stata software versions 13 and 14 (StataCorp, College Station, TX). We used hospitalization as the unit of analysis, unless otherwise specified. We used 2-sided significance testing and considered a *P* value less than 0.05 to be significant.

The median number of rehospitalizations following the index hospitalization was chosen as the reference group (typical recovery) in the multinomial logistic regression in order to test the hypothesis that different factors may influence the transition from complex or failed recovery to typical recovery and from typical to uncomplicated recovery. We performed a multinomial logistic regression to examine if any patient characteristics were associated with an uncomplicated recovery (alive with no hospitalizations for 1 year following discharge) or a complex or failed recovery (greater than 2 hospitalizations or death by 1 year) as compared to the typical recovery of 1 rehospitalization following the index hospitalization by evaluating the relative risk ratios (RRR). To account for multiple hospitalizations for pneumonia per person, we used a clustered sandwich estimator to adjust standard errors.[24,25] McFadden R^2 were calculated to account for the variance predicted by the models for each cohort.

3. Results

There were 2,731 hospitalizations for pneumonia in the FFS cohort; 23,536 in the VA cohort; and 39,147 in KPNC. FFS patients were older (mean age, 78.3 ± 10 years), majority female (52.1%), with a moderate comorbidity burden (Charlson Comorbidity Index median score 3, IQR 2–5). Median hospital

Table 1

Demographic information and hospitalization characteristics.

Demographic or hospitalization characteristics	VA (N = 23,536)	FFS (N = 2731)	KPNC (N = 39,147)
Years of data included	2013–2014	1998–2009	2010–2014
Number of hospitals	113	908	21
Age, mean, SD	70.7 (12.5)	78.3 (10)	71.8 (16.2)
Male, n, %	22,773 (97)	1153 (47.9)	19,367 (49.5)
Race/ethnicity, n, %			
White	18,145 (77)	1968 (81.8)	28,115 (71.8)
Black/African American	3648 (16)	347 (14.4)	3467 (8.9)
Other/missing	1743 (8)	92 (3.8)	7565 (19.3)
Charlson score, median, IQR	2 (1–3)	3 (2–5)	2 (1–3)
Hospital length of stay, d, median, IQR	4 (3–8)	5 (3–8)	3.7 (2.1–6.5)
Admitted to intensive care unit, n, %	1034 (4.0)	372 (15.5)	10,834 (27.7)

FFS = Fee for Service, KPNC = Kaiser Permanente Northern California, IQR = interquartile range 25–75%, SD = standard deviation, VA = Veterans Administration.

length of stay was 5 days (IQR, 3–18 d). Veteran patients were predominately white (77%), male (97%), and had a mean age of 70 (SD, 12.5). KPNC patients were 50.5% female with a mean age of 71.8 (SD 16.2) years, with a lower comorbidity burden (Charlson Comorbidity Index median score 2, IQR 1–3). (Table 1; see also Supplemental Table 1, http://links.lww.com/MD/B820 which shows data for just 2005–9 FFS, with no substantive differences.)

In the FFS cohort, 9% of all patients who survived pneumonia experienced 2 rehospitalizations and a full year of survival (Fig. 1; see also Supplemental Figure 1, http://links.lww.com/MD/B820 which shows data for just 2005–9 FFS, with no substantive differences). One-third (33.3%) died within the next year. Of those who survived the full year, 29.8% were never hospitalized again, suggesting an uncomplicated recovery. There was also a subgroup who were repeatedly hospitalized, yet still survived a full year—with 11.9% hospitalized at least 3 times.

In the VA, 14.1% of the patients were hospitalized once in the year after discharge and survived. As in FFS, one-third (30.2%) died within the next year. Of those who survived the full year, 35.9% were never hospitalized again. As in FFS, a subgroup was repeatedly hospitalized; 11.9% survived a full year but were hospitalized at least 3 times.

Only 9.1% of patients in KPNC, as in the VA, experienced 1 hospitalization and a full year of survival. One quarter (26.8%) died within the next year with only 2 patients dying within 1 day of the index hospitalization. However, 46.1% were never hospitalized again. There was again a subgroup who was repeatedly hospitalized yet survived a full year—with 11.7% being hospitalized at least 3 times.

Among pneumonia patients discharged alive, older patients and those with more comorbidity were more likely to have a complex or failed recovery (Table 2). Greater lengths of stay were associated with increased likelihood of poor outcomes in FFS and VA, but did not influence the odds of better-than-typical recovery. Although the magnitude varied, the direction and significance of association were similar across all systems. However, these baseline characteristics did not capture much of the variance as reflected by the McFadden R^2 values of 7%, 6%, and 5% in the FFS, KPNC, and VA cohorts, respectively.

4. Discussion

Our data suggest that recovery after a hospitalization for pneumonia can take several different forms. Further, the distribution of recovery experiences following a hospitalization for pneumonia is quite similar despite the 3 different major US health systems. Broadly speaking, one-third of patients die in the year after a hospitalization for pneumonia, evidence of failed recovery. About one-third have a complex recovery, requiring at

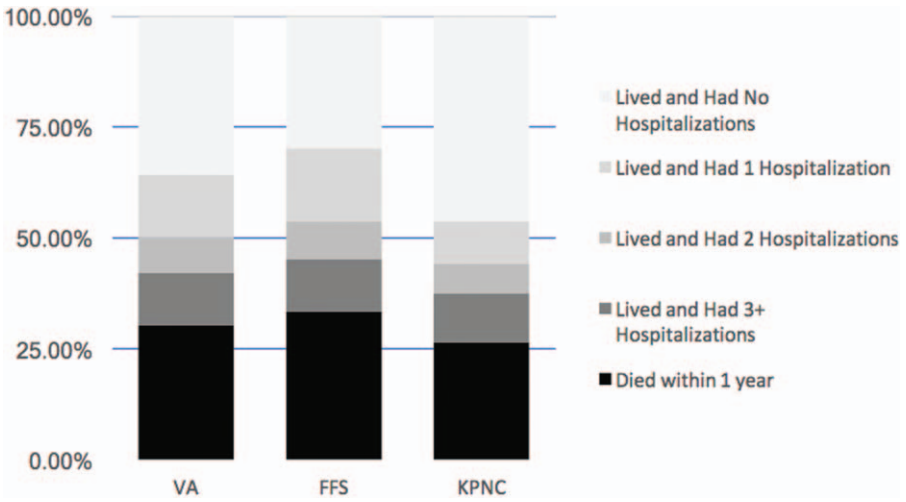

Figure 1. Distribution of patient outcomes following index hospitalization for pneumonia per health system.

Table 2

Association of patient-level characteristics with uncomplicated and complex or failed recoveries than typical recoveries from a multivariable logistic regression, compared to the experience of those only hospitalized once.

	Outcomes following Index Hospitalization compared to the experience of those only hospitalized once											
	FFS				VA				KPNC			
McFadden R^2	7%				5%				6%			
	Uncomplicated recovery		Complex or failed recovery		Uncomplicated recovery		Complex or failed recovery		Uncomplicated recovery		Complex or failed recovery	
	RRR	95%CI	RRR	95%CI	RRR	95% CI	RRR	95% CI	RRR	95% CI	RRR	95% CI
Age, per year	**0.98**	**0.97–1.00**	**1.02**	**1.00–1.03**	**0.99**	**0.98–1.00**	**1.02**	**1.02–1.02**	**0.99**	**0.99–0.99**	**1.02**	**1.01–1.02**
Race:												
African American, vs White	0.82	0.56–1.19	0.99	0.69–1.43	1.03	0.92–1.12	1.01	0.89–1.13	0.90	0.79–1.03	**1.17**	**1.02–1.35**
Other, vs White	0.81	0.46–1.41	0.92	0.49–1.72	1.12	0.80–1.57	1.06	0.75–1.49	1.02	0.92–1.12	0.93	0.84–1.03
Gender: female, vs male	0.90	0.70–1.15	0.84	0.65–1.09	1.09	0.87–1.35	**0.70**	**0.55–0.90**	1.04	0.96–1.12	0.95	0.88–1.02
ICU, vs ward	0.89	0.60–1.30	1.02	0.72–1.46	0.91	0.73–1.11	1.02	0.83–1.26	**0.80**	**0.73–0.88**	1.0	0.91–1.10
LOS, per day	1.01	0.98–1.05	**1.07**	**1.04–1.10**	0.91	0.73–1.12	**1.02**	**1.01–1.03**	**0.99**	**0.99–1.00**	1.00	1.00–1.00
Charlson Index, per point	**0.88**	**0.83–0.93**	**1.17**	**1.11–1.22**	**0.91**	**0.88–0.93**	**1.18**	**1.15–1.20**	**0.92**	**0.89–0.95**	**1.39**	**1.35–1.44**

CI = confidence intervals, FFS = Fee for Service, ICU = intensive care units, KPNC = Kaiser Permanente Northern California, RRR = relative risk ratio, LOS = length of stay, VA = Veterans Administration.
The comparison group for each cohort was patients whose recovery was notable for 1 rehospitalization following their index admission for pneumonia.
The P value is < .05 and is statistically significant.

least 1 re-hospitalization. About one-third of patients (half of those who survive the year) do so without any need for rehospitalization suggesting an uncomplicated recovery.

Such heterogeneity is the norm in biology. In a paper entitled “The median isn't the message,” Stephen J Gould wrote regarding his own expected clinical course after a diagnosis of abdominal mesothelioma, “Variation is the hard reality, not a set of imperfect measures for a central tendency. Means and medians are the abstractions.”[26] By this he meant that the population median or mean may rarely characterize an individual patient's experience. Our data suggest that fewer than 1 in 5 patients across 3 large health systems experience the median, making it a poor tool for prognostication and thus potentially misleading in the context of advice given to individual patients. Our data also suggest important similarities in patterns of recovery after pneumonia across health systems, opening the possibility of robust cross-system aids in prognostication. Although there is some variation in the median between health systems—1 rehospitalization in VA and KPNC versus 2 in FFS—the similarities in the distributions in Fig. 1 are to us more striking; nonetheless, the reasons for these differences are not clearly explained by standard risk factors and warrant further exploration.

Accurate prognostication is critical to guiding medical management. The expected prognosis directs treatment recommendations and shared decision-making, whereas deviations from the expected course prompt providers to investigate alternative diagnoses. A substantial evidence-base informs prognostication during the acute phase of pneumonia, including duration of cough,[27] time until blood culture positivity if bacteremic,[28] duration of illness until clinical stability,[29–33] and time to expected radiographic resolution.[34,35] Yet the low variance explained by conventional risk factors in our data across each of 3 different systems suggests that individualized, precision prognostication regarding subsequent health remains elusive for patients surviving hospitalization for pneumonia.

Although heterogeneity in prognosis and outcomes is not unexpected, understanding the extent of the heterogeneity and the factors driving it is an important step in beginning to identify the different patient phenotypes who may benefit from different interventions. The varied patterns of recovery after pneumonia suggest the need for—and potential yield of—mechanistic studies to uncover the processes generating these patterns. Our analyses support the notion that 2 broad hypotheses on what is the nature of post-pneumonia trajectories exist. The first is that a limited set of distinct recovery trajectories exists. Alternatively, it may be that each patient has a unique path of recovery informed by stochastic and unpredictable (but potentially quantifiable) additional factors, which could be favorable or unfavorable.

These hypotheses have distinct implications. If there are a handful of characterizable trajectories, then early detection of a patient's trajectory, followed by personalized intervention and prognostication based on that trajectory may be possible—a proactive approach to recovery. On the other hand, if recovery is largely driven by (randomly distributed) favorable or unfavorable factors, then the analysis of these factors, rather than of trajectories, should receive priority.

Our data also suggest the value of prognostic information to address multiple potential outcomes, not merely the risk of 1 extreme state of death. Indeed, the results of our multinomial regression suggest that a simple ordinal model, that assumes that morbidity and mortality are neatly arranged on a single dimension, may poorly fit the data. Information on the likely

post-pneumonia course(s) would enable informed, shared decision-making regarding advanced directives and selection of further treatments. Such information might not only improve the care of pneumonia survivors, but also limit the burden for spouses and care-takers who participate in these weighty decisions. Until such information is available, our uncertainty regarding anticipated recovery should be acknowledged and reflected in our prognostication.

Our work is not without limitations. We have studied pneumonia as diagnosed by physicians in situ; we have not and could not arbitrate pneumonia cases across such a wide range of hospitals and health systems. However, we used a standard validated definition to identify hospitalizations for pneumonia. Likewise, we do not have reliable information on the causative organisms or treatment regiments used. It is likely that aspects of the hospital course beyond ICU use and length of stay are associated with—indeed, may cause—different aspects of recovery. Unfortunately, existing literature and data sources neither let us characterize that well, nor allow us to understand the relationship between these rehospitalizations and other patient-centered aspects of recovery, such as disability and cognitive functioning.

We have shown that patients experience markedly different patterns of recovery in the year after a hospitalization for pneumonia. Older age, increased length of hospital stay, and greater comorbidity burden are weakly associated with a complex or failed recovery. Our current models, however, have limited ability to predict the likely recovery path for an individual patient. Understanding the likely recovery trajectory will assist clinicians, patients, and caregivers to prepare for possible challenges that may be encountered during recovery and facilitate conversations about prognostication and advanced care planning.

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References

[1] Heron M. Deaths: Leading Causes for 2013. Natl Vital Stat Rep 2016; 65:1–95.
[2] Thomas CP, Ryan M, Chapman JD, et al. Incidence and cost of pneumonia in medicare beneficiaries. Chest 2012;142:973–81.
[3] Niederman MS. Community-acquired pneumonia: the U.S. perspective. Semin Respir Crit Care Med 2009;30:179–88.
[4] Jasti H, Mortensen EM, Obrosky DS, et al. Causes and risk factors for rehospitalization of patients hospitalized with community-acquired pneumonia. Clin Infect Dis 2008;46:550–6.
[5] Lindenauer PK, Bernheim SM, Grady JN, et al. The performance of US hospitals as reflected in risk-standardized 30-day mortality and readmission rates for medicare beneficiaries with pneumonia. J Hosp Med 2010;5:E12–8.
[6] Prescott HC, Sjoding MW, Iwashyna TJ. Diagnoses of early and late readmissions after hospitalization for pneumonia. A systematic review. Ann Am Thorac Soc 2014;11:1091–100.
[7] Johnstone J, Eurich DT, Majumdar SR, et al. Long-term morbidity and mortality after hospitalization with community-acquired pneumonia: a population-based cohort study. Medicine (Baltimore) 2008;87:329–34.
[8] Eurich DT, Marrie TJ, Minhas-Sandhu JK, et al. Ten-year mortality after community-acquired pneumonia. A prospective vohort. Am J Respir Crit Care Med 2015;192:597–604.
[9] Kaplan V, Clermont G, Griffin MF, et al. Pneumonia: still the old man's friend? Arch Intern Med 2003;163:317–23.
[10] Bordon J, Wiemken T, Peyrani P, et al. Decrease in long-term survival for hospitalized patients with community-acquired pneumonia. Chest 2010;138:279–83.
[11] Waterer GW, Kessler LA, Wunderink RG. Medium-term survival after hospitalization with community-acquired pneumonia. Am J Respir Crit Care Med 2004;169:910–4.
[12] Davydow DS, Hough CL, Levine DA, et al. Functional disability, cognitive impairment, and depression after hospitalization for pneumonia. Am J Med 2013;126:615–24. e615.
[13] Sonnega A, Faul JD, Ofstedal MB, et al. Cohort profile: the Health and Retirement Study (HRS). Int J Epidemiol 2014;43:576–85.
[14] Fihn SD, Francis J, Clancy C, et al. Insights from advanced analytics at the Veterans Health Administration. Health Aff (Millwood) 2014;33: 1203–11.
[15] Render ML, Kim HM, Deddens J, et al. Variation in outcomes in Veterans Affairs intensive care units with a computerized severity measure. Crit Care Med 2005;33:930–9.
[16] Escobar GJ, Gardner MN, Greene JD, et al. Risk-adjusting hospital mortality using a comprehensive electronic record in an integrated health care delivery system. Med Care 2013;51:446–53.
[17] Selby JV. Linking automated databases for research in managed care settings. Ann Intern Med 1997;127(8 Pt 2):719–24.
[18] Aronsky D, Haug PJ, Lagor C, et al. Accuracy of administrative data for identifying patients with pneumonia. Am J Med Qual 2005;20:319–28.
[19] Dean NC, Bateman KA, Donnelly SM, et al. Improved clinical outcomes with utilization of a community-acquired pneumonia guideline. Chest 2006;130:794–9.
[20] Rothberg MB, Pekow PS, Priya A, et al. Variation in diagnostic coding of patients with pneumonia and its association with hospital risk-standardized mortality rates: a cross-sectional analysis. Ann Intern Med 2014;160:380–8.
[21] Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613–9.
[22] Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
[23] Kramer AA, Zimmerman JE. Assessing the calibration of mortality benchmarks in critical care: The Hosmer–Lemeshow test revisited. Crit Care Med 2007;35:2052–6.
[24] Rabe-Hesketh S, Skrondal A. Multilevel and Longitudinal Modeling Using Stata. Stata Press Publication, College Station, TX:2012.
[25] Molenberghs G, Verbeke G. SpringerLinkModels for Discrete Longitudinal Data. Springer, New York, London:2005.
[26] Gould SJ. The median isn't the message. Virtual Mentor 2013;15:77–81.
[27] Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(suppl 2):S27–72.
[28] Doern GV, Brueggemann AB, Dunne WM, et al. Four-day incubation period for blood culture bottles processed with the Difco ESP blood culture system. J Clin Microbiol 1997;35:1290–2.
[29] Akram AR, Chalmers JD, Taylor JK, et al. An evaluation of clinical stability criteria to predict hospital course in community-acquired pneumonia. Clin Microbiol Infect 2013;19:1174–80.
[30] Halm EA, Fine MJ, Marrie TJ, et al. Time to clinical stability in patients hospitalized with community-acquired pneumonia: implications for practice guidelines. JAMA 1998;279:1452–7.
[31] Menendez R, Torres A, Rodriguez de Castro F, et al. Reaching stability in community-acquired pneumonia: the effects of the severity of disease, treatment, and the characteristics of patients. Clin Infect Dis 2004;39:1783–90.
[32] Aliberti S, Peyrani P, Filardo G, et al. Association between time to clinical stability and outcomes after discharge in hospitalized patients with community-acquired pneumonia. Chest 2011;140:482–8.
[33] Aliberti S, Zanaboni AM, Wiemken T, et al. Criteria for clinical stability in hospitalised patients with community-acquired pneumonia. Eur Respir J 2013;42:742–9.
[34] Marrie TJ. Normal resolution of community-acquired pneumonia. Semin Respir Infect 1992;7:256–70.
[35] Lim WS, Baudouin SV, George RC, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax 2009;64(suppl 3):iii1–55.