Research Article

Antibiotic Prescriptions for Upper Respiratory Infection in the Emergency Department: A Population-Based Study

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Study Objective. Antibiotics prescriptions for upper respiratory infections (URI) are not uncommon, but the benefits for these groups had seldom been evaluated. We aimed to utilize a sampled National Health Insurance (NHI) claims data containing one million beneficiaries to explore if the use of antibiotics could reduce the possibility of unscheduled returns. **Methods.** We identified patients presented to ambulatory clinics with the discharged diagnoses of URI. The prescriptions of antibiotics were identified. We further matched each patient in the antibiotic group to the patient in the control group by selected covariates using a standard propensity score greedy-matching algorithm. The risks of unscheduled revisits were compared between the two groups. **Results.** A total of 6915140 visits were identified between 2005 and 2010. The proportions of antibiotics prescriptions are similar among these years, ranging from 9.99% to 13.38 %. In the propensity score assignment, 9190 patients (4595 in each group) were further selected. The odds ratio of unscheduled revisits among antibiotics group and control group was 0.92 (95% CI, 0.70–1.22) with *P* value equal to 0.569. **Conclusions.** Overall, antibiotics prescriptions did not seem to decrease the unscheduled revisits in patients presented to the ED with URI. Emergency physicians should reduce the unnecessary prescriptions and save antibiotics to patients with real benefits.

1. Introduction

For every clinician, whetherto treat adult patients with upper respiratory tract infections (URIs) with antibiotics was daily encountered clinical dilemma. It had been shown that oral antibiotic seldom had real therapeutic effect for acute bronchitis, since virus was the most common pathogen [1]. Overly prescribed antibiotics benefit patients little but raise the possibility of antimicrobial resistance and increase the medical cost. Recent guideline suggests that a period of observation without antibiotics use for most of URIs was reasonable and was associated with reducing the inappropriate

use [2]. Nevertheless, in 2012, a study based in the emergency departments (EDs) still revealed that 74.0% of thecases of acute bronchitis in adults were discharged with antibiotics [3]. This discrepancy suggested that either there was significant gap for knowledge translation or reflected the reality that clinicians have other considerations on this issue.

It has been found that, although most of time unnecessary, oral antibiotics use for URIs may fulfill patient expectations and increase satisfaction [4]. Since patient dissatisfaction was frequently associated with unscheduled returns [5], we hypothesized that antibiotic use might reduce unscheduled returns by shortening the disease course. To date, there

has been no research existing to prove the effectiveness of such strategy. This study utilized large-scale administrative data to explore the associations between antibiotics use for URI and unplanned return visits after index visits. Results of this study would provide clinicians with further insight on this frequently encountered situation.

2. Materials and Methods

2.1. Study Setting. The National Health Insurance program, which provides compulsory universal health insurance, was implemented in Taiwan in 1995. It enrolls up to 99% of the Taiwanese population and contracts with 97% of all medical providers [6, 7]. The database contains comprehensive information on insured subjects, including dates of clinical visits, diagnostic codes, details of prescriptions, and expenditure amounts. A random sample with 1,000,000 people based on the 2005 reimbursement data was established for public access, and the group did not differ statistically significantly from the larger cohort in age, gender, or health care costs, as reported by the Taiwan National Health Research Institute [8]. The sampled group was used as our study cohort. Since all identifying personal information was stripped from the secondary files before analysis, the Institutional Review Board of Buddhist Dalin Tzu Chi General Hospital, Taiwan, waived the requirement for written informed consent from the patients involved.

2.2. Patients. We identified patients older than 18 years who visited ambulatory clinics during 2005–2010 with a diagnosis of URIs (ICD-9-CM 490 and 465-466.19). Unscheduled returns were defined if the patients came back to any clinic in Taiwan with URIs and the interval of adjacent visits was shorter than the days of prescriptions. Use of any kind of oral antibiotics available in Taiwan was identified (i.e., Cephalexin, Cephadrine, Cefaclor, Cefibuten, Azithromycin, Clarithromycin, Erythromycin, Penicillin, Dicloxacillin, Amoxicillin, Amoxicillin and clavulanic acid, Sultamicillin, Ciprofloxacin, Gemifloxacin, Levofloxacin, Moxifloxacin, Nitroxoline, Norfloxacin, Sulfamethoxazole and trimethoprim, Doxycycline, Minocycline, Tetracycline, Clindamycin, Fosfomycin, and Metronidazole). The following covariates were also retrieved for each patient: age, sex, socioeconomic status (SES), smoking status, hypertension, coronary artery disease (CAD), asthma, chronic obstructive pulmonary disease (COPD), diabetes, and Charlson Comorbidity Index Score (CCIS) [9, 10]. The insurance enrollee category was used as a proxy measure of SES. Patients receiving antibiotics would be classed into the antibiotic group; patients who did not receive antibiotics during visits would be labeled as the control group.

2.3. Propensity Score Methods. In this study, the propensity score was the conditional probability for using antibiotics under possible confounders. We used the generalized estimating equation (GEE) method [11] to account for potential clustering among health care facilities and individual patients. Age, sex, SES, urbanization, smoking

status, hypertension, CAD, asthma, COPD, diabetes, and CCIS were added into a multivariable logistic regression model to predict the effect of antibiotic prescription [12]. The predicted probability from the model was used as the propensity score for each patient. We then matched each patient in the antibiotic group to the patient in the control group with the closest propensity score using a standard greedy-matching algorithm [13–15]. After the 1:1 matched groups were assembled, the primary outcome was compared accordingly.

2.4. Statistical Analysis. Continuous variables were compared with the *t*-test and categorical variables with the χ^2 test. Ninety-five percent confidence interval (CI) and *P* value were reported. *P* < 0.05 was considered significant. All analyses were performed using Statistical Analysis Software for Windows, version V.9.2 (SAS Institute Inc, Cary, NC).

3. Results

We identified 6915140 episodes of URIs during the 6-year study period. There were 406042 patients (5.87%) in the antibiotic group and 6509098 (94.13%) in the control group. The frequencies of antibiotics in the visits with diagnoses of URIs during the six years were 6.8%, 5.5%, 5.7%, 5.6%, 5.5%, and 6.0%, respectively. The baseline characteristics of both groups are shown in Table 1. Before adjustment for possible confounding variables, the mean age and the overall CCIS in the antibiotic group are higher than the control group, and so the total costs. The rates of unscheduled returns are similar between the two groups before adjusting for covariates (2.1% versus 2.4%, *P* value = 0.1684).

In the propensity score assignment, the possible covariates mentioned above were added into the multivariable generalized estimating equation (GEE) model to predict the possibility of antibiotic use. The propensity score-matching process selected 4595 patients from the antibiotic group and the other 4595 from the control group for further analysis. Baseline characteristics were similar in the 2 groups (Table 2). In the propensity score-matched subcohort, the antibiotic use was again not found to be associated with decreased unscheduled returns compared with the control group (2.1% versus 2.3%, *P* value = 0.5692). Of note, antibiotic use was associated with higher medical costs before and after adjusting for covariates.

3.1. Limitations. Several limitations rise when using insurance reimbursement database. First, the selection bias occurred when the inclusion criteria were based on doctor entry disease coding. When prescribing antibiotics for patients with URIs, the physician might intentionally discard any code related with URIs for fearing of being censored by peer review, which would not only be withholding the reimbursement but also eliciting financial penalties under Bureau of National Health Insurance's policy. It was impossible for investigators to have any information of those omitted patients; therefore, it would not be able to confirm the direction of the bias. However, it was hard to believe that any

TABLE 1: Baseline characteristics of the antibiotic group and the control group.

Variables	Antibiotic group (n = 5800)		Control group (n = 44597)		P value
	No.	%	No.	%	
Male	2585	45.43	19499	44.80	0.367
Patient age (SD)	46.02	20.51	41.70	18.94	<0.001
Socioeconomic status					0.074
Low	2807	49.33	20894	48.00	
Moderate	2133	37.49	16487	37.88	
High	750	13.18	6146	14.12	
Smoking status	125	2.16	1118	2.51	0.104
Hypertension	1980	34.14	12557	28.16	<0.001
CAD	1211	20.88	7669	17.20	<0.001
Asthma	1260	21.72	8335	18.69	<0.001
COPD	911	15.71	4703	10.55	<0.001
Diabetes	1139	19.64	7170	16.08	<0.001
Charlson Comorbidity Index Score					<0.001
0	1438	24.79	14101	31.62	
1	1812	31.24	14281	32.02	
≥2	2550	43.97	16215	36.36	
Total costs (SD)	79.61	79.94	46.31	44.46	<0.001
Unscheduled returns	121	2.09	1150	2.58	0.024

TABLE 2: Baseline characteristics of the propensity score-matched subcohort.

Variables	Antibiotic group (n = 5733)		Control group (n = 5733)		P value
	No.	%	No.	%	
Male	2556	45.46	2461	43.77	0.072
Patient age (SD)	45.86	20.45	45.69	20.37	0.648
Socioeconomic status					0.247
Low	2763	49.14	2825	50.24	
Moderate	2112	37.56	2105	37.44	
High	748	13.3	693	12.32	
Smoking status	122	2.13	102	1.78	0.177
Hypertension	1949	34.00	1984	34.61	0.491
CAD	1180	20.58	1141	19.90	0.365
Asthma	1221	21.30	1264	22.05	0.330
COPD	874	15.25	889	15.51	0.700
Diabetes	1111	19.38	1179	20.57	0.112
Charlson Comorbidity Index Score					0.948
0	1438	25.08	1435	25.03	
1	1798	31.36	1814	31.64	
≥2	2497	43.55	2484	43.33	
Total costs (SD)	78.70	75.96	49.67	46.28	<0.001
Unscheduled returns	121	2.11	152	2.65	0.058

clinical benefit would ever exist in this group, since physicians were not confident enough to justify the use of the antibiotics.

Second, for the same reason, some physicians may adopt another strategy by intentionally not claiming antibiotics when the diagnoses including URIs, especially if the drug is cheap. The “antibiotics give away” practice caused

misclassification bias, which diluted the potential benefit of antibiotics prescriptions and biased the study result toward null. However, considering the very closed point of estimation between propensity score-matched group (2.1% versus 2.3%) and the strong power of this study, it would require significant misclassification for the results to be changed.

Third, our studies included patients with a primary diagnosis of several URIs. Technically speaking, a priori subgroup analysis for each individual diagnosis can be performed; however, the retrospective design made it difficult to access the magnitude of misclassification bias on diagnosis accuracy. Although drugs prescription should take individual risk and benefit into account, we believe that, as a whole, all included patients shared a common disease entity and the message delivered by this study has its practical clinical implication.

4. Discussion

In this study, we found that adult patients who were discharged from ED with or without antibiotic prescriptions for URIs had similar rate of unscheduled return visits. After being adjusted for predefined confounders, rates of return visits were not significantly different between groups, and the fact that antibiotics group cost more in total expenditure further dissuade the antibiotics use for the purpose.

Under the circumstance of ED overcrowding, EPs generally would like to decrease preventable return visits. Medical errors, inadequate physician-patient communication, and lack of proper observation duration were reported as factors contributing to return ED visits [5, 16, 17]. Giving antibiotics may decrease the rate of return visits through its real therapeutic effect or improving patient satisfaction (i.e., placebo effect). This study, empowered by large-scale population data, yet failed to prove that prescribing antibiotics was an effective method to prevent return visits.

The yearly antibiotics prescription rate in this study was ranging from 10.0% to 13.4% over the 5-year period. To our knowledge, there was no benchmark existing for the rate. Even from public health point of view, it can be definitely said that 0% was not an ideal goal since antibiotics may be helpful, especially for individuals with significant comorbidities, with prolonged fever, or at extreme ages. However, it should also be noticed that, for target population, even 1% drop would lead to significant resource saving, needless to say the impact on antibiotics resistance. EPs who are aware of this study would realize that antibiotics should not be given to patients with URIs solely for the purpose of return visits avoidance.

Generally speaking, a well-executed double-blinded, randomized controlled trial would be the best way to test the hypothesis associated with treatment choices; however, since the “placebo effect” may also contribute to the avoidance of return visits, it was undesirable to use the double blind design unless only the pharmacological effect was concerned. By the way, a randomized control trial with primary end point not related to true therapeutic effect but just frequency of unscheduled visits would not be ethically sound. We constructed a retrospective cohort from administrative data and applied propensity score to account for possible confounding factors, such as age, gender, and comorbidities. Although residual confounding may exist, we do not think that it would alter the study results.

The advantage of using the population-based database was that the study could have enough power, despite that the baseline return visits rate was low and the expected difference

between groups was small. The external validity was excellent since the database had been already verified by previous study [18]. Unless there will be significant access barrier to ED service (i.e., raise of registration fee), the conclusion of the study will not be easily biased in the next decade.

5. Conclusions

For adult patients, antibiotics prescriptions written for URIs increase total cost without reducing the rate of unscheduled ED return visits.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

- [1] V. Snow, C. Mottur-Pilson, and R. Gonzales, “Principles of appropriate antibiotic use for treatment of acute bronchitis in adults,” *Annals of Internal Medicine*, vol. 134, no. 6, pp. 518–520, 2001.
- [2] D. M. Wong, D. A. Blumberg, and L. G. Lowe, “Guidelines for the use of antibiotics in acute upper respiratory tract infections,” *American Family Physician*, vol. 74, no. 6, pp. 956–969, 2006.
- [3] J. C. Kroening-Roche, A. Soroudi, E. M. Castillo, and G. M. Vilke, “Antibiotic and bronchodilator prescribing for acute bronchitis in the emergency department,” *Journal of Emergency Medicine*, vol. 43, no. 2, pp. 221–227, 2012.
- [4] C. R. Stearns, R. Gonzales, C. A. Camargo Jr., J. Maselli, and J. P. Metlay, “Antibiotic prescriptions are associated with increased patient satisfaction with emergency department visits for acute respiratory tract infections,” *Academic Emergency Medicine*, vol. 16, no. 10, pp. 934–941, 2009.
- [5] S. Nuñez, A. Hexdall, and A. Aguirre-Jaime, “Unscheduled returns to the emergency department: an outcome of medical errors?” *Quality and Safety in Health Care*, vol. 15, no. 2, pp. 102–108, 2006.
- [6] Y. K. Lee, C. C. Lee, C. C. Chen, C. H. Wong, and Y. C. Su, “High risk of “failure” among emergency physicians compared with other specialists: a nationwide cohort study,” *Emergency Medicine Journal*, vol. 30, no. 8, pp. 620–622, 2013.
- [7] Y. K. Lee, S. W. Hou, C. C. Lee, C. Y. Hsu, Y. S. Huang, and Y. C. Su, “Increased risk of dementia in patients with mild traumatic brain injury: a nationwide cohort study,” *PLoS ONE*, vol. 8, Article ID e62422, 2013.
- [8] S. W. Hou, Y. K. Lee, C. Y. Hsu, C. C. Lee, and Y. C. Su, “Increased risk of acute pancreatitis in patients with chronic hemodialysis: a 4-year follow-up study,” *PLoS ONE*, vol. 8, Article ID e71801, 2013.
- [9] M. E. Charlson, P. Pompei, K. A. Ales, and C. R. MacKenzie, “A new method of classifying prognostic comorbidity in longitudinal studies: development and validation,” *Journal of Chronic Diseases*, vol. 40, no. 5, pp. 373–383, 1987.
- [10] R. A. Deyo, D. C. Cherkin, and M. A. Ciol, “Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases,” *Journal of Clinical Epidemiology*, vol. 45, no. 6, pp. 613–619, 1992.

- [11] S. L. Zeger, K.-Y. Liang, and P. S. Albert, "Models for longitudinal data: a generalized estimating equation approach," *Biometrics*, vol. 44, no. 4, pp. 1049–1060, 1988.
- [12] Z. L. Zhehui Luo, J. C. Gardiner, and C. J. Bradley, "Applying propensity score methods in medical research: pitfalls and prospects," *Medical Care Research and Review*, vol. 67, no. 5, pp. 528–554, 2010.
- [13] J. D. Seeger, P. L. Williams, and A. M. Walker, "An application of propensity score matching using claims data," *Pharmacoepidemiology and Drug Safety*, vol. 14, no. 7, pp. 465–476, 2005.
- [14] H.-L. Guan, H.-Y. Lin, Y.-K. Lee, C.-Y. Hsu, and Y.-C. Su, "Early endoscopy can shorten the duration of hospitalization in suspected variceal hemorrhage," *ISRN Emergency Medicine*, vol. 2013, Article ID 839126, 6 pages, 2013.
- [15] Y. K. Lee, C. C. Chen, H. Y. Lin, C. Y. Hsu, and Y. C. Su, "Propofol for sedation can shorten the duration of ED stay in joints reduction," *The American Journal of Emergency Medicine*, vol. 30, no. 8, pp. 1352–1356, 2012.
- [16] S. N. Hastings, A. Barrett, M. Weinberger et al., "Older patients' understanding of emergency department discharge information and its relationship with adverse outcomes," *Journal of Patient Safety*, vol. 7, no. 1, pp. 19–25, 2011.
- [17] I. Imsuwan, "Characteristics of unscheduled emergency department return visit patients within 48 hours in Thammasat University Hospital," *Journal of the Medical Association of Thailand*, vol. 94, supplement 7, pp. S73–S80, 2011.
- [18] J.-J. Sheu, H.-Y. Chiou, J.-H. Kang, Y.-H. Chen, and H.-C. Lin, "Tuberculosis and the risk of ischemic stroke: a 3-year follow-up study," *Stroke*, vol. 41, no. 2, pp. 244–249, 2010.