



Background

Recurrent cellulitis is a vexing clinical problem with huge financial burden on healthcare resources. Though intramuscular antibiotics had been suggested as a prevention strategy but the evidence is scarce.

Methods

We conducted a cohort study by using Taiwan's National Health Insurance Research Database (NHIRD) between 2000 and 2008. Patients received intramuscular benzathine penicillin 2.4 MU every 4 weeks at least three prescriptions within half a year were enrolled and followed for one year since the first dose. (Figure 1) The prevention efficacy was determined by comparing the incidence of recurrent cellulitis in the prophylactic period to non-prophylactic period in each enrolled subject by a Poisson regression model. The prophylactic period was defined as 4 weeks after the date of each dose of benzathine penicillin injection and non-prophylactic period was the time not covered by penicillin during the follow-up period.

Table 1. Demographic characteristics of cases and matched controls in index date

	without prophylaxis (N=823) N(%)	with prophylaxis (N=206) N(%)	P Value
Gender(Male)	452 (54.92)	120 (58.25)	0.3894
Age*	62.20 (17.19)	63.59 (16.51)	0.2961
<65	394 (47.87)	95 (46.12)	0.6515
≥65	429 (52.13)	111 (53.88)	
No. of comorbidities			
No	422 (51.28)	59 (28.64)	<.0001
1	247 (30.01)	79 (38.35)	
≥2	154 (18.71)	68 (33.01)	
Diabetes mellitus	230 (27.95)	73 (35.44)	0.0349
Chronic renal failure	38 (4.62)	15 (7.28)	0.1218
Congestive heart failure	38 (4.62)	19 (9.22)	0.0097
Obesity	5 (0.61)	5 (2.43)	0.0322
Cirrhosis	38 (4.62)	8 (3.88)	0.6486
Impaired venous drainage	63 (7.65)	20 (9.71)	0.333
Malignancy of lower extremity	21 (2.55)	7 (3.4)	0.5043
Previous fracture	2 (0.24)	0 (0)	1.0000
Joint replacement of lower extremity	46 (5.59)	13 (6.31)	0.6904
Previous myocardial infraction	12 (1.46)	6 (2.91)	0.2282
Open chest coronary artery angioplasty	0 (0)	0 (0)	
Tinea pedis	113 (13.73)	69 (33.5)	<0.0001

Figure 1.

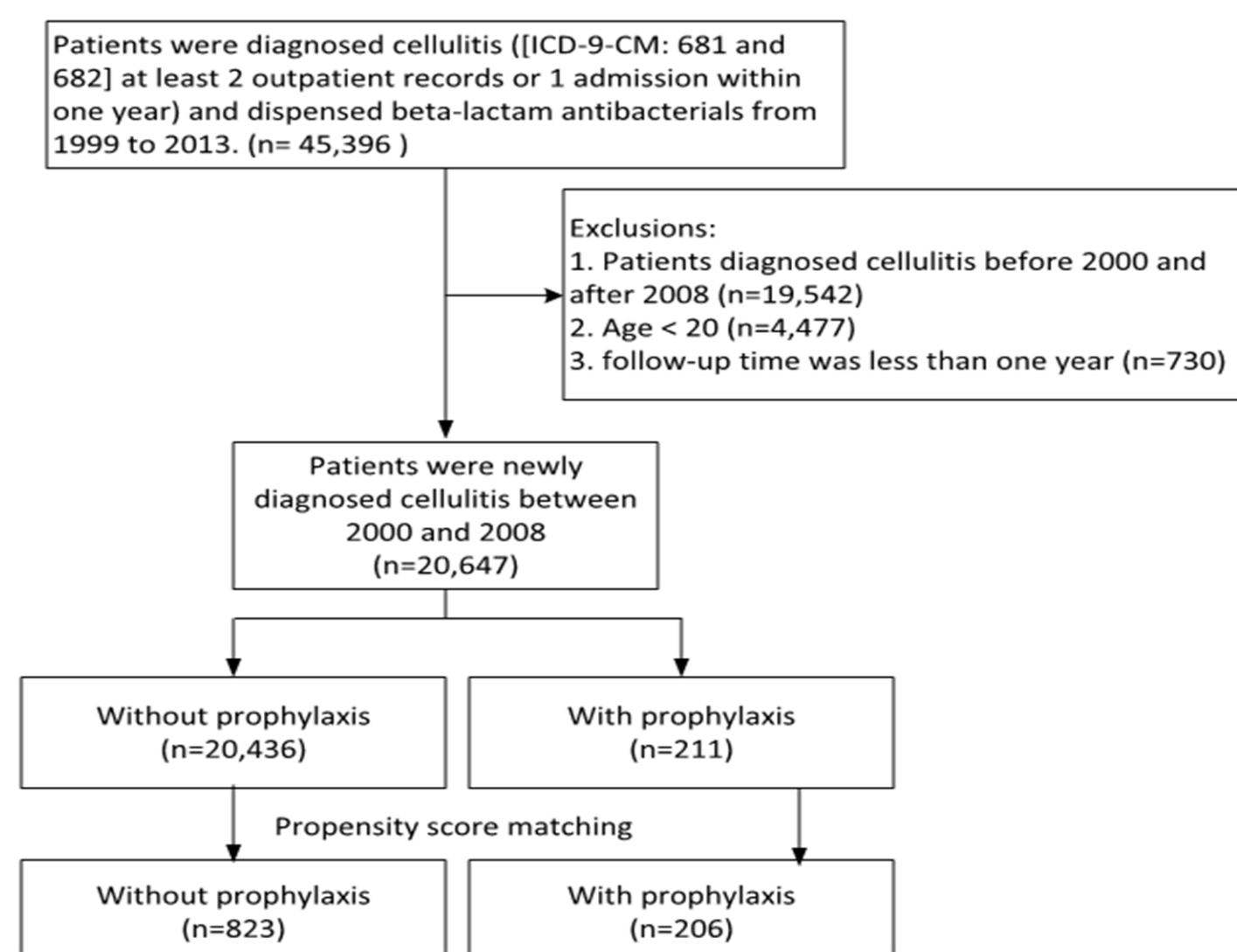


Figure 2.

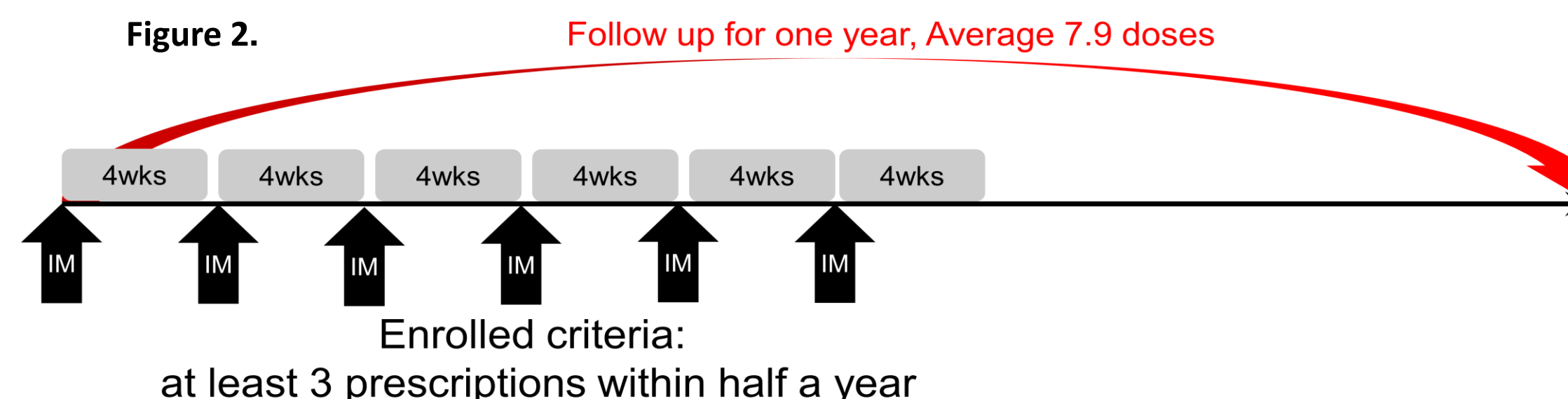


Figure 3.

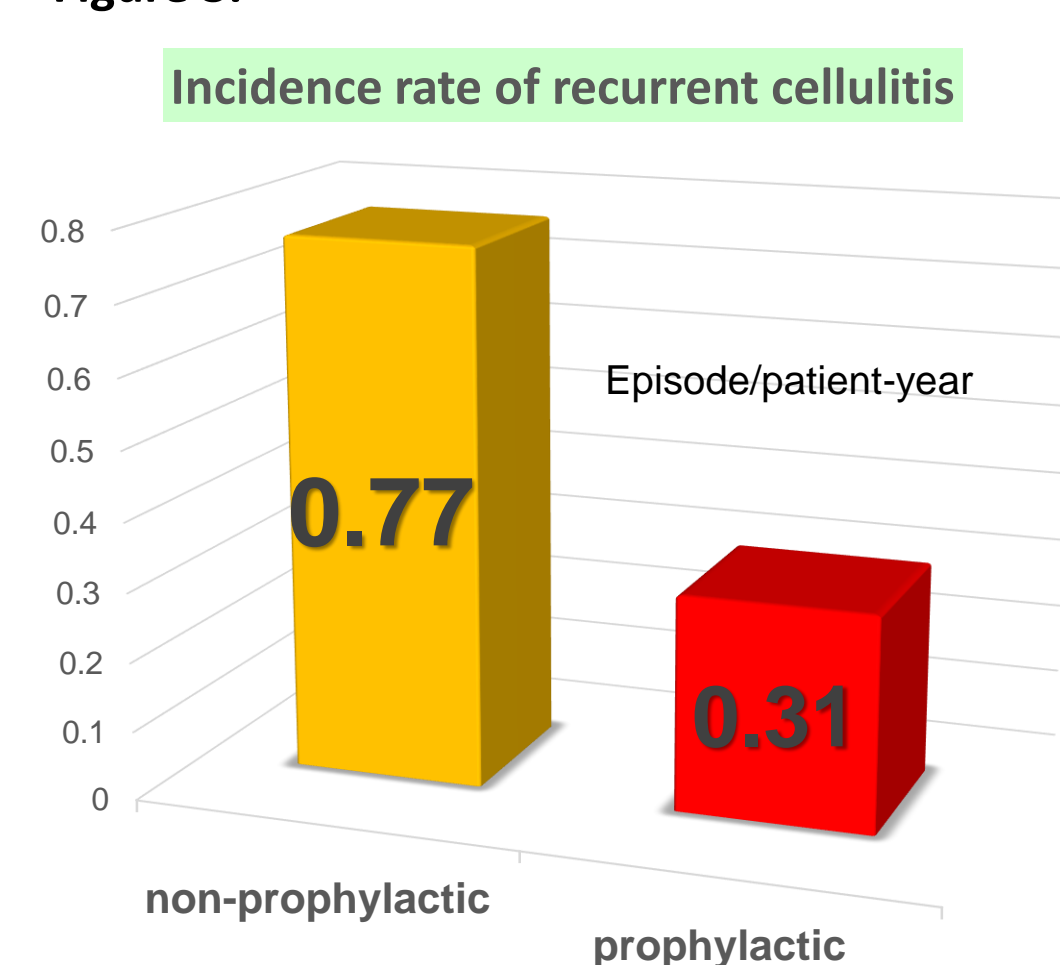


Table 2. Outcome analysis of Poisson regression model

	Univariate			Multivariate		
	RR	95% CI	p	RR	95% CI	p
Prophylaxis period (yes/no)	0.30	(0.14-0.68)	0.004	0.30	(0.13-0.69)	0.005
Gender (male/female)	1.42	(0.58-3.47)	0.443	0.79	(0.44-1.41)	0.426
Age (years)	1.01	(0.98-1.04)	0.378	0.99	(0.97-1.02)	0.518
Diabetes mellitus (yes/no)	1.67	(0.51-5.42)	0.393	1.53	(0.47-5.04)	0.481
Chronic renal failure (yes/no)	0.97	(0.29-3.31)	0.963	0.82	(0.18-3.64)	0.789
Congestive heart failure (yes/no)	1.58	(0.62-4.03)	0.343	2.13	(0.69-6.53)	0.186
Cirrhosis (yes/no)	0.59	(0.14-2.43)	0.461	0.36	(0.08-1.57)	0.175
Impaired venous drainage (yes/no)	2.04	(0.82-5.06)	0.124	2.78	(1.20-6.48)	0.018
Malignancy of lower extremity (yes/no)	1.58	(0.34-7.43)	0.564	1.25	(0.28-5.60)	0.775
Joint replacement of lower extremity (yes/no)	0.54	(0.16-1.87)	0.334	0.36	(0.09-1.40)	0.140
Myocardial infraction (yes/no)	1.20	(0.25-5.88)	0.820	1.06	(0.14-8.28)	0.957
Tinea pedis (yes/no)	2.39	(0.77-7.42)	0.133	3.04	(1.17-7.90)	0.022

Results

A total of 211 patients were enrolled, including 123(58.3%) men. An average of 7.9 doses of IM benzathine penicillin were given in the study period. (Figure 2) The incidence rate of recurrent cellulitis in the prophylactic period was 0.31 episode/patient-year, significantly lower than that of 0.77 episodes/patient-year in the non-prophylactic period (p = 0.004). (Figure 3) The common underlying diseases of enrolled patients included diabetes mellitus (73, 35.4%), tinea pedis (69, 33.5%), impaired venous drainage (20, 9.7%), joint replacement of lower extremity (13, 6.3%) and edema status including congestive heart failure (19, 9.2%), chronic renal failure (15, 7.3%), and cirrhosis (8, 3.9%). (Table 1). In multivariate analysis of Poisson regression model, penicillin prophylaxis was associated with lower recurrence (relative risk (RR), 0.30; 95% confidence interval (CI), 0.13-0.69, p=0.005), in contrast, impaired venous drainage (RR 2.78; CI, 1.20-6.48, p=0.018) and tinea pedis (RR 3.04; CI, 1.17-7.90, p=0.022) were associated with higher risk of recurrence (Table 2).

Discussions

Our study was nationwide population and multiple center study and showed prophylactic intramuscular benzathine penicillin 2.4 MIU at 4 week interval could **reduce 70% incidence rate of recurrent cellulitis**. It was also the most exposure participants study about intramuscular benzathine penicillin for recurrent cellulitis. Past systemic review study and IDSA guideline showed oral prophylactic antibiotic could be 45% reduction in the risk of a repeat episode of cellulitis, but intramuscular benzathine penicillin was weakness evidence. The recent one retrospective study in single medical center showed strong positive and decreased incidence of recurrent cellulitis from 1.25 to 0.73 episodes per person per year. Our study showed intramuscular benzathine penicillin had much better response of prevent recurrent cellulitis.

Conclusions

The study was the largest cohort that demonstrated intramuscular injection of 2.4 million units benzathine penicillin with 4-week interval significantly reduced the incidence of recurrent cellulitis.

Reference:
1. Choon Chiat Oh a, Henry Chung Hung Ko. Antibiotic prophylaxis for preventing recurrent cellulitis: A systematic review and meta-analysis. Journal of Infection (2014) 69, 26e34
2. Hsien-Meng Chen, Yu-Lin Li. The experience of intramuscular benzathine penicillin for prophylaxis of recurrent cellulitis: A cohort study. Journal of Microbiology, Immunology and Infection (2015) xx, 1e6
3. Thomas KS, Crook AM, Nunn AJ, Foster KA, Mason JM, Chalmers JR, et al. Penicillin to prevent recurrent leg cellulitis. N Engl J Med 2013; 368:1695-703
4. Dennis L. Stevens, Alan L. Bisno, Henry F. Chambers, Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases Advance Access published June 18, 2014