

Supplemental Table 1 International Classification of Disease 10<sup>th</sup> (ICD-10) version codes and standardized procedural codes to identify renal diseases.

Description	ICD-10 code
Acute nephritic syndrome	N00X
Rapidly progressive nephritic syndrome	N01X
Recurrent and persistent haematuria	N02X
Chronic nephritic syndrome	N03X
Nephrotic syndrome	N04X
Unspecified nephritic syndrome	N05X
Isolated proteinuria with specified morphological lesion	N06X
Hereditary nephropathy, not elsewhere classified	N07X
Glomerular disorders in diseases classified elsewhere	N08X
Acute tubulo-interstitial nephritis	N10X
Chronic tubulo-interstitial nephritis	N118, N119
Tubulo-interstitial nephritis, not specified as acute or chronic	N12X
Obstructive and reflux uropathy	N13X
Drug- and heavy-metal-induced tubulo-interstitial and tubular conditions	N14X
Other renal tubulo-interstitial diseases	N15X
Renal tubulo-interstitial disorders in diseases classified elsewhere	N16X
Acute renal failure	N17X
Chronic kidney disease	N18X
Unspecified kidney failure	N19X
Other disorders resulting from impaired renal tubular function	N258
Disorder resulting from impaired renal tubular function, unspecified	N259
Unspecified contracted kidney	N26X
Other disorders of kidney and ureter, not elsewhere classified	N28X
Description	Procedural codes
Hemodialysis, Peritoneal dialysis or renal replacement therapy	C102, J038, J038-2, J039, J041, J042

Supplemental Table 2 Definition of the study drugs.

Class or drug name	ATC index code
Proton pump inhibitors (PPIs)	
Esomeprazole	(WHO) A02BC05
Lansoprazole	(WHO) A02BC03, A02BD03, A02BD07, B01AC56
Omeprazole	(WHO) A02BC01
Rabeprazole	(WHO) A02BC04, A02BD12, A02BD13
Vonoprazan	(WHO) A02BC08, A02BD14, A02BD15
Non-steroidal anti-inflammatory drugs (NSAIDs) †	(EphMRA) M01A1
Penicillin antibiotics †	(EphMRA) J01C1, J01C2; (WHO) A02BD03, A02BD07, A02BD12, A02BD13, A02BD14, A02BD15
Macrolide antibiotics †	(EphMRA) J01F-; (WHO) A02BD07, A02BD12, A02BD14
Cephalosporin antibiotics †	(EphMRA) J01D1, J01D2
Fluoroquinolone antibiotics †	(EphMRA) J01G1, J01G2

The study drugs were identified using the ATC index codes developed by the European Pharmaceutical Market Research Association (EphMRA) or World Health Organization (WHO). †Topical agents were excluded.

Supplemental Table 3 Drugs suspected to increase risk of AKI.

Class name	EphMRA ATC index code	Class name	EphMRA ATC index code
H2 blocker	A02B1	Fluoroquinolone antibiotic	J01G1, J01G2
Loop diuretic	C03A2	Aminoglycoside antibiotic	J01K-
Thiazide diuretic	C03A3	Monobactam antibiotic	J01P1
Tetracycline antibiotic	J01A-	Carbapenem antibiotic	J01P2
Penicillin antibiotic	J01C1, J01C2	NSAIDs	M01A1, M01A3, M02A-
Cephalosporin antibiotic	J01D1, J01D2	Contrast media	T01A-, T01B-
Macrolide antibiotic	J01F-		

Drug name			
Miconazole	Polymyxin B	Amphotericin B	Vancomycin
Sulfasalazine	Mesalazine	Acetylsalicylate	Dextran
Hydroxyethyl starch	Mannitol	Ephedrine	Triamterene
Polidocanol	Captopril	Acyclovir	Tacrolimus
Trimethoprim-Sulfamethoxazole	Teicoplanin	Fluconazole	Itraconazole
Voriconazole	Rifampicin	Foscarnet	Indinavir
Telaprevir	Simeprevir	Tenofovir	Adefovir
Oseltamivir	Immunoglobulin	Ifosfamide	Streptozocin
Methotrexate	Pemetrexed	Cytarabine	Tegafur
Bleomycin	Mitomycin C	Cisplatin	Imatinib
Sunitinib	Sorafenib	Temsirolimus	Interferon alfa
Interferon beta	Sirolimus	Cyclosporine	Azathioprine
Allopurinol	Alendronate	Zoledronic acid	Cocaine
Acetaminophen	Phenytoin	Carbamazepine	Valproic acid
Clozapine	Lithium	Edaravone	Pentamidine
Deferasirox			

This list of drugs is based on the formulary described in the 'Clinical Practice Guideline for Drug-induced Kidney Injury in Japan 2016' published by the Japanese Society of Nephrology. To identify the nephrotoxic drugs in database, the EphMRA ATC codes or the specific drug names were used.

Supplemental Table 4 Characteristics of current PPI users in cases and controls.

Characteristics	Current PPI users	
	Cases (n = 148)	Controls (n = 655)
Age, years, mean (SD)	54 (13)	55 (13)
Female, n (%)	43 (29.1)	195 (29.8)
Duration of follow-up, days, mean (SD)	313 (404)	319 (431)
Comorbidity, n (%)		
Hypertension	40 (27.0)	225 (34.4)
Congestive heart failure	12 (8.1)	39 (6.0)
Diabetes	22 (14.9)	122 (18.6)
Liver disease	15 (10.1)	78 (11.9)
Pulmonary disease	10 (6.8)	48 (7.3)
Cancer	32 (21.6)	38 (5.8)
Charlson comorbidity index, median (IQR)	1 (0 to 3)	0 (0 to 2)
PPIs prescribed at the last time, n (%)		
Lansoprazole	54 (36.5)	222 (33.9)
Esomeprazole	48 (32.4)	180 (27.5)
Rabeprazole	29 (19.6)	140 (21.4)
Omeprazole	10 (6.8)	59 (9.0)
Vonoprazan	7 (4.7)	54 (8.2)
Current use of nephrotoxic drugs, n (%) <sup>†</sup>	113 (77.9)	349 (53.3)

SD, standard deviation; IQR, interquartile range. <sup>†</sup>Three cases (2.0%) had missing data.

Supplemental Table 5 Sensitivity analyses.

Current drug use	Cases	Controls	Matched odds ratio (95% CI) †
Setting the index date 1 week before the diagnosis (Cases, n = 294; Controls, n = 2,920)			
Current use of PPIs			
With NSAIDs (Yes/No)	44/82	75/422	4.04 (2.27 to 7.42)
With penicillins (Yes/No)	12/114	41/456	1.54 (0.65 to 3.59)
With macrolides (Yes/No)	8/118	50/447	0.76 (0.29 to 1.79)
With cephalosporins (Yes/No)	16/110	25/472	2.63 (1.25 to 5.56)
With fluoroquinolones (Yes/No)	7/119	19/478	1.66 (0.59 to 4.36)
Following patients for up to 120 days from the cohort entry (Cases, n = 99; Controls, n = 990)			
Current use of PPIs			
With NSAIDs (Yes/No)	29/41	66/318	3.50 (1.91 to 6.53)
With penicillins (Yes/No)	10/60	98/286	0.49 (0.23 to 0.98)
With macrolides (Yes/No)	7/63	94/290	0.32 (0.12 to 0.72)
With cephalosporins (Yes/No)	16/54	36/348	3.44 (1.61 to 7.40)
With fluoroquinolones (Yes/No)	12/58	21/363	4.65 (1.87 to 12.10)
Including patients diagnosed with AIN into cases (Cases, n = 475; Controls, n = 4,721)			
Current use of PPIs			
With NSAIDs (Yes/No)	68/142	186/824	2.01 (1.35 to 2.99)
With penicillins (Yes/No)	40/170	118/892	1.50 (0.95 to 2.35)
With macrolides (Yes/No)	34/176	138/872	1.16 (0.74 to 1.78)
With cephalosporins (Yes/No)	30/180	77/933	2.00 (1.17 to 3.40)
With fluoroquinolones (Yes/No)	20/190	44/966	2.11 (1.09 to 3.96)
Including patients with previous renal diseases into the study cohort (Cases, n = 517; Controls, n = 5,143)			
Current use of PPIs			
With NSAIDs (Yes/No)	80/164	180/943	2.80 (1.96 to 4.02)
With penicillins (Yes/No)	27/217	129/994	1.12 (0.68 to 1.80)
With macrolides (Yes/No)	23/221	160/963	0.69 (0.41 to 1.11)
With cephalosporins (Yes/No)	54/190	80/1,043	3.81 (2.46 to 5.92)
With fluoroquinolones (Yes/No)	28/216	60/1,063	2.24 (1.31 to 3.80)

CI, confidence interval. †Odds ratios of AKI for current drug combinations compared with PPIs alone were estimated using the conditional logistic regression model.