

Supplementary Tables: Proton pump inhibitors and risk of acute interstitial nephritis

Supplementary Table 1. Socioeconomic status of cases and matched controls

	Definite Cases (n=46)	Controls (n=460)	All Cases (n=72)	Controls (n=719)
NZDep06 quintile* [n(%)]				
1	9 (19.6)	85 (18.5)	10 (13.9)	131 (18.2)
2	11 (23.9)	94 (20.4)	16 (22.2)	147 (20.5)
3	8 (17.4)	106 (23.0)	13 (18.1)	166 (23.1)
4	9 (19.6)	109 (23.7)	17 (23.6)	175 (24.3)
5	9 (19.6)	66 (14.4)	16 (22.2)	100 (13.9)

*New Zealand Deprivation Index 2006, an area-based measure of socioeconomic deprivation based on census data (1 = least deprived)

Supplementary Table 2. Total daily dose in current users of the proton pump inhibitors omeprazole, pantoprazole, and lansoprazole at the last dispensing before the index date

	Definite Cases (n=35)	Controls (n=207)	All Cases (n=55)	Controls (n=332)
“Low” dose*	5 (14.3)	14 (6.8)	5 (9.1)	22 (6.6)
“Standard” dose†	22 (62.9)	137 (66.2)	35 (63.6)	212 (63.9)
“High” dose‡	8 (22.9)	56 (27.1)	15 (27.3)	98 (29.5)

*Omeprazole<20mg, pantoprazole<40mg, lansoprazole<30mg

†Omeprazole=20mg, pantoprazole=40mg, lansoprazole=30mg

‡Omeprazole>20mg, pantoprazole>40mg, lansoprazole>30mg

Supplementary Table 3. Risk of acute interstitial nephritis in current users of the proton pump inhibitors omeprazole, pantoprazole, or lansoprazole (by total daily dose) compared to past users

	Cases	Controls	Matched odds ratio (95% CI)	P-value
Definite cases*				
“Low” dose [†]	5	14	10.75 (2.89 – 39.92)	<0.001
“Standard” dose [‡]	22	137	4.87 (1.99 – 11.93)	0.001
“High” dose [§]	8	56	4.14 (1.43 – 11.99)	0.009
Past use	7	197	1.0	—
All cases				
“Low” dose [†]	5	22	6.46 (2.02 – 20.68)	0.002
“Standard” dose [‡]	35	212	4.83 (2.34 – 9.98)	<0.001
“High” dose [§]	15	98	4.38 (1.92 – 9.99)	<0.001
Past use	12	298	1.0	—

*Verified by discharge letter and renal biopsy

[†]Omeprazole<20mg, pantoprazole<40mg, lansoprazole<30mg

[‡]Omeprazole=20mg, pantoprazole=40mg, lansoprazole=30mg

[§]Omeprazole>20mg, pantoprazole>40mg, lansoprazole>30mg

^{||}Definite and probable (verified by discharge letter only) cases

Supplementary Table 4. Risk of acute interstitial nephritis in current users of the proton pump inhibitors omeprazole, pantoprazole, or lansoprazole, by duration of current use

	Cases	Controls	Adjusted* unmatched odds ratio (95% CI)	P-value
Definite cases				
	n=18	n=101		
≤180 days current use	15	83	1.12 (0.29 – 4.31)	0.866
>180 days current use (reference)	3	18	1.0	—
All cases				
	n=24	n=164		
≤180 days current use	21	133	1.69 (0.47 – 6.09)	0.419
>180 days current use (reference)	3	31	1.0	—

*Adjusted for the matching factors (birth year and sex)

Supplementary Table 5. International Classification of Diseases 9th revision Australian Modification codes (ICD-9-AM) used to exclude study cohort members with kidney disease diagnoses before cohort entry

Description	ICD-9-AM
Acute glomerulonephritis	5800, 5804, 58081, 58089, 5809
Nephrotic syndrome	5810, 5811, 5812, 5813, 58181, 58189, 5819
Chronic glomerulonephritis	5820, 5821, 5822, 5824, 58281, 58289, 5829
Nephritis and nephropathy	5830, 5831, 5832, 5834, 5836, 5837, 58381, 58389, 5839
Acute renal failure	5845, 5846, 5847, 5848, 5849
Chronic renal impairment	5851
Chronic renal failure	5859
Renal failure, unspecified	586
Chronic pyelonephritis	59000, 59001
Acute pyelonephritis	59010, 59011
Renal and perinephric abscess	5902
Pyelonephritis, unspecified	59080
Pyelitis or pyelonephritis in diseases classified elsewhere	59081
Postural proteinuria	5936

Supplementary Table 6. International Classification of Diseases 10th revision Australian Modification codes (ICD-10-AM) used to exclude study cohort members with kidney disease diagnoses before cohort entry

Description	ICD-10-AM
Acute nephritic syndrome	N000, N001, N002, N003, N004, N005, N006, N007, N008, N009
Rapidly progressive nephritic syndrome	N010, N011, N012, N013, N014, N015, N016, N017, N018, N019
Recurrent and persistent haematuria	N020, N021, N022, N023, N024, N025, N026, N027, N028, N029
Chronic nephritic syndrome	N030, N031, N032, N033, N034, N035, N036, N037, N038, N039
Nephrotic syndrome	N040, N041, N042, N043, N044, N045, N046, N047, N048, N049
Unspecified nephritic syndrome	N050, N051, N052, N053, N054, N055, N056, N057, N058, N059
Isolated proteinuria	N060, N061, N062, N063, N064, N065, N066, N067, N068, N069
Hereditary nephropathy	N070, N071, N072, N073, N074, N075, N076, N077, N078, N079
Glomerular disorders	N080, N081, N082, N083, N084, N085, N088
Acute tubulo-interstitial nephritis	N10
Other chronic tubulo-interstitial nephritis	N118
Chronic tubulo-interstitial nephritis, unspecified	N119
Tubulo-interstitial nephritis, not specified as acute or chronic	N12
Analgesic nephropathy	N140
Nephropathy induced by other drugs, medicaments and biological substances	N141
Nephropathy induced by unspecified drug, medicament or biological substance	N142
Nephropathy induced by heavy metals	N143
Toxic nephropathy, not elsewhere classified	N144
Balkan nephropathy	N150
Renal and perinephric abscess	N151
Other specified renal tubulo-interstitial diseases	N158
Renal tubulo-interstitial disease, unspecified	N159
Renal tubulo-interstitial disorders	N160, N161, N162, N163, N164, N165, N168
Acute renal failure	N170, N171, N172, N178, N179
End-stage renal disease	N180
Other chronic renal failure	N188
Unspecified chronic renal failure	N1890
Chronic renal impairment	N1891

Supplementary Table 7. International Classification of Diseases 10th revision Australian Modification codes (ICD-10-AM) that were used to identify, and then exclude, potential cases who had a kidney or urinary tract infection (patients concurrently diagnosed with N10 or N12 and any of the ICD-10-AM codes listed in the table were excluded, regardless of whether other ICD-10-AM codes were listed)

ICD-10-AM	Description
A4151	Sepsis due to other Gram-negative organisms
B962	<i>Escherichia coli</i> [<i>E.coli</i>] as the cause of disease classified to other chapters
N110	Non-obstructive reflux-associated chronic pyelonephritis
N111	Chronic obstructive pyelonephritis
N309	Cystitis, unspecified
N390	Urinary tract infection, site not specified
O230	Infections of kidney in pregnancy
O234	Unspecified infection of urinary tract in pregnancy
O862	Urinary tract infection following delivery

Supplementary Table 8. International Classification of Diseases 10th revision Australian Modification codes (ICD-10-AM) that were used to identify, and then exclude, potential cases who had a kidney or urinary tract infection and had not already been excluded according to Table A3 (patients concurrently diagnosed with N10 or N12 and any of the ICD-10-AM codes listed in the table were excluded, provided there were no other ICD-10-AM codes listed)

ICD-10-AM	Description
B950 – B958	Streptococcus and staphylococcus as the cause of diseases classified to other chapters
B960 – B968	Other specified bacterial agents as the cause of diseases classified to other chapters
B970 – B978	Viral agents as the cause of disease classified to other chapters

Supplementary Table 9. Government-subsidised prescription drugs listed in the New Zealand formulary known or suspected of increasing the risk of interstitial nephritis, by therapeutic class

<p>NSAIDs Diclofenac sodium Diflunisal Fenoprofen calcium Flurbiprofen Ibuprofen Indomethacin Ketoprofen Mefenamic acid Meloxicam Mesalazine Naproxen Naproxen sodium Phenylbutazone Piroxicam Sulindac Tenoxicam Tiaprofenic acid</p> <p>Other analgesics Nefopam hydrochloride Paracetamol Paracetamol with codeine Tramadol Tramadol hydrochloride</p> <p>Aspirin Aspirin Aspirin with chloroform Aspirin with codeine Aspirin with paracetamol and codeine</p> <p>Other anti-coagulants Phenindione Warfarin sodium</p> <p>Antibiotics Amoxicillin Amoxicillin clavulanate Azithromycin Aztreonam Benzathine benzylpenicillin</p>	<p>Benzylpenicillin sodium (Penicillin G) Cefaclor monohydrate Cefamandole nafate Cefazolin sodium Cefoxitin sodium Ceftriaxone sodium Cefuroxime axetil Cefuroxime sodium Cephalexin monohydrate Cephalothin sodium Cephradine Ciprofloxacin Clarithromycin</p> <p>Other antimicrobials Abacavir sulphate Abacavir sulphate with lamivudine Aciclovir Adefovir dipivoxil Atazanavir sulphate Dapsone Dapsone with pyrimethamine Darunavir Didanosine Efavirenz Emtricitabine Enfuvirtide Entecavir Ethambutol Ethambutol hydrochloride Etravirine Hexamine hippurate Hydroxychloroquine sulphate Indinavir Isoniazid Lamivudine Lopinavir with ritonavir Nevirapine Pyrazinamide Quinine sulphate</p>	<p>Raltegravir potassium Rifabutin Rifampicin Ritonavir Stavudine Tenofovir disoproxil fumarate Valaciclovir Zidovudine Zidovudine with lamivudine</p> <p>Anxiolytics Alprazolam Buspirone hydrochloride Diazepam Lorazepam Oxazepam</p> <p>Anti-epilepsy Carbamazepine Clobazam Clonazepam Ethosuximide Gabapentin Lamotrigine Levetiracetam Paraldehyde Phenobarbitone Phenobarbitone sodium Phenytoin sodium Primidone Sodium valproate Topiramate Vigabatrin</p> <p>Diuretics Amiloride Amiloride with frusemide Amiloride with hydrochlorothiazide Bendrofluazide Bumetanide Chlorothiazide Chlorthalidone Furosemide Indapamide Triamterene with hydrochlorothiazide</p>	<p>ACE inhibitors Captopril Captopril with hydrochlorothiazide Cilazapril Cilazapril with hydrochlorothiazide Enalapril Enalapril with hydrochlorothiazide Lisinopril Lisinopril with hydrochlorothiazide Perindopril Quinapril Quinapril with hydrochlorothiazide Trandolapril</p> <p>Angiotensin II antagonists Candesartan Losartan Losartan with hydrochlorothiazide</p> <p>Beta blockers Atenolol Atenolol with chlorthalidone Carvedilol Celiprolol Labetalol Metoprolol succinate Metoprolol tartrate Nadolol Pindolol Pindolol with clopamide Propranolol Sotalol Timolol Timolol maleate Timolol maleate with pilocarpine</p> <p>Calcium channel blockers Amlodipine Diltiazem hydrochloride Felodipine Isradipine</p>	<p>Nifedipine Perhexiline maleate Verapamil hydrochloride</p> <p>H2 receptor antagonists Cimetidine Famotidine Ranitidine hydrochloride</p> <p>Immune modulators Interferon alpha-2a Interferon alpha-2a with ribavirin Interferon alpha-2b Interferon alpha-n Interferon beta-1-alpha Interferon beta-1-beta Interferon gamma-1b Pegylated interferon alpha-2a Pegylated interferon alpha-2b Pegylated interferon alpha-2b with ribavirin</p> <p>Other drugs Allopurinol Azathioprine Bismuth carbonate Bismuth subcitrate, metronidazole and tetracycline Bismuth subnitrate Carbimazole Chlorpropamide Clofibrate Clozapine Griseofulvin Methyldopa Methyldopa with hydrochlorothiazide Penicillamine Probenecid Propylthiouracil Sulphinpyrazone</p>
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