Figure S1. Consort Diagram

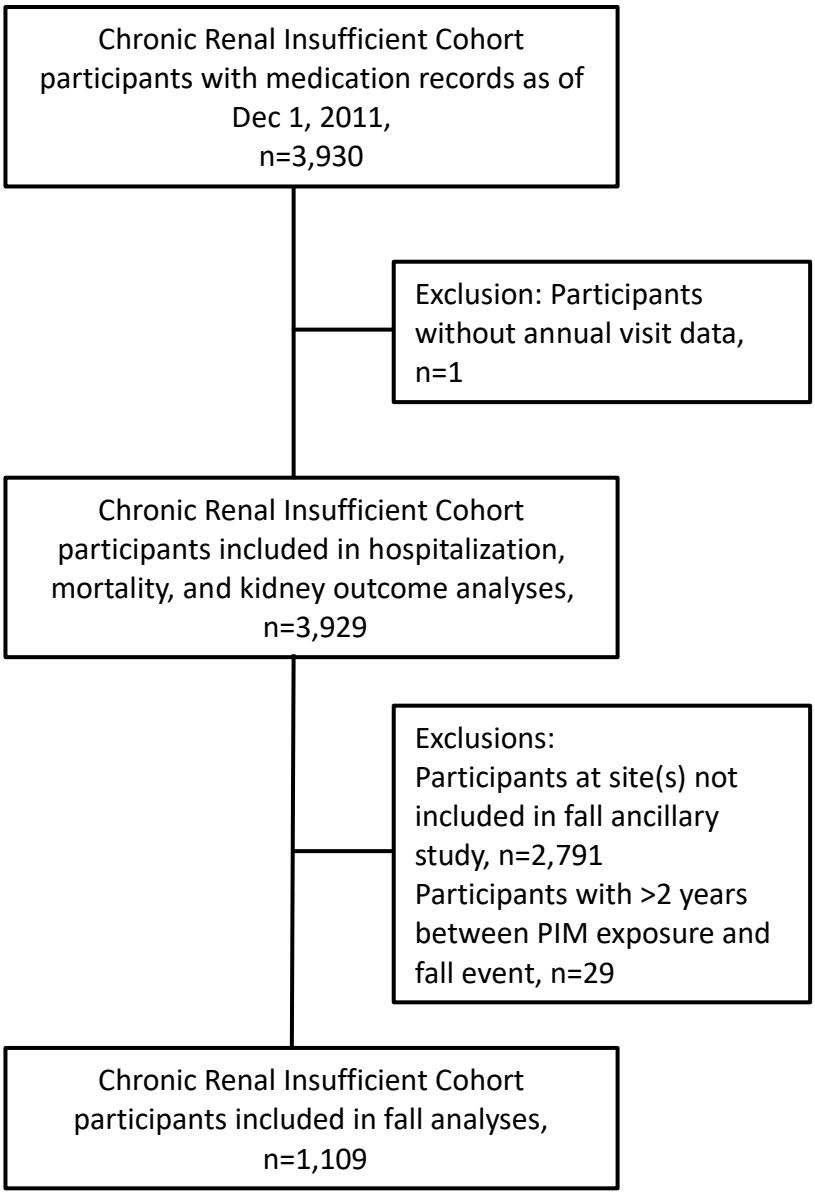

Table S1. Potentially Inappropriate Medications Included in Exposure Variable

Category	Medication Name(s)
Anticholinergics	First-generation antihistamines Brompheniramine Carbinoxamine Chrlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Dimenhydrinate Diphenhydramine (oral) Doxylamine Hydroxyzine Meclizine Promethazine Triprolidine
	Anti-parkinsonian agents Benztropine (oral) Trihexyphenidyl
	Antispasmodics Atropine (excludes ophthalmic) Belladonna alkaloids Clidinium-Chlordiazepoxide Dicyclomine Hyoscyamine Propantheline Scopolamine
Antithrombotics	Dipyridamole
	Ticlopidine
Anti-infective	Nitrofurantoin
Cardiovascular	Peripheral alpha-1 blockers Doxazosin Prazosin Terazosin
	Central alpha blockers Clonidine Guanabenz Guanfacine Methyldopa Reserpine
	Disopyramide
	Dronedarone
	Digoxin
	Nifedipine (immediate release)
	Amiodarone
Central Nervous System	Antidepressants Amitriptyline Amoxapine

	Clomipramine Desipramine Doxepin Imipramine Nortriptyline Paroxetine Protriptyline Trimipramine
	Anti-psychotics (first- and second-generation
	Barbiturates Amobarbital Butabarbital Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital
	Benzodiazepines Short- and Intermediate-acting Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam Long-acting Clorazepate Chlordiazepoxide Clonazepam Diazepam Flurazepam Quazepam
	Meprobamate
	Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zolpidem Zaleplon
	Ergoloid mesylates Isoxsuprine
Endocrine	Androgens Methyltestosterone Testosterone
	Desiccated thyroid
	Estrogens (with or without progresterone)
	Growth hormone
	Insulin
	Megestrol
	Sulfonylureas (long-duration) Chrlorpropamide

	Glyburide
Gastrointestinal	Metoclopramide
	Mineral oil (oral)
	Proton-pump inhibitors
Pain Medications	Meperidine Non-cyclooxygenase-selective NSAIDS (oral) Aspirin Diflunisal Etodolac Fenoprofen Ibuprofen Ketoprofen Meclofenamate Mefenamic acid Meloxicam Nabumetone Naproxen Oxaprozin Piroxicam Sulindac Tolmetin Indomethacin Ketorolac
	Pentazocine
	Skeletal muscle relaxants Carisoprodol Chlorzoxazone Cyclobenzaprine Metaxalone Methocarbamol Orphenadrine
Genitourinary	Desmopressin

Table S2. Baseline Cohort Characteristics based on Ever taking a PIM during study observation period

Characteristic	**Overall N= 3929**	**Ever PIM N= 3151**	**Never PIM N=778**
Demographics			
Age (years)	57.7 (10.9)	58.4 (10.4)	54.8 (12.5)
Age <65	2789 (71.0%)	2200 (69.8%)	589 (75.7%)
Age 65-70	741 (18.9%)	608 (19.3%)	133 (17.1%)
Age >70	399 (10.2%)	343 (10.9%)	56 (7.2%)
Female	1775 (45.2%)	1466 (46.5%)	309 (39.7%)
Non-Hispanic Black	1646 (41.9%)	1356 (43%)	290 (37.3%)
Non-Hispanic White	1635 (41.6%)	1333 (42.3%)	302 (38.8%)
Hispanic	495 (12.6%)	349 (11.1%)	146 (18.8%)
Other	153 (3.9%)	113 (3.6%)	40 (5.1%)
Clinical Characteristics			
eGFR	44.8 (16.8)	45.0 (16.8)	44.1 (16.5)
Chronic Kidney Disease Stage at Baseline			
Stage I/II	694 (17.7%)	569 (18.1%)	125 (16.1%)
Stage IIIA	1090 (27.7%)	876 (27.8%)	214 (27.5%)
Stage IIIB	1338 (34.1%)	1066 (33.8%)	272 (35%)
Stage IV/V	807 (20.5%)	640 (20.3%)	167 (21.5%)
Urine Protein/CreatinineRatio	1.0 (2.4)	1.0 (2.4)	1.2 (2.3)
BMI Categories			
BMI >30	2174 (55.5%)	1824 (58.1%)	350 (45%)
BMI 25-30	1121 (28.6%)	853 (27.2%)	268 (34.4%)
BMI <25	623 (15.9%)	463 (14.7%)	160 (20.6%)
Diabetes	1908 (48.6%)	1556 (49.4%)	352 (45.2%)
CVD	1315 (33.5%)	1116 (35.4%)	199 (25.6%)
Hypertension	3390 (86.3%)	2741 (87%)	649 (83.4%)
Arthritis	492 (13.2%)	432 (14.5%)	60 (8.1%)
Number of Medications	8.9 (4.5)	9.5 (4.6)	6.3 (3.3)
Number of PIMs	0.9 (1.1)	1.2 (1.1)	0.0 (0.0)
Nephrology Care	2596 (66.1%)	2071 (65.7%)	525 (67.5%)

Data reported as N (%) or mean (SD)

Abbreviations: BMI, body mass index; CVD, cardiovascular disease, eGFR, estimated glomerular filtration rate; PIM, potentially inappropriate medication

Table S3. Sensitivity analysis of fully adjusted model (Model 3) with additional adjustment for number of hospitalizations reported from the prior year

		OR (95% CI) or RR (95% CI)[a]
Outcome	Exposure	Adjusted Model[b]
Hospitalizations	No PIM	[Reference]
	1 PIM	1.09 (1.00 - 1.17)
	2 PIMs	1.18 (1.07 - 1.30)
	≥3 PIMs	1.25 (1.11 - 1.42)
	Any PIM	1.12 (1.04 - 1.20)
Death	No PIM	[Reference]
	1 PIM	1.18 (0.91, 1.54)
	2 PIMs	1.61 (1.20, 2.15)
	≥3 PIMs	1.62 (1.11, 2.37)
	Any PIM	1.34 (1.06, 1.69)
KRT	No PIM	[Reference]
	1 PIM	1.20 (0.95, 1.52)
	2 PIMs	1.11 (0.82, 1.51)
	≥3 PIMs	1.12 (0.72, 1.74)
	Any PIM	1.18 (0.94, 1.46)
Renal Composite outcome[c]	No PIM	[Reference]
	1 PIM	1.13 (0.93, 1.38)
	2 PIMs	1.06 (0.82, 1.37)
	≥3 PIMs	1.12 (0.78, 1.62)
	Any PIM	1.11 (0.93, 1.34)
Falls	No PIM	[Reference]
	1 PIM	1.34 (0.87, 2.08)
	2 PIMs	1.25 (0.70, 2.24)
	≥3 PIMs	2.72 (1.46, 5.08)
	Any PIM	1.44 (0.97, 2.14)

Abbreviations: PIM, potentially inappropriate medications; KRT, initiation of kidney replacement therapy; OR, odds ratio; RR, rate ratio

[a]Rate ratio for hospitalization model

[b]Model is adjusted for age, other demographics and participant site, eGFR, BMI, diabetes, any CVD, hypertension, arthritis, and prior nephrology care, number of medications, and number of hospitalizations in the prior year

[c]Renal composite outcome is defined as occurrence of ESKD or halving of baseline estimated glomerular filtration rate

Table S4. Sensitivity analysis of fully adjusted model (Model 3) in a subgroup of visits from the cohort with eGFR<45

		OR (95% CI) or RR (95% CI)[a]
Outcome	Exposure	Adjusted Model[b] for eGFR<45 subgoup
Hospitalizations	No PIM	[Reference]
	1 PIM	1.07 (0.99 - 1.17)
	2 PIMs	1.16 (1.03 - 1.30)
	≥3 PIMs	1.28 (1.11 - 1.46)
	Any PIM	1.11 (1.02 - 1.20)
Death	No PIM	[Reference]
	1 PIM	1.23 (0.93, 1.65)
	2 PIMs	1.52 (1.10, 2.10)
	≥3 PIMs	1.45 (0.95, 2.21)
	Any PIM	1.33 (1.02, 1.73)
KRT	No PIM	[Reference]
	1 PIM	1.15 (0.92, 1.43)
	2 PIMs	1.06 (0.79, 1.42)
	≥3 PIMs	1.20 (0.80, 1.80)
	Any PIM	1.13 (0.91, 1.39)
Renal Composite outcome[c]	No PIM	[Reference]
	1 PIM	1.05 (0.87, 1.28)
	2 PIMs	1.02 (0.79, 1.32)
	≥3 PIMs	1.18 (0.82, 1.69)
	Any PIM	1.05 (0.88, 1.26)
Falls	No PIM	[Reference]
	1 PIM	0.98 (0.54, 1.81)
	2 PIMs	0.82 (0.35, 1.90)
	≥3 PIMs	3.76 (1.65, 8.55)
	Any PIM	1.14 (0.67, 1.94)

Abbreviations: PIM, potentially inappropriate medications; KRT, initiation of kidney replacement therapy; OR, odds ratio; RR, rate ratio

[a]Rate ratio for hospitalization model

[b]Model is adjusted for age, other demographics and participant site, eGFR, BMI, diabetes, any CVD, hypertension, arthritis, and prior nephrology care, number of medications

[c]Renal composite outcome is defined as occurrence of ESKD or halving of baseline estimated glomerular filtration rate

Table S5. Number of all visits (Rate) when PIMs reported used by Cohort Members who died in Total and By Age Group

Medication	**Total**	**Age <65**	**Age 65-70**	**Age >70**	**P-value**
proton pump inhibitor	601 (35.1)	297 (31.9)	134 (32.3)	170 (34.7)	0.7
Alpha blockers	311 (18.2)	84 (9.0)	110 (26.5)	117 (23.9)	<0.001
central alpha agonists	256 (14.9)	168 (18.0)	51 (12.3)	37 (7.6)	<0.001
antidepressants	190 (11.1)	125 (13.4)	20 (4.8)	45 (9.2)	<0.001
anticholinergic	184 (10.7)	96 (10.3)	35 (8.4)	53 (10.8)	0.5
NSAIDS	161 (9.4)	84 (9.0)	28 (6.8)	49 (10.0)	0.2
benzodiazepines	146 (8.5)	85 (9.1)	25 (6.0)	36 (7.4)	0.1
digoxin	138 (8.1)	69 (7.4)	36 (8.7)	33 (6.7)	0.6
metoclopramide	85 (5.0)	64 (6.9)	12 (2.9)	9 (1.8)	<0.001
amiodarone	70 (4.1)	30 (3.2)	13 (3.1)	27 (5.5)	0.1
muscle relaxant	66 (3.9)	44 (4.7)	12 (2.9)	10 (2.0)	0.02
antispasmodics	47 (2.7)	21 (2.3)	11 (2.7)	15 (3.1)	0.7
antipsychotic	44 (2.6)	34 (3.7)	5 (1.2)	5 (1.0)	0.001
Z-drugs	34 (2.0)	20 (2.1)	3 (0.7)	11 (2.2)	0.1

This is list of the most common PIMs among those who died during follow-up.

Data expressed as number of visits (rate)

Rate defined as number of PIMs per 100 person-year

Age group is based on age at reported medication use

Table S6. Adjusted association between common PIMs in the cohort [proton pump inhibitors (PPIs) and alpha blockers] and adverse outcomes of hospitalization and death

		OR (95% CI) or RR (95% CI)[a]			
Outcome	Exposure	Unadjusted	Model 1[b]	Model 2[c]	Model 3[d]
Hospitalizations	No PPI	[Reference]	[Reference]	[Reference]	Reference]
	Any PPI	1.28 (1.17 - 1.39)	1.28 (1.17 - 1.39)	1.21 (1.12 - 1.31)	1.13 (1.04 - 1.23)
	No alpha blocker	[Reference]	[Reference]	[Reference]	Reference]
	Any alpha blocker	1.15 (1.02 - 1.29)	1.16 (1.03 - 1.31)	1.16 (1.04 - 1.31)	1.09 (0.97 - 1.23)
Death	No PPI	[Reference]	Reference]	Reference]	Reference]
	Any PPI	1.55 (1.27, 1.89)	1.45 (1.19, 1.78)	1.25 (1.00, 1.56)	1.11 (0.88, 1.40)
	No alpha blocker	[Reference]	[Reference]	[Reference]	Reference]
	Any alpha blocker	1.45 (1.12, 1.86)	1.01 (0.77, 1.31)	0.91 (0.68, 1.23)	0.81 (0.60, 1.09)

Abbreviations: PPIs, proton pump inhibitors, OR, odds ratio; RR, rate ratio

[a]Relative risk for hospitalization model

[b]Model 1 adjusted for age, other demographics and participant site.

[c]Model 2 is adjusted for Model 1 covariates and eGFR, BMI, diabetes, any CVD, hypertension, arthritis, and prior nephrology care.

[d]Model 3 is adjusted for Model 2 covariates and number of medications