

**Supplemental Material for Manuscript:**  
**Primary Care Prescriptions of Potentially Nephrotoxic Medications in Children with Chronic**  
**Kidney Disease**  
**A Matched Cohort Study**

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## **Supplemental Table 1: Codes Defining CKD for Study Inclusion**

**Table 1A: CPRD Read Codes**

| <b>Medcode</b> | <b>Read term (Code description)</b>                          |
|----------------|--|
| 16929          | Anaemia secondary to renal failure                           |
| 22205          | Lupus nephritis  |
| 12465          | Membranoproliferative nephritis unspecified                  |
| 5291           | Membranous nephritis unspecified                             |
| 57987          | Hyperten heart&renal dis+both(congestv)heart and renal fail  |
| 28684          | Hypertensive heart and renal disease with renal failure      |
| 4668           | Hypertensive renal disease                                   |
| 15106          | Hypertensive renal disease NOS                               |
| 32423          | Hypertensive renal disease with renal failure                |
| 41148          | Renal tubulo-interstitial disorder in SLE                    |
| 107216         | [X]Hereditary nephropathy, unspecif morphological changes    |
| 53940          | [X]Other chronic renal failure                               |
| 101453         | [X]Other chronic tubulo-interstitial nephritis               |
| 72877          | [X]Other cystic kidney diseases                              |
| 104079         | Acquired renal cystic disease                                |
| 100205         | Acute-on-chronic renal failure                               |
| 25394          | Anaemia secondary to chronic renal failure                   |
| 8607           | Analgesic nephropathy  |
| 105143         | Autosomal dominant polycystic kidney disease                 |
| 105919         | Autosomal recessive polycystic kidney disease                |
| 99139          | Balkan nephropathy   |
| 21423          | Berger's IgA or IgG nephropathy                              |
| 9500           | Bilateral renal dysplasia                                    |
| 38774          | Bilateral small kidneys                                      |
| 56893          | Chron neph syn difus mesangial prolifrtiv glomerulonephritis |
| 57168          | Chron nephritic syndrom difuse membranous glomerulonephritis |
| 65400          | Chronic diffuse glomerulonephritis                           |
| 4669           | Chronic focal glomerulonephritis                             |
| 7804           | Chronic glomerulonephritis                                   |
| 97758          | Chronic glomerulonephritis + diseases EC                     |
| 15097          | Chronic glomerulonephritis NOS                               |
| 106060         | Chronic infective interstitial nephritis                     |
| 104981         | Chronic kidney disease                                       |
| 30735          | Chronic kidney disease annual review                         |
| 19473          | Chronic kidney disease monitoring                            |

|        |   |
|--------|---|
| 71271  | Chronic kidney disease monitoring administration            |
| 30739  | Chronic kidney disease monitoring first letter              |
| 72962  | Chronic kidney disease monitoring second letter             |
| 69679  | Chronic kidney disease monitoring telephone invite          |
| 72964  | Chronic kidney disease monitoring third letter              |
| 88494  | Chronic kidney disease monitoring verbal invite             |
| 108766 | Chronic kidney disease self-management plan agreed          |
| 105392 | Chronic kidney disease stage 1                              |
| 29013  | Chronic kidney disease stage 1                              |
| 94789  | Chronic kidney disease stage 1 with proteinuria             |
| 95572  | Chronic kidney disease stage 1 without proteinuria          |
| 12586  | Chronic kidney disease stage 2                              |
| 105383 | Chronic kidney disease stage 2                              |
| 95146  | Chronic kidney disease stage 2 with proteinuria             |
| 95121  | Chronic kidney disease stage 2 without proteinuria          |
| 12566  | Chronic kidney disease stage 3                              |
| 104619 | Chronic kidney disease stage 3                              |
| 94793  | Chronic kidney disease stage 3 with proteinuria             |
| 95123  | Chronic kidney disease stage 3 without proteinuria          |
| 94965  | Chronic kidney disease stage 3A                             |
| 95408  | Chronic kidney disease stage 3A with proteinuria            |
| 95175  | Chronic kidney disease stage 3A without proteinuria         |
| 95179  | Chronic kidney disease stage 3B                             |
| 95178  | Chronic kidney disease stage 3B with proteinuria            |
| 95177  | Chronic kidney disease stage 3B without proteinuria         |
| 12479  | Chronic kidney disease stage 4                              |
| 104963 | Chronic kidney disease stage 4                              |
| 95122  | Chronic kidney disease stage 4 with proteinuria             |
| 95406  | Chronic kidney disease stage 4 without proteinuria          |
| 105151 | Chronic kidney disease stage 5                              |
| 12585  | Chronic kidney disease stage 5                              |
| 95508  | Chronic kidney disease stage 5 with proteinuria             |
| 95405  | Chronic kidney disease stage 5 without proteinuria          |
| 61494  | Chronic membranoproliferative glomerulonephritis            |
| 10809  | Chronic membranous glomerulonephritis                       |
| 73026  | Chronic neph syn difus mesangiocapillary glomerulonephritis |
| 60857  | Chronic nephritic syn diffuse crescentic glomerulonephritis |
| 48855  | Chronic obstructive pyelonephritis                          |
| 34998  | Chronic proliferative glomerulonephritis                    |

|        |   |
|--------|---|
| 4654   | Chronic pyelonephritis                              |
| 48111  | Chronic pyelonephritis NOS                          |
| 57568  | Chronic pyelonephritis with medullary necrosis      |
| 99631  | Chronic pyelonephritis without medullary necrosis   |
| 65064  | Chronic rapidly progressive glomerulonephritis      |
| 512    | Chronic renal failure                               |
| 12720  | Chronic renal impairment                            |
| 10081  | Chronic uraemia                                     |
| 97980  | CKD stage 1 with proteinuria                        |
| 111022 | CKD stage 1 without proteinuria                     |
| 97979  | CKD stage 2 with proteinuria                        |
| 97978  | CKD stage 2 without proteinuria                     |
| 95145  | CKD stage 3 with proteinuria                        |
| 95188  | CKD stage 3 without proteinuria                     |
| 95571  | CKD stage 3A with proteinuria                       |
| 95176  | CKD stage 3A without proteinuria                    |
| 95180  | CKD stage 3B with proteinuria                       |
| 100633 | CKD stage 3B without proteinuria                    |
| 99312  | CKD stage 4 with proteinuria                        |
| 97587  | CKD stage 4 without proteinuria                     |
| 99160  | CKD stage 5 with proteinuria                        |
| 97683  | CKD stage 5 without proteinuria                     |
| 110033 | CKD with GFR category G1 & albuminuria category A1  |
| 110003 | CKD with GFR category G1 & albuminuria category A2  |
| 110484 | CKD with GFR category G1 & albuminuria category A3  |
| 110269 | CKD with GFR category G2 & albuminuria category A1  |
| 110108 | CKD with GFR category G2 & albuminuria category A2  |
| 110251 | CKD with GFR category G2 & albuminuria category A3  |
| 109804 | CKD with GFR category G3a & albuminuria category A1 |
| 109805 | CKD with GFR category G3a & albuminuria category A2 |
| 109905 | CKD with GFR category G3a & albuminuria category A3 |
| 109963 | CKD with GFR category G3b & albuminuria category A1 |
| 109657 | CKD with GFR category G3b & albuminuria category A2 |
| 109990 | CKD with GFR category G3b & albuminuria category A3 |
| 109980 | CKD with GFR category G4 & albuminuria category A1  |
| 109904 | CKD with GFR category G4 & albuminuria category A2  |
| 110626 | CKD with GFR category G4 & albuminuria category A3  |
| 110133 | CKD with GFR category G5 & albuminuria category A1  |
| 109981 | CKD with GFR category G5 & albuminuria category A2  |

|        |  |
|--------|--|
| 110467 | CKD with GFR category G5 & albuminuria category A3           |
| 107881 | Clinical diabetic nephropathy                                |
| 15917  | Congenital cystic kidney disease                             |
| 50331  | Congenital cystic kidney disease NOS                         |
| 20629  | Congenital cystic renal disease                              |
| 47342  | Congenital renal failure                                     |
| 9240   | Cystic kidney disease NEC                                    |
| 35107  | Diabetes mellitus with nephropathy NOS                       |
| 2475   | Diabetic nephropathy   |
| 95422  | Did not attend chronic kidney disease monitoring clinic      |
| 10063  | Dysplasia of kidney  |
| 54798  | Dysplasia of kidney NOS                                      |
| 6712   | End stage renal failure                                      |
| 53852  | End stage renal failure                                      |
| 8330   | End-stage renal disease                                      |
| 40100  | Exc chronic kidney disease quality indicators: Inform dissen |
| 12860  | Except chronic kidney disease qual indic: Patient unsuitable |
| 46626  | Exception reporting: chronic kidney disease quality indicato |
| 24384  | Familial glomerulonephritis in Alport's syndrome             |
| 67486  | Fibrocystic kidney disease                                   |
| 21687  | Gout due to impairment of renal function                     |
| 51113  | Hereditary nephropathy NEC, minor glomerular abnormality     |
| 41239  | Hereditary nephropathy NEC,focal+segmnt glomerular lesion    |
| 36205  | Hereditary nephropathy not elsewhere classified              |
| 91738  | Hereditary nephropathy, NEC, dense deposit disease           |
| 62980  | Hereditary nephropathy, unspecif morphological changes       |
| 44270  | Hereditry nephropathy NEC,difus membran glomerulnephritis    |
| 50305  | Hypocomplementaemic persistent glomerulonephritis NEC        |
| 56939  | Hypokalaemic nephropathy                                     |
| 85659  | IgA nephropathy  |
| 102163 | Insulin dependent diabetes mellitus with nephropathy         |
| 57621  | Insulin dependent diabetes mellitus with nephropathy         |
| 111077 | Juvenile nephropathic cystinosis                             |
| 18331  | Multicystic renal dysplasia                                  |
| 68112  | Nephropathic amyloidosis                                     |
| 11875  | Nephropathy - chronic  |
| 59365  | Non-insulin dependent diabetes mellitus with nephropathy     |
| 35360  | Nonobstructive reflux-associated chronic pyelonephritis      |
| 60960  | Other chronic glomerulonephritis                             |

|        |   |
|--------|---|
| 63615  | Other chronic glomerulonephritis NOS                          |
| 59031  | Other congenital cystic kidney disease NOS                    |
| 59018  | Other specified congenital cystic kidney disease              |
| 4504   | Polycystic kidney   |
| 4503   | Polycystic kidney disease                                     |
| 56852  | Polycystic kidney disease NOS                                 |
| 4505   | Polycystic kidneys, adult type                                |
| 21381  | Polycystic kidneys, infantile type                            |
| 19454  | Polyneuropathy in uraemia                                     |
| 89332  | Predicted stage chronic kidney disease                        |
| 105302 | Proteinuric diabetic nephropathy                              |
| 60856  | Recur+persist haematuria difus crescentic glomerulonephritis  |
| 61317  | Recur+persist haematuria difus membranous glomerulonephritis  |
| 49642  | Recur+persist haemuria df mesangial prolif glomerulonephritis |
| 60484  | Recur+persist hmuria df mesangiocapillary glomerulonephritis  |
| 105657 | Renal dysplasia and retinal aplasia                           |
| 22876  | Renal fibrosis  |
| 41013  | Renal function impairment with growth failure                 |
| 45880  | Rovsing's operation for polycystic kidney                     |
| 107027 | Sickle cell nephropathy                                       |
| 7154   | Small kidney of unknown cause                                 |
| 38768  | Small kidneys unspecified                                     |
| 10418  | Type 1 diabetes mellitus with nephropathy                     |
| 24836  | Type 2 diabetes mellitus with nephropathy                     |
| 12640  | Type 2 diabetes mellitus with nephropathy                     |
| 66872  | Type I diabetes mellitus with nephropathy                     |
| 64571  | Type II diabetes mellitus with nephropathy                    |
| 102201 | Type II diabetes mellitus with nephropathy                    |
| 24120  | Unilateral renal dysplasia                                    |
| 43919  | Unilateral small kidney                                       |
| 105369 | Unilateral small kidney with contralateral hypertrophy        |
| 105742 | Aneurysm of anastomotic site of dialysis AV fistula           |
| 107188 | Aneurysm of dialysis arteriovenous fistula                    |
| 107220 | Aneurysm of needle site of dialysis arteriovenous fistula     |
| 110095 | Aneurysm of superficialised artery of dialysis AV fistula     |
| 60302  | Creation of graft fistula for dialysis                        |
| 106975 | Haemorrhage of dialysis arteriovenous fistula                 |
| 107260 | Infection of dialysis arteriovenous fistula                   |
| 108213 | Infection of dialysis arteriovenous graft                     |

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|        |  |
|--------|--|
| 96347  | Ligation of arteriovenous dialysis fistula   |
| 107719 | Ligation of arteriovenous dialysis graft     |
| 107082 | Occlusion of dialysis arteriovenous fistula  |
| 109135 | Occlusion of dialysis arteriovenous graft    |
| 108116 | Occlusion of dialysis vascular access        |
| 108423 | Rupture of dialysis arteriovenous graft      |
| 59315  | Stenosis of arteriovenous dialysis fistula   |
| 108699 | Stenosis of dialysis arteriovenous graft     |
| 106720 | Thrombosis of dialysis arteriovenous fistula |



**Table 1B: ICD-10 Diagnostic Codes**

| ICD-10 Code | Code Description  |
|-------------|---|
| N05.1       | Unspecified nephritic syndrome with focal and segmental glomerular lesions                        |
| N05.2       | Unspecified nephritic syndrome with diffuse membranous glomerulonephritis                         |
| N05.5       | Unspecified nephritic syndrome with diffuse mesangiocapillary glomerulonephritis                  |
| N05.6       | Unspecified nephritic syndrome with dense deposit disease   |
| N13.8       | Other obstructive and reflux nephropathy  |
| N13.9       | Obstructive and reflux nephropathy unspecified  |
| N13.73      | VUR with reflux nephropathy with hydroureter  |
| M32.14      | Glomerular disease in systemic lupus erythematosus  |
| N06.1       | Isolated proteinuria with focal and segmental glomerular lesions                                  |
| N06.2       | Isolated proteinuria with diffuse membranous glomerulonephritis                                   |
| N06.5       | Isolated proteinuria with diffuse mesangiocapillary glomerulonephritis                            |
| N06.6       | Isolated proteinuria with dense deposit disease   |
| N04.1       | Nephrotic syndrome with focal and segmental glomerular lesions                                    |
| N04.2       | Nephrotic syndrome with diffuse membranous GN   |
| N04.5       | Nephrotic syndrome with diffuse mesangiocapillary glomerulonephritis                              |
| N04.6       | Nephrotic syndrome with dense deposit disease   |
| N27.0       | Small kidney, unilateral  |
| N27.9       | Small kidney, unspecified   |
| Q60.1       | Renal agenesis bilateral  |
| Q60.3       | Renal hypoplasia, unilateral  |
| Q60.5       | Renal hypoplasia, unspecified (congenital hypoplasia, oligomeganephronia)                         |
| D63.1       | Anemia in chronic kidney disease  |
| M32.15      | Tubulo-interstitial nephropathy in SLE  |
| I12.0       | Hypertensive CKD with stage 5 CKD or end stage renal disease                                      |
| I12.9       | Hypertensive CKD with stage 1-4 or unspecified CKD  |
| I13         | Hypertensive heart and CKD  |
| I13.0       | Hypertensive heart and chronic kidney disease with heart failure and stage 1-4 CKD or unspecified |
| I13.1       | Hypertensive heart and chronic kidney disease without heart failure                               |
| I13.2       | Hypertensive heart and chronic kidney disease with heart failure and stage 5 or end stage CKD     |
| M10.3       | Gout due to renal impairment  |
| M1A.3       | Chronic gout due to renal impairment  |
| N02         | Recurrent and persistent hematuria  |
| N02.1       | Recurrent and persistent hematuria with focal and segmental glomerular lesions                    |
| N02.2       | Recurrent and persistent hematuria with diffuse membranous glomerulonephritis                     |
| N02.3       | Recurrent and persistent hematuria with diffuse mesangial proliferative glomerulonephritis        |
| N02.4       | Recurrent and persistent hematuria with diffuse endocapillary proliferative glomerulonephritis    |
| N02.5       | Recurrent and persistent hematuria with diffuse mesangiocapillary glomerulonephritis              |
| N02.6       | Recurrent and persistent hematuria with dense deposit disease                                     |
| N02.7       | Recurrent and persistent hematuria with diffuse crescentic glomerulonephritis                     |
| N02.8       | Recurrent and persistent hematuria with other morphologic changes                                 |
| N02.9       | Recurrent and persistent hematuria with unspecified morphologic changes                           |
| N03         | Chronic nephritic syndrome  |
| N03.0       | Chronic nephritic syndrome with minor glomerular abnormality                                      |
| N03.1       | Chronic nephritic syndrome with focal and segmental glomerular lesions                            |
| N03.2       | Chronic nephritic syndrome with diffuse membranous glomerulonephritis                             |
| N03.3       | Chronic nephritic syndrome with diffuse mesangial proliferative glomerulonephritis                |
| N03.4       | Chronic nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis            |

|        |  |
|--------|--|
| N03.5  | Chronic nephritic syndrome with diffuse mesangiocapillary glomerulonephritis                                     |
| N03.6  | Chronic nephritic syndrome with dense deposit disease  |
| N03.7  | Chronic nephritic syndrome with diffuse crescentic glomerulonephritis  |
| N03.8  | Chronic nephritic syndrome with other morphologic changes  |
| N03.9  | Chronic nephritic syndrome with unspecified morphologic changes  |
| N07    | Hereditary nephropathy, not elsewhere classified   |
| N07.0  | Hereditary nephropathy, not elsewhere classified with minor glomerular abnormality                               |
| N07.1  | Hereditary nephropathy, not elsewhere classified with focal and segmental glomerular lesions                     |
| N07.2  | Hereditary nephropathy, not elsewhere classified with diffuse membranous glomerulonephritis                      |
| N07.3  | Hereditary nephropathy, not elsewhere classified with diffuse mesangial proliferative glomerulonephritis         |
| N07.4  | Hereditary nephropathy, not elsewhere classified with diffuse endocapillary proliferative glomerulonephritis     |
| N07.5  | Hereditary nephropathy, not elsewhere classified with diffuse mesangiocapillary glomerulonephritis               |
| N07.6  | Hereditary nephropathy, not elsewhere classified with dense deposit disease                                      |
| N07.7  | Hereditary nephropathy, not elsewhere classified with diffuse crescentic glomerulonephritis                      |
| N07.8  | Hereditary nephropathy, not elsewhere classified with other morphologic lesions                                  |
| N07.9  | Hereditary nephropathy, not elsewhere classified with unspecified morphologic lesions                            |
| N11    | Chronic tubule-interstitial nephritis  |
| N11.0  | Nonobstructive reflux-associated chronic pyelonephritis  |
| N11.1  | Chronic obstructive pyelonephritis   |
| N11.8  | Other chronic tubulo-interstitial nephritis  |
| N11.9  | Chronic tubulo-interstitial nephritis, unspecified   |
| N14.0  | Analgesic nephropathy  |
| N15.0  | Balkan nephropathy   |
| N18    | Chronic kidney disease   |
| N18.1  | Chronic kidney disease, stage 1 (Kidney damage with normal or increased GFR ( $\geq 90$ mL/min))                 |
| N18.2  | Chronic kidney disease, stage 2 (Kidney damage with mild decreased GFR (60-89 mL/min))                           |
| N18.3  | Chronic kidney disease, stage 3 (Kidney damage with moderately decreased GFR (30-59 mL/min))                     |
| N18.4  | Chronic kidney disease, stage 4 (Kidney damage with severely decreased GFR (15-29 mL/min))                       |
| N18.5  | Chronic kidney disease, stage 5  |
| N18.6  | End stage renal disease  |
| N18.9  | Chronic kidney disease, unspecified  |
| N25.0  | Renal osteodystrophy   |
| N25.81 | Secondary hyperparathyroidism of renal origin  |
| N27.1  | Small kidney bilateral   |
| O10.2  | Pre-existing hypertensive chronic kidney disease complicating pregnancy, childbirth and the puerperium           |
| O10.3  | Pre-existing hypertensive heart and chronic kidney disease complicating pregnancy, childbirth and the puerperium |
| P96.0  | Congenital renal failure   |
| Q60.4  | Renal hypoplasia, bilateral  |
| Q60.6  | Potter's syndrome  |
| Q61.02 | Congenital multiple renal cysts  |
| Q61.1  | Polycystic kidney, infantile type  |
| Q61.19 | Other polycystic kidney, infantile type  |

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|--------|--|
| Q61.2  | Polycystic kidney, adult type  |
| Q61.3  | Polycystic kidney, unspecified   |
| Q61.4  | Renal dyaplsia (multicystic dysplastic, multycystic)   |
| Q61.5  | Medullary cystic kidney (UTD: end-stage renal disease (ESRD) onset that is highly variable, usually between the ages of 20 and 70 years) |
| Q61.8  | Other cystic kidney diseases (applicable to fibrocystic kidney, fibrocystic renal degeneration or disease)                               |
| Q61.9  | Cystic kidney diease, unspecified (includes Meckel gruber syndrome)  |
| Q87.81 | Alport syndrome  |

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**Table 1C: OPCS-4 Procedure Codes**

| OPCS4 Code | Code Description                             |
|------------|--|
| L74.6      | Creation of graft fistula for dialysis       |
| M02.1      | Nephrectomy and excision of perirenal tissue |
| M02.2      | Nephroureterectomy NEC                       |
| M02.3      | Bilateral nephrectomy                        |
| M02.5      | Nephrectomy NEC                              |
| M02.7      | Other specified total excision of kidney     |
| M02.9      | Unspecified total excision of kidney         |

**Supplemental Table 2: Nonspecific Renal Codes Defining Exclusion from the Unexposed Cohort**

**Table 2A: CPRD Read Codes**

| Medcode | Read term (Code Description)                                 |
|---------|--|
| 5451    | [D]Albuminuria   |
| 22327   | [D]Kidney function test abnormal                             |
| 10924   | [D]Microalbuminuria  |
| 11248   | [D]Proteinuria   |
| 38284   | [D]Proteinuria NOS   |
| 10768   | [D]Renal function test abnormal                              |
| 34320   | [D]Renal scarring  |
| 98067   | [X]Hydronephrosis with ureteral stricture NEC                |
| 72478   | [X]Nephropathy induced by other drugs+biological substances  |
| 72621   | [X]Other and unspecified hydronephrosis                      |
| 70157   | [X]Other disorders of kidney and ureter                      |
| 96819   | [X]Other disorders resulting/impaired renal tubular function |
| 56896   | [X]Other specified disorders of kidney and ureter            |
| 64030   | [X]Persistent proteinuria, unspecified                       |
| 61930   | [X]Renal failure   |
| 94842   | [X]Renal tubulo-interstitial diseases                        |
| 103757  | [X]Tubulo-interstit nephritis, not specif as acute or chron  |
| 63000   | Benign hypertensive heart and renal disease                  |
| 43935   | Benign hypertensive renal disease                            |
| 105634  | Candida pyelonephritis                                       |
| 62045   | Closed injury of kidney                                      |
| 31549   | Compensation for renal failure                               |
| 5379    | Congenital hydronephrosis                                    |
| 26001   | Deteriorating renal function                                 |
| 110092  | Emphysematous pyelonephritis                                 |
| 52969   | Gouty nephropathy  |
| 61145   | Gouty nephropathy NOS  |
| 6774    | H/O: kidney disease  |
| 8828    | H/O: nephritis   |
| 9959    | H/O: renal disease   |
| 3277    | Hydronephrosis   |
| 27302   | Hydronephrosis NOS   |
| 8522    | Hydronephrosis with pelviureteric junction obstruction       |
| 27592   | Hydronephrosis with renal and ureteral calculous obstruction |
| 28159   | Hydronephrosis with ureteral stricture NEC                   |

|        |   |
|--------|---|
| 10410  | Hydronephrosis with ureteropelvic junction obstruction                      |
| 6842   | Impaired renal function   |
| 8919   | Impaired renal function disorder  |
| 25980  | Impaired renal function disorder NOS  |
| 105967 | Inherited renal tubule insufficiency with cholestatic jaundice              |
| 16496  | Injury to kidney  |
| 52339  | Injury to kidney NOS  |
| 102947 | Ischaemic nephropathy   |
| 43611  | Isolated proteinuria with specified morphological lesion                    |
| 101572 | Isolated proteinuria, with other specific morphological changes             |
| 59992  | Isolated proteinuria, with unspecified morphological changes                |
| 2991   | Kidney and ureter disease NOS   |
| 39598  | Kidney failure as a complication of care                                    |
| 107771 | Kidney failure unspecified  |
| 66213  | Kidney injury due to birth trauma   |
| 110554 | Kidney injury with open wound into cavity, unspecified                      |
| 71500  | Kidney injury without mention of open wound into cavity NOS                 |
| 62728  | Kidney injury without open wound into cavity, unspecified                   |
| 67232  | Malignant hypertensive heart and renal disease                              |
| 39649  | Malignant hypertensive renal disease  |
| 33580  | Nephritis and nephropathy unspecified                                       |
| 4850   | Nephritis and nephropathy unspecified                                       |
| 2773   | Nephritis, nephrosis and nephrotic syndrome                                 |
| 15780  | Nephritis, nephrosis and nephrotic syndrome NOS                             |
| 41159  | Nephropathy induced by other drugs, medicines and biological substances     |
| 57784  | Nephropathy induced by unspecified drug, medicament or biological substance |
| 38312  | Nephropathy NOS in pregnancy without hypertension                           |
| 11873  | Nephropathy, unspecified  |
| 11436  | Non-functioning kidney  |
| 39840  | Other impaired renal function disorder                                      |
| 50804  | Other impaired renal function disorder NOS                                  |
| 34669  | Other interstitial nephritis  |
| 36273  | Other kidney and ureter disorders   |
| 44657  | Other kidney and ureteric disorders   |
| 34675  | Other kidney and ureteric disorders NOS                                     |
| 8098   | Other kidney disorders  |
| 27335  | Other nephritis and nephrosis in diseases EC                                |
| 44055  | Other nephritis and nephrosis NOS   |
| 35065  | Other nephritis and nephrosis unspecified                                   |

|        |  |
|--------|--|
| 48022  | Other specified compensation for renal failure             |
| 49150  | Other specified nephritis, nephrosis or nephrotic syndrome |
| 16465  | Persistent proteinuria, unspecified                        |
| 16008  | Proliferative nephritis unspecified                        |
| 1802   | Proteinuria  |
| 58164  | Rapidly progressive nephritis unspecified                  |
| 107765 | Renal disorders in systemic disease                        |
| 11554  | Renal failure as a complication of care                    |
| 350    | Renal failure unspecified                                  |
| 106860 | Renal failure-associated hyperphosphataemia                |
| 3980   | Renal function tests abnormal                              |
| 25763  | Renal function tests borderline                            |
| 11787  | Renal impairment   |
| 18770  | Renal injury due to birth trauma                           |
| 64622  | Renal tubulo-interstitial disorder/ neoplastic diseases    |
| 45523  | Renal tubulo-interstitial disorders in diseases EC         |
| 106045 | Renal vascular disease                                     |
| 10460  | Renal vascular disorders                                   |
| 15340  | Renal vascular disorders NOS                               |
| 20516  | Salt-losing nephritis                                      |
| 50893  | Toxic nephropathy, not elsewhere classified                |
| 52272  | Tuberculous nephropathy                                    |
| 49235  | Tuberculous pyelonephritis                                 |
| 23990  | Tubulo-interstit nephritis, not specif as acute or chron   |
| 30294  | Type 1 diabetes mellitus with persistent microalbuminuria  |
| 30323  | Type 1 diabetes mellitus with persistent proteinuria       |
| 18390  | Type 2 diabetes mellitus with persistent microalbuminuria  |
| 26054  | Type 2 diabetes mellitus with persistent proteinuria       |
| 102620 | Type I diabetes mellitus with persistent microalbuminuria  |
| 85991  | Type II diabetes mellitus with persistent microalbuminuria |
| 60796  | Type II diabetes mellitus with persistent proteinuria      |
| 47080  | Unspecified renal disease in pregnancy                     |
| 96724  | Unspecified renal disease in pregnancy - delivered         |
| 54938  | Unspecified renal disease in pregnancy unspecified         |
| 4809   | Uraemia NOS  |
| 106058 | Urate nephropathy  |
| 106213 | Uric acid nephropathy                                      |
| 11992  | Vascular disorders of kidney                               |
| 38572  | Xanthogranulomatous pyelonephritis                         |

**Table 2B: HES ICD-10 Codes**

| ICD-10 Code | Code Description   |
|-------------|--|
| E08.2       | Diabetes mellitus due to underlying condition with kidney complications                                      |
| E09.2       | Drug or chemical induced DM with kidney complications  |
| E10.2       | Type 1 DM with diabetic kidney complications   |
| E11.2       | Type 2 DM with diabetic kidney complications   |
| E13.2       | Other specified DM with kidney complication  |
| R80.1       | Persistent proteinuria, unspecified  |
| N04.0       | Nephrotic syndrome with minor glomerular abnormality   |
| N04.3       | Nephrotic syndrome with diffuse mesangial proliferative glomerulonephritis                                   |
| N04.4       | Nephrotic syndrome with diffuse endocapillary proliferative glomerulonephritis                               |
| N04.7       | Nephrotic syndrome with diffuse crescentic GN  |
| N04.8       | Nephrotic syndrome with other morphologic changes  |
| N04.9       | Nephrotic syndrome with unspecified morphologic changes  |
| D86.84      | Sarcoid pyelonephritis   |
| I15.1       | Hypertension secondary to other renal disorders  |
| I70.1       | Atherosclerosis of renal artery  |
| I72.2       | Aneurysm of renal artery   |
| I75.81      | Atheroembolism of kidney (excluded because code asks to specify AKI or CKD with separate code if applicable) |
| I77.73      | Dissection of renal artery   |
| M31.31      | Wegner's granulomatosis with renal involvement   |
| M35.04      | Sicca syndrome with tubulo-interstitial nephropathy  |
| N05.0       | Unspecified nephritic syndrome with minor glomerular abnormality   |
| N05.3       | Unspecified nephritic syndrome with diffuse mesangial proliferative glomerulonephritis                       |
| N05.4       | Unspecified nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis                   |
| N05.7       | Unspecified nephritic syndrome with diffuse crescentic glomerulonephritis                                    |
| N05.8       | Unspecified nephritic syndrome with other morphologic changes  |
| N05.9       | Unspecified nephritic syndrome with unspecified morphologic changes  |
| N06.0       | Isolated proteinuria with minor glomerular abnormality   |
| N06.3       | Isolated proteinuria with diffuse mesangial proliferative glomerulonephritis                                 |
| N06.4       | Isolated proteinuria with diffuse endocapillary proliferative glomerulonephritis                             |
| N06.7       | Isolated proteinuria with diffuse crescentic glomerulonephritis  |
| N06.8       | Isolated proteinuria with other morphologic lesion   |
| N06.9       | Isolated proteinuria with unspecified morphologic lesion   |
| N08         | Glomerular disorders in diseases classified elsewhere  |
| N12         | Tubulointerstitial nephritis not specified as acute or chronic   |
| N13.0       | HN with UP junction obstruction  |
| N13.1       | HN with ureteral stricture, NEC  |
| N13.2       | HN with renal and ureteral calculous obstruction   |
| N13.4       | Hydroureter  |
| N13.7       | Vesicoureteral reflux  |
| N14.1       | Nephropathy induced by other drugs, medicaments and biological substances                                    |
| N14.2       | Nephropathy induced by unspecified drug, medicament or biologic substance                                    |
| N14.3       | Nephropathy induced by heavy metals  |
| N14.4       | Toxic nephropathy not elsewhere classified   |
| N15.8       | Other specified renal tubule-interstitial disease  |
| N15.9       | Renal tubule-interstitial disease, unspecified   |
| N16         | Renal tubule-interstitial disorders in diseases classified elsewhere   |
| N19         | Unspecified kidney failure   |
| N25.8       | Other disorders resulting from impaired renal tubular function   |



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|         |   |
|---------|---|
| N25.9   | Disorder resulting from impaired renal tubular function, unspecified            |
| N26.1   | Atrophy of kidney (terminal) – includes renal atrophy; unilateral renal atrophy |
| N28.8   | Other specified disorders of kidney and ureter                                  |
| N28.9   | Disorder of kidney and ureter, unspecified                                      |
| N29     | Other disorders of kidney and ureter in diseases classified elsewhere           |
| N39.8   | Other specified disorders of urinary system                                     |
| N39.9   | Disorder of urinary system, unspecified   |
| N99.0   | Postprocedural (acute) (chronic) kidney failure                                 |
| O26.83  | Pregnancy related renal disease   |
| O26.839 | Pregnancy-related renal disease   |
| Q27.1   | Congenital renal artery stenosis  |
| Q27.2   | Other congenital malformations of renal artery                                  |
| Q27.34  | Arteriovenous malformation of renal vessel                                      |
| Q60.0   | Renal agenesis, unilateral  |
| Q60.2   | Renal agenesis unspecified  |
| Q62.1   | Congenital occlusion of ureter  |
| Q62.2   | Congenital megaureter   |
| Q62.31  | Congenital ureterocele, orthotopic  |
| R94.4   | Abnormal results of kidney function studies                                     |
| S35.40  | Unspecified injury of renal blood vessel  |
| S35.41  | Laceration of renal blood vessel (artery/vein)                                  |
| S35.49  | Other specified injury of renal blood vessel                                    |
| S37.0   | Injury of kidney (excludes acute nontraumatic kidney injury)                    |
| T81.711 | Complication of a renal artery following a procedure, NEC                       |
| Z52.4   | Kidney donor  |
| Z87.448 | Personal history of other diseases of urinary system                            |
| Z90.5   | Acquired absence of kidney (applies to total and partial nephrectomy)           |

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**Table 2C OPCS-4 Procedure Codes**

| OPCS-4 Code | Code Description                           |
|-------------|--|
| M02.4       | Excision of half of horseshoe kidney       |
| M03.1       | Heminephrectomy of duplex kidney           |
| M03.8       | Other specified partial excision of kidney |
| M03.9       | Unspecified partial excision of kidney     |

**Supplemental Table 3: List of Category A and Category B Potentially Nephrotoxic Medications Included in the Study**

**Table 3A: Category A Medications**

| Medications included in our definition | Medications prescribed by general practitioners to included patients during the study period |
|--|--|
| <b>Aminoglycosides</b>                 |  |
| Amikacin sulfate                       |  |
| Framycetin Sulphate                    |  |
| Gentamicin                             | Gentamicin   |
| Kanamycin                              |  |
| Neomycin                               |  |
| Netilmicin sulfate                     |  |
| Streptomycin                           |  |
| Tobramycin                             |  |
| Paromomycin                            |  |
| <b>NSAIDS</b>                          |  |
| Aceclofenac                            |  |
| Acemetacin                             |  |
| Celecoxib                              | Celecoxib  |
| Codeine Phosphate/Ibuprofen            |  |
| Dexibuprofen                           |  |
| Dexketoprofen trometamol               |  |
| Diclofenac                             | Diclofenac   |
| Diflunisal                             |  |
| Etodolac                               |  |
| Etoricoxib                             |  |
| Fenbufen                               |  |
| Fenoprofen calcium                     |  |
| Flurbiprofen                           |  |
| Ibuprofen                              | Ibuprofen  |
| Indometacin                            | Indometacin  |
| Ketoprofen                             | Ketoprofen   |
| Lornoxicam                             |  |
| Magnesium Trisilicate                  |  |
| Mefenamic acid                         | Mefenamic acid   |
| Meloxicam                              |  |
| Nabumetone                             |  |
| Naproxen                               | Naproxen   |
| Phenylbutazone                         |  |
| Piroxicam                              | Piroxicam  |
| Salsalate                              |  |
| Sulindac                               |  |
| Tenoxicam                              |  |
| Tiaprofenic acid                       |  |
| Tolfenamic Acid                        |  |
| Tolmetin Sodium                        |  |
| <b>Antivirals</b>                      |  |
| Aciclovir                              | Aciclovir  |
| Valaciclovir                           | Valaciclovir   |

|                               |                               |
|-------------------------------|-------------------------------|
| Ganciclovir                   |                               |
| Cidofovir                     |                               |
| Foscarnet sodium              |                               |
| Valganciclovir hydrochloride  | Valganciclovir hydrochloride  |
| Indinavir sulfate             |                               |
| Salicylates                   |                               |
| Balsalazide disodium          |                               |
| Mesalazine                    | Mesalazine                    |
| Olsalazine sodium             |                               |
| Sulfapyridine                 |                               |
| Sulfasalazine                 | Sulfasalazine                 |
| Aspirin                       |                               |
| Para-aminosalicylic Acid      |                               |
| Bismuth subsalicylate         |                               |
| Sodium salicylate             |                               |
| Acetylsalicylic acid          |                               |
| PPIs                          |                               |
| Esomeprazole                  | Esomeprazole                  |
| Lansoprazole                  | Lansoprazole                  |
| Omeprazole                    | Omeprazole                    |
| Pantoprazole                  |                               |
| Rabeprazole sodium            |                               |
| Other antimicrobials          |                               |
| Amphotericin                  |                               |
| Amphotericin B                |                               |
| Colistimethate sodium         | Colistimethate sodium         |
| Colistin sulfate              |                               |
| Sulfamethoxazole/Trimethoprim | Sulfamethoxazole/Trimethoprim |
| Vancomycin hydrochloride      | Vancomycin hydrochloride      |
| Piperacillin Sodium           |                               |
| Immunomodulators/suppressors  |                               |
| Ciclosporin                   | Ciclosporin                   |
| Cisplatin                     |                               |
| Ifosfamide                    |                               |
| Methotrexate                  | Methotrexate                  |
| Tacrolimus                    | Tacrolimus                    |
| Lithium                       |                               |
| Pamidronate                   |                               |

**Table 3B: Category B Medications**

| Medications included in our definition | Medications prescribed by general practitioners to included patients during the study period |
|--|--|
| ACE-Inhibitors                         |  |
| Captopril                              | Captopril  |
| Cilazapril                             |  |
| Enalapril                              | Enalapril  |
| Imidapril                              |  |
| Lisinopril                             | Lisinopril   |
| Moexipril hydrochloride                |  |
| Perindopril                            | Perindopril  |

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|  |  |
|--|--|
| Quinapril                                |  |
| Ramipril                                 | Ramipril                                 |
| Trandolapril                             |  |
| Angiotensin II Receptor Blockers         |  |
| Azilsartan                               |  |
| Candesartan                              |  |
| Eprosartan                               |  |
| Irbesartan                               | Irbesartan                               |
| Losartan                                 | Losartan                                 |
| Olmesartan                               |  |
| Telmisartan                              |  |
| Valsartan                                | Valsartan                                |
| Cephalosporins                           |  |
| Cefotaxime sodium                        |  |
| Ceftazidime pentahydrate                 |  |
| Cefuroxime axetil                        | Cefuroxime axetil                        |
| Cefaclor                                 | Cefaclor                                 |
| Cefadroxil monohydrate                   | Cefadroxil monohydrate                   |
| Cefalexin                                | Cefalexin                                |
| Cefamandole                              |  |
| Cefazolin sodium                         |  |
| Cefixime                                 | Cefixime                                 |
| Cefodizime                               |  |
| Cefoxitin sodium                         |  |
| Cefpodoxime proxetil                     |  |
| Cefprozil                                |  |
| Cefradine                                | Cefradine                                |
| Ceftibuten                               |  |
| Ceftizoxime                              |  |
| Ceftriaxone sodium                       | Ceftriaxone sodium                       |
| Other antibiotics                        |  |
| Cinoxacin                                |  |
| Ciprofloxacin                            | Ciprofloxacin                            |
| Dapsone                                  | Dapsone                                  |
| Enoxacin                                 |  |
| Levofloxacin                             | Levofloxacin                             |
| Moxifloxacin hydrochloride               |  |
| Nalidixic acid                           |  |
| Norfloxacin                              | Norfloxacin                              |
| Ofloxacin                                | Ofloxacin                                |
| Pentamidine isetionate                   |  |
| Rifampicin                               | Rifampicin                               |
| Penicillins                              |  |
| Amoxicillin                              | Amoxicillin                              |
| Amoxicillin sodium/Potassium clavulanate | Amoxicillin sodium/Potassium clavulanate |
| Ampicillin                               | Ampicillin                               |
| Bacampicillin                            |  |
| Benzympenicillin                         | Benzympenicillin                         |
| Flucloxacillin                           | Flucloxacillin                           |
| Phenoxymethylpenicillin potassium        | Phenoxymethylpenicillin potassium        |
| Pivampicillin                            |  |

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|                               |             |
|-------------------------------|-------------|
| Talampicillin                 |             |
| Ticarcillin Sodium            |             |
| Immunomodulators/suppressors  |             |
| Bevacizumab                   |             |
| Carboplatin                   |             |
| Interferon Alfa-2b            |             |
| Peginterferon Alfa-2b         |             |
| Sirolimus                     |             |
| Temsirolimus                  |             |
| Anti-epileptic                |             |
| Topiramate                    | Topiramate  |
| Zonisamide                    | Zonisamide  |
| HIV meds and other antivirals |             |
| Abacavir sulfate              |             |
| Adefovir dipivoxil            |             |
| Atazanavir sulfate            |             |
| Didanosine                    |             |
| Lamivudine                    |             |
| Ritonavir                     |             |
| Tenofovir                     |             |
| Contrast agents               |             |
| Iodixanol                     |             |
| Iohexol                       |             |
| Iopamidol                     |             |
| Ioversol                      |             |
| Meglumine gadopentetate       |             |
| Other                         |             |
| Auranofin                     |             |
| Propylthiouracil              |             |
| Zoledronic Acid               |             |
| Quinine                       |             |
| Clopidogrel                   |             |
| Ranitidine                    | Ranitidine  |
| Allopurinol                   |             |
| Hydralazine                   | Hydralazine |

**Supplemental Table 4: CKD Diagnosis and Procedure codes of Included Study Patients**

**Table 4A: CPRD Read Codes for Renal Disease**

| Code description   | Number of Patients |
|--|--------------------|
| <b>Cystic kidney disease</b>                                 | <b>100</b>         |
| Polycystic kidney disease                                    | 70                 |
| Congenital cystic kidney disease                             | 14                 |
| Cystic kidney disease  | 9                  |
| Multicystic renal dysplasia                                  | 5                  |
| Polycystic kidneys infantile type                            | 2                  |
| <b>Chronic kidney disease</b>                                | <b>99</b>          |
| Chronic kidney disease/CKD                                   | 29                 |
| Chronic renal failure  | 31                 |
| Except chronic kidney disease qual indic: Patient unsuitable | 17                 |
| Chronic renal impairment                                     | 11                 |
| Chronic kidney disease monitoring                            | 7                  |
| End-stage renal disease                                      | 4                  |
| <b>Nephropathy/nephritis</b>                                 | <b>72</b>          |
| Chronic pyelonephritis                                       | 16                 |
| IgA nephropathy  | 14                 |
| Berger's nephropathy   | 9                  |
| Chronic glomerulonephritis                                   | 9                  |
| Chronic nephropathy  | 8                  |
| Lupus nephritis  | 8                  |
| Familial GN in Alport's                                      | 3                  |
| Diabetic nephropathy   | 3                  |
| Chronic membranoproliferative glomerulonephritis             | 1                  |
| Membranoproliferative nephritis unspecified                  | 1                  |
| <b>Renal dysplasia/hypoplasia</b>                            | <b>70</b>          |
| Small kidney(s)  | 50                 |
| Kidney dysplasia   | 16                 |
| Unilateral renal dysplasia                                   | 3                  |
| Bilateral renal dysplasia                                    | 1                  |
| <b>Other</b>   | <b>10</b>          |
| Hypertensive renal disease                                   | 5                  |
| Renal fibrosis   | 4                  |
| Juvenile nephropathic cystinosis                             | 1                  |
| <b>Total</b>   | <b>351</b>         |

**Table 4B: HES ICD-10 Codes for Renal Disease**

| <b>Code description</b>  | <b>Number of Patients</b> |
|--|---------------------------|
| <b>Nephropathy/nephritis</b>   | <b>295</b>                |
| Obstructive and reflux nephropathy                                     | 115                       |
| Recurrent and persistent hematuria with morphological changes          | 91                        |
| Chronic tubulo-interstitial nephritis                                  | 24                        |
| Chronic nephritic syndrome with morphological changes                  | 17                        |
| Nonobstructive reflux-associated chronic pyelonephritis                | 15                        |
| Nephrotic syndrome with focal and segmental glomerular lesions         | 14                        |
| Unspecified nephritic syndrome with diffuse mesangiocapillary GN       | 6                         |
| Unspecified nephritic syndrome focal and segmental glomerular lesions  | 4                         |
| Nephrotic syndrome with diffuse mesangiocapillary glomerulonephritis   | 3                         |
| Hereditary nephropathy with morphological changes                      | 2                         |
| Chronic obstructive pyelonephritis                                     | 2                         |
| Unspecified nephritic syndrome with diffuse membranous GN              | 1                         |
| Isolated proteinuria with diffuse mesangiocapillary glomerulonephritis | 1                         |
| <b>Renal dysplasia/hypoplasia</b>                                      | <b>144</b>                |
| Small kidney(s)  | 79                        |
| Renal dysplasia  | 51                        |
| Renal hypoplasia   | 14                        |
| <b>Chronic kidney disease</b>  | <b>79</b>                 |
| Chronic kidney disease   | 58                        |
| Hypertensive chronic kidney disease stage 5 or end stage               | 11                        |
| Hypertensive chronic kidney disease stage 1-4 or unspecified           | 10                        |
| <b>Cystic kidney disease</b>   | <b>28</b>                 |
| Polycystic kidney, unspecified   | 15                        |
| Cystic kidney disease  | 8                         |
| Polycystic kidney, infantile type                                      | 5                         |
| <b>Other</b>   | <b>5</b>                  |
| Potter's syndrome  | 2                         |
| Congenital renal failure   | 2                         |
| Renal osteodystrophy   | 1                         |
| <b>Total</b>   | <b>551</b>                |



**Table 4C: HES OPCS-4 Procedure codes for Renal Disease**

| Code description                     | Number of Patients |
|--------------------------------------|--------------------|
| <b>Nephrectomy</b>                   | <b>106</b>         |
| Nephrectomy                          | 81                 |
| Nephrectoureterectomy                | 22                 |
| Unspecified total excision of kidney | 2                  |
| Bilateral nephrectomy                | 1                  |

**Table 4D: CPRD Read codes for Dialysis**

| Code description                                   | Number of Patients |
|--|--------------------|
| <b>Dialysis</b>                                    | <b>10</b>          |
| Peritoneal dialysis                                | 5                  |
| Dialysis for renal failure                         | 3                  |
| Haemodialysis                                      | 1                  |
| Removal of ambulatory peritoneal dialysis catheter | 1                  |

**Supplemental Table 5: Detailed proportions for Manuscript Figures 2 and 3**

Table 5A: Proportion and Total Number of CKD vs. Non-CKD Patients Who Received a Category A Medication, by Medication Class

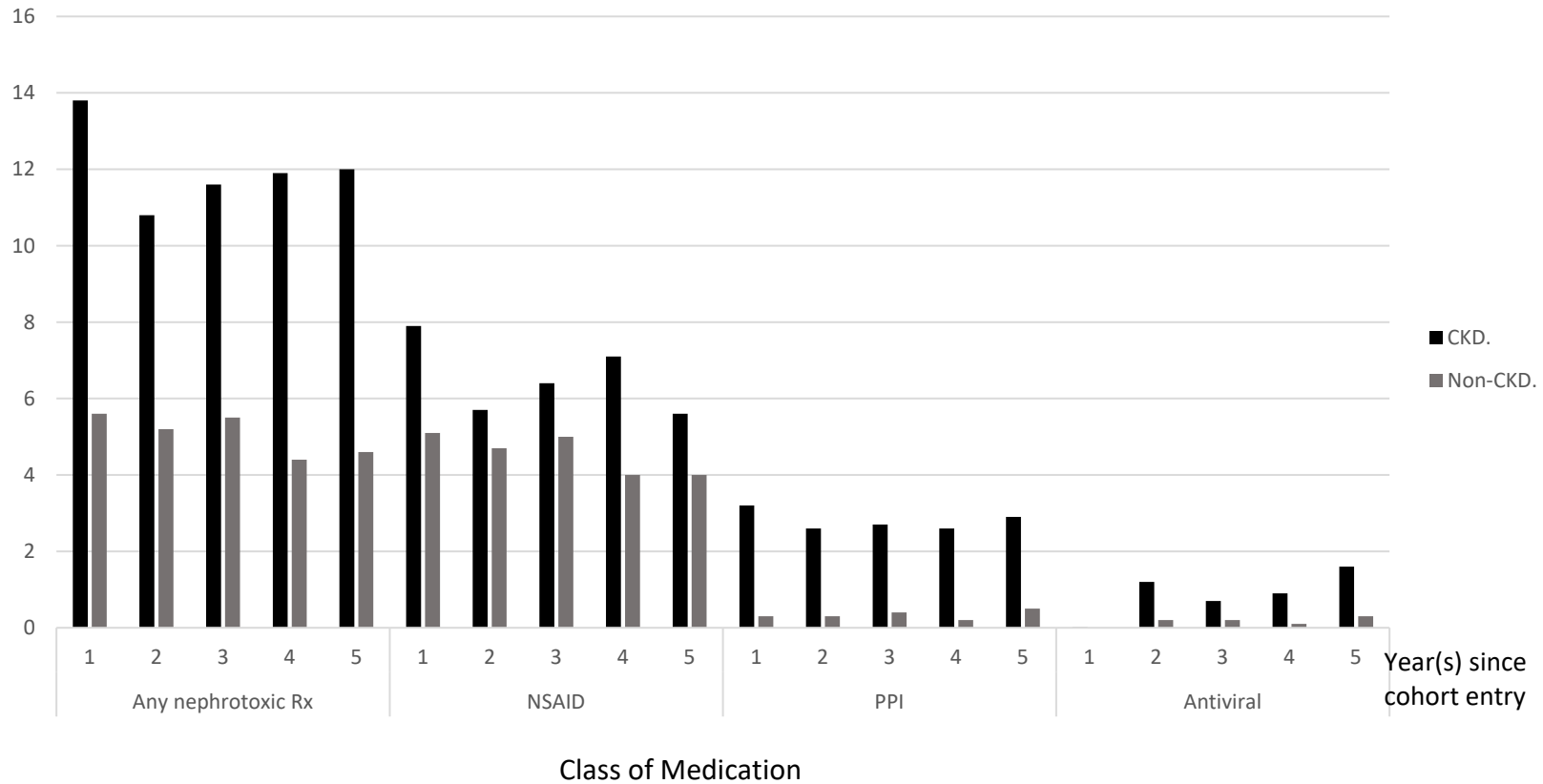
| Medication                           | CKD<br>n (%)          | Non-CKD<br>n (%)    |
|--------------------------------------|-----------------------|---------------------|
| Any potential nephrotoxic medication | 263 (26)              | 591 (15)            |
| NSAIDs                               | 175 (17)              | 543 (13)            |
| PPIs                                 | 56 (6)                | 40 (1)              |
| Immunomodulators                     | 41 (4)                | 0 (0)               |
| Other antibiotics                    | 30 (3)                | <5 <sup>a</sup> (0) |
| Antivirals                           | 25 (3)                | 27 (0.7)            |
| Salicylates                          | <5 <sup>a</sup> (0.2) | <5 <sup>a</sup> (0) |
| Aminoglycosides                      | <5 <sup>a</sup> (0.1) | 0 (0)               |

Table 5B: Proportion of CKD vs. Non-CKD Patients Who Received a Category A or Category B Medication, by Medication Class

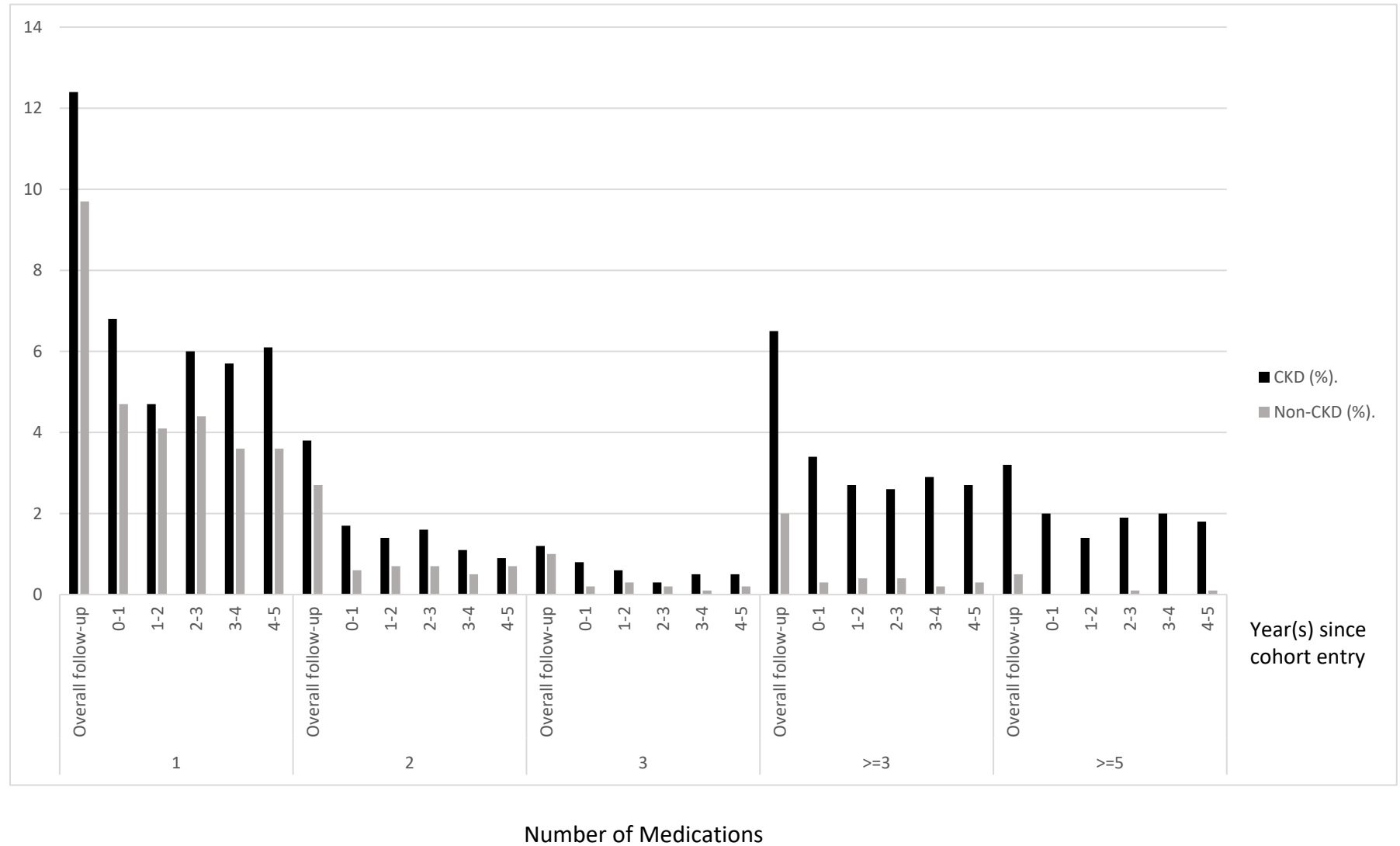
| Medication  | CKD<br>n (%)          | Non-CKD<br>n (%) |
|---|-----------------------|------------------|
| Any potential nephrotoxic medication  | 724 (71)              | 2036 (50)        |
| Any potential nephrotoxic medication<br>(excluding ACE-inhibitors and ARBs) | 695 (68)              | 2036 (50)        |
| Penicillins   | 579 (57)              | 1797 (44)        |
| Cephalosporins  | 186 (18)              | 160 (4)          |
| Other antibiotics (2)   | 55 (5)                | 19 (0.5)         |
| Ranitidine  | 48 (5)                | 25 (0.6)         |
| Anti-epileptics   | <5 <sup>a</sup> (0.3) | 5 (0.1)          |
| Hydralazine   | <5 <sup>a</sup> (0.3) | 0 (0)            |
| ACE-inhibitors  | 105 (10)              | 0 (0)            |
| Angiotensin-II receptor blockers  | 33 (3)                | 0 (0)            |

### Supplemental Figure 1: Trends in Category A Medication Prescribing by Year Since Cohort Entry

**Figure 5A: Percentage of Patients Receiving at least one Category A Medication by Year Since Cohort Entry**



**Figure 5B: Number of Category A Medications Prescribed Per Patient Throughout Entire Follow-Up and by Year Since Cohort Entry**



## **Supplemental Methods and Results corresponding to sections within the manuscript**

### **Study population**

Where exposed patients had fewer than 4 eligible matches, the general practitioner visits matching criterion was broadened to a categorization of 0, 1-3, or >3 general practitioner visits in the 12 months prior to cohort entry and in cases persisting with fewer than 4 matches, on 0-1 and >1 general practitioner visits.

### **Outcome definition**

We constructed our lists as follows: Category A medications included medications considered definitively nephrotoxic in at least two of the three reference studies. To this list, we added medications in the British National Formulary for Children belonging to the following medication classes: non-steroidal anti-inflammatory drugs (NSAIDs), aminoglycoside antibiotics, proton pump inhibitors and salicylates. We did not include angiotensin converting enzyme inhibitors to our Category A medication list despite some of these agents appearing in two or more of our reference studies due to their potential indication in CKD. Our second, Category B list was broadened to provide as wide a capture of potential nephrotoxic medications as possible. This list included our Category A medications plus medications considered to have nephrotoxic potential in any of the three reference studies or medications which only one of the three studies considered definitively nephrotoxic.

Each individual prescription was considered independently. The rationale being that repeated exposure to the same drug likely had a cumulative effect on kidney risk similarly to exposure to multiple different nephrotoxic drugs. Our study did not evaluate adherence to prescribed medications and the CPRD does not allow us to confirm the patient received a medication that was prescribed. Refills were therefore only captured if they were re-prescribed by the physician. We felt this was important to the design of our study as the main interest was to evaluate general practitioner prescribing behaviors and an outcome based on issued prescriptions was felt to best capture this.

Because each child had the possibility of receiving more than one prescription over the follow-up period, prescription counts occurring within a same child were likely to be more highly correlated than prescription counts between individual children. We accounted for this non-independence of observations with the use of modified sandwich variance estimators or robust variance estimators for the calculation of our confidence intervals.

### **Matching, CKD diagnosis and population characteristics**

There were 231 CKD patients (23%) with fewer than 4 eligible matches when matching on exact number of general practitioner visits in the year preceding cohort entry. These were instead matched on a categorization of 0, 1-3, or >3 general practitioner visits in the year preceding cohort entry. Eighteen CKD patients still did not have a minimum of four eligible matches and for these, categorization was broadened to 0-1 and >1 general practitioner visits. One CKD patient was left without any eligible matches and was excluded from the study.

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