Monitoring kidney function in primary care: an overview of current practice and identification of optimal strategies

Summary of Research in plain English

Monitoring of kidney function in primary care is important for two main reasons. Firstly, to diagnose chronic kidney disease especially in patients with conditions, such as diabetes or heart failure, which may affect their kidney function; secondly, to determine when to refer patients with existing kidney disease to specialist assessment such as if their kidney function becomes very poor or declines very quickly. Disease progression can be delayed if it is identified early.

Kidney function is usually tested through blood or urine tests. We would like to use the Clinical Practice Research Datalink (CPRD) to describe how many of these tests are carried out in usual practice in the UK, how many are used for initial diagnosis of kidney disease or for monitoring of existing disease, and to examine whether testing varies by region, calendar-period or the existence of major long-term conditions, such as heart disease, high blood pressure or diabetes.

As current national guidelines for how frequently patients should be tested are based on low-quality evidence, we would also like to use the CPRD to model different monitoring scenarios to identify the best strategy for testing, and to make recommendations on how often testing should occur for diagnosis and monitoring purposes.

Background and rationale

Chronic Kidney Disease (CKD) is a largely asymptomatic condition where kidney function and/or structure is abnormal (1,2). About 2 million adults in England have been diagnosed

with moderate to severe CKD, defined by persistent proteinuria or estimates of reduced glomerular filtration rate from serum creatinine (eGFR). CKD is associated with increased cardiovascular risk (predominantly stroke, ischaemic heart disease and heart failure) (3–7), and increased all-cause mortality (4–6), however disease progression can be delayed if it is identified early (1,8). The majority of patients (98%) are managed in primary care using a multifactorial approach of: repeated monitoring; maintenance of blood pressure below agreed guideline limits (140/90mmHg, or below 130/80mmHg in those with diabetes or raised proteinuria); treatment of hypertension with angiotensin-converting-enzyme inhibitors (ACE inhibitors) or Angiotensin II Receptor Blockers (ARBs); and encouragement to lead a healthy lifestyle (1).

Monitoring forms a major part in managing long term illness. It is an important element of health care; however, despite the substantial costs it entails, it has been neglected as an area for research. Guideline bodies often find there is a lack of evidence on which to make recommendations, for example regarding the frequency of monitoring (9). Although good monitoring can improve patient outcomes, poor monitoring may be an expensive waste of resources, not only incurring huge cost to the National Health Service (NHS) but also leading to inappropriate treatment and patient inconvenience as well as absence from work.

There has been a dramatic increase in the use of laboratory testing over recent decades, particularly repeat testing or monitoring. CKD management guidance from the National Institute for health and Care Excellence (NICE) (2) recommends that the frequency of serum creatinine monitoring should depend on the clinical situation, with more frequent monitoring in patients with poorer kidney function; figure 1 shows the recommended frequencies by category of eGFR and Albumin Creatinine Ratio (ACR).

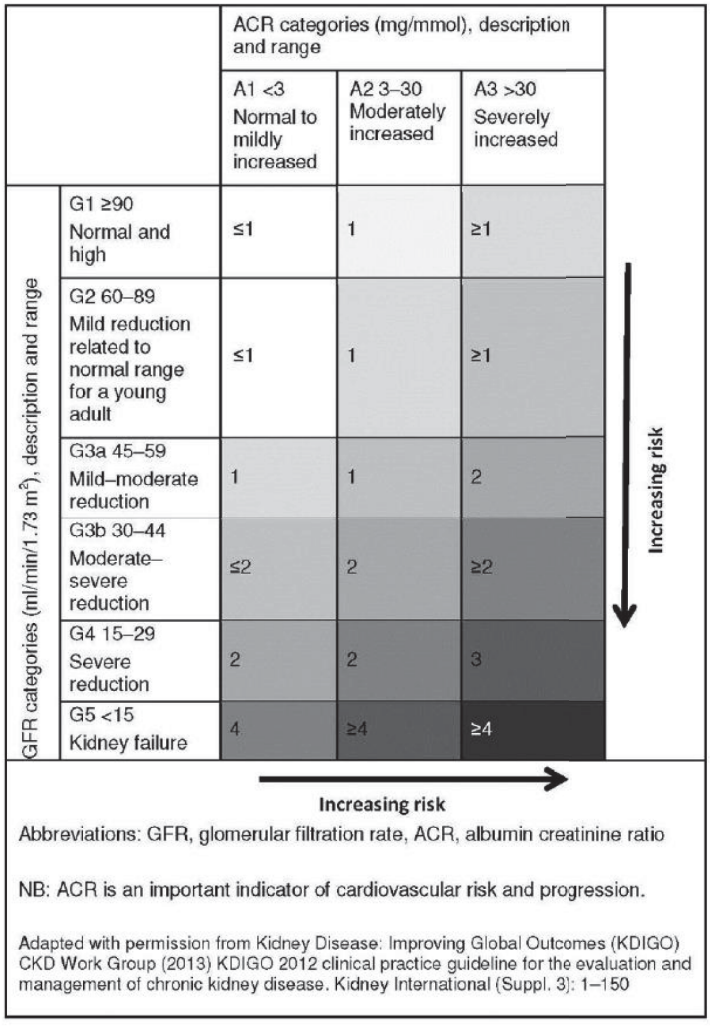

Figure 1: Frequency of monitoring of GFR (number of times per year, by GFR and ACR category) for people with, or at risk of, CKD. From the National Institute for health and Care Excellence Clinical Guideline 182: Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care (2)

NICE management guidelines also recommend that testing should be offered to people with a number of comorbidities such as diabetes, hypertension and cardiovascular diseases, but that age, gender and ethnicity should not be used for distinguishing whether or not a person should be tested (1). A recent study in south-west London found that testing was carried out unequally across different age, gender and ethnic groups (10), however variation in the rate of kidney function testing and potential differentials between different populations groups have not previously been characterised at the national level. The use of data from the CPRD would provide a comprehensive picture of current monitoring practice, allow us to estimate the proportion of tests that are for monitoring as opposed to diagnostic purposes, and

provide insight into evolving trends and potential differentials in testing. Kidney function testing is also recommended in subjects treated with certain medications, such as antihypertensive agents and non-steroidal anti-inflammatory drugs (NSAIDs) (2). Previous research within the General Practice Research Database (GPRD, now CPRD), has examined rates of creatinine testing (and other biochemical testing) in subjects beginning antihypertensive drug treatment (11,12). Our analyses will extend this previous work to examine testing rates in a wider population and for other prescriptions where creatinine and/or proteinuria testing is recommended.

Furthermore, while these guidelines do provide recommendations for the frequency of monitoring, the recommendation is largely based on the consensus opinion of the Guideline Development Group using indirect evidence on progression of CKD from a literature review; no economic analyses were found (2). Similar monitoring frequencies, based on consensus of the Guideline Development Group, were also recommended in earlier NICE guidelines (1), which also specifically recommended that further research is "undertaken to identify more accurate and cost effective methods of monitoring kidney function, especially in patients with [glomerular filtration rate] (GFR) 60 ml/min/1.73m2 or more" (1). We propose to address this evidence gap using previously described methods for the analysis of monitoring regimes (13–16).

Objective and specific aims

The overall objective of this study is to describe and improve kidney function testing in UK primary care. The tests of interest will be serum creatinine blood tests to determine a patient's estimated Glomerular Filtration Rate (eGFR), and proteinuria urine tests.

Aim 1: To describe rates of kidney function testing since the introduction of the Quality Outcomes Framework (QOF) for general practice.

The number of serum creatinine and proteinuria tests requested in each calendar year from 2005 to 2013 (9 years inclusive) will be examined by region (strategic health authority (SHA)), presence/absence of major patient comorbidities (diabetes, hypertension, cardiovascular disease, atrial fibrillation etc.) and subdivided into monitoring and diagnostic tests.

Aim 2: To identify the most effective monitoring strategy for different stages of CKD.

Current guidelines from NICE suggest a range of monitoring intervals by stage of CKD and category of ACR, however these recommendations are largely based on consensus opinion of the Guideline Development Group (GDG) (2). We will use a modelling approach to find evidence-based recommendations for intervals of monitoring different stages of CKD.

Study Type

Descriptive study (aim 1) and hypothesis generating (aim 2).

Study design

Open cohort study.

Sample size

A recent study of GP records from practices in south-west London found that 28% of men and 24% of women (aged 18 to 75+ years) had a serum creatinine test recorded in their general practice record (10). Assuming therefore that about one quarter of adults in the CPRD will have at least one serum creatinine test, we expect to have more than adequate data for our research questions regarding serum creatinine. Proteinuria testing is rare (~1%; reference (10)). To estimate a proportion of about 1%, with 95% confidence and precision +/-0.1%, requires 27,500 patients; therefore even our analyses of proteinuria should in general have sufficient data. However if any subgroup has fewer subjects than this, we will handle this through reporting of confidence intervals (as for all analyses) and cautious interpretation.

For aim 2, analysis will use repeated measurements of eGFR (calculated using recorded serum creatinine levels). Planned analysis methods do not require large numbers (17); our previous successful project on HbA1c monitoring in people with type 2 diabetes used data from a cohort of 200 subjects (16).

Data Linkage (if applicable)

ONS mortality linkage is requested. Cause of death data will be used to inform the individual simulation models we will fit for Aim 2. Linkage to integrated Hospital Episode Statistic (HES) data is also requested. Kidney dialysis, transplantation and end-stage renal disease are other important end points in our health economic modelling; while read codes are available within CPRD, we believe the addition of secondary care International Classification of Diseases (ICD) codes from integrated HES will improve the accuracy of ascertaining dates of these events.

Linkage to the Index of Multiple Deprivation is also requested. Recent evidence suggests that socioeconomic inequalities in the care for chronic conditions such as CKD have persisted, even after the introduction of pay for performance systems like the Quality Outcomes Framework (18). Describing potential differentials in current practice by level of deprivation is therefore an important part of analyses in aim 1, and deprivation may be a relevant covariate for analyses in aim 2.

Study population

This is an open cohort study of adult patients (≥ 18 years of age) registered at "up-to-standard" CPRD practices (both with and without linkage) and who are deemed to have "acceptable" patient records, excluding patients who were pregnant in the 12 months preceding study entry and patients who have had renal transplantation at any time prior to study entry. Analyses for aim 1 will include subjects from practices with and without linkage, other than analyses examining deprivation which will be restricted to linked practices. Analyses for aim 2 will all be restricted to practices with linkage available.

Follow-up

The study start date will be 1st January 2005 (this date is after the publication of the KDOQI guidelines (19) for classification of CKD in 2002, and after the introduction of QOF targets in UK primary care in 2004).

Eligible patients will be registered with the practice for a minimum of 12 months prior to study entry (to ensure adequate recording of baseline covariates). Eligibility will be defined using all available data prior to entry date.

Study end date will be 31st December 2013 (or date of last available linked data). Follow-up ends at this date or (if earlier) at time of death or transfer out of CPRD or (where applicable) date of becoming pregnant or undergoing renal transplantation or dialysis (when no read code diagnosis of acute kidney injury is also present).

Hence the study index date for each patient will be the latest of the following dates: study start date, practice up-to-standard date, date of 18th birthday and date of registration with the practice plus 12 months. Patient records will be censored at the earliest of the following dates: study end date, date of last upload of practice data, date of death, transfer out date, date of incident record of pregnancy within study period and date of incident record of renal transplantation or dialysis within study period.

Selection of comparison group(s) or controls

No comparison or control groups required .

Exposures, Outcomes, and Covariates

Aim 1: To describe rates of kidney function testing.

Outcomes:

- Number of serum creatinine tests

  The number of tests will be extracted using entity codes for serum creatinine (code 165) and read codes indicating serum creatinine testing (see Appendix for code list). A maximum of one test per date will be counted.

- Number of proteinuria urine tests

  The number of tests will be extracted using entity codes for urinalysis protein (287) and urine microalbumin (code 435). We will also use read codes indicating proteinuria testing (see Appendix for code list). A maximum of one test per date will be counted.

- Kidney function tests

  Read codes for kidney function tests that cannot be identified as creatinine or proteinuria tests using entity codes will also be counted separately (see appendix for read codes). A maximum of one test per date will be counted.

Exposures:

- Diagnosis of CKD. Stage of CKD will be defined using relevant diagnostic codes specifically indicating CKD with or without stage information (see Appendix for list of read codes).
  - In sensitivity analyses, we will additionally use eGFR values to define CKD stage (two consecutive eGFR values separated by 90 days or more within the relevant ranges(1)). This combination of diagnostic codes and eGFR values has been used to define CKD by stage in previous research using primary care data (20,21). GFR will be estimated using the Modification of Diet in Renal Disease (MDRD) equation (22), as recommended by the national guidelines over the study period (1).
  - Because eGFR readings over 60 ml/min/1.73m^2 are less accurate than lower readings, we will group stages 1 and 2 together into a "mildly impaired eGFR" group.
- Year of test

- Region (SHA)
- Age at test
- Major comorbidities including diabetes, hypertension, ischaemic heart disease, chronic heart failure, peripheral vascular disease, transient ischaemic attack and stroke, thyroid disease, atrial fibrillation, non-melanoma skin cancer and prescription of non-steroidal anti-inflammatory drugs (NSAID) (categories for length of use: no use, <1 year, 1-3 years, 3-5 years, ≥5years)
- Reason for testing (monitoring, diagnostic work-up, and drug toxicity monitoring) see Analysis section of this protocol for further detail).
- Gender
- Ethnicity
- Deprivation

We will define comorbidities using the recording of a relevant diagnostic code (read code) and/or a treatment codes as appropriate. These methods will be based on QOF coding and our previous experience using data from the GPRD/CPRD (protocol numbers 10_038, 10_071, 12_091R). For example, for each time point, history of cardiovascular disease, e.g. chronic heart failure, will be defined using the recording of at least one relevant read code prior to the time point of interest, whereas diabetes status at each time point will be defined using the recording of a relevant diagnostic code (read code) and/or a treatment code for diabetes prior to the time point of interest, and will exclude patients with secondary diabetes, for example gestational or corticosteroid-induced diabetes.

*Aim 2:*To identify the most effective monitoring strategy for different stages of CKD.

Analyses will be restricted to patients with a diagnosis of CKD, defined using relevant diagnostic codes (see Appendix).

Outcome:

- eGFR at study entry and at the time of each test

- Serum creatinine values will be obtained using entity code 165, and when associated with a relevant read code (see appendix for serum creatinine code list), general serum testing entity code.
- For our primary analysis we will use the CKD-EPI equation to calculate eGFR based on recorded values of serum creatinine, gender, age at test and ethnicity (23); this equation is recommended in current NICE guidelines (2)
- In sensitivity analyses we will compare to other estimates of eGFR: in particular, the MDRD equation (recommended by NICE over the period data were collected).

Exposures:

- Age at each test will be used as the unit of time.
- Gender
- Year of test
- Stage of CKD

NICE guidance recommends different monitoring intervals for patients with different stages of CKD, we will report results stratified by stage of CKD, grouped as CKD stages 1 and 2, stage 3a, stage 3b. Additionally, during model estimation, we will test whether model fit is improved by adjustment for or stratification by level of proteinuria (see Figure 1, NICE guidance).

Previous research has indicated that CKD screening is likely to be cost-effective in people at increased risk of kidney disease, such as those with hypertension or diabetes (24). Sensitivity analyses will examine whether blood pressure treatments and comorbidities (diabetes, hypertension), modify CKD progression. Health economic modelling will extend progression to stages 4 and 5, and will also use additional covariates (ethnicity, blood pressure (systolic and/or diastolic, last record in preceding two years), deprivation, smoking status (last record in preceding two years), BMI (last record in preceding two years), diabetes, cardiovascular disease, lipid profile (total cholesterol and HDL cholesterol, last record in preceding two

years)), subgroup size permitting, to evaluate effects driven by different monitoring regimens and treatments in the management of disease.

Analysis

Data management and analyses will be carried out using Stata 12.1 and R. (25,26).

Aim 1: To describe rates of kidney function testing.

Details of the number and clinical results (values) of serum creatinine and proteinuria tests requested by GPs during the study period for each patient will be analysed. Further demographic and comorbidity data on each patient will also be used for some analyses.

We will summarise rates of serum creatinine and proteinuria testing separately in tables.

The following will be reported for all patients and by diagnosed stage of CKD:

a) The number of patients with at least one record of testing (and additionally the number of patients with repeat tests; e.g. 2, 3, 4 or more tests).
b) Of those, the number with repeated tests versus those with isolated tests (e.g. first test in >2 years, not followed by another test in <2 years)
c) Tests will be subdivided into those concurrent with a prescription of drugs in which kidney function testing is recommended for monitoring purposes or prior to prescription.

The above categories are chosen to give an indication of the burden of testing attributable to CKD monitoring, diagnostic work-up, and drug toxicity monitoring. The denominator will include all adult patients (≥ 18 years of age) registered at "up-to-standard" CPRD practices (both with and without linkage) and who are deemed to have "acceptable" patient records, excluding patients who were pregnant in the 12 months preceding study entry and patients who have had renal transplantation at any time prior to study entry.

We will also examine numbers by age groups; by the presence/absence of major patient comorbidities (diabetes, hypertension etc.); and by NHS region.

Where appropriate, we will use statistical tests (e.g. Chi-squared tests) to formally test associations between patient characteristics, year or region on testing rates. To examine associations between covariates and testing for kidney function simultaneously across all time periods, we will use multi-level mixed effects logistic regression; analyses examining deprivation as a covariate will be restricted to patients registered at practices with linkage to IMD.

*Aim 2:*To identify the most effective monitoring strategy for different stages of CKD.

These analyses will use repeated measures of eGFR, appropriate diagnostic and referral codes for renal impairment or end-stage renal failure, and ONS data for date of death. We will build statistical models for the progression of CKD that account for the uncertainty or short-term variation in eGFR. Methods for estimating these parameters have been described in detail elsewhere (13,16); briefly we favour a random-effects modelling approach. We propose to treat eGFR as a continuous variable. However, model assumptions will be checked, and if substantially violated, we will instead model CKD stage as a categorical variable, using statistical models previously developed for diabetic nephropathy and diabetic conditions (27). We will evaluate the impact of different monitoring intervals for different levels of risk factors. Risk factors will include baseline eGFR or CKD stage, hypertension, proteinuria, age and history of cardiovascular events.

The main analysis will use standard deviations to quantify variability; in a methodological add-on we will compare this to the use of co-efficient of variation, variation independent of mean and standard deviation independent of the mean (28) for quantifying variability.

Individual patient simulation models, informed by the analysis on progression of CKD, will then be used to evaluate monitoring strategies that differ by timing and frequency of monitoring and management strategies. Current monitoring strategies will be compared with alternative strategies (e.g. biannual, annual and biennial monitoring, or other intervals as indicated by results) to identify the most effective and cost-effective scheme. For each monitoring strategy, we will estimate the incidence of true disease and probability of stage misclassification.

Parameter estimates from these models and data on risk factors listed above (along with estimates from ongoing systematic reviews and unit cost data, such as the cost of appointments and of procedures, from external sources (e.g. Unit Costs of Health and Social Care 2013 (29)) will contribute to the development of a cost-effectiveness model of monitoring patients with CKD in the UK population. For the purpose of evaluating costs, CPRD data will be used to establish the characteristics of people diagnosed with CKD and estimate numbers of appointments for the purpose of diagnosis and monitoring of kidney disease and other relevant primary care costs related to CKD stage. External data will be used for hospital and other healthcare costs of people diagnosed with CKD in UK (e.g. (30)). We have previously used these methods to provide transition probabilities for an economic model in an Health Technology Assessment funded project on monitoring diabetic nephropathy (31). Current guidelines for economic modelling will be followed in reporting and presenting the results of this analysis (32). The model will estimate the cost per quality-adjusted life year (QALY) of various screening and monitoring policies to help identify the optimal levels of screening, monitoring and management strategies in different patient groups a UK context.

Validation of the models:

We will use a number of approaches to assess the internal validity of the model, and validity of the results, as follows: internal validation will consist of checking that assumptions of the

model are met and that the model recreates the observed distributions of the stages of CKD, end stage renal disease and mortality over the time frame of the data (apparent validation). We will compare the model based estimates of intra-individual variation (biological and assay) in eGFR with estimates from the literature. Finally, we will use bootstrap resampling to produce estimates of uncertainty in the main model outputs (proportions of false positives and false negative tests).

Missing data

For the assessment of clinical diagnosis/ disease in individuals, we will assume that absence of any relevant medical read code in the clinical record means true absence of disease. For other covariate measures that may not be accurately/ regularly recorded at yearly intervals, we will use multiple imputation methods if the necessary assumptions are met (33).

The random-effects models, to be fitted as part of aim 2, fit time (age) as a continuous measure, and therefore allow for irregular repeat measures.

Patient or user group involvement

As part of the grant proposal, this project has been reviewed by individuals with long term conditions that require frequent monitoring, as well as nurse practitioners and GP commissioners. Patient and Public Involvement (PPI) members have also been invited to the Steering and Senior Management groups. A PPI expert is also involved as a strategic consultant in this programme of work.

Limitations of the study design, data sources, and analytic methods

In Aim 2 we are using a modelling approach rather than a randomised controlled trial of different approaches to monitoring kidney function, but we consider this a cost-effective way

to examine different monitoring schemes using statistical methods that have previously proven useful. Additionally, due to a limited time horizon of clinical trials, life-time results would still need to be based on a model.

An unavoidable limitation is that CRPD analyses often require the use of measurements taken at different times (e.g. blood pressure at one visit, weight at another) rather than concurrently, hence the decision to use multiple imputation methods for data that is missing during the relevant time periods.

The proposal as a whole is also subject to the usual caveats for statistical modelling based on observational data, and to the usual limitations of routinely collected data for research.

Plans for disseminating and communicating study results, including the presence or absence of any restrictions on the extent and timing of publication

The results from both project aims will be submitted for presentation at academic conferences and for publication in scientific journals. It is expected that Aims 1 and 2 will each form at least one publication, with both being prepared by Summer 2016; the results of cost-effectiveness analyses require input from the rest of the programme of work so will be finalised in 2017/2018.

Amendments

The following amendments are proposed.

Exposures, Outcomes and Covariates

This amendment affects analysis of Aim 2 only.

For Aim 2 only, we propose to define the inclusion criterion CKD, and exposure variable stage of CKD, from biochemical measurements (eGFR) instead of diagnostic codes. This is because our GP colleagues advise that not all patients with impaired eGFR may have been assigned CKD diagnostic codes. Aim 2 is to identify appropriate monitoring strategies for different stages of CKD by studying rate of change of eGFR in each stage of CKD. For this we wish to classify CKD, and its stages, as accurately as possible.

The methods for calculating eGFR from serum creatinine are already documented in the protocol.

(Note that for Aim 1 we will continue to assign the exposure variable CKD by recorded diagnostic codes rather than biochemical measurements. This is because the exposure in aim 1 is explicitly *diagnosis* of CKD: to describe the monitoring of CKD in those known to their GP to have CKD.)

Follow-up

For the cost-effectiveness analysis in Aim 2, a study start date of 1st July 2004 will be used (replacing the study start date of 1st January 2005), to ensure ten years of follow-up and hence give comparability of our results with the ten-year risk equations used in UK guidelines for prevention of CVD.

Plans for disseminating and communicating study results …

This amendment affects publication plans only. No additional analyses will be carried out, but we propose to publish separately an intermediate analysis that contributes to the cost-effectiveness modelling that is described in the Analysis section under subheading Aim 2.

The original protocol anticipated publication of the cost-effectiveness model as a single publication: components of the model would appear as a Table or a part of a Table or an Appendix.

In the light of current interest in CKD as a risk factor for cardiovascular disease, we now consider the component of the model quantifying risk of first CVD among CKD patients without previous cardiovascular disease to be of interest in its own right. We therefore additionally propose (a) a conference abstract (b) a student dissertation at MSc level and (c) potentially, a manuscript based on these, describing this component of the CVD submodel and its interpretation. Any such publication(s) would reflect the status of this as a part of a larger cost-effectiveness model of monitoring CKD rather than a stand-alone research project.

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Code lists

Code list for Chronic Kidney Disease

medcode	readcode	readterm	databasebuild
104981	K05..13	Chronic kidney disease	Sep-12
29013	1Z10.00	Chronic kidney disease stage 1	Feb-09
105392	K051.00	Chronic kidney disease stage 1	Dec-12
94789	1Z17.00	Chronic kidney disease stage 1 with proteinuria	Feb-09
95572	1Z18.00	Chronic kidney disease stage 1 without proteinuria	Feb-09
12586	1Z11.00	Chronic kidney disease stage 2	Feb-09
105383	K052.00	Chronic kidney disease stage 2	Dec-12
95146	1Z19.00	Chronic kidney disease stage 2 with proteinuria	Feb-09
95121	1Z1A.00	Chronic kidney disease stage 2 without proteinuria	Feb-09
12566	1Z12.00	Chronic kidney disease stage 3	Feb-09
104619	K053.00	Chronic kidney disease stage 3	Jul-12
94793	1Z1B.00	Chronic kidney disease stage 3 with proteinuria	Feb-09
95123	1Z1C.00	Chronic kidney disease stage 3 without proteinuria	Feb-09
94965	1Z15.00	Chronic kidney disease stage 3A	Feb-09
95408	1Z1D.00	Chronic kidney disease stage 3A with proteinuria	Feb-09
95175	1Z1E.00	Chronic kidney disease stage 3A without proteinuria	Feb-09

95179	1Z16.00	Chronic kidney disease stage 3B	Feb-09
95178	1Z1F.00	Chronic kidney disease stage 3B with proteinuria	Feb-09
95177	1Z1G.00	Chronic kidney disease stage 3B without proteinuria	Feb-09
12479	1Z13.00	Chronic kidney disease stage 4	Feb-09
104963	K054.00	Chronic kidney disease stage 4	Sep-12
95122	1Z1H.00	Chronic kidney disease stage 4 with proteinuria	Feb-09
95406	1Z1J.00	Chronic kidney disease stage 4 without proteinuria	Feb-09
12585	1Z14.00	Chronic kidney disease stage 5	Feb-09
105151	K055.00	Chronic kidney disease stage 5	Nov-12
95508	1Z1K.00	Chronic kidney disease stage 5 with proteinuria	Feb-09
95405	1Z1L.00	Chronic kidney disease stage 5 without proteinuria	Feb-09
97980	1Z17.11	CKD stage 1 with proteinuria	Nov-09
97979	1Z19.11	CKD stage 2 with proteinuria	Nov-09
97978	1Z1A.11	CKD stage 2 without proteinuria	Nov-09
95145	1Z1B.11	CKD stage 3 with proteinuria	Feb-09
95188	1Z1C.11	CKD stage 3 without proteinuria	Feb-09
95571	1Z1D.11	CKD stage 3A with proteinuria	Feb-09
95176	1Z1E.11	CKD stage 3A without proteinuria	Feb-09
95180	1Z1F.11	CKD stage 3B with proteinuria	Feb-09
100633	1Z1G.11	CKD stage 3B without proteinuria	Sep-10

99312	1Z1H.11	CKD stage 4 with proteinuria	May-10
97587	1Z1J.11	CKD stage 4 without proteinuria	Sep-09
99160	1Z1K.11	CKD stage 5 with proteinuria	Apr-10
97683	1Z1L.11	CKD stage 5 without proteinuria	Sep-09

Code list to indicate serum creatinine testing

medcode	readcode	read term
5	44J3.00	Serum creatinine
3927	44J3300	Serum creatinine raised
31277	44J3000	Serum creatinine abnormal
26903	44J3200	Serum creatinine normal
35545	44J3100	Serum creatinine low
42345	44J3z00	Serum creatinine NOS
45096	44JD.00	Corrected serum creatinine level
13736	44JF.00	Plasma creatinine level
62062	44JC.00	Corrected plasma creatinine level
27095	4Q40.00	Creatinine level
39905	4I37.11	Creatinine in sample
13736	44JF.00	Plasma creatinine level

Additional codes to indicate serum creatinine testing in aim 1.

medcode	readcode	read term
23250	451E.00	GFR calculated abbreviated MDRD

30898	451G.00	GFR calculated abbreviated MDRD adj for African Americ orign
19747	451F.00	Glomerular filtration rate
90871	7P14000	Glomerular filtration rate testing

Code list to indicate proteinuria testing

medcode	readcode	read term
1802	4678.00	Proteinuria
38284	R110z00	[D]Proteinuria NOS
11248	R110.00	[D]Proteinuria
13613	46N2.00	urine protein abnormal
14395	46N..00	urine protein
14429	46N3.00	urine total protein
27059	467Z.00	urine protein test NOS
27214	46NZ.00	urine protein NOS
43262	467H.00	random urine protein level
27266	44lD.00	Urine protein/creatinine ratio
44179	46N7.00	urine protein/creatinine index
5451	R110000	[D]Albuminuria
10924	R110300	[D]Microalbuminuria

14410	46N4.00	urine albumin
14563	46W..00	Urine microalbumin
17106	46W1.00	Urine microalbumin negative
28180	46W0.00	Urine microalbumin positive
31969	4I3B.11	Albumin in sample
39248	46N8.00	urine microalbumin profile
2607	46TC.00	Urine albumin:creatinine ratio
14113	44J7.00	Albumin / creatinine ratio
14391	46TD.00	Urine microalbumin:creatinine ratio

Kidney function testing

medcode	readcode	readterm
8662	8A6..11	kidney function monitoring
11995	451..11	kidney function tests
22327	R144.11	kidney function test abnormal
5458	8A6..00	Renal function monitoring
2998	451..00	Renal function tests
10768	R144.00	[D]Renal function test abnormal
3980	4512.00	Renal function tests abnormal

4265	4511.00	Renal function tests normal
26001	4519.00	Deteriorating renal function
13812	44J..00	Blood urea/renal function
25763	4516.00	Renal function tests borderline
26943	44JZ.00	Blood urea/renal function NOS
37236	451Z.00	Renal function test NOS
56293	4515.00	Differential renal function
101976	451H.00	Recovery of renal function