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Adherence to guidelines for creatinine and potassium monitoring and discontinuation following renin-angiotensin system blockade

Running title: Creatinine and potassium monitoring after ACEI/ARB initiation

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ABSTRACT

Objectives To examine adherence to serum creatinine and potassium monitoring and discontinuation guidelines following initiation of treatment with angiotensin converting-enzyme inhibitors (ACEI) or angiotensin-receptor blockers (ARB); and whether high-risk patients are monitored.

Design Population-based cohort study using electronic health records from the UK Clinical Practice Research Datalink and Hospital Episode Statistics.

Setting UK primary care, 2004–2014.

Subjects 223,814 new ACEI/ARB users.

Main outcome measures Proportion of patients with renal function monitoring before and after ACEI/ARB initiation; adverse renal outcomes (creatinine increase ≥30% or potassium levels >6 mmol/L) at first follow-up monitoring; and treatment discontinuation after such changes. Using logistic regression models, we also examined patient characteristics associated with such adverse outcomes, and with follow-up monitoring within the guideline-recommend two weeks of treatment initiation.

Results Ten percent of patients had neither baseline nor follow-up monitoring of creatinine within 12 months before and 2 months after initiation of an ACEI/ARB, 28% had monitoring only at baseline, 15% only at follow-up, and 47% both at baseline and follow-up. The median period between the most recent baseline monitoring and drug initiation was 40 days (interquartile range: 12-125 days). 34% of patients had baseline creatinine monitoring within one month before initiating therapy, but less than 10% also had the guideline-recommended follow-up test recorded within two weeks. Among patients experiencing a creatinine increase ≥30% (n=567, 1.2%) or potassium level >6 mmol/L (n=191, 0.4%), 80% continued treatment. Although patients with prior myocardial infarction, hypertension, or baseline potassium >5 mmol/L were at high risk of adverse renal outcomes after ACEI/ARB initiation, there was no evidence that they were more frequently monitored.

Conclusions Only one tenth of patients initiating ACEI/ARB therapy receive the guideline-recommended creatinine monitoring. Moreover, the vast majority of the patients fulfilling post-initiation discontinuation criteria for creatinine and potassium increases continue on treatment.

Strengths and limitations of this study:

- This is the largest monitoring study to date, examining both adherence to creatinine and potassium monitoring and discontinuation guidelines following initiation of angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers in UK primary care, and whether patients are monitored in accordance with their individual risk profile
- Use of the UK Clinical Practice Research Datalink and Hospital Episode Statistics ensured that the study was population-based and not restricted to specific demographic, hospital, or insurance groups.
- Blood tests performed in hospital systems were not recorded in the Clinical Practice Research Datalink, but the results were consistent for patients with no recent hospital admissions
- If the recording of creatinine levels was not missing completely at random, the associations between patient characteristics and creatinine increase may have been underestimated

INTRODUCTION

Renin angiotensin system blockade using angiotensin-converting enzyme inhibitors (ACEI) and angiotensin-receptor blockers (ARB) is a mainstay in treatment of hypertension,[1] heart failure,[2] diabetic microalbuminuria or proteinuric renal diseases,[3] and after myocardial infarction.[4] However, some patients experience a sudden decline in kidney function when initiating these drugs, presumably due to antagonism of the angiotensin II-mediated efferent arteriolar constriction or impaired kidney excretion of potassium.[5 6]

The potential impact on kidney function should be evaluated by comparing pre- and post-initiation levels of serum creatinine and potassium.[7] Discontinuation is recommended if the rise in creatinine exceeds 30% above baseline or if hyperkalaemia develops.[8] It is unclear whether these recommendations are routinely followed in clinical practice.[9]

A few studies have compared baseline and follow-up monitoring results,[9] but large studies using contemporary data with reference to current guidelines are lacking, and it is unknown whether patients' individual risk of renal impairment influence their likelihood of being monitored.[9] We therefore examined adherence to creatinine and potassium monitoring and treatment discontinuation guidelines following ACEI/ARB initiation in UK primary care, and whether patients are monitored in accordance with their individual risk profile.

METHODS

Data sources

We used the UK's Clinical Practice Research Datalink (CPRD) linked to hospital record data from the Hospital Episode Statistics (HES) database. The CPRD database contains primary care electronic health record data from 7% of the UK population (~15 million patient lives, with ~8 million currently under follow-up).[10] Patients included in the CPRD are largely representative of the UK population in terms of age, sex and ethnicity.[10 11] Information recorded in the database includes demographics such as sex and year of birth, the location of the general practice, medical diagnoses (based on 'Read' codes), drug prescriptions, and a

range of routine laboratory test results. HES records cover all hospital admissions for patients covered by the NHS who receive treatment either from English NHS trusts or independent providers.[10 11] Fifty-eight percent of general practices included in the CPRD have agreed to HES linkage.[10] We obtained linked data on socioeconomic status (index of multiple deprivation) based on area of residence.

Monitoring guidelines

Consistent with other international guidelines, the National Institute for Health and Care Excellence (NICE) recommend baseline testing of creatinine when initiating ACEI/ARB therapy in patients with hypertension,[1] heart failure,[2] myocardial infarction,[4] or chronic kidney disease (CKD).[3] The time interval for baseline testing is not further specified.[1-4] Among patients with heart failure, myocardial infarction, and chronic kidney disease, NICE recommends follow-up monitoring within 2 weeks of treatment initiation,[2-4] and for myocardial infarction patients at least annually thereafter.[4] A baseline assessment and follow-up test within 2 weeks are also recommended by the UK Renal Association,[12] as well as the frequently used online web resource General Practice (GP) Notebook.[13] GP Notebook additionally recommends monitoring 1, 3, 6, and 12 months after the first follow-up test.[13] NICE recommends not to initiate ACEI/ARBs in patients with a baseline potassium level >5 mmol/L and to discontinue therapy if potassium rises above 6 mmol/L.

ACEI/ARB initiators

We identified a cohort of all HES linked CPRD patients aged ≥18 years, who initiated ACEI/ARB treatment between January 1, 2004 and March 31, 2014. We did not include earlier calendar periods, as laboratory data before 2004 were incomplete due to interface problems between laboratory reporting software and GP practice software.[14] Also, creatinine testing was incentivised in 2004 with the introduction of the diabetes Quality and Outcomes

Framework (QOF) and further in 2006 with the CKD QOF.[14] To rule out any potential influence of incomplete data around 2004, we also examined the most recent 5-year calendar period separately in a sensitivity analysis. New users were defined as persons with at least one year of continuous registration in the CPRD before their first recorded ACEI/ARB prescription.

Laboratory data

All creatinine test results were extracted from the general practice records of the study population, using creatinine-specific codes in CPRD. Cross-reference was then made to creatinine test results identified from a broad Read code search. Any irrelevant codes were excluded. The same procedure was used to identify potassium test results.

Patient characteristics

We obtained information for all patients on age, sex, calendar period of ACEI/ARB initiation (2004–2008 and 2010–2014), socioeconomic status (quintiles of the 2004 index of multiple deprivation scores), lifestyle factors (smoking, alcohol intake, and body mass index), baseline potassium level (≤5 or >5 mmol/L), CKD, cardiovascular comorbidities (heart failure, myocardial infarction, hypertension, peripheral arterial disease, and arrhythmia), and diabetes.[15] We used algorithms for smoking status, alcohol intake, and body mass index based on the most recent records in the CPRD before ACEI/ARB initiation.[16 17] As measures of baseline creatinine and potassium levels, we used the single most recent measurement within 12 months before the first ACEI/ARB prescription. We calculated estimated glomerular filtration rate (eGFR) level from the most recent creatinine measurement and CKD stage from the CKD-EPI equation.[18] Cardiovascular comorbidities and diabetes were identified from both the CPRD and HES based on diagnoses recorded prior to ACEI/ARB initiation. The code lists for all variables are provided in the online repository at

https://clinicalcodes.rss.mhs.man.ac.uk/.[19]

Patient involvement

The study included no patient involvement

Statistical analysis

We described ACEI/ARB users according to patient characteristics, both overall and according to creatinine monitoring status (no baseline or follow-up monitoring, baseline only, follow-up only, and both baseline and follow-up monitoring). Baseline monitoring was defined as a test performed on the date of drug initiation or within either 12 months before (generous interval) or one month before initiation (more ideal interval assumed to be driven by planned ACEI/ARB initiation). To accord with the post-initiation monitoring interval recommended from previous trial data, we considered only follow-up monitoring within the first 2 months after drug initiation.[8]

We calculated the proportion of persons in the total cohort of new users who had baseline and follow-up monitoring (within 1, 3, and 12 months before drug initiation and within 2 weeks, 1 month, and 2 months after initiation). We then computed the proportion of persons with both baseline and initial follow-up monitoring within the guideline-recommended interval of 2 weeks following drug commencement.

We repeated the analyses for continuing users, in order to examine adherence to the stricter guideline recommendations for ongoing monitoring (*i.e.*, monitoring within 1, 3, 6, and 12 months after the first retest).[13] Continuation was defined as ACEI/ARB use beyond 30 days following the monitoring date, *i.e.*, when the end date of the first continuous course of therapy was after the date of the first monitoring date plus 30 days (to allow for stockpiling). The end date of each prescription was calculated by adding the prescription duration (total number of tablets prescribed divided by the specified number of tablets per day) to the

prescription date. In identifying continuous courses of therapy, we allowed for a 30-day gap between the end date of one prescription and the start of the next consecutive prescription.

In sensitivity analyses, we repeated the analyses (1) extending the follow-up window for the first follow-up monitoring from two to three weeks to account for minor delays; (2) including only the most recent calendar period (2009-2014) to account for temporal changes in data completeness and quality of care; (3) excluding patients with a hospital admission or discharge date within 1 month before or after their first ACEI/ARB prescription, in order to account for drug initiation and any subsequent renal function tests occurring in the hospital and therefore not captured in the CPRD; (4) focusing on specific patient subgroups (heart failure, myocardial infarction, hypertension, CKD (eGFR<60mls/min/1.73m^2), peripheral arterial disease, and diabetes); and (5) defining drug use continuation as ACEI/ARB use beyond 90 days (instead of 30 days) after the first retest date.

We used the subcohort of patients with both baseline and follow-up monitoring to calculate the proportion of patients with creatinine increases ≥30% or potassium levels >6 mmol/L at the first follow-up monitoring within 2 months after initiation, as well as the proportion of patients continuing treatment despite these contraindications for use.

Finally, we fitted a logistic regression model to identify patient characteristics associated with a severe decline in renal function (creatinine increase ≥30% or potassium level >6 mmol/L) and compared these characteristics with those associated with receiving post-initiation follow-up monitoring within 2 weeks. The model included age, sex, CKD stage, cardiovascular comorbidities, diabetes, and baseline potassium level (>5 vs. ≤5 mmol/L). In three additional model-based sensitivity analyses, we repeated the analyses (1) excluding patients with a recent hospitalization (as defined above); (2) omitting baseline potassium from the model to examine the extent of potential overfitting when both baseline potassium and CKD stage were kept in the model; and (3) also adjusting additional for ethnicity.

The study protocol was made available to the journal reviewers and approved by the London School of Hygiene and Tropical Medicine Ethics Committee (No. 6536) and the Independent Scientific Advisory Committee (ISAC) for Medicines and Healthcare Products Regulatory Agency (No. 16_025). All analyses were performed using STATA 14 statistical software package.

RESULTS

Serum creatinine monitoring before and after ACEI/ARB initiation

We identified 223,814 new users of ACEI/ARBs (Table 1). Among these patients, 21,411 (10%) had no baseline or follow-up creatinine tests within 12 months before and 2 months after treatment initiation, 63,359 (28%) had only a baseline test, 33,185 (15%) had only follow-up tests, and 105,859 (47%) had both baseline and follow-up tests. Median age varied only slightly between the groups (60, 62, 59, and 63 years, respectively) and there were no substantial differences in socioeconomic status, lifestyle factors, or peripheral arterial disease. Compared with patients with neither pre- nor post-initiation monitoring, patients with both were more likely to have diagnosed hypertension (76% vs. 61%) and diabetes (20% vs. 7%), but less likely to have diagnosed heart failure (4% vs. 7%), myocardial infarction (4% vs. 18%), and arrhythmia (7% vs. 10%). Among patients with baseline monitoring, 83% did not have CKD, 13% stage 3a, 3% stage 3b, 0.5% stage 4 CKD. In the same population, 7% commenced ACEI/ARB therapy despite baseline potassium above 5 mmol/L. The median number of days between baseline monitoring and first prescription date was 40 days (interquartile range: 12-125 days).

The proportion of patients receiving creatinine testing before initiating ACEI/ARB therapy was 76% within 12 months before treatment initiation, declining to 34% within one month before initiation (Table 2). The proportion with follow-up testing after treatment initiation was 29% within 2 weeks, increasing to 62% within 2 months. 21% of ACEI/ARB initiators had both a baseline test within 12 months before and a follow-up test within 2

weeks after starting treatment (Table 3). However, among patients undergoing testing within one month prior to treatment initiation, only 9% had also the recommended follow-up test within 2 weeks of treatment start. When we extended the follow-up window to three weeks, this proportion increased only to 14% (Table 3). Among patients continuing treatment, only 1% had follow-up measurements at 1, 3, 6, and 12 months after the first retest, in compliance with the strictest recommendation (eTable 1). These results were unchanged when the analysis was restricted to the most recent calendar period (eTable 1-2) and to patients with heart failure, myocardial infarction, hypertension, peripheral arterial disease, diabetes or no recent hospitalization (eTable 3). Only patients with CKD received a slightly higher degree of monitoring (13%) within two weeks following treatment initiation (eTable 3).

Serum creatinine and potassium changes after ACEI/ARB initiation

Among patients receiving the recommended renal function monitoring, 567 (1.2%) experienced a creatinine increase ≥30% and 191 (0.4%) a potassium level >6 mmol/L at their first follow-up test within two months of treatment initiation (1.4% received in total either) (Table 4). Among these patients, 80% continued treatment beyond 30 days following the monitoring date (Table 4). The sensitivity analysis showed that 65% of patients with a creatinine increase ≥30% and 60% of those with a potassium level >6 mmol/L continued also treatment beyond 90 days after the monitoring date (eTable 4). The results remained consistent for longer baseline monitoring intervals (eTable 4).

Patients at high risk for creatinine increases ≥30%

When we examined patient characteristics associated with a creatinine increase ≥30% and adjusted for the other characteristics in a multivariable analysis (Table 5), we found an increased odds ratio (OR) for women (1.6-fold increased), for age above 70 years (at least 1.3-fold increased), for CKD stage 4 (1.6-fold increased), heart failure (2.9-fold increased),

peripheral arterial disease (1.9-fold increased), myocardial infarction (1.6-fold increased), and hypertension (1.6-fold increased).

Patients at high risk for potassium >6 mmol/L

Baseline potassium level and CKD stage, but not age and sex, were associated with potassium levels >6 mmol/L after ACEI/ARB initiation. Thus, the OR was 7-fold increased for baseline potassium >5 mmol/L, two-fold increased for CKD stage 3a, 5-fold increased for stage 3b, and 11-fold increased for stage 4 (Table 5). Among cardiovascular comorbidities, heart failure was associated with the strongest OR of a potassium level >6 mmol/L (2.22, 95% CI: 1.38-3.58).

Monitoring high-risk patients

The odds of having a follow-up test within 2 weeks following drug initiation were higher for persons aged 70 years or above compared with ≤50 years (1.18, 95% CI: 1.13-1.23 for 70-79 years and 1.17, 95% CI: 1.11-1.23 for 80+ years). It was also increased for patients with CKD stage (1.41, 95% CI: 1.20-1.66), heart failure (1.16, 95% CI: 1.08-1.23), and peripheral arterial disease (1.11, 95% CI: 1.02-1.20). However, there was no substantially increased OR (>10%) associated with female sex (1.07, 95% CI: 1.04-1.09), prior history of myocardial infarction (0.77, 95% CI: 0.72-0.82), hypertension (1.05, 95% CI: 1.00-1.11), or baseline potassium >5 mmol/L (1.04, 95% CI: 0.99-1.09). When we excluded patients with a recent hospital admission, the reduced OR for myocardial infarction was no longer observed (0.93, 95% CI: 0.80-1.08) (eTable 5). Finally, the results remained consistent when we omitted adjustment for baseline potassium (data not shown) and when we adjusted additionally for ethnicity (eTable 5).

DISCUSSION

Only one tenth of patients initiating ACEI/ARBs in UK primary care appear to receive the guideline-recommended creatinine monitoring. One in 15 patients commenced ACEI/ARBs despite baseline potassium above the recommended level, which was also shown to be a strong predictor for severe post-initiation hyperkalaemia. Among monitored patients, a creatinine increase ≥30% or a potassium level >6 mmol/L occurred in almost 1.5% of patients, and most did not discontinue therapy despite guideline recommendations to stop. Although patients with prior myocardial infarction, hypertension, or a high baseline potassium level were at higher risk of sudden decline in kidney function after ACEI/ARB initiation, there was no evidence that these patient groups were monitored more frequently while initiating the drugs.

Strengths and limitations

Several issues should be considered when interpreting our study results. Its large sample size increased precision. Use of the CPRD ensured that the study was population-based and not restricted to specific demographic, hospital, or insurance groups.

We did not have access to blood tests performed in hospital systems, which may have been reported to GPs, but not recorded in CPRD. However, restricting the analysis to patients with no recent hospital admissions had little effect on our findings. Although some patients may also have been seen in outpatient specialty clinics, it is common practice for specialists to ask GPs to initiate new drugs such as ACEI/ARBs, with local biochemical monitoring, limiting misclassification.

Consistent with findings from other studies,[20] we found that approximately 50% of all ACEI/ARB initiators were monitored both before and after treatment start. If GPs are retesting renal function in patients at higher risk of adverse outcomes, we may have overestimated the proportion of patients with high potassium levels or creatinine increases compared with the untested lower-risk general population.

GP system software is used for issuing prescriptions, ensuring the accuracy of prescription data. However, it cannot be inferred that all patients actually redeemed their prescription at the pharmacy and start medication on the same day that it was prescribed.[18 21] Similarly, the estimated coverage of prescriptions may not be completely accurate due to such factors as stockpiling and irregular use. We also do not know whether GPs contacted patients with elevated laboratory results to advise them to stop taking the medication prior to the end of their prescriptions. However, 80% of patients who developed creatinine increase ≥30% after ACEI/ARB initiation were still issued a subsequent ACEI/ARB prescriptions.

We aimed to detect discontinuation related closely in time to first follow-up monitoring and hence likely resulting from an elevated creatinine or potassium result. We therefore defined continuation as ACEI/ARB use beyond 30 days (the median prescription duration) after the monitoring date. Extending the definition of continuous use beyond 90 days reduced the risk of misclassifying patients as continuing treatment when they had in fact stopped. However, extending the duration also increased the risk of identifying discontinuation due to other reasons than creatinine/potassium increase, *e.g.*, death or cough. Diagnoses recorded in the CPRD generally have been found to have adequate validity for research purposes,[22 23] particularly in the domains assessed by the QOF.[24 25]

In the logistic regression analysis to estimate factors associated with creatinine increase ≥30%, we excluded patients without pre and post measurements (complete case analysis). If the recording of creatinine levels was not missing completely at random, the associations between patient characteristics and creatinine increase may have been underestimated.[26] While this assumption could not be tested directly, examination of baseline characteristics revealed no major differences in age, sex, socioeconomic status, and lifestyle between patients with and without pre- and post-monitoring. Furthermore, the results were consistent for each individual patient group examined. Patients with no testing before or after treatment

initiation (including those with potentially haemolysed samples) only accounted for 10% of all ACEI/ARB initiators.

Comparison with other studies

To our knowledge, this is the largest study conducted to date on adherence to monitoring and discontinuation guidelines after ACEI/ARB initiation. Only one previous study[20] examined monitoring according to guideline-recommended intervals (<14 days). All others have used longer intervals (*e.g.*, 30 days[27] or 6 months[28 29]), which make interpretations and implications for clinical practice less clear. Poor adherence to monitoring guidelines after ACEI/ARB initiation is not restricted to the UK,[20 29 30] but has also been reported in the US[31-33], Canada,[34] and the Netherlands.[27 35] Owing to our sample size, we were able to show that the lack of monitoring occurred in all patient groups with an indication for ACEI/ARB therapy.

A recent Dutch study, including 3,353 patients initiating ACEI/ARBs between 2005-2011, found that 19% had creatinine measured within 30 days and 66% within one year.[27] Creatinine increases above 30% occurred in 1.6% of patients, and among these 70% did not discontinue treatment.[27] A Scottish study of 4,056 patients with type 2 diabetes, prescribed an ACEI/ARB between 2005-2009, found that 19% had both a baseline (within 90 days) and follow-up measurement (within 2 weeks) of initiation. Within this cohort, 1.7% had both a creatinine increase of ≥30% and potassium level ≥5.6 mmol/L.

The magnitude of the risk of severe renal impairment, as measured by creatinine increase in these observational studies, was consistent with our findings, but substantially higher than reported in clinical trials (*e.g.*, 0.2% in the ONTARGET trial).[36] It is not clear from the literature how often harm occurs around the time of initiation, when the risk of nephrotoxicity is thought to be greatest.[8] If physicians are to understand why follow-up monitoring within 2 weeks of treatment start matters, the short-term risks need to be clarified.

Until now, most studies have reported only on cumulative risk over entire courses of treatment, such as the 1.1% two-year risk for potassium of >6 mmol/L in the SOLVD trials of heart failure patients.[37] In contrast to clinical trial reviews, reporting a 0.2% (3/1818) risk of potassium >6 mmol/L, we found a 0.4% risk of hyperkalaemia already at time of first retesting after ACEI initiation.

Extending the previous literature, our results support that advanced age, advanced CKD, and heart failure, but not sex, increase the likelihood of being monitored.[20 27 31] Consistent with some,[27 31] but not all, previous studies,[29] we found no association for diabetes. However, these previous studies reporting an association for diabetes focused on monitoring within broader intervals (*e.g.*, 6 months),[29] where diabetes patients, irrespective of ACEI/ARB initiation, were likely to receive blood testing owing to the diabetes QOF programme.

Determinants of increases in creatinine levels after ACEI/ARB initiation are less well understood than for hyperkalemia, but increasing age is a consistently reported factor.[20] Advanced CKD and a range of cardiovascular comorbidities (mostly associated with atherosclerosis) were also important determinants in our patient cohort. Consistent with previous studies, we found that the risk of hyperkalemia risk associated with CKD (likely due to impaired ability of the cortical collecting tubule to secrete potassium), heart failure (likely due to decreased delivery of sodium to the distal nephron), and high pre-treatment potassium levels.[6 8 20 38] We did not observe an association with diabetes or increasing age, as could have been expected due to diabetic nephropathy or age-dependent hyporeninemic hypoaldosteronism.[6]

Clinical relevance

Several possible explanations exist for the divergence between the clinical guideline recommendations and the observed monitoring and response patterns in clinical practice. The

first is *clinician nonadherence* to ordering tests. This may be due to inconsistent recommendations for timing and frequency of monitoring over time,[6] consensus-based (rather than evidence-based) monitoring guidelines, and a lack of guidelines tailored to particular high-risk patients, such as those with CKD and heart failure. Although we found that follow-up monitoring correlated well with the risk of renal impairment after ACEI/ARB initiation for most patient groups, it was not observed for patients with myocardial infarction or pre-initiation high potassium. The second explanation may be *patient nonadherence* to ordered tests. This is particularly salient in UK primary care where blood samples may be taken in phlebotomy clinics that the patient has to visit rather than the GP practice. Patients may find it burdensome to have blood tests, and GPs have no direct economic incentives to ensure that they are done. A third barrier is *lack of evidence of the clinical importance* of monitoring and its cost-effectiveness. ACEI/ARB-induced renal impairment is rare in clinical trials, even among patients with multiple risk factors for atherosclerotic renal artery stenosis.[8 39] Trial results may therefore have led to a general perception that the rarity of renal impairment obviates the need for close monitoring. However, as observed in our data, the risks in real world practice may be somewhat higher and non-negligible. In addition, previous research has shown that potassium monitoring in high-risk patients with CKD and diabetes may reduce serious hyperkalaemia-associated adverse events.[40] Still, the extent to which an initial creatinine increase ≥30% translates into adverse long-term outcomes in real-world patients remains to be clarified in future studies.

Generalisability, implications, and conclusions

The majority of patients initiating treatment with ACEI/ARBs experience only minor changes in renal function. However, substantial increases in creatinine levels after ACEI/ARB initiation may not be as rare as previously suggested, reinforcing the need for adherence to clinical guidelines for both pre- and post-initiating monitoring. Moreover, the post-initiation

creatinine increase and potassium levels used in this study are widely recognised cut-off levels, making the results internationally applicable. The comparison with the previous literature also confirms that the lack of systematic monitoring is not exclusive to the UK. Of particular concern was that even when appropriate monitoring was performed, severe renal impairment only rarely led to treatment discontinuation. Individual patient counselling may also be helpful to ensure that those at highest risk are closely monitored. More work is needed to determine the prognostic importance of the changes in renal function that we have observed.

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Transparency declaration: The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Contributorship

LT conceived the study idea and acquired data permissions. MS, KM, and LT designed the study. MS and KM performed data management and established the cohort. MS, KM, and LT reviewed the literature. The analyses were carried out by MS. All authors participated in the discussion and interpretation of the results. MS organised the writing and wrote the initial drafts. All authors critically revised the manuscript for intellectual content and approved the final version. MS is the guarantor.

Data sharing: No additional data are available.

Disclosures: None

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Table 1. Characteristics of patients initiating angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers in the UK primary care during 2004-2014, by monitoring groups

	Serum creatinine monitoring*				Total
	No baseline or follow-up tests	Baseline test only	Follow-up test only	Baseline and follow-up test	
Total number	21,411 (100)	63,359 (100)	33,185 (100)	105,859 (100)	223,814 (100)
Female sex	8,882 (41)	27,722 (44)	14,570 (44)	49,109 (46)	100,283 (45)
Age (years)					
<50 years	5,019 (23)	13,697 (22)	8,732 (26)	19,910 (19)	47,358 (21)
50-59 years	5,485 (26)	15,135 (24)	9,115 (27)	24,866 (23)	54,601 (24)
60-69 years	4,863 (23)	15,586 (25)	7,776 (23)	27,790 (26)	56,015 (25)
70-79 years	3,579 (17)	12,193 (19)	5,066 (15)	22,152 (21)	42,990 (19)
80+ years	2,465 (12)	6,748 (11)	2,496 (8)	11,141 (11)	22,850 (10)
Calendar period					
2004-2008	14,814 (69)	40,667 (64)	19,808 (60)	60,902 (58)	136,191 (61)
2009-2014	6,597 (31)	22,692 (36)	13,377 (40)	44,957 (42)	87,623 (39)
SES quintiles					
1 (low)	5,153 (24)	15,290 (24)	8,533 (26)	25,577 (24)	54,553 (24)
2	4,725 (22)	14,331 (23)	7,887 (24)	24,851 (23)	51,794 (23)
3	4,341 (20)	13,028 (21)	6,890 (21)	22,629 (21)	46,888 (21)
4	4,254 (20)	12,140 (19)	5,931 (18)	19,318 (18)	41,643 (19)
5 (high)	2,925 (14)	8,508 (13)	3,898 (12)	13,359 (13)	28,690 (13)
Missing	13 (0)	62 (0)	46 (0)	125 (0)	246 (0)
Smoking status					
Never	7,860 (37)	22,496 (36)	12,229 (37)	36,895 (35)	79,480 (36)
Ever	13,433 (63)	40,797 (64)	20,915 (63)	68,939 (65)	144,084 (64)
Missing	118 (1)	66 (0)	41 (0)	25 (0)	250 (0)
Alcohol intake					
No use	2,556 (12)	7,819 (12)	3,409 (10)	11,088 (10)	24,872 (11)
Current	15,495 (72)	47,322 (75)	25,656 (77)	82,870 (78)	171,343 (77)
Former	1,328 (6)	4,499 (7)	1,933 (6)	7,490 (7)	15,250 (7)
Missing	2,032 (9)	3,719 (6)	2,187 (7)	4,411 (4)	12,349 (6)
BMI groups					
Underweight	282 (1)	700 (1)	304 (1)	1,008 (1)	2,294 (1)
Healthy weight	5,666 (26)	15,406 (24)	8,089 (24)	24,972 (24)	54,133 (24)
Overweight	7,677 (36)	23,755 (37)	12,484 (38)	40,556 (38)	84,472 (38)
Obesity	6,009 (28)	20,660 (33)	10,527 (32)	35,887 (34)	73,083 (33)
Missing	1,777 (8)	2,838 (4)	1,781 (5)	3,436 (3)	9,832 (4)
CKD (eGFR)†					
Stage ≤2 (≥60)	10,326 (48)	53,773 (85)	19,470 (59)	87,484 (83)	171,053 (76)
Stage 3a (45–59)	1,137 (5)	7,382 (12)	1,766 (5)	13,913 (13)	24,198 (11)
Stage 3b (30–44)	217 (1)	1,885 (3)	265 (1)	3,854 (4)	6,221 (3)
Stage 4 (15–29)	24 (0)	319 (1)	29 (0)	608 (1)	980 (0)
Not measured	9,707 (45)	0 (0)	11,655 (35)	0 (0)	21,362 (10)
CV comorbidities‡					
Heart failure	1,568 (7)	3,270 (5)	1,386 (4)	4,583 (4)	10,807 (5)
Myocardial infarction	3,881 (18)	4,653 (7)	3,203 (10)	4,620 (4)	16,357 (7)
Hypertension	13,023 (61)	44,273 (70)	24,195 (73)	80,946 (76)	162,437 (73)
Peripheral arterial disease	471 (2)	1,590 (3)	523 (2)	2,547 (2)	5,131 (2)
Arrhythmia	2,057 (10)	4,973 (8)	2,000 (6)	7,123 (7)	16,153 (7)
Diabetes mellitus	1,399 (7)	13,586 (21)	1,992 (6)	21,548 (20)	38,525 (17)

Abbreviations: CV, cardiovascular; CKD, chronic kidney disease; y, year
*Monitoring groups based on baseline (within 12 months before) and follow-up (within 2 months after) serum creatinine monitoring.
†Calculated from most recent creatinine measurement within 12 months before first prescription date.
‡Diagnosis ever registered before ACE/ARB initiation in CRPD or HES.

Table 2. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers, 2004-2014

	S-Creatinine, ≥1 test
Total number	n=223,814 (100%)
Baseline testing	
≤12 months before	169,218 (76%)
≤3 months before	115,348 (52%)
≤1 months before	75,476 (34%)
Follow-up testing	
≤2 weeks after	65,090 (29%)
≤1 month after	114,244 (51%)
≤2 months after	139,044 (62%)

Table 3. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations

	Clinical guidelines					All initiators n=223,814 (100%)	
	NICE Heart Failure	NICE MI	NICE/UKRA Hypertension	NICE CKD	GP Notebook	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)
Baseline testing	x	x	x	x	x	169,218 (76%)	75,476 (34%)
+ Follow-up test ≤2 weeks*	x	n/a	x	x	x	46,486 (21%)	19,679 (9%)
+ Follow-up test ≤3 weeks†						70,792 (32%)	30,451 (14%)

Abbreviations: CKD, chronic kidney disease; GP, General Practice; MI, myocardial infarction; n/a, not specified; UKRA, UK Renal Association

*Follow-up test among those with baseline measurements

† Sensitivity analysis illustrating the importance of 2 vs. 3-week cut-off interval in follow-up test intervals.

Table 4. Proportion of new users of angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers who continue or discontinue treatment according to guideline recommended cut-off levels of serum creatinine and potassium at follow-up testing*

	Continuation†	Discontinuation†	Total
Total number, %	42,942 (93.1)	3,178 (6.9)	46,120 (100)
Serum creatinine increase ≥30%, n (%)	462 (81.5)	105 (18.5)	567 (100)
Serum potassium >6 mmol/L, n (%)	150 (78.5)	41 (21.5)	191 (100)

*Calculated from the most recent measurements within 1 month before and 2 months after drug initiation.

† A patient was considered continuous users when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring + 30 days (to allow for stock piling and irregular use)

Table 5. Association between patient characteristics and serum creatinine increase ≥30% and follow-up monitoring within 2 weeks following initiation of renin-angiotensin system blockade

	Odds ratio (95% confidence intervals)					
Characteristics	**S-creatinine monitoring within 2 weeks**		**S-creatinine increase ≥30%***		**S-potassium increase ≥30%***	
	Age- and sex adjusted	Fully adjusted†	Age- and sex adjusted	Fully adjusted†	Age- and sex adjusted	Fully adjusted†
Female sex	1.07 (1.04-1.10)	1.07 (1.04-1.09)	1.39 (1.26-1.53)	1.63 (1.47-1.80)	0.87 (0.66-1.16)	0.94 (0.70-1.26)
Age (years)						
< 50 years	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
50-59 years	0.98 (0.94-1.01)	0.98 (0.95-1.02)	0.88 (0.74-1.05)	0.86 (0.72-1.03)	1.29 (0.79-2.11)	1.10 (0.67-1.81)
60-69 years	1.05 (1.02-1.09)	1.05 (1.01-1.09)	1.03 (0.88-1.21)	1.00 (0.85-1.19)	1.35 (0.84-2.17)	0.97 (0.60-1.58)
70-79 years	1.18 (1.14-1.23)	1.18 (1.13-1.23)	1.49 (1.27-1.74)	1.36 (1.15-1.61)	1.65 (1.02-2.66)	0.74 (0.43-1.26)
80+ years	1.20 (1.14-1.25)	1.17 (1.11-1.23)	2.72 (2.32-3.20)	2.02 (1.68-2.44)	2.75 (1.67-4.53)	0.73 (0.41-1.32)
CKD stage						
No CKD (≥60)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Stage 3a (45–59)	1.00 (0.96-1.04)	1.00 (0.96-1.04)	0.62 (0.53-0.73)	0.60 (0.51-0.70)	2.48 (1.66-3.71)	2.06 (1.36-3.11)
Stage 3b (30–44)	0.99 (0.93-1.06)	1.01 (0.94-1.08)	1.01 (0.82-1.24)	0.88 (0.71-1.09)	7.51 (4.75-11.9)	5.10 (3.16-8.22)
Stage 4 (15–29)	1.42 (1.21-1.67)	1.41 (1.20-1.66)	2.16 (1.52-3.05)	1.72 (1.18-2.51)	24.0 (13.5-42.6)	11.4 (6.07-21.4)
Comorbidities*						
Heart failure	1.15 (1.09-1.23)	1.16 (1.08-1.23)	4.00 (3.49-4.58)	2.93 (2.51-3.42)	2.90 (1.90-4.42)	2.22 (1.38-3.58)
MI	0.80 (0.75-0.85)	0.77 (0.72-0.82)	2.33 (1.98-2.74)	1.57 (1.32-1.87)	2.12 (1.33-3.39)	1.35 (0.80-2.25)
Hypertension	1.00 (0.97-1.02)	1.05 (1.00-1.11)	0.62 (0.56-0.68)	1.58 (1.36-1.84)	0.60 (0.45-0.80)	1.02 (0.63-1.65)
PAD	1.09 (1.01-1.18)	1.11 (1.02-1.20)	2.10 (1.70-2.60)	1.87 (1.50-2.33)	2.14 (1.18-3.86)	1.53 (0.82-2.88)
Arrhythmia	1.09 (1.03-1.14)	0.98 (0.95-1.01)	2.37 (2.07-2.71)	0.77 (0.69-0.86)	1.41 (0.90-2.21)	0.77 (0.56-1.05)
Diabetes mellitus	0.93 (0.90-0.96)	0.93 (0.90-0.96)	1.09 (0.97-1.22)	1.04 (0.92-1.18)	0.97 (0.69-1.36)	0.90 (0.63-1.29)
Baseline K>5 mmol/L	1.04 (1.00-1.10)	1.04 (0.99-1.09)	1.04 (0.86-1.25)	0.97 (0.80-1.17)	8.22 (6.14-11.0)	6.68 (4.94-9.02)

Abbreviations: CKD, chronic kidney disease; MI, myocardial infarction; PAD, peripheral arterial disease

* The increase was based on the difference between the most recent baseline measurements within 12 months before and first follow-up measurement within 2 months after drug initiation. All analyses were restricted to those with both baseline and follow-up measurements (n=105,859).

† Adjusted for sex, age, CKD, heart failure, MI, hypertension, PAD, arrhytmia, diabetes, and calendar period of prescription start

ONLINE SUPPLEMENTAL MATERIAL

eTable 1. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations, overall and in most recent calendar period (extended version of Table 3)

	Clinical guidelines						All initiators		Continuing users*	
	NICE Heart Failure	NICE CKD	NICE Hypertension	NICE MI	UK Renal Association	GP Notebook	Generous baseline interpretation (≤12 month)	Strict baseline interpretation (≤1 month)	Generous baseline interpretation (≤12 month)	Strict baseline interpretation (≤1 month)
2004-2014							n=223,814 (100%)		n=173,244 (100%)	
Baseline testing	x	x	x	x	x	x	169,218 (76%)	75,476 (34%)	132,156 (76%)	58,668 (34%)
Follow-up test (≤2 weeks)†	x	x	n/a	x	x	x	46,486 (21%)	19,679 (9%)	43,420 (25%)	18,457 (11%)
+ At least within one year after				x			36,424 (16%)	15,642 (7%)	34,336 (20%)	14,800 (9%)
+ 1 month thereafter‡						x	11,866 (5%)	5,643 (3%)	11,298 (7%)	5,388 (3%)
+ 1 and 3 months thereafter ‡						x	5,787 (3%)	2,933 (1%)	5,516 (3%)	2,791 (2%)
+ 1, 3, and 6 months thereafter ‡						x	3,390 (2%)	1,807 (1%)	3,201 (2%)	1,703 (1%)
+ 1, 3, 6, and 12 months thereafter‡						x	2,618 (1%)	1,439 (1%)	2,464 (1%)	1,353 (1%)
Follow-up test (≤3 weeks)§							70,792 (32%)	30,451 (14%)	66,340 (38%)	28,644 (17%)
2009-2014							n=87,623 (100%)		n=68,042 (100%)	
Baseline testing	x	x	x	x	x	x	67,649 (77%)	30,576 (35%)	52,760 (78%)	23,716 (35%)
Follow-up test (≤2 weeks)†	x	x	n/a	x	x	x	20,172 (23%)	8,707 (10%)	18,862 (28%)	8,169 (12%)
+ At least within one year after				x			15,416 (18%)	6,726 (8%)	14,557 (21%)	6,377 (9%)
+ 1 month thereafter‡						x	5,373 (6%)	2,607 (3%)	5,123 (8%)	2,500 (4%)
+ 1 and 3 months thereafter ‡						x	2,614 (3%)	1,365 (2%)	2,492 (4%)	1,302 (2%)
+ 1, 3, and 6 months thereafter ‡						x	1,525 (2%)	841 (1%)	1,437 (2%)	792 (1%)
+ 1, 3, 6, and 12 months thereafter‡						x	1,152 (1%)	650 (1%)	1,079 (2%)	606 (1%)
Follow-up test (≤3 weeks)§							31,007 (35%)	13,511 (15%)	29,081 (43%)	12,726 (19%)

Abbreviations: CKD, chronic kidney disease; GP, General Practice; MI, myocardial infarction; n/a, not specified

* A patient was considered continuous users when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring + 30 days (to allow for stock piling and irregular use)

†Follow-up test among those with baseline measurements

‡Within additional 1, 3, 6, and 12 months after correspond to within 1.5, 3.5, 6.5, and 12.5 months after ACE/ARB initiation, respectively.

§Sensitivity analysis illustrating the importance of 2 vs. 3 week cut-off interval in follow-up test intervals.

eTable 2. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers, overall and most recent calendar period (extended version of Table 1)

	S-Creatinine, ≥1 test, n (%)	
	Total cohort (n=223,814)	2009-2014 cohort (n=87,623)
Baseline testing		
≤12 months before	169,218 (75.6)	67,649 (77.2)
≤3 months before	115,348 (51.5)	46,925 (53.6)
≤1 months before	75,476 (33.7)	30,576 (34.9)
Follow-up testing		
≤2 weeks after	65,090 (29.1)	27,933 (31.9)
≤1 month after	114,244 (51.0)	48,877 (55.8)
≤2 months after	139,044 (62.1)	58,334 (66.6)

eTable 3. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations

	All initiators n=223,814 (100%)	
	Generous baseline interpretation (≤12 month)	**Strict baseline interpretation** (≤1 month)
Overall (n=223,814)		
Baseline testing	169,218 (76%)	75,476 (34%)
+ Follow-up test ≤2 weeks*	46,486 (21%)	19,679 (9%)
+ Follow-up test ≤3 weeks†	70,792 (32%)	30,451 (14%)
Overall, no recent hospitalization (n=197,291)		
Baseline testing	153,353 (78%)	68,883 (35%)
+ Follow-up test ≤2 weeks*	42,967 (22%)	18,222 (9%)
+ Follow-up test ≤3 weeks†	65,881 (33%)	28,375 (14%)
Heart failure patients (n=10,807)		
Baseline testing	7,853 (73%)	3,277 (30%)
+ Follow-up test ≤2 weeks*	2,229 (21%)	951 (9%)
+ Follow-up test ≤3 weeks†	3,085 (29%)	1,340 (12%)
Myocardial infarction patients (n=16,357)		
Baseline testing	9,273 (57%)	3,766 (23%)
+ Follow-up test ≤2 weeks*	1,816 (11%)	726 (4%)
+ Follow-up test ≤3 weeks†	2,645 (16%)	1,078 (7%)
Hypertension patients (n=162,437)		
Baseline testing	125,219 (77%)	54,174 (33%)
+ Follow-up test ≤2 weeks*	35,502 (22%)	14,559 (9%)
+ Follow-up test ≤3 weeks†	54,585 (34%)	22,710 (14%)
CKD patients (n=31,399)		
Baseline testing	27,961 (89%)	13,913 (44%)
+ Follow-up test ≤2 weeks*	8,457 (27%)	4,198 (13%)
+ Follow-up test ≤3 weeks†	12,482 (40%)	6,324 (20%)
PAD patients (n=5,131)		
Baseline testing	4,137 (81%)	1,671 (33%)
+ Follow-up test ≤2 weeks*	1,198 (23%)	458 (9%)
+ Follow-up test ≤3 weeks†	1,751 (34%)	698 (14%)
Diabetes patients (n=38,525)		
Baseline testing	35,134 (91%)	15,907 (41%)
+ Follow-up test ≤2 weeks*	9,161 (24%)	3,794 (10%)
+ Follow-up test ≤3 weeks†	14,093 (37%)	5,994 (16%)

Abbreviations: CKD, chronic kidney disease; GP, General Practice; MI, myocardial infarction; n/a, not specified; UKRA, UK Renal Association

*Follow-up test among those with baseline measurements

† Sensitivity analysis illustrating the importance of 2 vs. 3-week cut-off interval in follow-up test intervals.

eTable 4. Proportion of new users of ACEI/ARB who continue or discontinue treatment according to guideline recommended cut-off levels of serum creatinine and potassium at follow-up testing

	Wide monitoring interval (12 month before to the first monitoring within 2 month after)			Narrow monitoring interval (1 month before to the first monitoring within 2 month after)		
	Continuation*	Discontinuation*	Total	Continuation*	Discontinuation*	Total
+ 30 day window						
Total number, %	113,210 (92.5)	9,170 (7.5)	122,380 (100)	48,772 (93.0)	3,676 (7.0)	52,448 (100)
S-creatinine increase ≥30%, n (%)	1,679 (80.7)	401 (19.3)	2,080 (100)	541 (81.5)	123 (18.5)	664 (100)
S-potassium >6 mmol/L, n (%)	472 (81.9)	104 (18.1)	576 (100)	204 (80.6)	49 (19.4)	253 (100)
+ 90 day window						
Total number, %	86,620 (81.8)	19,239 (18.2)	105,859 (100)	37,920 (82.2)	8,200 (17.8)	46,120 (100)
S-creatinine increase ≥30%, n (%)	1,111 (64.7)	605 (35.3)	1,716 (100)	372 (65.6)	195 (34.4)	567 (100)
S-potassium >6 mmol/L, n (%)	261 (61.0)	167 (39.0)	428 (100)	110 (57.6)	81 (42.4)	191 (100)

Calculated from the measurements closest to the first prescription date in the corresponding intervals, i.e., the most recent baseline measurements and the first follow-up measurement.

* A patient was considered continuous users when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring + 30 days or + 90days (to allow for stock piling and irregular use)

eTable 5. Association between patient characteristics and serum creatinine increase ≥30% and follow-up monitoring within 2 weeks following initiation of renin-angiotensin system blockade

	Adjusted odds ratio (95% confidence intervals)					
	Additional adjustment for ethnicity†			Excluding patient with hospitalisation within 30 days†		
Characteristics	**S-creatinine monitoring within 2 weeks**	**S-creatinine increase ≥30%***	**S-potassium >6 mmol/L***	**S-creatinine monitoring within 2 weeks**	**S-creatinine increase ≥30%***	**S-potassium >6 mmol/L***
Female sex	1.04 (1.01-1.08)	1.91 (1.64-2.23)	1.09 (0.70-1.71)	1.06 (1.04-1.09)	1.66 (1.48-1.86)	0.94 (0.69-1.27)
Age (years)						
< 50 years	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
50-59 years	0.97 (0.92-1.02)	0.91 (0.71-1.16)	1.65 (0.77-3.52)	0.99 (0.95-1.03)	0.86 (0.71-1.05)	1.17 (0.70-1.98)
60-69 years	1.04 (0.99-1.10)	0.86 (0.68-1.10)	1.23 (0.57-2.65)	1.07 (1.02-1.11)	1.05 (0.87-1.26)	0.98 (0.58-1.64)
70-79 years	1.22 (1.15-1.30)	1.22 (0.96-1.55)	0.83 (0.36-1.95)	1.19 (1.14-1.24)	1.40 (1.16-1.68)	0.72 (0.41-1.27)
80+ years	1.15 (1.06-1.24)	1.61 (1.21-2.14)	0.58 (0.21-1.58)	1.17 (1.11-1.24)	2.16 (1.76-2.66)	0.71 (0.38-1.33)
CKD stage						
No CKD (≥60)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Stage 3a (45–59)	1.00 (0.94-1.06)	0.51 (0.39-0.66)	1.82 (0.93-3.55)	1.00 (0.96-1.04)	0.58 (0.49-0.70)	2.40 (1.57-3.68)
Stage 3b (30–44)	1.06 (0.95-1.17)	0.99 (0.71-1.39)	5.66 (2.70-11.9)	0.98 (0.92-1.06)	0.92 (0.73-1.17)	5.15 (3.09-8.58)
Stage 4 (15–29)	1.51 (1.17-1.94)	1.65 (0.87-3.12)	15.0 (5.84-38.8)	1.42 (1.20-1.70)	1.86 (1.23-2.81)	12.2 (6.29-23.7)
Comorbidities*						
Heart failure	1.10 (0.99-1.21)	3.07 (2.41-3.91)	2.16 (0.96-4.85)	1.15 (1.06-1.24)	2.57 (2.11-3.13)	2.68 (1.59-4.51)
MI	0.78 (0.72-0.86)	1.76 (1.35-2.30)	1.10 (0.46-2.63)	0.89 (0.82-0.97)	1.59 (1.23-2.06)	1.89 (1.05-3.41)
Hypertension	0.97 (0.90-1.05)	1.51 (1.19-1.92)	1.01 (0.44-2.30)	1.04 (0.99-1.11)	1.40 (1.16-1.68)	0.81 (0.46-1.42)
PAD	1.09 (0.96-1.23)	1.63 (1.13-2.35)	1.52 (0.54-4.29)	1.16 (1.06-1.26)	1.74 (1.34-2.27)	1.75 (0.92-3.32)
Arrhythmia	0.96 (0.92-1.01)	0.84 (0.71-0.99)	0.72 (0.44-1.17)	0.98 (0.94-1.01)	0.80 (0.71-0.91)	0.74 (0.53-1.03)
Diabetes mellitus	0.91 (0.87-0.96)	1.15 (0.96-1.37)	0.58 (0.31-1.09)	0.93 (0.90-0.96)	1.06 (0.93-1.22)	0.93 (0.64-1.35)
Baseline K>6 mmol/L	1.05 (0.98-1.13)	0.86 (0.63-1.15)	7.98 (5.06-12.6)	1.03 (0.98-1.08)	1.01 (0.82-1.24)	6.44 (4.69-8.84)

Abbreviations: CKD, chronic kidney disease; MI, myocardial infarction; PAD, peripheral arterial disease

* The increase was based on the difference between the most recent baseline measurements within 12 months before and first follow-up measurement within 2 months after drug initiation. All analyses were restricted to those with both baseline and follow-up measurements (n=105,859).

† The main model was adjusted for sex, age, CKD, heart failure, MI, hypertension, PAD, arrhytmia, diabetes, and calendar period of prescription start

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	a) 3, 6 b) 3	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1.1 3, 5 1.2 3 1.3 3
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	5		
Objectives	3	State specific objectives, including any prespecified hypotheses	5		
Methods					
Study Design	4	Present key elements of study design early in the paper	5		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the	a) 5-6	RECORD 6.1: The methods of study population selection (such as codes or	6.1) 5-6 6.2) 5-6, 13-14

		sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	6.3) Not needed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	5-7	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7		
Bias	9	Describe any efforts to address potential sources of bias	8-9		
Study size	10	Explain how the study size was	6-7		

		arrived at			
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5-9		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	8-9		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	12.1) 5-6 12.2) 5-6
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-	12.3) 5-6

				level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	5-6, 9-12	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	13.1) 5-6, 9-12
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	9-12, Table 1		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	9-12		
Main results	16	(a) Give unadjusted estimates	9-12		

		and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	9-12		
Discussion					
Key results	18	Summarise key results with reference to study objectives	12		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-14	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	12-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17		
Generalisability	21	Discuss the generalisability (external validity) of the study results	17		

Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2		
Accessibility of protocol, raw data, and programming code		..	7, protocol made available for reviewers	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	7, protocol made available for reviewers

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Adherence to guidelines for creatinine and potassium monitoring and discontinuation following renin-angiotensin system blockade: a UK general practice-based cohort study

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Adherence to guidelines for creatinine and potassium monitoring and discontinuation following renin-angiotensin system blockade: a UK general practice-based cohort study

Running title: Creatinine and potassium monitoring after ACEI/ARB initiation

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ABSTRACT

Objectives To examine adherence to serum creatinine and potassium monitoring and discontinuation guidelines following initiation of treatment with angiotensin converting-enzyme inhibitors (ACEI) or angiotensin-receptor blockers (ARB); and whether high-risk patients are monitored.

Design General practice-based cohort study using electronic health records from the UK Clinical Practice Research Datalink and Hospital Episode Statistics.

Setting UK primary care, 2004–2014.

Subjects 223,814 new ACEI/ARB users.

Main outcome measures Proportion of patients with renal function monitoring before and after ACEI/ARB initiation; creatinine increase ≥30% or potassium levels >6 mmol/L at first follow-up monitoring; and treatment discontinuation after such changes. Using logistic regression models, we also examined patient characteristics associated with these biochemical changes, and with follow-up monitoring within the guideline-recommendation of two weeks after treatment initiation.

Results Ten percent of patients had neither baseline nor follow-up monitoring of creatinine within 12 months before and 2 months after initiation of an ACEI/ARB, 28% had monitoring only at baseline, 15% only at follow-up, and 47% both at baseline and follow-up. The median period between the most recent baseline monitoring and drug initiation was 40 days (interquartile range: 12-125 days). 34% of patients had baseline creatinine monitoring within one month before initiating therapy, but less than 10% also had the guideline-recommended follow-up test recorded within two weeks. Among patients experiencing a creatinine increase ≥30% (n=567, 1.2%) or potassium level >6 mmol/L (n=191, 0.4%), 80% continued treatment. Although patients with prior myocardial infarction, hypertension, or baseline potassium >5 mmol/L were at high risk of ≥30% increase in creatinine after ACEI/ARB initiation, there was no evidence that they were more frequently monitored.

Conclusions Only one tenth of patients initiating ACEI/ARB therapy receive the guideline-recommended creatinine monitoring. Moreover, the vast majority of the patients fulfilling post-initiation discontinuation criteria for creatinine and potassium increases continue on treatment.

Article Summary:

- This is the largest monitoring study to date, examining both adherence to creatinine and potassium monitoring and discontinuation guidelines following initiation of angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers in UK primary care, and whether patients are monitored in accordance with their individual risk profile
- Use of the UK Clinical Practice Research Datalink and Hospital Episode Statistics ensured that the study was population-based and not restricted to specific demographic, hospital, or insurance groups.
- Blood tests performed in hospital systems were not recorded in the Clinical Practice Research Datalink, but the results were consistent for patients with no recent hospital admissions
- If the recording of creatinine levels was not missing completely at random, the associations between patient characteristics and creatinine increase may have been underestimated

INTRODUCTION

Renin angiotensin system blockade using angiotensin-converting enzyme inhibitors (ACEI) and angiotensin-receptor blockers (ARB) is a mainstay in treatment of hypertension,[1] heart failure,[2] diabetic microalbuminuria or proteinuric renal diseases,[3] and after myocardial infarction.[4] However, some patients experience a sudden decline in kidney function when initiating these drugs, presumably due to antagonism of the angiotensin II-mediated efferent arteriolar constriction or impaired kidney excretion of potassium.[5 6]

The potential impact on kidney function should be evaluated by comparing pre- and post-initiation levels of serum creatinine and potassium.[7] Discontinuation is recommended if the rise in creatinine exceeds 30% above baseline or if hyperkalaemia develops.[8] It is unclear whether these recommendations are routinely followed in clinical practice.[9]

A few studies have compared baseline and follow-up monitoring results,[9] but large studies using contemporary data with reference to current guidelines are lacking, and it is unknown whether patients' individual risk of renal impairment influence their likelihood of being monitored.[9] We therefore examined adherence to creatinine and potassium monitoring and treatment discontinuation guidelines following ACEI/ARB initiation in UK primary care, and whether patients are monitored in accordance with their individual risk profile.

METHODS

Data sources

We used the UK's Clinical Practice Research Datalink (CPRD) linked to hospital record data from the Hospital Episode Statistics (HES) database. The CPRD database contains primary care electronic health record data from 7% of the UK population (~15 million patient lives, with ~8 million currently under follow-up).[10] Patients included in the CPRD are largely representative of the UK population in terms of age, sex and ethnicity.[10 11] Information recorded in the database includes demographics such as sex and year of birth, the location of the general practice, medical diagnoses (based on 'Read' codes), drug prescriptions, and a

range of routine laboratory test results. HES records cover all hospital admissions for patients covered by the NHS who receive treatment either from English NHS trusts or independent providers.[10 11] Fifty-eight percent of general practices included in the CPRD have agreed to HES linkage.[10] We obtained linked data on socioeconomic status (index of multiple deprivation) based on area of residence.

Monitoring guidelines

Consistent with other international guidelines, the National Institute for Health and Care Excellence (NICE) recommend baseline testing of creatinine when initiating ACEI/ARB therapy in patients with hypertension,[1] heart failure,[2] myocardial infarction,[4] or chronic kidney disease (CKD).[3] The time interval for baseline testing is not further specified.[1-4] Among patients with heart failure, myocardial infarction, and chronic kidney disease, NICE recommends follow-up monitoring within 2 weeks of treatment initiation,[2-4] and for myocardial infarction patients at least annually thereafter.[4] A baseline assessment and follow-up test within 2 weeks are also recommended by the UK Renal Association,[12] as well as the frequently used online web resource General Practice (GP) Notebook.[13] GP Notebook additionally recommends monitoring 1, 3, 6, and 12 months after the first follow-up test.[13] NICE recommends not to initiate ACEI/ARBs in patients with a baseline potassium level >5 mmol/L and to discontinue therapy if potassium rises above 6 mmol/L.

ACEI/ARB initiators

We identified a cohort of all HES linked CPRD patients aged ≥18 years, who initiated ACEI/ARB treatment between January 1, 2004 and March 31, 2014. We did not include earlier calendar periods, as laboratory data before 2004 were incomplete due to interface problems between laboratory reporting software and GP practice software.[14] Also, creatinine testing was incentivised in 2004 with the introduction of the diabetes Quality and Outcomes

Framework (QOF) and further in 2006 with the CKD QOF.[14] To rule out any potential influence of incomplete data around 2004, we also examined the most recent 5-year calendar period separately in a sensitivity analysis. New users were defined as persons with at least one year of continuous registration in the CPRD before their first recorded ACEI/ARB prescription.

Laboratory data

All creatinine test results were extracted from the general practice records of the study population, using creatinine-specific codes in CPRD. Cross-reference was then made to creatinine test results identified from a broad Read code search. Any irrelevant codes were excluded. Renal function testing in the UK includes creatinine and potassium so it can be inferred that testing frequency is similar to creatinine for potassium. When we conducted analyses related to potassium levels, we repeated the procedure used to identify creatinine levels for potassium test results.

Patient characteristics

We obtained information for all patients on age, sex, calendar period of ACEI/ARB initiation (2004–2008 and 2010–2014), socioeconomic status (quintiles of the 2004 index of multiple deprivation scores), lifestyle factors (smoking, alcohol intake, and body mass index), baseline potassium level (≤5 or >5 mmol/L), CKD, cardiovascular comorbidities (heart failure, myocardial infarction, hypertension, peripheral arterial disease, and arrhythmia), and diabetes.[15] We used algorithms for smoking status, alcohol intake, and body mass index based on the most recent records in the CPRD before ACEI/ARB initiation.[16 17] As measures of baseline creatinine and potassium levels, we used the single most recent measurement within 12 months before the first ACEI/ARB prescription. We calculated estimated glomerular filtration rate (eGFR) level from the most recent creatinine measurement and

CKD stage from the CKD-EPI equation.[18] Cardiovascular comorbidities and diabetes were identified from both the CPRD and HES based on diagnoses recorded prior to ACEI/ARB initiation. The code lists for all variables are provided in the Appendix.

Patient involvement

The study included no patient involvement

Statistical analysis

We described ACEI/ARB users according to patient characteristics, both overall and according to creatinine monitoring status (no baseline or follow-up monitoring, baseline only, follow-up only, and both baseline and follow-up monitoring). Baseline monitoring was defined as a test performed on the date of drug initiation or within either 12 months before (generous interval) or one month before initiation (more ideal interval assumed to be driven by planned ACEI/ARB initiation). To accord with the post-initiation monitoring interval recommended from previous trial data, we considered only follow-up monitoring within the first 2 months after drug initiation.[8]

We calculated the proportion of persons in the total cohort of new users who had baseline and follow-up monitoring (within 1, 3, and 12 months before drug initiation and within 2 weeks, 1 month, and 2 months after initiation). We then computed the proportion of persons with both baseline and initial follow-up monitoring within the guideline-recommended interval of 2 weeks following drug commencement.

We repeated the analyses for continuing users, in order to examine adherence to the stricter guideline recommendations for ongoing monitoring (*i.e.*, monitoring within 1, 3, 6, and 12 months after the first retest).[13] Continuation was defined as ACEI/ARB use beyond 30 days following the monitoring date, *i.e.*, when the end date of the first continuous course of therapy was after the date of the first monitoring date plus 30 days (to allow for stockpiling).

The end date of each prescription was calculated by adding the prescription duration (total number of tablets prescribed divided by the specified number of tablets per day) to the prescription date. In identifying continuous courses of therapy, we allowed for a 30-day gap between the end date of one prescription and the start of the next consecutive prescription.

In sensitivity analyses, we repeated the analyses (1) extending the follow-up window for the first follow-up monitoring from two to three weeks to account for minor delays; (2) including only the most recent calendar period (2009-2014) to account for temporal changes in data completeness and quality of care; (3) excluding patients with a hospital admission or discharge date within 1 month before or after their first ACEI/ARB prescription, in order to account for drug initiation and any subsequent renal function tests occurring in the hospital and therefore not captured in the CPRD; (4) focusing on specific patient subgroups (heart failure, myocardial infarction, hypertension, CKD (eGFR<60mls/min/1.73m^2), peripheral arterial disease, and diabetes); and (5) defining drug use continuation as ACEI/ARB use beyond 90 days (instead of 30 days) after the first retest date.

We used the subcohort of patients with both baseline and follow-up monitoring to calculate the proportion of patients with creatinine increases ≥30% or potassium levels >6 mmol/L at the first follow-up monitoring within 2 months after initiation, as well as the proportion of patients continuing treatment despite these contraindications for use.

Finally, we fitted a logistic regression model to identify patient characteristics associated with a severe decline in renal function (creatinine increase ≥30% or potassium level >6 mmol/L) and compared these characteristics with those associated with receiving post-initiation follow-up monitoring within 2 weeks. The model included age, sex, CKD stage, cardiovascular comorbidities, diabetes, and baseline potassium level (>5 vs. ≤5 mmol/L). In three additional model-based sensitivity analyses, we repeated the analyses (1) excluding patients with a recent hospitalization (as defined above); (2) omitting baseline potassium from the model to examine the extent of potential overfitting when both baseline

potassium and CKD stage were kept in the model; and (3) also adjusting additional for ethnicity.

The study protocol was made available to the journal reviewers and approved by the London School of Hygiene and Tropical Medicine Ethics Committee (No. 6536) and the Independent Scientific Advisory Committee (ISAC) for Medicines and Healthcare Products Regulatory Agency (No. 16_025). All analyses were performed using STATA 14 statistical software package.

RESULTS

Serum creatinine monitoring before and after ACEI/ARB initiation

We identified 223,814 new users of ACEI/ARB. We compared these patients in four groups: 21,411 (10%) had no baseline or follow-up creatinine tests within 12 months before and 2 months after treatment initiation, 63,359 (28%) had only a baseline test, 33,185 (15%) had only follow-up tests, and 105,859 (47%) had both baseline and follow-up tests. (Table 1). Median age varied only slightly between the groups (60, 62, 59, and 63 years, respectively) and there were no substantial differences in socioeconomic status, lifestyle factors, or peripheral arterial disease. Compared with patients with neither pre- nor post-initiation monitoring, patients with both were more likely to have diagnosed hypertension (76% vs. 61%) and diabetes (20% vs. 7%), but less likely to have diagnosed heart failure (4% vs. 7%), myocardial infarction (4% vs. 18%), and arrhythmia (7% vs. 10%). Among patients with baseline monitoring, 83% did not have CKD, 13% stage 3a, 3% stage 3b, 0.5% stage 4 CKD. In the same population, 7% commenced ACEI/ARB therapy despite baseline potassium above 5 mmol/L. The median number of days between baseline monitoring and first prescription date was 40 days (interquartile range: 12-125 days).

Among all patients initiating ACEI/ARB therapy, the proportion of patients receiving creatinine testing before was 76% within 12 months before treatment initiation, declining to 34% within one month before initiation (Table 2). The proportion with follow-up testing after

treatment initiation was 29% within 2 weeks, increasing to 62% within 2 months. Among ACEI/ARB initiators who had a baseline test within 12 months, 21% also had a follow-up test within 2 weeks after starting treatment (Table 3). However, among patients undergoing testing within one month prior to treatment initiation, only 9% had also the recommended follow-up test within 2 weeks of treatment start. When we extended the follow-up window to three weeks, this proportion increased only to 14% (Table 3). Among patients continuing treatment, only 1% had follow-up measurements at 1, 3, 6, and 12 months after the first retest, in compliance with the strictest recommendation (eTable 1). These results were unchanged when the analysis was restricted to the most recent calendar period (eTable 1-2) and to patients with heart failure, myocardial infarction, hypertension, peripheral arterial disease, diabetes or no recent hospitalization (eTable 3). Only patients with CKD received a slightly higher degree of monitoring (13%) within two weeks following treatment initiation (eTable 3). The proportion with follow-up testing after treatment initiation was also unchanged when results were stratified by date of ACEI/ARB initiation in two-year intervals (eTable 4).

Serum creatinine and potassium changes after ACEI/ARB initiation

Among patients receiving the recommended renal function monitoring, 567 (1.2%) experienced a creatinine increase ≥30% and 191 (0.4%) a potassium level >6 mmol/L at their first follow-up test within two months of treatment initiation (1.4% received in total either) (Table 4). Among these patients, 80% continued treatment beyond 30 days following the monitoring date (Table 4). The sensitivity analysis showed that 65% of patients with a creatinine increase ≥30% and 60% of those with a potassium level >6 mmol/L continued also treatment beyond 90 days after the monitoring date (eTable 5). The results remained consistent for longer baseline monitoring intervals (eTable 5).

Patients at high risk for creatinine increases ≥30%

When we examined patient characteristics associated with a creatinine increase ≥30% and adjusted for the other characteristics in a multivariable analysis (Table 5), we found an increased odds ratio (OR) for women (1.6-fold increased), for age above 70 years (at least 1.3-fold increased), for CKD stage 4 (1.6-fold increased), heart failure (2.9-fold increased), peripheral arterial disease (1.9-fold increased), myocardial infarction (1.6-fold increased), and hypertension (1.6-fold increased).

Patients at high risk for potassium >6 mmol/L

Baseline potassium level and CKD stage, but not age and sex, were associated with potassium levels >6 mmol/L after ACEI/ARB initiation. Thus, the OR was 7-fold increased for baseline potassium >5 mmol/L, two-fold increased for CKD stage 3a, 5-fold increased for stage 3b, and 11-fold increased for stage 4 (Table 5). Among cardiovascular comorbidities, heart failure was associated with the strongest OR of a potassium level >6 mmol/L (2.22, 95% CI: 1.38-3.58).

Monitoring high-risk patients

Some characteristics associated with an increased odds of having ≥30% rise in creatinine were also associated with a greater likelihood of having a follow-up test within 2 weeks following drug initiation. These included older age: persons aged 70 years or above compared with ≤50 years (1.18, 95% CI: 1.13-1.23 for 70-79 years and 1.17, 95% CI: 1.11-1.23 for 80+ years), CKD stage 4 compared to no CKD (1.41, 95% CI: 1.20-1.66), heart failure (1.16, 95% CI: 1.08-1.23), and peripheral arterial disease (1.11, 95% CI: 1.02-1.20). However, other characteristics associated with an increased odds of having ≥30% rise in creatinine were not associated with a greater likelihood of having a follow-up test within 2 weeks following drug initiation: there was no substantially increased OR (>10%) associated with female sex (1.07,

95% CI: 1.04-1.09), prior history of myocardial infarction (0.77, 95% CI: 0.72-0.82), hypertension (1.05, 95% CI: 1.00-1.11), or baseline potassium >5 mmol/L (1.04, 95% CI: 0.99-1.09). When we excluded patients with a recent hospital admission, the reduced OR for myocardial infarction was no longer observed (0.93, 95% CI: 0.80-1.08) (eTable 6). Finally, the results remained consistent when we omitted adjustment for baseline potassium (data not shown) and when we adjusted additionally for ethnicity (eTable 6).

DISCUSSION

Only one tenth of patients initiating ACEI/ARBs in UK primary care appear to receive the guideline-recommended creatinine monitoring. One in 15 patients commenced ACEI/ARBs despite baseline potassium above the recommended level, which was also shown to be a strong predictor for severe post-initiation hyperkalaemia. Among monitored patients, a creatinine increase ≥30% or a potassium level >6 mmol/L occurred in almost 1.5% of patients, and most did not discontinue therapy despite guideline recommendations to stop. Although patients with prior myocardial infarction, hypertension, or a high baseline potassium level were at higher risk of sudden decline in kidney function after ACEI/ARB initiation, there was no evidence that these patient groups were monitored more frequently while initiating the drugs.

Strengths and limitations

Several issues should be considered when interpreting our study results. Its large sample size increased precision. Use of the CPRD ensured that the study was general practice-based and not restricted to specific demographic, hospital, or insurance groups.

Over the time course of this study multiple factors have impacted on prescribing of ACEI/ARB and measurement of renal function in primary care, for example the introduction of the relevant NICE guidelines, and QOF reimbursement for testing in certain sub-groups. We also did not have information about clinical initiatives such as heart failure nurses and

ACEI/ARB stopping rules ('sick-day rules'). While our main results provide summary measures over a ten-year period, sensitivity analyses confirm that despite these changes, the proportion receiving the guideline suggested biochemical monitoring does not vary during the study period. We did not have access to blood tests performed in hospital systems, which may have been reported to GPs, but not recorded in CPRD. However, restricting the analysis to patients with no recent hospital admissions who were most likely to have had renal function measured and acted upon in secondary care had little effect on our findings. We did not examine testing during initiation of dual blockade with ACEI and ARB as this combination is now used very infrequently for patients with severe comorbidities who are likely to be monitored in secondary care. Although some patients may also have been seen in outpatient specialty clinics, it is common practice for specialists to ask GPs to initiate new drugs such as ACEI/ARBs, with local biochemical monitoring, limiting misclassification.

Consistent with findings from other studies,[19] we found that approximately 50% of all ACEI/ARB initiators were monitored both before and after treatment start. If GPs are retesting renal function in patients at higher risk of substantial biochemical changes, we may have overestimated the proportion of patients with high potassium levels or creatinine increases compared with the untested lower-risk general population.

GP system software is used for issuing prescriptions, ensuring the accuracy of prescription data. However, it cannot be inferred that all patients actually redeemed their prescription at the pharmacy and start medication on the same day that it was prescribed.[18 20] Similarly, the estimated coverage of prescriptions may not be completely accurate due to such factors as stockpiling and irregular use. We also do not know whether GPs contacted patients with elevated laboratory results to advise them to stop taking the medication prior to the end of their prescriptions. However, 80% of patients who developed creatinine increase ≥30% after ACEI/ARB initiation were still issued a subsequent ACEI/ARB prescription.

We aimed to detect discontinuation related closely in time to first follow-up monitoring

and hence likely resulting from an elevated creatinine or potassium result. We therefore defined continuation as ACEI/ARB use beyond 30 days (the median prescription duration) after the monitoring date. Extending the definition of continuous use beyond 90 days reduced the risk of misclassifying patients as continuing treatment when they had in fact stopped. However, extending the duration also increased the risk of identifying discontinuation due to other reasons than creatinine/potassium increase, *e.g.*, death or cough. Diagnoses recorded in the CPRD generally have been found to have adequate validity for research purposes,[21 22] particularly in the domains assessed by the QOF.[23 24]

In the logistic regression analysis to estimate factors associated with creatinine increase ≥30%, we excluded patients without pre and post measurements (complete case analysis). If the recording of creatinine levels was not missing completely at random, the associations between patient characteristics and creatinine increase may have been underestimated.[25] While this assumption could not be tested directly, examination of baseline characteristics revealed no major differences in age, sex, socioeconomic status, and lifestyle between patients with and without pre- and post-monitoring. Furthermore, the results were consistent for each individual patient group examined. Patients with no testing before or after treatment initiation (including those with potentially haemolysed samples) only accounted for 10% of all ACEI/ARB initiators.

Comparison with other studies

To our knowledge, this is the largest study conducted to date on adherence to monitoring and discontinuation guidelines after ACEI/ARB initiation. Only one previous study[19] examined monitoring according to guideline-recommended intervals (<14 days). All others have used longer intervals (*e.g.*, 30 days[26] or 6 months[27 28]), which make interpretations and implications for clinical practice less clear. Poor adherence to monitoring guidelines after ACEI/ARB initiation is not restricted to the UK,[19 28 29] but has also been reported in the US[30-

[32], Canada,[33] and the Netherlands.[26 34] Owing to our sample size, we were able to show that the lack of monitoring occurred in all patient groups with an indication for ACEI/ARB therapy.

A recent Dutch study, including 3,353 patients initiating ACEI/ARBs between 2005-2011, found that 19% had creatinine measured within 30 days and 66% within one year.[26] Creatinine increases above 30% occurred in 1.6% of patients, and among these 70% did not discontinue treatment.[26] A Scottish study of 4,056 patients with type 2 diabetes, prescribed an ACEI/ARB between 2005-2009, found that 19% had both a baseline (within 90 days) and follow-up measurement (within 2 weeks) of initiation. Within this cohort, 1.7% had both a creatinine increase of ≥30% and potassium level ≥5.6 mmol/L.

The magnitude of the risk of severe renal impairment, as measured by creatinine increase in these observational studies, was consistent with our findings, but substantially higher than reported in clinical trials (*e.g.*, 0.2% in the ONTARGET trial).[35] It is not clear from the literature how often harm occurs around the time of initiation, when the risk of nephrotoxicity is thought to be greatest.[8] If physicians are to understand why follow-up monitoring within 2 weeks of treatment start matters, the short-term risks need to be clarified. Until now, most studies have reported only on cumulative risk over entire courses of treatment, such as the 1.1% two-year risk for potassium of >6 mmol/L in the SOLVD trials of heart failure patients.[36] In contrast to clinical trial reviews, reporting a 0.2% (3/1818) risk of potassium >6 mmol/L, we found a 0.4% risk of hyperkalaemia already at time of first retesting after ACEI initiation.

Extending the previous literature, our results support that advanced age, advanced CKD, and heart failure, but not sex, increase the likelihood of being monitored.[19 26 30] Consistent with some,[26 30] but not all, previous studies,[28] we found no association for diabetes. However, these previous studies reporting an association for diabetes focused on monitoring within broader intervals (*e.g.*, 6 months),[28] where diabetes patients, irrespective of

ACEI/ARB initiation, were likely to receive blood testing owing to the diabetes QOF programme.

Determinants of increases in creatinine levels after ACEI/ARB initiation are less well understood than for hyperkalaemia, but increasing age is a consistently reported factor.[19] Advanced CKD and a range of cardiovascular comorbidities (mostly associated with atherosclerosis) were also important determinants in our patient cohort. Consistent with previous studies, we found that the risk of hyperkalaemia was associated with CKD (likely due to impaired ability of the cortical collecting tubule to secrete potassium), heart failure (likely due to decreased delivery of sodium to the distal nephron), and high pre-treatment potassium levels.[6 8 19 37] We did not observe an association with diabetes or increasing age, as could have been expected due to diabetic nephropathy or age-dependent hyporeninemic hypoaldosteronism.[6]

Clinical relevance

Several possible explanations exist for the divergence between the clinical guideline recommendations and the observed monitoring and response patterns in clinical practice. The first is *clinician nonadherence* to ordering tests. This may be due to inconsistent recommendations for timing and frequency of monitoring over time,[6] consensus-based (rather than evidence-based) monitoring guidelines, and a lack of guidelines tailored to particular high-risk patients, such as those with CKD and heart failure. Although we found that follow-up monitoring correlated well with the risk of renal impairment after ACEI/ARB initiation for most patient groups, it was not observed for patients with myocardial infarction or pre-initiation high potassium. The second explanation may be *patient nonadherence* to ordered tests. This is particularly salient in UK primary care where blood samples may be taken in phlebotomy clinics that the patient has to visit rather than the GP practice. Patients may find it burdensome to have blood tests, and GPs have no direct economic incentives to ensure that

they are done. A third barrier is *lack of evidence of the clinical importance* of monitoring and its cost-effectiveness. ACEI/ARB-induced renal impairment is rare in clinical trials, even among patients with multiple risk factors for atherosclerotic renal artery stenosis.[8 38] Trial results may therefore have led to a general perception that the rarity of renal impairment obviates the need for close monitoring. However, as observed in our data, the risks in real world practice may be somewhat higher and non-negligible. In addition, previous research has shown that potassium monitoring in high-risk patients with CKD and diabetes may reduce serious hyperkalaemia-associated adverse events.[39] Still, the extent to which an initial creatinine increase ≥30% translates into adverse long-term outcomes in real-world patients remains to be clarified in future studies.

Generalisability, implications, and conclusions

The majority of patients initiating treatment with ACEI/ARBs experience only minor changes in renal function. However, substantial increases in creatinine levels after ACEI/ARB initiation may not be as rare as previously suggested, reinforcing the need for adherence to clinical guidelines for both pre- and post-initiating monitoring. Moreover, the post-initiation creatinine increase and potassium levels used in this study are widely recognised cut-off levels, making the results internationally applicable. The comparison with the previous literature also confirms that the lack of systematic monitoring is not exclusive to the UK. Of particular concern was that even when appropriate monitoring was performed, severe renal impairment only rarely led to treatment discontinuation. Individual patient counselling may also be helpful to ensure that those at highest risk are closely monitored. More work is needed to determine the prognostic importance of the changes in renal function that we have observed.

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Transparency declaration: The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Contributions

LT conceived the study idea and acquired data permissions. MS, KM, and LT designed the study. MS and KM performed data management and established the cohort. MS, KM, and LT reviewed the literature. The analyses were carried out by MS. All authors participated in the discussion and interpretation of the results. MS organised the writing and wrote the initial drafts. All authors critically revised the manuscript for intellectual content and approved the final version. MS is the guarantor.

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Table 1. Characteristics of patients initiating angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers in the UK primary care during 2004-2014, by monitoring groups

	Serum creatinine monitoring*				Total
	No baseline or follow-up tests	Baseline test only	Follow-up test only	Baseline and follow-up test	
Total number	21,411 (100)	63,359 (100)	33,185 (100)	105,859 (100)	223,814 (100)
Female sex	8,882 (41)	27,722 (44)	14,570 (44)	49,109 (46)	100,283 (45)
Age (years)					
<50 years	5,019 (23)	13,697 (22)	8,732 (26)	19,910 (19)	47,358 (21)
50-59 years	5,485 (26)	15,135 (24)	9,115 (27)	24,866 (23)	54,601 (24)
60-69 years	4,863 (23)	15,586 (25)	7,776 (23)	27,790 (26)	56,015 (25)
70-79 years	3,579 (17)	12,193 (19)	5,066 (15)	22,152 (21)	42,990 (19)
80+ years	2,465 (12)	6,748 (11)	2,496 (8)	11,141 (11)	22,850 (10)
Calendar period					
2004-2008	14,814 (69)	40,667 (64)	19,808 (60)	60,902 (58)	136,191 (61)
2009-2014	6,597 (31)	22,692 (36)	13,377 (40)	44,957 (42)	87,623 (39)
SES quintiles					
1 (low)	5,153 (24)	15,290 (24)	8,533 (26)	25,577 (24)	54,553 (24)
2	4,725 (22)	14,331 (23)	7,887 (24)	24,851 (23)	51,794 (23)
3	4,341 (20)	13,028 (21)	6,890 (21)	22,629 (21)	46,888 (21)
4	4,254 (20)	12,140 (19)	5,931 (18)	19,318 (18)	41,643 (19)
5 (high)	2,925 (14)	8,508 (13)	3,898 (12)	13,359 (13)	28,690 (13)
Missing	13 (0)	62 (0)	46 (0)	125 (0)	246 (0)
Smoking status					
Never	7,860 (37)	22,496 (36)	12,229 (37)	36,895 (35)	79,480 (36)
Ever	13,433 (63)	40,797 (64)	20,915 (63)	68,939 (65)	144,084 (64)
Missing	118 (1)	66 (0)	41 (0)	25 (0)	250 (0)
Alcohol intake					
No use	2,556 (12)	7,819 (12)	3,409 (10)	11,088 (10)	24,872 (11)
Current	15,495 (72)	47,322 (75)	25,656 (77)	82,870 (78)	171,343 (77)
Former	1,328 (6)	4,499 (7)	1,933 (6)	7,490 (7)	15,250 (7)
Missing	2,032 (9)	3,719 (6)	2,187 (7)	4,411 (4)	12,349 (6)
BMI groups					
Underweight	282 (1)	700 (1)	304 (1)	1,008 (1)	2,294 (1)
Healthy weight	5,666 (26)	15,406 (24)	8,089 (24)	24,972 (24)	54,133 (24)
Overweight	7,677 (36)	23,755 (37)	12,484 (38)	40,556 (38)	84,472 (38)
Obesity	6,009 (28)	20,660 (33)	10,527 (32)	35,887 (34)	73,083 (33)
Missing	1,777 (8)	2,838 (4)	1,781 (5)	3,436 (3)	9,832 (4)
CKD (eGFR)†					
Stage ≤2 (≥60)	10,326 (48)	53,773 (85)	19,470 (59)	87,484 (83)	171,053 (76)
Stage 3a (45–59)	1,137 (5)	7,382 (12)	1,766 (5)	13,913 (13)	24,198 (11)
Stage 3b (30–44)	217 (1)	1,885 (3)	265 (1)	3,854 (4)	6,221 (3)
Stage 4 (15–29)	24 (0)	319 (1)	29 (0)	608 (1)	980 (0)
Not measured	9,707 (45)	0 (0)	11,655 (35)	0 (0)	21,362 (10)
CV comorbidities‡					
Heart failure	1,568 (7)	3,270 (5)	1,386 (4)	4,583 (4)	10,807 (5)
Myocardial infarction	3,881 (18)	4,653 (7)	3,203 (10)	4,620 (4)	16,357 (7)
Hypertension	13,023 (61)	44,273 (70)	24,195 (73)	80,946 (76)	162,437 (73)
Peripheral arterial disease	471 (2)	1,590 (3)	523 (2)	2,547 (2)	5,131 (2)
Arrhythmia	2,057 (10)	4,973 (8)	2,000 (6)	7,123 (7)	16,153 (7)
Diabetes mellitus	1,399 (7)	13,586 (21)	1,992 (6)	21,548 (20)	38,525 (17)

Abbreviations: CV, cardiovascular; CKD, chronic kidney disease; y, year

*Monitoring groups based on baseline (within 12 months before) and follow-up (within 2 months after) serum creatinine monitoring.

†Calculated from most recent creatinine measurement within 12 months before first prescription date.

‡Diagnosis ever registered before ACE/ARB initiation in CRPD or HES.

Table 2. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers, 2004-2014

	S-Creatinine, ≥1 test
Total number	n=223,814 (100%)
Baseline testing	
≤12 months before	169,218 (76%)
≤3 months before	115,348 (52%)
≤1 months before	75,476 (34%)
Follow-up testing	
≤2 weeks after	65,090 (29%)
≤1 month after	114,244 (51%)
≤2 months after	139,044 (62%)

Table 3. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations

	Clinical guidelines					All initiators n=223,814 (100%)	
	NICE Heart Failure	NICE MI	NICE/UKRA Hypertension	NICE CKD	GP Notebook	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)
Baseline testing	x	x	x	x	x	169,218 (76%)	75,476 (34%)
+ Follow-up test ≤2 weeks*	x	n/a	x	x	x	46,486 (21%)	19,679 (9%)
+ Follow-up test ≤3 weeks†						70,792 (32%)	30,451 (14%)

Abbreviations: CKD, chronic kidney disease; GP, General Practice; MI, myocardial infarction
*Follow-up test among those with baseline measurements
† Sensitivity analysis illustrating the importance of 2 vs. 3-week cut-off interval in follow-up test intervals.

Table 4. Proportion of new users of angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers who continue or discontinue treatment according to guideline recommended cut-off levels of serum creatinine and potassium at follow-up testing*

	Continuation†	Discontinuation†	Total
Total number, %	42,942 (93.1)	3,178 (6.9)	46,120 (100)
Serum creatinine increase ≥30%, n (%)	462 (81.5)	105 (18.5)	567 (100)
Serum potassium >6 mmol/L, n (%)	150 (78.5)	41 (21.5)	191 (100)

*Calculated from the most recent measurements within 1 month before and 2 months after drug initiation.
† A patient was considered continuous users when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring + 30 days (to allow for stock piling and irregular use)

Table 5. Association between patient characteristics and serum creatinine increase ≥30% and follow-up monitoring within 2 weeks following initiation of renin-angiotensin system blockade

	Odds ratio (95% confidence intervals)					
Characteristics	**S-creatinine monitoring within 2 weeks**		**S-creatinine increase ≥30%***		**S-potassium increase ≥30%***	
	Age- and sex adjusted	Fully adjusted†	Age- and sex adjusted	Fully adjusted†	Age- and sex adjusted	Fully adjusted†
Female sex	1.07 (1.04-1.10)	1.07 (1.04-1.09)	1.39 (1.26-1.53)	1.63 (1.47-1.80)	0.87 (0.66-1.16)	0.94 (0.70-1.26)
Age (years)						
< 50 years	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
50-59 years	0.98 (0.94-1.01)	0.98 (0.95-1.02)	0.88 (0.74-1.05)	0.86 (0.72-1.03)	1.29 (0.79-2.11)	1.10 (0.67-1.81)
60-69 years	1.05 (1.02-1.09)	1.05 (1.01-1.09)	1.03 (0.88-1.21)	1.00 (0.85-1.19)	1.35 (0.84-2.17)	0.97 (0.60-1.58)
70-79 years	1.18 (1.14-1.23)	1.18 (1.13-1.23)	1.49 (1.27-1.74)	1.36 (1.15-1.61)	1.65 (1.02-2.66)	0.74 (0.43-1.26)
80+ years	1.20 (1.14-1.25)	1.17 (1.11-1.23)	2.72 (2.32-3.20)	2.02 (1.68-2.44)	2.75 (1.67-4.53)	0.73 (0.41-1.32)
CKD stage						
No CKD (≥60)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Stage 3a (45–59)	1.00 (0.96-1.04)	1.00 (0.96-1.04)	0.62 (0.53-0.73)	0.60 (0.51-0.70)	2.48 (1.66-3.71)	2.06 (1.36-3.11)
Stage 3b (30–44)	0.99 (0.93-1.06)	1.01 (0.94-1.08)	1.01 (0.82-1.24)	0.88 (0.71-1.09)	7.51 (4.75-11.9)	5.10 (3.16-8.22)
Stage 4 (15–29)	1.42 (1.21-1.67)	1.41 (1.20-1.66)	2.16 (1.52-3.05)	1.72 (1.18-2.51)	24.0 (13.5-42.6)	11.4 (6.07-21.4)
Comorbidities*						
Heart failure	1.15 (1.09-1.23)	1.16 (1.08-1.23)	4.00 (3.49-4.58)	2.93 (2.51-3.42)	2.90 (1.90-4.42)	2.22 (1.38-3.58)
MI	0.80 (0.75-0.85)	0.77 (0.72-0.82)	2.33 (1.98-2.74)	1.57 (1.32-1.87)	2.12 (1.33-3.39)	1.35 (0.80-2.25)
Hypertension	1.00 (0.97-1.02)	1.05 (1.00-1.11)	0.62 (0.56-0.68)	1.58 (1.36-1.84)	0.60 (0.45-0.80)	1.02 (0.63-1.65)
PAD	1.09 (1.01-1.18)	1.11 (1.02-1.20)	2.10 (1.70-2.60)	1.87 (1.50-2.33)	2.14 (1.18-3.86)	1.53 (0.82-2.88)
Arrhythmia	1.09 (1.03-1.14)	0.98 (0.95-1.01)	2.37 (2.07-2.71)	0.77 (0.69-0.86)	1.41 (0.90-2.21)	0.77 (0.56-1.05)
Diabetes mellitus	0.93 (0.90-0.96)	0.93 (0.90-0.96)	1.09 (0.97-1.22)	1.04 (0.92-1.18)	0.97 (0.69-1.36)	0.90 (0.63-1.29)
Baseline K>5 mmol/L	1.04 (1.00-1.10)	1.04 (0.99-1.09)	1.04 (0.86-1.25)	0.97 (0.80-1.17)	8.22 (6.14-11.0)	6.68 (4.94-9.02)

Abbreviations: CKD, chronic kidney disease; MI, myocardial infarction; PAD, peripheral arterial disease

* The increase was based on the difference between the most recent baseline measurements within 12 months before and first follow-up measurement within 2 months after drug initiation. All analyses were restricted to those with both baseline and follow-up measurements (n=105,859).

† Adjusted for sex, age, CKD, heart failure, MI, hypertension, PAD, arrhythmia, diabetes, and calendar period of prescription start

ONLINE SUPPLEMENTAL MATERIAL

eTable 1. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations, overall and in most recent calendar period (extended version of Table 3)

	Clinical guidelines						All initiators		Continuing users*	
	NICE Heart Failure	NICE CKD	NICE Hypertension	NICE MI	UK Renal Association	GP Notebook	Generous baseline interpretation (≤12 month)	Strict baseline interpretation (≤1 month)	Generous baseline interpretation (≤12 month)	Strict baseline interpretation (≤1 month)
2004-2014							n=223,814 (100%)		n=173,244 (100%)	
Baseline testing	x	x	x	x	x	x	169,218 (76%)	75,476 (34%)	131,756 (76%)	58,668 (34%)
Follow-up test (≤2 weeks)†	x	x	n/a	x	x	x	46,486 (21%)	19,679 (9%)	43,420 (25%)	18,457 (11%)
+ At least within one year after				x			36,424 (16%)	15,642 (7%)	34,356 (20%)	14,800 (9%)
+ 1 month thereafter‡						x	11,866 (5%)	5,643 (3%)	11,398 (7%)	5,388 (3%)
+ 1 and 3 months thereafter ‡						x	5,787 (3%)	2,933 (1%)	5,556 (3%)	2,791 (2%)
+ 1, 3, and 6 months thereafter ‡						x	3,390 (2%)	1,807 (1%)	3,281 (2%)	1,703 (1%)
+ 1, 3, 6, and 12 months thereafter‡						x	2,618 (1%)	1,439 (1%)	2,484 (1%)	1,353 (1%)
Follow-up test (≤3 weeks)§							70,792 (32%)	30,451 (14%)	66,340 (38%)	28,644 (17%)
2009-2014							n=87,623 (100%)		n=68,042 (100%)	
Baseline testing	x	x	x	x	x	x	67,649 (77%)	30,576 (35%)	52,780 (78%)	23,716 (35%)
Follow-up test (≤2 weeks)†	x	x	n/a	x	x	x	20,172 (23%)	8,707 (10%)	18,862 (28%)	8,169 (12%)
+ At least within one year after				x			15,416 (18%)	6,726 (8%)	14,557 (21%)	6,377 (9%)
+ 1 month thereafter‡						x	5,373 (6%)	2,607 (3%)	5,123 (8%)	2,500 (4%)
+ 1 and 3 months thereafter ‡						x	2,614 (3%)	1,365 (2%)	2,492 (4%)	1,302 (2%)
+ 1, 3, and 6 months thereafter ‡						x	1,525 (2%)	841 (1%)	1,457 (2%)	792 (1%)
+ 1, 3, 6, and 12 months thereafter‡						x	1,152 (1%)	650 (1%)	1,089 (2%)	606 (1%)
Follow-up test (≤3 weeks)§							31,007 (35%)	13,511 (15%)	29,091 (43%)	12,726 (19%)

Abbreviations: CKD, chronic kidney disease; GP, General Practice; MI, myocardial infarction; n/a, not specified

* A patient was considered continuous users when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring + 30 days (to allow for stock piling and irregular use)

†Follow-up test among those with baseline measurements

‡Within additional 1, 3, 6, and 12 months after correspond to within 1.5, 3.5, 6.5, and 12.5 months after ACE/ARB initiation, respectively.

§Sensitivity analysis illustrating the importance of 2 vs. 3-week cut-off interval in follow-up test intervals.

eTable 2. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating angiotensin converting-enzyme inhibitors or angiotensin-receptor blockers, overall and most recent calendar period (extended version of Table 1)

	S-Creatinine, ≥1 test, n (%)	
	Total cohort (n=223,814)	2009-2014 cohort (n=87,623)
Baseline testing		
≤12 months before	169,218 (75.6)	67,649 (77.2)
≤3 months before	115,348 (51.5)	46,925 (53.6)
≤1 months before	75,476 (33.7)	30,576 (34.9)
Follow-up testing		
≤2 weeks after	65,090 (29.1)	27,933 (31.9)
≤1 month after	114,244 (51.0)	48,877 (55.8)
≤2 months after	139,044 (62.1)	58,334 (66.6)

eTable 3. Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations

	All initiators n=223,814 (100%)	
	Generous baseline interpretation (≤12 month)	**Strict baseline interpretation** (≤1 month)
Overall (n=223,814)		
Baseline testing	169,218 (76%)	75,476 (34%)
+ Follow-up test ≤2 weeks*	46,486 (21%)	19,679 (9%)
+ Follow-up test ≤3 weeks†	70,792 (32%)	30,451 (14%)
Overall, no recent hospitalization (n=197,291)		
Baseline testing	153,353 (78%)	68,883 (35%)
+ Follow-up test ≤2 weeks*	42,967 (22%)	18,222 (9%)
+ Follow-up test ≤3 weeks†	65,881 (33%)	28,375 (14%)
Heart failure patients (n=10,807)		
Baseline testing	7,853 (73%)	3,277 (30%)
+ Follow-up test ≤2 weeks*	2,229 (21%)	951 (9%)
+ Follow-up test ≤3 weeks†	3,085 (29%)	1,340 (12%)
Myocardial infarction patients (n=16,357)		
Baseline testing	9,273 (57%)	3,766 (23%)
+ Follow-up test ≤2 weeks*	1,816 (11%)	726 (4%)
+ Follow-up test ≤3 weeks†	2,645 (16%)	1,078 (7%)
Hypertension patients (n=162,437)		
Baseline testing	125,219 (77%)	54,174 (33%)
+ Follow-up test ≤2 weeks*	35,502 (22%)	14,559 (9%)
+ Follow-up test ≤3 weeks†	54,585 (34%)	22,710 (14%)
CKD patients (n=31,399)		
Baseline testing	27,961 (89%)	13,913 (44%)
+ Follow-up test ≤2 weeks*	8,457 (27%)	4,198 (13%)
+ Follow-up test ≤3 weeks†	12,482 (40%)	6,324 (20%)
PAD patients (n=5,131)		
Baseline testing	4,137 (81%)	1,671 (33%)
+ Follow-up test ≤2 weeks*	1,198 (23%)	458 (9%)
+ Follow-up test ≤3 weeks†	1,751 (34%)	698 (14%)
Diabetes patients (n=38,525)		
Baseline testing	35,134 (91%)	15,907 (41%)
+ Follow-up test ≤2 weeks*	9,161 (24%)	3,794 (10%)
+ Follow-up test ≤3 weeks†	14,093 (37%)	5,994 (16%)

Abbreviations: CKD, chronic kidney disease

*Follow-up test among those with baseline measurements

† Sensitivity analysis illustrating the importance of 2 vs. 3-week cut-off interval in follow-up test intervals.

eTable 4: Prevalence of baseline and follow-up serum creatinine monitoring among patients initiating renin-angiotensin system blockade according to clinical guideline recommendations, stratified by year of ACEI/ARB initiation, 2004-2014

	All initiators n=223,814		**2004/2005** n=51,529		**2006/2007** n=59,881		**2008/2009** n=47,472		**2010/2011** n=37,183		**2012/2014** n=27,749	
	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)	Wide baseline interval (≤12 month)	Ideal baseline interval (≤1 month)
Baseline testing	169,218 (76%)	75,476 (34%)	36,649 (71%)	14,710 (29%)	45,801 (76%)	21,079 (35%)	36,585 (77%)	17,265 (36%)	28,727 (77%)	13,045 (35%)	21,443 (77%)	9,377 (34%)
+ Follow-up test ≤2 weeks*	46,486 (21%)	19,679 (9%)	8,139 (16%)	2,929 (6%)	12,587 (21%)	5,509 (9%)	10,595 (22%)	4,769 (10%)	8,623 (23%)	3,720 (10%)	6,556 (24%)	2,752 (10%)
+ Follow-up test ≤3 weeks†	70,792 (32%)	30,451 (14%)	12,222 (24%)	4,550 (9%)	19,102 (32%)	8,504 (14%)	16,229 (34%)	7,392 (16%)	13,127 (35%)	5,768 (16%)	10,054 (36%)	4,237 (15%)

*Follow-up test among those with baseline measurements

† Sensitivity analysis illustrating the importance of 2 vs. 3-week cut-off interval in follow-up test intervals.

eTable 5. Proportion of new users of ACEI/ARB who continue or discontinue treatment according to guideline recommended cut-off levels of serum creatinine and potassium at follow-up testing

	Wide monitoring interval (12 month before to the first monitoring within 2 month after)			Narrow monitoring interval (1 month before to the first monitoring within 2 month after)		
	Continuation*	Discontinuation*	Total	Continuation*	Discontinuation*	Total
+ 30 day window						
Total number, %	113,210 (92.5)	9,170 (7.5)	122,380 (100)	48,772 (93.0)	3,676 (7.0)	52,448 (100)
S-creatinine increase ≥30%, n (%)	1,679 (80.7)	401 (19.3)	2,080 (100)	541 (81.5)	123 (18.5)	664 (100)
S-potassium >6 mmol/L, n (%)	472 (81.9)	104 (18.1)	576 (100)	204 (80.6)	49 (19.4)	253 (100)
+ 90 day window						
Total number, %	86,620 (81.8)	19,239 (18.2)	105,859 (100)	37,920 (82.2)	8,200 (17.8)	46,120 (100)
S-creatinine increase ≥30%, n (%)	1,111 (64.7)	605 (35.3)	1,716 (100)	372 (65.6)	195 (34.4)	567 (100)
S-potassium >6 mmol/L, n (%)	261 (61.0)	167 (39.0)	428 (100)	110 (57.6)	81 (42.4)	191 (100)

Calculated from the measurements closest to the first prescription date in the corresponding intervals, i.e., the most recent baseline measurements and the first follow-up measurement.

* A patient was considered continuous users when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring + 30 days or + 90days (to allow for stock piling and irregular use)

eTable 6. Association between patient characteristics and serum creatinine increase ≥30% and follow-up monitoring within 2 weeks following initiation of renin-angiotensin system blockade

	Adjusted odds ratio (95% confidence intervals)					
	Additional adjustment for ethnicity†			Excluding patient with hospitalisation within 30 days†		
Characteristics	**S-creatinine monitoring within 2 weeks**	**S-creatinine increase ≥30%***	**S-potassium >6 mmol/L***	**S-creatinine monitoring within 2 weeks**	**S-creatinine increase ≥30%***	**S-potassium >6 mmol/L***
Female sex	1.04 (1.01-1.08)	1.91 (1.64-2.23)	1.09 (0.70-1.71)	1.06 (1.04-1.09)	1.66 (1.46-1.86)	0.94 (0.69-1.27)
Age (years)						
< 50 years	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
50-59 years	0.97 (0.92-1.02)	0.91 (0.71-1.16)	1.65 (0.77-3.52)	0.99 (0.95-1.03)	0.86 (0.74-1.05)	1.17 (0.70-1.98)
60-69 years	1.04 (0.99-1.10)	0.86 (0.68-1.10)	1.23 (0.57-2.65)	1.07 (1.02-1.11)	1.05 (0.88-1.26)	0.98 (0.58-1.64)
70-79 years	1.22 (1.15-1.30)	1.22 (0.96-1.55)	0.83 (0.36-1.95)	1.19 (1.14-1.24)	1.40 (1.18-1.68)	0.72 (0.41-1.27)
80+ years	1.15 (1.06-1.24)	1.61 (1.21-2.14)	0.58 (0.21-1.58)	1.17 (1.11-1.24)	2.16 (1.76-2.66)	0.71 (0.38-1.33)
CKD stage						
No CKD (≥60)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Stage 3a (45–59)	1.00 (0.94-1.06)	0.51 (0.39-0.66)	1.82 (0.93-3.55)	1.00 (0.96-1.04)	0.58 (0.49-0.70)	2.40 (1.57-3.68)
Stage 3b (30–44)	1.06 (0.95-1.17)	0.99 (0.71-1.39)	5.66 (2.70-11.9)	0.98 (0.92-1.06)	0.92 (0.79-1.07)	5.15 (3.09-8.58)
Stage 4 (15–29)	1.51 (1.17-1.94)	1.65 (0.87-3.12)	15.0 (5.84-38.8)	1.42 (1.20-1.70)	1.86 (1.52-2.31)	12.2 (6.29-23.7)
Comorbidities*						
Heart failure	1.10 (0.99-1.21)	3.07 (2.41-3.91)	2.16 (0.96-4.85)	1.15 (1.06-1.24)	2.57 (2.19-3.03)	2.68 (1.59-4.51)
MI	0.78 (0.72-0.86)	1.76 (1.35-2.30)	1.10 (0.46-2.63)	0.89 (0.82-0.97)	1.59 (1.23-2.06)	1.89 (1.05-3.41)
Hypertension	0.97 (0.90-1.05)	1.51 (1.19-1.92)	1.01 (0.44-2.30)	1.04 (0.99-1.11)	1.40 (1.11-1.68)	0.81 (0.46-1.42)
PAD	1.09 (0.96-1.23)	1.63 (1.13-2.35)	1.52 (0.54-4.29)	1.16 (1.06-1.26)	1.74 (1.33-2.27)	1.75 (0.92-3.32)
Arrhythmia	0.96 (0.92-1.01)	0.84 (0.71-0.99)	0.72 (0.44-1.17)	0.98 (0.94-1.01)	0.80 (0.71-0.91)	0.74 (0.53-1.03)
Diabetes mellitus	0.91 (0.87-0.96)	1.15 (0.96-1.37)	0.58 (0.31-1.09)	0.93 (0.90-0.96)	1.06 (0.93-1.22)	0.93 (0.64-1.35)
Baseline K>6 mmol/L	1.05 (0.98-1.13)	0.86 (0.63-1.15)	7.98 (5.06-12.6)	1.03 (0.98-1.08)	1.01 (0.88-1.14)	6.44 (4.69-8.84)

Abbreviations: CKD, chronic kidney disease; MI, myocardial infarction; PAD, peripheral arterial disease

* The increase was based on the difference between the most recent baseline measurements within 12 months before and first follow-up measurement within 2 months after drug initiation. All analyses were restricted to those with both baseline and follow-up measurements (n=105,859).

† The main model was adjusted for sex, age, CKD, heart failure, MI, hypertension, PAD, arrhythmia, diabetes, and calendar period of prescription start

Appendix: Code list

Serum creatinine

Code	Classification	Description
4....00	Read	laboratory procedures
41...00	Read	laboratory procedures -general
4....11	Read	investigation-laboratory
4....12	Read	test - laboratory
412..00	Read	laboratory procedure performed
413..00	Read	laboratory test requested
41B..00	Read	laboratory test due
41BZ.00	Read	laboratory test nos due
41G..00	Read	laboratory administration procedures
41G3.00	Read	specimen received in laboratory
41H..00	Read	review of patient laboratory test report
44J..00	Read	blood urea/renal function
44J3.00	Read	serum creatinine
44J3000	Read	serum creatinine abnormal
44J3100	Read	serum creatinine low
44J3200	Read	serum creatinine normal
44J3300	Read	serum creatinine raised
44J3z00	Read	serum creatinine nos
44JC.00	Read	corrected plasma creatinine level
44JD.00	Read	corrected serum creatinine level
44JF.00	Read	plasma creatinine level
44JZ.00	Read	blood urea/renal function nos
451..00	Read	renal function tests
4511	Read	renal function tests normal
4512	Read	renal function tests abnormal
4515	Read	differential renal function
4516	Read	renal function tests borderline
4519	Read	deteriorating renal function
451H.00	Read	recovery of renal function
451Z.00	Read	renal function test nos
4Q40.00	Read	creatinine level
4Z...00	Read	laboratory procedure nos
8A6..00	Read	renal function monitoring
8H7P.11	Read	refer to pathology laboratory
8HP..00	Read	referral for laboratory tests
98F..00	Read	reason for repeat laboratory test
9b0P.00	Read	laboratory request
9b0Q.00	Read	laboratory result
9mG..00	Read	renal function monitoring invitation
9mG0.00	Read	renal function monitoring invitation first letter
9N1Q.00	Read	seen in diabetic clinic

C345.00	Read	gout due to impairment of renal function
K060.11	Read	impaired renal function
K08..00	Read	impaired renal function disorder
K08y.00	Read	other impaired renal function disorder
K08y300	Read	renal function impairment with growth failure
K08yz00	Read	other impaired renal function disorder nos
K08z.00	Read	impaired renal function disorder nos
R144.00	Read	[d]renal function test abnormal
R1yz.11	Read	[d]unexplained laboratory result
ZV72600	Read	[v]laboratory examination

Serum potassium

Code	Classification	Description
44I4.00	Read	serum potassium
4....12	Read	test - laboratory
4Z...00	Read	laboratory procedure nos
451..00	Read	renal function tests
C368.00	Read	hypokalaemia
412..00	Read	laboratory procedure performed
4512.00	Read	renal function tests abnormal
4511.00	Read	renal function tests normal
8A6..00	Read	renal function monitoring
C367.00	Read	hyperkalaemia
K060.11	Read	impaired renal function
4....11	Read	investigation-laboratory
K08..00	Read	impaired renal function disorder
R144.00	Read	[d]renal function test abnormal
8HP..00	Read	referral for laboratory tests
4....00	Read	laboratory procedures
44J..00	Read	blood urea/renal function
44h8.00	Read	plasma potassium level
44h0.00	Read	blood potassium level
4I46.00	Read	sweat potassium level
413..00	Read	laboratory test requested
C345.00	Read	gout due to impairment of renal function
41...00	Read	laboratory procedures -general
41B..00	Read	laboratory test due
411..00	Read	laboratory test not necessary
4516.00	Read	renal function tests borderline
K08z.00	Read	impaired renal function disorder nos
4519.00	Read	deteriorating renal function
44I4200	Read	low serum potassium level
44I4000	Read	normal serum potassium level
44I4100	Read	raised serum potassium level
44JZ.00	Read	blood urea/renal function nos

1F34.00	Read	dietary potassium - low
1F3..11	Read	dietary potassium intake
41BZ.00	Read	laboratory test nos due
ZC61c00	Read	potassium supplementation
ZV72600	Read	[v]laboratory examination
451Z.00	Read	renal function test nos
K08y.00	Read	other impaired renal function disorder
4Q42.00	Read	potassium level
R1yz.11	Read	[d]unexplained laboratory result
ZC28.00	Read	advice to change potassium intake
4I34.11	Read	potassium in sample
9b0Q.00	Read	laboratory result
K08yz00	Read	other impaired renal function disorder nos
4515.00	Read	differential renal function
1F36.00	Read	dietary potassium - high
4I34.00	Read	fluid sample potassium
1F35.00	Read	dietary potassium - average
5714.00	Read	potassium 40 whole body count
41G..00	Read	laboratory administration procedures
41H..00	Read	review of patient laboratory test report
9b0P.00	Read	laboratory request
8B77.00	Read	potassium supplementation
451H.00	Read	recovery of renal function
9mG..00	Read	renal function monitoring invitation
98F..00	Read	reason for repeat laboratory test
13BD.00	Read	low potassium diet
9mG0.00	Read	renal function monitoring invitation first letter
41G3.00	Read	specimen received in laboratory
4IA5.00	Read	unsatisfactory laboratory analysis

End stage renal disease

Code	Classification	Description
14S2.00	Read	h/o: kidney recipient
14V2.00	Read	h/o: renal dialysis
14V2.11	Read	h/o: kidney dialysis
1Z14.00	Read	chronic kidney disease stage 5
1Z1K.00	Read	chronic kidney disease stage 5 with proteinuria
1Z1K.11	Read	ckd stage 5 with proteinuria
1Z1L.00	Read	chronic kidney disease stage 5 without proteinuria
1Z1L.11	Read	ckd stage 5 without proteinuria
4I29.00	Read	peritoneal dialysis sample
4N0..00	Read	dialysis fluid urea level
4N2..00	Read	dialysis fluid glucose level
67P4100	Read	discussion about kidney transplantation
7A60.00	Read	arteriovenous shunt

7A60000	Read	insertion of arteriovenous prosthesis
7A60100	Read	creation of arteriovenous fistula nec
7A60111	Read	creation of radial-cephalic fistula
7A60112	Read	creation of brachial-cephalic fistula
7A60200	Read	attention to arteriovenous shunt
7A60300	Read	removal of infected arteriovenous shunt
7A60400	Read	banding of arteriovenous fistula
7A60500	Read	thrombectomy of arteriovenous fistula
7A60600	Read	creation of graft fistula for dialysis
7A60y00	Read	other specified arteriovenous shunt
7A60z00	Read	arteriovenous shunt nos
7A61100	Read	repair of acquired arteriovenous fistula
7A61111	Read	ligation of acquired arteriovenous fistula
7A61400	Read	ligation of acquired arteriovenous fistula
7A61900	Read	ligation of arteriovenous dialysis fistula
7A61A00	Read	ligation of arteriovenous dialysis graft
7B00.00	Read	transplantation of kidney
7B00100	Read	transplantation of kidney from live donor
7B00111	Read	allotransplantation of kidney from live donor
7B00200	Read	transplantation of kidney from cadaver
7B00211	Read	allotransplantation of kidney from cadaver
7B00212	Read	cadaveric renal transplant
7B00300	Read	allotransplantation of kidney from cadaver heart-beating
7B00400	Read	allotransplantation kidney from cadaver heart non-beating
7B00600	Read	xenograft renal transplant
7B00y00	Read	other specified transplantation of kidney
7B00z00	Read	transplantation of kidney nos
7B01500	Read	transplant nephrectomy
7B01511	Read	excision of rejected transplanted kidney
7B06300	Read	exploration of renal transplant
7B0F.00	Read	interventions associated with transplantation of kidney
7B0F100	Read	pre-transplantation of kidney work-up
7B0F300	Read	post-transplantation of kidney examination
7B0Fy00	Read	os interventions associated with transplantation of kidney
7B0Fz00	Read	interventions associated with transplantation of kidney nos
7L1A.00	Read	compensation for renal failure
7L1A000	Read	renal dialysis
7L1A011	Read	thomas intravascular shunt for dialysis
7L1A100	Read	peritoneal dialysis
7L1A.11	Read	dialysis for renal failure
7L1A200	Read	haemodialysis nec
7L1A300	Read	haemofiltration
7L1A400	Read	automated peritoneal dialysis
7L1A500	Read	continuous ambulatory peritoneal dialysis
7L1A600	Read	peritoneal dialysis nec

7L1Ay00	Read	other specified compensation for renal failure
7L1Az00	Read	compensation for renal failure nos
7L1B.00	Read	placement ambulatory apparatus compensation renal failure
7L1B000	Read	insertion of ambulatory peritoneal dialysis catheter
7L1B100	Read	removal of ambulatory peritoneal dialysis catheter
7L1B.11	Read	placement ambulatory dialysis apparatus - compens renal fail
7L1B200	Read	flushing of peritoneal dialysis catheter
7L1By00	Read	placement ambulatory apparatus- compensate renal failure os
7L1C.00	Read	placement other apparatus for compensation for renal failure
7L1C000	Read	insertion of temporary peritoneal dialysis catheter
7L1Cy00	Read	placement other apparatus- compensate for renal failure os
7L1Cz00	Read	placement other apparatus- compensate for renal failure nos
8L50.00	Read	renal transplant planned
9b8K.00	Read	transplantation surgery
9Ot5.00	Read	predicted stage chronic kidney disease
G72C.00	Read	ruptured aneurysm of dialysis vascular access
G72D.00	Read	aneurysm of dialysis arteriovenous fistula
G72D100	Read	aneurysm of needle site of dialysis arteriovenous fistula
G72D200	Read	aneurysm of anastomotic site of dialysis av fistula
G760.00	Read	acquired arteriovenous fistula
Gy1..00	Read	stenosis of dialysis vascular access
Gy21.00	Read	thrombosis of dialysis arteriovenous fistula
Gy3..00	Read	occlusion of dialysis vascular access
Gy31.00	Read	occlusion of dialysis arteriovenous fistula
Gy40.00	Read	infection of dialysis arteriovenous graft
Gy41.00	Read	infection of dialysis arteriovenous fistula
Gy51.00	Read	haemorrhage of dialysis arteriovenous fistula
Gy60.00	Read	rupture of dialysis arteriovenous graft
K050.00	Read	end stage renal failure
K05..12	Read	end stage renal failure
K055.00	Read	chronic kidney disease stage 5
K0B5.00	Read	renal tubulo-interstitial disordrs in transplant rejectn
K0D..00	Read	end-stage renal disease
Kyu1C00	Read	[x]renal tubulo-interstitial disorders/transplant rejection
SP01500	Read	mechanical complication of dialysis catheter
SP01700	Read	mechanical complication of arterio-venous surgical fistula
SP05613	Read	[x] peritoneal dialysis associated peritonitis
SP06B00	Read	continuous ambulatory peritoneal dialysis associated perit
SP07G00	Read	stenosis of arteriovenous dialysis fistula
SP07N00	Read	arteriovenous fistula thrombosis
SP08011	Read	det.ren.func.after ren.transpl
SP08300	Read	kidney transplant failure and rejection
SP08J00	Read	chronic rejection of renal transplant
SP08N00	Read	unexplained episode of renal transplant dysfunction
SP08R00	Read	renal transplant rejection

SP08T00	Read	urological complication of renal transplant
SP08W00	Read	vascular complication of renal transplant
SP0E.00	Read	disorders associated with peritoneal dialysis
SP0G.00	Read	anaphylactoid reaction due to haemodialysis
TA02000	Read	accid cut
TA22.00	Read	failure of sterile precautions during perfusion
TA22000	Read	failure of sterile precautions during kidney dialysis
TB00100	Read	kidney transplant with complication
TB00111	Read	renal transplant with complication
TB11.00	Read	kidney dialysis with complication
TB11.11	Read	renal dialysis with complication
U612200	Read	[x]failure sterile precautions dur kidney dialys/other perf
Z1A..00	Read	dialysis training
Z1A1.00	Read	peritoneal dialysis training
Z1A2.00	Read	haemodialysis training
Z919.00	Read	care of haemodialysis equipment
Z919100	Read	priming haemodialysis lines
Z919300	Read	reversing haemodialysis lines
Z91A.00	Read	peritoneal dialysis bag procedure
ZV42000	Read	[v]kidney transplanted
ZV45100	Read	[v]renal dialysis status
ZV56.00	Read	[v]aftercare involving intermittent dialysis
ZV56000	Read	[v]aftercare involving extracorporeal dialysis
ZV56011	Read	[v]aftercare involving renal dialysis nos
ZV56100	Read	[v]preparatory care for dialysis
ZV56y00	Read	[v]other specified aftercare involving intermittent dialysis
ZV56y11	Read	[v]aftercare involving peritoneal dialysis
ZVu3G00	Read	[x]other dialysis
I77.0	ICD-10	arteriovenous fistula
N16.5	ICD-10	renal tubulo-interstitial disorders in transplant rejection
N18.5	ICD-10	chronic kidney disease
T82.4	ICD-10	mechanical complication of vascular dialysis catheter
T86.1	ICD-10	kidney transplant failure and rejection
Y60.2	ICD-10	during kidney dialysis or other perfusion
Y61.2	ICD-10	during kidney dialysis or other perfusion
Y62.2	ICD-10	during kidney dialysis or other perfusion
Y84.1	ICD-10	kidney dialysis
Z49	ICD-10	care involving dialysis
Z49.0	ICD-10	preparatory care for dialysis
Z49.1	ICD-10	extracorporeal dialysis
Z49.2	ICD-10	other dialysis
Z94.0	ICD-10	kidney transplant status
Z99.2	ICD-10	dependence on renal dialysis

Ischemic heart disease

Code	Classification	Description
14A3.00	Read	h/o: myocardial infarct <60
14A4.00	Read	h/o: myocardial infarct >60
14A5.00	Read	h/o: angina pectoris
14AA.00	Read	h/o: heart disease nos
14AH.00	Read	h/o: myocardial infarction in last year
14AJ.00	Read	h/o: angina in last year
14AL.00	Read	h/o: treatment for ischaemic heart disease
14AT.00	Read	history of myocardial infarction
14AW.00	Read	h/o acute coronary syndrome
182A.00	Read	Chest pain on exertion
187..00	Read	frequency of angina
1J61.00	Read	suspected ischaemic heart disease
3213111	Read	Positive exercise ECG test
322..00	Read	ecg: myocardial ischaemia
3222	Read	ecg:shows myocardial ischaemia
322Z.00	Read	ecg: myocardial ischaemia nos
323..00	Read	ecg: myocardial infarction
3232	Read	ecg: old myocardial infarction
3233	Read	ecg: antero-septal infarct.
3234	Read	ecg:posterior/inferior infarct
3235	Read	ecg: subendocardial infarct
3236	Read	ecg: lateral infarction
323Z.00	Read	ecg: myocardial infarct nos
32B..00	Read	ecg: q wave
32B2.00	Read	ecg: q wave abnormal
32B3.00	Read	ecg: q wave pathological
32BZ.00	Read	ecg: q wave nos
32E4.00	Read	ecg: s-t depression
44H3.00	Read	cardiac enzymes abnormal
44H3000	Read	cardiac enzymes abnormal - first set
44HJ.00	Read	Plasma creatinine phosphokinase MB isoenzyme level
44MH.00	Read	Plasma troponin T level
44p2.00	Read	cardiac troponin positive
5533	Read	angiocardiography abnormal
5543	Read	coronary arteriograph.abnormal
5C11.00	Read	radionuclide heart study abnormal
661M000	Read	angina self-management plan agreed
662..00	Read	Cardiac disease monitoring
662..11	Read	Heart disease monitoring
662K.00	Read	angina control
662K000	Read	angina control - good
662K100	Read	angina control - poor
662K200	Read	angina control - improving
662K300	Read	angina control - worsening

662Kz00	Read	angina control nos
662N.00	Read	CHD monitoring
662Z.00	Read	Cardiac disease monitoring NOS
66f..00	Read	Cardiovascular disease monitoring
66f1.00	Read	Cardiovascular disease interim monitoring
6A2..00	Read	coronary heart disease annual review
6A4..00	Read	coronary heart disease review
7920	Read	saphenous vein graft replacement of coronary artery
7920000	Read	saphenous vein graft replacement of one coronary artery
7920100	Read	saphenous vein graft replacement of two coronary arteries
7920.11.00	Read	saphenous vein graft bypass of coronary artery
7920200	Read	saphenous vein graft replacement of three coronary arteries
7920300	Read	saphenous vein graft replacement of four+ coronary arteries
7920y00	Read	saphenous vein graft replacement of coronary artery os
7920z00	Read	saphenous vein graft replacement coronary artery nos
7921	Read	other autograft replacement of coronary artery
7921000	Read	autograft replacement of one coronary artery nec
792..11	Read	coronary artery bypass graft operations
7921100	Read	autograft replacement of two coronary arteries nec
7921.11.00	Read	other autograft bypass of coronary artery
7921200	Read	autograft replacement of three coronary arteries nec
7921300	Read	autograft replacement of four of more coronary arteries nec
7921y00	Read	other autograft replacement of coronary artery os
7921z00	Read	other autograft replacement of coronary artery nos
7922	Read	allograft replacement of coronary artery
7922000	Read	allograft replacement of one coronary artery
7922100	Read	allograft replacement of two coronary arteries
7922.11.00	Read	allograft bypass of coronary artery
7922200	Read	allograft replacement of three coronary arteries
7922300	Read	allograft replacement of four or more coronary arteries
7922y00	Read	other specified allograft replacement of coronary artery
7922z00	Read	allograft replacement of coronary artery nos
7923	Read	prosthetic replacement of coronary artery
7923000	Read	prosthetic replacement of one coronary artery
7923100	Read	prosthetic replacement of two coronary arteries
7923.11.00	Read	prosthetic bypass of coronary artery
7923200	Read	prosthetic replacement of three coronary arteries
7923300	Read	prosthetic replacement of four or more coronary arteries
7923z00	Read	prosthetic replacement of coronary artery nos
7924	Read	revision of bypass for coronary artery
7924000	Read	revision of bypass for one coronary artery
7924100	Read	revision of bypass for two coronary arteries
7924200	Read	revision of bypass for three coronary arteries
7924y00	Read	other specified revision of bypass for coronary artery
7924z00	Read	revision of bypass for coronary artery nos

7925	Read	connection of mammary artery to coronary artery
7925000	Read	double anastomosis of mammary arteries to coronary arteries
7925100	Read	double implant of mammary arteries into coronary arteries
7925.11.00	Read	creation of bypass from mammary artery to coronary artery
7925300	Read	single anastomosis of mammary artery to coronary artery nec
7925311	Read	lima single anastomosis
7925312	Read	rima single anastomosis
7925400	Read	single implantation of mammary artery into coronary artery
7925y00	Read	connection of mammary artery to coronary artery os
7925z00	Read	connection of mammary artery to coronary artery nos
7926	Read	connection of other thoracic artery to coronary artery
7926000	Read	double anastom thoracic arteries to coronary arteries nec
7926200	Read	single anastomosis of thoracic artery to coronary artery nec
7926300	Read	single implantation thoracic artery into coronary artery nec
7926z00	Read	connection of other thoracic artery to coronary artery nos
7927500	Read	open angioplasty of coronary artery
7928	Read	transluminal balloon angioplasty of coronary artery
7928000	Read	percut transluminal balloon angioplasty one coronary artery
7928100	Read	percut translum balloon angioplasty mult coronary arteries
7928.11.00	Read	percutaneous balloon coronary angioplasty
7928200	Read	percut translum balloon angioplasty bypass graft coronary a
7928300	Read	percut translum cutting balloon angioplasty coronary artery
7928y00	Read	transluminal balloon angioplasty of coronary artery os
7928z00	Read	transluminal balloon angioplasty of coronary artery nos
7929000	Read	percutaneous transluminal laser coronary angioplasty
7929100	Read	percut transluminal coronary thrombolysis with streptokinase
7929111	Read	percut translum coronary thrombolytic therapy- streptokinase
7929300	Read	rotary blade coronary angioplasty
7929400	Read	insertion of coronary artery stent
7929500	Read	insertion of drug-eluting coronary artery stent
7929600	Read	percutaneous transluminal atherectomy of coronary artery
792B000	Read	endarterectomy of coronary artery nec
792C.00	Read	other replacement of coronary artery
792C000	Read	replacement of coronary arteries using multiple methods
792Cy00	Read	other specified replacement of coronary artery
792Cz00	Read	replacement of coronary artery nos
792D.00	Read	other bypass of coronary artery
792Dy00	Read	other specified other bypass of coronary artery
792Dz00	Read	other bypass of coronary artery nos
793G.00	Read	perc translumin balloon angioplasty stenting coronary artery
793G000	Read	perc translum ball angio insert 1-2 drug elut stents cor art
793G100	Read	perc tran ball angio ins 3 or more drug elut stents cor art
793G200	Read	perc translum balloon angioplasty insert 1-2 stents cor art
793G300	Read	percutaneous cor balloon angiop 3 more stents cor art nec
793Gy00	Read	os perc translumina balloon angioplast stenting coronary art

793Gz00	Read	perc translum balloon angioplasty stenting coronary art nos
7A4B800	Read	percut translum thrombolysis femoral graft streptokinase
7A54000	Read	percutaneous transluminal angioplasty of artery nec
7A54500	Read	rotary blade angioplasty
7A54700	Read	percutaneous transluminal thrombolysis of artery
7A54800	Read	percutaneous transluminal atherectomy
7A56000	Read	percutaneous transluminal arterial thrombolysis reconstruct
7A56400	Read	percutaneous transluminal balloon angioplasty of artery
7A6G100	Read	peroperative angioplasty
7A6H300	Read	prosthetic graft patch angioplasty
7A6H400	Read	percutaneous transluminal angioplasty of vascular graft
7A6S300	Read	percutaneous transluminal venous thrombolysis nec
889A.00	Read	diab mellit insulin-glucose infus acute myocardial infarct
8B27.00	Read	antianginal therapy
8B3k.00	Read	coronary heart disease medication review
8BGC.00	Read	long term dual antiplatelet drug therapy indicated
8CMP.00	Read	coronary heart disease care plan
8F9..00	Read	Cardiac rehabilitation
8F90.00	Read	Cardiac rehabilitation - phase 1
8F91.00	Read	Cardiac rehabilitation - phase 2
8F92.00	Read	Cardiac rehabilitation - phase 3
8F93.00	Read	Cardiac rehabilitation - phase 4
8H2V.00	Read	admit ischaemic heart disease emergency
8H7v.00	Read	Referral to cardiac rehabilitation nurse
8I37.00	Read	Coronary heart disease monitoring refused
8I3a.00	Read	Cardiac rehabilitation declined
8IEY.00	Read	referral to angina plan self-management programme declined
8L40.00	Read	coronary artery bypass graft operation planned
8L41.00	Read	coronary angioplasty planned
8LF..00	Read	coronary angiography planned
8T04.00	Read	referral to angina plan self-management programme
9Ob..00	Read	Coronary heart disease monitoring administration
9Ob0.00	Read	Attends coronary heart disease monitoring
9Ob1.00	Read	Refuses coronary heart disease monitoring
9Ob2.00	Read	Coronary heart disease monitoring default
9Ob3.00	Read	Coronary heart disease monitoring 1st letter
9Ob4.00	Read	Coronary heart disease monitoring 2nd letter
9Ob5.00	Read	Coronary heart disease monitoring 3rd letter
9Ob6.00	Read	Coronary heart disease monitoring verbal invitation
9Ob8.00	Read	Coronary heart disease monitoring check done
9Ob9.00	Read	Coronary heart disease monitoring telephone invite
G....12	Read	Cardiac diseases
G....13	Read	Heart diseases
G3...00	Read	ischaemic heart disease
G30..00	Read	acute myocardial infarction

G300.00	Read	acute anterolateral infarction
G301.00	Read	other specified anterior myocardial infarction
G301000	Read	acute anteroapical infarction
G30..11	Read	attack - heart
G301100	Read	acute anteroseptal infarction
G30..12	Read	coronary thrombosis
G30..13	Read	cardiac rupture following myocardial infarction (mi)
G30..14	Read	heart attack
G30..15	Read	mi - acute myocardial infarction
G30..16	Read	thrombosis - coronary
G30..17	Read	silent myocardial infarction
G301z00	Read	anterior myocardial infarction nos
G302.00	Read	acute inferolateral infarction
G303.00	Read	acute inferoposterior infarction
G304.00	Read	posterior myocardial infarction nos
G305.00	Read	lateral myocardial infarction nos
G306.00	Read	true posterior myocardial infarction
G307.00	Read	acute subendocardial infarction
G307000	Read	acute non-q wave infarction
G307100	Read	acute non-st segment elevation myocardial infarction
G308.00	Read	inferior myocardial infarction nos
G309.00	Read	acute q-wave infarct
G30A.00	Read	mural thrombosis
G30B.00	Read	acute posterolateral myocardial infarction
G30X.00	Read	acute transmural myocardial infarction of unspecif site
G30X000	Read	acute st segment elevation myocardial infarction
G30y.00	Read	other acute myocardial infarction
G30y000	Read	acute atrial infarction
G30y100	Read	acute papillary muscle infarction
G30y200	Read	acute septal infarction
G30yz00	Read	other acute myocardial infarction nos
G30z.00	Read	acute myocardial infarction nos
G31..00	Read	other acute and subacute ischaemic heart disease
G310.00	Read	postmyocardial infarction syndrome
G310.11	Read	dressler's syndrome
G3...11	Read	arteriosclerotic heart disease
G311.00	Read	preinfarction syndrome
G311000	Read	myocardial infarction aborted
G311011	Read	mi - myocardial infarction aborted
G311100	Read	unstable angina
G311.11	Read	crescendo angina
G311.12	Read	impending infarction
G311.13	Read	unstable angina
G311.14	Read	angina at rest
G311200	Read	angina at rest

G311300	Read	refractory angina
G311400	Read	worsening angina
G311500	Read	acute coronary syndrome
G311z00	Read	preinfarction syndrome nos
G3...12	Read	atherosclerotic heart disease
G312.00	Read	coronary thrombosis not resulting in myocardial infarction
G3...13	Read	ihd - ischaemic heart disease
G31y.00	Read	other acute and subacute ischaemic heart disease
G31y000	Read	acute coronary insufficiency
G31y100	Read	microinfarction of heart
G31y200	Read	subendocardial ischaemia
G31y300	Read	transient myocardial ischaemia
G31yz00	Read	other acute and subacute ischaemic heart disease nos
G32..00	Read	old myocardial infarction
G32..11	Read	healed myocardial infarction
G32..12	Read	personal history of myocardial infarction
G33..00	Read	angina pectoris
G330.00	Read	angina decubitus
G330000	Read	nocturnal angina
G330z00	Read	angina decubitus nos
G331.11	Read	variant angina pectoris
G332.00	Read	coronary artery spasm
G33z.00	Read	angina pectoris nos
G33z000	Read	status anginosus
G33z100	Read	stenocardia
G33z200	Read	syncope anginosa
G33z300	Read	angina on effort
G33z400	Read	ischaemic chest pain
G33z500	Read	post infarct angina
G33z600	Read	new onset angina
G33z700	Read	stable angina
G33zz00	Read	angina pectoris nos
G34..00	Read	other chronic ischaemic heart disease
G340.00	Read	coronary atherosclerosis
G340000	Read	single coronary vessel disease
G340100	Read	double coronary vessel disease
G340.11	Read	triple vessel disease of the heart
G340.12	Read	coronary artery disease
G341.00	Read	Aneurysm of heart
G341000	Read	Ventricular cardiac aneurysm
G341100	Read	Other cardiac wall aneurysm
G341.11	Read	Cardiac aneurysm
G341z00	Read	Aneurysm of heart NOS
G342.00	Read	atherosclerotic cardiovascular disease
G343.00	Read	Ischaemic cardiomyopathy

G344.00	Read	silent myocardial ischaemia
G34y.00	Read	other specified chronic ischaemic heart disease
G34y000	Read	chronic coronary insufficiency
G34y100	Read	chronic myocardial ischaemia
G34yz00	Read	other specified chronic ischaemic heart disease nos
G34z.00	Read	other chronic ischaemic heart disease nos
G34z000	Read	asymptomatic coronary heart disease
G35..00	Read	subsequent myocardial infarction
G350.00	Read	subsequent myocardial infarction of anterior wall
G351.00	Read	subsequent myocardial infarction of inferior wall
G353.00	Read	subsequent myocardial infarction of other sites
G35X.00	Read	subsequent myocardial infarction of unspecified site
G36..00	Read	certain current complication follow acute myocardial infarct
G360.00	Read	haemopericardium/current comp folow acut myocard infarct
G361.00	Read	atrial septal defect/curr comp folow acut myocardal infarct
G362.00	Read	ventric septal defect/curr comp fol acut myocardal infarctn
G363.00	Read	ruptur cardiac wall w'out haemopericard/cur comp fol ac mi
G364.00	Read	ruptur chordae tendinae/curr comp fol acute myocard infarct
G365.00	Read	rupture papillary muscle/curr comp fol acute myocard infarct
G366.00	Read	thrombosis atrium
G38..00	Read	postoperative myocardial infarction
G380.00	Read	postoperative transmural myocardial infarction anterior wall
G381.00	Read	postoperative transmural myocardial infarction inferior wall
G383.00	Read	postoperative transmural myocardial infarction unspec site
G384.00	Read	postoperative subendocardial myocardial infarction
G38z.00	Read	postoperative myocardial infarction
G39..00	Read	coronary microvascular disease
G3y..00	Read	other specified ischaemic heart disease
G3z..00	Read	ischaemic heart disease nos
G5...00	Read	other forms of heart disease
G501.00	Read	post infarction pericarditis
G574000	Read	Ventricular fibrillation
G5y..00	Read	other specified heart disease
G5yyz00	Read	Other ill-defined heart disease NOS
G5yz.00	Read	other heart disease nos
G5z..00	Read	heart disease nos
Gyu3.00	Read	[x]ischaemic heart diseases
Gyu3000	Read	[x]other forms of angina pectoris
Gyu3200	Read	[x]other forms of acute ischaemic heart disease
Gyu3300	Read	[x]other forms of chronic ischaemic heart disease
Gyu3400	Read	[x]acute transmural myocardial infarction of unspecif site
Gyu3600	Read	[x]subsequent myocardial infarction of unspecified site
Gyu5.00	Read	[x]other forms of heart disease
Gyu7000	Read	[x]atherosclerosis of other arteries
SP00300	Read	mechanical complication of coronary bypass

SP07600	Read	coronary artery bypass graft occlusion
Z677.00	Read	Cardiac rehabilitation class
ZL22200	Read	Under care of cardiac rehabilitation nurse
ZV45700	Read	[v]presence of aortocoronary bypass graft
ZV45800	Read	[v]presence of coronary angioplasty implant and graft
ZV45K00	Read	[v]presence of coronary artery bypass graft
ZV45K11	Read	[v]presence of coronary artery bypass graft - cabg
ZV45L00	Read	[v]status following coronary angioplasty nos
ZV57900	Read	[V]Cardiac rehabilitation
I20	ICD-10	angina pectoris
I20.0	ICD-10	unstable angina
I20.1	ICD-10	angina pectoris with documented spasm
I20.8	ICD-10	other forms of angina pectoris
I20.9	ICD-10	angina pectoris
I21	ICD-10	acute myocardial infarction
I21.0	ICD-10	acute transmural myocardial infarction of anterior wall
I21.1	ICD-10	acute transmural myocardial infarction of inferior wall
I21.2	ICD-10	acute transmural myocardial infarction of other sites
I21.3	ICD-10	acute transmural myocardial infarction of unspecified site
I21.4	ICD-10	acute subendocardial myocardial infarction
I21.9	ICD-10	acute myocardial infarction
I22	ICD-10	subsequent myocardial infarction
I22.0	ICD-10	subsequent myocardial infarction of anterior wall
I22.1	ICD-10	subsequent myocardial infarction of inferior wall
I22.8	ICD-10	subsequent myocardial infarction of other sites
I22.9	ICD-10	subsequent myocardial infarction of unspecified site
I23	ICD-10	certain current complications following acute myocardial infarction
I23.0	ICD-10	haemopericardium as current complication following acute myocardial infarction
I23.1	ICD-10	atrial septal defect as current complication following acute myocardial infarction
I23.2	ICD-10	ventricular septal defect as current complication following acute myocardial infarction
I23.3	ICD-10	rupture of cardiac wall without haemopericardium as current complication following acute myocardial
I23.4	ICD-10	rupture of chordae tendineae as current complication following acute myocardial infarction
I23.5	ICD-10	rupture of papillary muscle as current complication following acute myocardial infarction
I23.6	ICD-10	thrombosis of atrium
I23.8	ICD-10	other current complications following acute myocardial infarction
I24	ICD-10	other acute ischaemic heart diseases
I24.0	ICD-10	coronary thrombosis not resulting in myocardial infarction
I24.1	ICD-10	dressler's syndrome
I24.8	ICD-10	other forms of acute ischaemic heart disease
I24.9	ICD-10	acute ischaemic heart disease
I25	ICD-10	chronic ischaemic heart disease
I25.0	ICD-10	atherosclerotic cardiovascular disease
I25.1	ICD-10	atherosclerotic heart disease
I25.2	ICD-10	old myocardial infarction
I25.5	ICD-10	ischaemic cardiomyopathy

I25.6	ICD-10	silent myocardial ischaemia
I25.8	ICD-10	other forms of chronic ischaemic heart disease
I25.9	ICD-10	chronic ischaemic heart disease
T82.2	ICD-10	mechanical complication of coronary artery bypass and valve grafts
Z95.5	ICD-10	presence of coronary angioplasty implant and graft

Heart failure

Code	Classification	Description
14A6.00	Read	h/o: heart failure
14AM.00	Read	h/o: heart failure in last year
1736	Read	paroxysmal nocturnal dyspnoea
1J60.00	Read	suspected heart failure
1O1..00	Read	heart failure confirmed
388D.00	Read	new york heart assoc classification heart failure symptoms
585f.00	Read	echocardiogram shows left ventricular systolic dysfunction
585g.00	Read	echocardiogram shows left ventricular diastolic dysfunction
661M500	Read	heart failure self-management plan agreed
662f.00	Read	new york heart association classification - class i
662g.00	Read	new york heart association classification - class ii
662h.00	Read	new york heart association classification - class iii
662i.00	Read	new york heart association classification - class iv
662p.00	Read	heart failure 6 month review
662T.00	Read	congestive heart failure monitoring
662W.00	Read	heart failure annual review
679W100	Read	education about deteriorating heart failure
679X.00	Read	heart failure education
67D4.00	Read	heart failure information given to patient
8B29.00	Read	cardiac failure therapy
8CeC.00	Read	preferred place of care for next exacerbation heart failure
8CL3.00	Read	heart failure care plan discussed with patient
8CMK.00	Read	has heart failure management plan
8CMW800	Read	heart failure clinical pathway
8H2S.00	Read	admit heart failure emergency
8HBE.00	Read	heart failure follow-up
8Hg8.00	Read	discharge from practice nurse heart failure clinic
8HgD.00	Read	discharge from heart failure nurse service
8HHb.00	Read	referral to heart failure nurse
8HHz.00	Read	referral to heart failure exercise programme
8Hk0.00	Read	referred to heart failure education group
8HTL.00	Read	referral to heart failure clinic
8HTL000	Read	referral to rapid access heart failure clinic
8IE0.00	Read	referral to heart failure education group declined
8IE1.00	Read	referral to heart failure exercise programme declined
9h1..00	Read	exception reporting: lvd quality indicators

9h11.00	Read	excepted from lvd quality indicators: patient unsuitable
9h12.00	Read	excepted from lvd quality indicators: informed dissent
9hH..00	Read	exception reporting: heart failure quality indicators
9hH0.00	Read	excepted heart failure quality indicators: patient unsuitabl
9hH1.00	Read	excepted heart failure quality indicators: informed dissent
9N0k.00	Read	seen in heart failure clinic
9N2p.00	Read	seen by community heart failure nurse
9N4s.00	Read	did not attend practice nurse heart failure clinic
9N4w.00	Read	did not attend heart failure clinic
9N6T.00	Read	referred by heart failure nurse specialist
9On..00	Read	left ventricular dysfunction monitoring administration
9On0.00	Read	left ventricular dysfunction monitoring first letter
9On1.00	Read	left ventricular dysfunction monitoring second letter
9On2.00	Read	left ventricular dysfunction monitoring third letter
9On3.00	Read	left ventricular dysfunction monitoring verbal invite
9On4.00	Read	left ventricular dysfunction monitoring telephone invite
9Or..00	Read	heart failure monitoring administration
9Or0.00	Read	heart failure review completed
9Or1.00	Read	heart failure monitoring telephone invite
9Or2.00	Read	heart failure monitoring verbal invite
9Or3.00	Read	heart failure monitoring first letter
9Or4.00	Read	heart failure monitoring second letter
9Or5.00	Read	heart failure monitoring third letter
G1yz100	Read	rheumatic left ventricular failure
G210.00	Read	malignant hypertensive heart disease
G210100	Read	malignant hypertensive heart disease with ccf
G211100	Read	benign hypertensive heart disease with ccf
G21z100	Read	hypertensive heart disease nos with ccf
G230.00	Read	malignant hypertensive heart and renal disease
G232.00	Read	hypertensive heart&renal dis wth (congestive) heart failure
G234.00	Read	hyperten heart&renal dis+both(congestv)heart and renal fail
G400.00	Read	acute cor pulmonale
G41z.11	Read	chronic cor pulmonale
G554000	Read	congestive cardiomyopathy
G554011	Read	congestive obstructive cardiomyopathy
G557100	Read	beriberi heart disease
G58..00	Read	heart failure
G580.00	Read	congestive heart failure
G580000	Read	acute congestive heart failure
G580100	Read	chronic congestive heart failure
G580.11	Read	congestive cardiac failure
G580.12	Read	right heart failure
G580.13	Read	right ventricular failure
G580.14	Read	biventricular failure
G580200	Read	decompensated cardiac failure

G580300	Read	compensated cardiac failure
G580400	Read	congestive heart failure due to valvular disease
G581.00	Read	left ventricular failure
G581000	Read	acute left ventricular failure
G58..11	Read	cardiac failure
G581.11	Read	asthma - cardiac
G581.13	Read	impaired left ventricular function
G582.00	Read	acute heart failure
G583.00	Read	heart failure with normal ejection fraction
G583.11	Read	hfnef - heart failure with normal ejection fraction
G583.12	Read	heart failure with preserved ejection fraction
G584.00	Read	right ventricular failure
G58z.00	Read	heart failure nos
G58z.11	Read	weak heart
G58z.12	Read	cardiac failure nos
G5y4z00	Read	post cardiac operation heart failure nos
G5yy900	Read	left ventricular systolic dysfunction
G5yyA00	Read	left ventricular diastolic dysfunction
G5yyB00	Read	right ventricular diastolic dysfunction
Q48y100	Read	congenital cardiac failure
R2y1000	Read	[d]cardiorespiratory failure
SP11111	Read	heart failure as a complication of care
ZRad.00	Read	new york heart assoc classification heart failure symptoms
I11.0	ICD-10	hypertensive heart disease with (congestive) heart failure
I13.0	ICD-10	hypertensive heart and renal disease with (congestive) heart failure
I13.2	ICD-10	hypertensive heart and renal disease with both (congestive) heart failure and renal failure
I26.0	ICD-10	pulmonary embolism with mention of acute cor pulmonale
I50	ICD-10	heart failure
I50.0	ICD-10	congestive heart failure
I50.1	ICD-10	left ventricular failure
I50.9	ICD-10	heart failure

Hypertension

Code	Classification	Description
14A2.00	Read	h/o: hypertension
1JD..00	Read	suspected hypertension
2126100	Read	hypertension resolved
212K.00	Read	hypertension resolved
246M.00	Read	white coat hypertension
662..12	Read	hypertension monitoring
6624	Read	borderline hyperten:yearly obs
6627	Read	good hypertension control
6628	Read	poor hypertension control
6629	Read	hypertension:follow-up default

662b.00	Read	moderate hypertension control
662c.00	Read	hypertension six month review
662d.00	Read	hypertension annual review
662F.00	Read	hypertension treatm. started
662G.00	Read	hypertensive treatm.changed
662H.00	Read	hypertension treatm.stopped
662O.00	Read	on treatment for hypertension
662P.00	Read	hypertension monitoring
662P000	Read	hypertension 9 month review
662q.00	Read	trial reduction of antihypertensive therapy
662r.00	Read	trial withdrawal of antihypertensive therapy
67H8.00	Read	lifestyle advice regarding hypertension
7Q01.00	Read	high cost hypertension drugs
7Q01y00	Read	other specified high cost hypertension drugs
8B26.00	Read	antihypertensive therapy
8BL0.00	Read	patient on maximal tolerated antihypertensive therapy
8CR4.00	Read	hypertension clinical management plan
8HT5.00	Read	referral to hypertension clinic
8I3N.00	Read	hypertension treatment refused
9h3..00	Read	exception reporting: hypertension quality indicators
9h31.00	Read	excepted from hypertension qual indicators: patient unsuit
9h32.00	Read	excepted from hypertension qual indicators: informed dissent
9N03.00	Read	seen in hypertension clinic
9N1y200	Read	seen in hypertension clinic
9N4L.00	Read	dna - did not attend hypertension clinic
9OI..00	Read	hypertension monitoring admin.
9OI1.00	Read	attends hypertension monitor.
9OI..11	Read	hypertension clinic admin.
9OI2.00	Read	refuses hypertension monitor.
9OI3.00	Read	hyperten.monitor offer default
9OI4.00	Read	hypertens.monitor.1st letter
9OI5.00	Read	hypertens.monitor 2nd letter
9OI6.00	Read	hypertens.monitor 3rd letter
9OI7.00	Read	hypertens.monitor verbal inv.
9OI8.00	Read	hypertens.monitor phone invite
9OI9.00	Read	hypertens.monitor deleted
9OIA.00	Read	hypertension monitor.chck done
9OIA.11	Read	hypertension monitored
9OIZ.00	Read	hypertens.monitoring admin.nos
F404200	Read	blind hypertensive eye
F421300	Read	hypertensive retinopathy
G2...00	Read	hypertensive disease
G20..00	Read	essential hypertension
G200.00	Read	malignant essential hypertension
G201.00	Read	benign essential hypertension

G20..11	Read	high blood pressure
G20..12	Read	primary hypertension
G202.00	Read	systolic hypertension
G203.00	Read	diastolic hypertension
G20z.00	Read	essential hypertension nos
G20z.11	Read	hypertension nos
G21..00	Read	hypertensive heart disease
G210.00	Read	malignant hypertensive heart disease
G210000	Read	malignant hypertensive heart disease without ccf
G210100	Read	malignant hypertensive heart disease with ccf
G210z00	Read	malignant hypertensive heart disease nos
G2...11	Read	bp - hypertensive disease
G211.00	Read	benign hypertensive heart disease
G211000	Read	benign hypertensive heart disease without ccf
G211100	Read	benign hypertensive heart disease with ccf
G211z00	Read	benign hypertensive heart disease nos
G21z.00	Read	hypertensive heart disease nos
G21z000	Read	hypertensive heart disease nos without ccf
G21z011	Read	cardiomegaly - hypertensive
G21z100	Read	hypertensive heart disease nos with ccf
G21zz00	Read	hypertensive heart disease nos
G22..00	Read	hypertensive renal disease
G220.00	Read	malignant hypertensive renal disease
G221.00	Read	benign hypertensive renal disease
G22..11	Read	nephrosclerosis
G222.00	Read	hypertensive renal disease with renal failure
G22z.00	Read	hypertensive renal disease nos
G22z.11	Read	renal hypertension
G23..00	Read	hypertensive heart and renal disease
G230.00	Read	malignant hypertensive heart and renal disease
G231.00	Read	benign hypertensive heart and renal disease
G232.00	Read	hypertensive heart&renal dis wth (congestive) heart failure
G233.00	Read	hypertensive heart and renal disease with renal failure
G234.00	Read	hyperten heart&renal dis+both(congestv)heart and renal fail
G23z.00	Read	hypertensive heart and renal disease nos
G24..00	Read	secondary hypertension
G240.00	Read	secondary malignant hypertension
G240000	Read	secondary malignant renovascular hypertension
G240z00	Read	secondary malignant hypertension nos
G241.00	Read	secondary benign hypertension
G241000	Read	secondary benign renovascular hypertension
G241z00	Read	secondary benign hypertension nos
G244.00	Read	hypertension secondary to endocrine disorders
G24z.00	Read	secondary hypertension nos
G24z000	Read	secondary renovascular hypertension nos

G24z100	Read	hypertension secondary to drug
G24zz00	Read	secondary hypertension nos
G25..00	Read	stage 1 hypertension (nice - nat ins for hth clin excl 2011)
G25..11	Read	stage 1 hypertension
G26..00	Read	severe hypertension (nat inst for health clinical ex 2011)
G26..11	Read	severe hypertension
G27..00	Read	hypertension resistant to drug therapy
G28..00	Read	stage 2 hypertension (nice - nat ins for hth clin excl 2011)
G2y..00	Read	other specified hypertensive disease
G2z..00	Read	hypertensive disease nos
G672.00	Read	hypertensive encephalopathy
G672.11	Read	hypertensive crisis
Gyu2.00	Read	[x]hypertensive diseases
Gyu2000	Read	[x]other secondary hypertension
Gyu2100	Read	[x]hypertension secondary to other renal disorders
L122.00	Read	other pre-existing hypertension in preg/childbirth/puerp
L122000	Read	other pre-existing hypertension in preg/childb/puerp unspec
L122100	Read	other pre-existing hypertension in preg/childb/puerp - deliv
L122300	Read	other pre-exist hypertension in preg/childb/puerp-not deliv
L122z00	Read	other pre-existing hypertension in preg/childb/puerp nos
L127.00	Read	pre-eclampsia or eclampsia with pre-existing hypertension
L127z00	Read	pre-eclampsia or eclampsia + pre-existing hypertension nos
L128.00	Read	pre-exist hypertension compl preg childbirth and puerperium
L128000	Read	pre-exist hyperten heart dis compl preg childbth+puerperium
L128200	Read	pre-exist 2ndry hypertens comp preg childbth and puerperium
TJC7.00	Read	adverse reaction to other antihypertensives
TJC7z00	Read	adverse reaction to antihypertensives nos
U60C500	Read	[x]oth antihyperten drug caus advers eff in therap use
U60C511	Read	[x] adverse reaction to other antihypertensives
U60C51A	Read	[x] adverse reaction to antihypertensives nos
I10	ICD-10	essential (primary) hypertension
I11	ICD-10	hypertensive heart disease
I11.0	ICD-10	hypertensive heart disease with (congestive) heart failure
I11.9	ICD-10	hypertensive heart disease without (congestive) heart failure
I12	ICD-10	hypertensive renal disease
I12.0	ICD-10	hypertensive renal disease with renal failure
I12.9	ICD-10	hypertensive renal disease without renal failure
I13	ICD-10	hypertensive heart and renal disease
I13.0	ICD-10	hypertensive heart and renal disease with (congestive) heart failure
I13.1	ICD-10	hypertensive heart and renal disease with renal failure
I13.2	ICD-10	hypertensive heart and renal disease with both (congestive) heart failure and renal failure
I13.9	ICD-10	hypertensive heart and renal disease
I15	ICD-10	secondary hypertension
I15.0	ICD-10	renovascular hypertension
I15.1	ICD-10	hypertension secondary to other renal disorders

I15.2	ICD-10	hypertension secondary to endocrine disorders
I15.8	ICD-10	other secondary hypertension
I15.9	ICD-10	secondary hypertension
I67.4	ICD-10	hypertensive encephalopathy

Arrhytmia

Code	Classification	Description
14AN.00	Read	h/o: atrial fibrillation
14AR.00	Read	history of atrial flutter
212R.00	Read	atrial fibrillation resolved
327..00	Read	ecg: supraventricular arrhythmia
3272	Read	ecg: atrial fibrillation
3273	Read	ecg: atrial flutter
328..00	Read	ecg: ventricular arrhythmia
3282	Read	ecg: ventricular tachycardia
328Z.00	Read	ecg: ventricular arrhythmia nos
662S.00	Read	atrial fibrillation monitoring
6A9..00	Read	atrial fibrillation annual review
7936A00	Read	implant intravenous pacemaker for atrial fibrillation
8CMW200	Read	atrial fibrillation care pathway
8HTy.00	Read	referral to atrial fibrillation clinic
9hF..00	Read	exception reporting: atrial fibrillation quality indicators
9hF1.00	Read	excepted from atrial fibrillation qual indic: inform dissent
9Os..00	Read	atrial fibrillation monitoring administration
9Os0.00	Read	atrial fibrillation monitoring first letter
9Os1.00	Read	atrial fibrillation monitoring second letter
9Os2.00	Read	atrial fibrillation monitoring third letter
9Os3.00	Read	atrial fibrillation monitoring verbal invite
9Os4.00	Read	atrial fibrillation monitoring telephone invite
G559.00	Read	arrhythmogenic right ventricular cardiomyopathy
G55A.11	Read	tachycardia-induced cardiomyopathy
G56..00	Read	conduction disorders
G56..11	Read	conduction disorders of heart
G567400	Read	wolff-parkinson-white syndrome
G56y.00	Read	other conduction disorders
G56y000	Read	lown-ganong-levine syndrome
G56zz00	Read	conduction disorders nos
G57..00	Read	cardiac dysrhythmias
G570.00	Read	paroxysmal supraventricular tachycardia
G570000	Read	paroxysmal atrial tachycardia
G570100	Read	paroxysmal atrioventricular tachycardia
G570200	Read	paroxysmal junctional tachycardia
G570300	Read	paroxysmal nodal tachycardia
G570z00	Read	paroxysmal supraventricular tachycardia nos
G571.00	Read	paroxysmal ventricular tachycardia

G57..11	Read	cardiac arrhythmias
G571.11	Read	ventricular tachycardia
G572.00	Read	paroxysmal tachycardia unspecified
G572000	Read	essential paroxysmal tachycardia
G572z00	Read	paroxysmal tachycardia nos
G573.00	Read	atrial fibrillation and flutter
G573000	Read	atrial fibrillation
G573100	Read	atrial flutter
G573200	Read	paroxysmal atrial fibrillation
G573300	Read	non-rheumatic atrial fibrillation
G573400	Read	permanent atrial fibrillation
G573500	Read	persistent atrial fibrillation
G573600	Read	paroxysmal atrial flutter
G573z00	Read	atrial fibrillation and flutter nos
G574.00	Read	ventricular fibrillation and flutter
G574100	Read	ventricular flutter
G574z00	Read	ventricular fibrillation and flutter nos
G576300	Read	atrial premature depolarization
G576400	Read	junctional premature depolarization
G576500	Read	ventricular premature depolarization
G57y.00	Read	other cardiac dysrhythmias
G57y600	Read	nodal rhythm disorder
G57y900	Read	supraventricular tachycardia nos
G57yA00	Read	re-entry ventricular arrhythmia
G57yz00	Read	other cardiac dysrhythmia nos
G57z.00	Read	cardiac dysrhythmia nos
Gyu5a00	Read	[x]other specified cardiac arrhythmias
I45.6	ICD-10	pre-excitation syndrome
I47	ICD-10	paroxysmal tachycardia
I47.0	ICD-10	re-entry ventricular arrhythmia
I47.1	ICD-10	supraventricular tachycardia
I47.2	ICD-10	ventricular tachycardia
I47.9	ICD-10	paroxysmal tachycardia
I48	ICD-10	atrial fibrillation and flutter
I49	ICD-10	other cardiac arrhythmias
I49.0	ICD-10	ventricular fibrillation and flutter
I49.1	ICD-10	atrial premature depolarization
I49.2	ICD-10	junctional premature depolarization
I49.3	ICD-10	ventricular premature depolarization
I49.4	ICD-10	other and unspecified premature depolarization
I49.5	ICD-10	sick sinus syndrome
R00.0	ICD-10	tachycardia

Peripheral arterial disease

Code	Classification	Description

G73z000	Read	intermittent claudication
G73z011	Read	claudication
G73..12	Read	ischaemia of legs
G73zz00	Read	peripheral vascular disease nos
G73z.00	Read	peripheral vascular disease nos
G73yz00	Read	other specified peripheral vascular disease nos
G73..11	Read	peripheral ischaemic vascular disease
G73..00	Read	other peripheral vascular disease
G73..13	Read	peripheral ischaemia
2G63.00	Read	ischaemic toe
G702.00	Read	Extremity artery atheroma
G742z00	Read	peripheral arterial embolism and thrombosis nos
G702z00	Read	Extremity artery atheroma NOS
G76A.00	Read	arterial insufficiency
G73y100	Read	Peripheral angiopathic disease EC NOS
R055011	Read	[d]peripheral circulatory failure
G73y.00	Read	other specified peripheral vascular disease
14NB.00	Read	h/o: peripheral vascular disease procedure
Gyu7400	Read	[x]other specified peripheral vascular diseases
7A56600	Read	percutaneous transluminal placement peripheral stent artery
G733.00	Read	ischaemic foot
G73z012	Read	vascular claudication
G734.00	Read	peripheral arterial disease
16I..00	Read	claudication distance
I70.2	ICD-10	atherosclerosis of arteries of extremities
I70.20	ICD-10	atherosclerosis of arteries of extremities
I70.21	ICD-10	atherosclerosis of arteries of extremities
I73	ICD-10	other peripheral vascular diseases
I73.8	ICD-10	other specified peripheral vascular diseases
I73.9	ICD-10	peripheral vascular disease, unspecified
I79.2	ICD-10	peripheral angiopathy in diseases classified elsewhere

Mycardial infarction

Code	Classification	Description
14A3.00	Read	H/O: myocardial infarct <60
14A4.00	Read	H/O: myocardial infarct >60
14AH.00	Read	H/O: Myocardial infarction in last year
323..00	Read	ECG: myocardial infarction
3232.00.00	Read	ECG: old myocardial infarction
3233.00.00	Read	ECG: antero-septal infarct.
3234.00.00	Read	ECG:posterior/inferior infarct
3235.00.00	Read	ECG: subendocardial infarct
3236.00.00	Read	ECG: lateral infarction
323Z.00	Read	ECG: myocardial infarct NOS
32B2.00	Read	ECG: Q wave abnormal

32B3.00	Read	ECG: Q wave pathological
32E3.00	Read	ECG: S-T elevation
44H3.00	Read	Cardiac enzymes abnormal
44H3000	Read	Cardiac enzymes abnormal - first set
44p2.00	Read	Cardiac troponin positive
7929100	Read	Percut transluminal coronary thrombolysis with streptokinase
7929111	Read	Percut translum coronary thrombolytic therapy- streptokinase
889A.00	Read	Diab mellit insulin-glucose infus acute myocardial infarct
8B3a.00	Read	Door to needle time
8B3g.00	Read	Pain to thrombolysis time
G30..00	Read	Acute myocardial infarction
G30..11	Read	Attack - heart
G30..12	Read	Coronary thrombosis
G30..13	Read	Cardiac rupture following myocardial infarction (MI)
G30..14	Read	Heart attack
G30..15	Read	MI - acute myocardial infarction
G30..16	Read	Thrombosis - coronary
G30..17	Read	Silent myocardial infarction
G300.00	Read	Acute anterolateral infarction
G301.00	Read	Other specified anterior myocardial infarction
G301000	Read	Acute anteroapical infarction
G301100	Read	Acute anteroseptal infarction
G301z00	Read	Anterior myocardial infarction NOS
G302.00	Read	Acute inferolateral infarction
G303.00	Read	Acute inferoposterior infarction
G304.00	Read	Posterior myocardial infarction NOS
G305.00	Read	Lateral myocardial infarction NOS
G306.00	Read	True posterior myocardial infarction
G307.00	Read	Acute subendocardial infarction
G307000	Read	Acute non-Q wave infarction
G307100	Read	Acute non-ST segment elevation myocardial infarction
G308.00	Read	Inferior myocardial infarction NOS
G309.00	Read	Acute Q-wave infarct
G30A.00	Read	Mural thrombosis
G30B.00	Read	Acute posterolateral myocardial infarction
G30X.00	Read	Acute transmural myocardial infarction of unspecif site
G30X000	Read	Acute ST segment elevation myocardial infarction
G30y.00	Read	Other acute myocardial infarction
G30y000	Read	Acute atrial infarction
G30y100	Read	Acute papillary muscle infarction
G30y200	Read	Acute septal infarction
G30yz00	Read	Other acute myocardial infarction NOS
G30z.00	Read	Acute myocardial infarction NOS
G310.00	Read	Postmyocardial infarction syndrome
G310.11	Read	Dressler's syndrome

G31y100	Read	Microinfarction of heart
G32..00	Read	Old myocardial infarction
G32..11	Read	Healed myocardial infarction
G32..12	Read	Personal history of myocardial infarction
G33z500	Read	Post infarct angina
G35..00	Read	Subsequent myocardial infarction
G350.00	Read	Subsequent myocardial infarction of anterior wall
G351.00	Read	Subsequent myocardial infarction of inferior wall
G353.00	Read	Subsequent myocardial infarction of other sites
G35X.00	Read	Subsequent myocardial infarction of unspecified site
G36..00	Read	Certain current complication follow acute myocardial infarct
G360.00	Read	Haemopericardium/current comp folow acut myocard infarct
G361.00	Read	Atrial septal defect/curr comp folow acut myocardal infarct
G362.00	Read	Ventric septal defect/curr comp fol acut myocardal infarctn
G363.00	Read	Ruptur cardiac wall w'out haemopericard/cur comp fol ac MI
G364.00	Read	Ruptur chordae tendinae/curr comp fol acute myocard infarct
G365.00	Read	Rupture papillary muscle/curr comp fol acute myocard infarct
G366.00	Read	Thrombosis atrium,auric append&vent/curr comp foll acute MI
G38..00	Read	Postoperative myocardial infarction
G380.00	Read	Postoperative transmural myocardial infarction anterior wall
G381.00	Read	Postoperative transmural myocardial infarction inferior wall
G384.00	Read	Postoperative subendocardial myocardial infarction
G38z.00	Read	Postoperative myocardial infarction, unspecified
G501.00	Read	Post infarction pericarditis
Gyu3400	Read	[X]Acute transmural myocardial infarction of unspecif site
I21	ICD-10	Acute myocardial infarction
I22	ICD-10	Subsequent myocardial infarction
I23	ICD-10	Certain current complications following acute myocardial infarction

Diabetes mellitus

Code	Classification	Description
13AB.00	Read	diabetic lipid lowering diet
13AC.00	Read	diabetic weight reducing diet
13B1.00	Read	diabetic diet
13L4.11	Read	diabetic child
1434	Read	h/o: diabetes mellitus
14F4.00	Read	h/o: admission in last year for diabetes foot problem
14P3.00	Read	h/o: insulin therapy
2BBF.00	Read	retinal abnormality - diabetes related
2BBJ.00	Read	o/e - no right diabetic retinopathy
2BBk.00	Read	o/e - right eye stable treated prolif diabetic retinopathy
2BBK.00	Read	o/e - no left diabetic retinopathy
2BBl.00	Read	o/e - left eye stable treated prolif diabetic retinopathy
2BBL.00	Read	o/e - diabetic maculopathy present both eyes
2BBM.00	Read	o/e - diabetic maculopathy absent both eyes

2BBo.00	Read	o/e - sight threatening diabetic retinopathy
2BBP.00	Read	o/e - right eye background diabetic retinopathy
2BBQ.00	Read	o/e - left eye background diabetic retinopathy
2BBr.00	Read	impaired vision due to diabetic retinopathy
2BBR.00	Read	o/e - right eye preproliferative diabetic retinopathy
2BBS.00	Read	o/e - left eye preproliferative diabetic retinopathy
2BBT.00	Read	o/e - right eye proliferative diabetic retinopathy
2BBV.00	Read	o/e - left eye proliferative diabetic retinopathy
2BBW.00	Read	o/e - right eye diabetic maculopathy
2BBX.00	Read	o/e - left eye diabetic maculopathy
2G51000	Read	foot abnormality - diabetes related
2G5A.00	Read	o/e - right diabetic foot at risk
2G5B.00	Read	o/e - left diabetic foot at risk
2G5C.00	Read	foot abnormality - diabetes related
2G5d.00	Read	o/e - left diabetic foot at increased risk
2G5e.00	Read	o/e - right diabetic foot at increased risk
2G5E.00	Read	o/e - right diabetic foot at low risk
2G5F.00	Read	o/e - right diabetic foot at moderate risk
2G5G.00	Read	o/e - right diabetic foot at high risk
2G5H.00	Read	o/e - right diabetic foot - ulcerated
2G5I.00	Read	o/e - left diabetic foot at low risk
2G5J.00	Read	o/e - left diabetic foot at moderate risk
2G5K.00	Read	o/e - left diabetic foot at high risk
2G5L.00	Read	o/e - left diabetic foot - ulcerated
2G5V.00	Read	o/e - right chronic diabetic foot ulcer
2G5W.00	Read	o/e - left chronic diabetic foot ulcer
3881	Read	education score - diabetes
3882	Read	diabetes well being questionnaire
3883	Read	diabetes treatment satisfaction questionnaire
42c..00	Read	hba1 - diabetic control
42c0.00	Read	hba1 < 7% - good control
42c1.00	Read	hba1 7 - 10% - borderline control
42c2.00	Read	hba1 > 10% - bad control
42W..00	Read	hb. a1c - diabetic control
42W1.00	Read	hb. a1c < 7% - good control
42W2.00	Read	hb. a1c 7-10% - borderline
42W3.00	Read	hb. a1c > 10% - bad control
42WZ.00	Read	hb. a1c - diabetic control nos
44T9.00	Read	glucometer blood sugar
44UZ.00	Read	blood glucose 14+ mmol/l
44Uz.11	Read	blood hyperglycaemia nos
44V3.00	Read	glucose tol. test diabetic
661N400	Read	diabetes self-management plan review
66A..00	Read	diabetic monitoring
66A1.00	Read	initial diabetic assessment

66A2.00	Read	follow-up diabetic assessment
66A3.00	Read	diabetic on diet only
66A4.00	Read	diabetic on oral treatment
66A5.00	Read	diabetic on insulin
66A8.00	Read	has seen dietician - diabetes
66A9.00	Read	understands diet - diabetes
66Aa.00	Read	diabetic diet - poor compliance
66AA.11	Read	injection sites - diabetic
66Ab.00	Read	diabetic foot examination
66Ac.00	Read	diabetic peripheral neuropathy screening
66AC.00	Read	blood sugar charts
66AD.00	Read	fundoscopy - diabetic check
66Ae.00	Read	hba1c target
66AE.00	Read	feet examination
66Af.00	Read	patient diabetes education review
66Ag.00	Read	insulin needles changed daily
66AG.00	Read	diabetic drug side effects
66Ah.00	Read	insulin needles changed for each injection
66AH.00	Read	diabetic treatment changed
66AH000	Read	conversion to insulin
66AH100	Read	conversion to insulin in secondary care
66AH200	Read	conversion to insulin by diabetes specialist nurse
66Ai.00	Read	diabetic 6 month review
66AI.00	Read	diabetic - good control
66Aj.00	Read	insulin needles changed less than once a day
66AJ.00	Read	diabetic - poor control
66AJ000	Read	chronic hyperglycaemia
66AJ100	Read	brittle diabetes
66AJ.11	Read	unstable diabetes
66AJ200	Read	loss of hypoglycaemic warning
66AJz00	Read	diabetic - poor control nos
66Ak.00	Read	diabetic monitoring - lower risk albumin excretion
66AK.00	Read	diabetic - cooperative patient
66Al.00	Read	diabetic monitoring - higher risk albumin excretion
66AL.00	Read	diabetic-uncooperative patient
66Am.00	Read	insulin dose changed
66AM.00	Read	diabetic - follow-up default
66An.00	Read	diabetes type 1 review
66AN.00	Read	date diabetic treatment start
66Ao.00	Read	diabetes type 2 review
66Ap.00	Read	insulin treatment initiated
66AP.00	Read	diabetes: practice programme
66Aq.00	Read	diabetic foot screen
66AQ.00	Read	diabetes: shared care programme
66AQ000	Read	unsuitable for diabetes year of care programme

66AQ100	Read	declined consent for diabetes year of care programme
66AR.00	Read	diabetes management plan given
66As.00	Read	diabetic on subcutaneous treatment
66AS.00	Read	diabetic annual review
66AS000	Read	diabetes year of care annual review
66At.00	Read	diabetic dietary review
66AT.00	Read	annual diabetic blood test
66At000	Read	type i diabetic dietary review
66At011	Read	type 1 diabetic dietary review
66At100	Read	type ii diabetic dietary review
66At111	Read	type 2 diabetic dietary review
66Au.00	Read	diabetic erectile dysfunction review
66AU.00	Read	diabetes care by hospital only
66Av.00	Read	diabetic assessment of erectile dysfunction
66AV.00	Read	diabetic on insulin and oral treatment
66Aw.00	Read	insulin dose
66AW.00	Read	diabetic foot risk assessment
66AY.00	Read	diabetic diet - good compliance
66AZ.00	Read	diabetic monitoring nos
66b1.00	Read	diabetic monitoring not required
66o..00	Read	further diabetic monitoring
6761	Read	diabetic pre-pregnancy counselling
679c.00	Read	insulin administration education
679L.00	Read	health education - diabetes
679L000	Read	education in self management of diabetes
679L200	Read	education about diabetes and driving
679L211	Read	advice about diabetes and driving
679R.00	Read	patient offered diabetes structured education programme
67D8.00	Read	provision of diabetes clinical summary
68A7.00	Read	diabetic retinopathy screening
68A9.00	Read	diabetic retinopathy screening offered
68AB.00	Read	diabetic digital retinopathy screening offered
7276	Read	pan retinal photocoagulation for diabetes
7L10000	Read	continuous subcutaneous infusion of insulin
7L10011	Read	subcutaneous infusion with insulin pump
7L19800	Read	subcutaneous injection of insulin
7L19J00	Read	subcutaneous injection of exenatide
889A.00	Read	diab mellit insulin-glucose infus acute myocardial infarct
8A12.00	Read	diabetic crisis monitoring
8A13.00	Read	diabetic stabilisation
8A17.00	Read	self monitoring of blood glucose
8B3l.00	Read	diabetes medication review
8BAi.00	Read	insulin passport completed
8BAj.00	Read	informed dissent not to carry insulin passport
8BAm.00	Read	insulin passport checked

8BL2.00	Read	patient on maximal tolerated therapy for diabetes
8CA4100	Read	pt advised re diabetic diet
8CAQ.00	Read	advice about blood glucose control
8CE0100	Read	insulin alert patient information booklet given
8CE0200	Read	insulin passport given
8CMW700	Read	diabetes clinical pathway
8CP2.00	Read	transition of diabetes care options discussed
8CR2.00	Read	diabetes clinical management plan
8CS0.00	Read	diabetes care plan agreed
8H2J.00	Read	admit diabetic emergency
8H3O.00	Read	non-urgent diabetic admission
8H4e.00	Read	referral to diabetes special interest general practitioner
8H4F.00	Read	referral to diabetologist
8H7C.00	Read	refer
8H7f.00	Read	referral to diabetes nurse
8H7r.00	Read	refer to diabetic foot screener
8HBG.00	Read	diabetic retinopathy 12 month review
8HBH.00	Read	diabetic retinopathy 6 month review
8Hg4.00	Read	discharged from care of diabetes specialist nurse
8HgC.00	Read	discharged from diabetes shared care programme
8HHy.00	Read	referral to diabetic register
8Hj0.00	Read	referral to diabetes structured education programme
8Hj3.00	Read	referral to dafne diabetes structured education programme
8Hj4.00	Read	referral to desmond diabetes structured education programme
8Hj5.00	Read	referral to xpert diabetes structured education programme
8HKE.00	Read	diabetology d.v. requested
8Hl1.00	Read	referral for diabetic retinopathy screening
8Hl4.00	Read	referral to community diabetes specialist nurse
8Hlc.00	Read	referral to community diabetes service
8HLE.00	Read	diabetology d.v. done
8HME.00	Read	listed for diabetology admissn
8HTe.00	Read	referral to diabetes preconception counselling clinic
8HTE100	Read	referral to community diabetes clinic
8HTi.00	Read	referral to multidisciplinary diabetic clinic
8HTk.00	Read	referral to diabetic eye clinic
8HVU.00	Read	private referral to diabetologist
8I2P.00	Read	sulphonylureas contraindicated
8I2S.00	Read	glitazones contraindicated
8I3k.00	Read	insulin therapy declined
8I3W.00	Read	diabetic foot examination declined
8I3X.00	Read	diabetic retinopathy screening refused
8I57.00	Read	patient held diabetic record declined
8I6F.00	Read	diabetic retinopathy screening not indicated
8I6G.00	Read	diabetic foot examination not indicated
8I7B.00	Read	metformin not tolerated

8I7C.00	Read	sulphonylureas not tolerated
8I81.00	Read	did not complete diabetes structured education programme
8I82.00	Read	did not complete dafne diabetes structured education program
8I83.00	Read	did not complete desmond diabetes structured educat program
8I84.00	Read	did not complete xpert diabetes structured education program
8IAs.00	Read	diabetic dietary review declined
8IE2.00	Read	diabetes care plan declined
8IEa.00	Read	referral to dafne diabetes structured educn prog declined
8IEQ.00	Read	referral to community diabetes specialist nurse declined
8OA3.00	Read	provision of written information about diabetes and driving
9360	Read	patient held diabetic record issued
93C4.00	Read	patient consent given for addition to diabetic register
9b92000	Read	diabetic medicine
9h4..00	Read	exception reporting: diabetes quality indicators
9h41.00	Read	excepted from diabetes qual indicators: patient unsuitable
9h42.00	Read	excepted from diabetes quality indicators: informed dissent
9kL..00	Read	insulin initiation - enhanced services administration
9m00.00	Read	eligible for diabetic retinopathy screening
9M00.00	Read	informed consent for diabetes national audit
9m0A.00	Read	declined diabetic retinopathy screening
9M10.00	Read	informed dissent for diabetes national audit
9N0m.00	Read	seen in diabetic nurse consultant clinic
9N0n.00	Read	seen in community diabetes specialist clinic
9N0o.00	Read	seen in community diabetic specialist nurse clinic
9N1i.00	Read	seen in diabetic foot clinic
9N1o.00	Read	seen in multidisciplinary diabetic clinic
9N1Q.00	Read	seen in diabetic clinic
9N1v.00	Read	seen in diabetic eye clinic
9N2d.00	Read	seen by diabetologist
9N2i.00	Read	seen by diabetic liaison nurse
9N4I.00	Read	dna - did not attend diabetic clinic
9N4p.00	Read	did not attend diabetic retinopathy clinic
9NiA.00	Read	did not attend diabetes structured education programme
9NiC.00	Read	did not attend dafne diabetes structured education programme
9NiD.00	Read	did not attend desmond diabetes structured education program
9NiE.00	Read	did not attend xpert diabetes structured education programme
9NiZ.00	Read	did not attend diabetes foot screening
9Nl4.00	Read	seen by general practitioner special interest in diabetes
9NM0.00	Read	attending diabetes clinic
9NN8.00	Read	under care of diabetologist
9NN9.00	Read	under care of diabetes specialist nurse
9NND.00	Read	under care of diabetic foot screener
9OL..00	Read	diabetes monitoring admin.
9OL1.00	Read	attends diabetes monitoring
9OL..11	Read	diabetes clinic administration

9OL2.00	Read	refuses diabetes monitoring
9OL3.00	Read	diabetes monitoring default
9OL4.00	Read	diabetes monitoring 1st letter
9OL5.00	Read	diabetes monitoring 2nd letter
9OL6.00	Read	diabetes monitoring 3rd letter
9OL7.00	Read	diabetes monitor.verbal invite
9OL8.00	Read	diabetes monitor.phone invite
9OL9.00	Read	diabetes monitoring deleted
9OLA.00	Read	diabetes monitor. check done
9OLA.11	Read	diabetes monitored
9OLB.00	Read	attended diabetes structured education programme
9OLD.00	Read	diabetic patient unsuitable for digital retinal photography
9OLE.00	Read	attended desmond structured programme
9OLF.00	Read	diabetes structured education programme completed
9OLG.00	Read	attended xpert diabetes structured education programme
9OLH.00	Read	attended dafne diabetes structured education programme
9OLJ.00	Read	dafne diabetes structured education programme completed
9OLK.00	Read	desmond diabetes structured education programme completed
9OLL.00	Read	xpert diabetes structured education programme completed
9OLM.00	Read	diabetes structured education programme declined
9OLN.00	Read	diabetes monitor invitation by sms (short message service)
9OLZ.00	Read	diabetes monitoring admin.nos
9Oy..00	Read	diabetes screening administration
9Oy0000	Read	diabetic foot screening invitation
9Oy0200	Read	diabetic foot screening invitation first letter
9Oy0300	Read	diabetic foot screening invitation second letter
9Oy0400	Read	diabetic foot screening invitation third letter
C10..00	Read	diabetes mellitus
C100.00	Read	diabetes mellitus with no mention of complication
C100000	Read	diabetes mellitus
C100011	Read	insulin dependent diabetes mellitus
C100100	Read	diabetes mellitus
C100111	Read	maturity onset diabetes
C100112	Read	non-insulin dependent diabetes mellitus
C100z00	Read	diabetes mellitus nos with no mention of complication
C101.00	Read	diabetes mellitus with ketoacidosis
C101000	Read	diabetes mellitus
C101100	Read	diabetes mellitus
C101y00	Read	other specified diabetes mellitus with ketoacidosis
C101z00	Read	diabetes mellitus nos with ketoacidosis
C102.00	Read	diabetes mellitus with hyperosmolar coma
C102000	Read	diabetes mellitus
C102100	Read	diabetes mellitus
C102z00	Read	diabetes mellitus nos with hyperosmolar coma
C103.00	Read	diabetes mellitus with ketoacidotic coma

C103000	Read	diabetes mellitus
C103100	Read	diabetes mellitus
C103y00	Read	other specified diabetes mellitus with coma
C103z00	Read	diabetes mellitus nos with ketoacidotic coma
C104.00	Read	diabetes mellitus with renal manifestation
C104000	Read	diabetes mellitus
C104100	Read	diabetes mellitus
C104.11	Read	diabetic nephropathy
C104y00	Read	other specified diabetes mellitus with renal complications
C104z00	Read	diabetes mellitus with nephropathy nos
C105.00	Read	diabetes mellitus with ophthalmic manifestation
C105000	Read	diabetes mellitus
C105100	Read	diabetes mellitus
C105y00	Read	other specified diabetes mellitus with ophthalmic complicatn
C105z00	Read	diabetes mellitus nos with ophthalmic manifestation
C106.00	Read	diabetes mellitus with neurological manifestation
C106000	Read	diabetes mellitus
C106100	Read	diabetes mellitus
C106.11	Read	diabetic amyotrophy
C106.12	Read	diabetes mellitus with neuropathy
C106.13	Read	diabetes mellitus with polyneuropathy
C106y00	Read	other specified diabetes mellitus with neurological comps
C106z00	Read	diabetes mellitus nos with neurological manifestation
C107.00	Read	diabetes mellitus with peripheral circulatory disorder
C107000	Read	diabetes mellitus
C107100	Read	diabetes mellitus
C107.11	Read	diabetes mellitus with gangrene
C107.12	Read	diabetes with gangrene
C107200	Read	diabetes mellitus
C107300	Read	iddm with peripheral circulatory disorder
C107400	Read	niddm with peripheral circulatory disorder
C107z00	Read	diabetes mellitus nos with peripheral circulatory disorder
C108.00	Read	insulin dependent diabetes mellitus
C108000	Read	insulin-dependent diabetes mellitus with renal complications
C108011	Read	type i diabetes mellitus with renal complications
C108012	Read	type 1 diabetes mellitus with renal complications
C108100	Read	insulin-dependent diabetes mellitus with ophthalmic comps
C108.11	Read	iddm-insulin dependent diabetes mellitus
C108112	Read	type 1 diabetes mellitus with ophthalmic complications
C108.12	Read	type 1 diabetes mellitus
C108.13	Read	type i diabetes mellitus
C108200	Read	insulin-dependent diabetes mellitus with neurological comps
C108211	Read	type i diabetes mellitus with neurological complications
C108212	Read	type 1 diabetes mellitus with neurological complications
C108300	Read	insulin dependent diabetes mellitus with multiple complicatn

C108311	Read	type i diabetes mellitus with multiple complications
C108400	Read	unstable insulin dependent diabetes mellitus
C108411	Read	unstable type i diabetes mellitus
C108412	Read	unstable type 1 diabetes mellitus
C108500	Read	insulin dependent diabetes mellitus with ulcer
C108511	Read	type i diabetes mellitus with ulcer
C108512	Read	type 1 diabetes mellitus with ulcer
C108600	Read	insulin dependent diabetes mellitus with gangrene
C108700	Read	insulin dependent diabetes mellitus with retinopathy
C108711	Read	type i diabetes mellitus with retinopathy
C108712	Read	type 1 diabetes mellitus with retinopathy
C108800	Read	insulin dependent diabetes mellitus - poor control
C108811	Read	type i diabetes mellitus - poor control
C108812	Read	type 1 diabetes mellitus - poor control
C108900	Read	insulin dependent diabetes maturity onset
C108911	Read	type i diabetes mellitus maturity onset
C108912	Read	type 1 diabetes mellitus maturity onset
C108A00	Read	insulin-dependent diabetes without complication
C108A11	Read	type i diabetes mellitus without complication
C108B00	Read	insulin dependent diabetes mellitus with mononeuropathy
C108B11	Read	type i diabetes mellitus with mononeuropathy
C108C00	Read	insulin dependent diabetes mellitus with polyneuropathy
C108D00	Read	insulin dependent diabetes mellitus with nephropathy
C108D11	Read	type i diabetes mellitus with nephropathy
C108E00	Read	insulin dependent diabetes mellitus with hypoglycaemic coma
C108E11	Read	type i diabetes mellitus with hypoglycaemic coma
C108E12	Read	type 1 diabetes mellitus with hypoglycaemic coma
C108F00	Read	insulin dependent diabetes mellitus with diabetic cataract
C108F11	Read	type i diabetes mellitus with diabetic cataract
C108G00	Read	insulin dependent diab mell with peripheral angiopathy
C108H00	Read	insulin dependent diabetes mellitus with arthropathy
C108H11	Read	type i diabetes mellitus with arthropathy
C108J00	Read	insulin dependent diab mell with neuropathic arthropathy
C108J11	Read	type i diabetes mellitus with neuropathic arthropathy
C108J12	Read	type 1 diabetes mellitus with neuropathic arthropathy
C108y00	Read	other specified diabetes mellitus with multiple comps
C108z00	Read	unspecified diabetes mellitus with multiple complications
C109.00	Read	non-insulin dependent diabetes mellitus
C109000	Read	non-insulin-dependent diabetes mellitus with renal comps
C109011	Read	type ii diabetes mellitus with renal complications
C109012	Read	type 2 diabetes mellitus with renal complications
C109100	Read	non-insulin-dependent diabetes mellitus with ophthalm comps
C109.11	Read	niddm - non-insulin dependent diabetes mellitus
C109111	Read	type ii diabetes mellitus with ophthalmic complications
C109112	Read	type 2 diabetes mellitus with ophthalmic complications

C109.12	Read	type 2 diabetes mellitus
C109.13	Read	type ii diabetes mellitus
C109200	Read	non-insulin-dependent diabetes mellitus with neuro comps
C109211	Read	type ii diabetes mellitus with neurological complications
C109212	Read	type 2 diabetes mellitus with neurological complications
C109300	Read	non-insulin-dependent diabetes mellitus with multiple comps
C109312	Read	type 2 diabetes mellitus with multiple complications
C109400	Read	non-insulin dependent diabetes mellitus with ulcer
C109411	Read	type ii diabetes mellitus with ulcer
C109412	Read	type 2 diabetes mellitus with ulcer
C109500	Read	non-insulin dependent diabetes mellitus with gangrene
C109511	Read	type ii diabetes mellitus with gangrene
C109512	Read	type 2 diabetes mellitus with gangrene
C109600	Read	non-insulin-dependent diabetes mellitus with retinopathy
C109611	Read	type ii diabetes mellitus with retinopathy
C109612	Read	type 2 diabetes mellitus with retinopathy
C109700	Read	non-insulin dependent diabetes mellitus - poor control
C109711	Read	type ii diabetes mellitus - poor control
C109712	Read	type 2 diabetes mellitus - poor control
C109900	Read	non-insulin-dependent diabetes mellitus without complication
C109912	Read	type 2 diabetes mellitus without complication
C109A00	Read	non-insulin dependent diabetes mellitus with mononeuropathy
C109A11	Read	type ii diabetes mellitus with mononeuropathy
C109B00	Read	non-insulin dependent diabetes mellitus with polyneuropathy
C109B11	Read	type ii diabetes mellitus with polyneuropathy
C109C00	Read	non-insulin dependent diabetes mellitus with nephropathy
C109C11	Read	type ii diabetes mellitus with nephropathy
C109C12	Read	type 2 diabetes mellitus with nephropathy
C109D00	Read	non-insulin dependent diabetes mellitus with hypoglyca coma
C109D11	Read	type ii diabetes mellitus with hypoglycaemic coma
C109D12	Read	type 2 diabetes mellitus with hypoglycaemic coma
C109E00	Read	non-insulin depend diabetes mellitus with diabetic cataract
C109E11	Read	type ii diabetes mellitus with diabetic cataract
C109E12	Read	type 2 diabetes mellitus with diabetic cataract
C109F00	Read	non-insulin-dependent d m with peripheral angiopath
C109F11	Read	type ii diabetes mellitus with peripheral angiopathy
C109F12	Read	type 2 diabetes mellitus with peripheral angiopathy
C109G00	Read	non-insulin dependent diabetes mellitus with arthropathy
C109G11	Read	type ii diabetes mellitus with arthropathy
C109G12	Read	type 2 diabetes mellitus with arthropathy
C109H00	Read	non-insulin dependent d m with neuropathic arthropathy
C109H11	Read	type ii diabetes mellitus with neuropathic arthropathy
C109H12	Read	type 2 diabetes mellitus with neuropathic arthropathy
C109J00	Read	insulin treated type 2 diabetes mellitus
C109J11	Read	insulin treated non-insulin dependent diabetes mellitus

C109J12	Read	insulin treated type ii diabetes mellitus
C109K00	Read	hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10B.00	Read	diabetes mellitus induced by steroids
C10B000	Read	steroid induced diabetes mellitus without complication
C10C.00	Read	diabetes mellitus autosomal dominant
C10C.11	Read	maturity onset diabetes in youth
C10C.12	Read	maturity onset diabetes in youth type 1
C10D.00	Read	diabetes mellitus autosomal dominant type 2
C10D.11	Read	maturity onset diabetes in youth type 2
C10E.00	Read	type 1 diabetes mellitus
C10E000	Read	type 1 diabetes mellitus with renal complications
C10E012	Read	insulin-dependent diabetes mellitus with renal complications
C10E100	Read	type 1 diabetes mellitus with ophthalmic complications
C10E.11	Read	type i diabetes mellitus
C10E111	Read	type i diabetes mellitus with ophthalmic complications
C10E112	Read	insulin-dependent diabetes mellitus with ophthalmic comps
C10E.12	Read	insulin dependent diabetes mellitus
C10E200	Read	type 1 diabetes mellitus with neurological complications
C10E212	Read	insulin-dependent diabetes mellitus with neurological comps
C10E300	Read	type 1 diabetes mellitus with multiple complications
C10E311	Read	type i diabetes mellitus with multiple complications
C10E312	Read	insulin dependent diabetes mellitus with multiple complicat
C10E400	Read	unstable type 1 diabetes mellitus
C10E411	Read	unstable type i diabetes mellitus
C10E412	Read	unstable insulin dependent diabetes mellitus
C10E500	Read	type 1 diabetes mellitus with ulcer
C10E511	Read	type i diabetes mellitus with ulcer
C10E512	Read	insulin dependent diabetes mellitus with ulcer
C10E600	Read	type 1 diabetes mellitus with gangrene
C10E611	Read	type i diabetes mellitus with gangrene
C10E700	Read	type 1 diabetes mellitus with retinopathy
C10E711	Read	type i diabetes mellitus with retinopathy
C10E712	Read	insulin dependent diabetes mellitus with retinopathy
C10E800	Read	type 1 diabetes mellitus - poor control
C10E811	Read	type i diabetes mellitus - poor control
C10E812	Read	insulin dependent diabetes mellitus - poor control
C10E900	Read	type 1 diabetes mellitus maturity onset
C10E911	Read	type i diabetes mellitus maturity onset
C10E912	Read	insulin dependent diabetes maturity onset
C10EA00	Read	type 1 diabetes mellitus without complication
C10EA11	Read	type i diabetes mellitus without complication
C10EA12	Read	insulin-dependent diabetes without complication
C10EB00	Read	type 1 diabetes mellitus with mononeuropathy
C10EC00	Read	type 1 diabetes mellitus with polyneuropathy
C10EC11	Read	type i diabetes mellitus with polyneuropathy

C10EC12	Read	insulin dependent diabetes mellitus with polyneuropathy
C10ED00	Read	type 1 diabetes mellitus with nephropathy
C10ED12	Read	insulin dependent diabetes mellitus with nephropathy
C10EE00	Read	type 1 diabetes mellitus with hypoglycaemic coma
C10EE12	Read	insulin dependent diabetes mellitus with hypoglycaemic coma
C10EF00	Read	type 1 diabetes mellitus with diabetic cataract
C10EF12	Read	insulin dependent diabetes mellitus with diabetic cataract
C10EG00	Read	type 1 diabetes mellitus with peripheral angiopathy
C10EH00	Read	type 1 diabetes mellitus with arthropathy
C10EJ00	Read	type 1 diabetes mellitus with neuropathic arthropathy
C10EK00	Read	type 1 diabetes mellitus with persistent proteinuria
C10EL00	Read	type 1 diabetes mellitus with persistent microalbuminuria
C10EL11	Read	type i diabetes mellitus with persistent microalbuminuria
C10EM00	Read	type 1 diabetes mellitus with ketoacidosis
C10EM11	Read	type i diabetes mellitus with ketoacidosis
C10EN00	Read	type 1 diabetes mellitus with ketoacidotic coma
C10EN11	Read	type i diabetes mellitus with ketoacidotic coma
C10EP00	Read	type 1 diabetes mellitus with exudative maculopathy
C10EP11	Read	type i diabetes mellitus with exudative maculopathy
C10EQ00	Read	type 1 diabetes mellitus with gastroparesis
C10ER00	Read	latent autoimmune diabetes mellitus in adult
C10F.00	Read	type 2 diabetes mellitus
C10F000	Read	type 2 diabetes mellitus with renal complications
C10F011	Read	type ii diabetes mellitus with renal complications
C10F100	Read	type 2 diabetes mellitus with ophthalmic complications
C10F.11	Read	type ii diabetes mellitus
C10F111	Read	type ii diabetes mellitus with ophthalmic complications
C10F200	Read	type 2 diabetes mellitus with neurological complications
C10F211	Read	type ii diabetes mellitus with neurological complications
C10F300	Read	type 2 diabetes mellitus with multiple complications
C10F311	Read	type ii diabetes mellitus with multiple complications
C10F400	Read	type 2 diabetes mellitus with ulcer
C10F411	Read	type ii diabetes mellitus with ulcer
C10F500	Read	type 2 diabetes mellitus with gangrene
C10F511	Read	type ii diabetes mellitus with gangrene
C10F600	Read	type 2 diabetes mellitus with retinopathy
C10F611	Read	type ii diabetes mellitus with retinopathy
C10F700	Read	type 2 diabetes mellitus - poor control
C10F711	Read	type ii diabetes mellitus - poor control
C10F900	Read	type 2 diabetes mellitus without complication
C10F911	Read	type ii diabetes mellitus without complication
C10FA00	Read	type 2 diabetes mellitus with mononeuropathy
C10FA11	Read	type ii diabetes mellitus with mononeuropathy
C10FB00	Read	type 2 diabetes mellitus with polyneuropathy
C10FB11	Read	type ii diabetes mellitus with polyneuropathy

C10FC00	Read	type 2 diabetes mellitus with nephropathy
C10FC11	Read	type ii diabetes mellitus with nephropathy
C10FD00	Read	type 2 diabetes mellitus with hypoglycaemic coma
C10FD11	Read	type ii diabetes mellitus with hypoglycaemic coma
C10FE00	Read	type 2 diabetes mellitus with diabetic cataract
C10FE11	Read	type ii diabetes mellitus with diabetic cataract
C10FF00	Read	type 2 diabetes mellitus with peripheral angiopathy
C10FF11	Read	type ii diabetes mellitus with peripheral angiopathy
C10FG00	Read	type 2 diabetes mellitus with arthropathy
C10FG11	Read	type ii diabetes mellitus with arthropathy
C10FH00	Read	type 2 diabetes mellitus with neuropathic arthropathy
C10FJ00	Read	insulin treated type 2 diabetes mellitus
C10FJ11	Read	insulin treated type ii diabetes mellitus
C10FK00	Read	hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10FK11	Read	hyperosmolar non-ketotic state in type ii diabetes mellitus
C10FL00	Read	type 2 diabetes mellitus with persistent proteinuria
C10FL11	Read	type ii diabetes mellitus with persistent proteinuria
C10FM00	Read	type 2 diabetes mellitus with persistent microalbuminuria
C10FM11	Read	type ii diabetes mellitus with persistent microalbuminuria
C10FN00	Read	type 2 diabetes mellitus with ketoacidosis
C10FN11	Read	type ii diabetes mellitus with ketoacidosis
C10FP00	Read	type 2 diabetes mellitus with ketoacidotic coma
C10FP11	Read	type ii diabetes mellitus with ketoacidotic coma
C10FQ00	Read	type 2 diabetes mellitus with exudative maculopathy
C10FR00	Read	type 2 diabetes mellitus with gastroparesis
C10FS00	Read	maternally inherited diabetes mellitus
C10G.00	Read	secondary pancreatic diabetes mellitus
C10G000	Read	secondary pancreatic diabetes mellitus without complication
C10M.00	Read	lipoatrophic diabetes mellitus
C10N.00	Read	secondary diabetes mellitus
C10N000	Read	secondary diabetes mellitus without complication
C10N100	Read	cystic fibrosis related diabetes mellitus
C10y.00	Read	diabetes mellitus with other specified manifestation
C10y100	Read	diabetes mellitus
C10yy00	Read	other specified diabetes mellitus with other spec comps
C10yz00	Read	diabetes mellitus nos with other specified manifestation
C10z.00	Read	diabetes mellitus with unspecified complication
C10z000	Read	diabetes mellitus
C10z100	Read	diabetes mellitus
C10zy00	Read	other specified diabetes mellitus with unspecified comps
C10zz00	Read	diabetes mellitus nos with unspecified complication
C110000	Read	iatrogenic hyperinsulinism
C110.11	Read	insulin coma
C11y000	Read	steroid induced diabetes
C314.11	Read	renal diabetes

C350011	Read	bronzed diabetes
Cyu2.00	Read	[x]diabetes mellitus
Cyu2000	Read	[x]other specified diabetes mellitus
Cyu2300	Read	[x]unspecified diabetes mellitus with renal complications
F171100	Read	autonomic neuropathy due to diabetes
F345000	Read	diabetic mononeuritis multiplex
F35z000	Read	diabetic mononeuritis nos
F372.00	Read	polyneuropathy in diabetes
F372000	Read	acute painful diabetic neuropathy
F372100	Read	chronic painful diabetic neuropathy
F372.11	Read	diabetic polyneuropathy
F372.12	Read	diabetic neuropathy
F372200	Read	asymptomatic diabetic neuropathy
F381300	Read	myasthenic syndrome due to diabetic amyotrophy
F381311	Read	diabetic amyotrophy
F3y0.00	Read	diabetic mononeuropathy
F420.00	Read	diabetic retinopathy
F420000	Read	background diabetic retinopathy
F420100	Read	proliferative diabetic retinopathy
F420200	Read	preproliferative diabetic retinopathy
F420300	Read	advanced diabetic maculopathy
F420400	Read	diabetic maculopathy
F420500	Read	advanced diabetic retinal disease
F420600	Read	non proliferative diabetic retinopathy
F420700	Read	high risk proliferative diabetic retinopathy
F420800	Read	high risk non proliferative diabetic retinopathy
F420z00	Read	diabetic retinopathy nos
F440700	Read	diabetic iritis
F464000	Read	diabetic cataract
G73y000	Read	diabetic peripheral angiopathy
K01x100	Read	nephrotic syndrome in diabetes mellitus
K01x111	Read	kimmelstiel - wilson disease
K08yA00	Read	proteinuric diabetic nephropathy
K08yA11	Read	clinical diabetic nephropathy
K27y700	Read	erectile dysfunction due to diabetes mellitus
Kyu0300	Read	[x]glomerular disorders in diabetes mellitus
L180500	Read	pre-existing diabetes mellitus
L180600	Read	pre-existing diabetes mellitus
L180X00	Read	pre-existing diabetes mellitus
M037200	Read	cellulitis in diabetic foot
M21yC00	Read	insulin lipohypertrophy
M21yC11	Read	insulin site lipohypertrophy
M271000	Read	ischaemic ulcer diabetic foot
M271100	Read	neuropathic diabetic ulcer - foot
M271200	Read	mixed diabetic ulcer - foot

N030000	Read	diabetic cheiroarthropathy
N030011	Read	diabetic cheiropathy
N030100	Read	diabetic charcot arthropathy
R054200	Read	[d]gangrene of toe in diabetic
R054300	Read	[d]widespread diabetic foot gangrene
R105712	Read	[d]hyperglycaemia
Ryu8A00	Read	[x]hyperglycaemia
TJ23.00	Read	adverse reaction to insulins and antidiabetic agents
TJ23000	Read	adverse reaction to insulins
TJ23200	Read	adverse reaction to chlorpropamide
TJ23300	Read	adverse reaction to glibenclamide
TJ23400	Read	adverse reaction to gliclazide
TJ23500	Read	adverse reaction to glipizide
TJ23800	Read	adverse reaction to tolazamide
TJ23900	Read	adverse reaction to tolbutamide
TJ23A00	Read	adverse reaction to metformin hydrochloride
TJ23B00	Read	adverse reaction to glucagon
TJ23z00	Read	adverse reaction to insulins and antidiabetic agents nos
U602300	Read	[x]insul/oral hypoglyc drugs caus adverse eff therapeut use
U602311	Read	[x] adverse reaction to insulins and antidiabetic agents
U602312	Read	[x] adverse reaction to insulins
U602315	Read	[x] adverse reaction to glibenclamide
U602316	Read	[x] adverse reaction to gliclazide
U602317	Read	[x] adverse reaction to glipzide
U602318	Read	[x] adverse reaction to gliquidone
U60231A	Read	[x] adverse reaction to tolazamide
U60231B	Read	[x] adverse reaction to tolbutamide
U60231C	Read	[x] adverse reaction to metformin hydrochloride
U60231E	Read	[x] adverse reaction to insulins and antidiabetic agents nos
ZC2C800	Read	dietary advice for diabetes mellitus
ZC2C900	Read	dietary advice for type i diabetes
ZC2CA00	Read	dietary advice for type ii diabetes
ZL22500	Read	under care of diabetic liaison nurse
ZL62500	Read	referral to diabetes nurse
ZL62600	Read	referral to diabetic liaison nurse
ZLA2500	Read	seen by diabetic liaison nurse
ZLD7500	Read	discharge by diabetic liaison nurse
ZRB4.00	Read	diabetes clinic satisfaction questionnaire
ZRB4.11	Read	csq - diabetes clinic satisfaction questionnaire
ZRB5.00	Read	diabetes treatment satisfaction questionnaire
ZRB5.11	Read	dtsq - diabetes treatment satisfaction questionnaire
ZRB6.00	Read	diabetes wellbeing questionnaire
ZRB6.11	Read	dwbq - diabetes wellbeing questionnaire
ZRBa.00	Read	education score - diabetes
ZRbH.00	Read	perceived control of insulin-dependent diabetes

ZV65312	Read	[v]dietary counselling in diabetes mellitus
ZV6DA00	Read	[v]admitted for commencement of insulin
ZV6DB00	Read	[v]admitted for conversion to insulin
E10	ICD-10	insulin-dependent diabetes mellitus
E10.0	ICD-10	insulin-dependent diabetes mellitus
E10.1	ICD-10	insulin-dependent diabetes mellitus
E10.2	ICD-10	insulin-dependent diabetes mellitus
E10.3	ICD-10	insulin-dependent diabetes mellitus
E10.4	ICD-10	insulin-dependent diabetes mellitus
E10.5	ICD-10	insulin-dependent diabetes mellitus
E10.6	ICD-10	insulin-dependent diabetes mellitus
E10.7	ICD-10	insulin-dependent diabetes mellitus
E10.8	ICD-10	insulin-dependent diabetes mellitus
E10.9	ICD-10	insulin-dependent diabetes mellitus
E11	ICD-10	non-insulin-dependent diabetes mellitus
E11.0	ICD-10	non-insulin-dependent diabetes mellitus
E11.1	ICD-10	non-insulin-dependent diabetes mellitus
E11.2	ICD-10	non-insulin-dependent diabetes mellitus
E11.3	ICD-10	non-insulin-dependent diabetes mellitus
E11.4	ICD-10	non-insulin-dependent diabetes mellitus
E11.5	ICD-10	non-insulin-dependent diabetes mellitus
E11.6	ICD-10	non-insulin-dependent diabetes mellitus
E11.7	ICD-10	non-insulin-dependent diabetes mellitus
E11.8	ICD-10	non-insulin-dependent diabetes mellitus
E11.9	ICD-10	non-insulin-dependent diabetes mellitus
E13	ICD-10	other specified diabetes mellitus
E13.0	ICD-10	other specified diabetes mellitus
E13.1	ICD-10	other specified diabetes mellitus
E13.2	ICD-10	other specified diabetes mellitus
E13.3	ICD-10	other specified diabetes mellitus
E13.4	ICD-10	other specified diabetes mellitus
E13.5	ICD-10	other specified diabetes mellitus
E13.6	ICD-10	other specified diabetes mellitus
E13.7	ICD-10	other specified diabetes mellitus
E13.8	ICD-10	other specified diabetes mellitus
E13.9	ICD-10	other specified diabetes mellitus
E14	ICD-10	unspecified diabetes mellitus
E14.0	ICD-10	unspecified diabetes mellitus
E14.1	ICD-10	unspecified diabetes mellitus
E14.2	ICD-10	unspecified diabetes mellitus
E14.3	ICD-10	unspecified diabetes mellitus
E14.4	ICD-10	unspecified diabetes mellitus
E14.5	ICD-10	unspecified diabetes mellitus
E14.6	ICD-10	unspecified diabetes mellitus
E14.7	ICD-10	unspecified diabetes mellitus

E14.8	ICD-10	unspecified diabetes mellitus
E14.9	ICD-10	unspecified diabetes mellitus
G59.0	ICD-10	diabetic mononeuropathy
G63.2	ICD-10	diabetic polyneuropathy
H28.0	ICD-10	diabetic cataract
H36.0	ICD-10	diabetic retinopathy
M14.2	ICD-10	diabetic arthropathy
N08.3	ICD-10	glomerular disorders in diabetes mellitus
Y42.3	ICD-10	insulin and oral hypoglycaemic [antidiabetic] drugs

Death

Date of death registered in CPRD

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	a) 1, 3 b) 3	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and time period within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1.1) 1, 3 1.2) 1, 3 1.3) 3
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	5		
Objectives	3	State specific objectives, including any prespecified hypotheses	5		
Methods					
Study Design	4	Present key elements of study design early in the paper	5-6		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7		

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	a) 5-7 b) Not applicable	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	6.1) 5-7 6.2) 5-6, 15 6.3) Not needed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	5-7	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	5-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7		

Bias	9	Describe any efforts to address potential sources of bias	8-10		
Study size	10	Explain how the study size was arrived at	6-7		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5-10		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	8-10		
Data access and cleaning methods		5-7		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	12.1) 5-6 12.2) 5-7

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		5-6		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	12.3) 5-6
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	6, 10-13	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	13.1) 6, 10-13
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	10-11, Table 1		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure	10-13		

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10-13		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10-13		
Discussion					
Key results	18	Summarise key results with reference to study objectives	13		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-15	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	13-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	18,19		

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	18		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20		
Accessibility of protocol, raw data, and programming code		..	20, Appendix, protocol made available for reviewers	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	20, Appendix, protocol made available for reviewers

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

36/bmjopen-2016-012818 on 9 January 2017. Downloaded from

Correction: Adherence to guidelines for creatinine and potassium monitoring and discontinuation following renin–angiotensin system blockade: a UK general practice-based cohort study

Schmidt M, Mansfield KE, Bhaskaran K, *et al*. Adherence to guidelines for creatinine and potassium monitoring and discontinuation following renin–angiotensin system blockade: a UK general practice-based cohort study. *BMJ Open* 2017;**7**:e012818. doi: 10.1136/bmjopen-2016-012818

In the 3rd column of Table 5 the heading 'Serum potassium increase ≥30%*' should read 'Serum potassium increase >6 mmol/L'.

BMJ Open 2017;**7**:e012818corr1. doi:10.1136/bmjopen-2016-012818corr1