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Application of prescribing recommendations in older people with reduced kidney function in general practice: a cross-sectional study

Wood S.^a, Petty D.^b, Glidewell L.^a, Raynor D. K.^c

- a. Academic Unit of Primary Care, Institute of Health Sciences, University of Leeds
- b. School of Pharmacy and Medical Sciences, University of Bradford
- c. School of Healthcare, University of Leeds

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Corresponding Author:

Dr Su Wood

Academic Unit of Primary Care
Leeds Institute of Health Sciences
University of Leeds
Worsley Building
University of Leeds
LS2 9UT

S.I.Wood@leeds.ac.uk

Abstract

Background

Kidney function reduces with age, increasing the risk of harm from increased blood levels of many medicines. Although estimated glomerular filtration rate (eGFR) is reported, for prescribing decisions in those aged ≥ 65 years, creatinine clearance (Cockcroft–Gault) gives a more accurate estimate of kidney function.

Aim

To explore the extent of prescribing outside recommendations for people aged ≥ 65 years with reduced kidney function in primary care and to assess the impact of using eGFR instead of creatinine clearance to calculate kidney function.

Design and setting

A cross-sectional survey of anonymised prescribing data in people aged ≥ 65 years from all 80 general practices (70 900 patients) in a North of England former primary care trust.

Method

The prevalence of prescribing outside recommendations was analysed for eight exemplar drugs. Data were collected for age, sex, actual weight, serum creatinine and eGFR. Kidney function as creatinine clearance (Cockcroft–Gault) was calculated using actual body weight and estimated ideal body weight.

Results

Kidney function was too low for recommended prescribing in 4–40% of people aged ≥ 65 years, and in 24–80% of people aged ≥ 85 years, despite more than 90% of patients having recent recorded kidney function results. Using eGFR overestimated kidney function for 3–28% of those aged ≥ 65 years, and for 13–58% of those aged ≥ 85 years. Increased age predicted higher odds of having a kidney function estimate too low for recommended prescribing of the study drugs.

Conclusion

Prescribing recommendations when kidney function is reduced are not applied for many people aged ≥ 65 years in primary care. Using eGFR considerably overestimates kidney function for prescribing, so creatinine clearance (Cockcroft–Gault) should be assessed when prescribing for these people. Interventions are needed to aid prescribers when kidney function is reduced.

How this fits in

- Internationally, studies have found that recommendations for prescribing in patients with reduced kidney function are often not applied, with increased risk of patient harm and hospital admissions.
- How medicines affected by renal impairment are prescribed to those aged ≥ 65 years in UK primary care was previously unknown.
- This survey found many people aged ≥ 65 years in UK general practice had a recorded estimate of kidney function, but not had drugs adjusted. Data were available to calculate creatinine clearance (Cockcroft-Gault); when creatinine clearance estimates were applied even more patients were identified as at a risk.
- The findings from this study have informed an update to the *British National Formulary* to recommend the Cockcroft and Gault formula as the preferred method for estimating renal function in elderly patients.

Introduction

Prescribing when a patient's kidney function is reduced should include consideration of the risk from increased blood levels when drugs excreted renally are eliminated more slowly.¹ With ageing, a progressive loss of functional capabilities in most body organs, changed responses to receptor stimulation and decreased homeostatic mechanisms, have implications for drug handling. Of these changes, excretion is the most significant and important age-related pharmacokinetic change, and is both predictable and measurable. Two-thirds of people aged 70–80 years have approximately half the kidney function of a 'young adult'^{2,3}, with an average decline of approximately 1ml/min annually after 30yrs old, decreasing more rapidly after 65⁴.

Harm and hospitalisation are potential outcomes when recommendations for altering prescribing are not applied. In other European countries, a large primary care study found drug use not recommended when kidney function was reduced in people aged ≥ 65 years caused a 40% increase

in all-cause mortality,⁵ a third of hospital admissions related to adverse drug reactions were judged to be due to renal impairment in those aged ≥65 years⁶, and one-third of adverse drug reactions in people aged ≥65 years during their hospital stay were associated with reduced kidney function⁷.

The National Institute for Health and Care Excellence (NICE) guidance on chronic kidney disease (CKD)⁸ recommends 'review of medications', and now the NICE acute kidney injury (AKI) guidelines⁹ and alerts are requiring GPs to review medicines after an AKI episode. These include drugs that are a direct risk to the kidney, such as non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs); and drugs that are more likely to cause adverse drug reactions when blood levels are increased as a result of slower elimination, such as metformin, gabapentin, and pregabalin). Reduced kidney function can also reduce the effectiveness of some drugs, such as thiazides and nitrofurantoin.

Estimated Glomerular Filtration Rate (eGFR) has been reported with pathology results since the introduction of the CKD guidelines in 2003, and is calculated using the 'Modification of Diet in Renal Disease' (MDRD) equation¹⁰, and more recently the CKD Epidemiology Collaboration (CKD-EPI) formula¹¹. eGFR was developed to provide staging for CKD and does not have a weight component, therefore, making it straight forward for pathology to report. Drug dosing studies, however, have used the Cockcroft-Gault equation¹² to estimate kidney function as 'creatinine clearance' (CrCl). Cockcroft-Gault includes a weight component: ideal body weight to factor muscle mass, not body fat, as creatinine is produced from muscle turnover.¹³ The equations give progressively different results with increasing age, and studies focussed on prescribing for older people have concluded that Cockcroft-Gault should continue to be used for prescribing decisions.^{14,15} Studies using gentamicin have shown that blood levels are more closely estimated by creatinine clearance: while Cockcroft-Gault underestimates kidney function and effect on drug blood levels by 10% across all older ages, eGFR overestimates kidney function increasingly as age increases by 29% up to 69%,¹⁶ meaning the safer estimate to use is Cockcroft-Gault^{17,18}. Use of eGFR for prescribing decisions, rather than Cockcroft-Gault, has been shown to lead to more frequent major bleeding events with glycoprotein-IIb/IIIa-inhibitors¹⁹, and increases the likelihood of adverse drug reactions²⁰, hospitalisation⁶, or ineffectiveness²¹.

International studies have found prescribing outside recommendations for older people with reduced kidney function^{5,22}, but, while a similar problem has been shown in a UK hospital²³, to the authors' knowledge, no studies have been conducted in UK general practice. The aim of this study was to assess whether drugs are prescribed according to the *British National Formulary* (BNF)¹³ and Electronic Medicines Compendium (eMC), summary of product characteristics (www.medicines.org.uk/emc/) when kidney function is reduced, for people aged ≥65 years across a healthcare population. The study also set out to determine the impact of using eGFR instead of creatinine clearance (Cockcroft-Gault) on drug and dosage decisions.

Method

A cross-sectional survey was conducted on prescribing data from all 80 general practices in a north of England former Primary Care Trust (PCT).

Two drugs, or drug classes, were identified in each of four categories in reduced kidney function:

- Drugs that should be avoided.
- Drugs that should have a dose reduction.
- Drugs that are ineffective.
- Drugs that require caution as they are known to frequently cause adverse drug reactions in renal impairment.

The eight choices of drugs were based on findings in a previous case-note-review of five practices in the PCT²⁴. Drugs were selected on the strength of the BNF/SPC (summaries of product characteristics) recommendations and the literature,^{5,21-22,25-32} impact on patients,^{28,33-40} and independent expert advice from a renal physician, geriatrician, hospital renal pharmacist, and an antibiotics expert pharmacist (Table 1).

Data collection

Data collection were age, sex, actual weight and date last recorded, serum creatinine and date last recorded, eGFR and date last recorded, or no eGFR ever recorded. These data were used to calculate creatinine clearance using actual body weight (CrCl-AW) and creatinine clearance using estimated ideal body weight (CrCl-IBW).

Searches were run for all patients prescribed each drug by a PCT data analyst at the end of October 2011 to extract data from general practice systems. All practices used the TPP SystemOne clinical information system.

Data analysis

Data quality and missing data analyses were performed, and a descriptive analysis to give:

- The numbers of people aged ≥ 65 years with eGFR < 60 ml/minute/1.73 m² (NICE CKD level).
- The numbers of people aged ≥ 65 years taking each of the study drugs.

For each of the eight drugs the number of patients in age bands ≥ 65 , 65-74, 75-85, and ≥ 85 yrs were assessed; for seven drugs on the repeat medication list, and for nitrofurantoin, at least one prescription in the previous 12 months, described as 'patient drug events'. For each drug the following data were collected and/or calculated:

- The number of 'patient drug events' where a serum creatinine level had been recorded in the previous 15 months, and the estimated kidney function was too low for the recommended use, calculated using eGFR, CrCl-AW and CrCl-IBW.
- The number of 'patient drug events' that would be missed if eGFR, or actual weight in Cockcroft-Gault, were used.
- The number of 'patient drug events' for each drug where there was no kidney function estimate on the record.
- Spearman correlation between age and level of kidney function (using SPSS version 21).
- Logistic regression analysis to explore the effect of people aged ≥ 65 years on the likelihood of having a kidney function too low for appropriate prescribing of the drug (using SPSS version 21).

Data oversight was provided by the supervisory research team.

Results

Thirteen percent of the PCT population were aged ≥ 65 years (70,900/ 549,533), and 1.8% (9,723) were aged ≥ 85 years; 26% of those aged ≥ 65 years, and 50% of those aged ≥ 85 years, had a documented eGFR < 60 ml/min/1.73m².

A recent kidney function test in the previous 15 months was found on the patient record for 83% of patients prescribed NSAIDs, and for 97% prescribed metformin. Only 0.2%-9.7% of the patient drug events had no eGFR, and 0%-5.7% did not have the parameters to calculate CrCl-IBW.

Figure 1 shows the numbers of patients prescribed each of the drugs studied; an ACEI or ARB was found to be prescribed for 40% of the 70,900 patients ≥ 65 years.

Prevalence of kidney function found to be too low for recommended prescribing

The number of patient drug events where a recent kidney function was available but was too low for the recommended drug use ranged from 39.6% (95% CI = 35.8-43.4%) for nitrofurantoin to 3.5% (95% CI = 0-11.2%) for NSAIDs in those aged ≥ 65 years, and 79.5% (95% CI = 75.1-83.9%) (nitrofurantoin) to 24.2% (95% CI = 16.4-32.1%) (metformin) for the patients aged ≥ 85 years (Table 2).

Figure 2 shows an example line plot charting the range of kidney function (CrCl-IBW in the previous 15 months) for nitrofurantoin at each age level for those aged ≥ 65 years. All cases below the line at CrCl-IBW 45ml/min had a kidney function likely to be too low for the drug to be effective, and more likely to cause adverse drug reactions.²⁸

Impact of the different equations to estimate kidney function

Using eGFR to estimate the level of kidney function suggested a much lower number of alterations required for drug or dose choice than would be the case using CrCl-IBW (Figure 3). Use of eGFR, rather than CrCl-IBW, would mean that the suggested altering or stopping of the study drugs would be missed for 3% to 28% of those aged ≥ 65 years, and 13% to 58% for those aged ≥ 85 years.

Using actual weight in the Cockcroft-Gault equation also found fewer patients that might need prescribing alteration, but to a lesser extent than using eGFR: the suggested altering or stopping of the study drugs would be missed for 1-10% of patients aged ≥ 65 years..

Effect of increased age

Kidney function reduced with age for all groups studied using Spearman correlation, for example, for nitrofurantoin [$r = -0.608$, $n = 3,185$ $p < 0.001$].

Logistic regression analysis found that, compared to age band 65-74yrs, 'patient drug events' for those aged 75-84yrs had higher odds of being prescribed drugs where the kidney function was too low, and even higher odds for those ≥ 85 years (Table 3). For example, for nitrofurantoin, using CrCl-IBW the patient drug events for people aged 74-84 years had 5.64 (95% CI = 4.58-6.95) times greater odds of being prescribed drugs where the kidney function was too low for recommended use, and 29.23 (95% CI = 22.75-37.56) times greater odds for those aged ≥ 85 years.

Discussion

Summary

Prescribing of drugs outside recommendations for use in reduced kidney function was widespread for the eight representative drugs in the study population. Using eGFR, rather than CrCl-IBW, considerably underestimated potential risk to patients, particularly those aged ≥ 85 years.

Strengths and limitations

The study population was from a large PCT with a broad range of prescribers. A deprivation score higher than the England average, a lower life expectancy, and a slightly younger population⁴⁰, suggests that the study findings might be an under-estimation of the problem in the UK. Only a small number of data were excluded, where no kidney function data was available, giving confidence in the findings being representative.

Anonymised 'patient drug events' were collected, but it is likely that many were prescribed more than one drug. Inferences cannot be made on the group of drugs as a whole in this study, or the prevalence of a patient having more than one drug affected by level of kidney function. A case-note-review in five GP practices found that 25% of patients aged ≥ 65 years were prescribed an average of two drugs where the kidney function was too low for recommended use, and 70 different drugs were involved²⁴.

Comparison with existing literature

International prevalence studies in primary and secondary care^{5,22,25-32}, have reported high numbers of drug use and dosing outside recommendations. A French multi-centre prospective primary care study found 13.3% of patients ≥ 65 years with a kidney function too low for recommended use, 52.5% in those with eGFR 30–59, and 96% with eGFR < 30 ml/minute/1.73 m².⁵ A retrospective case-record analysis from patients over 70 years in a UK hospital found 13% having 'potentially inappropriate prescribing'.²³

A recent kidney function level was recorded in the patient record for most (90%) people aged ≥ 65 years prescribed the included drugs in the current study. The UK Quality Outcomes Framework (QOF)⁴⁸ targets may have helped as kidney function testing has been incentivised, for example in diabetes. However, renal impairment did not seem to lead to altered prescribing in all four categories of drugs studied, which may impact on patient safety from increased blood levels, sensitivity, or ineffectiveness. For all drugs studied, the dose could have been reduced or an alternative treatment chosen, such as atorvastatin, which is not affected by level of kidney function, instead of simvastatin, or alternative anti-hypertensive or antidiabetic medication.

Increased age predicted higher odds of having a kidney function estimate too low for recommended prescribing. This analysis did not address the possibility of confounders, but there is broad evidence of progressive loss of kidney function with aging^{2,3}. Those aged ≥ 65 years are more likely to have a lower kidney function, and so a lower reserve to react to assaults such as dehydration or nephrotoxicity of drugs. Renal impairment, polypharmacy, and identified drugs such as NSAIDs are included as 'deficits' identified which can occur with aging and combine to increase 'frailty' which in turn increases the risk of adverse outcomes.⁴⁴

The equation used to estimate kidney function for prescribing decisions made a substantial difference to whether prescribing might be reviewed because of renal impairment in people aged ≥ 65 years. Many other studies report underestimation of kidney function when different equations

are used, ranging from an Italian hospital study that found 9.8% dosing outside recommendations if eGFR was used,⁵⁰ to a Spanish hospital study of nephrotoxic drugs which found a 65% dosing outside recommendations.⁵¹ A US primary care study found 40% of patients should have been recommended different doses, and 22% of those reviewed would have had different recommendations based on the equation chosen.⁵² The current study found that using eGFR would mean that many people needing a review of prescribing would be missed. It also showed that using actual weight in the Cockcroft-Gault equation would miss drugs that might need review; an ideal body weight, or actual if lower body weight, should be used in the Cockcroft-Gault calculation to give an indication of muscle mass.^{13,14}

Implications for practice and research

Treatment of multi-morbidity has resulted in the increasing numbers of older people being prescribed more long term medicines, the mean being seven for people aged ≥ 80 years,⁵³ and 60% of the billion items dispensed in the community in England are for people aged ≥ 65 years.⁵⁴ As many older people are prescribed multiple medications, there is the likelihood that people will be taking more than one drug eliminated via the kidneys, increasing the complexity of the impact. Applying BNF recommendations for prescribing (or avoidance of prescribing) in renal impairment could reduce the risk of adverse drug reactions, particularly for the oldest and most frail patient.

In 2017 the BNF reviewed this evidence and updated their recommendation in the 'Prescribing in Renal Impairment' section to state that '*...the Cockcroft and Gault formula is the preferred method for estimating renal function in elderly patients aged 75 years and over*'^{13,55}. Electronic patient record systems, e.g. SystemOne and EMIS, have a 'renal calculator' to enable prescribers to calculate, and code, creatinine clearance Cockcroft-Gault; smartphone apps are also available and easy to use. Pharmacists have been shown to significantly reduce prescribing outside recommendations in reduced kidney function⁵⁶; they can audit, highlight for review, and do medication reviews, for high risk populations.

The data required to calculate creatinine clearance and identify affected drugs are already available in the prescribing and consultation systems; it would be possible to develop patient and drug specific decision support to suggest safer doses or alternative drugs, both at initiation and at medication review. Further research has been undertaken to understand why GPs often do not apply renal impairment recommendations when prescribing, and to inform an intervention to aid prescribing in reduced kidney function.⁵⁷

Guidelines should consider recommendations for drug use and level of kidney function.⁵⁸ CKD and AKI guidelines could include guidance on prescribing (and avoiding prescribing) to both reduce risk to the kidney, and reduce adverse drug reactions from renally excreted drugs. The NHS England 'Think Kidneys' resources include an 'AKI medicines optimisation toolkit' (www.thinkkidneys.nhs.uk) aimed at prescribers in hospitals which could be usefully extended to primary care. Non-prescription medicines could be important for future research, for example NSAIDs bought from pharmacies or retail outlets.

Conclusion

Prescribing recommendations in reduced kidney function were not applied for a large number of people aged ≥ 65 years, in this first UK general practice study. Assessment of Cockcroft-Gault creatinine clearance to estimate kidney function level when making prescribing decisions for people aged ≥ 65 years will find more at risk of higher drug blood levels than eGFR, and reduce the risk of harm.

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Ethical approval

Not required for this study.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

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category: recommendation when kidney function is reduced	drug	BNF ¹³ / SPC recommendation	% prescribing outside recommendations, or dose suggested may need review, in a case-note review study ²⁴	references where prescribing outside recommendations was reported	evidence of potential impact for patients	comments from independent experts in the field (a renal physician with a national role, geriatrician, hospital renal pharmacist, and an antibiotics expert pharmacist)
avoid	alendronic acid	SPC - 'not recommended' BNF: 'avoid if CrCl<35ml/min'	4.0	Breton et al (2011) ⁵ Khanal et al.(2015) ²²	<ul style="list-style-type: none"> Alendronic acid accumulates in the bones, with a terminal half-life of over ten years.⁴¹ MHRA review of risks: associated with an increased risk of atypical stress fractures of the proximal femoral shaft; low but increased risk of atrial fibrillation.³³ 	Agreed to be included.
	metformin	SPC: 'contra-indication < 30 mL/min'	2.0	Breton et al (2011) ⁵ Khanal et al (2015) ²² Schmidt-Mende et al (2012) ²⁵	<ul style="list-style-type: none"> Increased risk of lactic acidosis especially with dehydration.³⁴ 	Suggested by a renal physician and a geriatrician as they see admissions to hospital caused by metformin when kidney function is low.
reduce the dose	simvastatin	SPC/BNF: 'CrCl < 30 ml/min: dosages above 10 mg/day should be carefully considered and, if deemed necessary, implemented cautiously.'	8.8	Breton et al (2011) ⁵	<ul style="list-style-type: none"> Total drug (AUC) 2-3 times greater when kidney function is low (Personal communication by S Wood to Merck Sharp & Dohme, 12 October 2011) (ie greater than the effect of the drug interaction with amlodipine: AUC for simvastatin increased by 1.58-1.77 fold²⁵) MHRA: 'increased plasma concentrations of simvastatin are associated with an increased risk of myopathy and/or rhabdomyolysis.'³⁵ 	Agreed to be included as a widely used drug with an alternative available (atorvastatin does not need dose alteration when kidney function is low ⁴²).
	gabapentin and pregabalin	table of reduced doses at specified levels of CrCl	0.2	Breton et al (2011) ⁵	<ul style="list-style-type: none"> High risk from the common adverse effects of somnolence, dizziness, ataxia, and fatigue.^{43,44} There has been a 46% rise in prescribing of gabapentin and 53% rise in pregabalin prescribing since 2011.³⁶ 	Added at the suggestion of the renal pharmacist because of frequent side effects seen in the renal unit.
ineffective	thiazides	BNF: 'likely to be ineffective at CrCl<30ml/min'	17.0	Howard et al (2003) ²⁶	<ul style="list-style-type: none"> Unlikely to be effective below 30ml/min.⁴⁵ Increased risk of adverse events such as electrolyte imbalance.²⁵ 	Agreed to be included.
	nitrofurantoin	BNF: 'likely to be ineffective at CrCl<45ml/min' SPC: contraindicated <45ml/min; may be used with caution 30-44ml/min - only prescribe to such patients to treat lower urinary tract infection with suspected or proven multidrug resistant pathogens when the benefits of nitrofurantoin are considered to outweigh the risks of side effects.	0.2 (on repeat)	Farag et al (2014) ²⁷ Geerts et al (2013) ²⁸ Howard and Wood (2013) ²¹	<ul style="list-style-type: none"> MHRA: 'The antibacterial efficacy depends on the renal secretion of nitrofurantoin into the urinary tract. In patients with renal impairment, renal secretion of nitrofurantoin is reduced. This may reduce the antibacterial efficacy, increase the risk of side effects (eg, nausea, vomiting, loss of appetite), and may result in treatment failures.'³⁷ The drug may not work increasing risk from infection.⁴⁶ An audit in a large GP practice found older people with renal impairment were more likely to need further antibiotics²¹ Raised blood levels increases the risk of pulmonary, hepatic, neurological, haematological, and gastrointestinal side effects during treatment.; <50 ml/min significantly increased the risk of pulmonary adverse events leading to hospitalisation (HR 4.1, CI 1.39-13.09)²⁸ 	Agreed to be included; issue raised after discussion with a pharmacist with international expertise in antibiotics.
caution as ADRs are likely	NSAIDs	BNF: 'caution in reduced kidney function' (study parameter set at <30ml/min)	1.7	Evans et al (1995) ²⁹ Guthrie et al (2011) ³⁰ Howard et al (2003) ²⁶ Ingrasciotta et al (2014) ³¹	<ul style="list-style-type: none"> Sodium and water retention may occur and renal function may deteriorate, possibly leading to renal failure; deterioration in renal function has also been reported after topical use.¹³ Chronic use of NSAIDs is a risk factor for progression of CKD.⁸ Frequently cited as causing admissions³⁸ 	Agreed to be included: NSAIDs affect all stages of kidney function and are frequently a cause of hospital admission.
	ACEIs and ARBs	BNF: 'caution in reduced kidney function' (study parameter set at <30ml/min)	26.0	Breton et al (2011) ⁵ Handler et al (2014) ³² Khanal et al (2015) ²² Schmidt-Mende et al (2012) ²⁵	<ul style="list-style-type: none"> Ramipril SPC: CrCl <60 ml/min maximum dose is 5mg.⁴⁷ Hyperkalaemia and other side-effects of ACE inhibitors are more common, and the dose may need to be reduced.¹³ Can cause impairment of kidney function which may progress and become severe (at particular risk are the elderly).¹³ 'STOP-ACE' study is investigating whether the risk to the kidney may outweigh any beneficial effect if <30 ml/min.³⁹ 	Although ACEIs and ARBs are used in renal disease, they can also be nephrotoxic so the consultant experts suggested inclusion.

Abbreviations: ACEIs – angiotensin-converting enzyme inhibitors; ARBs – angiotensin II receptor blockers; CrCl – creatinine clearance; NSAIDs – non-steroidal anti-inflammatories.

Table 1: Choices of drugs and drug classes to investigate in the survey

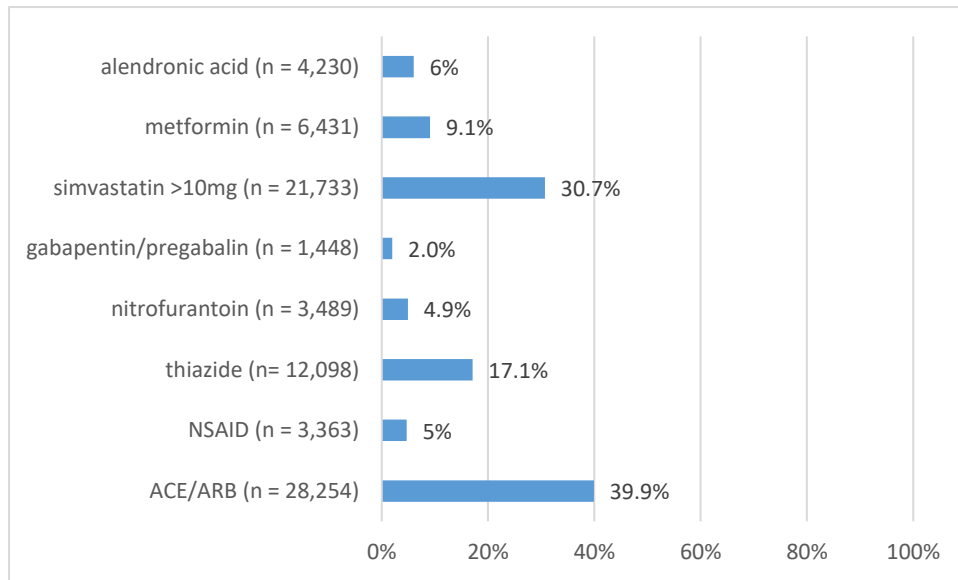


Figure 1: Number of people aged ≥ 65 years in the PCT prescribed each of the study drugs

drug	aged 65yrs and older				aged 65-74yrs				aged 75-84yrs				aged 85yrs and older			
	total	kidney function < recmd'd	%	95% CI	total	kidney function < recmd'd	%	95% CI	total	kidney function < recmd'd	%	95% CI	total	kidney function < recmd'd	%	95% CI
alendronic acid	3,400	804	23.6	(19.2-28.1)	1,120	49	4.4	(3.6-5.1)	1,532	342	22.3	(20.1-24.6)	748	413	55.2	(48.6-61.8)
metformin	6,276	267	4.3	(1.2-7.3)	3,491	30	0.9	(0.81-0.91)	2,319	124	5.3	(4.9-5.8)	466	113	24.2	(16.4-32.1)
simvastatin > 10mg	19,434	1,465	7.5	(6.6-8.5)	9,894	167	1.7	1.65-1.72	7,494	643	8.6	(8.4-8.8)	2,046	655	32.0	(29.9-34.1)
gabapentin or pregabalin	1,209	132	10.9	(0-25.7)	598	43	7.2	(5.0-9.4)	450	56	12.4	(7.6-17.3)	161	33	20.5	(0.3-40.7)
nitrofurantoin	3,185	1,262	39.6	(35.8-43.4)	1,206	141	11.7	(10.0-13.4)	1,242	535	43.1	(39.1-47.0)	737	586	79.5	(75.1-83.9)
thiazide	10,805	797	7.4	(5.7-9.1)	5,371	62	1.2	(1.11-1.20)	4,189	303	7.2	(6.9-7.6)	1,245	432	34.7	(31.1-38.3)
NSAID	2,483	86	3.5	(0-11.2)	1,577	8	0.5	(0.44-0.57)	762	36	4.7	(3.5-5.9)	144	42	29.2	(0.5-57.9)
ACE/ARB	26,109	2,521	9.7	(9.0-10.3)	12,663	288	2.3	(2.24-2.31)	10,280	1,062	10.3	(10.2-10.5)	3,166	1,171	37.0	(35.5-38.5)

Table 2: Number of drugs prescribed for people aged ≥65 years with a kidney function estimate (CrCl-CG IBW) in the previous 15 months below that for recommended use.

Patients with no eGFR on the record, or kidney function data older than 15 months, were excluded for the final analysis (9911/96 900 (10.2%).

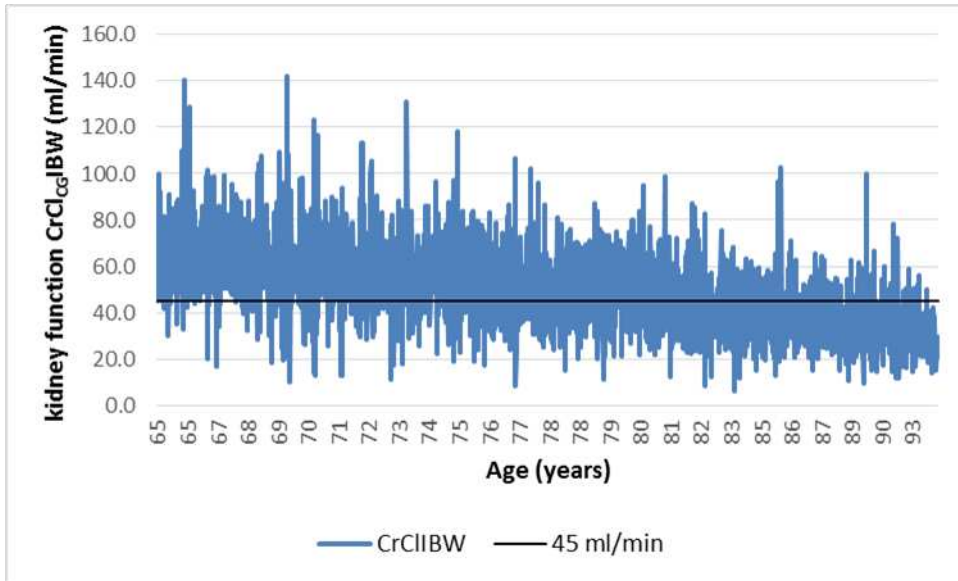


Figure 2: Line plot charting the range of kidney function using creatinine clearance Cockcroft-Gault(CrCl-IBW) within the previous 15 months, for nitrofurantoin prescribed for people at each age level 65 years and older.

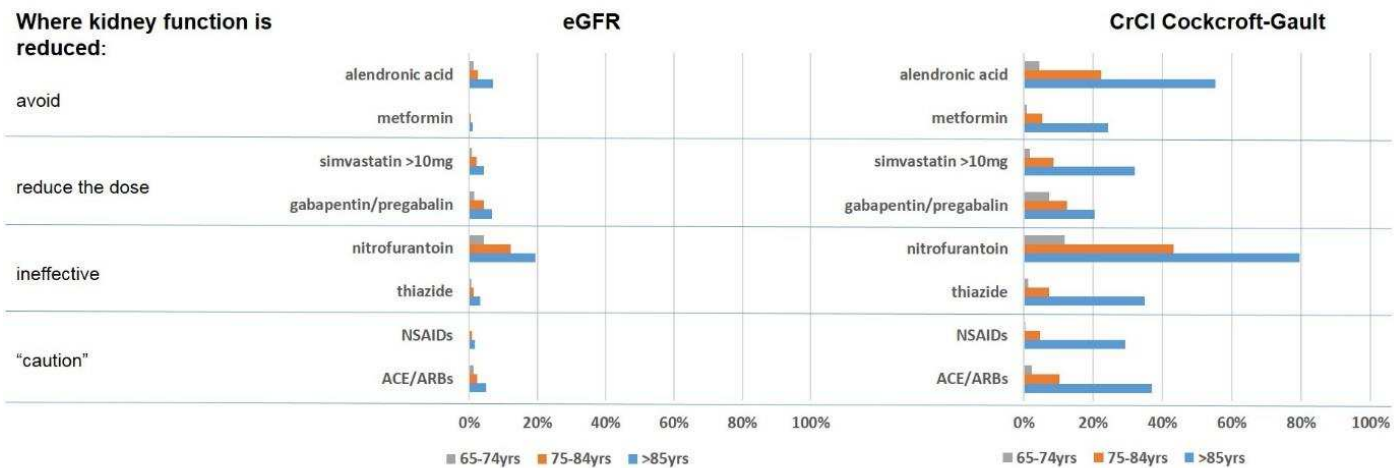


Figure 3: A chart of the percentage of patients found with a kidney function too low for recommended use of the drug using eGFR compared to creatinine clearance (CrCl) Cockcroft-Gault in the 3 older age bands.

		65-74yrs	75-84yrs		85 years and older	
			odds ratio		odds ratio	
alendronic acid	eGFR	1	1.96	(1.08-3.56)	5.49	(3.07-9.81)
	CrCl-CG AW	1	5.11	(3.59-7.26)	24.12	(16.93-34.36)
	CrCl-CG IBW	1	6.28	(4.61-8.57)	26.95	(19.56-37.13)
metformin	eGFR	1	2.26	(0.80-6.35)	6.15	(1.87-6.35)
	CrCl-CG AW	1	5.90	(3.20-10.88)	48.64	(26.70-88.61)
	CrCl-CG IBW	1	6.52	(4.36-9.75)	36.93	(24.33-58.05)
simvastatin >10mg	eGFR	1	2.45	(1.89-3.17)	4.98	(3.71-6.70)
	CrCl-CG AW	1	5.03	(4.06-6.23)	30.64	(24.73-37.95)
	CrCl-CG IBW	1	5.47	(4.60-6.50)	27.43	(22.93-32.80)
thiazides	eGFR	1	2.19	(1.42-3.37)	5.29	(3.32-8.43)
	CrCl-CG AW	1	5.60	(3.96-7.93)	49.67	(35.52-69.44)
	CrCl-CG IBW	1	6.68	(5.07-8.80)	45.50	(34.52-59.98)
NSAIDs	eGFR	1	4.20	(1.05-16.84)	3.68	(0.38-35.57)
	CrCl-CG AW	1	3.50	(1.52-8.03)	43.93	(20.31-95.03)
	CrCl-CG IBW	1	9.73	(4.50-21.03)	80.76	(36.94-176.55)
ACE/ARBs	eGFR	1	1.81	(1.49-2.21)	3.84	(3.09-4.78)
	CrCl-CG AW	1	4.73	(3.98-5.61)	29.01	(24.27-34.38)
	CrCl-CG IBW	1	4.95	(4.33-5.65)	25.22	(21.99-28.93)
Gabapentin/pregabalin	eGFR	1	2.73	(1.27-5.89)	4.28	(1.78-10.26)
	CrCl-CG AW	1	2.97	(1.55-5.72)	9.96	(5.25-18.88)
	CrCl-CG IBW	1	1.83	(1.21-2.79)	3.33	(2.03-5.45)
nitrofurantoin	eGFR	1	3.03	(4.20-4.18)	5.24	(3.78-7.27)
	CrCl-CG AW	1	6.79	(5.16-8.92)	41.33	(30.87-55.36)
	CrCl-CG IBW	1	5.64	(4.58-6.95)	29.23	(22.75-37.56)

Table 3: The odds of having a kidney function too low for the drug with increased age compared to those aged 65-74 years, using eGFR, creatinine clearance calculated using actual weight (CrCl-AW), and ideal body weight (CrCl-IBW)