University Hospitals of North Midlands NHS
NHS Trust

The diagnosis and management of chronic kidney disease in adults

Guidelines for general practice

2017

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On behalf of the Renal Department at UHNM NHS Trust

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Purpose and acknowledgements

These guidelines have been compiled by Dr Andrew McClean (Consultant Nephrologist) on behalf of the Renal Department at University Hospitals of North Midlands, in collaboration with Dr Bhushan Rao (General Practitioner and Clinical Associate at North Staffordshire CCG), and are intended to help local General Practitioners and other primary care health professionals in the management of patients with Chronic Kidney Disease (CKD). They are primarily intended for the use of staff working within the catchment area of University Hospitals of North Midlands.

The information in these guidelines is largely adapted from a variety of NICE clinical guidelines, supplemented with evidence from other government and peer-reviewed sources. A full list of references can be found at the end of this document (Section 11). In compiling this document the author also reviewed previous local guidelines and contributions were made by primary and secondary care colleagues including Dr Ruth Chambers, Dr Kerry Tomlinson, Dr Chris Thompson, Dr Madhu Menon, Dr Richard Fish, and Dr Dominic de Takats.

Disclaimer

The information provided herein is intended to be used for guidance only; clinical judgment must always be applied to individual cases, and patients' wishes should be taken into account in making joint management decisions. These guidelines are based on the evidence and guidelines available at the time of compilation, and new guidelines may become available regionally and nationally which supersede these recommendations. These guidelines may be used by clinicians working outside of the intended user-base, but particular attention must be paid to any differences in local guidelines and referral pathways.

Contents

1. Introduction

Chronic kidney disease (CKD) is not a single entity, but rather it is caused by a heterogeneous group of diseases. It is defined by the presence of reduced kidney function and / or other markers of kidney damage irrespective of the underlying cause, and to distinguish CKD from acute kidney disorders these abnormalities must persist for at least three months. The prognosis and management, however, are influenced by the causative disease.

1.1. Prevalence

It is very difficult to accurately gauge the prevalence of CKD in the general population since it is often asymptomatic and undiagnosed. The Public Health England (PHE) CKD prevalence model (based on previous studies and 2011 census data) predicted that in 2014 there were likely to be 2.6 million people in England aged 16 or over with CKD G3-G5 (then called stages 3-5), which was equivalent to 6.1% of the population of that age group (1). The same PHE model estimated the prevalence of CKD G3-G5 in the Stoke-on-Trent CCG to be 5.9% in 2014.

However the Quality and Outcomes Framework (QOF) data (available at http://content.digital.nhs.uk/article/2021/Website-Search?productid=23378&q=QOF+data&sort=Relevance&size=10&page=1&area=both#top) suggests that CKD is almost certainly being underdiagnosed. The 2014-15 QOF data showed that across the whole of England only 4.13% of patients over the age of 18 years were on a register of CKD G3-G5, and that the local recorded prevalence was only 4.10% for North Staffordshire CCG, 3.97% for Stoke-on-Trent CCG, and 3.80% for Stafford and Surrounds CCG. The most recent (2015-16) data shows even lower recorded prevalence, with 4.10% on a register nationally, 4.10% in North Staffordshire CCG practices, 3.90% in Stoke-on-Trent CCG practices, and 3.58% in Stafford and Surrounds CCG practices. This underdiagnosis may in part be due to the lack of symptoms associated with early CKD, but it may also be due to inadequate screening of high-risk groups, and suboptimal recognition and monitoring of early (G1 and G2) CKD.

1.2. Influencing the progression of CKD

Perhaps the most important reason to diagnose CKD early is for the opportunity to slow the progression of CKD: in theory slowing the progression might delay the need for renal replacement therapy until later in life, or even reduce the percentage of patients who ever progress to renal failure in their lifetime. Indeed there is evidence that optimal management of blood pressure (2), proteinuria (3-5), and other factors can slow CKD progression.

1.3. Late presentation of CKD

The Renal Registry collects data regarding the presentation and treatment of patients from all UK Renal Units. This data shows that far more patients present late to renal services locally than to most other units across the UK: the latest report (based on 2015 data) shows that 25.3% of patients presented to the Renal Department at University Hospitals of North Midlands NHS Trust less than 90 days before they needed to start renal replacement therapy (i.e. dialysis or transplantation), compared to a UK average of only 18.0%. In fact 40% of all patients starting dialysis in our unit that year were known to renal services for less than a year. Late presentation increases the cost of CKD care to the health economy, and even more importantly means that patients are much less likely to start dialysis with definitive access (e.g. a fistula), and have higher rates of morbidity and mortality (6).

1.4. Modifying comorbidities

CKD is an independent risk factor for cardiovascular disease (CVD), and patients are 6-fold more likely to die from CVD than to ever reach renal failure (7). Early diagnosis of CKD allows modification of CVD risk factors.

1.5. Summary

CKD may manifest clinically in a variety of ways depending on the underlying disease and on the severity of any functional impairment. Crucially, unless there are disease-specific symptoms, CKD is often asymptomatic until there is at least moderate impairment. Early identification is desirable because it offers an opportunity to modify the rate of progression of CKD, to ensure that referral is appropriate and timely, and to modify important comorbidities such as cardiovascular disease.

The purpose of this document is to help primary care clinicians in the Stoke and North Staffordshire areas to identify, classify and manage patients with CKD under their care and to identify which of those patients will require referral to secondary care in a timely fashion. Our aim was to assimilate the various national and international guidelines and other useful pieces of evidence, and to present them in a format which is readable but comprehensive. This guidance has been fully referenced throughout to those source documents.

2. Who should be investigated for chronic kidney disease?

Despite the high cost of dialysis, transplantation, and other interventions used in the management of end-stage kidney disease, indiscriminate population screening is not cost-effective (8). In one Dutch study where 40,856 people aged 28 to 75 years from the general population were screened for CKD, only 26 reached RRT during 9 years of follow-up (9).

Resources should therefore be concentrated into screening for CKD in high-risk groups who have particular comorbidities, have had a previous episode of AKI, have a relevant family history, or are taking certain medications.

NICE recommend that CKD screening should consist of a blood test for excretory function (estimated glomerular filtration rate, eGFR), as well as urine testing for haematuria (with a dipstick) and proteinuria (urine albumin:creatinine ratio, ACR) (10). At present many GP practices perform CKD screening in at-risk groups with only eGFR and do not routinely screen the urine, and it is clear that introducing the NICE guidance in full would have significant implications for practice workload and costs. However it is also clear that proteinuria is a significant risk factor for all-cause and cardiovascular mortality even in the absence of reduced renal excretory function, and also that detection and reduction of proteinuria in a patient with CKD may reduce the rate of disease progression. It is therefore recommended that full screening of blood and urine should at least be carried out in the following circumstances: when there is significant clinical suspicion of CKD or nephrotic syndrome; in those patients where knowledge of cardiovascular risk or the diagnosis of early stage CKD is likely to alter treatment; in diabetic patients. Full blood and urine screening should also be used for monitoring progression of CKD once a diagnosis has been established. See section 3 for further details of these investigations.

2.1. Comorbidity

People with the following diseases should be screened for CKD at least annually (10):

- Diabetes mellitus;
- Hypertension;
- Ischaemic heart disease;
- Heart failure (with reduced or preserved ejection fraction);
- Peripheral vascular disease;
- Cerebrovascular disease;
- Structural renal tract disease;
- Recurrent renal calculi;

- Diseases which might cause urinary tract obstruction, e.g. prostatic disease;
- Multisystem inflammatory diseases with potential kidney involvement, e.g. systemic lupus erythematosus or ANCA-associated vasculitis;
- Anyone opportunistically found to have proteinuria or haematuria on urine dipstick.

2.2. Acute kidney injury (AKI)

There is an increased risk of CKD after an episode of AKI, even when the renal function returns to normal levels in the recovery phase (11, 12). Recommended follow-up monitoring is as follows:

- Patients should have a check U&E within six weeks of discharge, and the frequency of testing thereafter is dependent on the patient's eGFR as per the category of CKD that eGFR puts them in (see section 5 for details of this).
- **N.B.: The patient should be monitored for at least 2-3 years - even if the follow-up U&E shows that serum creatinine has returned to baseline** (10).

2.3. Medications

People taking prescription medications which may cause or worsen chronic kidney disease should be screened for CKD at least annually. Such drugs include, but are not limited to:

- Non-steroidal anti-inflammatory drugs (NSAIDS). In people already known to have CKD all possible efforts should be made to avoid or stop the use of this class of drugs;
- Angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin-II receptor antagonists (ARB);
- Diuretics;
- Aminosalicylates, e.g mesalazine;
- Lithium (6-monthly monitoring recommended (13));
- Calcineurin inhibitors (e.g. ciclosporin or tacrolimus).

2.4. Family history

Adults with a family history of either: a) known hereditary kidney disease (e.g. polycystic kidney disease), or b) end-stage kidney disease (GFR category G5 – see section 4) should be screened for CKD if this has not been done before (10). It is not normally necessary to repeat this screening unless doing so is specifically advised by a nephrologist or genetics service (provided no abnormalities are found).

3. Which investigations should be used to identify CKD?

If CKD is suspected, patients should be investigated for evidence of reduced glomerular filtration rate, haematuria, and proteinuria. Other tests may also be indicated depending on the clinical context.

3.1. Estimating glomerular filtration rate

Attempting to directly measure glomerular filtration rate (GFR) is relatively complex, and is not usually necessary for patients being managed in the community. However it is not reasonable to rely on creatinine alone, as a 'normal' creatinine may vary widely from individual to individual. Instead the GFR should be estimated using equations based on serum markers such as creatinine (known as 'estimated glomerular filtration rate', or eGFR).

In keeping with 2014 NICE guidance, our laboratories at UHNM use the 'Chronic Kidney Disease Epidemiology Collaboration' (CKD-EPI) formula to calculate eGFR based on a patient's serum creatinine, age and gender. The CKD-EPI formula has important advantages over the formula we used previously, the Modification of Diet in Renal Disease (MDRD) formula:

- Although both equations become progressively less accurate at higher GFR levels, in a validation study the CKD-EPI equation was shown to more accurate than MDRD in those with GFRs greater than 60 mL/min per 1.73 m2 (and as accurate in those with lower GFR) (14).
- Using CKD-EPI results in a lower reported prevalence of CKD (11.5% vs 13%) and better risk prediction compared with MDRD (15, 16). In other words, some people who would be diagnosed as having CKD if we used the MDRD equation can be reassured that they don't have CKD now that we are using the CKD-EPI equation.

The following points must be borne in mind when using creatinine-based eGFR calculations:

- Some UK hospital laboratories are still reporting eGFR using the MDRD equation. This must be considered if you are comparing the results of samples processed in different hospitals. If in doubt, free eGFR calculators are available on the internet (e.g. http://ckdepi.org/equations/gfr-calculator/).
- eGFR results derived from the CKD-EPI formula (or the MDRD equation) should be adjusted for black ethnicity, but this is not done automatically by the laboratory, so the reported results for people of African-Caribbean or African family origin must be multiplied manually by a factor of 1.159.
- Standard eGFR equations are not validated for use in children or pregnant women.

- Creatinine is derived from the metabolism of skeletal muscle and from dietary meat intake, and therefore eGFR equations which use creatinine will be less accurate in those with extremes or abnormalities of muscle mass (e.g. amputees, patients with sarcopenia, body-builders) or certain diets (e.g. vegetarians or athletes consuming creatine supplements).
- Because creatinine is influenced by diet, it may also be appropriate to ask your patient not to eat meat for 12 hours before testing eGFR. This is not usually necessary, but you may wish to do this if a very accurate result is essential, e.g. if the eGFR is borderline for the diagnosis or exclusion of CKD.
- 10-40% of urinary creatinine is actively secreted into the urine by the proximal tubules (17). This is important because:
    - Drugs that reduce tubular creatinine excretion (e.g. trimethoprim or cimetidine) will cause a rise in serum creatinine that might be interpreted as an acute kidney injury, although the increase is self-limiting and reversible on stopping the offending drug.
    - Conversely, creatinine secretion is increased in nephrotic syndrome and sickle cell disease, and eGFR estimations based in creatinine may be falsely reassuring in these settings.

3.1.1. Using cystatin C to estimate GFR

NICE guidance now includes the use of Cystatin C as an alternative to creatinine in estimating GFR ('eGFRcystatinC'). The main theoretical advantage of cystatin C over creatinine is that cystatin C is produced by most cell types in the body and not only by muscle, so for example it may be more reliable in people with extremes of muscle mass.

However there are problems with using cystatin C to estimate GFR - for example the serum cystatin C concentration has been shown to be affected by several factors including thyroid disease (18) and diabetes (19). There are also concerns that it may lead to false reassurance, since a proportion of patients who will be told they don't have CKD on the basis of the result will in fact go on to develop CKD in future years.

At UHNM our biochemistry laboratories have decided to offer the measurement of cystatin C, and the calculation of eGFR using this value, in keeping with the NICE recommendations. However it should only be used in one very specific scenario (see section 4.4 for details) and is <u>not</u> a replacement for creatinine.

3.2. Haematuria

If chronic kidney disease (or acute kidney injury) is suspected, it is essential to test for invisible haematuria (also called non-visible haematuria or microscopic

haematuria) using a reagent strip, because the presence or absence of haematuria helps to refine the differential diagnosis of the underlying cause.

A dipstick haematuria of 1+ or greater requires further evaluation as follows:

- Any opportunistic detection of invisible haematuria should prompt full screening for CKD with eGFR and urinary ACR.
- Diagnose 'persistent invisible haematuria' if two out of three consecutive reagent strip tests are positive. This is important because –
    - Persistent invisible haematuria should prompt investigation for urinary tract malignancy in appropriate age groups. Full details of who should be investigated for malignancy are beyond the scope of these guidelines, and NICE guidance 'NG12' should be consulted (20).
    - Persistent invisible haematuria should prompt annual screening with repeat testing for haematuria, serum eGFR, urinary ACR, and blood pressure for as long as the haematuria persists.

3.3. Proteinuria

Proteinuria should be tested for and quantified in the following situations:

- All people with diabetes mellitus, regardless of eGFR (see section 2.1);
- People without diabetes but with an eGFR < 60ml/min/1.73m^2.
- Those with an eGFR > 60ml/min/1.73m^2 but a clinical suspicion of CKD. See section 2 for details of when CKD should be suspected and screened for.

The preferred investigation for the detection and quantification of proteinuria is urinary albumin:creatinine ratio (ACR), which has a greater sensitivity than protein:creatinine ratio (PCR) at low levels of proteinuria. Urine dipstick is not an acceptable method of quantifying proteinuria, unless the reagent strip is capable of measuring albumin at low concentrations and expressing the result as an ACR.

Further points to consider:

- Transient proteinuria is common, particularly in younger people. Causes include exercise, fever and urinary tract infection. Therefore when proteinuria is initially detected at an ACR of between 3 – 70mg/mmol, this should be confirmed with a further early morning sample.
- A *confirmed* ACR of >3mg/mmol should always be considered to be clinically important proteinuria (see section 4.2 for further details).
- An ACR of >70mg/mmol is very unlikely to be transient, and a repeat sample is not necessary for confirmation.
- If the ACR is >70mg/mmol, PCR may alternatively be used for subsequent monitoring, but note that the results of urinary ACR and PCR are not directly equivalent.

- Urine ACR will not detect Bence Jones Protein, which must be tested separately if required.

3.4. Investigating for the underlying cause

It is important to investigate the underlying cause of CKD, particularly as the cause might be treatable or even reversible, e.g. diabetes mellitus, hypertension, myeloma, glomerulonephritis or urinary tract obstruction. The exact nature of the tests required should be determined on the basis of the likely differential diagnosis following history-taking and examination. **There is no standard 'renal screen'**.

3.4.1. Ultrasound

Ultrasound scan of the renal tract is often required. In particular it should be requested in the following situations:

- There is accelerated progression of CKD (see section 6);
- Visible or persistent invisible haematuria (see section 3.2);
- Symptoms compatible with urinary tract obstruction;
- Family history of polycystic kidney disease. However, ultrasound in this situation should only be done in adults, and following appropriate counselling. In most cases this process should be coordinated by a specialist physician;
- Newly diagnosed CKD with an eGFR < 30ml/min/1.73m^2;
- When a patient is being referred to renal services for further evaluation of their CKD. This is usually essential information for the reviewing nephrologist, so requesting USS before or at the time of referral will result in better and speedier care for your patient, and for some patients will mean that only a single outpatient review is required;
- A renal biopsy may be required (a decision which should be made by a consultant nephrologist).

4. How should chronic kidney disease be diagnosed and classified?

To diagnose CKD, abnormalities must have been present and documented for at least three months. For example, to diagnose CKD on the basis of a reduced eGFR, there must be at least two recorded eGFRs of a suitable level (see below), taken at least three months apart.

When a person is found to have a newly reduced eGFR, the eGFR must be repeated within two weeks to exclude acute kidney injury.

The classification of CKD was changed in the 2014 iteration of the NICE CKD clinical guidelines (10), bringing them in line with the 2013 'Kidney Disease Improving Global Outcomes' (KDIGO) guidelines (21). CKD should now be classified not only by the level of excretory function (now known as 'GFR category'), but also by the degree of proteinuria, known as 'ACR category'.

4.1. GFR category

'GFR category' is essentially what used to be called 'CKD stage' in older guidance, where the severity of CKD is classified according to eGFR, with categories G1-G5 replacing what used to be known as CKD stages 1-5:

eGFR (ml/min/1.73m^2)	Description	GFR Category
≥90 and other markers	Normal or high	**G1**
60-89 and other markers	Mild reduction relative to normal range for a young adult	**G2**
45-59	Mild-moderate reduction	**G3a**
30-44	Moderate-severe reduction	**G3b**
15-29	Severe reduction	**G4**
<15	Kidney failure	**G5**

People with an eGFR ≥ 60ml/min/1.73m^2 should NOT be diagnosed with CKD unless there are also other markers of kidney disease.

Acceptable markers to allow the diagnosis of categories G1 and G2 include:

- Albuminuria (ACR > 3mg/mmol);
- Haematuria;
- Electrolyte or acid-base abnormalities *if caused by tubular disorders*;
- Structural abnormalities of the kidneys found on imaging (e.g.hydronephrosis, horse-shoe kidney, polycystic kidneys);
- History of renal transplantation;
- Histological abnormalities of the kidneys.

4.2. ACR category

New to the 2014 NICE CKD guidelines (and 2012 KDIGO guidelines) is the inclusion of an 'ACR category' in the classification of CKD. Studies have found that albuminuria is an independent predictor of mortality and kidney failure (22), and adding a description of the severity of albuminuria therefore conveys additional prognostic information. Albuminuria should now be classified as follows:

- ACR <3mg/mmol = ACR category A1;
- ACR 3-30mg/mmol = ACR category A2;
- ACR >30mg/mmol = ACR category A3.

4.3. Putting it together

When describing the classification of a patient's CKD you should now list the 'GRF category' first, then the 'ACR category', without a space in-between. For example:

A person with eGFR=81 and ACR=54 would have CKD category G2A3;

A person with eGFR=36 and ACR=21 would have CKD category G3bA2.

Remember that CKD should also be classified according to the proven or presumed underlying disease process (e.g. diabetic nephropathy), as that information will help inform the management and prognosis of the condition. You might for example classify an individual as having "CKD category G3bA1 due to hypertensive nephrosclerosis".

4.4. When should you consider checking eGFRcystatinC?

Because of the inaccuracies of eGFR (particularly at higher values), some people may be misdiagnosed as having CKD when in fact their kidneys are healthy. In an effort to reduce this problem of over-diagnosis, NICE now suggest measuring cystatin C to estimate GFR in one specific situation - patients who have:

- An 'eGFRcreatinine' of 45-59 ml/min/1.73m^2 and an ACR of less than 3mg/mmol (i.e. CKD category G3aA1), *and*
- No other marker of kidney disease. If there is another marker of kidney disease (e.g. non-visible haematuria), cystatin C should <u>not</u> be tested.

If such a person is subsequently found to have an eGFRcystatinC of > 60ml/min/1.73m^2, they should not be diagnosed with CKD.

As mentioned previously, there is debate about the usefulness of this test (section 3.1.1). Nonetheless the biochemistry laboratory at UHNM have decided to offer the test in keeping with NICE guidance. The introduction of this test will be fully audited by the laboratory to assess its clinical usefulness.

5. How often should patients with chronic kidney disease be monitored? Which tests should be done?

Each time you review a patient with CKD, it is recommended to measure:

- Serum creatinine and CKD-EPI eGFR. Use this to estimate the current rate of change of eGFR, which is as important as the absolute value;
- Urine dipstick, for the detection of haematuria;
- ACR to quantify proteinuria;
- Blood pressure;
- Consider whether to test for anaemia, CKD-MBD, lipids etc. (see section 7).

There may be situations when it is reasonable to check urine dipstick and ACR less frequently - e.g. if a patient has moderate CKD but has never had significant proteinuria previously the clinician may feel that an annual ACR is sufficient.

The frequency of monitoring should be tailored to the individual, taking into consideration the whole clinical context, including:

- The underlying cause of CKD;
- Recent rate of progression (but note that CKD progression is frequently not linear);
- Comorbidities, especially heart failure;
- Changes to treatment (especially diuretics or ACE-I / ARB);
- Intercurrent illness;
- Previous decision to manage CKD conservatively (i.e. without dialysis), when less frequent monitoring might be appropriate.

If decisions are made to monitor more or less frequently than might be considered usual, this should be discussed with the patient.

The following table suggests a reasonable frequency of monitoring based on CKD classification (adapted from NICE guidance (10):

<table>
<tr><th colspan="2" rowspan="2"></th><th colspan="3">ACR Category</th></tr>
<tr><th>A1</th><th>A2</th><th>A3</th></tr>
<tr><td rowspan="6">GFR Category</td><td>G1</td><td colspan="2" rowspan="3">Annually</td><td rowspan="3">6-monthly</td></tr>
<tr><td>G2</td></tr>
<tr><td>G3a</td></tr>
<tr><td>G3b</td><td colspan="2">6 monthly</td><td rowspan="2">4 monthly</td></tr>
<tr><td>G4</td><td colspan="2">4-6 monthly</td></tr>
<tr><td>G5</td><td colspan="3">At least every 3 months</td></tr>
</table>

6. Progression

The 'rate of progression' of CKD describes how quickly a patient's eGFR is worsening over time. Formal assessment of the rate of progression is important because it allows clinicians to estimate when (if ever) the patient is likely to develop CKD G5 (renal failure) and therefore whether they might eventually need renal replacement therapy.

Interpret this result in the context of the patient's current age and eGFR - for example, a drop in eGFR of 10 ml/min/1.73m^2 in five years is relatively slow and may not be concerning in a 75 year old with a current eGFR of 62, but the same rate of decline would be of great concern in a 32 year old with a current eGFR of 40, because that person would be far more likely to require dialysis or renal transplantation in their lifetime.

Caution should be used in interpreting small changes in eGFR, particularly if there are only a small number of results to base your evaluation on. Assessment of progression is easier if you review as many results as possible, and if you look at all results over the course of at least a year. This is also made much easier by graphing the results – this function is easily available in 'ICE'.

At UHNM we are currently working on an automatic 'CKD alert' which will be available to General Practice to help you with this assessment by generating an estimated rate of progression for all relevant eGFR results.

6.1. Modifying rate of progression

There are several factors known to be associated with rate of progression of CKD (10), and apart from ethnicity all are potentially modifiable:

- African, African-Caribbean, or Asian family origin;
- Hypertension;
- Proteinuria;
- Diabetes mellitus;
- Smoking;
- Chronic NSAID use;
- Cardiovascular disease;
- Untreated urinary outflow tract obstruction;
- Acute kidney injury.

It is important to address these risk factors, and specifically to discuss with the patient that modifying these risk factors (e.g. through smoking cessation or compliance with anti-hypertensive medications) might help to reduce the risk of adverse outcomes.

6.2. Accelerated progression

It is especially important to recognise accelerated progression of CKD, because it greatly increases the risk of progression to CKD G5 (kidney failure), and patients with accelerated progression should normally be referred to secondary care renal services (see section 9).

Accelerated progression is defined as a sustained decrease in eGFR of (10):

- 25% or more and a change in GFR category within 12 months;

AND / OR

- 15 ml/min/1.73m^2 or more within 12 months.

7. The pharmacological management of chronic kidney disease

7.1. Hypertension

Hypertension (HTN) is an important risk factor both for the development (section 2.1) and progression (section 6) of CKD. Full details of HTN management are beyond the scope of these guidelines, and clinicians should refer to NICE guideline CG127 (23). However, it is important to remember that the target blood pressure is lower for CKD patients who also have diabetes mellitus or significant proteinuria:

- In people with CKD and either DM or an ACR of ≥ 70mg/mmol, aim for a systolic BP of 120-130, and a diastolic BP of below 80mmHg;
- In others with CKD, aim for systolic BP of 120-140, and a diastolic BP of below 90mmHg.

7.2. Using ACE-inhibitors and angiotensin receptor blockers in chronic kidney disease

The choice of antihypertensive agent should normally be as per NICE hypertension guidance (CG127) (23). However, there are three situations where people with CKD should specifically be offered an ACE-I or ARB – people with:

- DM, and an ACR of ≥3mg/mmol (ACR category A2 or A3);
- HTN, and an ACR of ≥30mg/mmol (ACR category A3);
- An ACR ≥ 70mg/mmol - irrespective of HTN or cardiovascular disease.

7.2.1. ACE-I and ARB in combination

Previously the combination of an ACE-I and an ARB was sometimes used for treatment of hypertension or proteinuria for patients with CKD; however this combination should NOT be used any longer since it increases the risk of adverse events including syncope, hyperkalaemia and AKI, especially in patients with DM or vascular disease (24, 25).

7.2.2. Starting or adjusting the dose of an ACE-I or ARB in CKD

- Always check urea and electrolytes (U&E) before starting or increasing the dose of these drugs.
- If the pre-treatment potassium is > 5mmol/L, do not start the ACE-I or ARB unless following specialist advice. Instead, investigate and manage any other factors contributing towards hyperkalaemia (e.g. other medications, metabolic acidosis, or dietary intake). Once any other factors have been addressed, recheck U&E and consider whether it is now safe to start an ACE-I or ARB.
- **U&E must be checked again 1-2 weeks after starting or increasing the dose of an ACE-I or ARB**. React to these results as follows:

- Creatinine will often rise (and eGFR will therefore fall) after starting or increasing the dose of an ACE-I or ARB. This is a normal physiological response, since ACE-I prevent vasoconstriction of the efferent arterioles within the nephron. Only revert to the previous (lower) dose if the rise in creatinine is >30% or the fall in eGFR is >25% of the baseline value. If the change is less marked, continue the new dose but recheck U&E in a further 1-2 weeks to make sure the renal function has not worsened further. A mild reduction in renal function should be tolerated because of the known longer-term benefits of these drugs.
- If the serum potassium concentration rises to ≥ 6mmol/L, stop or reduce the ACE-I / ARB back to the previous dose.
- If an ACE-I / ARB has to be stopped or reduced because of a drop in renal function or an unsafe potassium, investigate and manage any other causes (e.g. volume depletion, UTI, urinary tract obstruction, metabolic acidosis, other drugs). Recheck U&E after appropriate management and consider restarting the ACE-I / ARB if this result is safe.

7.3. Cardiovascular risk reduction

CKD is an independent risk factor for cardiovascular disease, and people with CKD are 6-fold more likely to die as a result of cardiovascular disease than they are to reach kidney failure (CKD G5) (7). Cardiovascular risk reduction is therefore an essential part of the management of people with CKD, and should be addressed early in the course of the disease.

7.3.1. Statins

There is conflicting evidence as to whether statins can influence the rate of progression of CKD or the level of proteinuria, and statins cannot be recommended on that basis. However, the SHARP trial showed that people with CKD who were NOT on dialysis had a lower incidence of their primary outcome of coronary death, myocardial infarction, ischemic stroke, or any revascularization procedure when treated with simvastatin and ezetimibe compared with placebo (26). This was not the case for those already on dialysis treatment. Therefore:

- All people with CKD who are not on dialysis should be offered atorvastatin 20mg once daily whether or not they have known cardiovascular disease (27).
- Target a greater than 40% reduction in non-HDL cholesterol, and increase the atorvastatin dose if this target is not achieved.

If eGFR is < 30ml/min/1.73m^2, seek advice from a nephrologist before using doses higher than 20mg (27).

7.3.2. Oral antiplatelets and anticoagulants

A meta-analysis of 50 randomised trials (27,139 patients) showed that for patients with CKD, antiplatelet therapy significantly reduced the risk of fatal or non-fatal myocardial infarction, but did not reduce the incidence of stroke. However the study also found that antiplatelet treatment significantly increased the risk of major bleeding (15 additional major bleeding episodes for every 1,000 patients with CKD treated) (28). In view of this, antiplatelet drugs should be offered to CKD patients for the *secondary* prevention of CVD, but careful consideration must be given where there are added bleeding risks or when considering the use of dual antiplatelet therapy. Patients should be counselled accordingly.

Anticoagulants, and not antiplatelets, should be used for the prevention of thromboembolic events in patients with CKD and atrial fibrillation (AF).

NICE recommend the use of apixaban (a 'novel oral anticoagulant', NOAC) in preference to warfarin for those people with an eGFR of 30–50 ml/min/1.73m^2 and non-valvular atrial fibrillation who have 1 or more of the following risk factors: prior stroke or transient ischaemic attack; age 75 years or older; hypertension; diabetes mellitus; symptomatic heart failure (10).

Patients with eGFR of less than 30 ml/min/1.73m^2 were excluded from most trials of NOACs (including apixaban), so warfarin is recommended if anticoagulation is required in CKD G4 or G5.

7.4. Anaemia

Anaemia due to CKD is extremely unusual if the eGFR is > 60ml/min/1.73m^2, and in such patients other causes of anaemia are much more likely than 'renal anaemia'. Further investigation should always be undertaken unless you judge these investigations to be inappropriate for your individual patient. If you do not plan to investigate, your reasons for this should be discussed with the patient.

Conversely, if eGFR is < 45ml/min/1.73m^2 you should check the haemoglobin (Hb) level if you have not already done so. The frequency of further monitoring of the Hb will depend on the result and the overall clinical scenario, but it is often appropriate to check the Hb each time you are checking the eGFR (see section 5).

When you find anaemia for the first time in CKD, or if the Hb changes more quickly than you expect, always consider alternative causes. At the very least B12 and folate

should always be checked, and any abnormalities of B12 and folate should be corrected before you consider diagnosing anaemia due to CKD.

Clues that suggest the anaemia might be due to another cause and that more thorough investigation is indicated include:

- High or low MCV (anaemia due to CKD is usually but not always normocytic);
- Abnormalities of the white blood cell or platelet counts;
- Very low serum ferritin, although iron stores may be relatively low in CKD;
- Any signs or symptoms of blood loss or haemolysis.

7.4.1. When should anaemia due to CKD be further investigated and treated?

- Hb falls to 110 g/L or less,

OR

- The patient develops symptoms attributable to anaemia.

For further details of the management of anaemia in CKD, including how to assess and replenish iron stores, please consult NICE guideline NG8 (29).

At the present time, ESA (erythropoiesis-stimulating agent) therapy can only be prescribed in our locality by Secondary Care. If you think your patient with anaemia *due to CKD* may benefit from an ESA, please seek further advice from the renal team at UHNM.

7.5. Metabolic acidosis

Metabolic acidosis is relatively common in moderate-to-severe CKD, and may result in multiple problems including increased protein catabolism and insulin resistance (30). In addition, bicarbonate supplementation appears to slow the progression of CKD (31), possibly even in mild disease and in the absence of overt acidosis (32).

NICE recommend the use of oral sodium bicarbonate if eGFR is less than 30 ml/min/1.73m^2 (CKD G4 or G5) and the serum bicarbonate concentration is less than 20mmol/litre. However, since the testing of serum bicarbonate concentration is not currently being offered to primary care by the UHNM biochemistry laboratory, oral sodium bicarbonate should only normally be prescribed when recommended by a secondary care physician.

7.6. Bone metabolism and osteoporosis

The management of CKD-mineral and bone disorders (CKD-MBD) should normally be directed by a nephrologist, and evidence in this area is lacking. However, the following points should be remembered:

- Calcium, phosphate, vitamin D and parathyroid hormone (PTH) levels should NOT be routinely measured in CKD G1, G2 or G3 (i.e. when eGFR > 30 ml/min/1.73m^2). Frequency of monitoring of these levels in patients with CKD G4 and G5 should be individualised, taking into consideration factors such as the trend in measured values and the patient's wishes.
- Guidelines suggest maintaining calcium (corrected for albumin concentration) and phosphate concentrations within normal limits in CKD patients who are not yet on dialysis.
- Offer cholecalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency but NOT to treat or prevent CKD-MBD. For further information about vitamin D replacement, please see local guideline 'Recommendations for the Assessment and Management of Vitamin D Status in Symptomatic / High Risk Adults'.
- Alfacalcidol (1-alpha-hydroxycholecalciferol) or calcitriol (1-25-dihydroxycholecalciferol) may be used to treat secondary hyperparathyroidism, but only once abnormalities of calcium, phosphate and vitamin D have first been corrected. There is little evidence to guide the optimum PTH levels in CKD, and treatment should only be offered if PTH concentration is above normal limits and progressively rising.
- Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with a GFR of 30 ml/min/1.73m2 or more (GFR category G1, G2 or G3).
- When eGFR < 30 ml/min/1.73m^2 it is virtually impossible to differentiate between osteoporosis and CKD-MBD, and the advice of a consultant nephrologist or rheumatologist should be sought before commencing treatment.

7.7. Avoiding acute kidney injury - sick day rules

It is essential that patients know which of their medications they must stop when they have diarrhoea and vomiting or fever and reduced appetite (such as diuretics and ACE-inhibitors). Opportunities for such education include: when starting such a medication; when carrying out a medication review; following episodes of AKI.

A 'Sick Day Rules' leaflet produced by Dr Chris Thompson (consultant nephrologist at UHNM NHS Trust) is included in appendix 1 of this document. This leaflet can be found at: http://vmwebsrv/patientleaflets/Summary.aspx (search in 'find leaflet' through drop down – 'Specialised Medicine'), and it should be given to any patient on such medications.

7.8. Vaccination

Patients with moderate and severe CKD are more vulnerable to infection, and so the following vaccinations should be given to all patients with CKD stages G4 and G5, as well as those with renal transplants or on any form of dialysis:

- Seasonal influenza vaccine should be offered every year (see page 14, chapter 19 (v10_0) of The Green Book (33));
- Pneumococcal vaccine (PPV23) should be offered every 5 years (see page 302, chapter 25 (v6_0) of The Green Book (33));
- Hepatitis B vaccination should be offered to everyone who might have renal replacement therapy in the future. This will require a course of vaccinations, usually over 6 months, and should be started when the eGFR is around 20-25 ml/min/1.73m^2. If the first course is unsuccessful (as evidenced by HBsAb levels 2-3 months post-vaccination), we currently recommend a second full course with a different preparation. Patients in whom hepatitis B vaccination is appropriate will normally also be under the care of the renal team at UHNM, who will normally indicate the appropriate time to initiate the vaccination and whether any boosters or further courses are indicated in clinic letters (see page 170, chapter 18 (v3_0) of The Green Book (33)).

8. Non-Pharmacological Management

8.1. Education and patient activation

Involving patients in their own care improves patient activation, which in turn improves patient experience and even measurable health outcomes (34). Patients should therefore be given appropriate information tailored to their stage and underlying cause of CKD, and there should be joint decision making at all stages.

Any education programmes developed locally should involve patients in the earliest stages of their design (a principle known as ‘co-production’). They should also make use of peer support and ‘expert patients’ where possible.

8.2. Promoting self-management

Encouraging the following aspects of self-management will serve to improve patient activation, and would therefore be expected to improve outcomes:

- Remind patients to come for regular blood tests to monitor kidney function;
- Undertake regular reviews of patients’ medications, and aim to educate patients on the reasons why they are prescribed each drug. Actively address adherence to medication (35, 36). Encourage patients to take medication as prescribed and to report any side effects;
- Emphasise that reducing raised BP is an essential factor in preventing the progression of CKD. Tell patients that reducing BP is predominantly to reduce their chance of getting a heart attack/stroke or dying as well as reducing chance of needing dialysis/transplant;
- Advise patients to monitor their BP at home e.g. weekly; then bring home readings to their surgery consultations. Ensure that the patient is using a maintained and validated monitor;
- Encourage smoking cessation;
- Advise people with diabetes about blood sugar control;
- Advise about restricting excessive alcohol;
- Self-medication:
    - Give advice on over the counter medicines, especially avoidance of anti-inflammatory drugs;
    - Encourage patients to report use of complementary therapies such as Chinese herbal medicine
- As discussed in section 7.7, educate patients about when they should STOP their tablets: if they vomit and are unable to keep fluids down for > 6 hours; have diarrhoea > 5 times per day; have a fever and do not eat or drink for >24 hours.

8.3. Lifestyle modification

Many of the risk factors for CKD progression are modifiable, but only by changes in lifestyle (e.g. smoking cessation, weight loss).

When managing hypertension it is particularly essential to address lifestyle factors such as weight loss, salt intake, exercise.

Consider referring patients to a dietitian (unless the renal team have already done so), particularly if there are concerns about: malnutrition, potassium or phosphate, diabetic control, weight loss.

9. Who should be referred to the specialist renal services?

People with CKD in the following groups should normally be referred for specialist assessment by a nephrologist:

- eGFR less than 30 ml/min/1.73m^2, i.e. GFR category G4 or G5;
- Accelerated progression of CKD (see section 6);
- ACR ≥ 70 mg/mmol, unless known to be caused by DM and already appropriately treated;
- ACR ≥ 30 mg/mmol, i.e. ACR category A3, if there is also invisible haematuria;
- Hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs *at therapeutic doses*;
- Known or suspected rare or genetic causes of CKD
- Suspected renal artery stenosis.

This list is only a guide, and there will be circumstances when it is appropriate to refer outside of these indications. The patient's wishes should be taken into consideration before referring, as should their comorbidities.

10. Contacting the renal team at University Hospitals of North Midlands NHS Trust

10.1. When urgent advice or admission is required

Please call the switchboard at Royal Stoke University Hospital:

- 9am-5pm Monday to Friday, you will be put through to a phone carried by the renal consultant covering the renal ward (W124). They will help to facilitate admission to the renal ward or urgent assessment by the renal team if that is appropriate and necessary.
- Outside of normal working hours you will be put through to the renal middle-grade doctor on-call, who will seek consultant advice if necessary and will help to facilitate admission if appropriate.

Where admission is necessary for a patient who is known to the renal team, and if it is an appropriate problem, we will always attempt to facilitate direct admission so that our mutual patients do not need to attend A&E or AMU.

10.2. Non-urgent advice

If your patient is already known to one of the consultant renal physicians, please always contact that consultant directly for advice. If urgent advice is required please contact their secretary (through RSUH switchboard), but if the query is non-urgent please seek advice through a letter addressed to the consultant and posted or faxed to the renal unit at UHNM.

'Choose and Book Advice and Guidance' should ONLY be used when your patient is not already known to the renal team at UHNM. Please also note that this service is only suitable for straightforward questions; if broader management advice is required, it is more appropriate to make an outpatient referral.

10.3. Outpatient referrals

Referrals to the renal team at UHNM may be made either through Choose and Book, or by writing / faxing a letter directly. In either case, a referral should always contain the following information as a minimum:

- Clear reason for referral ("Please see and advise" may result in you not gaining the advice you require, or even rejection of the referral);
- Past medical history and up to date medication list;
- Current eGFR (within 3 months of referral date);

- Previous eGFR results, or a clear indication of the rate of progression;
- Current urine dip result – haematuria positive / negative (within 3 months of referral date);
- Recent urine ACR (within 3 months of referral date);
- USS result if appropriate – please see section 3.4.1 for details.

If this information is not included in the referral, the correct treatment may be unnecessarily delayed by the need for these tests to be done at or after the first appointment. Also, your patient may be allocated a routine appointment when missing information would have indicated the need for an urgent appointment.

All referrals are screened by a consultant nephrologist, and if the referral is rejected you should expect a letter indicating why an outpatient appointment is not required.

11. References

1. Chronic kidney disease (CKD) prevalence model: Public Health England; 2014. Available from: http://www.yhpho.org.uk/resource/view.aspx?RID=204689.
2. Anderson AH, Yang W, Townsend RR, Pan Q, Chertow GM, Kusek JW, et al. Time-updated systolic blood pressure and the progression of chronic kidney disease: a cohort study. Annals of internal medicine. 2015 Feb 17;162(4):258-65. PubMed PMID: 25686166. Pubmed Central PMCID: PMC4404622. Epub 2015/02/17. eng.
3. Jafar TH, Stark PC, Schmid CH, Landa M, Maschio G, de Jong PE, et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. Annals of internal medicine. 2003 Aug 19;139(4):244-52. PubMed PMID: 12965979. Epub 2003/09/11. eng.
4. Yu HT. Progression of chronic renal failure. Arch Intern Med. 2003 Jun 23;163(12):1417-29. PubMed PMID: 12824091. Epub 2003/06/26. eng.
5. Sarafidis PA, Khosla N, Bakris GL. Antihypertensive therapy in the presence of proteinuria. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2007 Jan;49(1):12-26. PubMed PMID: 17185142. Epub 2006/12/23. eng.
6. NEPHRON: 18th Annual Report of the Renal Association: UK Renal Registry; 2016. Available from: https://www.renalreg.org/reports/2015-eighteenth-annual-report/.
7. Borg GA. Psychophysical bases of perceived exertion. Medicine and science in sports and exercise. 1982;14(5):377-81. PubMed PMID: 7154893.
8. Manns B, Hemmelgarn B, Tonelli M, Au F, Chiasson TC, Dong J, et al. Population based screening for chronic kidney disease: cost effectiveness study. Bmj. 2010 Nov 08;341:c5869. PubMed PMID: 21059726. Pubmed Central PMCID: PMC2975430. Epub 2010/11/10. eng.
9. van der Velde M, Halbesma N, de Charro FT, Bakker SJL, de Zeeuw D, de Jong PE, et al. Screening for Albuminuria Identifies Individuals at Increased Renal Risk. Journal of the American Society of Nephrology : JASN. 2009 06/27/received

10/29/accepted;20(4):852-62. PubMed PMID: PMC2663830.
10. Chronic kidney disease in adults: assessment and management (Clinical guideline 182). National Institute for Health and Clinical Excellence; 2014 (Updated 2015). Available from: www.nice.org.uk/guidance/cg182.
11. Bucaloiu ID, Kirchner HL, Norfolk ER, Hartle JE, 2nd, Perkins RM. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. Kidney international. 2012 Mar;81(5):477-85. PubMed PMID: 22157656. Epub 2011/12/14. eng.
12. Jones J, Holmen J, De Graauw J, Jovanovich A, Thornton S, Chonchol M. Association of complete recovery from acute kidney injury with incident CKD stage 3 and all-cause mortality. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2012 Sep;60(3):402-8. PubMed PMID: 22541737. Pubmed Central PMCID: PMC3422603. Epub 2012/05/01. eng.
13. Joint Formulary Committee. British National Formulary London: BMJ Group and Pharmaceutical Press; 2016. 72:[
14. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Annals of internal

medicine. 2009 May 05;150(9):604-12. PubMed PMID: 19414839. Pubmed Central PMCID: PMC2763564. Epub 2009/05/06. eng.
15. Matsushita K, Mahmoodi BK, Woodward M, Emberson JR, Jafar TH, Jee SH, et al. Comparison of risk prediction using the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate. JAMA : the journal of the American Medical Association. 2012 May 09;307(18):1941-51. PubMed PMID: 22570462. Pubmed Central PMCID: PMC3837430. Epub 2012/05/10. eng.
16. Matsushita K, Selvin E, Bash LD, Astor BC, Coresh J. Risk implications of the new CKD Epidemiology Collaboration (CKD-EPI) equation compared with the MDRD Study equation for estimated GFR: the Atherosclerosis Risk in Communities (ARIC) Study. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2010 Apr;55(4):648-59. PubMed PMID: 20189275. Pubmed Central PMCID: PMC2858455. Epub 2010/03/02. eng.
17. Shemesh O, Golbetz H, Kriss JP, Myers BD. Limitations of creatinine as a filtration marker in glomerulopathic patients. Kidney international. 1985 Nov;28(5):830-8. PubMed PMID: 2418254. Epub 1985/11/01. eng.
18. Manetti L, Pardini E, Genovesi M, Campomori A, Grasso L, Morselli LL, et al. Thyroid function differently affects serum cystatin C and creatinine concentrations. Journal of endocrinological investigation. 2005 Apr;28(4):346-9. PubMed PMID: 15966508. Epub 2005/06/22. eng.
19. Stevens LA, Schmid CH, Greene T, Li L, Beck GJ, Joffe MM, et al. Factors other than glomerular filtration rate affect serum cystatin C levels. Kidney international. 2009 Mar;75(6):652-60. PubMed PMID: 19119287. Pubmed Central PMCID: PMC4557800. Epub 2009/01/03. eng.
20. Suspected cancer: recognition and referral (NICE Guideline 12): National Institute for Health and Care Excellence; 2015. Available from: https://www.nice.org.uk/guidance/ng12.
21. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements. 2013;3(1):1-150.
22. Astor BC, Matsushita K, Gansevoort RT, van der Velde M, Woodward M, Levey AS, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. Kidney international.79(12):1331-40.
23. Hypertension in adults: diagnosis and management (Clinical guideline 127): National Institute for Health and Clinical Excellence; 2011 (Updated 2016). Available from: https://www.nice.org.uk/guidance/cg127.
24. Fried LF, Emanuele N, Zhang JH, Brophy M, Conner TA, Duckworth W, et al. Combined Angiotensin Inhibition for the Treatment of Diabetic Nephropathy. New England Journal of Medicine. 2013;369(20):1892-903. PubMed PMID: 24206457.
25. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. The New England journal of medicine. 2008 Apr 10;358(15):1547-59. PubMed PMID: 18378520. Epub 2008/04/02. eng.
26. Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. 2011 Jun 25;377(9784):2181-92. PubMed PMID: 21663949. Pubmed Central PMCID: PMC3145073. Epub 2011/06/15. Eng.

27. Cardiovascular disease: risk assessment and reduction, including lipid modification (Clinical guideline 181). National Institute for Health and Clinical Excellence; 2014 (Updated 2016). Available from: https://www.nice.org.uk/guidance/cg181.
28. Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, et al. Antiplatelet agents for chronic kidney disease. Cochrane database of systematic reviews. 2013 Feb 28(2):CD008834. PubMed PMID: 23450589. Epub 2013/03/02. Eng.
29. Chronic kidney disease: managing anaemia (NICE Guideline NG8) 2015. Available from: https://www.nice.org.uk/guidance/ng8.
30. Kopple JD, Kalantar-Zadeh K, Mehrotra R. Risks of chronic metabolic acidosis in patients with chronic kidney disease. Kidney international Supplement. 2005 Jun(95):S21-7. PubMed PMID: 15882309. Epub 2005/05/11. Eng.
31. de Brito-Ashurst I, Varagunam M, Raftery MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. Journal of the American Society of Nephrology : JASN. 2009 Sep;20(9):2075-84. PubMed PMID: 19608703. Pubmed Central PMCID: PMC2736774. Epub 2009/07/18. Eng.
32. Goraya N, Simoni J, Jo CH, Wesson DE. Treatment of metabolic acidosis in patients with stage 3 chronic kidney disease with fruits and vegetables or oral bicarbonate reduces urine angiotensinogen and preserves glomerular filtration rate. Kidney international. 2014 Nov;86(5):1031-8. PubMed PMID: 24694986. Epub 2014/04/04. Eng.
33. Immunisation against infectious disease ('The Green Book'): Public Health England; 2013 (Updated 2014). Available from: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book.
34. Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. Health affairs (Project Hope). 2013 Feb;32(2):207-14. PubMed PMID: 23381511. Epub 2013/02/06. eng.
35. Osterberg L, Blaschke T. Adherence to medication. New England Journal of Medicine. 2005;353(5):487-97.
36. Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Archives of internal medicine. 2007;167(6):540-9.

12. Appendix 1 – UHNM Acute Kidney Injury 'Sick Day Rules' leaflet

University Hospitals of North Midlands NHS
NHS Trust

My Medication:

What Should I do When I am Poorly?

Patient Information Leaflet

For patients on an Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors) \ Angiotensin Receptor Blockers (ARBs), Diuretic ("Water") tablets, Non-steroidal anti-inflammatory pain relievers (NSAIDs) or Tolvaptan.

University Hospitals of North Midlands NHS
NHS Trust

Staffordshire and Stoke on Trent Partnership NHS
NHS Trust

PROUD TO CARE

Version 2.

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Are you prescribed, as routine medication, any of the following?

ACE Inhibitors: a medicine for high blood pressure and heart conditions

medicines ending in "pril"

e.g., **Lisinopril, Perindopril, Ramipril, Captopril**

ARBs: high blood pressure medicines ending in "sartan"

e.g., **Losartan, Valsartan, Candesartan, Irbesartan**

Diuretics: sometimes called "water tablets" for excess fluid and high blood pressure

e.g., **Furosemide, Spironolactone, Bendroflumethiazide, Amiloride, Co-Amilofruse, Bumetanide, Metolazone, Indapamide, Eplerenone**

NSAIDs: anti-inflammatory pain killers should be generally avoided if you have CKD or heart failure.

e.g., **Ibuprofen, Naproxen, Diclofenac, Indometacin, Meloxicam, Nabumetone, Celecoxib**

Tolvaptan: Used for progressive Autosomal Dominant Polycystic Kidney disease or conditions causing low sodium.

If YES, your kidneys could be at risk if you have an upset stomach or fever.

Doctors prescribe medication to keep you well, but sometimes the unexpected happens and you become 'sick' with something else. Here's some simple advice to remember to help prevent things getting worse.

If you have any of the following symptoms **STOP** the tablets listed overleaf until your symptoms have resolved.

- Vomiting and unable to keep fluids down for greater than 6 hours
- Diarrhoea more than 5 times per day
- Fever and not eating or drinking for 24 hours

You can restart them when you are better or speak to your GP or out of hours doctor if you are not better in 48 hours.

For out of hours advice contact **NHS 111**

If you have diabetes please contact your GP as additional advice may be applicable

Ask your GP, Pharmacist or Hospital Consultant if you are unsure

University Hospitals of North Midlands NHS Trust