**National Institute for Health and Care Excellence**

# Chronic Kidney Disease (update)
# Guideline Consultation Table
# 21st February – 4th April 2014

| Type | Stakeholder | Order No | Document | Page No | Line No | Comments<br>Please insert each new comment in a new row. | Developer's Response<br>Please respond to each comment |
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| SH | Aintree University Hospital NHS Foundation Trust | 1 | FULL | 4 | Table | Categorising G1-G5 is fine. However the Terms for G2 as mild renal impairment creates discrepancy and either over doing (e.g. elderly with eGFR 60 and 58 is labelled as CKD and goes through all the pre-procedure, pre-contrast work up including resultant cancellation of procedures and important diagnostic investigations) or under doing (in a 28 yr old patient eGR 62 is low and is significant impairment which needs to be dealt with as a matter of urgency). The lack of clarity in this stage has resulted in delays for both the sides.<br>Unfortunately there is no correction factor added for ageing kidney labelling an elderly with CKD 2 or 3A results in patient's frustration difficulty in acceptance which is understandable | Thank you for your comment. For clarification the table on page 4 illustrates the GFR categories used in the KDIGO guideline and were included in the introduction in order to provide background information.<br>We have stated in our classification table (table 1 of the NICE guideline) that people in G1 or G2 with normal to mildly increased levels of albuminuria (3 mg/mmol: A1) should not be diagnosed as having CKD. |
| SH | Aintree University Hospital NHS Foundation Trust | 2 | FULL | 5 | Table | There should be clarification and management plan laid out for non-renal professionals to guide them dealing with ACR3-30 category as NICE suggests not al these patients should be refer unless ACR over 70 except those with haematuria. Our Audit findings suggest ACR over 25-30 compares with significant proteinuria of over 1gm per day and requires nephrology input. | Thank you for your comment. For clarification these were the ACR categories used in the KDIGO guideline and were included in the introduction in order to provide background information. |

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| | | | | | | Happy to supply the details of analysis ( awaiting publication) | |
| SH | Aintree University Hospital NHS Foundation Trust | 3 | FULL | 12 | Do not diagnose… | There is discrepancy here compared to the staging table which confuses non-renal professionals | Thank you for your comment. We do not agree that there is a discrepancy between this recommendation table, it clarifies the recommendation above (to consider using eGFRcystatin C at initial diagnosis to confirm or rule out the diagnosis in people with eGFR 45-59). |
| SH | Aintree University Hospital NHS Foundation Trust | 4 | FULL | 14 | table | There is no CKD 1 stage to suggest CKD for patients with structural abnormalities and normal eGFR for example patients with ADPKD and no proteinuria | Thank you for your comment. The definition of CKD has not changed and remains 'abnormalities of kidney structure or function for greater than 3 months….', we will modify the classification table to clarify this. |
| SH | Aintree University Hospital NHS Foundation Trust | 5 | FULL | 20 | proteinuria | ? Diagnostic implications of raised ACR with dipstick negative urine for protein and implications on change in management in majority of population in community with many Long Term Conditions. Also same comments from no. 1 will apply here. | Thank you for your comment. This section was not prioritised as part of the guideline update. |
| SH | Aintree University Hospital NHS Foundation Trust | 6 | FULL | 31 | Referral criteria | ACR over between 30 and 70 if associated with reduced eGFR less than 60 requires referral. Also in a young person inappropriate eto wait for ACR>70 as ACR of between 25-30 is comparable with significant proteinuria of 1gms/day (our own audit findings, awaiting publication. Happy to supply the details) | Thank you for your comment. This section was not prioritised as part of the guideline update. |
| SH | Boehringer Ingelheim | 1 | FULL | 60 | 28 | With reference to the statement: "Consider apixaban in preference to warfarin in people with a confirmed eGFR of 15-50 ml/min/1.73 $m^2$ and non-valvular atrial fibrillation who have 1 or | Thank you for your comment. We have updated the evidence review (chapter 10.3) to incorporate this pre-specified subgroup analysis (Hijazi, Z et al. Efficacy and safety of dabigatran compared with warfarin in relation to baseline renal function in patients with atrial fibrillation: a RE-LY |

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| | | | | | | more risk factors".<br><br>• It is unclear as to how this advice has been determined in favour of apixaban relative to the other licensed NOACs. The guidance does not reflect the marked efficacy of dabigatran 150mg in reducing stroke for a cohort of patients with a creatinine clearance of between 30 and 50 ml/min. On review of this and similar sub-groups across the relevant randomized controlled trials of licensed NOACs, dabigatran 150mg shows the largest reduction in stroke and systemic embolism when compared to warfarin, with similar risk of major bleeding compared to warfarin.<br><br>Reference: Hart RG et al. Stroke prevention in atrial fibrillation patients with chronic kidney disease. Canadian J of Cardiology 2013; 29, S71-S78. | (Randomized Evaluation of Long-term Anticoagulation Therapy) trial analysis. Circulation 129(9), 961-970. 4-3-2014) and also updated the clinical and economic searches to ensure no other papers had been published since.<br>The GDG agreed that while dabigatran did appear to reduce the rate of stroke and systemic embolism compared to warfarin at doses of 150 mg twice daily, however there was no consistent benefit at 110mg twice daily. At 150 mg twice daily, in the group with GFR between 30-50 ml/min/1.73 $m^2$, warfarin was superior to dabigatran in causing less bleeding. The GDG agreed that as the safety benefits in terms of major bleeding in the most renal impaired group demonstrated with apixaban were not replicated with dabigatran, there was not sufficient evidence to recommend that dabigatran should be used in preference to warfarin in this group. The GDG were also aware that advice in the SPC is for doses of 150 mg of dabigatran not to be used in people aged over 80 years. |
| SH | Boehringer Ingelheim | 2 | FULL | 60 | 28 | Please note that a likely consequence of this proposed guideline advice is that a significant number of patients are likely to be recommended a dose of apixaban which has limited independent evidence for efficacy in stroke prevention. For example, on examining the main apixaban study in AF, namely ARISTOTLE, 24.3% of patients with a creatinine clearance of less than 50 ml/min were given either 2.5 mg of apixaban or the 'low-dose placebo'. This regime was tested on only 428 patients within ARISTOTLE (n=9088; total | Thank you for your comment. The GDG considered the number of people in the subgroup with eGFR <50ml/min when the analysis was reviewed. There were 3017 people in this group which the GDG agree is strong enough to warrant a recommendation to consider apixaban in this specific population. It has been noted that this study excluded people with creatinine clearance of <25 ml/min, and therefore the recommendation has been reworded to state that this should be in people with a confirmed eGFR of 30-50 ml/min/1.73$m^2$ to be consistent with the evidence and the licensed indication. |

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| | | | | | | number of patients in apixaban group).<br><br>Reference: Hohnloser SH et al. Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the<br>ARISTOTLE trial. European Heart Journal (2012) 33, 2821–2830. | |
| SH | Boehringer Ingelheim | 3 | FULL | 60 | 28 | It should be noted that there is no data from the NOAC randomized control trials (RCTs) that have studied patients with CrCL of <25ml/min. In fact, patients with CrCL<30ml/min were excluded from rivaroxaban and dabigatran trials in AF, and patients with CrCL<25ml/min were excluded from apixaban trials in AF.<br><br>• In addition, please note that the current ESC 2012 Guideline on management of AF recommends against the use of NOACs in patients with CrCL <30ml/min.<br><br>Reference: Camm AJ et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J 2012; 33: 2719–2747.<br>See last point in table on page 2730. | Thank you for your comment and for highlighting this. We have amended the recommendation accordingly. As there was a very small percentage of people with eGFR <30 included in the trial, the GDG agreed that for consistency with ranges usually reported, and kidney disease classification, the recommendation should state 30-50 ml/min/1.73 $m^2$. |
| SH | Bonpharma Ltd | 3 | FULL | General | General | Though what is meant when the terms eGFR and GFR are used is covered it could be made somewhat clearer by having a table at the beginning of the document. | Thank you for your comment. These terms are defined in the glossary, at the end of the full guideline. |
| SH | Bonpharma | 12 | FULL | General | General | Though mention is made of diet the | Thank you for your comment. This issue is outside the scope |

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| | Ltd | | | | | potential benefits of water soluble vitamins (WSV) supplementation is neglected. The use WSV's is recommended by both the renal association guidelines and EBPG in dialysis patients and may also be of benefit in some CKD patients. This is especially likely to be the case in patients on conservative management programs where diets to reduce potassium intake will also be likely to reduce WSV intake. http://onlinelibrary.wiley.com/doi/10.1111/sdi.12099/pdf | of this guideline update. |
| SH | Bonpharma Ltd | 13 | FULL | General | General | Much discussion is made of the diagnosis of CKD. It would be helpful if mention could be made of the importance of Primary Care in the early identification of CKD to enable optimal management. This is true of both GP's and especially the practice nurse who is potentially the first line of defence. Providing improved support for primary care to enable better earlier diagnosis can only be of value. Specific computer software can be used which makes patient identification in primary care easier and highlighting its availability would be of value. An example of this is the CLAHRC IMPAKT project. http://www.clahrc-lnr.nihr.ac.uk/impakt | Thank you for your comment. Early identification is highlighted in the guideline title and encapsulated in the recommendation which instructs clinicians to offer testing for CKD in those groups at risk. This was highlighted by the GDG as one of the key recommendations. |
| SH | Bonpharma Ltd | 14 | FULL | General | General | The importance of the whole MDT in managing CKD patients is widely recognised. It would be helpful if some comment is included regarding the value | Thank you for your comment. We have included a comment on the importance of the MDT in the introduction. |

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| | | | | | | of the MDT. | |
| SH | Bonpharma Ltd | 6 | FULL | 222-223 | | The document makes comment regarding the importance of diet thoughts does not address the need for dietetic support from a specialist dietitan especially as the patients CKD progresses. | Thank you for your comment. NICE recommendation style is to not specify the healthcare professional who should deliver the interventions or management programmes that are recommended. It is expected that these will be appropriately trained professionals. |
| SH | Bonpharma Ltd | 1 | FULL | 17 | 18-19 | Might it be useful to here to highlight that late diagnosis is associated with poorer outcomes with significant costs to patients, their families and society as a whole? | Thank you for your comment. Late diagnosis is mentioned in the introduction. We will repeat this point at the end of line 19 on page 17. |
| SH | Bonpharma Ltd | 2 | FULL | 17 | 18-19 | It may also be worthwhile making it clear that CKD is more a marker of CKD risk than it is of a future need for dialysis of transplant. | Thank you for your comment. We assume you mean that CKD is more a marker of **CVD** risk than it is of a future need for dialysis of transplant? We agree this is important to highlight. This is stated in the full guideline introduction. |
| SH | Bonpharma Ltd | 4 | FULL | 55 | 9 | As CKD is more a marker of CV risk than of the future need for dialysis or transplant would it not be wise to expand this to include CKD4? | Thank you for your comment. This recommendation is intended to highlight those who should be tested for presence of CKD, where the evidence suggests that they are at higher risk than the general population; therefore we do not agree that everyone with a family history of stage 4 CKD should be included here. |
| SH | Bonpharma Ltd | 5 | FULL | 58 | 16 | Does this include patients who enter a conservative management program? | Thank you for your comment. This is intended to cover all people with CKD who are within the scope of this guideline and therefore does include patients who enter a conservative management program. |
| SH | Bonpharma Ltd | 7 | FULL | 179 | 7-14 | An important point and one that could be made clearer for the benefit of those who mistakenly believe that patients with early stage CKD are likely to need dialysis or transplantation in the longer term. The use of the pyramid model may be helpful here as it shows how the numbers of patients decreases with falling eGFR as a result of increased | Thank you for your comment. Whilst we agree that this is important, these are the standard form of evidence statements used by NICE and are intended to be a narrative summary of the evidence reviewed. |

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| | | | | | | mortality. | |
| SH | Bonpharma Ltd | 9 | FULL | 342 | 16 | It is interesting to note the association between iron deficiency and strokes (Shovlin et al 2014). Studies have shown that this may also be the case in patients with CKD (TREAT). Managing iron availability may be helpful in such situations. This is of course independent of an effect upon Hb levels and requires further studies. | Thank you for your comment and this information. |
| SH | Bonpharma Ltd | 10 | FULL | 378 | 21 | Currently pharmaceutical vitamin D3 supplements are only available as relatively low dose (800iu). Though potentially suitable for maintenance therapy they are not well suited to correction dosing as they require patients to take large number of tablets or capsules. As a consequence the current alternative is to prescribe nutritional grade or named patient supplies which can be associated with significant costs. In addition the nutritional grade products are not subject to the same controls as pharmaceutical products. | Thank you for your comment. The recommendation highlights where there is best evidence for treatment, guides for the appropriate dose should be informed by the SPC. |
| SH | Bonpharma Ltd | 11 | FULL | 381 | 25 | Though Hb levels are important markers some view them as potentially misleading. Sadly NICE is no doubt constrained by the scope of guidelines and as such is unable to address what may be the more important issue, that of iron availability. Data from patients with CHF for example shows that though low Hb levels are associated with poorer outcomes so is what many would regard | Thank you for your comment. Recommendation 86 (previously recommendation 85) in the full guideline is the 2008 recommendation and was not prioritised for update – however, in the draft consultation version of the full guideline this has been highlighted as a 'new 2014 recommendation' in error. We apologise for the confusion caused. This will be corrected (highlighting removed to indicate this is part of the guideline that was not updated) in the final published version. |

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| | | | | | | as an appropriate Hb level with low iron. It seems plausible that this may also be the case patients with CKD. It may be that in the future a Hb levels will be regarded with less significance that markers of iron availability. Eg. http://www.ncbi.nlm.nih.gov/pubmed/24644024 | |
| SH | Bonpharma Ltd | 8 | FULL | 387 | 5 | The daily dose should read 1.8 g and not 1.8 mg. In addition none of the currently approved products enables this dosing. Recently some units have reported supply issues with sodium bicarbonate preparations which are likely to be exasperated by this Guideline. | Thank you for your comment. This typo has been fixed. |
| SH | Bristol-Myers Squibb | 1 | GENERAL | General | General | BMS have no comments on the draft guideline | Thank you for your comment. |
| SH | British Dietetic Association – Renal Nutrition Group | 1 | FULL | General | General | throughout the document it states renal failure, kidney disease and CKD. This it should be kidney disease (not failure) and CKD not renal failure. Need to be consistent. | Thank you for your comment. We acknowledge the inconsistency and have amended the recommendations and guideline text where appropriate to use the term kidney disease instead of renal failure. |
| SH | British Dietetic Association – Renal Nutrition Group | 2 | FULL | General | General | We think the document would be more user friendly and positive if self-management section was mentioned earlier | Thank you for your comment. The structure of the guideline was arranged according to identification, classification, monitoring progression and then management. We agree that self-management is a very important part of management, and have placed it before pharmacotherapy to highlight this, but do not agree that it should be moved to earlier in the guideline. |
| SH | British Dietetic Association – | 11 | FULL | General | General | all requirements for intervention should include kg/ IBW | Thank you for your comment, guides for the appropriate dose of interventions should be informed by the SPC. Where g/kg/day has been stated, it is direct reporting from the doses |

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| | Renal Nutrition Group | | | | | | stipulated in the included studies. |
| SH | British Dietetic Association – Renal Nutrition Group | 13 | FULL | General | General | Perhaps HCO3 should be mentioned – not specifically as a dietary intervention as such, but the knock-on effect on K and protein catabolism. | Thank you for your comment. Please refer to chapter 14 of the full guideline (recommendation 87). |
| SH | British Dietetic Association – Renal Nutrition Group | 6 | FULL | 222 | 29-30 | maybe need to highlight that potassium restriction may be required to allow for use of ACE-i and ARB's. | Thank you for your comment. We will add on line 29 'Hyperkalaemia is also a problem in people with advanced renal failure particularly those taking renin angiotensin-aldosterone system antagonists'. |
| SH | British Dietetic Association – Renal Nutrition Group | 3 | FULL | 222 | 14 | instead of restriction a person (line 14) suggest ...modification an individual ... | Thank you for your comment. 'Restriction' has been changed to 'modification'. |
| SH | British Dietetic Association – Renal Nutrition Group | 4 | FULL | 222 | 20 | too few calories; suggest inadequate calories leads… | Thank you for your comment. This change has been made. |
| SH | British Dietetic Association – Renal | 5 | FULL | 222 | 25 | line 25 onwards (paragraph) contradicts NICE hyperphosphataemia guidance which recommends first line treatment is diet | Thank you for your comment. We will change this to 'Dietary restrictions may not adequately control phosphate in severe renal failure and phosphate binders…' |

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| | Nutrition Group | | | | | | |
| SH | British Dietetic Association – Renal Nutrition Group | 7 | FULL | 223 | 12 | should refer to fluid not water intake | Thank you for your comment. However, we think 'water intake' is appropriate in this context. |
| SH | British Dietetic Association – Renal Nutrition Group | 8 | FULL | 223 | 14 | Should refer to specialist renal dietitian not an appropriately training individual | Thank you for your comment. NICE recommendation style is to not specify the healthcare professional who should deliver the interventions or management programmes that are recommended. It is expected that these will be appropriately trained professionals. |
| SH | British Dietetic Association – Renal Nutrition Group | 9 | FULL | 223 | 36, 38 | Is this a typing error - should it be hyper not hypophosphataemia? | Thank you for your comment. Yes we agree it should be 'hyper' and will fix this typo. |
| SH | British Dietetic Association – Renal Nutrition Group | 12 | FULL | 224 | 5-6 | Need to stipulate that if patient should be advised 0.6-0.8g/kg/day (should be IBW) this increases the risk of malnutrition therefore 0.8-1g/kgIBW is though to be more acceptable | Thank you for your comment. This was the level of protein restriction that was considered as a low protein diet in the studies reviewed, it is not the level that is recommended. This guideline has not recommended low protein diets. |
| SH | British Dietetic Association – Renal | 10 | FULL | 224 | 1 | As above | Thank you for your comment.<br>Yes we agree it should be 'hyper' and will fix this typo. |

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| | Nutrition Group | | | | | | |
| SH | British Kidney Patient Association | 1 | FULL | 54 | 7 | The classification table (27) is complex and we suggest that the information in it is clarified to make it easier for kidney patients and their families to relate to or to lend itself to an informed discussion. Perhaps some worked examples would help to demonstrate that. The guidelines are a good opportunity to help patients understand whether they do or do not have CKD and what it means so we would like this to be expanded. | Thank you for your comment. We have amended the classification table with the intention of making it easier for healthcare professionals and people with kidney disease. We agree that your suggestion of worked examples would be helpful, and have added these to the 'terms used in this guideline' section of the NICE guideline and in the 'linking evidence to recommendations' section in the full guideline (page 119) to accompany the table and facilitate implementation. We have also added detail to the 'linking evidence to recommendations' section to highlight that it is important that people with CKD are made aware that both the eGFR and ACR levels are important, and that this should be highlighted when the classification was explained. |
| SH | British Kidney Patient Association | 2 | FULL | 57 | 23 | People worried about CKD will contact organisations like the BKPA for advice and would benefit from guidance from their GP on who they can turn to. Please can the suggested decisions include 'signpost' to sources of advice in the voluntary sector and elsewhere. | Thank you for your comment. When the guideline is published, there will also be an accompanying version called 'Information for the public'. Information on the relevant patient organisations will be provided in this version of the guideline produced by NICE. |
| SH | British Kidney Patient Association | 3 | FULL | 57 | 40 | This would better read 'Discuss and explain conservative management where appropriate' | Thank you for your comment. These bullet points are provided as suggested topics for inclusion in education programmes, and therefore we do not agree that the wording needs to be amended. |
| SH | British Kidney Patient Association | 4 | FULL | 58 | 4 | As there a number of important changes in the way CKD patients can be guided, the wording might be improved to include a comment to encourage GPs to 'update knowledge on the 2014 guidance' as the classification explanation is more complex. | Thank you for your comment. We agree that healthcare professionals should update their knowledge with the publication of updated guidance. |

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| SH | British Kidney Patient Association | 5 | GENERAL | | | We suggest that, just as examples of how the new classification would help lay readers, patients and families, some examples are given for GPs to aid their understanding of how to use the guidelines and to explain their import to their patients, and to encourage the sharing of decisions about their treatment. | Thank you for your comment. To accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations. This recommendation has been highlighted as an area that will require implementation support. |
| SH | British Kidney Patient Association | 6 | GENERAL NICE VERSION | | | Please note our earlier comments about explaining for the lay reader how to relate e.g. A3 to G2...ACR and Gfr tables on pp 4 & 5 and the relationship between the two. The further tables 1 and 2 on pp7 and 8 will be a challenge to many of our patients and simplification would benefit them greatly. | Thank you for your comment. We agree that your suggestion of worked examples would be helpful, and have added these to the 'terms used in this guideline' section of the NICE guideline and in the 'linking evidence to recommendations' section in the full guideline (page 119) to accompany the table and facilitate implementation. We have amended the tables to simplify them where possible.<br>In addition, when the guideline is published, there will also be an accompanying version called 'Information for the public'. This will provide further explanation of each of the recommendations tailored to lay readers. |
| SH | British Medical Association | 6 | NICE | General | General | On the whole, we think this is useful as a reference for management, but the implications, if the guideline were to be followed fully and properly for every patient, could be considerable in primary care. | Thank you for your comment. To accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations in all healthcare settings, including in primary care. |
| SH | British Medical Association | 1 | NICE | 3-5 | - | We welcome the narrowing of the focus to patients with CKD3b-5 which is more appropriate. | Thank you for your comment. |
| SH | British Medical Association | 2 | NICE | 3-5 | - | We are concerned that the current labelling of patients with CKD1-3 is not welcome by many patients; it creates a large degree of unnecessary anxiety and confusion and should be abandoned. | Thank you for your comment. We acknowledge that disease labelling can cause anxiety in patients. The revised classification criteria, including the addition of albuminuria clarifies that those with CKD 1 or 2 without any other marker of kidney damage should not be classified as having CKD. However, those with increasing levels of albuminuria are at a |

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| | | | | | | | higher risk of adverse outcomes than the general population, as are people with CKD 3 (NB. These are now termed G1, G2, G3 etc. with albuminuria classified as either A1, A2 or A3). This includes increased risk of CVD and unnecessary harm due to AKI. |
| SH | British Medical Association | 3 | NICE | 19 | 1.1.15 | We welcome the recommendation not to diagnose CKD in people with moderate reductions in eGFRcreatinine where that reduction is unlikely to impact on their wellbeing. | Thank you for your comment. |
| SH | British Medical Association | 4 | NICE | 21 | 1.1.27 | Many people are take NSAIDs over the counter so will be missed. In addition, many people are prescribed NSAIDs but often do not take them; this section should be clarified to reflect this.<br><br>Topical NSAIDs should be excluded from this general principle. | Thank you for your comment. This is true of many drugs, not just NSAIDs, and people with CKD will be told they have CKD. We did not review topical NSAIDs. |
| SH | British Medical Association | 5 | NICE | 24 | 1.2.2 | Although we would agree that management of CKD should not solely be determined by age, there is little mention on how age affects treatment decisions. For example, monitoring eGFR in elderly patients often reflects their decreased muscle mass (and ageing kidneys) and treatment may not be appropriate. Although we do not want to disadvantage older patients, robust evidence is lacking in this age group, and some guidance on age appropriate treatments would be useful. | Thank you for your comment. You will note that the PICO for almost all the review questions included people over the age of 75 as a separate population. Where data allowed subgrouping by age this has been conducted, for example the economic analysis around cystatin C testing (although the results were not markedly different). As you state, there was limited evidence for this population in most data. Please also note that where the GDG were particularly concerned a research recommendation has been made (please see research recommendation 2.3 in the NICE version on RAAS antagonists). |
| SH | British Renal Society | 6 | FULL | Section 4.4 | General | Strongly support the recommendations for research. | Thank you for your comment. |
| SH | British Renal | 5 | FULL | Section | Line 1 | There is a strong rationale for using the | Thank you for your comment. The classification table has |

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| | Society | | | 4.3, recommendation 27, page 54 | | KDIGO classification system but I am concerned that it is too complex for everyday use in primary care. I suggest that the guideline should promote the use of both the old and new systems, at least initially. This would be analogous to the way the TNM classification system is often used in oncology practice. Thus a person would be referred to as having CKD stage 3b (G3bA3). I note that the guidelines themselves still make reference to "CKD stage 1-5". | been amended with the intention of clarifying it for clinical use. The GDG agreed it was important to highlight that both GFR and albuminuria are required for classification to indicate increased risk and the need for better vigilance and awareness of risk, for example risk of acute kidney injury.<br>In addition to simplifying the table, we have added an explanation of the classifications with examples, to aid people in relating these to the 'stages'.<br>We acknowledge your comment that the consultation version of this guideline itself was not supportive of the use of the new classification by still retaining the term 'stages'. We have now amended the recommendations accordingly to relate to, for example G3bA3, as appropriate. |
| SH | British Renal Society | 2 | FULL | Section 1.1, page 17 | Line 12 | The term "established renal failure" should be dropped. It is imprecise, unnecessary and it is not used in any other country | Thank you for your comment. We agree and will change to 'end-stage kidney disease (ESKD)' where appropriate. |
| SH | British Renal Society | 3 | FULL | Section 4.3, recommendation 2, page 51, | line 24 | The change to CKD-EPI GFR will make it difficult to assess trends over time in people with previous MDRD GFR estimates. I suggest that the guideline should promote the reporting of both the MDRD and CKD-EPI GFR for a transition period of several years. | Thank you for comment. The GDG considered and noted in the 'linking evidence to recommendations section' (page 101 of the full guideline) that there would need to be a coordinated country wide approach to implementation. Online tools, such as those produced by the UK Renal Association or the National kidney disease education programme (NKDEP), are available to convert the values, which may be of assistance. Recommending means of implementation is beyond the remit of this guideline, but to accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations when the guideline is published. This recommendation has been highlighted as an area that may require implementation support. |
| SH | British Renal Society | 4 | FULL | Section 4.3, recommendation | Line 32 | The recommendation to consider confirming a diagnosis of CKD with cystatin C in people with CKD-EPI GFR 45-59ml/min is not supported by | Thank you for your comment. This is not contradicted as recommendation 1.1.15 in the NICE version refers to people with 'no other marker of kidney disease'**.** We do not see a conflict in the language. 'Consider' using it where |

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| | | | | 15 page 52, | | compelling evidence. The softer "consider" in 15 is contradicted by the "do not" in 16. This is an important issue because people with stage G3aA1 make up the majority of people with CKD stage 3 in primary care, thus large numbers will be affected. At present cystatin C assays are available only in a small number of laboratories. Thus there are substantial resource implications for establishing the assays in laboratories and testing the majority of people with CKD stage 3. Several studies are currently investigating the clinical utility of cystatin C measurements and the results of these should be awaited before a recommendation is made. | appropriate, and if the result is negative 'do not' diagnose CKD.<br><br>This recommendation is in part intended to help address the concerns that there is over diagnosis of CKD in people who fall within this group. Cystatin C has been demonstrated as having a lower number of false positive results at eGFR 45-59. This has been stated in the 'linking evidence to recommendations' section (section 5.7.3 of the full guideline). The GDG has considered the evidence for use of cystatin C including economic modelling. We acknowledge that the evidence to populate the model was not as strong as we would have liked and that was one of the reasons that the recommendation started with a relatively weak 'consider'. However, the model was based on the diagnostic evidence from the guideline's systematic review, recommendations from NICE guidance and the expertise of the clinicians on the guideline development group, in line with NICE methods. We have reworded the header of this section to clarify that this should be done to confirm or rule out the diagnosis of CKD. This should be a one-off test, not to be repeated in people who fall within this eGFR range. We have amended the recommendation to state: 'Consider using eGFRcystatinC at initial diagnosis to confirm or rule out CKD…' and updated recommendation number 36 (p55 of the full guideline) to state that monitoring should be with eGFRcreatinine. |
| SH | British Renal Society | 1 | FULL VERSION | General | | There is a welcome emphasis on patient involvement and self-management. | Thank you for your comment. |
| SH | British Society of Interventional Radiology | 1 | NICE VERSION | | | No comments on this consultation | Thank you for your comment. |

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| SH | Department of Heath | 1 | GENERAL | General | General | The Department of Health has no substantive comments to make, regarding this consultation. | Thank you for your comment. |
| SH | Diabetes UK | 1 | NICE | General | General | It would be helpful if the NICE guideline was clarified, as the recommendations for monitoring and frequency of testing are a bit unclear. In one table there are recommendations for monitoring, which are sound. But then the text and another table include the need for 3 eGFR measures in 90 days to determine if someone has progressive CKD. | Thank you for your comment. We think the tables are clear. These recommendations are about two different things – monitoring and progression. We will add subheadings '**Frequency of monitoring'** and **'Defining progression'** to clarify this in the full list of recommendations in the full guideline. |
| SH | Kidney Research UK | 6 | FULL | 249 - 252 | all | We strongly support the recommendation for research: 'Does the provision of educational and supportive interventions to people with CKD by healthcare professionals increase patients' skills and confidence in managing their conditions and improve clinical outcomes?' As mentioned above, we have already invested in a research study that addressed this exact issue.<br><br>Kidney Research UK is currently project managing, on behalf of all renal stakeholders, a consultation process to develop a National Renal Research Strategy, ref; http://www.kidneyresearchuk.org/national-renal-research-strategy | Thank you for your comment. |
| SH | Kidney Research UK | 2 | FULL | 12<br>20<br>21 | 17<br>15<br>25 | The term "established renal failure" should be dropped. It is imprecise, unnecessary and it is not used in any | Thank you for your comment. We agree and will change to 'end-stage kidney disease (ESKD)' where appropriate. |

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| | | | | | | other country. | |
| SH | Kidney Research UK | 1 | FULL | 42<br>207 | 18<br>20 | We welcome the increased emphasis on patient involvement and self-management in their treatment care. There already exists evidence based, piloted and implemented information available for patients (and professionals), please see : https://www.kidneyresearchuk.org/health-information/resources/package-of-innovation | Thank you for this information. |
| SH | Kidney Research UK | 3 | FULL | 50<br>51<br>51<br>63 | 7<br>25<br>32<br>22 | The change to CKD-EPI GFR will make it difficult to assess trends over time in people with previous MDRD GFR estimates. We suggest that the guideline should promote the reporting of both the MDRD and CKD-EPI GFR for a transition period of several years. Research funded by Kidney Research UK (QI-CKD Study) has shown that the CKD prevalence rates using the CKD-EPI equation are lower than those using the MDRD equation. Our study showed that CKD-EPI identifies a smaller, higher-risk population at CKD3a. Consideration also needs to be given to the ethnicity of the UK population where existing published evidence shows that the BAME members are 5 times more at risk of CKD. | Thank you for comment. The GDG considered and noted in the 'linking evidence to recommendations section' (section 5.7.1 of the full guideline) that there would need to be a coordinated country wide approach to implementation. Online tools, such as those produced by the UK Renal Association or the National kidney disease education programme (NKDEP), are available to convert the values, which may be of assistance. Recommending means of implementation is beyond the remit of this guideline, but to accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations when the guideline is published. This recommendation has been highlighted as an area that may require implementation support.<br><br>With respect to ethnicity and chronic kidney disease, although there is observational data that indicates a greater risk of end-stage kidney disease receiving dialysis and/or transplantation in BAME members there is no evidence to support a difference in prevalence of CKD by ethnicity. A recommendation is included within the guidance to state: "Do not use age, gender or ethnicity as risk markers to test people for CKD" (NICE version, recommendation 1.1.29). |

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| SH | Kidney Research UK | 4 | FULL | 50<br>50<br>52<br>50-52 | 16<br>20<br>15 vs 16<br>As above | The recommendation to consider confirming a diagnosis of CKD in people with CKD-EPI GFR 45-59ml/min is not supported by compelling evidence.<br>The softer "consider" in 1.1.14 is contradicted by the "do not" in 1.1.15.<br>This is an important issue because people with stage G3aA1 make up the majority of people with CKD stage 3 in primary care, thus large numbers will be affected.<br>At present cystatin C assays are available only in a small number of laboratories. Thus there are substantial resource implications for establishing the assays in laboratories and testing the majority of people with CKD stage 3.<br>Several studies are currently investigating the clinical utility of cystatin C measurements and we recommend that the results of these should be awaited before a recommendation is made. | Thank you for your comment. This is not contradicted as recommendation 1.1.15 in the NICE version refers to people with 'no other marker of kidney disease'**.** We do not see a conflict in the language. 'Consider' using it where appropriate, and if the result is negative 'do not' diagnose CKD.<br><br>This recommendation is in part intended to help address the concerns that there is over diagnosis of CKD in people who fall within this group. Cystatin C has been demonstrated as having a lower number of false positive results at eGFR 45-59. This has been stated in the 'linking evidence to recommendations' section (section 5.7.3 of the full guideline). The GDG has considered the evidence for use of cystatin C including economic modelling. We acknowledge that the evidence to populate the model was not as strong as we would have liked and that was one of the reasons that the recommendation started with a relatively weak 'consider'. However, the model was based on the diagnostic evidence from the guideline's systematic review, recommendations from NICE guidance and the expertise of the clinicians on the guideline development group, in line with NICE methods.<br>We have reworded the header of this section to clarify that this should be done to confirm or rule out the diagnosis of CKD. This should be a one-off test, not to be repeated in people who fall within this eGFR range. We have amended the recommendation to state: 'Consider using eGFRcystatinC at initial diagnosis to confirm or rule out CKD…' and updated recommendation number 36 (p55 of the full guideline) to state that monitoring should be with eGFRcreatinine. |
| SH | Kidney Research UK | 5 | FULL | 83 | 30 | There is a strong rationale for using the KDIGO classification system but we are concerned that it is too complex for everyday use in primary care. We suggest that the guideline should promote the use of both the old and new | Thank you for your comment. The classification table has been amended with the intention of clarifying it for clinical use. The GDG agreed it was important to highlight that both GFR and albuminuria are important for classification to highlight increased risk and the need for better vigilance and awareness of risk, for example risk of acute kidney injury. |

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| | | | | | | systems, at least initially. This would be analogous to the way the TNM classification system is often used in oncology practice. Thus a person would be referred to as having CKD stage 3b (G3bA3). We note that the guidelines themselves still make reference to "CKD stage 1-5". | In addition to simplifying the table, we have added an explanation of the classifications with examples, to aid people in relating these to the 'stages'.<br>We acknowledge your comment that the consultation version of this guideline itself was not supportive of the use of the new classification by still retaining the term 'stages'. We have now amended the recommendations accordingly to relate to, for example G3bA3, as appropriate. |
| SH | Merck Sharp and Dohme | 1 | NICE VERSION | 21 | 1.1.28 | MSD agrees with the emphasis in the guideline for focusing on comorbid patients with CKD such as patients with diabetes, hypertension, CVD, etc. | Thank you for your comment. |
| SH | Merck Sharp and Dohme | 3 | NICE VERSION | 25 | 1.3.2 | MSD agrees with tailoring the frequency of eGFR monitoring according to the points in this section. We believe the point "comorbidities, especially heart failure" should be changed to "comorbidities, especially heart failure, CVD and diabetes". | Thank you for your comment. The GDG wanted to specifically emphasis people with heart failure; adding these other comorbidities would change the emphasis. |
| SH | Merck Sharp and Dohme | 2 | NICE VERSION | 23 and 25 to 26 | 1.2 and 1.3 | MSD note that classification of CKD and frequency of monitoring is now classified using a combination of eGFR and ACR categories. In the full guideline on page 117 the GDG noted that "it may need support in implementation". MSD agree with this point. Testing both eGFR and ACR would add an extra burden and cost to diagnosis and monitoring. It is imperative that the introduction of this new classification and monitoring does not lead to a decrease in health care for the patient. NICE need to consider how this will be implemented and perhaps incentivised. | Thank you for your comment. The GDG agreed it was important to highlight that both GFR and albuminuria are required for classification to indicate increased risk and the need for better vigilance and awareness of risk, for example risk of acute kidney injury.<br>In addition to simplifying the table, we have added an explanation of the classifications with examples, to aid people in relating these to the 'stages'.<br>To accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations. This recommendation has been highlighted as an area that may require implementation support. |
| SH | National | 5 | NICE | 29-30 | 1.4 – | The amended recommendations for | Thank you for your comment. |

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| | Kidney Federation (NKF) | | | | 1.4.11 | Information and Education, including low protein diets, self-management & the use of Renal Patient View. | |
| SH | National Kidney Federation (NKF) | 1 | NICE | 17 | 1.1.14 - 1.1.15 | The NKF fully welcomes the recommendations for measuring kidney function and in particular when to diagnose CKD. | Thank you for your comment. |
| SH | National Kidney Federation (NKF) | 2 | NICE | 23 | 1.2 | The NKF appreciate the use of Table 1 in the classification of CKD using GFR and ACR categories and find it particular useful to illustrate the increasing risk from CKD. | Thank you for your comment. |
| SH | National Kidney Federation (NKF) | 3 | NICE | 25 | 1.3 | The NKF find the use of Table 2 particular helpful and would hope that this can be picked up by Primary Care and used with patients/carers in the explanation of CKD monitoring and progression as well as in Secondary Care when needed. | Thank you for your comment. |
| SH | National Kidney Federation (NKF) | 4 | NICE | 27 | 1.3.16 | The risk factors for progression which are new to 2014 are to be welcomed and align with the 'matrix' working of NHS England in Cardiovascular Disease (Diabetes, Renal, Cardiac & Stroke). | Thank you for your comment. |
| SH | National Kidney Federation (NKF) | 6 | NICE | 36 | 1.7.4 - 1.7.7 | The new advice, for management of mineral bone disorders is also welcomed. | Thank you for your comment. |
| SH | NCGC - Type 1 diabetes (update) guideline development group | 1 | FULL | General | General | It was felt that a review of AF and CV disease as a single question was beyond the scope of the CKD guidance. Whilst offering an opinion on the ideal treatment purely from a kidney perspective, it did seem that the recommendation was directly in contrast | Thank you for your comment. Part of the remit of the guideline update was to look at reducing cardiovascular risk in people with CKD. The recommendations are derived from the best available clinical and cost effectiveness evidence. The only evidence available for this review question was indirect evidence from people with cardiovascular disease who also had CKD. The recommendation was made |

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| | | | | | | to other NICE guidelines and technology appraisals. | specifically for people with AF to be consistent with the evidence, and was drafted to be consistent with the technology appraisal, with more specific direction for people with CKD. |
| SH | NCGC - Type 1 diabetes (update) guideline development group | 2 | FULL | 342 | | In the case of secondary treatment of ACS - the recommendations made have not considered prasugrel due to a lack of relevant studies in CKD. However this drug is particularly important in the diabetes population, as diabetes is a specific indication for the use of this drug. Whilst we support the acknowledgement that bleeding risk is increased in patients with CKD (recommendation 76), we were not happy that the recommendations made appeared to override the recommendations made in TA182 and felt that a risk benefit decision should be made based on the patient and not just on their renal function. | Thank you for your comment. Prasugrel was included in the review protocol, but that no evidence was found to support recommending its use in this population. This recommendation was based on the evidence reviewed The recommendation was made specifically for people with AF to be consistent with the best available evidence, and was drafted to be consistent with the technology appraisal, with more specific direction for people with CKD. |
| SH | NCGC - Type 1 diabetes (update) guideline development group | 3 | FULL | 342 | | In regards to recommendation 77 we were unsure why diabetes had been listed as a particular population in which to consider apixaban. None of the evidence reviewed seemed to highlight that the diabetes population particularly benefited from this drug. We support the recommendation for patients who have particularly poor renal function (with diabetes or otherwise) but did not feel that all patients with diabetes should be considered in this category. Patient's with CKD3 may benefit as much from the other NOAC and should not be | Thank you for your comment. In order to be consistent with the technology appraisal, the risk factors in which treatment should be considered were taken directly from the TA recommendation. |

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| | | | | | | restricted. | |
| SH | NHS England | 9 | FULL | All | | The term "established renal failure" should be dropped. It is imprecise, unnecessary and it is not used in any other country | Thank you for your comment. We agree and will change to 'end-stage kidney disease (ESKD)' where appropriate. |
| SH | NHS England | 2 | FULL | 5.7 | 2 | Adoption of CKD EPI in place of MDRD. The change to CKD-EPI GFR will make it difficult to assess trends over time in people with previous MDRD GFR estimates. Ii is suggested that the guideline should promote the reporting of both the MDRD and CKD-EPI GFR for a transition period of several years. Although CKD-EPI is more 'accurate' at higher GFR, the clinical utility of MDRD vs CKD-EPI has not been evaluated. Dual reporting may allow this question to be answered. Reporting eGFR from 90 downwards may create confusion in assessing whether an individual has CKD or not (bullet point 9). This is reflected in statements11, suggesting that GFR 60-90 need careful interpretation. | Thank you for your comment. The GDG considered and noted in the 'linking evidence to recommendations section' (section 5.7.3 of the full guideline) that there would need to be a coordinated country wide approach to implementation. Online tools, such as those produced by the UK Renal Association or the National kidney disease education programme (NKDEP), are available to convert the values, which may be of assistance, and therefore we do not think that suggesting dual reporting would be beneficial. Recommending means of implementation is beyond the remit of this guideline, but costings and implementation tools will be produced to facilitate the implementation of recommendations when the guideline is published. This recommendation has been highlighted as an area that may require implementation support.<br><br>We do not agree that the clinical utility of CKD-EPI versus MDRD has not been evaluated. For example, in direct comparisons from large population cohorts CKD-EPI corresponds to crude risk much better than MDRD (JAMA. 2012;307(18):1941-1951). 34.7% of eGFR 45-59 were reclassified upward to 60-89 by CKD-EPI and the CIR (crude incidence rate) for all-cause mortality was 9.9 vs 34.5 for those reclassified upward vs. not reclassified vs. downward among those with eGFR 45-59. Therefore on a crude basis the 34.7% of those with eGFR 45-59 moved to 60+ have more than 3-fold lower mortality risk (9.9/34.5). eTable 6 shows this is 2-fold for high risk cohorts and eTable 7 for CKD cohorts. For CVD mortality CIRs are 2.7, 13.0 and 52.3 |

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| | | | | | | | – >4-fold lower risk for those reclassified upward. For ESRD it is 0.5 vs. 0.8 vs. 1.6 – less than 2-fold lower for those reclassified upward so less pronounced.<br><br>In another publication (Am J Kidney Dis. 60(2):241-249) a similar percentage (30.8%) were reclassified upwards from eGFR 45-59 to 60-89 and again with the outcomes all-cause mortality, acute myocardial infarction, end-stage renal disease, and progression of CKD the CKD-EPI equation was better at categorising individuals at clinical risk than the MDRD Study equation. |
| SH | NHS England | 4 | FULL | 6 | all | The new classification system needs careful<br>consideration. Whilst it is undoubtedly more precise indefining risk for an individual, the introduction of such aclassification system into practice would require a significant investment in education within primary and secondary care.<br>The current classification system has resulted in a<br>significant improvement in late presentation of end stage renal failure. Clearly, there is less evidence in cardiovascular risk and modification and in the field of Acute Kidney Injury.<br>The review on degree of proteinuria and risk is excellent, but it does not provide a justification for a new classification system to manage populations by non specialists - it is probably too complex and untested for everyday use in primary care. The guideline could | Thank you for your comment. The classification table has been amended with the intention of clarifying it for clinical use. The GDG agreed it was important to highlight that both GFR and albuminuria are required for classification to indicate increased risk and the need for better vigilance and awareness of risk, for example risk of acute kidney injury.<br>In addition to simplifying the table, we have added an explanation of the classifications with examples, to aid people in relating these to the 'stages'.<br>We acknowledge your comment that the consultation version of this guideline itself was not supportive of the use of the new classification by still retaining the term 'stages'. We have now amended the recommendations accordingly to relate to, for example G3bA3, as appropriate. |

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| | | | | | | promote the use of both the old and new systems, at least initially. This would be analogous to the way the TNM classification system is often used in oncology practice. Thus a person would be referred to as having CKD stage 3b (G3bA3). This would allow a comparison of use in populations.<br>Please note that the guidelines themselves still make reference to "CKD stage 1-5" and do not use the new classification system. | |
| SH | NHS England | 3 | FULL | 5.7.3 | 6 | Cystatin C is recommended (consider) to clarify<br>diagnosis of CKD (point 15) but implied as mandatory(16).<br>The use of Cystatin C in this setting needs very careful consideration. There is currently an NIHR funded study (http://www.nets.nihr.ac.uk/projects/hta/1110301)<br>designed to answer whether CyC has utility.<br>On a practical level, there is limited availability of this test across England.<br>The economic agreement is weak.<br>Within the guidance it notes that retesting can render the model incorrect.<br>The principle group of people to be investigated will reside within general practice. There is no guidance to manage the use of this test.<br>Consequently, there is a need for more studies (such as the above quoted work in progress) before widespread adoption into NHS England. | Thank you for your comment. This is stated as 'consider' and the intention is not to imply that it is mandatory, although economic modelling supports its use. Recommendation 16 in the full guideline provides guidance *if* this test has been done.<br>This recommendation is in part intended to help address the concerns that there is over diagnosis of CKD in people who fall within this group. Cystatin C has been demonstrated as having a lower number of false positive results at eGFR 45-59. This has been stated in the 'linking evidence to recommendations' section (section 5.7.3 of the full guideline).<br>We acknowledge that implementation will require support. The Cystatin C test is not currently offered by many laboratories in the UK but the vast majority of laboratories have access to analytical systems that either offer the test within their standard company menu or could set up the assay on an automated platform in open channel mode. To accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations. This recommendation has been highlighted as an area that will require implementation support. |

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| SH | NHS England | 5 | FULL | 8.6.6 | 2 | This new recommendation set is welcome. | Thank you for your comment. |
| SH | NHS England | 6 | FULL | 12.2.6 | 12 | There is no mention of whether bisphosphonates are contraindicated in CKD stage 4 and 5. | Thank you for your comment.<br>This chapter was not prioritised as part of the update of this guideline. |
| SH | NHS England | 7 | FULL | 14.1.6 | 24 | There is no mention of the ongoing NIHR funded trial of NaBic in the elderly (http://bicarb.org.uk) This will (hopefully) provide very important information about the appropriateness of NaBic in this setting. There should be a statement around its use in CKD1-3 and in addition patients on dialysis should be generally excluded (CKD 5 covers the dialysis population). | Thank you or your comment. As you state there is a funded trial in progress but this trial will not report for some time. There is no evidence to drive a statement surrounding use of bicarbonate supplementation in stage 1-3 CKD. Dialysis patients are outside the scope of this guideline but not all patients with a GFR<15 ml/min/1.73 $m^2$ are either receiving, or will receive renal replacement therapy. We have clarified this in the LETR section. |
| SH | NHS England | 1 | FULL AND NICE | General | General | The guideline is well written reflecting it's maturity. | Thank you for your comment. |
| SH | NHS England | 8 | NICE | | | The research recommendations are welcome. | Thank you for your comment. |
| SH | Renal Association | 1 | FULL | General | Number | **Renal Association Feedback on Draft Revised CKD Guidance Consultation 4th April 2014**<br><br>Feedback from the UK Renal Association on NICE draft guideline: Chronic kidney disease: Early identification and management of chronic kidney disease in adults in primary and secondary care<br><br>The Renal Association commend the guideline group development members for their excellent work. The first version of this guideline (2008) has made a | Thank you for your comment. The GDG acknowledges that the recommendation of adoption of CKD-EPIcreat represents a change in clinical practice. This will be thoroughly reflected in the implementation tools developed to facilitate uptake of the recommendation.<br><br>We acknowledge that training does represent an opportunity cost for this and other guidelines. But, we do not usually include training costs in our economic evaluations because training that can be delivered at medical/nursing school need not represent an incremental cost to the NHS. Other training might be only required in the short term to bring existing staff up to speed. And therefore training costs would have a negligible impact on the long-term cost-effectiveness of the guideline's recommendations. |

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| | | | | | | major contribution to improvements in care of patients with chronic kidney disease (CKD). The majority of the updates in this draft version are highly appropriate; they represent the development of the evidence base in terms of classification, monitoring and management in the time period since 2008.<br><br>We have limited our comments to those areas where we feel that further work is needed before the guideline is accepted for publication in it's present form.<br><br>The major recommendation in the guideline that will have an impact on clinical practice is (i) the change from estimation of GFR by the abbreviated (4-variable) MDRD equation to CKD-EPI creatinine; (ii) the utilisation of cystatin c for assessment of patients with CKD3aA1. Both these recommendations require careful consideration; we would recommend that work is required to understand the implications of the recommendations at a practice level, with a focus on the impact on patients with pre-existing CKD.<br><br>The introduction of eGFR into clinical practice and the alignment of the measurement to the Quality and Outcomes Framework was a major development in the accuracy of the management of CKD. It is a widely held | We have alerted NICE's implementation team to the need for training.<br><br>In direct comparisons from large population cohorts CKD-EPI corresponds to crude risk much better than MDRD. In the JAMA paper (JAMA. 2012;307(18):1941-1951) 34.7% of eGFR 45-59 get reclassified upward to 60-89 and the CIR (crude incidence rate) for all-cause mortality is 9.9 vs. 34.5 for those reclassified upward vs. not reclassified vs. downward among those with 45-59. Therefore on a crude basis the 34.7% of those with eGFR 45-59 moved to 60+ have more than 3-fold lower mortality risk (9.9/34.5). eTable 6 shows this is 2-fold for high risk cohorts and eTable 7 for CKD cohorts.<br><br>For CVD mortality CIRs are 2.7, 13.0 and 52.3 – >4-fold lower risk for those reclassified upward.<br><br>For ESRD it is 0.5 vs. 0.8 vs. 1.6 – less than 2-fold lower for those reclassified upward so less pronounced.<br><br>In the AJKD paper (Am J Kidney Dis. 2012 60(2):241-249) a similar percentage (30.8%) were reclassified upwards from eGFR 45-59 to 60-89 and again with the outcomes all-cause mortality, acute myocardial infarction, end-stage renal disease, and progression of CKD the CKD-EPI equation was better at categorising individuals at clinical risk than the MDRD Study equation.<br><br>The recommendation to consider using cystatinC is in part intended to help address the concerns that there is over diagnosis of CKD in people who fall within this group. Cystatin C has been demonstrated as having a lower number of false positive results at eGFR 45-59. This has been stated in the 'linking evidence to recommendations' section (section |

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| | | | | | | view amongst both primary and secondary care that this has led to better care, particularly through the CKD QOF. Although there is a lack of high quality evidence to confirm this, there is surrogate evidence to support; people who have been placed on the CKD register do have better management of those factors that are associated with adverse outcomes (e.g. hypertension) and the numbers of patients progressing to end-stage kidney disease in the UK are lower than the numbers projected before the introduction. The shortfalls in the MDRD equation are recognised and the CKD-EPI equations are more accurate, particularly for the reclassification of people with CKD3a.<br><br>(i) Recommending the adoption of CKD-EPIcreat should be based on careful evaluation of the potential impact of this change. Good clinical practice will involve a fully trained health care professional explaining to the patient how the calculation utilising serum or plasma creatinine to estimate kidney function (eGFR) has changed and that this change may lead to a reclassification of the patient as not having CKD or a different stage of CKD. That will require further follow-up as indicated in the proposed guideline, training the professionals involved for communication and assessing the support required for patients, | 5.7.3 of the full guideline). The GDG has considered the evidence for use of cystatin C including economic modelling. We acknowledge that the evidence to populate the model was not as strong as we would have liked and that was one of the reasons that the recommendation started with a relatively weak 'consider'. However, the model was based on the diagnostic evidence from the guideline's systematic review, recommendations from NICE guidance and the expertise of the clinicians on the guideline development group, in line with NICE methods.<br>We have reworded the header of this section to clarify that this should be done to confirm or rule out the diagnosis of CKD. This should be a one-off test, not to be repeated in people who fall within this eGFR range. We have amended the recommendation to state 'consider using eGFRcystatinC at initial diagnosis to confirm or rule out CKD**…**' and updated recommendation number 36 (p55 of the full guideline) to state that monitoring should be with eGFRcreatinine. |

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| | | | | | | professionals and referral pathways. It is not clear if these costs have been incorporated into the economic analysis.<br><br>(ii) The recommendation that CKD-EPIcys should be used to further assess a patient with CKD3aA1 will include the majority of patients with stage 3-5 CKD; again, careful assessment of the implications of this change are required.<br><br>Practicing clinicians in primary and secondary care recognise that patients have become increasingly informed about CKD and the estimating equations that are used to classify CKD. We believe that the impact of the changes to the testing recommended in the guideline and which are summarised in algorithm A should be carefully evaluated in pilot studies in primary care before their generalisation to mainstream clinical practice. We believe that most health care professionals involved in the management of patients with CKD will focus on algorithm A; primary care will require substantial support to implement that pathway accurately such that there is no detrimental impact on the improvements in management of CKD seen since the first edition of the guideline, by committing a lot of time to re-education of patients and health-care professionals when primary care specifically and the NHS generally is undergoing major | |

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| | | | | | | structural changes with many competing priorities. | |
| SH | Royal College of General Practitioners | 5 | FULL | General | General | We found that failing to monitor ACR or GFR in UK primary care was associated with an increased risk of cardiovascular disease and mortality in people with diabetes (McGovern, Rusholme et al. 2013). This paper highlights the need to undertake the routine renal screening of people with diabetes as recommended by this guideline. – SL | Thank you for this information. |
| SH | Royal College of General Practitioners | 4 | FULL | 17 | 7 | Even where CKD is recognised, primary care clinician confidence in managing CKD is low (Tahir, Dmitrieva et al. 2011). – SL | Thank you for this information. |
| SH | Royal College of General Practitioners | 6 | FULL | 207 | 2 | Under the section on Information and Education, I would propose the addition of a statement about the need to inform patients of their CKD at the point of diagnosis. Evidence suggests that GPs are reluctant to inform people they have CKD because of the concern that they are labelling someone as having a disease (Blakeman T, Protheroe J, Chew-Graham C, Rogers A, Kennedy A Understanding the management of early-stage chronic kidney disease in primary care: a qualitative study. Br J Gen Pract. 2012;62(597):e233-42). Also, there is evidence that a high proportion of people with CKD stage 3 are not aware that they have the condition. This forms an inevitable | Thank you for your comment. Although the 2008 recommendation 46 (now recommendation 47 in the 2014 full guideline) states that people with CKD should be involved in development of education and information programmes from the outset, and recommendation 33 (now recommendation 32 in the 2014 full guideline) begins 'Agree a plan to establish the cause of CKD during an informed discussion with the person with CKD', we agree this can be strengthened by adding an extra bullet to recommendation 54 (now recommendation 55 in the 2014 full guideline) 'Ensure that systems are in place to: inform people with CKD of their diagnosis' and have amended this recommendation accordingly. |

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| | | | | | | barrier to subsequent discussion of risk and or treatment strategies.( McIntyre NJ, Fluck R, McIntyre C, Taal M. Treatment needs and diagnosis awareness in primary care patients with chronic kidney disease.Br J Gen Pract. 2012;62(597):e227-32). – SF | |
| SH | Royal College of General Practitioners | 2 | FULL | 256 | 1 | In a RCT we demonstrate that audit-based-education in general practice improves blood pressure control in people with CKD (de Lusignan, Gallagher et al. 2013). We have also performed a review of other primary care quality improvement strategies for the management of hypertension in CKD (Gallagher, de Lusignan et al. 2010). – SL | Thank you for this information. The section on optimal blood pressure ranges was not prioritised as part of the update for this guideline, and therefore no new evidence was reviewed. |
| SH | Royal College of General Practitioners | 1 | FULL | 356 | 26-42 | In addition to the studies cited we have also shown that serum phosphate increases with decreasing renal function in the and furthermore elevated levels in both CKD stage 1-2 and CKD stages 3-5 are associated with increased cardiovascular events (McGovern, de Lusignan et al. 2013). - SL | Thank you for this information. This section was not prioritised as part of the update for this guideline, and therefore no new evidence was reviewed. |
| SH | Royal College of General Practitioners | 3 | FULL | 381 | 21 | Following on from this study we have produced more recent descriptive analysis of anaemia prevalence and type in the general population (Dmitrieva, de Lusignan et al. 2013). – SL | Thank you for this information. This section was not prioritised as part of the update for this guideline and therefore the background text has not been updated. |
| SH | Royal College of General Practitioners | 7 | GENERAL | General | General | **References:**<br><br>de Lusignan, S., H. Gallagher, et al. (2013). "Audit-based education lowers | Thank you for your comment and this information – our responses to your individual comments above detail why these references were not included as part of this guideline update. |

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| | | | | | | systolic blood pressure in chronic kidney disease: the Quality Improvement in CKD (QICKD) trial results." Kidney Int **84**(3): 609-620.<br>Strict control of systolic blood pressure is known to slow progression of chronic kidney disease (CKD). Here we compared audit-based education (ABE) to guidelines and prompts or usual practice in lowering systolic blood pressure in people with CKD. This 2-year cluster randomized trial included 93 volunteer general practices randomized into three arms with 30 ABE practices, 32 with guidelines and prompts, and 31 usual practices. An intervention effect on the primary outcome, systolic blood pressure, was calculated using a multilevel model to predict changes after the intervention. The prevalence of CKD was 7.29% (41,183 of 565,016 patients) with all cardiovascular comorbidities more common in those with CKD. Our models showed that the systolic blood pressure was significantly lowered by 2.41 mm Hg (CI 0.59-4.29 mm Hg), in the ABE practices with an odds ratio of achieving at least a 5 mm Hg reduction in systolic blood pressure of 1.24 (CI 1.05- | |

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| | | | | | | 1.45). Practices exposed to guidelines and prompts produced no significant change compared to usual practice. Male gender, ABE, ischemic heart disease, and congestive heart failure were independently associated with a greater lowering of systolic blood pressure but the converse applied to hypertension and age over 75 years. There were no reports of harm. Thus, individuals receiving ABE are more likely to achieve a lower blood pressure than those receiving only usual practice. The findings should be interpreted with caution due to the wide confidence intervals.<br><br>There are also extensive tables of data listed at the end of the main QICKD trial report:<br>**http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3778715/**<br><br>The main supplementary data file is at:<br><br>**http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3778715/bin/ki201396x1.tif**<br><br>Dmitrieva, O., S. de Lusignan, et al. (2013). "Association of anaemia in primary care patients with chronic | |

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| | | | | | | kidney disease: cross sectional study of quality improvement in chronic kidney disease (QICKD) trial data." BMC Nephrol **14**: 24.<br>BACKGROUND: Anaemia is a known risk factor for cardiovascular disease and treating anaemia in chronic kidney disease (CKD) may improve outcomes. However, little is known about the scope to improve primary care management of anaemia in CKD. METHODS: An observational study (N = 1,099,292) with a nationally representative sample using anonymised routine primary care data from 127 Quality Improvement in CKD trial practices (ISRCTN5631023731). We explored variables associated with anaemia in CKD: eGFR, haemoglobin (Hb), mean corpuscular volume (MCV), iron status, cardiovascular comorbidities, and use of therapy which associated with gastrointestinal bleeding, oral iron and deprivation score. We developed a linear regression model to identify variables amenable to improved primary care management. RESULTS: The prevalence of Stage 3-5 | |

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| | | | | | | CKD was 6.76%. Hb was lower in CKD (13.2 g/dl) than without (13.7 g/dl). 22.2% of people with CKD had World Health Organization defined anaemia; 8.6% had Hb </= 11 g/dl; 3% Hb </= 10 g/dl; and 1% Hb </= 9 g/dl. Normocytic anaemia was present in 80.5% with Hb </= 11; 72.7% with Hb </= 10 g/dl; and 67.6% with Hb </= 9 g/dl; microcytic anaemia in 13.4% with Hb </= 11 g/dl; 20.8% with Hb </= 10 g/dl; and 24.9% where Hb </= 9 g/dl. 82.7% of people with microcytic and 58.8% with normocytic anaemia (Hb </= 11 g/dl) had a low ferritin (<100 ug/mL). Hypertension (67.2% vs. 54%) and diabetes (30.7% vs. 15.4%) were more prevalent in CKD and anaemia; 61% had been prescribed aspirin; 73% non-steroidal anti-inflammatory drugs (NSAIDs); 14.1% warfarin 12.4% clopidogrel; and 53.1% aspirin and NSAID. 56.3% of people with CKD and anaemia had been prescribed oral iron. The main limitations of the study are that routine data are inevitably incomplete and definitions of anaemia have not been standardised. CONCLUSIONS: Medication | |

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| | | | | | | review is needed in people with CKD and anaemia prior to considering erythropoietin or parenteral iron. Iron stores may be depleted in over >60% of people with normocytic anaemia. Prescribing oral iron has not corrected anaemia.<br><br>Gallagher, H., S. de Lusignan, et al. (2010). "Quality-improvement strategies for the management of hypertension in chronic kidney disease in primary care: a systematic review." Br J Gen Pract **60**(575): e258-265.<br>BACKGROUND: Chronic kidney disease (CKD) is a relatively recently recognised condition. People with CKD are much more likely to suffer from cardiovascular events than progress to established renal failure. Controlling systolic blood pressure should slow the progression of disease and reduce mortality and morbidity. However, no systematic review has been conducted to explore the effectiveness of quality-improvement interventions to lower blood pressure in people with CKD. AIM: To assess the effectiveness of quality-improvement interventions to reduce systolic blood pressure in people with CKD in primary | |

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| | | | | | | care, in order to reduce cardiovascular risk and slow the progression of renal disease. METHOD: Papers were identified from the trial data bases of the Cochrane Effective Practice and Organisation of Care Group (EPOC) and Cochrane renal groups. In a three-round process, at least two investigators read the papers independently. Studies were initially excluded based on their abstracts, if these were not relevant to primary care. Next, full papers were read, and again excluded on relevance. Quantitative and, where this was not possible, qualitative analyses of the findings were performed. RESULTS: The selected studies were usually carried out on high-risk populations including ethnic minorities. The interventions were most often led by nurses or pharmacists. Three randomised trials showed a combined effect of a reduction in systolic blood pressure of 10.50 mmHg (95% confidence interval [CI] = 5.34 to 18.41 mmHg). One non-randomised study showed a reduction in systolic blood pressure of 9.30 mmHg (95% CI = 3.01 to 15.58 | |

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| | | | | | | mmHg). CONCLUSION: Quality-improvement interventions can be effective in lowing blood pressure, and potentially in reducing cardiovascular risk and slowing progression in CKD. Trials are needed in low-risk populations to see if the same improvements can be achieved.<br><br>McGovern, A. P., S. de Lusignan, et al. (2013). "Serum Phosphate as a Risk Factor for Cardiovascular Events in People with and without Chronic Kidney Disease: A Large Community Based Cohort Study." PLoS One **8**(9): e74996. BACKGROUND: Serum phosphate is a known risk factor for cardiovascular events and mortality in people with chronic kidney disease (CKD), however data on the association of these outcomes with serum phosphate in the general population are scarce. We investigate this relationship in people with and without CKD in a large community-based population. METHODS: Three groups from an adult cohort of the Quality Improvement in Chronic Kidney Disease (QICKD) cluster randomised trial (ISRCTN56023731) were followed over a period of 2.5 years: people with normal renal function (N = 24,184), people with CKD stages 1-2 (N = 20,356), and people with CKD stages 3-5 (N = 13,292). We used a multilevel | |

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| | | | | | | logistic regression model to determine the association between serum phosphate, in these groups, and a composite outcome of all-cause mortality, cardiovascular events, and advanced coronary artery disease. We adjusted for known cardiovascular risk factors. FINDINGS: Higher phosphate levels were found to correlate with increased cardiovascular risk. In people with normal renal function and CKD stages 1-2, Phosphate levels between 1.25 and 1.50 mmol/l were associated with increased cardiovascular events; odds ratio (OR) 1.36 (95% CI 1.06-1.74; p = 0.016) in people with normal renal function and OR 1.40 (95% CI 1.09-1.81; p = 0.010) in people with CKD stages 1-2. Hypophosphatemia (<0.75 mmol/l) was associated with fewer cardiovascular events in people with normal renal function; OR 0.59 (95% CI 0.36-0.97; p = 0.049). In people with CKD stages 3-5, hyperphosphatemia (>1.50 mmol/l) was associated with increased cardiovascular risk; OR 2.34 (95% CI 1.64-3.32; p<0.001). Other phosphate ranges were not found to have a significant impact on cardiovascular events in people with CKD stages 3-5. CONCLUSIONS: Serum phosphate is associated with cardiovascular events in people with and without CKD. Further research is required to determine the mechanisms underlying these associations. | |

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| | | | | | | McGovern, A. P., B. Rusholme, et al. (2013). "Association of chronic kidney disease (CKD) and failure to monitor renal function with adverse outcomes in people with diabetes: a primary care cohort study." BMC Nephrol **14**: 198. BACKGROUND: Chronic kidney disease (CKD) is a known risk factor for cardiovascular events and all-cause mortality. We investigate the relationship between CKD stage, proteinuria, hypertension and these adverse outcomes in the people with diabetes. We also study the outcomes of people who did not have monitoring of renal function. METHODS: A cohort of people with type 1 and 2 diabetes (N = 35,502) from the Quality Improvement in Chronic Kidney Disease (QICKD) cluster randomised trial was followed up over 2.5 years. A composite of all-cause mortality, cardiovascular events, and end stage renal failure comprised the outcome measure. A multilevel logistic regression model was used to determine correlates with this outcome. Known cardiovascular and renal risk factors were adjusted for. RESULTS: Proteinuria and reduced estimated glomerular filtration rate (eGFR) were independently associated with adverse outcomes in people with diabetes. People with an eGFR <60 ml/min, proteinuria, and hypertension have the greatest odds ratio (OR) of adverse | |

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| | | | | | | outcome; 1.58 (95% CI 1.36-1.83). Renal function was not monitored in 4460 (12.6%) people. Unmonitored renal function was associated with adverse events; OR 1.35 (95% CI 1.13-1.63) in people with hypertension and OR 1.32 (95% CI 1.07-1.64) in those without. CONCLUSIONS: Proteinuria, eGFR < 60 ml/min, and failure to monitor renal function are associated with cardiovascular and renal events and mortality in people with diabetes.<br><br>Tahir, M. A., O. Dmitrieva, et al. (2011). "Confidence and quality in managing CKD compared with other cardiovascular diseases and diabetes mellitus: a linked study of questionnaire and routine primary care data." BMC Fam Pract **12**: 83.<br>BACKGROUND: Much of chronic disease is managed in primary care and chronic kidney disease (CKD) is a recent addition. We are conducting a cluster randomised study of quality improvement interventions in CKD (QICKD) - Clinical Trials Registration: ISRCTN56023731. CKD registers have a lower than expected prevalence and an initial focus group study suggested variable levels of confidence in managing CKD. Our objective is to compare practitioner confidence and achievement of quality indicators for CKD with hypertension and diabetes. METHOD: We validated a new | |

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| | | | | | | questionnaire to test confidence. We compared confidence with achievement of pay-for-performance indicators (P4P) and implementation of evidence-based guidance. We achieved a 74% (148/201) response rate. RESULTS: 87% (n = 128) of respondents are confident in managing hypertension (HT) compared with 59% (n = 87) in managing HT in CKD (HT+CKD); and with 61% (n = 90) in HT, CKD and diabetes (CKD+HT+DM). 85.2% (P4P) and 62.5% (National targets) of patients with hypertension are at target; in patients with HT and CKD 65.1% and 53.3%; in patients with HT, CKD and DM 67.8% and 29.6%. Confidence in managing proteinuria in CKD is low (42%, n = 62). 87% of respondents knew BP treatment thresholds in CKD, but only 53% when proteinuria is factored in. Male GPs, younger (< 35 yrs), and older (> 54 yrs) clinicians are more confident than females and 35 to 54 year olds in managing CKD. 84% of patients with hypertension treated with angiotensin modulating drugs achieve achieved P4P targets compared to 67% of patients with CKD. CONCLUSIONS: Practitioners are less likely to achieve management targets where their confidence is low.<br><br>There are further QICKD trial papers either in-press or published. | |

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| SH | Royal College of Nursing | 1 | GENERAL | General | General | The Royal College of Nursing is a registered stakeholder for Clinical Guideline for Chronic Kidney Disease,<br><br>The Royal College of Nursing was invited to comment on recommendations for the update of this guideline.<br><br>The document was circulated to nurses caring for people with kidney disease. Find below comments received from the reviewers. | Thank you for your comment. |
| SH | Royal College of Nursing | 4 | NICE | General | | There are many changes in the guidance that will affect primary care practice, so ongoing education of GPs and practice nurses is crucial. Many primary care staff are still not conversant with 2008 recommendations, and these new recommendations are likely to cause confusion, especially regarding the use of both eGFR and ACR in staging, and the correction factor to be used with CKD-EPI. | Thank you for your comment. To accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations. These recommendations have been highlighted as an area that may require implementation support. |
| SH | Royal College of Nursing | 2 | NICE | 29 | 1.4.2 | Suggest that this section could be reworded, as not all bullet points are written as questions, and the section needs to be re-ordered according to the patient pathway. For example:<br><br>*What is CKD and how does it affect people?*<br><br>*What questions should people ask about their kidneys?*<br><br>*What can people do to manage and* | Thank you for your comment. This question was not included in the 2014 update because at the time of undertaking the review for deciding whether to update the guideline (October-November 2011) no new evidence was identified in this area, and therefore this topic was not prioritised for update. |

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| | | | | | | *influence their own condition?*<br><br>*What complications or side effects may occur as a result of medication?*<br><br>*What treatments are available for CKD, what are their advantages and disadvantages, complications and side-effects?*<br><br>*In what ways could CKD and its treatment affect people's daily life, social activities, work opportunities and financial situation, including benefits and allowances available?*<br>*How can people cope with and adjust to CKD and what sources of psychological support are available?*<br><br>*What is involved with the different types of renal replacement therapy (such as the frequency and length of time of dialysis treatment sessions or exchanges and pre-emptive transplantation)?*<br><br>*What is the preparation required for different types of renal replacement therapy (such as having a fistula or peritoneal catheter)?*<br><br>*What does conservative management mean?* | |
| SH | Royal | 3 | NICE | 30 | 1.4.10 | Suggest include 'smoking cessation' | Thank you for your comment. We have included this |

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| | College of Nursing | | | | | here<br><br>…support self-management (this includes providing information about blood pressure, smoking cessation, exercise, diet and medicines) | suggestion. |
| SH | Royal College of Pathologists | 6 | FULL | general | | New classification of stage of CKD, with risk stratification for cardiovascular disease is helpful and clear | Thank you for your comment. |
| SH | Royal College of Pathologists | 1 | FULL | 47 | N/A | Flow sheet useful and easy to follow | Thank you for your comment. |
| SH | Royal College of Pathologists | 2 | FULL | 47 | N/A | Use of cystatin C as described will have a significant financial effect on all laboratories. Although overall this will have a financial benefit, the cost to the labs needs to be accounted for | Thank you for your comment. We have reworded the header of this section to clarify that this should be done to confirm or rule out the diagnosis of CKD. This should be a one-off test, not to be repeated in people who fall within this eGFR range. We have amended the recommendation to state 'Consider using eGFRcystatinC at initial diagnosis to confirm or rule out CKD… ' to highlight when this test could be considered. Recommendation number 36 in the full guideline has also been updated to state that monitoring should be with eGFRcreatinine.<br><br>As you note, the use of the test should reduce costs to the NHS overall, although lab costs are likely to increase. So to accompany this guideline, costings and implementation tools will be produced to facilitate the implementation of recommendations. This recommendation has been highlighted as an area that will require implementation support.<br><br>Increases in laboratory costs will be dependent on who pays |

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| | | | | | | | for the test. We would envisage that introduction of this test will be dependent on Clinical Commissioning Groups agreeing to pay for it through the commissioning process. |
| SH | Royal College of Pathologists | 3 | FULL | 49 | N/A | Pink section ' ergocalciferol to people to people' repeated | Thank you for your comment. This has been corrected. |
| SH | Royal College of Pathologists | 9 | FULL | 50 | 12 | WE SHOULD NOT DEFINE NEQAS AS THE ONLY SUITABLE EXTERNAL QA. LABORATORIES MAY CHOOSE WHICH QA THEY WISH TO USE | Thank you for your comment. We agree it should state "a national external quality assessment scheme" and have amended the recommendation accordingly. |
| SH | Royal College of Pathologists | 4 | FULL | 50 | 36 | CKD monitoring mentions renal stones but flow chart says recurrent renal stones. Further instances just say renal stones. Need to make clear whether it applies to a single episode of stones or only if there is a recurrence | Thank you for your comment. This applies to recurrent renal stones and has been clarified throughout the guideline documents. |
| SH | Royal College of Pathologists | 8 | FULL | 52 | 20 | Should laboratories have a role in saying that eGFR 60-90 needs to be interpreted with caution? | Thank you for your comment. Whilst laboratories may choose to do this on their reports the GDG does not feel this should be mandated in the guideline. |
| SH | Royal College of Pathologists | 5 | FULL | 53 | 1 | Suggest make clear that PCR may be needed in patients at risk of tubular rather than glomerular disease | Thank you for your comment. Most patients with a tubular lesion will also have albuminuria. Testing for tubular proteinuria using a total protein approach almost certainly has very poor sensitivity for detecting tubular disease. When an isolated tubular lesion is suspected this is best investigated by measuring a specific tubular protein using an immunoassay. However, most CKD is not tubular disease so this issue is outside scope of the guideline update. |
| SH | Royal College of Pathologists | 7 | FULL | 54 | 16 | Does not define frequency of monitoring. Suggest that recommendation 36 that states how to work out frequency of monitoring is placed immediately after recommendation 31 | Thank you for your comment; however we do not agree that these recommendations should be re-ordered. Although frequency of monitoring is defined in a recommendation placed later in the guideline, the GDG agree this recommendation needs to be placed after the classification section. Recommendation 28 (previously recommendation |

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| | | | | | | | 31) in the full guideline is intended to highlight who should be tested for CKD initially, not those that should be monitored on an ongoing basis. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 1 | FULL | 50 | 7 | MDRD was validated in a cohort with established CKD whereas EPI cohort was validated in a cohort with a large number of 'normal' subjects. It is therefore not surprising that EPI outperforms MDRD in CKD 1 and 2. However in those with GFR <60 MDRD performs better (http://www.ncbi.nlm.nih.gov/pubmed/?term=earley+and+mdrd). I am therefore unsure what is to be gained from the change of equation UNLESS it can be shown to trigger specific interventions that improve patient outcomes. We need to move away from the " NET RECLASSIFICATION INDEX" to an idea of "NET RETREATMENT INDEX or NET IMPROVEMENT INDEX" – i.e. it doesn't really matter which equation performs better at classifying patients rather will a change of equation improve patient-centred outcomes… there has been no research presented to show that moving from MDRD to EPI will have any impact on patient outcomes. Furthermore if one is serious about getting the right equation I am not clear why BIS equations for the elderly have not been mentioned as these are clearly the only equations that have been specifically developed in an elderly cohort | Thank you for your comment. The outcomes against which equations were assessed were those traditionally used to do so – namely accuracy, bias and precision. Overall CKD-EPI provides a big improvement in reducing bias in GFR estimation, the improvement in precision is more moderate. In the Earley paper you refer to P30 values for the CKD-EPIcreatinine equation were slightly superior to those of the MDRD equation in most studies that had undertaken a head-to-head comparison. The gain is in risk associations.<br><br>In direct comparisons from large population cohorts CKD-EPI corresponds to crude risk much better than MDRD. In the JAMA paper (JAMA. 2012;307(18):1941-1951) 34.7% of eGFR 45-59 get reclassified upward to 60-89 and the CIR (crude incidence rate) for all-cause mortality is 9.9 vs. 34.5 for those reclassified upward vs. not reclassified vs. downward among those with 45-59. Therefore on a crude basis the 34.7% of those with eGFR 45-59 moved to 60+ have more than 3-fold lower mortality risk (9.9/34.5). eTable 6 shows this is 2-fold for high risk cohorts and eTable 7 for CKD cohorts.<br><br>For CVD mortality CIRs are 2.7, 13.0 and 52.3 – >4-fold lower risk for those reclassified upward.<br><br>For ESRD it is 0.5 vs. 0.8 vs. 1.6 – less than 2-fold lower for those reclassified upward so less pronounced.<br><br>In the AJKD paper (Am J Kidney Dis. 60(2):241-249) a similar percentage (30.8%) were reclassified upwards from eGFR 45-59 to 60-89 and again with the outcomes all-cause mortality, acute myocardial infarction, end-stage renal |

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| | | | | | | | disease, and progression of CKD the CKD-EPI equation was better at categorising individuals at clinical risk than the MDRD Study equation.<br><br>With reference to BIS, we agree that BIS1 (the creatinine equation) performed better than other equations in an elderly German population (P30 was 88% compared to CKD-EPI of 78% and MDRD 71%). However, this study was published after the cut-off date for evidence to be included in the guideline. Since the draft guideline was completed the BIS1 equation has been externally validated in an elderly French population, where the P30 was 78% compared to 82% with the CKD-EPI equation (J Nephrol 2013;26(4):716-723), and an elderly English population, BIS1 P30 88% compared to CKD-EPI 83% (Am J Kidney Dis. 2014 Feb 12 epub ahead of print). Incidentally, in the analysis of patient level data that was conducted for the economic model, it was observed that CKD-EPI$_{creat}$ seemed to over-diagnose CKD *less* in older patients than in younger patients (Positive predicted value=80% cf67-70% in younger people compared to mGFR) – see for example Table 191 and L.2 of Appendix L. Most studies to date comparing estimating GFR equations have been cross-sectional studies, but in clinical practice GFR is commonly used to assess change in kidney function over time. A recent study confirms the utility of estimated GFR using the CKD-EPIcreat equation to monitor changes of measured GFR, with only 15% of individuals showing a change in error in GFR (measured minus estimated) exceeding +3 mL/min/1.73 m2/year (Padala S, Tighiouart H, Inker LA et al. Accuracy of a GFR estimating equation over time in people with a wide range of kidney function. Am J Kidney Dis 2012;60(2):217-224). |
| SH | Sheffield Teaching Hospitals NHS | 2 | FULL | 50 | 15 | Use of eGFRCysC is an interesting idea to confirm CKD between 45 and 59mls/min.<br>However I am concerned that i) the | Thank you for your comment. The recommendation to use cystatin C was deliberately couched as 'consider' although economic modelling supported its use. This recommendation is in part intended to help address the concerns that there is |

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| | Foundation Trust | | | | | problems with cystatin C haven't been full recognised – obesity, steroid use and in particular thyroid disease – the latter being prevalent in the elderly. Whilst the guidelines acknowledge this its unrealistic to expect GPs to be able to interpret cystatin c levels in patients with thyroid disease… the danger is one of overtesting ii) there has been no clinical study evaluating the cost-effectiveness of cystatin C. The modelling data is at best speculative, assuming that differing CKD stages and the label of CKD carry different costs.This would have been an ideal research recommendation rather than a 'priority' for implementation. Again no experimental/clinical data to show that clinical use of Cystatin C will improve patient centred outcomes. | over diagnosis of CKD in people who fall within this group. Cystatin C has been demonstrated as having a lower number of false positive results at eGFR 45-59. This has been stated in the 'linking evidence to recommendations' section (section 5.7.3 of the full guideline). We acknowledged the potential influence of uncontrolled thyroid disease ('Interpret eGFRcystatinC with caution in people with uncontrolled thyroid disease as eGFRcystatinC values may be falsely elevated in people with hypothyroidism and reduced in people with hyperthyroidism') and although we agree that thyroid disease is prevalent in the elderly uncontrolled thyroid disease is not.<br><br>We acknowledge that the evidence to populate the model was not as strong as we would have liked and that was one of the reasons that the recommendation started with a relatively weak 'consider'. However, the model was based on the diagnostic evidence from the guideline's systematic review, recommendations from NICE guidance and the expertise of the clinicians on the guideline development group, in line with NICE methods. The assumption that the label of CKD can incur increased cost seems a plausible one, considering that different management/monitoring is recommended in this and other guidelines.<br><br>Please also note that the 'key priorities for implementation' (KPIs) are the recommendations that the GDG has selected as being the recommendations that are most likely to have a high impact on patients' outcomes and on reducing variations in clinical management (as per the NICE Guidelines manual). Although this recommendation is worded as 'consider', the GDG agreed it was important to highlight it as a KPI as it is likely to require support in implementing, and also will change practice, as some people who perhaps previously were |

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| | | | | | | | incorrectly diagnosed as having CKD3a, may be diagnosed as not having CKD following confirmation with a CystatinC test. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 3 | FULL | 50 | 24 | The acceptance of the KDIGO staging without evidence to show that staging improves clinical decision making and patient outcomes compared to the 2008 classification is disappointing. I have done many education sessions for GPs/non-nephrologists on the KDIGO classification and the consensus is that it adds a significant layer of complexity to the classification ( 16 categories!!) without making a difference to clinical management. The rationale for change is not clear. In particular whilst the A1 and A2 categories make sense from an epidemiological/research basis there is little evidence to show how documenting A1 or A2 levels of proteinuria actually impact on clinical decision making…Indeed whilst A2 associated with a higher risk of CV and kidney endpoints there is no evidence to show that knowledge of A2 levels of albuminuria can trigger a specific intervention beyond BP control. The classification system needs to work for non-nephrologists and as it stands its not clear what improvement this offers non-nephrologists compared to the previous classification. Needs to be big consultation with bodies like RCGP | Thank you for your comment. The proposed classification was based on an updated review of the evidence (reported in chapter 6), and the KDIGO staging was an extension of the internationally accepted and adopted modifications to the classification that NICE had recommended in CG73. The rationale for subdivision of ACR categories was based on prognosis data showing increased risk of progression at higher levels of albuminuria. We have followed that part of the KDIGO classification for that reason but accept that other than in diabetes specific intervention trials are lacking. What the A2 category serves to do though is highlight increased risk and the need for better vigilance and awareness of risk, for example risk of acute kidney injury. |
| SH | Sheffield Teaching Hospitals | 7 | FULL | 58 | 26-36 | Its completely inappropriate that all patients with CKD4 should be referred to nephrologists… this recommendation | Thank you for your comment. This was part of the 2008 guideline. At the time of undertaking the review for deciding whether to update the guideline (October-November 2011) |

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| | NHS Foundation Trust | | | | | has never had any serious cost-effectiveness analysis. The reality is that most people with CKD 4 will be elderly and (s work on the veterans cohort from o'Hare shows) are extremely unlikely to reach ESRD within their lifetime. In fact the risk of ESRD in a G4A1 patient in their 70s and 80s is negligible. The guidline should focus on referring those with progressive disease who are likely to need RRT within their lifetime. The rest should clearly get appropriate CVD/anaemia management but don't necessarily need to see a nephrologist. Focus on patients with CKD 4 getting the right treatment rather than who delivers that treatment. CRISIS study shows that even in a referred cohort progression is relatively rare and therefore its not sustainable to offer nephrology assessment for all ckd 4 patients irrespecticve of age.<br>The research recommendations should focus on developing collaborative models of CKD care with GPs morbid elderly so that those with low risk of progressuion get the appropriate treatment in the community.<br>As for this trigger for referral 'sustained decrease in GFR of 25% or more and a change in GFR category or 32 sustained decrease in GFR of 15 ml/min/1.73 m2 or more'there is no timeframe given for allowed period of decline | no new evidence was identified regarding referral criteria. This was also not raised during consultation of the draft scope for the update, and therefore this topic was not reviewed in the updated guidance.<br><br>The amendments made to this recommendation relate only to updating GFR and ACR terminology for consistency with the updated classification criteria and definition of progression that have been reviewed in this update.<br><br>We do agree that 'blanket' referral of all patients with GFR less than 30ml/min may be inappropriate, which is reflected in the recommendation wording with the insertion of 'normally'. The subsequent paragraph clearly states "Consider discussing management issues with a specialist by letter, email or telephone in cases where it may not be necessary for the person with CKD to be seen by the specialist. (see recommendation 59 in the full guideline/recommendation 1.5.3 in the NICE version). Furthermore, recommendation 58 in the full guideline/recommendation 1.5.2 in the NICE version says "take into account co-morbidities when referring" and recommendation 40 in the full guideline/1.3.5 in the NICE version specifically addresses this in terms of planning intervention and assessing CKD progression.<br><br>Regarding your comment on trigger for referral 'sustained decrease in GFR of 25% or more and a change in GFR category or a sustained decrease in GFR of 15 ml/min/1.73 $m^2$ or more'; a timeframe of 12 months is given (recommendation 40 in the full guideline/1.3.5 in the NICE version). We agree that this should also be included in related recommendations and have now added a separate recommendation to define accelerated progression (recommendation 38 in the full guideline/1.3.3 in the NICE |

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| | | | | | | | version), and referred to this in related recommendations. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 4 | FULL | 59 | Lines 10 and 13 | The recommendation that all diabetics with CKD should have a systolic BP of less than 130 is not borne out by robust evidence. Most will be Type 2 diabetics with a high risk of falls.<br>The KDIGO guidelines highlight this by saying that the evidence base for the 130 BP target with A2 levels of albuminuria is 2D. Similarly the evidence that ACEi/ARBs should be used in those with A2 levels of albuminuria is 2D.<br>Furthermore the very small benefit (in terms of stroke risk) of bringing the target down from 140 to 130 is offset by higher risk of complications of therapy.<br>NICE should avoid guidance based on 2D levels of evidence. This is a big issue in primary care and would strongly suggest that the guidelines around BP targets be based on the recent American Diabetic association guidelines which are much more pragmatic and recognise the difficulty in treating BP in diabetics. The recommendation for ACEi and the lower BP target of 130 should be in those who would benefit most from that lower target –namely those with A3 levels of proteinuria.<br>Also guidelines on BP don't make clear whether office BP ( as opposed to self-monitoring or 24hr ABPM) is acceptable in the CKD population | Thank you for your comment.<br>This question was not included in the 2014 update because at the time of undertaking the review for deciding whether to update the guideline (October-November 2011) no new evidence was identified in this area, and therefore this topic was not prioritised for update.<br>We would point out however that the recommendation in this treatment group is a range from 120-129 mmHg systolic, reflecting our previous concerns about over-control of blood pressure (see Figure 4 in section 9.2 of the full guideline).<br><br>For advice relating to measuring blood pressure and lifestyle interventions to reduce blood pressure, we have referred to NICE clinical guideline 127 (Hypertension). |
| SH | Sheffield Teaching | 5 | FULL | 60 | Lines 9-23 | Guidelines regarding ACei use – need to recognise that the decline in GFR (25%) | Thank you for your comment. The GDG were concerned about the indiscriminate use of RAAS antagonists where |

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| | Hospitals NHS Foundation Trust | | | | | or rise in serum creatinine (30%) maybe acceptable in those with CKD 123 but perhaps less so in CKD 4 or 5… do we really think its acceptable for somebody with a GFR of 15 to have an acceptable decline in GFR by 25% | there is no specific indication and were careful to record this. We have also called for research about the clinical effectiveness of RAAS antagonists in older people with CKD. We would be disappointed if somebody with a clear indication for RAAS antagonism and a GFR of 15 was not under the care of a nephrologist. A decline in GFR of 25% in somebody with a GFR of 15 would take them to 11.25.<br><br>Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 6 | FULL | 60 | 38 | Realise this is opinion based recommendation on CKD-MBD but if you are going to tell clinicians to monitor ca, P and PTH in CKD4 and 5 you should also tell them to measure vitamin D – PTH uninterpretable without vitamin D levels and identification of D deficiency will clearly change management | Thank you for your comment. The evidence relating to measurement of vitamin D was not prioritised as part of the guideline update because at the time of undertaking the review for deciding whether to update the guideline (October-November 2011) no new evidence was identified in this area. This was also not raised during consultation of the draft scope for the update, and therefore this topic was not reviewed in the updated guidance.<br>We do obviously recommend that people with vitamin D deficiency should be treated where it has been identified (see recommendations 82 and 83 of the full guideline). |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 8 | FULL | 61 | 18 | Disappointing that despite that the fact there are no licensed treatments for progressive CKD and a paucity of trials evaluating new therapies in progression there was no research recommendation made about the need to evaluate new agents for progressive kidney disease and how trials into progression should be conducted. | Thank you for your comment. We are only able to make research recommendations concerning clinical questions that we have specifically reviewed, and therefore cannot advise on the absence of adequate evidence e.g. asymptomatic hyperuricaemia. |

**These organisations were approached but did not respond:**

A Little Wish

AbbVie

Alder Hey Children's NHS Foundation Trust

Allocate Software PLC

Amgen UK

AMORE health Ltd

AMORE Studies Group

Association for Continence Advice

Association for Family Therapy and Systemic Practice in the UK

Association of Anaesthetists of Great Britain and Ireland

Association of British Clinical Diabetologists

Association of British Healthcare Industries

Association of Clinical Pathologists

Association of Renal Industries

Astrazeneca UK Ltd

Barnsley Hospital NHS Foundation Trust

Barts and the London NHS Trust

Baxter Healthcare

Betsi Cadwaladr University Health Board

Birmingham, Sandwell and Solihull Cardiac and Stroke Network

Blood Pressure UK

Boots

Bradford District Care Trust

British Association for Counselling and Psychotherapy

British Association For Paediatric Nephrology

British Association of Critical Care Nurses

British Association of Paediatric Nephrology
British Association of Social Workers
British Association of Urological Surgeons
British Geriatrics Society
British Hypertension Society
British Lymphology Society
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Nuclear Medicine Society
British Psychological Society
British Red Cross
British Society for Immunology
British Society of Urogynaecology
British Transplantation Society
Calderstones Partnerships NHS Foundation Trust
Cambridge University Hospitals NHS Foundation Trust
Camden Link
Capsulation PPS
Capsulation PPS
Cardiff and Vale University Health Board
Care Quality Commission
Central & North West London NHS Foundation Trust
Central London Community Health Care NHS Trust
Church Grange Surgery
CIS' ters
Clarity Informatics Ltd

CM&D Pharma Limited

Community District Nurses Association

Coventry and Warwickshire Cardiac Network

Covidien Ltd.

Croydon Clinical Commissioning Group

Croydon Health Services NHS Trust

Croydon University Hospital

Cybex Ventures

David Lewis Centre, The

Department for Communities and Local Government

Department of Health, Social Services and Public Safety - Northern Ireland

Dept of Primary Health Care Sciences, University of Oxford

Derbyshire Mental Health Services NHS Trust

Division of Public Health & Primary Health Care

Drinksense

East and North Hertfordshire NHS Trust

East Kent Hospitals University NHS Foundation Trust

Economic and Social Research Council

Education for Health

Elcena Jeffers Foundation

Ethical Medicines Industry Group

Faculty of Pain Medicine of the Royal College of Anaesthetists

Faculty of Public Health

Fellowship of Postgraduate Medicine

Five Boroughs Partnership NHS Trust

Fresenius Medical Care

GE Healthcare

Genzyme Therapeutics
George Eliot Hospital NHS Trust
GlaxoSmithKline
Great Western Hospitals NHS Foundation Trust
Greater Manchester and Cheshire Cardiac and Stroke Network
Guidelines and Audit Implementation Network
Guy's and St Thomas' NHS Foundation Trust
Harrogate and District NHS Foundation Trust
Harrow Local Involvement Network
Health & Social Care Information Centre
Health and Care Professions Council
Health and Safety Executive
Healthcare Improvement Scotland
Healthcare Infection Society
Healthcare Inspectorate Wales
Healthcare Quality Improvement Partnership
Healthwatch East Sussex
Heart of England NHS Foundation Trust
Help the Hospices
Herts Valleys Clinical Commissioning Group
Hindu Council UK
Hockley Medical Practice
Hospira UK Limited
Hughes Syndrome Foundation
Humber NHS Foundation Trust
Independent Healthcare Advisory Services
Institute of Biomedical Science

Integrity Care Services Ltd.
Intuitive Surgical
iQudos
Isabel Hospice
James Whale Fund for Kidney Cancer
KCARE
Kimal PLC
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Leeds North Clinical Commisioning Group
Leeds Teaching Hospitals NHS Trust
Lilly UK
Local Government Association
Luton and Dunstable Hospital NHS Trust
Maquet UK Ltd
McDonald Obstetric Medicine Society
Medicines and Healthcare products Regulatory Agency
Mental Health Act Commission
Ministry of Defence (MOD)
Monash Health
Mother and Infant Research Unit
MSD Ltd
Myeloma UK
National Association of Primary Care
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health

National Deaf Children's Society
National Institute for Health Research - Health Technology Assessment Programme
National Institute for Health Research

National Osteoporosis Society
National Patient Safety Agency
National Public Health Service for Wales
NDR UK
Neonatal & Paediatric Pharmacists Group
NHS Barnsley Clinical Commissioning Group
NHS Blood and Transplant
NHS Clinical Knowledge Summaries
NHS Connecting for Health
NHS County Durham and Darlington
NHS Cumbria Clinical Commissioning Group
NHS Derbyshire county
NHS Direct
NHS Greater Manchester Commissioning Support Unit
NHS Health at Work
NHS Improvement
NHS Kirklees
NHS Luton CCG
NHS Medway Clinical Commissioning Group
NHS National Specialised Commissioning Team
NHS Plus
NHS Plymouth
NHS Portsmouth Clinical Commissioning Group

NHS Sheffield
NHS Sheffield CCG
NHS South Central vascular Network
NHS South Cheshire CCG
NHS Wakefield CCG
NHS Warwickshire North CCG
NHS West Hampshire CCG
NHS West Lancashire CCG
North Cheshire Hospitals NHS Trust
North of England Commissioning Support
North West London Critical Care Network
North West London Hospitals NHS Trust
Northern Ireland Nephrology Forum
Nottingham City Council
Nottingham City Hospital
Nova Biomedical UK
Novartis Pharmaceuticals
NS Technomed
Nursing and Midwifery Council
Nutricia Clinical Care
Nutrition and Diet Resources UK
Nutrition Society
Otsuka Pharmaceuticals
Oxford Nutrition Ltd
Oxfordshire Clinical Commissioning Group
Parenteral and Enteral Nutrition Group
Parkwood Healthcare

PERIGON Healthcare Ltd

Pfizer

Pharmacosmos

Pharmametrics GmbH

PHE Alcohol and Drugs, Health & Wellbeing Directorate

Pilgrims Hospices in East Kent

Polycystic Kidney Disease Charity

PrescQIPP NHS Programme

Primary Care Cardiovascular Society

Primary Care Pharmacists Association

Primrose Bank Medical Centre

Public Health England

Public Health Wales NHS Trust

Queen Elizabeth Hospital

Queen Elizabeth Hospital King's Lynn NHS Trust

Ramsey Group Practice

Randox Laboratories Limited

Regional Public Health Agency for Northern Ireland

Renal Nutrition Group, British Dietetic Association

Robert Jones & Agnes Hunt Orthopaedic & District Hospital NHS Trust

Roche Diagnostics

Roche Products

Royal Berkshire NHS Foundation Trust

Royal Brompton Hospital & Harefield NHS Trust

Royal College of Anaesthetists

Royal College of General Practitioners in Wales

Royal College of Midwives

Royal College of Obstetricians and Gynaecologists

Royal College of Paediatrics and Child Health

Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition

Royal College of Physicians

Royal College of Physicians and Surgeons of Glasgow

Royal College of Physicians of Edinburgh

Royal College of Psychiatrists

Royal College of Radiologists

Royal College of Surgeons of England

Royal Free Hospital

Royal Free Hospital NHS Foundation Trust

Royal Pharmaceutical Society

Royal Society of Medicine

Royal Surrey County Hospital NHS Trust

Sandoz Ltd

Sanofi

Scottish Intercollegiate Guidelines Network

Sheffield Childrens Hospital

Shine

Shire Pharmaceuticals Ltd

Sickle Cell Society

Siemens Medical Solutions Diagnostics

Sigma-tau Spa

SNDRi

Social Care Institute for Excellence

Society and College of Radiographers

Solvay

South Asian Health Foundation
South East Staffordshire and Seisdon Pennisula CCG
South London & Maudsley NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
Southport and Ormskirk Hospital NHS Trust
St Mary's Hospital
Staffordshire and Stoke on Trent Partnership NHS Trust
Stockport Clinical Commissioning Group
Syner-Med
Takeda UK Ltd
Thames Ambulance Service Ltd
The Association for Clinical Biochemistry & Laboratory Medicine
The British In Vitro Diagnostics Association
The Hindu Forum of Britain
The Intensive Care Society
The Patients Association
The Phoenix Partnership
The Rotherham NHS Foundation Trust
The UK Renal Registry
ToHealth
Torbay and Southern Devon Health and Care NHS Trus
UK National Screening Committee
UK Renal Pharmacy Group
United Lincolnshire Hospitals NHS
University Hospital Birmingham NHS Foundation Trust
University Hospitals Birmingham
University of Dundee

University of Nottingham
Vascular Society of Great Britain and Ireland
Vifor Pharma UK Ltd
Vitaline Pharmaceuticals
Walsall Local Involvement Network
Wandsworth Clinical Commissioning Group
Welsh Government
Welsh Kidney Patients Association
Welsh Renal Clinical Network
Welsh Scientific Advisory Committee
West Midlands Ambulance Service NHS Trust
West Sussex Public Health
West Yorkshire Cardiac Network
Western Health and Social Care Trust
Western Sussex Hospitals NHS Trust
Westminster Local Involvement Network
Whipps Cross University Hospital NHS Trust
Wigan Borough Clinical Commissioning Group
Wirral University Teaching Hospital NHS Foundation Trust
Worcestershire Acute Hospitals Trust
Wye Valley NHS Trust
York Hospitals NHS Foundation Trust
Yorkshire & the Humber Specialised Commissioning Group
Yorkshire and Humber Strategic Clinical Networks