

National Institute for Health and Clinical Excellence

Acute Kidney Injury  
Guideline Consultation Comments Table

	Stakeholder	Order No	Document	Page No	Line No	Comments	Developer's Response
						Please insert each new comment in a new row.	Please respond to each comment
1.	Abbvie	1	Full	35	5	Suggest addition of cardiothoracic surgery as risk factor Reference: <ul style="list-style-type: none"> <li>Thakar CV, Arrigain S, Worley S et al. A clinical score to predict acute renal failure after cardiac surgery. <i>J Am Soc Nephrol</i> 2005; 16:162–168</li> <li><a href="#">Demirjian S</a> et al. Predictive models for acute kidney injury following cardiac surgery. <i>Am J Kidney Dis.</i> 2012 Mar;59(3):382-9</li> </ul>	Thank you for your comment. The GDG was aware that risk assessment tools are relatively well established in the field of cardiac surgery but felt that they were too specific to be utilised effectively for a general population (please refer to the 'Recommendations and link to evidence' section for this recommendation for further discussion). Cardiac surgery per se as compared to other forms of surgery e.g. vascular surgery has not been identified as a form of surgery at increased risk.
2.	Abbvie	2	Full	35	6	Suggest addition of proteinuria as a risk factor, in addition to CKD defined as eGFR <60ml/min/ml2 Reference: <ul style="list-style-type: none"> <li><a href="#">Hsu RK</a>, Hsu CY et al. Proteinuria and reduced glomerular filtration rate as risk factors for acute kidney injury. <i>Curr Opin Nephrol Hypertens.</i> 2011;20:211-7</li> </ul>	Thank you for your comment. This list is in relation to risks associated with surgery and as such this paper would not have been included in this review.
3.	Abbvie	3	Full	35	13	Additional risk factors in adults having surgery: complex or prolonged surgery, prior MI, and COPD References: <ul style="list-style-type: none"> <li>Thakar CV, Arrigain S, Worley S et al. A clinical score to predict acute renal failure after cardiac surgery. <i>J Am Soc Nephrol</i> 2005; 16:162–168</li> <li>Kiers HD, Boogaard M, Schoenmakers M et al. Comparison and clinical suitability of eight prediction models for</li> </ul>	Thank you for your comment. The GDG was aware that risk assessment tools are relatively well established in the field of cardiac surgery but felt that they were too specific to be utilised effectively for a general population (please refer to the 'Recommendations and link to evidence' section for this recommendation for further discussion). We note your references but cardiac surgery per se as compared to other forms of surgery e.g. vascular surgery has not been identified as a form of surgery at increased risk. Furthermore, as outlined in the

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						<p>cardiac surgery-related acute kidney injury. Nephrol Dial Transplant 2013;28:245-351</p> <ul style="list-style-type: none"> <li>Englberger L, Suri RM, Li Z et al. Validation of Clinical Scores Predicting Severe Acute Kidney Injury After Cardiac Surgery. Am J Kidney Dis 2010;56:623-631</li> <li>Huen SC, Parikh CR. Predicting Acute Kidney Injury After Cardiac Surgery: A Systematic Review. Ann Thorac Surg 2012;93:337-347</li> <li>Mariscalco G, Lorusso R, Dominici C et al. Acute Kidney Injury: A Relevant Complication After Cardiac Surgery. Ann Thorac Surg 2011;92:1539-1547</li> <li><a href="#">Demirjian S</a> et al. Predictive models for acute kidney injury following cardiac surgery. <a href="#">Am J Kidney Dis</a>. 2012 Mar;59(3):382-9</li> </ul>	<p>'Recommendations and link to evidence' section, the GDG felt it was important to make recommendations which are relevant to the majority of patients undergoing surgery and there was a focus on highlighting risk factors which were modifiable.</p> <p>The GDG is aware that complex surgery, prior MI and COPD are risk factors for AKI after cardiac surgery. However, there is insufficient evidence that these factors also increase the risk of AKI after general surgery.</p>
4.	Abbvie	4	Full	37	22	<p>Add risk factors: cardiothoracic surgery, proteinuria, complex or prolonged surgery, prior MI, and COPD</p> <p>Same references as used in comment 1-3</p>	<p>Thank you for your comment. The GDG was aware that risk assessment tools are relatively well established in the field of cardiac surgery but felt that they were too specific to be utilised effectively for a general population (please refer to the 'Recommendations and link to evidence' section for this recommendation for further discussion).</p> <p>We note your references but cardiac surgery per se as compared to other forms of surgery e.g. vascular surgery has not been identified as a form of surgery at increased risk.</p> <p>Furthermore, as outlined in the 'Recommendations and link to evidence' section, the GDG felt it was important to make recommendations which are relevant to the majority of patients undergoing surgery and there was a focus on highlighting risk factors which were modifiable.</p>

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							The GDG is aware that complex surgery, prior MI and COPD are risk factors for AKI after cardiac surgery. However, there is insufficient evidence that these factors also increase the risk of AKI after general surgery.
5.	Abbvie	5	Full	40	15	eGFR is only applicable in a steady state and should not be used to diagnose AKI	Thank you for your comment. eGFR is not mentioned in the page and line number you give. However, we agree that eGFR is only applicable in the steady state and nowhere in the guideline have we recommended that it be used to detect AKI. The only reference to GFR on page 40, in line 12 refers to AKI in children: - a 25% or greater fall in eGFR in children and young people. GFR is used in the pRIFLE definition, the standard definition used by paediatricians. The reasons for this are complex, including adjustment of eGFR to an adult body size, but the paediatric community does find this aspect of the definition useful. We acknowledge your concerns in terms of creatinine kinetics.
6.	Abbvie	6	Full	41	37	Patient should be referred for follow up with a nephrologist or general practitioner in outpatient care as the patient can develop CKD as a long term outcome References: <ul style="list-style-type: none"> <li>• Harel Z, Wald R, Bargman JM et al. Nephrologist follow-up improves all-cause mortality of severe acute kidney injury survivors. <i>Kidney Int.</i> 2013 Jan 16;doi: 10.1038/ki.2012.451</li> <li>• Goldstein SL, Jaber BL, Faubel S et al. AKI Transition of Care: A Potential Opportunity to Detect and Prevent CKD. <i>Clin J Am Soc Nephrol</i> 2013;8:476-483</li> </ul>	Thank you for your comment. The links between AKI and CKD were not in the scope of the guideline or its evidence reviews. The GDG is aware of the rapidly developing understanding of the relationship between AKI episodes, and risk and progression of CKD and therefore have amended the 'Recommendations and link to evidence' section for monitoring and follow up after AKI (section 79.5) to include clearer discussion on monitoring and follow up of renal function after an episode of AKI.

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						<ul style="list-style-type: none"> <li><i>Ishani A, Nelson D, Clotheir B et al. The Magnitude of Acute Serum Creatinine Increase After Cardiac Surgery and the Risk of Chronic Kidney Disease, Progression of Kidney Disease, and Death. Arch Intern Med 2011;171:226-233</i></li> </ul>	
7.	Abbvie	7	Full	42	26	<p>Recommend follow up with a nephrologist in 3 months <i>Same references as used in comment 6</i></p>	<p>Thank you for your comment. The GDG felt that this would depend on the clinical situation and it was not appropriate to make a general recommendation when and by whom a patient with AKI should be followed up. The GDG acknowledged that more knowledge was needed to understand the long-term effects of AKI and the need for follow-up arrangements better and made some research recommendations to this effect.</p>
8.	Abbvie	8	Full	43	1	<p>Additional Key Research Recommendations: 1. Utilization, validity and reliability of AKI risk assessment tools and scores 2. Biomarkers use for subclinical AKI and impact of management on progression of AKI</p>	<p>Thank you for your comments. In response:</p> <ol style="list-style-type: none"> <li>1. Thank you for the suggestion, the GDG did not feel that the research recommendation suggestion in this format was a priority. Decisions about inclusion of research recommendations were based on factors such as: <ul style="list-style-type: none"> <li>• the importance to patients or the population</li> <li>• national priorities</li> <li>• potential impact on the NHS and future NICE guidance</li> <li>• ethical and technical feasibility</li> </ul> </li> <li>2. Biomarkers were not considered in this guideline and as such we are not able to make any research recommendations in this area.</li> </ol>
9.	Abbvie	9	Full	44	30	<p>In Adult risk assessment tools, why are Risk scores looking only at patients undergoing cardiac surgery excluded? (cf comment on pages 30 – 31 Appendix C)</p>	<p>Thank you for your comment. The GDG was aware that risk assessment tools are relatively well established in the field of cardiac surgery but felt that they were too specific to be utilised effectively for a general population</p>

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						References: Same references as used in comment 3	(please refer to the 'Recommendations and link to evidence' section for this recommendation for further discussion). Cardiac surgery per se as compared to other forms of surgery e.g. vascular surgery has not been identified as a form of surgery at increased risk.
10.	Abbvie	10	Full	19	general	Consider "readmission" and "discharge status compared to care prior to admission" as outcomes <i>References:</i> <ul style="list-style-type: none"> <li>• <i>Morris DS, Rohrbach J, Rogers M, et al. The Surgical Revolving Door: Risk Factors for Hospital Readmission. J of Surgical Research 2011;170:297-301</i></li> <li>• <i>Thakar CV, Parikh PJ, Liu Y et al. Acute kidney injury (AKI) and risk of readmissions in patients with heart failure. Am J Cardiol. 2012; 109:1482-6.</i></li> </ul>	Thank you for your comment. Outcomes for each clinical question are decided separately at the protocol stage and only those considered by the GDG to be critical or important for decision making are selected. It is not possible or desirable to produce a complete list of all outcomes reported by studies. The outcomes that were chosen by the GDG were those they felt were of greatest importance to the individual reviews. In addition, data "readmission" and "discharge status compared to care prior to admission" would not be available in most of the literature. Although these 2 papers that are stated report these outcomes, the vast majority of AKI papers would not do so. They are not outcomes of key clinical interest and not useful to inform recommendations. The GDG felt that if mortality could be improved this would have a great impact on all other outcomes.
11.	Abbvie	11	Full	Appendix C 30 – 31	9 - 1	In Adult risk assessment tools, why are Risk scores looking only at patients undergoing cardiac surgery excluded? <i>Same references as used in comment 3</i>	Thank you for your comment. The GDG was aware that risk assessment tools are relatively well established in the field of cardiac surgery but felt that they were too specific to be utilised effectively for a general population (please refer to the Linking Evidence to Recommendations for this recommendation for further discussion). Cardiac surgery per se as compared to other forms of surgery e.g. vascular surgery has not been identified as a form of surgery at increased risk.
12.	Baxter Healthcare	1	Full	General		We would like to congratulate NICE and the Guideline Development Group (GDG) on the	Thank you for your comment. The GDG is pleased that you have found it to be a useful and comprehensive

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	Ltd					production of such a comprehensive and well researched document.	guideline.
13.	Baxter Healthcare Ltd	2	Full	168		We agree with the recommended approach to diagnose acute kidney injury, in line with (p)RIFLE, AKIN or KDIGO, however current use of these methods is not widespread nor standard practice. Will NICE therefore be issuing supporting tools that could help with uptake and use of such methods at point of care and therefore lead to more accurate and timely diagnosis?	Thank you for your comment. NICE are developing implementation tools that will be available at the time of publication of the guideline to help with local implementation.
14.	Baxter Healthcare Ltd	3	Full	36	25	We understand that the reason for omitting IV Fluid Management from these guidelines is due to the forthcoming publication of the NICE Guideline on IV Fluid Therapy. However, would NICE consider including direct reference to this guideline within this document? Fluid management is a vital part of AKI care before RRT but was excluded in the scope as there is the specific IV fluid guideline – however, the clinician needs to see the importance and evidence of IV fluid in AKI management – not only in terms of volume of fluid but also type of fluid (crystalloid vs. colloid) Such a link would also be helpful from this document to the clinical guideline for the care of the acutely ill patient. We believe that these links will help clinicians using the guideline to join up the different elements of care.	Thank you for your comment. As the NICE Clinical Guideline on intravenous fluid therapy has not yet been published we are unable to reference it in the current guideline. Links to relevant NICE guidelines can be made a later stage through the NICE Pathways available online if this is appropriate. All related NICE guidelines including intravenous fluids are listed in section 2.6 in the full guideline and 3.2 in the NICE version.
15.	Baxter Healthcare Ltd	4	Full	General		The scope of this guideline excludes guidance on the treatment of AKI with renal replacement therapy. Would NICE and this GDG consider the urgent development of a new set of guidelines for the Management of AKI with Renal Replacement Therapy?	Thank you for your comment. We are aware that the previous facility to suggest topics for guideline development to NICE no longer exists as the Institute focusses on developing and maintaining a core library of topics to inform the quality standard programme. It is beyond the remit of this GDG to develop guidance in this

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							area but we note that the NICE core library of topics includes a topic on Renal replacement therapy. We will ensure that NICE are aware of the detail of your comment when considering the remit of this work. The full list of topics can be found here <a href="http://www.nice.org.uk/guidance/cg/indevelopment/GuidelineReferralsUnderpinStandards.jsp">http://www.nice.org.uk/guidance/cg/indevelopment/GuidelineReferralsUnderpinStandards.jsp</a>
16.	Baxter Healthcare Ltd	5	Full	242	20	We are pleased to see that the guideline includes the recommendation to discuss treatment options with patients requiring long term renal replacement therapy after discharge following AKI. Would the GDG and NICE consider including direct reference to the appropriate NICE Guidance on RRT treatment options that is included in the CKD Guideline (CG73) and Peritoneal Dialysis (CG175). We believe that this will help clinicians who use the guideline to deliver a seamless clinical pathway.	Thank you for your comment. We agree that any reference that highlights potential renal replacement therapy options for individuals should be welcomed as it would hopefully encourage early discussion of potential choices for the individual. The CKD Guideline (CG73) and Peritoneal Dialysis (CG125) are both mentioned in the related guidance section of the full guideline (section 2.6). These will also be linked into the AKI guideline pathway which will further support the link between these guidelines. This pathway will be available on the NICE website on publication of the guideline.
17.	Bristol Myers Squibb	1	Full	General		Bristol-Myers Squibb Pharmaceuticals Ltd welcomes the publication of this document. We are grateful for sharing the draft with us.	Thank you for your comment. We are pleased that the guideline has been welcomed by Bristol-Myers Squibb Pharmaceuticals Ltd.
18.	British Association of Critical Care Nurses	1	Full	General		The CG is wide ranging and seems to cover all patients.	Thank you for your comment.
19.	British Association of Critical Care Nurses	2	Full	General		The document is rather long and may not be user friendly to healthcare professionals. This needs to be considered.	Thank you for your comment. We are aware that the full guideline may seem a large document but its purpose is to provide full detail of the evidence reviewed and discussions behind the recommendations. This guidance is also available in other formats, including the NICE Guideline which provides the recommendations only. The NICE Pathway will provide a visual

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							representation of the recommendations and implementation tools will be developed.
20.	British Association of Critical Care Nurses	3	Full	35		We note that there is mention that systems should be in place to measure urine output now that it is no longer part of the EWS if hospitals are using NEWS. We wonder what the group advice as we consider that unless patients are catheterised urine output well is very inaccurate.	<p>Thank you for your comment. We agree that this is a difficult area. We discussed the NEWS system with its developers in the early stages of this guideline development. We state that urine output should be monitored in patients at risk of AKI. We are aware that the NEWS chart does contain a specific space to collect data on urine output if deemed necessary.</p> <p>The scope and clinical questions did not prioritise techniques for monitoring urine output in non catheterised patients and therefore we cannot comment further.</p>
21.	British Association of Critical Care Nurses	4	Full	General		We would like to see more emphasis on the importance of early management of the presenting problem in the majority, namely hypotension and hypovolaemia with sepsis often at the root.	<p>Thank you for your comment. We agree that these are important causes of AKI. Treatment of sepsis or hypotension /hypovolaemia per se is not in the scope of the guideline. This has now been noted in the introduction, and the importance of the causes noted in section 7.1.6 (recommendation 26).</p> <p>Section 9.4.2 deals with the evidence of clinical and cost effectiveness of early compared to delayed referral to <i>nephrology</i>. The discussion of early versus late intervention is hampered by limited evidence. The GDG agree that correct early management of the presenting problem is crucial in preventing an AKI but feel that this is best undertaken at local level as the clinical circumstances you mention are more generic than specific to AKI.</p>
22.	British Association of Critical Care Nurses	5	Full	General		We would like more on the prevention of contrast-induced AKI with pre-procedure crystalloids	Thank you for your comment. The studies reviewed in the section on prevention of contrast induced AKI (section 6.2 of the full guideline) included pre and post procedure fluids and therefore we feel this area is already well covered in the guideline..

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23.	British Association of Critical Care Nurses	6	Full	General		Could more advice be given on the type of fluids used and impact on AKI	NICE is in the process of developing a separate clinical guideline on intravenous fluid therapy. Please see the NICE website: <a href="#">Intravenous fluid therapy</a> . To avoid duplication between pieces of NICE guidance, the use of fluids and impact on AKI has been covered by the NICE intravenous fluids guideline currently in development. A member from the AKI GDG provided advice to the intravenous fluids GDG during development of their recommendations. This guideline has only assessed the use of intravenous fluids in the prevention of contrast induced AKI.
24.	British Association of Critical Care Nurses	7	Full	General		Why is there no mention of the risk of transfusion and AKI?	Thank you for this query. The need for blood transfusion is usually a marker of severity of illness but in the experience of the GDG, it is not a common risk factor for AKI, and therefore was not included in our consensus listing of major risk factors.
25.	British Association of Critical Care Nurses	8	Full	General		As the document is very long we think that key points do need to be emphasised. Such as:- Spot the at risk group Do some blood tests Treat any treatable cause while actively and rapidly restoring circulatory volume and blood pressure They may need antibiotics and or surgery Escalate if they do not respond and are deemed suitable Those patients with complicated diagnosis should be referred to the renal physicians.	Thank you for your comment. We are aware that the full guideline may seem a large document but its purpose is to provide full detail of the evidence reviewed and discussions behind the recommendations. This guidance is also available in other formats, including the NICE Guideline which provides the recommendations only. The NICE Pathway will provide a visual representation of the recommendations and implementation tools will be developed to support the implementation of our recommendations which address some of the key points you highlight

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26.	British Association of Critical Care Nurses	8	Full	General		It may be useful to separate out adult, children and young people to enable healthcare professional to access the sections that they require more readily	We have considered and sought advice from GDG and NICE editors. We feel that the way the guidance is currently laid out is easier to follow in linking the evidence to the recommendations made. The NICE pathway will identify key recommendations of relevance to individual groups
27.	British Association of Critical Care Nurses	9	Full	40		No 27. Should we not be considering urine dipstick testing for all patients and not just for those who AKI is suspected or diagnosed?	Thank you for your comment. Our focus is on the prevention, detection and management of AKI. As such the use of urine dipstick for all emergency admissions, as recommended by NCEPOD, is beyond the scope of this guideline.
28.	British Association of Paediatric Nephrology	1	NICE	5		The link to the DH 'Seeking consent:working with children' could not be found. We think consent can be given by children under the age of 16 but to refuse treatment they need to be 18, is this distinction covered by the DH guidance?	Thank you for your comment. We have passed your comment to NICE and this has now been amended. We are unable to give guidance on the interpretation of this document but it appears to address the issues of consent and refusal for treatment. The link is also included here for ease. <a href="https://www.gov.uk/government/publications/reference-guide-to-consent-for-examination-or-treatment-second-edition">https://www.gov.uk/government/publications/reference-guide-to-consent-for-examination-or-treatment-second-edition</a>
29.	British Association of Paediatric Nephrology	2	NICE	11		Suggest: Ongoing assessment of the condition of <u>adult</u> patients in hospital	Thank you. We have not amended as you suggest as we feel that this sub-title is sufficient for its purpose.
30.	British Association of Paediatric Nephrology	3	NICE	22		1.5.8 would be better placed before 1.5.6	Thank you for your suggestion. The GDG has carefully considered the order of the recommendations and felt that this is the most helpful to clinicians. The GDG noted that recommendation 1.5.6 was intended to ensure early discussion if there was a <i>possibility</i> of renal replacement therapy whereas recommendation 1.5.8 provides a definite indication and as such takes place further down the pathway.. Therefore, the GDG did not

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							wish to change the order of the recommendations.
31.	British Association of Paediatric Nephrology	4	NICE	23		1.5.15 should be placed before 1.5.12	Thank you for your suggestion. The GDG has carefully considered the order of the recommendations and feels that the way they are currently laid out is more helpful in first referring the most urgent cases, treating patients whose cause of AKI is clear outside of nephrology services then guidance is provided for other cases. The GDG has chosen not to reorder these recommendations.
32.	British Association of Paediatric Nephrology	5	NICE	24		1.6.2 Is this related to long-term treatment of underlying diseases or long-term treatment of CKD resulting from the AKI	Thank you for your comment. This recommendation refers to both as appropriate and relevant to the individual patient. Full discussion of the nature of particular information requirements are provided in the linking evidence to recommendation section for this recommendation in the full guideline.
33.	British Association of Paediatric Nephrology	6	NICE	26		ESRD is more commonly called established renal failure (ERF).	Thank you for your comment. The GDG believes that from their experience as clinical practitioners in this area that end-stage renal disease (ESRD) is the term more commonly used and understood. They noted that the UK Renal Registry 2012 report also uses this term use this terminology.
34.	British Association of Urological Surgeons	1	Full	34	32	Iodinated contrast agents, while potentially causing renal damage seldom do and while I agree that these factors need to be taken into account, contrast should be given if deemed necessary	Thank you for your comment. We agree. The recommendation does not suggest withholding contrast but does advise clinicians to be aware of the risks of AKI in individuals receiving contrast. The recommendation also specifies that risk assessment should not delay emergency imaging. A detailed discussion is also included in the "Linking evidence to recommendation" section for this recommendation.
35.	British Association of Urological	2	Full	118-191	General	Urological relief of obstruction. This section is fine and I have no issues with it	Thank you for your comment.

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36.	British Association of Urological Surgeons	3	Full	202 ff	General	By renal replacement therapy the guides are referring to dialysis or Haemofiltration . Renal transplantation is not mentioned presumably because these guidelines are only dealing with acute renal injury rather than chronic	Thank you for your comment. Renal replacement therapy does refer to dialysis or haemofiltration in this context. Renal transplantation is beyond the scope of this guideline as you suggest as this is generally the management for a longer term chronic condition.
37.	British Society of Interventional Radiology (BSIR)	1	Full	General		<p>Daycase angiography helps reduce the burden on hospital beds, reduces waiting times for angiography and in our unit, has scored highly on patient satisfaction surveys. I have some concern regarding the interpretation of recommendation 16 on day case peripheral vascular intervention (Risk factors p-34).</p> <p>The vast majority of day case procedures are performed on patients who are &gt; 65years old and who will have intra-arterial contrast administered during angiography. Patients are all pre-assessed and if they are fit with no other co-morbidities (diabetes/heart failure etc), have a normal renal function and adequate home support they are generally deemed suitable for daycase angiography. If we were to exclude this group of patients (&gt; 65 years old), we would exclude the vast majority of suitable patients for day case angiography.</p> <p>As the guidelines state, there is as yet, no validated score to predict risk of CI-AKI in patients who present for peripheral arterial angiography. I accept that one risk factor on its own does not exclude a patient and that the</p>	<p>Thank you for your comment. The GDG is aware of this issue and has added discussion to the text of the "Linking evidence to recommendation" section to make this clear.</p> <p>In relation to the age cut off in the risk assessment recommendation for adults having iodinated contrast agents, the age cut-off has been amended to reflect the evidence rather than to promote consistency across the guideline. This age cut-off now reads age 75 or over.</p> <p>We have added text to the Linking evidence to recommendations section for this recommendation to outline the GDG thinking in this area of risk factors.. This indicates that clinical judgement is required to categorise risk and the fact that the GDG felt that in risk scoring, the risk of any adverse event typically rises dramatically the more risk factors a patient possesses. However, the evidence was such that the GDG was not in a position to state that any patient with any two or more risk factors, for example, is high risk.</p>

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						recommendation also serves to increase awareness. Would it be helpful to state within the guidelines that one risk factor on its own does not necessarily indicate that a patient is high risk, to avoid potential for misinterpretation?	
38.	Department of Health	1	Full	General		No Comment	Thank you.
39.	Faculty of Intensive Care Medicine	1	Full	General		<p>Long awaited advice that:</p> <p>1 provides for common definitions</p> <p>2 scotches most of the myths surrounding prevention and treatment of AKI</p> <p>3 provides sensible management guidelines for the patient with AKI or at risk of AKI</p> <p>Please remove the word "consider" from any of the headline recommendations as this is simply used as an excuse for inactivity.</p>	<p>Thank you for your comments.</p> <p>NICE recommendations are phrased according to the standards set in the NICE guideline manual. 'Consider' reflects the strength of the evidence base. Please refer to p7 of the NICE guideline – "We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient." This has therefore informed the use of consider throughout the guidance</p>
40.	Faculty of Intensive Care Medicine	2	Full	33	35	I would have thought that Extracellular Fluid Loss/Bleeding promotes recognition of the risk in those with GI loss of fluid, excess diuresis (therapeutic or otherwise), burns plus haemorrhage, rather than simply hypovolaemia which may be difficult to establish in its minor form and which sets up the kidney for injury with any additional insult e.g.sepsis/drugs.	Thank you for your comment. The GDG felt that this would be too much detail for a recommendation. The GDG listed the most common risk factors and acknowledged that the list cannot include all potential individual clinical conditions. The GDG chose to list general risk factors applicable to different diagnoses. For instance, patients with trauma, burns or haematological malignancy are at increased risk of AKI but these conditions were not mentioned separately. Instead, more general risk factors like hypovolaemia, sepsis, use of nephrotoxic drugs and obstruction are listed since they are the main reasons for AKI in this high risk group.

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							We have made no change to the recommendation but have added further discussion in the 'Recommendations and link to evidence' section to explain this and a definition of hypovolaemia to the glossary.
41.	Faculty of Intensive Care Medicine	3	Full	34		similar comments for paediatrics. Stating simply bloody diarrhoea rather than diarrhoea in general might be interpreted as the latter may be ignored even if severe.	<p>Thank you for your comment. We have included bloody diarrhoea to highlight Haemolytic Uraemic Syndrome. This is further discussed in the linking evidence to recommendations section for this recommendation.</p> <p>We have amended the wording of the paediatric recommendation to:  <i>'severe diarrhoea (children and young people with bloody diarrhoea are at particular risk to)</i> to ensure severe diarrhoea is not ignored as a risk factor for AKI. Hypovolaemia is also listed as a risk factor, causes of which would include severe diarrhoea.</p>
42.	Faculty of Intensive Care Medicine	4	Full	35		in dealing with the surgical patient the effects of nephrotoxic drugs alone seem to be emphasised (esp" NSAIDs after surgery"). There is no emphasis placed on patients on diuretics and other hypotensive agents or metformin in the setting of major surgery.	Thank you for your comment. The GDG wanted to highlight NSAIDs in particular as they are commonly used for post-operative pain relief. The GDG consider that other drugs would fall under drugs with nephrotoxic potential that is also outlined in the relevant recommendation.
43.	Faculty of Intensive Care Medicine	5	Full			In dealing with surgery there is no mention or reference to the effects of regional anaesthesia, in particular epidural anaesthesia on cardiovascular function particularly in the presence of antihypertensive agents	Thank you for your comment. This level of detail on anaesthesia was beyond the scope of this guideline and was therefore not prioritised for an evidence review.
44.	Faculty of Intensive Care Medicine	6	Full	37 para 3		There is no warning concerning the risk of iodinated contrast and diuretics or metformin	Thank you for your comment. We agree that discontinuation of diuretics and metformin should be considered before exposure to iodinated contrast. However, diuretics are only harmful if they cause hypovolaemia or are given to patients who are

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							hypovolaemic. Hypovolaemia has been included as a risk factor with the understanding that hypovolaemia can have many causes, including diuretic use. A definition for hypovolaemia and further explanatory text have been added to the 'Recommendations and link to evidence' section for further clarity. Metformin itself does not cause AKI. However, if AKI occurs, Metformin can lead to severe lactic acidosis. Since Metformin does not directly increase the risk of AKI, it was not included in the list of potential risk factors.
45.	Faculty of Intensive Care Medicine	7	Full	37		Ensure that risk assessment does not delay emergency imaging. end para 3. Should this not appear at the top of the list to emphasise that in the emergency situation that this should not be an excuse for delay.	Thank you for your comment. The GDG feel that this is most appropriately embedded in the recommendation as currently worded.
46.	Faculty of Intensive Care Medicine	8	Full	37		It would have reasonable to explain in what way renal physiology differed between the teenager and the young adult. (I don't believe it does)	Thank you for your comment .The GDG does not feel that it is the purpose of the guideline to provide such detail on renal physiology. Children and young people is the standard phraseology for paediatric guidelines. The GDG also felt that clinicians would be best placed to decide whether to use a recommendation for a child or young person or a recommendation for an adult depending on the individual patient and or their transition into adult services.
47.	Faculty of Intensive Care Medicine	9	Full	40 para 22		I think this should be stronger than just "consider". Surely it would be sensible to say stop and review on the basis of patient process. "Consider" allows no decision to be made. It should also include diuretics	Thank you for your comment. We are assuming you are referring to p39 recommendation number 22 in formulating our response. This is standard NICE writing style which reflects the strength of the evidence behind the recommendation (please see NICE version page 7). The use of diuretics was not included in the review and therefore could not be included in the recommendation

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48.	Faculty of Intensive Care Medicine	10	Full	40 para 23		again there is no concern raised as to patients on metformin or diuretics prior to contrast administration.	<p>Thank you for your comment. We are assuming you are referring to p40 recommendation 23 in formulating our response.</p> <p>We agree that discontinuation of diuretics and metformin should be considered before exposure to iodinated contrast. However, diuretics are only harmful if they cause hypovolaemia or are given to patients who are hypovolaemic. Hypovolaemia has been included as a risk factor in recommendation number 3 ( risk assessment in people having iodinated contrast) with the understanding that hypovolaemia can have many causes, including diuretic use. A definition for hypovolaemia and further explanatory text have been added to the 'Recommendations and link to evidence' section for further clarity.</p> <p>Metformin itself does not cause AKI. However, if AKI occurs, Metformin can lead to severe lactic acidosis. Since Metformin does not directly increase the risk of AKI, it was not included in the list of potential risk factors and as such we have made no amendments to this recommendation.</p>
49.	Faculty of Intensive Care Medicine	11	Full	40 para 30		I do not think that immediate equates with 6 hours. This should be no more than 2-3 hours.	Thank you. The GDG felt that 6 hours was sufficient to apply to an immediate category within their discussions on the evidence and when considering clinical practice issues. The rationale for this timing is indicated in the relevant linking evidence to recommendation in the guideline in section 8.2.6
50.	Faculty of Intensive Care Medicine	12	Full	41 para 34		This should be much firmer. There is no evidence that diuretics are a treatment for AKI and should not be administered on that basis. (Strictly speaking could be considered nephrotoxins). Suggest "Do not administer loop diuretics to treat AKI"	Thank you. The GDG feel that there are some defined circumstances where the use of loop diuretics may be appropriate and the GDG have made recommendations to guide practice whilst allowing for clinical discretion. These are further discussed in the Linking evidence to recommendation section for this recommendation (see section 9.2 of the full guideline)
51.	Faculty of	13	Full	41 para		Surely this should be acidaemia not acidosis	Thank you for your comment, but most clinicians would

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	Intensive Care Medicine			39		unless we mean treating a fully compensated excess of non volatile anion e.g. lactate, formate or glycollate	understand and use the term metabolic acidosis in their practice rather than acidaemia and therefore we have not amended our recommendation.
52.	Faculty of Intensive Care Medicine	14	Full	42 para 46		This should be within 12 hours as this is the time within which the patient should have been assessed by a consultant.	The GDG have set an upper limit in this recommendation. Earlier referral within this timeframe is beneficial where possible and should be based on individual circumstances. Please see 'Recommendations and link to evidence' section 9.5 of the full guideline for further information.
53.	Faculty of Intensive Care Medicine	15	Full	42 para 52		Would be worth adding, liver disease and chronic cardiac failure	Thank you for your comment. The GDG agrees that these are risk factors but for the purposes of this particular recommendation regarding information for patients, the GDG wished to highlight the information needs for those people with CKD and those with limited access to fluid as they felt that information about risks in these groups would possibly prevent future episodes of AKI if people were able to understand the impact of these two defined circumstances.
54.	Faculty of Intensive Care Medicine	16	Full	44	18	Should those patients taking long-term medication that affects renal compensatory mechanisms e.g. ACE, NSAID etc	Thank you for your comment. The GDG prioritised investigating risk scores where they felt most benefit to the NHS could be achieved. The patients you suggest are covered within the risk scores for all three patient groups assessed as part of this guideline
55.	Faculty of Intensive Care Medicine	17	Full	66	5.2.6	Add multisystem disease	Thank you for your comment. Multi system disease is covered in recommendation 8 in the full guideline.
56.	Faculty of Intensive Care Medicine	18	Full	69		in paediatric section discussion of children becoming unwell is it worth adding a small section on the efficient compensation by the young to stress to a limit beyond which they rapidly collapse. The importance is to recognise the early signs of compensation and plan a response to deal with rapid deterioration.	Thank you for your comment. The GDG felt this is captured by 'deteriorating PEWS' and that further discussion would be too much detail to include in this guideline

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57.	Faculty of Intensive Care Medicine	19	Full	81	6.1.4	Are the opportunity costs calculated correctly. If a consultant nurse or doctor is called to see a patient the time consumed in travelling, seeing the child and talking to staff/relatives is considerably more than 5 mins. I cannot agree with the statement of the NNT is cost neutral.	Thank you for your comment. We have added the following sentence to the section: "In addition to the time spent in actually carrying out PEWS, health care professionals could spend more than 5 minutes, for example to report the results." However we still consider the potential costs associated with this intervention to be likely offset by the benefits of preventing AKI. We have amended the text of the breakeven analysis to make it clearer that our calculations are a breakeven analysis and we were not trying to say that carrying out PEWS is cost neutral as this depends on the number of AKI prevented.
58.	Faculty of Intensive Care Medicine	20	Full	144	6.4.1	Need effect of epidural anaesthesia	Thank you for your comment. This level of detail on the types of anaesthesia, including epidural anaesthesia was beyond the scope. The relationship of different types of anaesthesia to AKI was not in the scope.
59.	Faculty of Intensive Care Medicine	21	Full	149		in the discussion regarding ACE /ARBs - there is no discussion of the positive feedback loop if a degree of AKI occurs then with continued dosing toxicity will develop.	Thank you for your comment. The GDG's aim was to provide a brief overview of the subject matter. We feel that such a pharmacokinetic point is too much detail for the guideline.
60.	Healthcare Improvement Scotland	1	Full	37	18	<p>Recommendation 5. Assessing risk factors in adults having surgery:</p> <p>Comment: We have been reviewing the evidence of NSAID use in the post-operative period. You may be aware of the Cochrane review: Lee A, Cooper MG, Craig JC, Knight JF, Keneally JP. Effects of nonsteroidal anti-inflammatory drugs on postoperative renal function in adults with normal renal function. Cochrane database of systematic reviews (Online) 2007(2): CD002765</p> <p>This concludes that "NSAIDS caused a clinically unimportant transient reduction in renal function in the early postoperative period in patients with</p>	<p>Thank you for your comment. Our recommendation does not exclude the use of NSAIDs in the peri operative period and we have clarified this in the Linking evidence to recommendation section. The GDG is aware that NSAIDs as a class have an increased nephrotoxic potential and as such felt it appropriate through consensus to draw attention to this fact.</p> <p>This recommendation was made following a review of the accuracy of risk assessment tools for predicting AKI and as such this study would not have come up in our review.</p>

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						<p>normal preoperative renal function. NSAIDS should not be withheld from adults with normal preoperative renal function because of concerns about postoperative renal impairment.”</p> <p>This does not seem to be cited in the draft guidance. We would be grateful if you could clarify the evidence base behind avoiding NSAID in all patients in the peri-operative period. The studies included in the Cochrane review excluded “higher risk” patients. We wonder whether this guidance should be limited to patients with other risk factors for AKI rather than all patients.</p>	
61.	Intensive Care Society	1	Full	11	12	“Creatinine levels” – “serum creatinine” would be preferable. eGFR should be mentioned at this stage.	Thank you for your comment. We have added in the phrase ‘serum or plasma’ in front of the word creatinine. eGFR is really only used for detection of AKI in children and to avoid confusion we have omitted mention of it at this stage.
62.	Intensive Care Society	2	Full	18	Table	Split infinitive. To specifically review.	Thank you, we have amended this.
63.	Intensive Care Society	3	Full	39	23	“Consider” – please define parameters. Also see below.	Thank you. NICE recommendations are phrased according to the standards set in the NICE guideline manual. ‘Consider’ reflects the strength of the evidence base. Please refer to p7 of the NICE guideline – “We use ‘consider’ when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient’s values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.”
64.	Intensive	4	Full	40	28	I would question this. The cause may be	Thank you for your comment. We assume you are

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	Care Society					presumptively identified, but diagnostic precision may not be known. (See also p184 line 15)	questioning recommendation 28: <i>Do not routinely offer ultrasound of the urinary tract when the cause for the acute kidney injury has been identified.</i>  The GDG have provided a clear rationale for this recommendation in chapter 8 that identified that a clear cause accompanied by rapid response to medical management would mean inappropriate use of ultrasound resource. The GDG feels that many patients have an easily demonstrable non obstructive cause of their AKI such as those critical care patients with severe sepsis that may respond well to medical management in whom ultrasound is not required.
65.	Intensive Care Society	5	Full	41	9	Does this also apply in cases of hypotension aggravating AKI where low dose dopamine may resolve this?	Thank you for your comment. The recommendation refers to dopamine for treatment of AKI per se. The GDG did not evaluate the evidence for the role of dopamine as a vasopressor in the setting of hypotension.
66.	Intensive Care Society	6	Full	104-134 and General		Evidence relating to NAC very equivocal. Suggest use of NAC in contrast induced AKI be restricted to clinical trials.	Thank you for your comment. NAC in combination with sodium chloride was the most cost effective regimen in the original economic model while NAC in combination with sodium bicarbonate was less cost-effective than sodium bicarbonate alone. Overall in the health economic analysis the difference in QALY gain between strategies with and without NAC was very small. The model results were uncertain and the GDG had other concerns over the cost-effectiveness of NAC which are detailed in the Linking Evidence to recommendations section of the relevant chapter (section 6.2.14). As a result, they decided to remove the existing recommendation and not to make any further research recommendations.
67.	Intensive Care Society	7	Full	170	Table	It would have been helpful for standardisation if a single definition eg AKIN were to be adopted by consensus	Thank you for your comment. There was insufficient evidence available to the GDG regarding the KDIGO classification system. We therefore do not have evidence to advocate adoption of one classification, e.g.

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							AKIN or KDIGO. The stages are very similar between RIFLE, AKIN and KDIGO (see introduction to the chapter and table 36). We have therefore advised that clinicians use a staging system chosen locally. We anticipate further national and international development of staging systems that may allow this in the future.
68.	Intensive Care Society	8	Full	184	15	See above 40/28	<p>Thank you for your comment. We assume you are questioning recommendation 28: <i>Do not routinely offer ultrasound of the urinary tract when the cause for the acute kidney injury has been identified.</i></p> <p>The GDG have provided a clear rationale for this recommendation in chapter 8 that identified that a clear cause accompanied by rapid response to medical management would mean inappropriate use of ultrasound resource. The GDG feels that many patients have an easily demonstrable non obstructive cause of their AKI such as those critical care patients with severe sepsis that may respond well to medical management in whom ultrasound is not required.</p>
69.	Intensive Care Society	9	Full	199	22-27	Hypotension not considered as a variable	Thank you for your comment. The part of the guideline you refer to is the clinical evidence statements for low dose dopamine in the management of AKI. As such only the outcomes as stated in the review protocol are discussed and hypotension was not one of the outcomes chosen by the GDG for this review because low dose dopamine in this situation is not used for hypotension.
70.	Intensive Care Society	10	Full	232	Table	Recommendation 45 – may require all ICU patients to be referred for review as there is often diagnostic uncertainty and this is not always fully appreciated in complex patients.	Thank you for your comment. We agree that the complexity of AKI in critically ill patients may not always be appreciated. However, in the absence of evidence-based criteria on when to refer an ICU patient with AKI for nephrology review and absence of strong data confirming that referral to nephrology changes the outcome in this scenario, the GDG was unable to recommend that all ICU patients with AKI needed to be reviewed by a nephrologist. Instead, the GDG

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							recommended that ICU clinicians should make a judgement whether any diagnostic uncertainty existed and/or whether there may be a case for disease specific management.
71.	Kidney Alliance	1	Full	11		There is increasing evidence that acute kidney injury is an important risk factor for incident chronic kidney disease and progression of existing chronic kidney disease. We suggest that this association is of sufficient importance to be mentioned in the introduction, particularly as it is under-appreciated in both primary and secondary care	Thank you for your helpful comments. The link between AKI and CKD were not in the scope of the guideline or its evidence reviews and therefore recommendations in this area could not be made. The GDG is aware of the rapidly developing understanding of the relationship between AKI episodes, and risk and progression of CKD and as such have amended the 'Recommendations and link to evidence' section for monitoring and follow up after AKI (recommendation 1.3.2, section 7.1.6) to include clearer discussion on the monitoring and follow up of renal function after an episode of AKI.
72.	Kidney Alliance	2	Full	33	28	CKD Stages 1 and 2 are also important risk factors for AKI. The KDIGO Clinical Practice Guidelines for CKD indicate that the adjusted relative risks for AKI are between 2.4 and 8.4 (depending on category) for people in eGFR categories >60ml/min/1.73m <sup>2</sup> and ACR categories >3mg/mmol (30mg/g). These are higher than the adjusted relative risks of AKI for the eGFR 45-60ml/min/1.73m <sup>2</sup> and ACR<1mg/mmol category. We suggest that all people with CKD are regarded as at risk of AKI. Proteinuria data is now increasingly available on pathology systems - a urine albumin should be available in 75-80% with diabetes (National Diabetes Audit)	The GDG acknowledged that CKD stages 1 and 2 are risk factors but wished to highlight the higher risk as it is known that the risk of AKI increases with worsening renal function. We have amended the recommendation as follows to make the inclusion of this group more explicit:  • <i>chronic kidney disease (adults with an estimated glomerular filtration rate [eGFR] less than 60 ml/min/1.73 m<sup>2</sup> are at particular risk)</i> Proteinuria is mainly a marker of CKD and has not been included as a risk factor for AKI.
73.	Kidney Alliance	3	Full	33	26	Is multiple myeloma per se a risk factor for acute kidney injury? (reviewed <a href="http://www.ncbi.nlm.nih.gov/pubmed/22045243">http://www.ncbi.nlm.nih.gov/pubmed/22045243</a> ). Not all such patients will have albuminuria or reduced eGFR.	The GDG listed the most common risk factors and acknowledged that the list cannot include all potential individual clinical conditions. The GDG chose to list general risk factors applicable to different diagnoses. For instance, patients with trauma, burns or haematological malignancy are at increased risk of AKI but these

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							conditions were not mentioned separately. Instead, more general risk factors like hypovolaemia, sepsis, use of nephrotoxic drugs and obstruction are listed since they are the main reasons for AKI in this high risk group We have made no change to the recommendation but have added the above text to the 'Recommendations and link to evidence' section to explain this.
74.	Kidney Alliance	4	Full	35	6	Proteinuria is a risk factor for acute kidney injury (see comment 2)	Thank you for your comment. Proteinuria was not identified as a risk in any of the risk scores we reviewed and the GDG felt that including CKD and diabetes as risk factors would include most of the population with proteinuria.
75.	Kidney Alliance	5	Full	35	35	"Inadequate response to treatment" is very open to interpretation, particularly for a condition where the natural history is variable. We suggest that this is recognised and if possible the phrase made more specific.	Thank you for your comment. The GDG felt that clinicians would be aware of those patients not responding to treatment through the exercise of their own clinical judgement. The rate of response will depend on how long patients have already had AKI, the aetiology of AKI and also the patient's underlying renal reserve. Therefore, it is not possible to give specific parameters or milestones. They did not feel it would be helpful to outline every clinical parameter where this would be the case and felt that the addition of the 'inadequate response to treatment' would capture this intent.
76.	Kidney Alliance	6	Full	35	39	"Pre-existing" CKD would be clearer with a definition of stage or eGFR	Thank you for your comment. The GDG feel that this does not add any clarity to the recommendation as CKD by definition has to be pre-existing.
77.	Kidney Alliance	7	Full	36	2	Should information provision to people at risk (recommendation 52) also be a key priority?	Thank you for your comment. All of the recommendations within a guideline are important. Key priorities for implementation are voted on by the Guideline development group according to the NICE Guidelines Manual "From the recommendations the GDG will identify between 5 and

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							10 key priorities for implementation; these are the recommendations that are most likely to have a high impact on patients' outcomes and on reducing variations in clinical management." <a href="http://publications.nice.org.uk/the-guidelines-manual-pmg6">http://publications.nice.org.uk/the-guidelines-manual-pmg6</a> . The GDG voting on this occasion did not include this as a key priority. NICE produce a version of this guidance called 'Information for the public' which will be available on the NICE website at publication. This document details the recommendations into an easy to read document explaining the care that people can expect as a result of the recommendations made in the guideline
78.	Kidney Alliance	8	Full	36	39	We would question whether a 3 -month cut-off is sufficient. Could the statement be qualified by indicating that in some situations it may not be? Significant changes will occur within this period, especially in the patient groups who are at highest risk, eg heart failure, heart failure + chronic kidney disease	Thank you for your comment. The other considerations section of the 'Recommendations and link to evidence' section (section 5.1.6) reads: "For a stable outpatient an eGFR value within the preceding 3 months was felt to be satisfactory when requesting an elective procedure." The recommendation allows for clinicians to measure eGFR before imaging if they feel that the patient circumstances require it in their clinical judgement.
79.	Kidney Alliance	9	Full	37	4	This states that those with eGFR<60ml/min/1.73m <sup>2</sup> are at increased risk of contrast nephropathy. This is inconsistent with page 34 line 34 which states that risk is increased at eGFR<30ml/min/1.73m <sup>2</sup> .	Thank you for bringing this to our attention. This was an error. We have amended this in the guideline document.
80.	Kidney Alliance	10	Full	39	20	Is the intention that iv volume expansion be offered to prevent contrast nephropathy to all in at-risk groups, eg everyone aged over 65? Could this be made more specific? Are there two different at-risk groups, those in whom volume expansion should be offered (eg eGFR<30ml/min/1.73m <sup>2</sup> , those with eGFR<45ml/min/1.73m <sup>2</sup> plus an additional risk	Thank you for your comment. After careful consideration of the evidence we have altered the bullet points of this recommendation so that at-risk groups regarding chronic kidney disease and older age are now defined as: <ul style="list-style-type: none"> <li>• <i>chronic kidney disease (people with an eGFR less than 40 ml/min/1.73 m<sup>2</sup> are at particular risk)</i></li> <li>• <i>age 75 years or over.</i></li> </ul>

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						factor), and those in whom it should be considered? Should offering volume expansion to those at highest risk - however they are defined - be a key priority? We have some reservations that the recommendation on volume expansion to all in at-risk groups will be implementable.	The GDG considered these groups to be at high risk of CI-AKI and thus would in general benefit from intravenous volume expansion as a preventative measure. Whilst a priority for implementation for radiology and cardiology departments, the GDG voted for their top 10 KPIs considering all recommendations and all settings in line with the NICE guideline manual methods (add hyperlink)
81.	Kidney Alliance	11	Full	41	5	The implication here is that diuretics should not be used to treat fluid overload or oedema in a patient in whom the renal function is not recovering. However might not it also sometimes be appropriate to use diuretics to treat pulmonary oedema in a patient in whom the acute kidney was stable, or even deteriorating if there was a clear clinical need, a good urine output and no other indication for RRT?	Thank you for your comment. We agree with the first part of your comment. Our recommendation indicates the appropriate circumstances in which loop diuretics could be used to manage treat fluid overload or oedema. The GDG feels that pulmonary oedema in the circumstances you describe would more likely benefit from renal replacement therapy, than from the uncertain diuretic effects in this situation. The actual benefit of diuretics in the face of deteriorating renal function has to be called into question, as shown by the evidence review and may also put the patient at avoidable risk of life threatening pulmonary oedema.
82.	Kidney Alliance	12	Full	144	25	NSAIDs also influence renal haemodynamics via their effect on prostaglandins and we suggest this is added to the discussion.	Thank you. The chapter discusses stopping ACEi/ARBs and the evidence around this. Therefore, discussion of NSAIDs would be out of place there. However, we agree with your point and have added more detail section 5.1.6.
83.	Kidney Alliance	13	Full	171		Does there need to be a formal recommendation somewhere on catheterisation, even if only to say decision should be based on clinical judgement? There is also no discussion of central venous pressure monitoring.	Thank you for your comment. Catheterisation was outside the scope of the guideline. However, the GDG did acknowledge this as an important issue and agrees that the decision regarding catheterisation should be based on clinical judgement and has therefore stated in the 'Recommendations and link to evidence' section that <i>"To some extent the decision regarding catheterisation remains a matter of clinical judgement."</i>

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							Central venous pressure monitoring was also outside the scope of this guideline and the GDG did not review the evidence and did not make any recommendations.
84.	Kidney Alliance	14	Full	179	Para 4	Could also refer to NICE CG73 when discussing inaccuracies associated with dipstick urinalysis.	Thank you for your comment. We have added a sentence to the 'Recommendations and link to evidence' section to refer to this guideline.
85.	Kidney Alliance	15	Full	189	21	Should bilateral upper tract obstruction also prompt urgent urological referral?	Thank you we agree and have added this to the recommendation.
86.	Kidney Alliance	16	Full	General		<p>Whilst we would agree that risk assessment and investigation in AKI are important, we question whether these guidelines are sufficient to improve outcomes</p> <ul style="list-style-type: none"> <li>- Patients with AKI will be treated in - and may move between - general ward, renal unit, HDU and ITU. Defining local pathways and referral criteria would seem essential.</li> <li>- One could also consider what might be included in specific care bundles to prevent and treat AKI, eg medication review, correction of hypovolaemia, prompt senior review etc. The elements within such bundles should be based on the highest quality evidence or national guidance, but the recommendations as they stand do not lend themselves to a description of what best care for AKI should look like.</li> </ul> <p>Greater focus on primary care would have been welcome. Up to 1% of hospital inpatients may have a diagnosis of community-acquired AKI, and one would imagine that a significant</p>	<p>Thank you for your comments. We agree that guidelines alone without change in care are unlikely to improve outcome. We encourage local implementation to improve AKI care, but written guidance on these service developments are not the direct remit of the guideline. The NICE implementation team will be looking at encouraging local implementation of the guidelines. We have identified referral criteria for nephrology within this guideline. We are also working with the RCGP on implementation</p> <p>Care bundles have been utilised in intensive care and sepsis care, but were not in the scope of this guideline and were therefore not the subject of a clinical review question.</p> <p>Whilst there are many recommendations that mainly relate to hospital care, a number of recommendations relate directly to primary care, and we worked with the benefit of an expert advisor from primary care who contributed to the Guideline development group discussions.</p> <p>NICE recommendations are not signposted 'as being for</p>

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						<p>proportion of these admissions are preventable. What interventions/actions other than holding ACEi/ARB might be useful?</p> <p>Recommendations on follow-up in the community after an episode of AKI would also be useful.</p>	<p>primary or hospital care. Some of the recommendations relevant to primary care are (titles paraphrased here):</p> <ul style="list-style-type: none"> <li>1.1.1 Identifying AKI in adults</li> <li>1.1.2 Identifying AKI in children</li> <li>1.1.3 Identifying ACKD</li> <li>1.1.4 Unclear clinical situations to consider AKI</li> <li>1.2.14 Situations to suspend ACEi/ARBs</li> <li>1.3.1 Detection of AKI</li> <li>1.3.2 Monitoring creatinine regularly</li> <li>1.3.3 Determining the cause</li> <li>1.4.1 Urinalysis</li> <li>1.5.15 and related - Referral to nephrology</li> <li>1.6.2 Info for patients/carers</li> </ul> <p>.</p> <p>We are unable to make recommendations in areas where we have not reviewed the evidence. We have, however, added further information to the "other considerations" section of the relevant 'Recommendations and link to evidence' section on follow up (recommendation 1.3.2, section 7.1.6) after an episode of AKI as we agree this is an important area.</p> <p>We went through a focussed scoping process including a four week stakeholder consultation on the scope where stakeholders highlighted critical areas to address. This feedback was taken into consideration and determined the scope of this guideline</p>
87.	MHRA	1	Full	General	General	No comment	Thank you.
88.	National Kidney Federation	1	Full	General	All	NKF welcomes the comprehensive nature of the consultation document. It addresses fully our concerns relating to avoidance, early detection and management of AKI, including specialist nephrological involvement, highlights known risk	Thank you for your comment. We are pleased that you find this a comprehensive and useful guideline.

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						factors, and deals very well with follow up care in the short and long term.	
89.	NHS England	1	Full	General		NICE guidance on AKI is to be welcomed. Improving the detection and management of AKI in both primary and secondary care reflects both the high frequency of its incidence, the poor outcomes associated with AKI and the current poor management as noted in the NCEPOD report "Acute Kidney Injury: Adding Insult to Injury".	Thank you for your comment
90.	NHS England	2	Full	General		The guidance for this clinical guideline as presented at this stage is long, yet appears to lack recommendations that when implemented will improve the situation.	<p>Thank you for your comment. We are aware that the full guideline may seem a large document but its purpose is to provide full detail of the evidence reviewed and discussions behind the recommendations. The recommendations included in the guideline have been made on the best available evidence and drafted by a multi professional GDG' This guidance is also available in other formats, including the: NICE Guideline which provides the recommendations only. The NICE Pathway will provide a visual representation of the recommendations and, and implementation tools will be developed.</p> <p>We disagree with your assertion that we have not made recommendations that when implemented will improve the situation. The GDG are satisfied that the recommendations they have made will improve care for patients. The NICE implementation team will provide support to the NHS to ensure that they are implemented in practice.</p>
91.	NHS England	3	Full	43		There is no mention of research into systems to improve detection.	Thank you for your comment .Research recommendations can only be made in areas where the evidence has been assessed. As we did not look at systems to improve detection in the guideline no research recommendation was made in this area. The GDG did however make a research recommendation for

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							a simplified staging system based on SI units which they believe would help to improve detection of AKI in the NHS.
92.	NHS England	4	Full	43		Primary care and research are not mentioned	Thank you for your comment. These research recommendations are not limited by healthcare setting and some of them are applicable to both primary and hospital care.
93.	NHS England	5	Full	43		Targeted education of the multiprofessional team is not considered.	Thank you for your comment. Research recommendations can only be made in areas where the evidence has been assessed. As the scope of the guideline did not include systems to improve detection in the guideline no research recommendation was made in this area. The scope was drafted and consulted on with key stakeholders before beginning development in line with NICE methods. Targeted education was not prioritised for inclusion,
94.	NHS England	6	Full	General		The term 'high risk' is consistently used in both the full and shorter publications. It is suggested that for clarity these high risk groups are not constantly listed, but summarised and referred to.	Thank you for your comment. After careful consideration we do not agree and believe the guidance is clearer in its current format to ensure readers are reminded of the detail of high risk groups. We believe that this will support better identification of those at risk by non-specialist clinicians and therefore improve care .
95.	NHS England	7	Full	85		The section on contrast nephropathy, whilst an excellent review, is overlong and confusing. Most importantly, the recommendations are not clear, but seem to imply intravenous hydration to all high risk groups. This has major implications for implementation and resource utilisation.	We are grateful for your identification of these issues. Owing to the complexity of the area, with multiple regimes to compare, health economic analysis and the requirement for a standard NICE format, the section will inevitably be quite long. We believe that this is as clear as possible. The GDG felt that IV hydration is the standard of care for all high risk patients. The evidence review and the economic model indicated that oral hydration was not a cost effective strategy for high risk patients, and was 'dominated' in that respect by some of the IV regimes which had higher initial costs but these were offset by lower CI-AKI costs. The reasons for this are now more clearly stated. The GDG has made clear that there are not high risk groups, but only high risk

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							patients. The 'Recommendations and link to evidence' section text now gives clearer guidance as to the use of clinical judgement in assessing risk. Unfortunately there were no defined risk tools that were identified as suitable following review. High risk patients will have to be identified by local protocols and Refer to recommendation on referral to nephrology 1.2.10
96.	NHS England	8	Full	135		The focus of medicines management for this section is on decision support tools in secondary care. Primary care medicines management and the implementation and research into 'sick day' medicine management and the role of primary care electronic systems should be considered, as well as medicines management itself.	Thank you. Medicines management reflects the fact that the evidence exclusively relates to secondary care. The GDG didn't prioritise a research recommendation for primary care medicines management because it was felt that primary has very well established medicines management systems.
97.	NHS England	9	Full	General		There is no discussion in section 6 of hydration strategies. This is of particular importance to the multiprofessional team.	Thank you for your comment. We assume this refers to oral versus IV strategies, or comparing different oral strategies. There was insufficient evidence to discuss one oral strategy versus another. We have made clear the GDG view that the evidence indicates that oral hydration for high risk patients is a suboptimal strategy. NICE are currently developing a clinical guideline in intravenous fluid therapy and the particular needs of the AKI population have been discussed within the context of that guideline. More detail can be found at this link <a href="http://guidance.nice.org.uk/CG/Wave25/5">http://guidance.nice.org.uk/CG/Wave25/5</a> . Development is also beginning on a similar guideline for children. This can be found here: <a href="http://www.nice.org.uk/guidance/cg/indevelopment/index.jsp?p=off">http://www.nice.org.uk/guidance/cg/indevelopment/index.jsp?p=off</a>
98.	NHS England	10	Full	151		The recommendation for the use of a formal staging for AKI is welcome but, accepting the lack of gold standard a recommendation to adopt a single system nationally would be helpful. There was no discussion of one key aspect of	Thank you for your comment. There was insufficient evidence available to the GDG regarding the KDIGO classification system. We therefore do not have evidence to advocate adoption of one classification, e.g. AKIN or KDIGO. The stages are very similar between

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						definition around defining baseline, a necessary precursor to implementing eAlerts – another important element to consider in driving improvement.	RIFLE, AKIN and KDIGO (see introduction to the chapter and table 36). We have therefore advised that clinicians use a staging system chosen locally. We anticipate further national and international development of staging systems in due course. The GDG noted that detailed discussion of e-alerts was outside the scope The following text has been added to the introduction to clarify baseline measurement: This prediction is prone to error, especially in the older patient most at risk of AKI, since it makes no allowance for pre-existing CKD and hence will over-diagnose AKI in this high-risk subgroup; among patients with below average muscle mass it will under-diagnose AKI. Back-calculation is difficult to implement in practice given that many laboratories use method-specific factors to adjust their biased creatinine results before calculating an eGFR and will vary depending on the creatinine method used. These issues are discussed in greater detail in section 7.1.1 of the full guideline.
99.	NHS England	11	Full	174		Identifying the cause of AKI is essential and the guidance here is welcome – in particular the central roles of urinalysis and ultrasound.	Thank you for your comment. We are pleased that the guidance on urinalysis and ultrasound are welcomed by NHS England.
100	NHS England	12	Full	General		The management section covers urological referral and guidance on the limited role of diuretics. These are broadly not contentious. Medicines management in the management of AKI (as opposed to modifying risk) is absent and should be considered. Guidelines for referral to renal specialists are to be welcomed, although specifics may be commented on by professional societies.	Thank you for your comment. We were unfortunately unable to cover all areas and focused upon those that stakeholders and GDG members initially suggested as critical areas to address. We went through a focussed scoping process including a four week stakeholder consultation on the scope where stakeholders highlighted critical areas to address. This feedback was taken into consideration and determined the scope of this guideline.
101	NHS England	13	Full	General		There is little to no consideration of recovery issues – areas that are absent are specifics in respect of renal recovery, rehabilitation for the person, medication review and the reinstatement	Thank you for your useful comments. In response to this we have strengthened our 'Recommendations and link to evidence' section on Medication review (section 6.3.6 and 6.4.6) and

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						of therapy stopped during and episode of AKI and finally the indications for follow up (to include the role and impact of AKI on CKD).	monitoring after AKI (section 9.5). Some of these areas are also covered in the information for patients and carers (IFP) that accompanies the guideline.  Rehabilitation and the link between AKI and CKD were not in the scope of the guideline. and therefore we have not been able to make specific recommendations in this area.
102	Renal Association Clinical Affairs Board	1	Full	General		The production of NICE guidelines to improve the management of AKI across the NHS is to be hugely commended, and will assist in increasing awareness of this very important disease area.	Thank you for your comment. We are pleased that you think this guideline will improve the management of AKI across the NHS.
103	Renal Association Clinical Affairs Board	2	Full	General		In general, many of the recommendations are in line with what is currently regarded as good practice; as noted in the introduction previous deficiencies have stemmed from the fact that these basic elements of care are not reliably delivered on a day to day basis. Therefore, consideration should be given to include specific comments that direct hospitals/acute care providers towards developing strategies to deliver the guidelines on a systematic, hospital wide basis.	Thank you for your comment. The NICE implementation team will develop implementation support materials to encourage implementation and uptake of the guidance. We will ensure that your comment is available to that team as they focus their support.
104	Renal Association Clinical Affairs Board	3	Full	General		Bearing in mind that these guidelines are aimed at all acute practitioners, there may be benefit to further condensing the Key Priorities for Implementation; currently these run over 5 pages and the NICE version takes up 36 pages. A clear one page summary is likely to help widespread dissemination and uptake.	Thank you for your comment. The Key Priorities for Implementation were voted on by the GDG according to the NICE Guidelines Manual "From the recommendations the GDG will identify between 5 and 10 key priorities for implementation; these are the recommendations that are most likely to have a high impact on patients' outcomes and on reducing variations in clinical management." <a href="http://publications.nice.org.uk/the-guidelines-manual-pmq6">http://publications.nice.org.uk/the-guidelines-manual-pmq6</a>

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							Other forms of the guideline such as the NICE pathway and implementation support tools will be developed to help address dissemination and uptake as it is important that the recommendations are outline in full in the NICE guideline.
105	Renal Association Clinical Affairs Board	4	NICE	11	1.2.2	The inclusion of specific reference to systems to pick up oliguria is very well made and its inclusion is important in view of changes to EWS in which urine output scoring is to be removed.	Thank you for your comment. We are pleased that you agree with this.
106	Renal Association Clinical Affairs Board	5	NICE	12	1.6.2	In the Key Priorities for implementation, it is not clear what the information is that 'should be given about long-term treatment options, monitoring, self-management and support', although this is elaborated upon to a certain degree later on in the guidance.	Thank you for the comment. It is not possible to discuss all the detail in the wording of the recommendation, hence the elaboration provided elsewhere in the guideline. Full detail behind this recommendation can be found in the linking evidence to recommendation for this recommendation in Chapter 10 of the full guideline
107	Renal Association Clinical Affairs Board	6	Full	General		It may valuable to emphasise that good communication to primary care following an episode of AKI is important to ensure appropriate monitoring of renal function, restarting chronic medications as appropriate, ongoing patient information, CKD care as appropriate.	<p>Thank you for your valuable comment. We have now added further information to our 'Recommendations and link to evidence' section sections on Medication review (recommendation 1.2.13) and monitoring in AKI (recommendation 1.3.2) in section 6.3.6 and 6.4.6 of the full guideline</p> <p>We have amended the 'Recommendations and link to evidence' section for monitoring and follow up after AKI (section 9.5 in the full guideline) to include further discussion on monitoring and follow up of renal function after discharge.</p> <p>Recommendation 1.6.2 states:  <i>1.6.2 Give information about long-term treatment options, monitoring, self-management and support to people who have had acute kidney injury (and/or their parent or carer, if appropriate) in collaboration with a</i></p>

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							<i>multidisciplinary team appropriate to the person's individual needs.</i> Some of these issues are also covered in the information for patients and carers (IFP) that accompanies the guideline and is specifically for use by the public.
108	Renal Association Clinical Affairs Board	7	NICE	11-12		Consideration should be given to include in the 'Key Priorities for Implementation' the recommendation that all patients with AKI should have urinalysis. This is currently omitted from the 'Key Priorities for Implementation' section but is a crucial step in the diagnostic pathway as highlighted in the main body of the recommendations.	Thank you for your comment. All of the recommendations within a guideline are important. Key priorities for implementation are voted on by the Guideline development group according to the NICE Guidelines Manual "From the recommendations the GDG will identify between 5 and 10 key priorities for implementation; these are the recommendations that are most likely to have a high impact on patients' outcomes and on reducing variations in clinical management." <a href="http://publications.nice.org.uk/the-guidelines-manual-pmg6">http://publications.nice.org.uk/the-guidelines-manual-pmg6</a> . Unfortunately this recommendation was not selected to appear in the Key priorities section.
109	Renal Association Clinical Affairs Board	8	NICE Full version	18 134	1.2.7	There is concern around the statement that all patients at risk of contrast induced nephropathy should be offered intravenous fluids. If this statement refers to all intravenous contrast procedures (including outpatient and daycase imaging and intervention) then this has big implications and may significantly increase hospital admissions for this purpose alone. If this statement is cross referenced with the list of patients at risk of CI-AKI then everyone over the age of 65 and everyone with a eGFR of <60 would need admission for intravenous fluids prior to any form of contrast administration. Further definition around the type of clinical scenario and type/volume of contrast proposed would help provide clarity here (i.e. intra-arterial contrast for PCI in an unstable patient carries a very different risk to an outpatient CT scan in a	Thank you for your comment. We have amended the recommendation to state 'increased' risk and the text of the 'Recommendations and link to evidence' section accordingly. After careful consideration of the evidence we have altered the bullet points of recommendation 1.1.6 so that increased -risk groups regarding chronic kidney disease and older age are now defined as: <ul style="list-style-type: none"> <li>• chronic kidney disease (people with an eGFR less than 40 ml/min/1.73 m2 are at particular risk)</li> <li>• age 75 years or over.</li> </ul> The GDG considered these groups to be at high risk of CI-AKI and thus would in general benefit from intravenous volume expansion as a preventative measure.

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						Please insert each new comment in a new row. stable patient who has received correct preparation). This is referred to on page 134 of the full guidelines but is not apparent in the NICE guidelines.	Please respond to each comment  We are unable to provide any further discussion beyond that included in the full guideline that you already refer to around the type or volume of contrast as this was not prioritised as a clinical question in the guideline as it was beyond the remit of guidelines for the prevention, detection and management of AKI. This level of detail is not recorded in the NICE guideline which details the recommendations only.  The GDG have asked the NICE implementation team to prioritise support in this area because of the challenges you allude to.
110	Renal Association Clinical Affairs Board	9	NICE Full version	20 155-173	1.3.1	This covers the identification of AKI using current criteria (AKIN/KDIGO) but omits advice to use staging systems to describe the severity of AKI. The full guidelines evaluate the performance of the different criteria, and find that in general the RIFLE and AKIN criteria perform similarly in terms of diagnosis and in terms of increasing stage associating with increased risk of short term mortality (no data yet for KDIGO but largely similar so unlikely that big differences will be seen). The GDG decided 'that whilst it was felt beneficial to use a system to stage AKI they did not wish to make a separate recommendation about using RIFLE or AKIN'. There would be value in explicitly stating that staging systems should be used to describe severity of AKI (probably doesn't matter too much which one). There would also be value in suggesting that hospitals consider mechanisms of monitoring the number of patients with AKI stage 3 as a method of driving systematic change on an organisational level.	Thank you for your comments. Our recommendations advocate the detection of an AKI in line with the relevant staging systems.  Your suggestion that we advise hospitals to monitor and report AKI is beyond the remit of this guideline.  There will be implementation tools available at the time of publication that will support the local implementation of the guideline including suggested audit measures.  The GDG advocates referral to nephrology of all stage 3 AKI and therefore clinicians will continue to need to stage AKI. By recommending detection of AKI by AKIN/RIFLE/KDIGO we feel that staging is inherent. This is made clear in the comments in the 'Recommendations and link to evidence' section (quoted below), and further expanded on in the bold sentences added in this section:  <b>Therefore whilst the GDG felt it was beneficial to use a system to stage AKI, they did not wish</b>

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							<b>to make a separate recommendation about using RIFLE or AKIN for prognosis. The evidence did not allow NICE to recommend a specific staging system. To be clear, this means that clinicians should be familiar with the stages of AKI (table 36), for example as given by AKIN or KDIGO. Clinicians should note that RIFLE, AKIN and KDIGO are closely related 'sister' definitions, with KDIGO being the most recent. AKI cases should be staged and the staging revised as needed during an illness.</b>
111	Renal Association Clinical Affairs Board	10	NICE	11	1.3.3	The emphasis placed on recording the cause of AKI is good - AKI is a syndrome and its implications and treatment differ significantly depending on underlying cause.	Thank you for your comment.
112	Renal Association Clinical Affairs Board	11	Full	General		The research recommendations are an important part of the documents. It will be key that well-designed projects addressing these areas are given priority from national funding bodies (such as Kidney Research UK) and are endorsed and supported by the AKI clinical study group.	Thank you for your comment. The GDG agrees that these are important areas that would benefit from further research and prioritised them as such.
113	Royal College of General Practitioners	1	Full	33	3	I went on to the NICE website and the AKI pathway doesn't exist	Thank you for your comment. The NICE Pathway associated with a clinical guideline will be published at the same time as the guideline.
114	Royal College of General Practitioners	2	Full	General		The document is obviously extremely detailed and much of its contents refer to 2ry and 3ry Care. The role of 1ry Care in terms of prevention, early identification and early referral are vital to the pathway and need to be articulated in a simple straightforward way. The current algorithm in Map of Medicine for Acute kidney Injury (AKI) – suspected (Primary Care)	Thank you for your comments. Our recommendations have not been signposted as being for primary or hospital care as they are relevant to many settings. The NICE pathway for AKI that is part of the web guidance gives a visual overview which is similar to the Map of Medicine. We agree that Map of Medicine could be updated following publication. The GDG are planning to work with the RCGP on

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						provides a good reference point for 1ry Care which could be updated following final publication of this document.	<p>implementation and have initiated discussions via the implementation team already.</p> <p>Some of the recommendations relevant to primary care are (titles paraphrased here):</p> <ul style="list-style-type: none"> <li>1.1.1 Identifying AKI in adults</li> <li>1.1.2 Identifying AKI in children</li> <li>1.1.3 Identifying ACKD</li> <li>1.1.4 Unclear clinical situations to consider AKI</li> <li>1.2.14 Situations to suspend ACEi/ARBs</li> <li>1.3.1 Detection of AKI</li> <li>1.3.2 Monitoring creatinine regularly</li> <li>1.3.3 Determining the cause</li> <li>1.4.1 Urinalysis</li> <li>1.5.15 - Referral to nephrology</li> <li>1.6.2 Info for patients/carers</li> </ul>
115	Royal College of General Practitioners	3	Full	33	32	I would like to seek clarity from the GDG with regard to past history of AKI. Relating to this page, page 36 line 21 and page 53. It would appear that there was no evidence examined with regard to a past history of AKI. Can the GDG tell me if they considered this to be an independent risk factor irrespective of the cause of the previous AKI. For example an episode of AKI in a young adult with normal underlying kidney function?	The GDG did not look specifically at evidence in this area but considered it would be important to include as a risk factor in any risk assessment because of the potential recurrence of AKI. This is discussed in the 'Recommendations and link to evidence' section for this recommendation.
116	Royal College of Nursing	1	Full	General		The Royal College of Nursing welcomes these draft guidelines. They are timely, comprehensive and relevant to NCEPODs AKI document which NICE acknowledges.	Thank you for your comment. We are pleased that the Royal College of Nursing welcomes this guideline.
117	Royal College of Nursing	2	Full	General		<p>The recommendations seem appropriate from the evidence based.</p> <p>As stated in the document, there is a clear relationship between suboptimal care and Acute</p>	Thank you for your comment. We believe this is covered fully in recommendation 1.2.1(Section 6.1.6 of full guideline) "Follow the recommendations in Acutely ill patients in hospital (NICE clinical guideline 50) on the use of track and trigger systems to identify adults who

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						Please insert each new comment in a new row. Kidney Injury (AKI). It would be helpful, therefore, if there is more emphasis in a recommendation that efforts should be made to avoid suboptimal care with utilisation of track and trigger detection tools and referral to critical care outreach nurses to try and prevent further deterioration.	Please respond to each comment are at risk of acute kidney injury because their clinical condition is deteriorating or is at risk of deteriorating".  The NICE implementation team will also be producing support tools to help implement the recommendations locally.
118	Royal College of Nursing	3	Full	General		The guidelines mention sepsis being a major risk factor for AKI and the use of volume expansion. The recent CHEST study has found that in volume expansion the use of starches increases the likelihood of AKI and patients going onto it require filtration. Could the evidence review state that due to the increase in AKI with intravenous starches, fluid expansion in sepsis should be avoided by using starch IV solutions?	The use of intravenous fluids will be covered by the NICE clinical guideline on Intravenous fluids currently in development ( <a href="http://guidance.nice.org.uk/CG/Wave25/5">http://guidance.nice.org.uk/CG/Wave25/5</a> ) . This guideline development group working on this guideline has included representation from the AKI GDG. We are unable to receive comments on behalf of that guideline, and look forward to your comments on that consultation separately.
119	Royal College of Nursing	4	Full	85	6.2.2	Under contrast induced AKI, the review focuses upon NAC, 0.9 saline and sodium bicarbonate. Aminophylline has also had some research studies focusing upon its role in preventing AKI with contrast. It is not clear why Aminophylline was not included in this review of the evidence? We know some hospitals that routinely use Aminophylline rather than NAC. This needs to be reflected within the evidence review and recommendations on Aminophylline use.	Thank you. The scope of the guideline included the evaluation of N-Acetylcysteine and/or intravenous fluids to prevent contrast-induced nephropathy. The value of aminophylline or any other drugs was beyond the scope and as such we have not made any recommendations on the use of other drugs.
120	Royal College of Nursing	5	NICE	22	1.5.8	It would be helpful if precise values (range) are provided for serum potassium "Refer patients for renal replacement therapy immediately if any of the following are not responding to medical management: Hyperkalaemia"	Thank you for your comment. There was no strong evidence reviewed that would allow the GDG to recommend specific potassium levels. The GDG acknowledged that the decision to initiate or withhold RRT varies by clinical factors and/or aetiology of AKI and also depends on the trends of urine output, potassium levels, degree of acidosis and overall severity of illness. They noted that each of these derangements often occur in combination. The GDG felt that providing

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							specific individual parameters and cut-off values for serum creatinine, urea or potassium would be unhelpful when compared to the clinician's overall assessment of the patient's condition and physiologic reserve and trends in blood results and urine output in considering when to refer for renal replacement therapy.
121	Royal College of Nursing	6	NICE	23	1.5.12	Should this be 'and' or 'and/or' – this needs clarification <i>“Do not refer patients to a nephrologist when there is a clear cause for acute kidney injury and the condition is responding promptly to medical management, unless they have a renal transplant.”</i>	Thank you for your comment. The GDG are happy with the wording of this recommendation using the term 'and' which implies that both points need to be met to not refer to a nephrologist.
122	Royal College of Nursing	7	NICE	24	1.6.1	Would prefer to see greater emphasis on informing the patient and family about AKI. The wording as it stands is open to ambiguity as clinicians may interpret 'appropriate' as meaning not important. Further explanation of 'appropriate' is recommended  “Discuss immediate treatment options, monitoring, prognosis and support options with the patient with acute kidney injury and/or their parent or carer if appropriate.”	Thank you for your comment. We have clarified the meaning and amended the recommendation to read as follows: <i>Discuss immediate treatment options, monitoring, prognosis and support options as soon as possible with the patient with acute kidney injury and/or, if appropriate, their parent or carer . Follow the recommendations on patient views and preferences and shared decision-making in <a href="#">Patient experience in adult NHS services (NICE clinical guidance 138)</a>.</i>
123	Royal College of Paediatrics and Child Health	1	Full	38	32	PEWS not fully validated. If used locally, then needs to have triggers, but cannot 'recommend' PEWS yet (Point 12)	Thank you for your comment. Having carefully considered the evidence on paediatric early warning scores, the GDG felt that although the evidence is not strong, the results are consistent in showing that they have fair to good discrimination between patients who are at risk of deteriorating and those who aren't. They also felt that having a scoring system would help to more easily identify patients who are deteriorating. Having reconsidered the evidence, the GDG agreed to make a

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							less strong recommendation and have amended the wording accordingly.
124	Royal College of Paediatrics and Child Health	2	Full	68	Methods, evidence and recommendation	PEWS advocated again: no evidence cited and there is no UK-wide consensus. We would agree that where a PEWS is used, deterioration should prompt consideration of AKI.	Thank you for your comment. The evidence considered by the GDG is summarised in chapter 6 of the full guideline. Although the evidence is not strong, the results are consistent in showing that PEWS have fair to good discrimination between patients who are at risk of deteriorating and those who aren't. The GDG agrees that deterioration of a PEWS score should prompt consideration of AKI and have made a recommendation in this regard. Recommendation number 9 lists special circumstances when children may be considered to be at greater risk of developing AKI. It is appropriate for these children to have, in addition to PEWS, observations that can alert the clinician to signs of impending AKI. These observations are renal specific and include the careful and accurate measurement of urine output, twice daily weight and biochemical testing to identify significant change in lactate, urea, creatinine, electrolytes and blood gases.
125	Royal College of Paediatrics and Child Health	3	Full	General	general	The 2 above both relate to the recommendation of PEWS. There has been a review of evidence for PEWS tools and evidence is weak. There is widespread acceptance of EWS in adult medicine and a desire to use such scores in children, but there is little consensus on which model works best; all papers have major biases and flaws. We think the wording in this guidance is too strong. It should alert to the possibility of AKI when PEWS is used and shows an unwell or deteriorating child and the guideline may suggest using an agreed tool should one be developed and implemented, but we do not think recommending the use of a PEWS tool is justified (by the evidence reviewed in the guideline).	Thank you for your comment. Although the evidence for PEWS had several limitations, the results were consistent in showing good measures of accuracy for their ability to predict PICU admission. Having reconsidered the evidence, the GDG agreed to make a less strong recommendation and have amended the wording accordingly.

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126	Royal College of Paediatrics and Child Health	4	Full	General		No specific comments from PICS other than it looks to be a very comprehensive guideline and David Milford has done a good job representing paediatric issues.	Thank you.
127	Royal College of Paediatrics and Child Health	5	Full	General		Congratulations to the GDG for such sensible, comprehensive guidance	Thank you for your comment. We are pleased that you find the guideline sensible and comprehensive.
128	Royal College of Paediatrics and Child Health	6	Full	38	14	It is very encouraging to see 'use of drugs with nephrotoxic potential, including NSAIDS' noted as a risk factor with AKI. It could perhaps be made clear that NSAIDs include ibuprofen, which is of course widely available.	Thank you for your comment. The GDG felt it most appropriate to mention class rather than individual drugs. We will look into specifically highlighting ibuprofen and other widely available NSAIDs in the Information for the Public version of the guideline to alert parents in particular to this fact.
129	Royal College of Physicians	1	Full	General		Please take this email as confirmation that the Royal College of Physicians has had sight of the response submitted by the Renal Association (RA) to the above guideline consultation. We wish to fully endorse the RA position.	Thank you. We have responded separately to all comments received from the Renal Association.
130	Royal Liverpool University Hospitals	1	Full	58	24	Assess the risk of acute kidney injury (AKI) in adults having surgery: Should also include :  Patients taking multiple antihypertensive (including on ACE inhibitor or Angiotensin receptor blockers)  Reason: as in many cases, the regular antihypertensive medications are given despite	Thank you for your comment. The evidence reviewed that informed this recommendation did not identify antihypertensive medication as a risk factor. This issue was not identified by the GDG as a key area to include through consensus. The GDG does discuss the risk of postoperative hypotension in section 5.1.6. of the full guideline.

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						low normal or Low BP post-surgery leading to AKI	
131	Royal Liverpool University Hospitals	2	Full	General		<p>Detecting Acute Kidney Injury:</p> <ol style="list-style-type: none"> <li>1. Electronic or lab based acute kidney injury (AKI) alert system is an useful adjuvant for early detection and we feels it should be included in the ' NICE AKI guideline'</li> <li>2. Many UK hospitals including our Royal Liverpool University Hospital renal unit in partnership with clinical biochemistry department have developed a real-time electronic checking and alerting system for patients who potentially have AKI (e-AKI alerts). Although, the diagnosis of AKI remains a clinical decision making process. However, the alert system can provide considerable benefits to patients by early detection and management of AKI as well as with prospective audit and service development.</li> </ol>	<p>Thank you for your comments. This was not directly in the scope for this guideline. However it was considered as part of early versus later referral for AKI. Although many support the introduction of alerts the actual evidence base for e-alerts is extremely limited, as shown by the early versus late referral review. The evidence review for guidelines looks for RCTs, prospective observational studies, and if needed retrospective observational studies. To show evidence of a beneficial intervention, the alerts have to be linked to action(s). Even in the review of early referral to nephrology, the one available study related to alerts had to be excluded. The GDG agreed this is an important topic and would form the basis of a good research topic particularly if such alerts are linked to packages of care. We have made a research recommendation around definitions of AKI which was within the scope and the findings of this would be crucial to inform use of e-alerts. Whilst we appreciate your comments, the available evidence does not permit the GDG to make a statement in support of alerts.</p>
132	Royal Liverpool University Hospitals	3	Full	General		<p>Summary: A summary flow chart can be added in the end of document for easy understanding and to aid usage of the guideline by general clinicians :</p> <p>One example, we use: 4 R</p>	<p>Thank you for your suggestion. The NICE pathway, available on the NICE website at publication, sets out the guidance in a similar format to the one you have suggested.</p>

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						<div style="border: 1px solid black; background-color: yellow; padding: 2px; margin-bottom: 5px;">RISK: Identify patients at risk of developing AKI</div> <div style="border: 1px solid black; background-color: orange; padding: 2px; margin-bottom: 5px;">Recognition: Early Detection of AKI</div> <div style="border: 1px solid black; background-color: red; padding: 2px; margin-bottom: 5px;">Response: Clinician review &amp; Management</div> <div style="border: 1px solid black; background-color: lightblue; padding: 2px; margin-bottom: 5px;">Referral: Renal team review</div> <p>Each box can be linked to the guideline summary box of - prevention, detection, management and referral</p>	
133	Society and College of Radiographers	1	Full	18 1.27, 1.28. 1.29 on page 18		One important point refers to procedures/precautions for iodinated contrast injection. The RCR have recently published recommendations which may agree, overlap or conflict. See <a href="http://www.rcr.ac.uk/publications.aspx?PageID=310&amp;PublicationID=391">http://www.rcr.ac.uk/publications.aspx?PageID=310&amp;PublicationID=391</a>	Thank you for bringing this to our attention. Two of our GDG members were also involved with developing the guidance you refer to and we are happy that our guidance is fit for purpose and is not contradictory.
134	UK Renal Pharmacy Group	1	Full	22	6	Text says not to offer low-dose dopamine to treat AKI. Should there also be a comment regarding the use of mannitol, which has also been a traditional "treatment" for AKI and has now been shown not to be effective?	Thank you for your comment. Mannitol was not prioritised by the GDG for review in this guideline. It has historically only been used in preventing AKI secondary to rhabdomyolysis or by kidney transplant surgeons to flush the organ prior to implantation and therefore was not included in the scope. The GDG felt that dopamine is much more widely used in current clinical practice and therefore warranted specific review.
135	UK Renal Pharmacy Group	2	Full	25	5	Information and Support – should there also be something about ensuring a full report of the AKI episode is fed back to the patient's GP? It is not uncommon for a patient to have an episode of	Thank you for your comments. The GDG agree and have added where possible some detail to their discussions behind this recommendation in chapter 10 of the full guideline. In the absence of a formal evidence

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						AKI but the discharge summary makes no mention of it, and the GP thinks that the missing ACEIs/ARBS/diuretics, etc are just an oversight. There should also be a clear plan for restarting any drugs which the patient had previously been taking, had been stopped during AKI, and now need to be restarted, which is communicated to the GP and the patient.	review in this area, the GDG were limited in the detail that they could provide.
136	UK Renal Registry	1	Full	General		Front page: Why is it confidential, does this just refer to the draft document?	Thank you for bringing this to our attention. This has now been amended in preparation for final publication.
137	UK Renal Registry	2	Full	11	8	It might be useful to state in the introduction that AKI is often a marker of circulatory failure which is a common feature of many severe illnesses. Circulatory failure affects all organs but problems with the kidneys are often detected before those in other organs, in part because good renal function requires a competent circulation and also because a simple and commonly performed blood test is available which requires little skill to interpret.	Thank you for your useful comment. Whilst not possible to provide a full and lengthy discussion of the issues in an introduction, we have added the following at the end of paragraph 1 of the introduction:  “For normal function the kidneys require a competent circulation. Conversely, it is known that renal function is vulnerable to even relative or quite modest hypotension or hypovolaemia. Hence AKI is a feature of many severe illnesses. Although these illnesses may affect many organs, the simple process of monitoring urine output and/or creatinine allow detection of AKI. “
138	UK Renal Registry	3	Full	17	12	Refers to sensitivity and specificity. Would positive and negative predictive value not be of more use here?	Thank you for your comment. Outcomes are agreed with the GDG at the protocol stage before the clinical review is undertaken. As this review was concerned with risk scores, and not a diagnostic test per se, it was decided that sensitivity, specificity and AUROC were the most useful outcomes for the GDG to base their recommendations on as calibration and discrimination are the most important factors here.
139	UK Renal Registry	4	Full	17	12	ACEI: even for a specialist readership, explain all abbreviations when they are first used.	Thank you, we have amended this and have also provided a glossary for reference in chapter 12 of the full guideline. ACEI is included in this glossary
140	UK Renal Registry	5	Full	29	7	Cost effectiveness: If evidence is available that a safe and efficacious treatment is available but is not currently deemed to be cost effective, is it	Thank you for your comment. Where evidence is available on interventions included in the scope and in the protocol of the review questions, this has been

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						mentioned in the guideline even although it cannot be recommended because it is too expensive or is it not mentioned at all?	presented in the guideline and considerations have been made. The results of the evidence review are presented in the 'Economic Evidence' sections in each chapter and the considerations on whether the strategy was or was not cost-effective have been made in the 'Linking Evidence to Recommendation' sections.
141	UK Renal Registry	6	Full	33	10	Have a high impact on reducing variation in care and outcomes (B): Should this not be improving quality? Simply reducing variation does not directly lead to improved quality. Finding variation may help to detect poor care but is not really the aim.	Thank you for your comment. The GDG agrees that improving quality is important. However, their decision had to be based on standard wording of criteria that are set out in the NICE guideline manual. 'Reducing variation' is one of these standard criteria. For more information please see section 9.4 of the NICE guideline manual ( <a href="http://publications.nice.org.uk/the-guidelines-manual-pmg6">http://publications.nice.org.uk/the-guidelines-manual-pmg6</a> )
142	UK Renal Registry	7	Full	33	25	Identifying acute kidney injury in adult patients with acute illness: ? add severe trauma, burns, medical condition know commonly to be associated with AKI. These need not be listed but eg HUS, tumour lysis syndrome, diarrhoea ...	Thank you for your comment. The GDG listed the most common risk factors and acknowledged that the list could include all potential individual clinical conditions. The GDG chose to list general risk factors applicable to different diagnoses. For instance, patients with trauma, burns or haematological malignancy are at increased risk of AKI but these conditions were not mentioned separately. Instead, more general risk factors like hypovolaemia, sepsis, use of nephrotoxic drugs and obstruction are listed since they are the main reasons for AKI in this high risk group. The corresponding paediatric recommendations mentions bloody diarrhoea which targets Haemolytic Uraemic Syndrome as a possible association.. We have made no change to the recommendation but have added the above text to the 'Recommendations and link to evidence' section to explain this.
143	UK Renal Registry	8	Full	33	34	Limited access to fluid because of neurological or cognitive impairment: ? add or because they have been told to fast 'nil by mouth' in anticipation of a procedure.	Thank you for your comment This recommendation is specifically made for acutely ill patients. This issue was raised specifically to draw attention to those groups who are unable to access

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							fluids without assistance. Being nil by mouth on its own is not a specific risk factor although the GDG did acknowledge in the 'Recommendations and link to evidence' section that prolonged periods of 'nil by mouth' prior to iodinated contrast should be avoided.
144	UK Renal Registry	9	Full	36	14	by measuring serum creatinine and comparing with baseline: Useful to give advice on what to do if a baseline serum creatinine measurement is not available and to remind readers that when interpreting a serum creatinine level in the absence of a base line reading, it is important to examine the patient to estimate muscle mass and BSA. Checking and recording of height and weight of all patients on admission if they are fit would help. Many patients with AKI have been admitted before and a Ht & (rough) Wt record would then be available.	Thank you for your comment. We agree with the general comment but the detailed assessment of creatinine and its relationship to muscle mass and GFR is beyond the scope of the guideline. Implementation support tools will be made available once the guideline is published. Further information about baseline creatinine has been added to the introduction to chapter 7 on detecting acute kidney injury.
145	UK Renal Registry	10	Full	39	32	Offer either isotonic sodium bicarbonate: Useful to say what this is. Many wards only have or have only herd of 8.4%.	Thank you for your comment. For clarity we have added the following to the linking evidence to recommendation section: "The GDG considered that isotonic sodium bicarbonate would be typically a solution of 1.26%. Strong solutions of sodium bicarbonate (up to 8.4%) would not be considered isotonic and are not to be used for this indication. "
146	UK Renal Registry	11	Full	40	1	Consider temporarily stopping ACE inhibitors and ARBs: ? add and ensure that a mechanism is in place to restart them or to ask the family doctor to review this when the patient recovers.	Thank you for your comment. Sections 6.4.6 and 6.5.6 have been amended to address these points. The GDG were unable to make an exact recommendation about when to restart ACE inhibitors and ARBs due to the lack of evidence, and so a research recommendation has been made in this area.
147	UK Renal Registry	12	Full	41	7	Re diuretics renal function is recovering in a patient not receiving renal replacement & therapy: ? add to	Thank you for your comment. The GDG feels that most of the readers would understand the term fluid overload and do not feel that the longer sentence suggested does

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						Please insert each new comment in a new row. treat circulatory sodium and water overload	Please respond to each comment not enhances clarity.
148	UK Renal Registry	13	Full	41	21	metabolic acidosis: Is there any evidence that RRT is of specific benefit to patients with eg lactic acidosis or ketoacidosis?	Thank you for your question. This very specific question was beyond the scope of the guideline and we are therefore unable to provide guidance..
149	UK Renal Registry	14	Full	41	27	... whole and not on an isolated urea, creatinine or potassium value: Could you offer guidance on what to look for in a patient with asymptomatic hyperkalaemia? ? refer to UK Resuscitation Council guideline (Alfonzo A. et al)	Thank you. The GDG felt that a patient may have hyperkalaemia alone without symptoms and this would require the exercise of some clinical judgement. The emphasis for this recommendation is to apply clinical judgement to the care of patients by assessing their condition as a whole and as such the management of the clinical situation you describe is beyond the scope of this guideline.
150	UK Renal Registry	15	Full	52		physiological age ...: This suggests that illness is inevitably associated with increasing age. Why not just say 'age and comorbidity'?	Thank you for your comment. We have changed this to 'age and comorbidity'.
151	UK Renal Registry	16	Full	61		nausea and vomiting, sleepiness or heart rhythm problems: While these may be associated with AKI, in the absence of data on the PPV and given their near ubiquity in many illnesses, do they help in the diagnosis of AKI? If not, suggest they are not mentioned.	Thank you for your comment. The GDG have included these as context for some of the symptoms of AKI but have not included them in their recommendations precisely because of the concerns you raised
152	UK Renal Registry	17	Full	62		Failure to diagnose AKI early may lead to ...: This is a key statement. Worth emphasising that most cases of severer or fatal illness associated with AKI start of as mild AKI. This is the time to make the diagnosis. If a confident diagnosis cannot be made quickly and if the patient is not rapidly improving, doctors who are not experienced in the full spectrum of AKI should seek help quickly. This can often be done by phoning a colleague to discuss immediate further investigations.	Thank you for your comment. The guideline includes recommendations on when patients should be referred to specialist nephrology services in chapter 9. For further clarity, we have added a sentence in 'Recommendations and link to evidence' section to sign post the reader to these recommendations.
153	University of Hertfordshi	1	Full	82	11	The Track and Trigger system is being converted to NEWS (National Early Warning Score). I am concerned that the omission of	The GDG understands your concerns. We discussed the NEWS system with its developers in the early stages of this guideline development. We state that urine output

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	re (Formerly Sheffield Kidney Institute)					Please insert each new comment in a new row. urine output on the scoring system will lead to poor evaluation of a patients urine output. In theory fluid assessment should be done as standard. However the early warning score that is used correctly draws the attention to urine output. I feel strongly that this is an error and should be advocated in this document. From a medical perspective this may be adequate. However as a nurse this is an important aspect that will lead to delays in identification of a problem.	Please respond to each comment should be monitored in patients at risk of AKI. We are aware that the NEWS chart does contain a specific space to collect data on urine output if deemed necessary. However, assessing the benefits and risks of different early warning scores was not in the scope of the guideline.

The following organisations were also invited to comment but did not do so:

Abbott GmbH & Co KG  
Aintree University Hospital NHS Foundation Trust  
Airedale NHS Trust  
Alder Hey Children's NHS Foundation Trust  
Alere  
Allocate Software PLC  
AMORE health Ltd  
AMORE Studies Group  
Association for Family Therapy and Systemic Practice in the UK  
Association of Anaesthetists of Great Britain and Ireland  
Association of British Insurers  
Association of Clinical Pathologists  
Association of Paediatric Anaesthetists of Great Britain and Ireland  
Association of Paediatric Emergency Medicine  
Association of Renal Industries  
Association of Renal Technologists  
Barnsley Hospital NHS Foundation Trust

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Barts and the London NHS Trust  
Black and Ethnic Minority Diabetes Association  
Bradford District Care Trust  
British Dietetic Association  
British Medical Association  
British Medical Journal  
British National Formulary  
British Nuclear Cardiology Society  
British Psychological Society  
British Renal Society  
British Society of Urogenital Radiology  
British Society of Urogynaecology  
Calderdale and Huddersfield NHS Trust  
Cambridge University Hospitals NHS Foundation Trust  
Camden Link  
Capsulation PPS  
Care Quality Commission (CQC)  
Central & North West London NHS Foundation Trust  
Chadderton Health Centre  
  
Chartered Society of Physiotherapy  
Clarity Informatics Ltd  
College of Emergency Medicine  
Commission for Social Care Inspection  
Covidien Ltd.  
Critical Care National Network Nurse Lead Forum  
Critical Care Network, Northern Ireland  
Croydon Health Services NHS Trust

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Cybex Ventures  
Deltex Medical  
Department for Communities and Local Government  
Department of Health, Social Services and Public Safety - Northern Ireland  
Drinksense  
Dudley Primary Care Trust  
East and North Hertfordshire NHS Trust  
East Kent Hospitals University NHS Foundation Trust  
Economic and Social Research Council  
Faculty of Sport and Exercise Medicine  
Five Boroughs Partnership NHS Trust  
Fresenius Medical Care  
Gambro UK  
GE Healthcare  
George Eliot Hospital NHS Trust  
GlaxoSmithKline  
Gloucestershire Hospitals NHS Foundation Trust  
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  
Hammersmith and Fulham Primary Care Trust  
Harrow Local Involvement Network  
Health Protection Agency  
Health Quality Improvement Partnership  
Healthcare Inspectorate Wales  
Herts & Beds Critical Care Network  
Hindu Council UK

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Hockley Medical Practice  
Independent Healthcare Advisory Services  
Institute of Biomedical Science  
KCARE  
Kidney Cancer UK  
  
Kidney Research UK  
L.IN.C.Medical  
Lancashire Care NHS Foundation Trust  
Leeds Teaching Hospitals NHS Trust  
Liverpool Community Health  
London Clinic  
Lothian University Hospitals Trust  
Maidstone and Tunbridge Wells NHS Trust  
Ministry of Defence  
National Confidential Enquiry into Patient Outcome and Death  
National Institute for Health Research Health Technology Assessment Programme  
National Patient Safety Agency  
National Public Health Service for Wales  
National Treatment Agency for Substance Misuse  
Newcastle upon Tyne Hospitals NHS Foundation Trust  
NHS Clinical Knowledge Summaries  
NHS Connecting for Health  
NHS Direct  
NHS Kidney Care  
NHS Plus  
NHS Sheffield  
NHS South Birmingham

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NHS Warwickshire Primary Care Trust  
NICE technical lead  
NOrF  
North central London acute kidney injury network  
North of England Critical Care Network  
North West London Critical Care Network  
Northamptonshire Primary Care Trust  
Northern Ireland Vascular Surgeons  
Nottingham City Council  
Nottingham City Hospital  
Nottingham University Hospitals NHS Trust  
Nova Biomedical UK  
Novartis Pharmaceuticals  
Parenteral and Enteral Nutrition Group  
Parkwood Healthcare  
PERIGON Healthcare Ltd  
  
Pharmametrics GmbH  
Pharmaxis Pharmaceuticals Ltd  
Public Health Wales NHS Trust  
Renal Nutrition Group, British Dietetic Association  
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 , Gastroenterology, Hepatology and Nutrition

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Royal College of Pathologists  
Royal College of Physicians and Surgeons of Glasgow  
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  
Sanofi  
Scottish Clinical Biochemistry Managed Diagnostic Network  
Scottish Intercollegiate Guidelines Network  
Sheffield Teaching Hospitals NHS Foundation Trust  
Shire Pharmaceuticals Ltd  
SNDRi  
Social Care Institute for Excellence  
Social Exclusion Task Force  
Society for Acute Medicine  
South East Coast Ambulance Service  
South London & Maudsley NHS Trust  
South Tees Hospitals NHS Trust  
South Wales Critical Care Network  
South West Yorkshire Partnership NHS Foundation Trust  
Southport and Ormskirk Hospital NHS Trust  
St Mary's Hospital  
Syner-Med  
The Association for Clinical Biochemistry

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The British In Vitro Diagnostics Association  
The Hindu Forum of Britain  
The Rotherham NHS Foundation Trust  
The University of Glamorgan  
UK Lung Cancer Coalition  
Unison  
University Hospital Birmingham NHS Foundation Trust  
University Hospital of North Staffordshire NHS Trust  
University Hospitals Birmingham  
University of Nottingham  
Vascular Society of Great Britain and Ireland  
Walsall Local Involvement Network  
Warrington and Halton Hospitals NHS Foundation Trust  
Welsh Government  
Welsh Kidney Patients Association  
Welsh Renal Clinical Network  
West Midlands Ambulance Service NHS Trust  
West Midlands Renal Network  
Western Cheshire Primary Care Trust  
Western Health and Social Care Trust  
Western Sussex Hospitals NHS Trust  
Wirral University Teaching Hospital NHS Foundation Trust  
Wye Valley NHS Trust  
York Hospitals NHS Foundation Trust

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