National Institute for Health and Care Excellence

4-year surveillance (2017) – Acute kidney injury: prevention, detection and management (2013) NICE guideline CG169

Appendix B: stakeholder consultation comments table

Consultation dates: 6 to 17 February 2017

Do you agree with the proposal not to update the guideline?

Stakeholder	Overall response	Comments	NICE response
Bristol Area Kidney Patient Association	No	As patients we are aware of the demographic time bomb as the population ages renal disease is more prevalent. The best and most cost effective treatment is early detection to manage the remaining kidney function for the natural lifetime of the patient. With medical advice the kidney can last longer with appropriate diet and lifestyle interventions encouraged by the medical profession to patients. We feel that if the guidance is not updated then this impetus will be diminished and an opportunity to extending lives at the most cost effective solution pre-treatment not dialysis or transplant is squandered. We do not wish treatment to be rationed in the elderly as unaffordable when it is better to invest in resources to maximise kidney function in stages 2 3 3a and 4. As patients we feel that the guidelines do not adequately stress the importance of early intervention but seems more attuned to expensive treatment. In patients opinion this is not best use of taxpayer's resources.	Thank you for your comment. The new evidence identified by the surveillance review did not have an impact on current recommendations, therefore we propose not to update the guideline. Whilst we are not updating the guidance, the evidence and input from our topic experts ensures that the guideline remains current and important for use in the NHS. No published evidence was identified during the surveillance review on the impact of dietary interventions specifically for the prevention or management of acute kidney injury (AKI). CG169 cross refers to NICE guideline CG138 - 'Patient experience in adult NHS services', where recommendations 1.2.6 and 1.2.7 emphasise that 'adequate and appropriate nutrition should be made available to patients. A research recommendation was drafted in CG169 on diet and other modifiable factors, as a package of care which may impact upon AKI outcomes: 'What is the clinical and cost effectiveness for outpatients with CKD stage 4/5 of an intensive tailored package of advice/care on prevention of AKI versus standard care on outcomes including incidence of AKI, mortality, need for RRT and hospital admission at 3 years?' No evidence which answers this particular research recommendation was found, and so the research recommendation will be retained.

			CG169 considers the care of patients aged 18 and over, in which those considered to be elderly (75 years and above) are included. As detailed in the scope, special consideration was given to 'older patients'. During the surveillance review, no evidence was identified that would cause any new health inequalities to arise. Topic experts also reported no new sources of health inequalities.
The Binding Site Group Limited	No	The point that we disagree on relates to section 1.4, in particular 1.4.2. Here urinalysis with a dipstick for the detection of 'protein' is recommended and we would like to suggest that this may not be sufficient for the detection of monoclonal serum free light chains as a cause of AKI. Monoclonal serum free light chains (generated in haematological malignancies such as Multiple Myeloma and AL Amyloidosis) are a well-known cause of AKI such as Cast Nephropathy, AL Amyloidosis, Light Chain Deposition Disease etc). In many instances rapid identification of monoclonal serum free light chains as a cause of the AKI is essential to minimise further renal damage and to maximise the chances of recovering renal function through the rapid initiation of treatment for the malignancy generating the monoclonal serum free light chains. The data further indicates that rapid diagnosis and therefore treatment improves overall survival in this population, particularly important as Myeloma patients who develop AKI are known to have shorter median survival than patients with AKI from other causes. NICE Guidance: 'NG35 Myeloma Diagnosis and Management' recommends serum free light chain analysis replaces urine analysis when investigating patients for suspected Myeloma. This recommendation was made based on the fact that urine analysis (for the detection of monoclonal serum free light chains as a cause for the AKI) is flawed for three reasons: 1. Urine is often not supplied. 2. The monoclonal free light chains don't always deposit in to the urine (due to renal reabsorption). 3. Urine analysis isn't sensitive enough to detect up to 5-10% of Myeloma and up to 15-20% of AL patients. Thus the problems associated with detecting monoclonal free light chains in the urine (identified in NG35) mean that the recommendation to use urine as the medium to access for 'protein' in a patient with AKI, may cause a delayed/missed diagnosis where monoclonal serum free light chains are causative, resulting in AKI progression and shortened overall survival.	Thank you for your comment. No published evidence was identified during the surveillance review, regarding urinalysis in AKI. No published evidence was identified that discussed monoclonal serum free light chains as a specific AKI biomarker. Patients with myeloma were not excluded from the scope of CG169, however no evidence to suggest this population should have a different management strategy was identified during the surveillance review. The guideline included the review question: What is the sensitivity and specificity of urine dipstick compared to urine microscopy and/or biopsy in the detection of proteinuria and haematuria as indicators of glomerulonephritis in AKI patients? No relevant evidence was identified during the 4 year surveillance reviews and therefore we did not identify an impact on current guideline recommendations.

		To minimise the use of serum free light chain analysis in the AKI group, it would be sensible to recommend that it is only used in those AKI patients over a certain age eg 50, and in those suspected of having an intrinsic cause of their AKI.	
Edwards Lifesciences	No	No comments	Thank you
Ortho Clinical Diagnostics	Yes	While we agree that no change to the guidelines are warranted right now, NICE should remain vigilant and should be prepared to re-visit this decision within the next 2 years, to evaluate if new data is available warranting the inclusion of biomarker testing in AKI guidelines. Biomarkers have now been recognized as clinically useful in the ICU setting **for patients at risk for moderate to severe AKI** and as such there will be increased research interest worldwide on their potential value in other hospital populations AND more specifically to the UK where **Acute kidney injury (AKI) is associated with as many as 100,000 deaths annually and is estimated to cost the NHS up to £620m per annum**	Thank you for your comment. New evidence was identified during the surveillance intelligence gathering regarding AKI specific biomarkers, however the evidence was mostly inconclusive and did not demonstrate an impact on clinical outcomes or practice. A UK-based, NIHR-funded, diagnostic Health Technology Assessment (HTA) of AKI-specific biomarkers, was identified. This study is yet to be published but if it is published at the time of the next surveillance review, its impact on current recommendations will be assessed.
Royal College of Pathologists	Yes	No comments	Thank you.
Astellas Pharma Ltd	Yes	No comments	Thank you.

Do you agree with the proposal to remove the research recommendation?

What is the clinical and cost effectiveness of rapid referral (within 12 hours) to nephrology services for adults with moderate to severe (stage 2 to 3) acute kidney injury not needing critical care?

Stakeholder	Overall response	Comments	NICE response
Bristol Area Kidney Patient Association	No	As a renal patient community with a permanent condition we are aware that as expert patients we have seen many of our community adversely effected with delays in treatment. We are aware that early intervention gives the best opportunity of slowing down the deteriorating function of the native kidney or graft. This is the best clinical outcome for the patient and the best value of NHS Taxpayer's resources and we are opposed to it being removed.	Thank you for your comment. We initially proposed to remove the research recommendation as we have identified new evidence (summarised in the Summary of Evidence) and an ongoing trial, which answers the research recommendation. However based on your comment, we will now retain this research recommendation.

The Binding Site Group Limited	Yes	No comments	Thank you.
Edwards Lifesciences	Yes	No comments	Thank you.
Ortho Clinical Diagnostics	No	Biomarkers have now been recognized as clinically useful in the ICU setting **for patients at risk for moderate to severe AKI** and as such there will be increased research interest worldwide on their potential value in other hospital populations AND more specifically to the UK where **Acute kidney injury (AKI) is associated with as many as 100,000 deaths annually and is estimated to cost the NHS up to £620m per annum.**	Thank you for your comment. We initially proposed to remove the research recommendation as we have identified new evidence (summarised in the Summary of Evidence) and an ongoing trial, which answers the research recommendation. However based on your comment, we will now retain this research recommendation.
Royal College of Pathologists	N/A	Not relevant to area of practice	Thank you for your comment.
Astellas Pharma Ltd	Yes	No comments	Thank you.

Do you have any comments on areas excluded from the scope of the guideline?

Stakeholder	Overall response	Comments	NICE response
Bristol Area Kidney Patient Association	Yes	When the guidance was compiled in our opinion there was not adequate specialist medical or expert patient involvement. The NICE recommendation to limit the range of immunosuppressant medication was overturned on appeal with intervention by the Renal Community and medical professionals. We feel that there is enough evidence for the guidance to be reviewed as a matter of priority.	Thank you for your comment. The process of recruiting a guideline committee to interpret the evidence, is detailed in the NICE Guidelines manual. In accordance to NICE methods, 2 expert patients or lay members are recruited, to ensure that patient perspective and involvement is captured and preserved throughout the guidance. The evidence identified during the surveillance intelligence gathering process supported current recommendations, hence we propose to not update the guideline with regard to immunosuppressant medications at this time. Ongoing trials were identified and will be followed up at the next surveillance cycle.
The Binding Site Group Limited	No	No comments	Thank you.

Edwards Lifesciences	Yes	Prevention of acute kidney injury (AKI) during surgery has been excluded from this guideline. In recent papers (2016 onwards) the incidence of AKI after surgery has been shown to range from 5% – 33% as referenced below: • SURGERY :5% Shara Feld (Feld, Tevis, Cobian, Craven, & Kennedy, 2016) • ANNALS : 33 % (Ozrazgat-Baslanti et al., 2016) • ANNALS RCS ENGLAND : 8-23 % (Ferguson et al., 2016) • PLOS ONE : 13.1 % (Kim, Bae, Ma, Kweon, & Kim, 2016) • ANAESTHESIA Analg 2016: 6.8 % (Long et al., 2016) AKI as a result of surgery can have serious consequences for patients in terms of mortality, both short and long term, and prolonged hospitalisation (Ferguson et al, 2016). Martensson et al 2014 (Current opinion in critical care, 20 (4), 451-9) discuss several approaches to prevent AKI after surgery including statins, aspirin and perioperative goal directed therapy. Perioperative goal directed therapy has been shown to reduce AKI by up to 30% (Brienza at al 2009, Critical Care Medicine, Vol 37, issue 6, pages 2079- 2090). In addition the following publications have shown that prolonged hypotension (mean arterial pressure <65 mm Hg) increases the risk of AKI. • Anaesthesiology 2017 (Salmasi et al., 2017) • Anaesthesiology 2015 (Sun, Wijeysundera, Tait, & Beattle, 2015) • Current Hypertension 2016 (Onuigbo & Agbasi, 2016) Perioperative goal directed therapy and prevention of perioperative hypotension should be considered as standard of care to prevent postoperative complications including AKI.	Thank you for your comment. Studies discussing the prevention of AKI after surgery, including both pharmacological and surgical interventions were identified during the surveillance process (summarised in the Summary of Evidence).NICE is planning a guideline on perioperative care and we will log this area for consideration in the scope of that guideline.
Ortho Clinical Diagnostics	No	No comments	Thank you for your comment.
Royal College of Pathologists	Yes	1) **Use of urine or serum NGAL (and other biomarkers) for the early diagnosis of AKI** These assays are not routinely available in clinical laboratories and there would be significant challenges to implementation across laboratories in the UK. Aside from the fact that there is no standard definition of AKI that is not based on serum creatinine, there are issues around:	Thank you for your comment. New evidence on the use of urine or serum neutrophil gelatinase associated lipocalin (NGAL) and other biomarkers were assessed and are summarised in the summary of evidence. The evidence did not have an impact on the current guideline. A new UK-based, NIHR-funded HTA investigating the diagnostic properties of NGAL and other biomarkers, was identified but

		- Cost of the assay (to include reagent, calibrator and control kits, potentially send-away/analyser costs if a laboratory does not have a specific analytical platform); NGAL is significantly more expensive than the serum creatinine assay - Variability between the various NGAL assays available in terms of their performance (and this should be taken into account when interpreting results from the various clinical/research studies measuring NGAL) - Lack of assay standardization and form of NGAL measured. - Lack of an established External Quality Assessment programme We would recommend an assessment of the technology and its clinical and cost effectiveness prior to any potential future recommendation for its routine use in clinical laboratories **2) Implementation of an AKI stage warning alert system and the communication of critical or unexpected results by laboratories** These areas were not covered by the original guidance and are relevant to the detection and management of AKI. The mandated implementation of a national algorithm, standardising the definition of AKI in laboratory information management systems has provided the ability to ensure that a timely and consistent approach to the detection and diagnosis of patients with AKI is taken across the NHS (NHS England, Level 3 Patient Safety Alert 2014). However: - The automated electronic systems in use are generally rudimentary and highly reliant on clinicians reviewing results in a timely manner. There remains a reliance on rapid, 'interruptive' communication by laboratory staff (typically via a telephone call) of markedly abnormal creatinine and/or potassium results to minimise risk of missed/delayed diagnosis as well as delayed treatment and thus reduce the risk of avoidable harm to patients - The provision of such a service is labour intensive for laboratories with associated opportunity costs particularly	has not yet published. The trial will be considered once published at the next surveillance review. New evidence on an AKI stage warning alert system was not identified during this surveillance cycle. However there is a currently a research recommendation addressing this issue: Can a simplified definition and staging system, based on SI units, be used to predict short- to medium-term outcomes in acute kidney injury? An ongoing study due to publish in 2016, assessing risk factors for AKI admission has been identified. This study is yet to be published but if it is published at the time of the next surveillance review, its impact on current recommendations will be assessed. A randomised controlled trial by Awdishu et al. 2016, identified in the surveillance process, evaluated the use of real-time alerting on appropriate prescribing in kidney disease. Topic experts agreed that the study supported current recommendations on electronic clinical decision tools. Recommendation 1.2.10 and 1.2.11 in CG169, endorse the use of clinical decision tools where feasible and mandate that they must be able to interact with laboratory data. As the evidence supports current recommendations, we will not update this area at this time. Management of AKI in the community was raised by topic experts. However, published evidence relevant to this area did not meet the inclusion criteria (randomised controlled trials or systematic reviews) of the 4 year surveillance review and its impact on the guideline cannot be considered at this time.

		given the ever increasing volume of requests and the number of AKI alerts generated on a daily basis across all settings. The Royal College of Pathologists are in the process of updating guidance for laboratories on the communication of critical or unexpected pathology results. The National AKI programme (Think Kidneys) has had an opportunity to influence this guidance as it relates to the communication of AKI stage warning test results and markedly potassium and creatinine results to both primary and secondary care clinicians. Any potential future recommendations by NICE in this area should take into account the significant challenges faced by laboratories in providing this service **3) The communication of AKI stage warning test results to primary care clinicians at discharge** This area was not covered by the original guidance and is relevant to patients whose hospital admission included an episode of AKI - High quality discharge communication is critical to patient safety. An important part of discharge communication is the timely handover of diagnostic tests ordered or to be ordered including results received and those requiring follow-up. - Breakdown in this aspect of communication is common and contributes to unsafe patient care (Ref: NHS England (2016) Standards for the communication of patient diagnostic results on discharge from hospital). - This area is particularly relevant to AKI given that patients with AKI may still be at risk after discharge (require AKI and CKD surveillance) and they are numerous. The majority are looked after by non-nephrologists while in hospital and after discharge very few receive outpatient nephrology follow up. Perhaps NICE should develop guidance on communication at discharge which future AKI guidance could refer to. There is a considerable evidence base. This should include specific guidance on the handover of diagnostic test results	

		4) AKI management in primary care Issues with community acquired acute kidney injury were not covered by the original guidance. This area is important given the potential scale of the problem (Ref: *Holmes J, Rainer T, Geen J et al. Acute Kidney Injury in the Era of the AKI E-alert) Clinical Journal of the American Society of Nephrology: CJASN 2016 Dec 7; 11(12)*. Primary care teams are well placed to raise AKI awareness and limit AKI risk in "at risk" patient groups, detect AKI and deliver simple interventions early as well as undertake post AKI reviews to detect new or worsening Chronic Kidney Disease post AKI, restart drugs suspended during AKI and limit risk of further AKI.	
Astellas Pharma Ltd	None	No comments	Thank you for your comment.

Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
Bristol Area Kidney Patient Association	Yes	There is growing imperial evidence that in some areas dialysis is not offered to all patients. If elderly >75 with co modalities then dialysis is not offered only end of life care. Some research may show this is appropriate but the lack of patient choice is unacceptable and the assumption that no treatments recommendations is made on financial not medical grounds.	Thank you for your comment. Short-term dialysis and other renal replacement therapies are discussed in this guideline on management of acute kidney disease In addition, a guideline addressing renal replacement therapy in chronic kidney disease is being developed.
The Binding Site Group Limited	No	No comments	Thank you.
Edwards Lifesciences	No	No comments	Thank you.
Ortho Clinical Diagnostics	No	No comments	Thank you.
Royal College of Pathologists	No	No comments	Thank you.
Astellas Pharma Ltd	None	No comments	Thank you.

Royal College of Paediatrics and Child Health
On this occasion we have not received any responses for this consultation – thank you for your comment.

Royal College of Nursing
The RCN has no comment – thank you for your response.

British Renal Society
Support the proposal not to update. – thank you for your comment.