Methods

This guidance was developed in accordance with the GAIN Guide to Developing Guidelines

Developing the review questions and outcomes

Review questions were developed using the PICO framework (patient, intervention, comparison and outcome) for intervention reviews, and with a framework of population, index tests, reference standard and target condition for reviews of diagnostic test accuracy. This was to guide the literature searching process and to facilitate the development of recommendations by the guideline development group (GDG). The questions were based on the key clinical areas identified in the scope.

For each review, question, the GDG chose up to 7 outcomes identifying which outcomes were critical to their decision making and which were important. This distinction helped the GDG to make judgements about the importance of the different outcomes and their impact on decision making. For example, mortality will usually be considered a critical outcome and would be given greater weight when considering the clinical effectiveness of an intervention than an important outcome with less serious consequences. The GDG decide on the relative importance in the review protocol before seeing the review. Further information on the outcome measures examined follows this section.

Scope Area	Review Questions	Outcomes
Clinical risk assessment in the identification an ongoing assessment of acute kidney injury	Which risk assessment tools are the most accurate for predicting AKI in at risk adult patients?	Sensitivity (%) and specificity (%)
Preventing deterioration: a) nephrotoxic drugs in patients with, or at high risk of AKI b) methods to monitor the use of nephrotoxic and other potentially toxic drugs in patients with suspected or confirmed AKI	What is the clinical and cost effectiveness of stopping compared to continuing chronic angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) therapy in patients with CKD to prevent AKI due to surgery, iodinated contrast, diarrhoea and vomiting, or sepsis?	Incidence of acute kidney injury • Cardiovascular events • All cause mortality • Number of patients needing RRT • Length of hospital stay
Preventing deterioration: a) nephrotoxic drugs in patients with, or at high risk of AKI b) methods to monitor the use of nephrotoxic and other potentially toxic drugs in patients with suspected or confirmed AKI	What is the clinical cost effectiveness for methods for preventing inappropriate use of nephrotoxic drugs in hospital inpatients?	Frequency of acute kidney injury due to nephrotoxic drugs • Mortality • Number of changes/ interventions • Time to discontinuation/ change in nephrotoxic drug • Incidence of adverse events • Length of stay
When to use ultrasound (US), and in which patients.	Which patients should have US for the diagnosis of the cause of AKI?	Main outcomes: • Sensitivity (%) and specificity (%) • Area under the ROC curve (AUROC) – measure of

		predictive accuracy Other outcomes: • Positive/negative predictive value • Positive/negative diagnostic likelihood ratios
Timing of relief of urological obstruction by methods such as nephrostomy.	In adults with AKI and upper tract urological obstruction, what is the clinical and cost effectiveness of early compared to delayed relief of obstruction by nephrostomy or stenting on mortality, severity of AKI, need for RRT and length of hospital stay?	• Mortality • Worsening of AKI (as defined by study) • Number of patients needing for RRT • Length of hospital stay • Adverse events (including bleeding, infection or injury to the obstructed kidney or to nearby organs)
Pharmacological management with: Low dose dopamine loop diuretics.	In adults with AKI, what is the clinical and cost effectiveness of loop diuretics compared to placebo on mortality, need for RRT, length of RRT, dialysis independence, length of hospital stay and hearing loss?	• Mortality • Number of patients needing RRT • Length of RRT • Dialysis independence • Length of hospital stay • Hearing loss
	In adults with AKI, what is the clinical and cost effectiveness of low dose dopamine compared to placebo on mortality, need for RRT, length of RRT, dialysis independence, length of hospital stay and cardiac arrythmias?	• Mortality • Number of patients needing RRT • Length of RRT • Dialysis independence • Length of hospital stay • Cardiac arrhythmias
At what stage should RRT be considered?	In patients with AKI, what is the clinical and cost effectiveness of initiating early RRT compared to delayed RRT on mortality, renal recovery, duration of RRT, length of critical care stay and HRQoL?	• Mortality • Renal recovery (as defined by study) • RRT duration • Length of ICU stay • HRQoL
Criteria for involving nephrology services	In patients with or suspected of having AKI, what is the clinical and cost effectiveness of early RRT compared to delayed referral to a nephrologist?	• Stage of AKI • Number of patients needing RRT • Mortality • Renal recovery (as defined by study) • Length of ICU stay • Length of hospital stay
Information and support for patients and carers.	What information and support do patients with acute kidney injury and their carers require?	• Patient /carer subjective reported outcomes • Patient/carer satisfaction • Patient preference

Clinical Literature Search

In order to identify the relevant literature systematic literature searches were order to answer the review questions as set out in the GAIN Guideline Development Guide.

Clinical databases were searched using relevant medical subject headings, free-text terms. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language. All searches were conducted using MEDLINE, Embase, Cochrane and HONNI. Additional subject specific databases were used for some questions: CINAHL for risk assessment tools, paediatric early warning scores, computerised decision tools, urinalysis, ultrasound, referring to nephrology and information and support for patients and carers; No papers after 30 November 2013 were considered. Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews and asking the GDG for known studies.

Evidence of Effectiveness

The evidence was reviewed following:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.

Full papers were reviewed against pre -specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population.

Relevant studies were critically appraised using the appropriate checklists as specified in The GAIN Guideline Development Guide.

Key information was extracted on the study's methods and PICO factors and results were presented in evidence tables.

Summaries of the evidence were generated by outcome and were presented as part of the GDG meetings:

Randomised studies: meta-analysed, where appropriate and reported in GRADE profiles

Prognostic studies: assessing risk factors data were presented as a range of values, usually in terms of the relative effect as reported by the authors and where possible reported in the GRADE profile format.

Inclusion/Exclusion

The GDG were consulted regarding the inclusion/exclusion and any uncertainty regarding inclusion/exclusion of selected studies. The guideline population was defined to be adults, children and young people. For some review questions, the review population was confined to special groups such as people at risk of AKI, people with AKI or people with chronic kidney disease.

Randomised trials, non-randomised trials, and observational studies (including prognostic studies) were included in the evidence reviews as appropriate. Laboratory studies (in vivo or in vitro) were excluded.

Conference abstracts were not automatically excluded from the review but were initially assessed against the inclusion criteria and reviewed only if no other full publication was available for a particular review

question or if it provided further data on published studies. Literature reviews, letters and editorials, foreign language publications and unpublished studies were excluded.

Updating the Guideline

A formal update review of a guideline is usually undertaken by GAIN 3 years after its publication.

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Stages of Chronic Kidney Disease

Stage	eGFR (ml /min/1.73 m^2)	Description	Qualifier
1	≥90	Kidney damage, normal or increased GFR	Kidney damage (presence of structural abnormalities and/or persistent haematuria, proteinuria or microalbuminuria) for ≥ 3 months
2	60-89	Kidney damage, mildly reduced GFR	
3a	45-59	Moderately reduced GFR ± other evidence of kidney damage	GFR < 60 ml/min for ≥ 3 months ± kidney damage
3b	30-44		
4	15-29	Severely reduced GFR ± other evidence of kidney damage	
5	<15	Established kidney failure	