**Methods**

This guidance was developed in accordance with the GAIN Advice for Guideline Development in Northern Ireland.

Evidence search took place during May 2015.

**Developing the review questions and outcomes**

All searches were run up to 30 November 2013. Searches were limited to retrieve material published in English.

Internet searches were carried out on various websites. Databases searched include Medline, Embase, Cinahl, PsycINFO and The Cochrane Library (Wiley). The main searches were supplemented by material identified by individual members of the development group.

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 identified 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.

<table>
<thead>
<tr>
<th>Review Question</th>
<th>Objectives</th>
<th>Population</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the accuracy of equations to estimate GFR as a measurement of kidney function?</td>
<td>Determine the most clinically and cost effective method of estimating GFR to assess kidney function</td>
<td>Adults over 18 with suspected CKD, Over 75 years, Minority ethnic groups</td>
<td>Critical: Accuracy, Bias, Precision, Important: Sensitivity, Specificity</td>
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<tr>
<td>For people with CKD what is the effect of proteinuria at any given eGFR on adverse outcomes (CKD progressions, AKI, all-cause mortality and cardiovascular mortality)?</td>
<td>Determine whether occurrence of adverse outcomes is different in people with different levels of proteinuria compared to those without any given eGFR.</td>
<td>Adults over 18 with suspected CKD, Over 75 years, Those with hypertension, Those with diabetes</td>
<td>Critical: CKD Progression - Change in eGFR, CKD Progression – Occurrence of end stage kidney disease, Cardiovascular mortality, AKI, Important: Cardiovascular events, Hospitalisation</td>
</tr>
<tr>
<td>Question</td>
<td>Outcome</td>
<td>Population</td>
<td>Key Outcomes</td>
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<td>For people with CKD, does the presence of diabetes have an effect on adverse outcomes at any given category of eGFR and ACR?</td>
<td>Determine whether occurrence of adverse outcomes is different in those with CKD associated with diabetes to those with CKD from another cause, at any given eGFR.</td>
<td>Adults over 18 with CKD</td>
<td>Critical: • CKD Progression - change in eGFR • CKD Progression – occurrence of end stage kidney disease • All-cause mortality • Cardiovascular mortality • Cardiovascular events</td>
</tr>
<tr>
<td>For people with CKD does the presence of hypertension have an effect on adverse outcomes at any given category of eGFR and ACR</td>
<td>Determine whether occurrence of adverse outcomes is different in those with CKD associated hypertension</td>
<td>Adults over 18 with CKD</td>
<td>Critical: • CKD Progression - change in eGFR • CKD Progression – occurrence of end stage kidney disease • All-cause mortality • Cardiovascular mortality • Cardiovascular events</td>
</tr>
</tbody>
</table>

**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 only. For some review questions, the review population was confined to:

- Identification and investigation of people who have or are at risk of developing CKD
- Classification of CKD
- The definition of CKD progression
- The relationship between Acute Kidney Injury (AKI) and CKD
- Pharmacotherapy for CKD.

Randomised trials, non-randomised trials, and observational studies (including prognostic studies) were included in the evidence reviews as appropriate. Laboratory studies 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.
Criteria, inclusions and exclusions were agreed by consensus of the full GDG.

**Updating the Guideline**

A formal update review of a guideline is usually undertaken by GAIN 3 years after its publication.
2. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. The EUCLID Study Group. Lancet. 1997; 349(9068):1787-1792
5. Malnutrition Universal Screening Tool ("MUST"). British Association for Parenteral and Enteral Nutrition (BAPEN), 2003


52. Burgess ED, Carides GW, Gerth WC, Marenette MA, Chabot I, Canadian Hypertension Society. Losartan reduces the costs associated with nephropathy and end-stage renal disease from type 2 diabetes: Economic evaluation of the RENAAL study from a Canadian perspective. Canadian Journal of Cardiology. 2004; 20(6):613-618


80. Dasgupta A, Steinhubl SR, Bhatt DL, Berger PB, Shao M, Mak KH et al. Clinical outcomes of patients with diabetic nephropathy randomized to clopidogrel plus aspirin versus aspirin alone (a post hoc
analysis of the clopidogrel for high atherothrombotic risk and ischemic stabilization, management, and avoidance [CHARISMA trial]. American Journal of Cardiology. 2009; 103(10):1359-1363


96. Earle KK, Porter KA, Ostberg J, Yudkin JS. Variation in the progression of diabetic nephropathy according to racial origin. Nephrology Dialysis and Transplantation. 2001; 16(2):286-290


103. Ford L and Berg J. Delay in separating blood samples affects creatinine measurement using the Roche kinetic Jaffe method, 2008


129. Halbesma N, Kuiken DS, Brantsma AH, Bakker SJ, Wetzels JF, de ZD et al. Macroalbuminuria is a better risk marker than low estimated GFR to identify individuals at risk for accelerated GFR loss in population screening. Journal of the American Society of Nephrology. 2006; 17(9):2582-2590


141. Hemmelgarn BR, Culleton BF, Ghali WA. Derivation and validation of a clinical index for prediction of rapid progression of kidney dysfunction. QJM. United Kingdom 2007; 100(2):87-92


143. Hendry BM, Viberti GC, Hummel S, Bagust A, Piercy J. Modelling and costing the consequences of using an ACE inhibitor to slow the progression of renal failure in type I diabetic patients. QJM. 1997; 90(4):277-282


Levin A, Stevens PE. Early detection of CKD: the benefits, limitations and effects on prognosis. Nature Reviews Nephrology.: Division of Nephrology, University of British Columbia, 1081 Burrard Street, Room 60101A, Vancouver, BC V6Z1Y8, Canada. alevin@providencehealth.bc.ca. 2011; 7(8):446-457


albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study). BMJ. 2004; 328(7438):495


293. Newsome BB, Warnock DG, McClellan WM, Herzog CA, Kiefe CI, Eggers PW et al. Long-term risk of mortality and end-stage renal disease among the elderly after small increases in serum creatinine


386. Stevens LA, Schmid CH, Greene T, Zhang Y, Beck GJ, Froissart M et al. Comparative performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study equations for estimating GFR levels above 60 mL/min/1.73 m2. American Journal of Kidney Diseases. 2010; 56(3):486-495


