



Surveillance report 2017 – Chronic kidney disease (stage 4 or 5): management of hyperphosphataemia (2013) NICE guideline CG157, Chronic kidney disease in adults: assessment and management (2014) NICE guideline CG182 and Chronic kidney disease: managing anaemia (2015) NICE guideline NG8

Surveillance report

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Surveillance decision

Following the joint surveillance review of the guidelines on [hyperphosphataemia in chronic kidney disease](#), [chronic kidney disease in adults](#) and [chronic kidney disease: managing anaemia](#), it is proposed that consideration be given to combining the 3 guidelines to ensure that recommendations on the management of chronic kidney disease are accessible from 1 clinical guideline.

We will plan an update of the guideline on [hyperphosphataemia in chronic kidney disease](#). The update will focus on:

- Cost effectiveness of phosphate binders for children, young people and adults with chronic kidney disease (CKD) stages 4–5, both on dialysis and not on dialysis.

We will plan an update of the guideline on [chronic kidney disease in adults](#). The update will focus on:

- Investigations for and classification of chronic kidney disease:
 - the use of the Tangri score in predicting the risk of progression to end stage renal disease (ESRD) in CKD patients.
- Defining progression:
 - The value of lesser declines in estimated glomerular filtration rate (eGFR) over a longer period than 1 year in identifying CKD patients at increased risk of progression.
- Anaemia identification in people with CKD (see update of the guideline on [chronic kidney disease: managing anaemia](#) below, which will be cross referred to).

We will plan an update of the guideline on [chronic kidney disease: managing anaemia](#). The update will focus on:

- Diagnostic role of glomerular filtration rate:
 - The trigger threshold of the eGFR for investigation of anaemia being due to CKD (a cross-referral will be added to this update from the guideline on [chronic kidney disease in adults](#)).

During surveillance editorial or factual corrections were identified for the guideline on [chronic kidney disease: managing anaemia](#).

Details are included in [appendix A3: summary of evidence from surveillance for the guideline on chronic kidney disease: managing anaemia](#).

Reason for the decision

Assessing the evidence

We found 162 studies through surveillance: 23 studies for the guideline on hyperphosphataemia in chronic kidney disease, 105 studies for the guideline on chronic kidney disease in adults and 34 studies for the guideline on chronic kidney disease: managing anaemia.

Evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guidelines, advised us about whether the following sections of the guidelines should be updated:

Hyperphosphataemia in chronic kidney disease

- For people with stage 4 or 5 CKD who are not on dialysis, are phosphate binders effective compared with placebo or other treatments in managing serum phosphate and its associated outcomes?
- For people with stage 5 CKD who are on dialysis, are phosphate binders effective compared to placebo or other treatments in managing serum phosphate and its associated outcomes?

Topic expert feedback indicated that sevelamer carbonate is available at a considerably reduced cost to hydrochloride as a generic version. Therefore the majority of topic experts highlighted a need to revise the health economic modelling, and to consider the carbonate version that was not included in the development of the guideline. Topic experts also agreed that:

- Practice relating to the use of combinations of phosphate binders had not changed sufficiently to justify inclusion in the economic model.
- They were unaware of any new evidence to inform cost effectiveness analysis for people with stage 4 or 5 CKD that are not on dialysis.
- The approach taken during the guideline development of adapting evidence from people with stage 5 CKD to those with stage 4 or 5 CKD remains an acceptable approach for the revised model.

- The limited evidence base on the effectiveness of phosphate binders in children has not changed since the guideline was developed.

Decision: These review questions should be updated.

Chronic kidney disease in adults

Investigations for chronic kidney disease

- What is the best combination of measures of kidney function and markers of kidney damage to identify people with CKD who are at increased risk of progression?

Classification of chronic kidney disease

- For people with suspected CKD, what is the effect of proteinuria at any given eGFR on adverse outcomes?

Topic expert feedback indicated that the Tangri score is accurate in predicting end stage renal disease (ESRD) with high discrimination. It was considered by the majority of topic experts to have a role in patient decision making and prognostication. Experts also felt that it could affect the referral pathway from primary to secondary care, with more timely access to dialysis due to better risk stratification. Patients could potentially be triaged using the Tangri score for intensive management versus discharge back to GP.

However, the Tangri score only predicts the risk of progressive CKD, but does not predict the additional risks of cardiovascular disease or related death. It was also highlighted that in primary care it is equally important to identify people at low risk of CKD progression but in whom acute conditions, such as episodes of kidney injury or cardiovascular events, could increase the level of risk. It was agreed that these factors will need to be considered during the update process.

The majority of topic experts also agreed that the two relevant review questions should be reviewed together in terms of the impact of the Tangri score. However, they advised caution to avoid confusing the recommendations relating to investigation and classification of CKD.

Decision: These review questions should be updated.

Frequency of monitoring

- In people with CKD, what constitutes a clinically significant decline in eGFR?

Topic expert feedback indicated that the standard annual review in clinical practice fits with a 1-year follow up, as recommended in chronic kidney disease in adults: assessment and management (NICE guideline CG182), as distinct from a 2- or 3-year follow up. However, as CKD is a long term condition, definitions of progression that are easy to use in practice over a longer time period are needed.

The finding that that a 30% change over 2 years is associated with a 5-fold increase in risk of ESRD was noted by experts to be a very significant new finding. It was considered to have the capability of identifying patients at high risk of ESRD who are likely to benefit from earlier referral, who will not be highlighted as such currently. Consequently it may result in a significant change in practice.

Further expert feedback highlighted a limitation of the guideline, which risks missing patients who decline by successive increments just below the currently recommended annual threshold. These patients could benefit from specialist review. A review of the current description of accelerated progression, which uses comparison of annual blood tests rather than trends over longer periods, was also suggested.

Additional topic expert feedback indicated that:

- The rate of decline should be 30% over 2 years to a threshold of less than 60 ml/min/1.73 ml², as distinct from 100 to 70 ml/min/1.73 ml², as even the CKD Epidemiology Collaboration (CKD-EPI) creatine equation has considerable imprecision above a GFR of 60 ml/min/1.73 ml².
- The smaller the rate of decline that is set to define progression the higher the sensitivity and the lower the specificity. The imprecision arises from the non-linear nature of CKD progression and the impact of related events, such as acute kidney injury.
- A rate of decline over a longer period may also affect other health parameters aside from CKD progression, such as cardiovascular complications and morbidity. It was suggested that incorporating a revised rate of decline into the guideline could complement the use of the Tangri score.

Decision: This review question should be updated.

Other complications

- Anaemia identification in people with CKD.

The recommendation in this area cross refers to the guideline on chronic kidney disease: managing anaemia. See below for details of the update.

Decision: This review question should be updated.

We also found evidence on the accuracy of equations to estimate glomerular filtration rate (GFR), information and education, and on referral criteria that supports current recommendations.

We found evidence on treatment for mild hyperkalaemia and on complementary therapies, which was not covered in the guideline. However, the evidence was insufficient to add new recommendations in these areas at this time.

Chronic kidney disease: managing anaemia

Diagnostic evaluation and assessment of anaemia

- Diagnostic role of glomerular filtration rate.

In developing the guideline on chronic kidney disease: managing anaemia, the guideline committee retained the previous 2006 recommendation for the trigger threshold of the eGFR for investigation of anaemia being due to CKD. Currently this is recommended to be below 60 ml/min/1.73 ml², although the rationale for this was consensus-based.

The majority of experts that contributed to the surveillance review agreed that a threshold below 60 ml/min/1.73 ml² was too high, did not reflect current practice and was out of date. The preferred threshold was agreed by the majority of experts to be less than 30 ml/min/1.73 ml² in current clinical practice today.

Some topic expert feedback indicated that separate thresholds may be required for people with CKD with and without diabetes. A threshold of less than 45 ml/min/1.73 ml² was suggested for people with diabetes. However, additional topic expert feedback indicated that people with diabetes may nonetheless benefit from some investigation if they develop anaemia above a threshold of 30 ml/min/1.73 ml² and that this occurs in practice. The use of a single threshold for all people could also avoid over-complication in clinical practice.

Decision: This review question should be updated.

We also found evidence on managing anaemia and on assessment and optimisation of erythropoiesis that supports current recommendations.

Equalities

We identified no equalities issues during the surveillance process.

Overall decision

After considering all the evidence and views of topic experts, we decided that a partial update is necessary for all three guidelines.

See [how we made the decision](#) for further information.

Commentary on selected evidence

With advice from topic experts we selected 3 studies for further commentary.

Hyperphosphataemia in chronic kidney disease: cost-effectiveness of phosphate binders in children, young people and adults

For [phosphate binders in children, young people and adults](#), we selected the network meta-analysis (NMA) by [Palmer et al. \(2016\)](#) for a full commentary. The reasons for selection were that it was highlighted by more than one topic expert as a significant addition to the body of evidence in this clinical area, and includes a large number of studies.

What the guideline recommends

For adults with CKD, NICE's guideline on [hyperphosphataemia in chronic kidney disease](#) recommends first line treatment with calcium acetate, to control serum phosphate in addition to dietary management. For adults with stage 4 or 5 CKD who are not on dialysis and who are taking a calcium-based binder, consideration of switching to a non-calcium-based binder is recommended if calcium-based phosphate binders are not tolerated, if hypercalcaemia develops, or if serum parathyroid hormone levels are low.

For adults with stage 5 CKD who are on dialysis and remain hyperphosphataemic despite adherence to the maximum recommended or tolerated dose of calcium-based phosphate binder, the guideline advises considering either combining with, or switching to, a non-calcium-based binder.

For adults with stage 5 CKD who are on dialysis and who are taking a calcium-based binder, if serum phosphate is controlled by the current diet and phosphate binder regimen but:

- serum calcium goes above the upper limit of normal, or
- serum parathyroid hormone levels are low

the guideline recommends consideration of either combining with, or switching to, sevelamer hydrochloride or lanthanum carbonate, having taken into account other causes of raised calcium.

Methods

The NMA by Palmer et al. (2016) compared the phosphate binders sevelamer, lanthanum, iron, calcium, colestilan, bixalomer, nicotinic acid, and magnesium, in adults with CKD.

Prior to the NMA, a pair-wise meta-analysis was conducted, using a random effects model, to determine treatment efficacy. For the NMA, heterogeneity was explored using a common variance, and direct and indirect estimates were compared to evaluate consistency.

Prespecified sensitivity analyses were also conducted for studies focusing on dialysis, patients younger than 60 years, longer than 12 months follow-up, and low baseline serum phosphorous. A post-hoc analysis was also conducted to compare all-cause mortality between sevelamer and calcium, incorporating a longer term follow-up study.

The inclusion criteria were:

- parallel-group randomised clinical trials (RCTs)
- a follow-up at least 4 weeks
- adults with CKD
- allocation to a phosphate binder, placebo, or standard care.

The analysis included a total of 12,562 patients from 77 studies, 62 (11,009 patients) of which were performed in a dialysis population. Risk of bias was assessed for the included studies according to methods outlined in the Cochrane handbook. The primary outcome was all-cause mortality. Additional outcomes were cardiovascular mortality, myocardial infarction, stroke, adverse events, serum phosphorus and calcium levels, and coronary artery calcification.

Results

Compared to placebo, The NMA found that no class of drug lowered mortality or cardiovascular events. All phosphate binders, except for colestilan, significantly lowered serum phosphorus levels, with iron performing best for this outcome (standardised mean difference –1.58, confidence interval [CI] –2.02 to –1.14). However, it should be noted that placebo-controlled trials were of short duration, with a maximum of 3 months.

Treatments were ranked according to their probability of being the best treatment for a specific outcome, and the surface under the cumulative ranking curve was estimated using the network rank command.

In terms of specific drug comparisons, the NMA results showed:

- Sevelamer significantly reduced all-cause mortality compared to calcium (odds ratio [OR] 0.39, 95% CI 0.21 to 0.74, $p=0.005$). However, when the INDEPENDENT trial ($n=466$) was removed from the analysis, the results were no longer significant (OR 0.61, 95% CI 0.37 to 1.01).
- Lanthanum was non-significant for all-cause mortality when compared to calcium (OR=0.78, 95% CI 0.16 to 3.72).
- Iron was non-significant for all-cause mortality when compared to calcium (OR=0.37, 95% CI 0.09 to 1.60).
- Colestilan was non-significant for all-cause mortality when compared to calcium (OR=0.55, 95% CI 0.07 to 4.43).
- Sevelamer significantly reduced coronary artery calcification scores compared to calcium (standardised mean difference -0.20 ; 95% CI -0.40 to -0.01). However, the clinical significance of this result was reduced due to the short duration of trials.
- There were no significant differences between non-calcium binders in terms of all-cause mortality.

Strengths and limitations

Strengths

- The meta-analysis only included RCTs.
- The network meta-analysis design enabled comparative analysis between specific phosphate-binder classes against each other or placebo, despite the lack of head-to-head trials. This included an assessment of heterogeneity, pre-specified sensitivity analysis and comparison of direct and indirect estimates to evaluate consistency.
- The meta-analysis enhanced the evidence base in this area, building on a previous NMA (28 studies, $n=8,335$) by including a larger number of studies and analyses.

Limitations

- The included placebo-controlled trials were of short duration, with a maximum of 3 months. The comparisons also varied considerably in terms of median follow-up, which may have influenced the reporting of outcomes.
- The included studies were of variable quality, with a high or unclear risk of bias.
- It was unclear whether attempts were made to identify unpublished studies.
- Imprecise results of testing for heterogeneity may have caused some inconsistency.
- The all-cause mortality benefit of sevelamer over calcium-based treatment was heavily dependent on a single large trial (INDEPENDENT). This benefit became non-significant when the trial was removed from the analysis.
- Both calcium acetate and calcium carbonate were considered together as calcium-based binders and compared with non-calcium-based binders. This overlooked the finding in NICE guideline CG157 that calcium acetate has a far lower, and therefore safer, calcium load than calcium carbonate.
- The impact of the results was limited by the exclusion of paediatric studies.
- The study did not undertake any cost-effectiveness analysis, such as to explore whether the benefits of sevelamer could justify its higher cost.
- The results reported in the abstract and the results section for adverse effects were discrepant with the adverse effects data presented in Figures 4 and 5.

Impact on guideline

While iron-based therapies were ranked first in the NMA for lowering serum phosphate, the guideline recommendations do not specify which non-calcium-based binder should be substituted or added if the serum phosphate is not controlled or adverse events, including hypercalcaemia, occur with calcium-based binders. The only exception to this is for children and young adults where the recommendations specify sevelamer for switching or as an add-on treatment. The exclusion of paediatric studies in the NMA by Palmer et al. (2016) therefore limited the impact of the results.

The results indicated that no drug class lowered mortality or cardiovascular events compared with placebo. However, topic expert feedback indicated that the durations of the trials appear too short to draw any definitive conclusions about treatment effects on mortality, cardiovascular events or vascular calcification.

The finding of an all-cause mortality benefit of sevelamer over calcium-based treatment was heavily dependent on the inclusion of the INDEPENDENT trial (n=466), which was one of few larger trials with a longer duration. When removed from the analysis, the effect of sevelamer on all-cause mortality was not significant, compared with calcium.

The findings are consistent with previous network and conventional meta-analyses in this area, which have been the subject of NICE Medicines Evidence Commentaries in 2014 and 2016.

Topic expert feedback indicated that further trials, with adequate power and duration covering both adults and children, are needed. This will determine whether phosphate binders reduce mortality, and if they do, whether any type of binder is superior for this outcome.

Cost effectiveness analysis was not included in the NMA by Palmer et al. Topic expert feedback indicated that sevelamer carbonate is available at considerably reduced cost compared to sevelamer hydrochloride as a generic version. There is therefore a potential need to revise the health economic modelling in NICE guideline CG157, and to consider sevelamer carbonate which was not included in the original guideline.

Chronic kidney disease in adults: investigations for chronic kidney disease – markers of kidney damage

For investigations for chronic kidney disease, we selected the individual patient data (IPD) meta-analysis by Tangri et al. (2016) for a full commentary. The reasons for selection were that it was highlighted by topic expert feedback, included a large overall sample, has a potential impact on guideline recommendations, and covers an emerging area of quantifying risk.

What the guideline recommends

NICE's guideline on chronic kidney disease in adults advises using the person's GFR and albumin:creatinine ratio (ACR) categories (see table 1 Classification of chronic kidney disease using GFR and ACR categories) to indicate their risk of adverse outcomes (for example, CKD progression, acute kidney injury, all-cause mortality and cardiovascular events) and discuss this with them. It does not currently make any recommendations on the use of equations for markers of kidney damage where CKD has been diagnosed.

Methods

The IPD meta-analysis by Tangri et al. (2016) evaluated the accuracy of kidney failure risk equations across a range of different geographic regions and patient populations. The equations,

which were originally validated in a Canadian population, use demographic and laboratory data to predict progression of CKD to kidney failure. The four-variable equation included age, sex, estimated glomerular filtration rate (eGFR), and albumin to creatinine ratio. The eight variable equation used the same four variables plus laboratory measurements of calcium, phosphate, bicarbonate, and albumin.

Cohorts participating in the Chronic Kidney Disease Prognosis Consortium (CKD-PC) were selected for validation based on data availability. The CKD-PC is a collaborative research group integrating data from more than 70 cohorts spanning 40 countries and involving 2 million individuals from general, high-risk, or CKD populations. Available data on end stage renal disease from people in the cohorts participating in the CKD-PC was included. A random-effects model was used to perform meta-analysis across studies. The studies were selected to include patients with stages 3 to 5 CKD with an eGFR less than 60 ml/min/1.73 ml² and an absence of kidney failure at baseline who had follow-up information on kidney failure, defined as treatment by dialysis or a kidney transplant.

The primary outcome was kidney failure, measured by treatment with dialysis or transplantation.

Calibration, defined as the difference between observed and predicted risk, was examined by comparing the observed 2-year and 5-year probability of kidney failure in individual cohorts to the predicted risk using the original and pooled risk equations.

In total, data from 31 cohorts were included covering 721,357 people with CKD, of which 23,829 experienced kidney failure. The median follow-up time was 4 years.

Results

Overall, the participants had a mean age of 74 years and a mean eGFR of 46 ml/min/1.73 ml². In the North American cohorts, there were 41% of participants with albuminuria and a kidney failure incidence of 7.5 per 1,000 patient years. In the non-North American cohorts there were 40% of participants with albuminuria and a kidney failure incidence of 7.8 per 1,000 patient years.

The original risk equations were found to differentiate people who developed kidney failure from those who did not across all included cohorts (overall C statistic 0.90, 95% CI 0.89 to 0.92 at 2 years; C statistic 0.88, 95% CI 0.86 to 0.90 at 5 years).

Calibration was found to be poorer among some non-North American cohorts, where the original risk equations overestimated risk. A calibration factor was therefore added to address this. This

reduced the baseline risk by 32.9% at 2 years and 16.5% at 5 years, resulting in improved calibration in non-North American cohorts at 2 years (12 of 15 studies $p=0.04$) and at 5 years (10 of 13 studies $p=0.02$).

Strengths and limitations

Strengths

- The meta-analysis pooled data from a very large overall sample.
- Meta-analysis was performed appropriately across studies using a random-effects model to allow for heterogeneity.
- The study validated the risk equations in non-north American cohorts, including those in the UK setting, which are more representative of the population and setting considered in the guideline.

Limitations

- The authors did not describe any search beyond the CKD-PC source. The studies within the CKD-PC may not reflect the entire set of existing studies, potentially introducing bias.
- The equations only predict risk over 2 or 5 years, which may restrict their applicability, due to varying patterns of decline among patients.
- Longer term risk of kidney failure beyond 5 years was not considered. This may affect other clinical decisions such as lifestyle modification, as acknowledged by the authors.
- The authors acknowledged that the risk prediction equation cannot be used to predict risk among those with mild impairment in kidney function, because these patients were not included in the model.
- The integrity of IPD was not fully reported, such as data consistency, baseline imbalance, and missing data.
- Risk of bias assessment of the included cohort studies was not reported.

Impact on guideline

NICE guideline CG182 does not include recommendations for the use of risk equations in assessing risk of progression for people already diagnosed with CKD. This new evidence and topic expert feedback supports the use of the Tangri risk equations in predicting ESRD in CKD patients, and has

a potential impact on the guideline to review the advice for determining the risk of progression and adverse outcomes.

Topic expert feedback further indicated that the equations have the potential to be used in primary and secondary care. In primary care, lower-risk patients could be managed without additional testing or treatment of CKD complications, whereas higher-risk patients could receive more intensive testing and early intervention.

However, the limitations of the model restrict its clinical value, and further evaluation and refinement may be necessary before implementation. For instance, the equations cannot be used currently to predict risk among those with mild impairment in kidney function, because these patients were not included in the model. Additionally the equations only predict risk over 2 or 5 years, which may restrict applicability, because the pattern of decline varies among patients. Topic expert feedback also highlighted that the equations cannot predict the risk of cardiovascular disease or death, and require validation in people with mild kidney disease. It was agreed that these factors will need to be considered during the update process.

Frequency of monitoring – defining progression by decline in eGFR

For [frequency of monitoring](#), we selected the IPD meta-analysis by [Coresh et al. \(2014\)](#) for a full commentary. The reasons for selection were that it was recommended by topic expert feedback, was based on a very large data set, and highlights the potential value of smaller declines to indicate CKD progression over 1 to 3 years.

What the guideline recommends

NICE's guideline on [chronic kidney disease in adults](#) defines accelerated progression of CKD as a sustained decrease in GFR of 25% or more and a change in GFR category over 12 months, or a sustained decrease in GFR of 15 ml/min/1.73 ml² per year (see recommendation [1.3.3](#)).

Methods

The IPD meta-analysis by [Coresh et al. \(2014\)](#) examined the association of decline in eGFR with subsequent progression to ESRD, and explored the role of smaller declines in eGFR over longer periods as potential alternative outcomes for CKD progression.

Participants with available outcome data from cohorts in the [CKD-PC](#) with a repeated measure of serum creatinine were included. Studies with at least 10 events and participants aged over 18 years

were included. ESRD cases before the baseline period were excluded. Baseline assessments in each cohort took place between 1975 and 2012.

In total, data were obtained from 35 cohorts (n=1,757,886) for analysis of mortality and change in eGFR.

The primary outcome was ESRD after the baseline period. This was defined as initiation of renal replacement therapy or death due to kidney disease other than acute kidney injury.

Results

Change in eGFR

- Over a baseline period of 1 year (n=1,530,648) there were 12,344 ESRD events over a mean follow-up of 3.1 years.
- Over a baseline period of 2 years (n=1,341,193), there were 8,532 subsequent ESRD events over a mean follow-up of 2.4 years.
- Over a baseline period of 3 years (n=1,080,274) there were 5,159 subsequent ESRD events over a mean follow-up of 2.0 years.

In terms of ESRD risk, 52% of ESRD cases had a –30% change in eGFR over 2 years, whereas only 16% of ESRD cases reached a –57% eGFR change in the same period. A change in eGFR of –30% was associated with an adjusted Hazard ratio (HR) of ESRD of 5.4 (95% CI 4.5 to 6.4) for a baseline eGFR less than 60 ml/min/1.73 ml². This result was similar over 1-year and 3-year baseline periods, as confirmed by sensitivity analysis. At a –57% decline, the risk was considerably higher (HR 32.1, 95% CI 22.3 to 46.3) for a baseline eGFR less than 60 ml/min/1.73 ml².

Mortality

- Over a baseline period of 1 year (n=1,757,886) there were 223,944 deaths from 27 cohorts.
- Over a baseline period of 2 years (n=1,589,257) there were 158,603 deaths from 32 cohorts.
- Over a baseline period of 3 years (n=1,259,477) there were 102,491 deaths from 34 cohorts.

From the mortality data analysed, there were considerably more people with an eGFR change of –30% or greater (cumulative prevalence of 7.1% (95% CI 6.6 to 7.7%)) compared to a –57% change or greater (cumulative prevalence of 0.97% (95% CI 0.70 to 1.25%)).

Compared to those with stable eGFR (0% change), the adjusted HR of all-cause mortality was higher with greater eGFR decline but was largely flat in the range of minimal decline (–10% change or less) or rise.

An association was found between a 30% decline in eGFR and a higher subsequent all-cause mortality risk, for both lower and higher baseline eGFR. The adjusted HR for a –30% change was 1.8 (95% CI 1.6 to 1.9) and this increased with greater declines.

Strengths and limitations

Strengths

- The study included a very large overall sample size.
- Meta-regression was conducted to assess variation in study characteristics and the robustness of findings. A large number of sensitivity analyses were also undertaken.

Limitations

- The authors did not explain how the included cohort studies were selected from the CKD-PC or whether any attempts were made to search for other additional studies.
- All of the included studies were observational in design, and methods for assessing risk of bias were not reported.
- Standardisation of serum creatinine values may have varied across time and studies. Percent change in eGFR-based on a single first and single last eGFR is less precise than alternative designs where multiple measures are available at each time point.
- Variation in design across cohorts introduced heterogeneity. However, the authors reported consistency across cohorts despite dramatic variation in design and populations.

Impact on guideline

The new evidence, based on a very large data set, highlights the potential value of smaller declines to indicate CKD progression over 1, 2 and 3 years. This is consistent with recommendations 1.3.3 and 1.3.5 in the NICE guideline on chronic kidney disease for 1-year follow up, which define increased risk of progression to ESRD as a sustained decrease in GFR of 25% or more over 12 months. The evidence reviewed for NICE guideline CG182 showed that a sustained drop in eGFR of 25% or a sustained drop of 15 ml/min/1.73 m² over the period of 1 year was associated

with an increased risk of mortality and progression to end stage kidney disease. There was more uncertainty of risk of progression with smaller declines in eGFR over longer periods.

Topic expert feedback indicated that the standard annual review in clinical practice fits with recommended 1-year follow up, as distinct from a 2- or 3-year follow up. However, additional topic expert feedback highlighted that CKD is a long-term condition, and that definitions of progression that are easy to apply in practice over a longer time period are needed.

The finding that a 30% change over 2 years is associated with a 5-fold increase in risk of ESRD was considered by topic experts to be very significant. It was considered that this has the potential to capture patients at high risk of ESRD who are likely to benefit from earlier referral and will not be highlighted as such currently. It may therefore impact on guideline recommendations and could potentially result in a change in practice.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of NICE's guideline on [hyperphosphataemia in chronic kidney disease](#) (CG157) in 2013, 4 years after the publication of NICE's guideline on [chronic kidney disease in adults](#) (CG182) in 2014 and 2 years after the publication of NICE's guideline on [chronic kidney disease: managing anaemia](#) (NG8) in 2015.

For details of the process and update decisions that are available, see [ensuring that published guidelines are current and accurate](#) in developing NICE guidelines: the manual.

The previous surveillance update decision for the guideline on [hyperphosphataemia in chronic kidney disease](#) is on our website. No previous surveillance was performed for the guidelines on [chronic kidney disease in adults](#) or [chronic kidney disease: managing anaemia](#).

New evidence

We found 13 studies in a search for systematic reviews and randomised controlled trials published between 25 November 2013 and 2 September 2016. We also considered 2 additional studies identified by members of the guideline committee who originally worked on this guideline.

We also considered evidence identified in previous surveillance 2 years after publication of the guideline. This included 8 studies identified by search.

From all sources, we considered 23 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See [appendix A1](#): summary of evidence from surveillance for details of all evidence considered, and references.

Chronic kidney disease in adults

We found 104 studies in a search for systematic reviews and randomised controlled trials published between 25 November 2013 and 2 September 2016. We also considered 1 additional study identified by members of the guideline committee who originally worked on this guideline.

From all sources, we considered 105 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See [appendix A2](#): summary of evidence from surveillance for details of all evidence considered, and references.

We found 32 studies in a search for systematic reviews and randomised controlled trials published between 14 August 2014 and 2 September 2016. We also considered 2 additional studies identified by members of the guideline committee who originally worked on this guideline.

From all sources, we considered 34 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See [appendix A3](#): summary of evidence from surveillance for details of all evidence considered, and references.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because 4-year surveillance reviews were performed, and the decision was to update all the guidelines, we did not consult on the decision.

See [ensuring that published guidelines are current and accurate](#) in developing NICE guidelines: the manual for more details on our consultation processes.

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