

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments Monday 21 May 2018 by 5pm email: RRT@nice.org.uk

	<p>Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly.</p> <p>We would like to hear your views on the draft recommendations presented in the guideline, and any comments you may have on the rationale and impact sections in the guideline and the evidence presented in the evidence reviews documents. We would also welcome views on the Equality Impact Assessment.</p> <p>We would like to hear your views on these questions:</p> <ol style="list-style-type: none">1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.2. Would implementation of any of the draft recommendations have significant cost implications?3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) <p>See section 3.9 of Developing NICE guidance: how to get involved for suggestions of general points to think about when commenting.</p>
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Renal Association UK https://renal.org/
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	[none]
Name of commentator person completing form:	Martin Wilkie

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Renal Replacement Therapy

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Type		[office use only]		
Comment number	Document [guideline, evidence review A, B, C etc., methods or other (please specify which)]	Page number Or ' <u>general</u> ' for comments on whole document	Line number Or ' <u>general</u> ' for comments on whole document	Comments.
Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.				
1	Guideline	General	General	<p><u>General points about the guideline –</u></p> <p>The Guideline Group are to be congratulated on their comprehensive approach to the report. The section on coordination of care [1.9] (including scheduling appointments, giving people the details of the person responsible for their care and considering multi-morbidity) is very welcome. However, we believe that the Guideline group has missed opportunities in several areas.</p> <ul style="list-style-type: none"> • Prediction of CKD progression: Consideration of the rate of decline of renal function is relevant to the discussion around the preparation of dialysis access. Validated tools exist to predict decline and if adopted could improve many of the statements and care eg...access within 6 months of dialysis, timing of pre-emptive transplant listing and timing of Transplant, conservative care. However existing risk prediction equations require validation in the NHS and should therefore be the subject of a research recommendation. • Choice of in-centre dialysis: We do not believe that the evidence is sufficient to recommend HDF preferentially over HD. • Choice of a home therapy: There is a missed opportunity to promote home dialytic therapies given benefits in quality of life, impact on outcomes and evidence of cost-effectiveness. There appears to be very little reference to the benefits of frequent regimens at home and patient

Please return to: RRT@nice.org.uk

Renal Replacement Therapy

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				<p>preferences and evidence around qualitative and cardiovascular benefits (2 RCTs – Culleton BF et al <i>JAMA</i> .1299-1291:(11)298;2007 .doi:10.1001 and FHN study <i>N Engl J Med</i> 2010; 363:2287-2300 DOI: 10.1056/NEJMoa1001593). The key reasons for low uptake are often extrinsic barriers and not patient related factors. This draft guidance it currently stands if circulated as i could have a detrimental impact on sustaining home programmes in NHS trusts, and would go against patient demand and preferences. It also contradicts existing research and other initiatives such as KQUIP and previous NICE guidance.</p> <ul style="list-style-type: none"> • A research recommendation should be to establish the clinical and cost effectiveness of frequent and extended home haemodialysis, considering the impact of frequency at home. • The use of peritoneal dialysis in unplanned start patients: this approach avoids the requirement for central venous catheters and is associated with increased uptake of PD. Data from the 18th Renal Registry Report, Multisite Dialysis Access audit, indicates PD is used half of renal units for at least some patients known to the service less than 90 days – this is more likely to occur through the use of percutaneous rather than surgical catheter insertion. • The use of assisted peritoneal dialysis – this service is commonly offered in the UK and provides a significant contribution to PD in the UK. • Young adult care: Stress the importance of a well organised young adult support clinic/service (including paediatric to adult care transition). The benefits are well described. Transplant outcomes remain inferior for 15-25 year olds • Conservative care: the quality of this is variably delivered across Renal/community Units. Should there be more focus on this? • Patient reported experience measures (PREMS): the UKRR has collected PREM data for the last 2 years, this information has potential to transform the quality of care. Should submission of such data to UKRR be recommended? <p>Communication</p> <p>There is no recommendation in the report around patients having access to their medical records including a requirement for all letters about the patient being copied in to all their correspondence from the renal team.</p> <p>MDT infrastructure</p>
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Renal Replacement Therapy

Consultation on draft guideline – deadline for comments Monday 21 May 2018 by 5pm email: RRT@nice.org.uk

				<p>There is no specific recommendation around care being delivered within a specialist clinic with an MDT framework.</p> <p>Financial modelling</p> <p>Care should be taken on utilizing reference costs. It is highly likely that these are not accurate.</p> <p>There are no recommendations for biochemical, haematological, fluid or BP parameters for patients on dialysis.</p> <p>Some of the points are clearly trying to encompass adult and paediatric populations with comments such as ‘developmental stage’ and this can make some of the text less fluid than if just dealing with adult OR paediatric populations.</p>
2	Guideline	Title		<p>As the guideline relates to an integrated programme of care for all people with End Stage Kidney Disease – renal replacement therapy as well as conservative care – we feel the title is misleading and excludes conservative care. Would the committee consider something like “end-stage kidney disease care” or “care for people with end-stage kidney disease”?</p>
3	Guideline	1	5	<p><u>Terminology</u></p> <p>Terminology is very important and there are many names for conservative care. Kidney Disease Improving Global Outcomes, the global non-profit organization developing and implementing evidence-based clinical practice guidelines in kidney disease (www.kdigo.org), held a controversies meeting that considered this and recommended adoption of the term “comprehensive conservative care” (Murtagh et al, 2016).</p> <p>Adoption of this KDIGO terminology was a key recommendation of the International Society of Nephrology end-stage kidney disease summit on integrating care in Sharjah, UAE, in March 2018. (Report in preparation.)</p> <p>We would suggest the guideline adopts the internationally recommended terminology – comprehensive conservative care.</p> <p>Reference</p> <p>Murtagh FE, Burns A, Moranne O, Morton RL, Naicker S. Supportive Care: Comprehensive Conservative Care in</p>

Please return to: RRT@nice.org.uk

Consultation on draft guideline – deadline for comments Monday 21 May 2018 by 5pm email: RRT@nice.org.uk

				End-Stage Kidney Disease. Clin J Am Soc Nephrol. 2016 Oct 7;11(10):1909-14.
5	Guideline	3	5	<p>1.1.2 <u>The rate of GFR decline and dialysis start.</u></p> <p>The RA responses to the GFR start recommendation are presented below. The main points of concern are for the accuracy of the eGFR equation at low GFRs and that rate of renal function decline should be factored into the renal replacement therapy preparation discussion.</p> <p><u>Concerns regarding the accuracy of the eGFR formula and Individualizing dialysis start</u></p> <p>The accuracy, precision and bias for eGFR when the GFR is <15 is significantly impaired. (http://cjasn.asnjournals.org/content/6/4/937.long) This is particularly true in sarcopenic older women in whom eGFR will significantly overestimate kidney function. Thus, although the timing of dialysis start bases its recommendations on findings from the IDEAL study, the conclusion should be qualified as a result of clinician judgement since in late start group of that study, the mean eGFR was actually 9.8ml/min and relatively few managed to start with an eGFR between 5-7. Therefore we should avoid suggesting a specific range of eGFR at which RRT should start but rather focus on individualising starting dialysis for each patient according to clinical characteristics.</p> <p>The other finding from IDEAL is that patients choosing PD were less likely to receive their chosen treatment if they were allocated to the late start group, therefore a comment about timely preparation of PD tube insertion and awareness of this would be appropriate (see Johnson D et al 2012 below).</p> <p>It would be useful to consider consideration of rate of decline of renal function in planning RRT start, since those in whom deterioration of kidney function progresses more rapidly are at greater risk of unplanned/unprepared start, and less at risk of unnecessarily early start. In anticipation of this patients with stage 5 CKD should be in a position to start dialysis with an eGFR of <10 ml/min.</p> <p>References:</p> <p>Tangri N, Grams ME, Levey AS, et al. Multinational assessment of accuracy of equations for predicting risk of kidney failure: A meta-analysis. JAMA 2016;315:164-74. Couchoud CG, Beuscart JB, Aldigier JC, et al. Development of a risk stratification algorithm to improve patient-centered care and decision making for incident elderly patients with end-stage renal disease. Kidney Int 2015;88:1178-86.</p> <p>Bansal N, Katz R, De Boer IH, et al. Development and validation of a model to predict 5-year risk of death without</p>

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				<p>ESRD among older adults with CKD. Clin J Am Soc Nephrol 2015;10:363-71. Ivory SE, Polkinghorne KR, Khandakar Y, et al. Predicting 6-month mortality risk of patients commencing dialysis treatment for end-stage kidney disease. Nephrol Dial Transplant 2017;32:1558-1565. Cooper BA et al A randomised, controlled trial of early versus late initiation of dialysis. NEJM 2010;363:609-619 Johnson D et al. Effect of timing of dialysis commencement on clinical outcomes of patient with planned initiation of peritoneal dialysis in the IDEAL trial. Perit Dial Int 2012 ;32:595-604</p>
6	Guideline	4	11	<p>Psychological support-focus on this is very welcome (and should enable business cases for increased appointments to meeting this requirement). However, it would also be reasonable to include focus on other multi-professional team support including access coordinators, transplant coordinators, anaemia coordinators etc..</p>
7	Guideline	4	24	<p>USS scanning pre Vascular Access - should this also include prior to placement of all AV access including AV grafts</p>
8	Guideline	5	20	<p>1.3.4 In many people who require RRT the benefits of transplantation will be outweighed by the risks. Accurate and supportive information and follow-up should be provided to individuals who are not felt to be fit for kidney transplantation. Many patients who are unfit ask if they can have a transplant. The likelihood is that more people would want an answer to this question but do not ask. Therefore it would represent good practice to discuss transplantation with all patients.</p> <p>The statement in the supporting evidence that transplantation offers a benefit across all ages is not corrected for age and comorbidity and contradicts the figures that show that only a subset of patients receiving dialysis are on the waiting list for transplantation despite being assessed for it. Time to equal risk and net survival benefit post transplantation rises with increasing age. In other words, the instantaneous risk of death increases markedly at the time of transplant and takes a longer to return to baseline in older and more highly co-morbid individuals.</p> <p>Reference</p> <p>Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. The New England journal of medicine. 1999 Dec 2;341(23):1725-30.</p>
9	Guideline	6	3	<p>1.3.6 Pre-emptive Transplantation and listing. This is a clear need within the community with major unwarranted variation between centres. Therefore, could the wording be strengthened to stress this is the gold standard</p>

Please return to: RRT@nice.org.uk

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				treatment of choice for suitable patients wherever possible. Should it be worded as “ ...offer pre-emptive live donor transplant and deceased donor transplant listing”. Many units list even when a LD may be available until donor availability is clear
10	Guideline	6	6	1.3.7 It is not clear why the BMI cut-off of 30 is used in this recommendation – since most units use higher BMI levels as part of eligibility criteria for transplantation and indeed the guideline itself suggests that there are benefits of transplantation at BMIs greater than 30
11	Guideline	6	10	<p>1.3.8 This draft guideline misses the opportunity to recommend ‘offering a home therapy as the preferred dialysis modality’ – which is in line with existing documents that support greater use of treatment outside hospital (eg NHS 5 Year Forward View 2014), as well as evidence that people who take a greater role in their own health care have better outcomes (Kings Fund; Supporting people to manage their health. An introduction to patient activation, 2014). There is evidence that home dialysis is associated with better quality of life and outcomes (registry data), avoidance of harm (eg the potential to avoid the 22% increase in mortality associated with the 3 day inter-dialytic gap), as well as health economic benefits. There appears to be very little reference to the benefits of frequent regimens at home evidence around qualitative and cardiovascular benefits (2 RCTs - Culleton et al and FHN study). The key reason for low uptake are often extrinsic barriers and not patient related factors. Furthermore, the absence of such a recommendation is at variance with previous NICE guidance (CG125 & TA 48) and initiatives from KQuIP. In the same way as many patients will not be suitable for a transplant many will not be suitable for a home dialysis therapy – but the key point all patients should be given this opportunity where possible.</p> <p>Equally there is no recommendation that patients on dialysis (eg centre based) should be given the opportunity to take a role in their own care (supported self-care / shared haemodialysis care).</p> <p>There is also no recognition of the role of assisted peritoneal dialysis although this is routinely available and widely used.</p> <p>References</p> <ul style="list-style-type: none"> • Culleton BF et al Effect of Frequent Nocturnal Hemodialysis vs Conventional Hemodialysis on Left Ventricular Mass and Quality of Life. A Randomized Controlled Trial <i>JAMA</i> .1299-1291:(11)298;2007 . doi:10.1001 • The FHN Trial Group. In-Center Hemodialysis Six Times per Week versus Three Times per Week. <i>N Engl J Med</i> 2010; 363:2287-2300 DOI: 10.1056/NEJMoa1001593

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				<ul style="list-style-type: none"> Marshall MR, Polkinghorne KR, Kerr PG, Agar JW, Hawley CM, McDonald SP. Temporal Changes in Mortality Risk by Dialysis Modality in the Australian & New Zealand Dialysis Population. <i>Am J Kidney Dis.</i> 2015;66(3):489-98. Nitsch D, Steenkamp R, Tomson CR, Roderick P, Ansell D, MacGregor MS. Outcomes in patients on home haemodialysis in England and Wales, 1997-2005: a comparative cohort analysis. <i>Nephrol Dial Transplant.</i> 2011;26(5):1670-7. Walker R, Marshall MR, Morton RL, McFarlane P, Howard K. The cost-effectiveness of contemporary home haemodialysis modalities compared with facility haemodialysis: a systematic review of full economic evaluations. <i>Nephrology (Carlton).</i> 2014;19(8):459-70. Pike E, Hamidi V, Ringerike T, Wisloff T, Klemp M. More Use of Peritoneal Dialysis Gives Significant Savings: A Systematic Review and Health Economic Decision Model. <i>J Clin Med Res.</i> 2017;9(2):104-16. Fotheringham J, Fogarty DG, El Nahas M, Campbell MJ, Farrington K. The mortality and hospitalization rates associated with the long interdialytic gap in thrice-weekly hemodialysis patients. <i>Kidney Int.</i> 2015;88(3):569-75.
12	Guideline	6	18	<p>Recommendation 1.3.11 For people who opt for dialysis via vascular access:</p> <ul style="list-style-type: none"> Offer HDF rather than HD if in centre (hospital or satellite unit) Offer either HDF or HD if at home, taking into account availability of home HDF, and patient preference. <p>We are very concerned that this draft NICE recommendation does not take into account the significant concerns that nephrologists in the UK and globally have regarding the evidence base generated by the current published RCTs comparing HD vs HDF.</p> <p>Randomization in the Spanish trial (Maduell et al, 2013) appears to be have been undermined or implemented incorrectly, because prognostic factors (especially age, diabetes, other co-morbidity and central venous catheter use) were clearly not balanced the intervention groups. Because patients in the HD group were at considerably</p>

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

			<p>higher risk of mortality, the longer survival in the HDF group did not necessarily arise from HDF leading to lower mortality than HD. This RCT contributes 47% weight to the morality TTE analysis (Fig 20, page 228 in the Evidence Review B) and 35% weight to the mortality RR analysis (Fig 21, page 228 in the Evidence Review B).</p> <p>The Turkish RCT (Ok et al, 2013) also has a number of significant flaws that mean the outcome of the trial is, at best, questionable. As the NICE drafting panel correctly pointed out, 10% of participants randomised to HDF in this RCT were withdrawn due to blood flow problems compared with 0% of participants randomised to HD. You state that “the study was not explicit as to the origin of this differential drop out, however it appeared as if the inclusion criteria (based on a fistula blood flow of >250ml/min) had been applied throughout the course of the trial in the in-centre HDF arm but not in the HD arm”. This is suggestive of selective removal of patients with low blood flow rates from the HDF arm. As older, more co-morbid patients have lower blood flow in their vascular access, this suggests there was selective removal of this group of patients from the HDF arm, once again strongly implying the reported outcomes are deeply flawed. This RCT also had multiple missing data points, with patients assumed to be alive. This must greatly increase the risk of bias associated with this RCT, which 18% weight of the mortality RR analysis (Fig 21, page 228 in Evidence Review B).</p> <p>These trials were included in the previous systematic reviews and meta analyses on this topic, which concluded that there was insufficient evidence to recommend the widespread adoption of HDF on the basis of the low quality of the evidence.</p> <ul style="list-style-type: none"> • Wang AY et al, 2014. • Nistor I et al, 2015. • Mostovaya IM et al, 2014. <p>There have only been two very small RCTs published since these systematic reviews and meta analyses:</p> <ul style="list-style-type: none"> • Mesaros-Devic et al, 2013: comparing HDF vs low-flux HD with 85 participants with 19 events. • Park et al, 2013: comparing HDF vs high-flux HD with 28 participants with 12 events. <p>When we re-ran the analyses (with fixed effects) excluding the Maduel and Ok data*, we got the following RRs (95% CIs):</p> <p>HDF vs low-flux HD: 0.89 (0.74-1.06) HDF vs high-flux HD: 1.65 (0.89-3.06)</p>
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Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				<p>HDF vs HD overall: 0.93 (0.78-1.11) The evidence in favour of HDF therefore relies on these two flawed RCTs. (We also question the appropriateness of fixed effects models for this analysis, see separate comment below.)</p> <p>It was on the basis of the previous systematic reviews and meta analyses that the following large RCTs have been competitively funded and are underway:</p> <ul style="list-style-type: none">• H4RT, The high-volume HDF vs high-flux HD Registry Trial, funded by NIHR HTA (15/80/52) £1.5m. Chief investigator Dr Fergus Caskey, Bristol, UK.• CONVINCE, The comparison of high-dose HDF with high-flux HD, funded by Horizon2020 €7m. Chief investigator Dr Peter Blankestijn, Utrecht, NL. <p>The H4RT was fully supported by the UK Kidney Research Consortium Dialysis Study Group, the UK renal community's expert group on dialysis. H4RT co-investigators include leading UK experts in HDF: Dr Andrew Davenport (London), Prof Ken Farrington (Stevenage), Dr Sandip Mitra (Manchester) and Dr Albert Power (Bristol).</p> <p>For all the above reasons, Kidney Disease Improving Global Outcomes, the global non-profit organization developing and implementing evidence-based clinical practice guidelines in kidney disease (www.kdigo.org) has decided not to review the evidence base for HDF until the RCTs currently testing the effectiveness of high-volume HDF are completed. (Personal communication Prof David Wheeler, co-chair of KDIGO 7th May 2018.)</p> <p>As we do not believe that the current published evidence supports the clinical effectiveness of HDF, nor do we believe there is any basis for concluding it is a more cost-effective treatment.</p> <p>We are also concerned that the guideline will recommend HDF for patients on home HD. Not only are the conclusions about the superiority of HDF unfounded, it also fails to recognise the additional risk patients on home HDF are at in terms of bacterial/ endotoxin contamination, but more importantly chemical contamination as carbon fibres are smaller and not back purged overnight. We feel this recommendation is unsafe.</p> <p>In conclusion, it is the view of the Renal Association, after listening to the advice of our member experts in HD and HDF, that this draft NICE recommendation is not supported by credible evidence. Further, we are concerned that if published it will imply superiority of HDF over HD and mean that currently funded RCTs in the UK and Europe,</p>
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Please return to: RRT@nice.org.uk

Renal Replacement Therapy

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				<p>designed to generate the evidence we feel is still needed, may have to be terminated early.</p> <p>Our reading of the evidence is that:</p> <ol style="list-style-type: none">1. There is good evidence that on-line HDF is as safe as high-flux HD.2. There is no evidence that standard on-line HDF improves mortality, though it may have other beneficial effects particularly reduction in intradialytic hypotension (though cooled dialysate may do just as well).3. There is some evidence that high volume on-line HDF improves mortality compared with high-flux HD, though in the only study to demonstrate this in an a priori analysis, baseline characteristics were not matched such that there was a significantly higher proportion of older, diabetic patients with cardiovascular disease and central venous catheters in the HD group – a poor prognostic factor. <p>We therefore urge the NICE drafting panel to await the outcome of the two large and well-designed RCTs that together, once reported, will provide the definitive evidence required to produce definitive NICE guidelines. Those guidelines would then have the support of the national and international nephrology community and can in turn be used to commission safe and cost-effective services. In the meantime we suggest a revised recommendation, such as:</p> <p>Current evidence suggests that high-flux HD and on-line HDF both provide satisfactory renal replacement. Patients who experience significant problems with intradialytic hypotension may benefit from on-line HDF or high-flux HDF with cooled dialysate. There is some evidence that high-volume HDF may reduce mortality risk compared to high-flux HD. Further trials are in progress including H4RT in the UK. Offering suitable patients the opportunity to participate in this study should be strongly considered.</p> <p>* This work was undertaken by Dr P Whiting, NIHR CLAHRC West, Bristol.</p> <p>References:</p> <ul style="list-style-type: none">• Susantitaphong P, Siribamrungwong M, Jaber BL. Convective therapies versus low-flux hemodialysis for chronic kidney failure: a meta-analysis of randomized controlled trials. <i>Nephrol Dial Transplant</i> 2013; 28(11): 2859-74.• Wang AY, Ninomiya T, Al-Kahwa A, et al. Effect of hemodiafiltration or hemofiltration compared with hemodialysis on mortality and cardiovascular disease in chronic kidney failure: a systematic review and meta-
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Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				<p>analysis of randomized trials. <i>Am J Kidney Dis</i> 2014; 63(6): 968-78.</p> <ul style="list-style-type: none"> • Nistor I, Palmer SC, Craig JC, et al. Haemodiafiltration, haemofiltration and haemodialysis for end-stage kidney disease. <i>Cochrane Database Syst Rev</i> 2015; 5: CD006258. • Mostovaya IM, Blankestijn PJ, Bots ML, et al. Clinical evidence on hemodiafiltration: a systematic review and a meta-analysis. <i>Seminars in dialysis</i> 2014; 27(2): 119-27. • Mesaros-Devcic I, Tomljanovic I, Mikolasevic I, et al. Survival of patients treated with online hemodiafiltration compared to conventional hemodialysis. <i>Collegium antropologicum</i> 2013; 37(3): 827-32 • Park KW, Kyun Bae S, Lee B, et al. The effect of on-line hemodiafiltration on heart rate variability in end-stage renal disease. <i>Kidney research and clinical practice</i> 2013; 32(3): 127-33.
13	Guideline	6	22	<p>1.4.1 There is no comment with regards to type of vascular access – line, fistula, graft. We would suggest that guideline group examine the latest evidence come to a conclusion with regards to the pros and cons of different access types (risks associated with the use of central venous catheters for example). The draft guideline is at variance with the NICE accredited Renal Association clinical practice guideline on vascular access for haemodialysis 6th Edition 2015 : “We recommend that all patients with end stage kidney disease who commence haemodialysis or are on long-term haemodialysis should dialyse with an arteriovenous fistula as first choice, an arteriovenous graft as second choice, a tunnelled venous catheter as third choice and a non-tunnelled temporary catheter as an option of necessity (Evidence level grade 1A).</p>
	Guideline	7	1	<p>1.4.2 There is general concern that the timing of peritoneal dialysis access is not given the same consideration as for vascular access. In the same way as with vascular access, PD access can be also problematic and indeed 3 month access survival is better for AVF/AVG than for PD catheters (88.4% in use 3 months from dialysis start vs 83.0% for PD catheters (Renal Registry multisite access audit 2017) ie both types of access have significant primary failure rates. Therefore it is better to place PD catheters earlier than absolutely required (ie above the target start GFR 5-7) to ensure that there is time to intervene if it does not work the first time. This does not mean that PD catheters cannot be placed and used immediately, with appropriate clinical care, as part of the management of unplanned start patients – but this is a separate issue from planned access.</p> <p>Reference</p> <p>Barnaby Hole et al <i>Nephron</i> 2017;137(suppl1):269–296</p>

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

14	Guideline	7	4	<p>1.4.3 This advice needs to be individualised based on the type of access that is planned. Further – the timing of dialysis start is influenced by the rate of decline of renal function and can be estimated using an appropriate Kidney Failure Risk equation as commented above.</p> <p>Para 1.8.6 – starting with a line or even an AV graft does not need a decision to be made 6 months before starting dialysis – they can be used either immediately or within a very few weeks. Page 22 of 29 line 13 – suggests that the 6 month advice is based on “common” practice not evidence of best practice and is designed to “standardise” practice – standardisation in itself should not be the goal of any guideline – the goal is improving patient care and use of resource and this has not been demonstrated.</p>
15	Guideline	7	18	<p>1.5.4 Patients should be made aware of the risk of encapsulating peritoneal sclerosis (EPS) and consideration should be given to offer the opportunity to switch modality after a numbers of years on PD to reduce this risk. However, switching dialysis modality is complex and has multiple components to it including the impact of co-morbidity and suitability for access. Comments about loss of ultrafiltration need to be more detailed or omitted as the relationship between that and the risk of EPS is related to complex components including the loss of the sodium dip (measured at 1 hour in the peritoneal equilibration test), and which is not routinely measured in the UK).</p> <p>This topic has been reviewed in an International Society of Peritoneal Dialysis Society (ISPD) guideline – the summary statements of that guideline provide a nuanced assessment. It would be perhaps more appropriate to state that EPS should be discussed with patients in the context of other risks that they face, but importantly this topic should be a subject for more detailed research.</p> <p>The conclusion of the ISPD EPS guideline is below :</p> <p><i>Encapsulating peritoneal sclerosis is a rare condition. There is no evidence to withhold PD as a treatment option because of fear of development of EPS. There is insufficient evidence to support a single rule about optimal length of time on PD to avoid the risk of EPS</i></p> <p><i>Each long-term patient needs to be considered individually, taking into account the following factors:</i></p> <ol style="list-style-type: none"> <i>1. Age and prognosis of patient;</i> <i>2. Length of time on PD;</i> <i>3. Quality of PD (dialysis adequacy, ultrafiltration, peritonitis frequency);</i> <i>4. Access to and suitability for transplantation;</i> <i>5. Potential risk of HD in the particular patient (hemodynamic stability, vascular access); and</i> <i>6. Quality of life of the patient.</i> <p><i>All these items should be discussed and any decision arrived at by shared decision-making.</i></p>

Please return to: RRT@nice.org.uk

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				<p>Reference: J Morelle et al, J Am Soc Nephrol. 2015 Oct;26(10):2521-33 E Brown et al, Perit Dial Int 2017; 37 : 362-374.</p>
16	Guideline	11	1	<p>Table 2 - Information about treatments – where is the evidence for these statements, are they comprehensive? Care needs to be taken that these statements are evidence based and not prejudicial, and adversely affect individual modality choice. Thus general statements should be made – but specifics avoided unless there is overwhelming evidence for these. For example people on peritoneal dialysis can swim if appropriate steps are taken to protect the peritoneal dialysis catheter exit site; post haemodialysis recovery time is not mentioned. It is more appropriate that high quality patient information is developed through appropriate research processes.</p>
17	Guideline	11	3	<p>1.8.2 Conservative management</p> <p>No recommendation around coordination with community services including referral to gold standard framework for patients requiring supportive or end of life care?</p>
18	Guideline	13	18	<p>Given our belief that the current evidence does not support a recommendation to offer HDF to all patients on in-centre HD, we believe the following key research recommendation should be added:</p> <p>HDF vs HD What is the clinical effectiveness and cost-effectiveness of high-volume HDF compared with high-flux HD for people who opt for in-centre dialysis via vascular access? Renal units offering HDF to their patients are encouraged to do so in the context of one of the RCTs currently evaluating this question, such as the NIHR HTA-funded H4RT. www.bristol.ac.uk/population-health-sciences/projects/h4rt-trial/ www.journalslibrary.nihr.ac.uk/programmes/hta/158052</p>
19	Guideline	15	2	<p>The Conservative Kidney Management Assessing Practice Patterns Study demonstrated marked differences in the care provided to patients choosing comprehensive conservative care in the UK and very big differences in the likelihood of someone choosing to prepare for dialysis or have comprehensive conservative care depending on which renal unit they attended. Investigating this further has been considered a priority for the renal community and we were encouraged by NIHR to move forwards from CKAMPPS to undertake a randomised controlled trial of preparing for renal dialysis versus preparing for comprehensive conservative care. This RCT, Prepare for Kidney Care, was funded by NIHR HTA in 2016 and is currently open and recruiting in England (15/57/39). Dr Fergus</p>

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Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				<p>Caskey, medical director of the Renal Association, UK Renal Registry is the chief investigator.</p> <p>We would therefore like to propose that the research recommendation “What is the clinical and cost effectiveness of conservative management versus dialysis in frail, older people?” is moved from an “other” to a “key” research recommendation.</p> <p>We also wonder whether the Committee would consider making the recommendation more specific, for example: <i>Where existing evidence suggests that RRT has a limited effect on prolonging survival and improving quality of life clinical teams are encouraged to support a shared decision about taking part in research that will generate that clinical effectiveness evidence for future patients. One such study is the NIHR-funded, multi-centre Prepare for Kidney Care study embedded in the UK Renal Registry.</i></p> <p>www.bristol.ac.uk/population-health-sciences/projects/prepare-kc-trial/ https://www.journalslibrary.nihr.ac.uk/programmes/hta/155739</p>
20	Guideline	18	28	<p>No evidence on benefit of transplantation on Quality of Life</p> <p>The document (P18) states ‘Evidence showed that if RRT is chosen, transplantation offers a clear advantage over dialysis in terms of extending life. This applied across all ages. There was no evidence on quality of life or hospitalisation, but in the committee’s experience these are likely to be improved by transplantation.’ The evidence evaluation does not appear to have included quality of life (systematic review by Tonelli in AJT 2011 as one example). Tonelli M et al, Systematic Review: Kidney Transplantation Compared With Dialysis in Clinically Relevant Outcomes. American Journal of Transplantation 2011; 11: 2093–2109.</p>
21	Guideline	28	23	<p>On page 28 the comment ‘The reported 1-year risk of death for people on RRT compared with the general population was approximately 22.0 for people aged 35 to 39 years’ needs amending/ clarifying.</p>
22	Evidence review B	57	5	<p>In relation to the treatment effect, we are surprised that it was the committee’s consensus that “if anything, HDF would be expected to be more effective in naïve patients as they would not have been exposed to potential downsides of less “efficient” forms of dialysis.” We believe that (if it works by removing middle-sized toxins) HDF</p>

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

				is likely to be <u>less</u> effective in people new to dialysis, as they have residual renal function which will continue to provide them with middle molecule clearance for first 6-24 months of treatment.
23	Evidence Review B	57 58	41 40	<p>We would like to challenge the statement “...there was evidence for all comparisons except for conservative management vs RRT, which was only available for age 75 years and older.”</p> <p>Due to the inclusion criteria chosen the Committee has included only two papers in this area – Murtagh FE et al 2007 and Chandna SM et al 2011 – both of which looked at only 75+.</p> <p>The Committee seem to have purposively excluded the paper by Hussain et al 2013 (it is included in the excluded studies table) and overlooked the paper by Verberne 2016, both of which demonstrate that “the extent to which RRT reduces mortality” is also “not clear” in the 70+ group. Both of these appear eligible for inclusion, in particular including multivariable adjustment in comparisons.</p> <p>We appreciate that an evidence bar has to be set somewhere, but by excluding lots of non-randomised studies that look at patients under 75 (included in the systematic review by Foote et al, 2016), the NICE conclusions fail to recognise that “the extent to which RRT reduces mortality” is “not clear” in some groups under 75.</p> <p>While we recognise the contribution of age, experts in comprehensive conservative care not on the Committee feel that co-morbidity and fragility are at least as important as age and worry about the use of an age threshold.</p> <p>We wonder whether the Committee would consider reviewing the excluded studies again and whether they could use that evidence, along with their experience, to re-consider whether the following statement might not apply to some groups of people under the age of 75: “From the evidence identified, it is not clear whether or to what extent RRT reduces mortality in frail, older people.”</p> <p>References:</p> <ul style="list-style-type: none"> • Murtagh FE, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE. Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. <i>Nephrology Dialysis Transplantation</i>. 2007; 22(7):1955-62.

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm email: RRT@nice.org.uk**

			<ul style="list-style-type: none"> Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. <i>Nephrology Dialysis Transplantation</i>. 2011; 26(5):1608-14. Hussain JA, Mooney A, Russon L. Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. <i>Palliative Medicine</i>. 2013; 27(9):829-39. Verberne WR, Geers AB, Jellema WT, Vincent HH, van Delden JJ, Bos WJ. Comparative Survival among Older Adults with Advanced Kidney Disease Managed Conservatively Versus with Dialysis. <i>Clin J Am Soc Nephrol</i>. 2016 Apr 7;11(4):633-40. Foote C, Kotwal S, Gallagher M, Cass A, Brown M, Jardine M. Survival outcomes of supportive care versus dialysis therapies for elderly patients with end-stage kidney disease: A systematic review and meta-analysis. <i>Nephrology (Carlton)</i>. 2016 Mar;21(3):241-53.
24	Evidence review B	106	<p>Table 29.</p> <p>There are various ways of delivering HDF which need to be taken into account in outcome comparisons. Earlier studies used off-line HDF rather than on-line HDF (which makes higher dose/ volume HDF possible, but requires production of sterile substitution fluid in each renal unit). Fluid can also be replaced before the filter (pre-dilution) or after the filter (post-dilution). The exclusion criteria do not mention these.</p> <p>It is also now widely believed that the dose/ volume of HDF is critically important, with clinical benefits predominantly seen in patients achieving high-volume HDF. This does not appear to have been considered by the NICE group.</p>
25	Evidence review B	228	<p>Fig 20 & 21:</p> <p>We are not sure why it was chosen to use fixed effects for these analyses. Fixed effect meta-analysis assumes all studies are estimating the same (common) treatment effect. Whereas random effect meta-analysis allows for some differences across studies in the true treatment effect due to differences in populations etc. We feel the latter is more appropriate for this analysis.</p> <p>When we reproduced the forest plots using a random effects model the effect was no longer statistically significant.</p>

Renal Replacement Therapy

Consultation on draft guideline – deadline for comments **Monday 21 May 2018 by 5pm** email: RRT@nice.org.uk

				<p>When we re-ran the analyses (with random effects)*, we got the following RRs (95% CIs): HDF vs low-flux HD: 0.66 (0.32-1.38) HDF vs high-flux HD: 0.92 (0.61-1.39) HDF vs HD overall: 0.84 (0.64-1.10) The evidence in favour of HDF therefore relies on the use of fixed effect models, which we do not believe are the most appropriate in this situation.</p> <p>* This work was undertaken by Dr P Whiting, NIHR CLAHRC West, Bristol.</p>
26	Evidence review B	271		<p>Studies excluded: Two RCTs comparing HDF and HD were included in previous systematic reviews and meta analyses, but not included in this one or listed in the table of excluded studies.</p> <ul style="list-style-type: none"> • Ward RA, Schmidt B, Hullin J, Hillebrand GF, Samtleben W. A comparison of on-line hemodiafiltration and high-flux hemodialysis: a prospective clinical study. <i>J Am Soc Nephrol</i> 2000; 11(12): 2344-50. • Locatelli F, Altieri P, Andrulli S, et al. Hemofiltration and hemodiafiltration reduce intradialytic hypotension in ESRD. <i>J Am Soc Nephrol</i> 2010; 21(10): 1798-807. <p>The reason that they were not picked up by the NICE search strategy is unclear.</p>

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Renal Replacement Therapy

Consultation on draft guideline – deadline for comments Monday 21 May 2018 by 5pm email: RRT@nice.org.uk

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