National Institute for Health and Care Excellence

DIAGNOSTICS ASSESSMENT PROGRAMME

Evidence overview

Multiple frequency bioimpedance devices to guide fluid management in people with chronic kidney disease having dialysis

This overview summarises the key issues for the diagnostics advisory committee's consideration. This document is intended to be read in conjunction with the final scope issued by NICE for the assessment and the diagnostics assessment report. A glossary of terms can be found in Appendix B.

1 Background

1.1 Introduction

The purpose of this assessment is to evaluate the clinical and cost effectiveness of using multiple frequency bioimpedance devices to monitor the hydration status of a person with chronic kidney disease who is having either haemodialysis or peritoneal dialysis treatment.

Dialysis is used to replace renal function in people with chronic kidney disease, including the removal of excess fluid from the blood. It is important that an appropriate volume of fluid is removed; removing too little will result in the person becoming overhydrated and may lead to oedema, increased blood pressure and an increased risk of cardiovascular events. Alternatively, if too much fluid is removed during dialysis the person will become underhydrated, which can result in the loss of residual renal function and an increased incidence of symptoms such as cramps, nausea and dizziness.

In current practice, the fluid status of a person on dialysis is generally determined by clinical assessment, which takes into account several clinical features and symptoms which suggest overhydration or underhydration. Clinical features include blood pressure, changes in residual renal function and weight, and the presence of oedema. Multiple frequency bioimpedance devices give an objective assessment of a person's fluid status, which can be used alongside clinical assessment to help make decisions about the amount of fluid to remove in dialysis. Using the devices may help to reduce the incidence of overhydration or underhydration and their associated clinical consequences.

Provisional recommendations on the use of these technologies will be formulated by the diagnostics advisory committee at the committee meeting on 17 January 2017.

1.2 Scope of the evaluation

Table 1 Scope of the evaluation

Decision question	Does the use of multiple frequency bioimpedance devices to assess fluid status in people with chronic kidney disease who are on dialysis represent a clinical- and cost-effective use of NHS resources?
Populations	People with chronic kidney disease who are on dialysis. This includes: • people who are on haemodialysis. • people who are on peritoneal dialysis. If evidence is available, further subgroups may include: • people for whom recommended configurations of electrodes cannot be used or who cannot assume recommended positions for measurements to be made • children younger than 5 years who may need monitoring more frequently • people at extremes of body composition • ethnicity.
Interventions	• BCM – Body Composition Monitor (Fresenius Medical Care) • BioScan 920-II (Maltron International)

	• BioScan touch i8 (Maltron International) • InBody S10 (InBody) • MultiScan 5000 (Bodystat) In conjunction with clinical assessment.
Comparator	Clinical assessment of the fluid status of people with chronic kidney disease who are on dialysis, and which takes into account the following factors: • presence of oedema • blood pressure • patient-reported symptoms of overhydration or underhydration • residual renal function • changes in weight • any pre-existing cardiovascular conditions.
Healthcare setting	All settings
Outcomes	Intermediate measures for consideration may include: • number and length of haemodialysis sessions • number of unplanned hospital appointments and stays caused by fluid overload or underhydration • use of antihypertensive medication • incidence of anaemia • blood pressure • left ventricular hypertrophy • arterial stiffness • incidence of overhydration or underhydration • changes of dialysis modality (from peritoneal dialysis to haemodialysis) because of fluid overload • adherence to recommended fluid intake.
	Clinical outcomes for consideration may include: • incidence of adverse cardiovascular events, including stroke and heart attack • mortality • residual renal function • incidence of oedema • incidence of peritonitis • incidence of adverse effects associated with hypotensive episodes (including cramps, fatigue,

	diarrhoea, nausea, dizziness, fainting).
	Patient-reported outcomes for consideration may include: • post-dialysis recovery time and fatigue • health-related quality of life
	Costs will be considered from an NHS and personal social services perspective. Costs for consideration may include: • cost of equipment and consumables • cost of staff and associated treatment • medical costs of monitoring, dialysis and care, such as hospital appointments and stay and medication • medical costs from adverse events including cardiovascular events and those associated with dialysis.
	The cost effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

Further details including descriptions of the interventions, comparator, care pathway and outcomes can be found in the final scope.

2 The evidence

This section summarises data from the diagnostics assessment report compiled by the external assessment group (EAG).

2.1 Clinical effectiveness

The EAG did a systematic review of the evidence on the clinical effectiveness of using multiple frequency bioimpedance devices (the BCM – Body Composition Monitor, BioScan 920-II, BioScan touch i8, InBody S10 or MultiScan 5000) in conjunction with clinical assessment to monitor the fluid status of people with chronic kidney disease who are on dialysis. Both randomised and non-randomised studies were eligible for inclusion. Details of

the systematic review can be found starting on page 21 of the diagnostics assessment report.

Overview of the included studies

Randomised controlled trials

Six randomised controlled trials (RCTs) were identified, all of which assessed use of the BCM – Body Composition Monitor (hereafter referred to as the BCM; Huan-Sheng et al. 2016; Hur et al. 2013; Luo et al. 2011; Onofriescu et al. 2012; Onofriescu et al. 2014; Ponce et al. 2014). However, 2 of these trials (Onofriescu et al. 2012 and Onofriescu 2014) may have reported the same trial or outcomes from an overlapping patient population. The frequency of using the device varied between studies, from twice monthly to every 3 months. Five of the studies were done outside the UK and 1 study did not state the location (Luo et al. 2011). Only 1 study included people having peritoneal dialysis (Luo et al. 2011), the remaining studies enrolled people having haemodialysis. Five trials included people aged 18 years or over and the remaining trial did not give the age-related exclusion criteria, however the mean age of participants was 52.4 years (standard deviation 13.1 years; Onofriescu et al. 2012). Other groups excluded from some of these studies were people with limb amputations, pregnant women and people with coronary stents, pacemakers or metallic implants. No RCTs were identified for the BioScan 920-II, BioScan touch i8, InBody S10 or the MultiScan 5000.

A description of the standard clinical assessment used to monitor fluid status in the comparator arms was not given in 4 RCTs. Two studies (Onofriescu et al. 2012; Onofriescu et al. 2014) reported that standard clinical assessment was based on measuring blood pressure, and the presence or absence of oedema and symptoms of hypotension and other hydration-related effects. The frequency of standard clinical assessments (either alone or alongside monitoring with the BCM device) was not given in the included RCTs.

Three of the trials had links to Fresenius Medical Care (Onofriescu et al. 2014; Ponce et al. 2014; Hur et al. 2013); although 2 of these (Onofriescu et al. 2014; Hur et al. 2013) stated that Fresenius Medical Care had no involvement in designing or carrying out the trials. One trial did not report the source of funding (Onofriescu et al. 2012) and the remaining 2 trials were supported by grants from independent sources (Luo et al. 2011; Huan-Sheng et al. 2016).

The Cochrane risk of bias tool was used to assess the risk of bias in the included RCTs. The EAG judged that 1 of the RCTs was at low risk of overall bias (Onofriescu et al. 2012), 1 was at high risk of bias (Luo et al. 2011) and the remaining 4 studies did not give enough information on which to make a robust judgement. Further detail on the critical appraisal of these studies can be found in the diagnostic assessment report starting on page 34.

Non-randomised studies

To supplement evidence from the RCTs, the EAG also searched for non-randomised studies. Because many such studies were identified (450 studies), the EAG focused on studies with at least 100 participants. Three studies involving paediatric populations were excluded by this criterion (and are discussed below). None of the excluded studies (with less than 100 participants) were UK-based, investigated devices other than the BCM or reported data on relevant outcomes that had not been identified in the included studies.

Eight non-randomised cohort studies, published in 9 papers, were identified (Castellano et al. 2014; Hoppe et al. 2015; Kim et al. 2012; Kim et al. 2015; Oei et al. 2016; O'Lone et al. 2014; Onofriescu et al. 2015; Santhakumaran et al. 2016; Wizemann et al. 2009), all of which assessed the BCM device. However, 2 of these studies (O'Lone et al. 2014 and Oei et al. 2016) may have overlapping patient populations. All participants included in the non-randomised studies had monitoring using the BCM. The frequency of device use varied widely between studies, from just once in the first week of dialysis

to 3 assessments per week. Two studies were done in the UK (O'Lone et al. 2014; Oei et al. 2016) and none of the studies enrolled paediatric patients. Most of the studies included people having haemodialysis (6 studies) rather than peritoneal dialysis (2 studies). No non-randomised studies were identified for the BioScan 920-II, the BioScan touch i8, the InBody S10, or the MultiScan 5000.

Three studies did not seem to be linked to Fresenius Medical Care (Kim et al. 2015; Oei et al. 2016; Hoppe et al. 2015), whereas the remaining 5 studies reported either funding from, or a connection with, the company.

The EAG assessed the risk of bias in the non-randomised studies using the Review Body for Interventional Procedures tool, which is designed for use with case-series. The key areas of concern highlighted by the EAG were that none of the included studies blinded participants or study personnel, and the characteristics of participants who withdrew from the studies were not reported. Further details on the risk of bias for the included non-randomised studies can be found in the diagnostics assessment report from page 37.

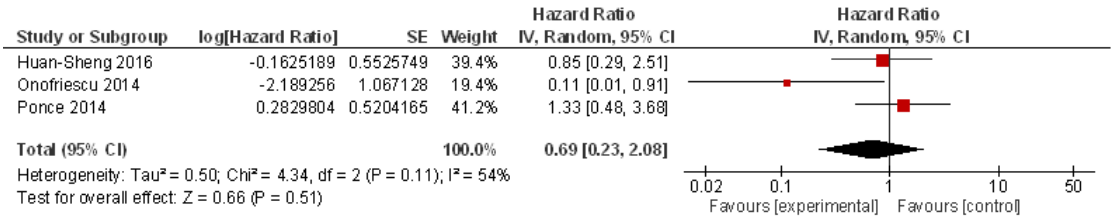
Further detail on the characteristics of participants in all included studies can be found starting on page 32 of the diagnostics assessment report.

Evidence on clinical outcomes

Mortality

Three RCTs reported data on mortality (Onofriescu et al. 2014; Ponce et al. 2014; Huan-Sheng et al. 2016) and were included in a meta-analysis (see figure 1). Use of the BCM device had no significant effect on mortality rates (pooled hazard ratio 0.69; 95% confidence interval [CI] 0.23 to 2.08; p=0.51) and there was moderate statistical heterogeneity between trials.

Figure 1 Meta-analysis of mortality hazard ratios



Three non-randomised studies had results for the effects of hydration status on mortality in subgroups of participants monitored with the BCM device. Kim et al. (2015) reported a higher incidence of mortality in overhydrated participants (defined by relative hydration state; odds ratio 2.57; 95% CI 1.08 to 6.13; p=0.033). In O'Lone et al. (2014), absolute overhydration had significant effect on the risk of mortality (hazard ratio 1.10; 95% CI 1.01 to 1.20; p=0.025) and Wizemann et al. (2009) reported that hydration state was an important predictor of mortality in patients having haemodialysis (adjusted hazard ratio 2.10; 90% CI 1.39 to 3.18; p=0.003).

Patient-reported adverse effects associated with dialysis

Huan-Sheng et al. (2016) reported significant differences in intradialytic complications between people monitored using the BCM device with standard clinical assessment and those monitored using standard clinical assessment alone. However, incidences were not consistently higher in 1 group. For people monitored using BCM, significantly higher incidences of cramping, chest tightness and headaches and significantly lower incidences of complications caused by hypotension during dialysis sessions and skin itching were reported. In this study there were also 4 patient-reported events of intradialytic fatigue in participants monitored using the BCM, and 5 such events in the standard assessment group. This difference was not statistically significant (p=0.7).

Hur et al. (2013) reported no significant difference in the frequency of intradialytic events between groups monitored with and without the BCM device at 12 months (66.6 and 63.9 events per 1000 dialysis sessions

respectively; p=0.4). Similarly, Onofriescu et al. (2014) found no difference in the incidence of hypotension or cramps (p=0.6). Ponce et al. (2014) reported no significant difference in the incidence of hypotensive events (defined as a drop in systolic blood pressure during dialysis by at least 30 mm of mercury [Hg] or to below 90 mm Hg) at 12 months.

Incidence of cardiovascular events

One RCT (Huan-Sheng et al. 2016) reported the incidence of cardiovascular-related events, although this was in combination with the incidence of acute fluid overload events. The incidence rate in people monitored with the BCM device was significantly lower than the control group (incidence rate ratio 0.50 per patient-year; 95% CI 0.26 to 0.94; p=0.03).

Three non-randomised studies gave the incidence of cardiovascular events among subgroups of people monitored using the BCM device. Kim et al. (2015) reported no statistically significant difference in the number of cardiovascular events per year between overhydrated and non-overhydrated subgroups as determined by the level of relative overhydration (p=0.13). Onofriescu et al. (2015) also found no statistically significant difference in the incidence of coronary heart disease, peripheral vascular disease, heart failure or stroke between subgroups with lower relative fluid overload (less than 17.4%) and higher relative fluid overload (over 17.4%). Hoppe et al. (2015) reported a non-significant difference in the incidence of acute myocardial infarction and stroke between people who had been having dialysis for a shorter length of time (short dialysis vintage) and people who had been having dialysis for a longer length of time (long dialysis vintage).

Residual renal function

No RCTs presented data on residual renal function, although 2 reported urinary output which could be used as a surrogate measure. Hur et al. (2013) found a significant increase in the proportion of patients with anuria, that is

when the kidneys no longer produce urine, and a significant decrease in urine output in patients without anuria in a group monitored using the BCM device. In the corresponding control group, there was no change in the proportion of patients with anuria and the decrease in urine output seen in patients without anuria was not significant. Luo et al. (2011) reported non-significant decreases in urine volume in groups monitored with and without the BCM device, although the BCM monitored group showed a larger decrease.

Evidence on intermediate outcomes

Blood pressure

All 6 included RCTs reported systolic blood pressure measurements. A pooled meta-analysis comparing the mean difference in systolic blood pressure between groups who were monitored with and without the BCM device found that use of the BCM device was associated with a significantly lower systolic blood pressure (pooled mean difference −3.48 mm Hg; 95% CI -5.96 to −1.00; p=0.006). If data from Onofriescu et al. (2012) was removed from the meta-analysis (because of possible study population overlap with Onofriescu et al. 2014), the effect size of BCM-guided monitoring was reduced and was no longer significant (pooled mean difference −2.46 mm Hg; 95% CI −5.07 to 0.15; p=0.06).

The EAG also carried out a subgroup analysis of systolic blood pressure according to the type of dialysis: peritoneal dialysis (1 study) or haemodialysis (5 studies). In the haemodialysis subgroup, use of the BCM device was associated with a significant decrease in systolic blood pressure (pooled mean difference −3.09 mm Hg; 95% CI −5.88 to −0.31; p=0.03). For patients having peritoneal dialysis, Luo et al. (2011) reported a mean decrease in systolic blood pressure of −6.08 mm Hg (95% CI −12.57 to 0.41) associated with use of the BCM device.

Four non-randomised studies reported on blood pressure among subgroups of people monitored using the BCM device. No statistically significant

differences in blood pressure were seen in the following subgroup comparisons:

- patients in whom the average overhydration decreased within 6 months compared with those in whom it did not decrease (Castellano et al. 2014)
- patients who had been having dialysis for a short length of time compared with those who had been having it for longer (Hoppe et al. 2015)
- patients with a high relative fluid overload (more than 17.4%) compared with those in whom it was low (less than 17.4%; Onofriescu et al. 2015).

Kim et al. (2012) reported that systolic blood pressure was higher in hyperhydrated patients when compared with dehydrated patients (significance not stated).

Arterial stiffness

Three RCTs reported on pulse wave velocity as a surrogate for arterial stiffness (Hur et al. 2013; Onofriescu et al. 2012; Onofriescu et al. 2014) and were included in a meta-analysis. Arterial stiffness is thought be associated with an increased risk of cardiovascular events in the longer term. Arterial stiffness was significantly reduced in patients who were monitored using the BCM device and standard clinical assessment compared with standard clinical assessment alone (mean difference −1.53 meters per second [m/s]; 95% CI −2.96 to −0.07; p=0.04), although there was high statistical heterogeneity between studies. If data from Onofriescu et al. (2012) was removed from the meta-analysis, the pooled effect still suggested lower arterial stiffness in the BCM monitored group but this effect size was no longer significant (mean difference −1.18 m/s; 95% CI −3.14 to 0.78; p=0.24).

Absolute overhydration

Five RCTs (Huan-Sheng et al. 2016; Hur et al. 2013; Luo et al. 2011; Onofriescu et al. 2012; Ponce et al. 2014) assessed absolute overhydration; that is, the volume of fluid by which the participants were above their target

volume (as determined by the BCM device). No data on underhydration were available. A meta-analysis of the mean difference in absolute overhydration volumes showed that absolute overhydration was significantly lower in groups monitored with the BCM device (mean difference = −0.39 litres, 95% CI −0.62 to −0.15, p=0.001).

The EAG carried out a subgroup analysis for absolute overhydration according to type of dialysis. They compared the pooled effect of using the BCM device on absolute overhydration in the overall group (all 5 studies) and a subgroup of studies on people having haemodialysis (4 of these studies). A difference in effect between the overall and haemodialysis subgroup was seen; however, the EAG stated that this was not large enough to suggest a significant dialysis effect.

Relative overhydration

Four RCTs had results for relative overhydration (Huan-Sheng et al. 2016; Onofriescu et al. 2012; Onofriescu et al. 2014; Ponce et al. 2014); that is, a person's absolute overhydration volume normalised against their total extracellular body water volume. A meta-analysis of the reported mean differences in the relative overhydration between groups monitored with and without the BCM device showed that relative overhydration was significantly lower when the BCM device was used (mean difference =−1.54; 95%CI −3.01 to −0.07; p=0.04).

Hospitalisation

Three RCTs reported data on hospitalisations. Huan-Sheng et al. (2016) reported a non-significant difference in all-cause hospitalisation in patient groups monitored with and without the BCM device (hazard ratio 1.19; 95% CI 0.79 to 1.80). Hur et al. (2013) found that the difference in rates of hospitalisation caused by new cardiovascular events in the control and BCM monitored groups was not statistically significant. In Ponce et al. (2014),

39.6% of participants in the BCM monitored group and 31.8% of the standard clinical assessment group were hospitalised at least once.

Two non-randomised studies reported data on hospitalisation. Kim et al. (2015) found no significant differences in the number of hospital days per event between overhydrated and non-overhydrated groups (as determined by the BCM device). Onofriescu et al. (2015) reported a significantly higher all-cause hospitalisation rate for patients classified as overhydrated when a relative overhydration value of 17.4% was used as a cut-off to define people as overhydrated, but not when a value of 15% was used.

Left ventricular hypertrophy and left ventricular mass index

Measures of left ventricular hypertrophy, and surrogates of this, such as left ventricular mass index, may be associated with longer-term cardiac morbidity. Hur et al. (2013) reported that left ventricular hypertrophy was present at 12 months in 44% of participants monitored using the BCM device and in 50% of participants monitored using standard clinical assessment alone. This was a non-significant reduction from baseline in both groups (67% and 53% respectively). However, there was a statistically significant reduction in left ventricular mass index from baseline in the group monitored using the BCM device ($p<0.001$), but not in the group monitored using standard clinical assessment ($p=0.9$).

Use of antihypertensive medication

Two non-randomised studies reported on the use of antihypertensive medication in subgroups of people monitored using the BCM device. In Castellano et al. (2014), consumption of antihypertensive medication was significantly higher in a subgroup who did not have reduced relative overhydration after 6 months of monitoring. Kim et al. (2012) found no significant difference in medication use between people who were dehydrated or hyperhydrated.

People under 18 years

Three non-randomised studies (published in 4 papers) that enrolled people under 18 years were identified by the EAG (all of which assessed the BCM). Full details are given in appendix 2 of the diagnostics assessment report. One of these studies (reported in Zaloszyc et al. [2013] and Zaloszyc et al. [2016]) investigated the association between relative hydration status (measured using the BCM device) and blood pressure in children having dialysis. The study authors concluded that hypertension was not always related to overhydration; and that using bioimpedance spectroscopy could prevent incorrect reduction of a child's target weight to try and reduce hypertension, when it is not caused by excess fluid.

Ongoing trials

Four ongoing trials that will report outcomes potentially relevant to this assessment were identified (described in table 5 on page 52 of the diagnostics assessment report). One of these trials, the BioImpedance Spectroscopy to maintain Renal Output (the BISTRO trial; ISRCTN11342007), will be UK based. This multi-centre study, funded by the National Institute for Health Research, has a primary outcome of time to anuria (loss of urine output). The study will involve random allocation of participants (adults starting haemodialysis because of chronic kidney disease stage 5) for either regular assessment with a bioimpedance device in addition to standard treatment or standard treatment alone. Secondary outcomes will include the rate of kidney function reduction, vascular access failure, cardiovascular events, hospital admissions, death and patient-reported outcomes, such as quality of life, dialysis symptoms and functional status (measured at baseline, then every 3 months for up to 24 months). The trial is scheduled to start recruiting in March 2017, with a planned publication date of February 2020.

2.2 Costs and cost effectiveness

Systematic review of cost-effectiveness evidence

The EAG carried out a systematic review to identify existing studies on the cost effectiveness of using multiple frequency bioimpedance devices to monitor the fluid status of people with chronic kidney disease who are on dialysis. Details of the review are reported in the diagnostics assessment report on page 53 onwards.

No studies reporting full economic evaluations relevant to the scope of this assessment were identified.

Economic analysis

The EAG developed a de novo economic model to assess the cost effectiveness of using multiple frequency bioimpedance testing to help guide fluid management decisions in people having dialysis for chronic kidney disease.

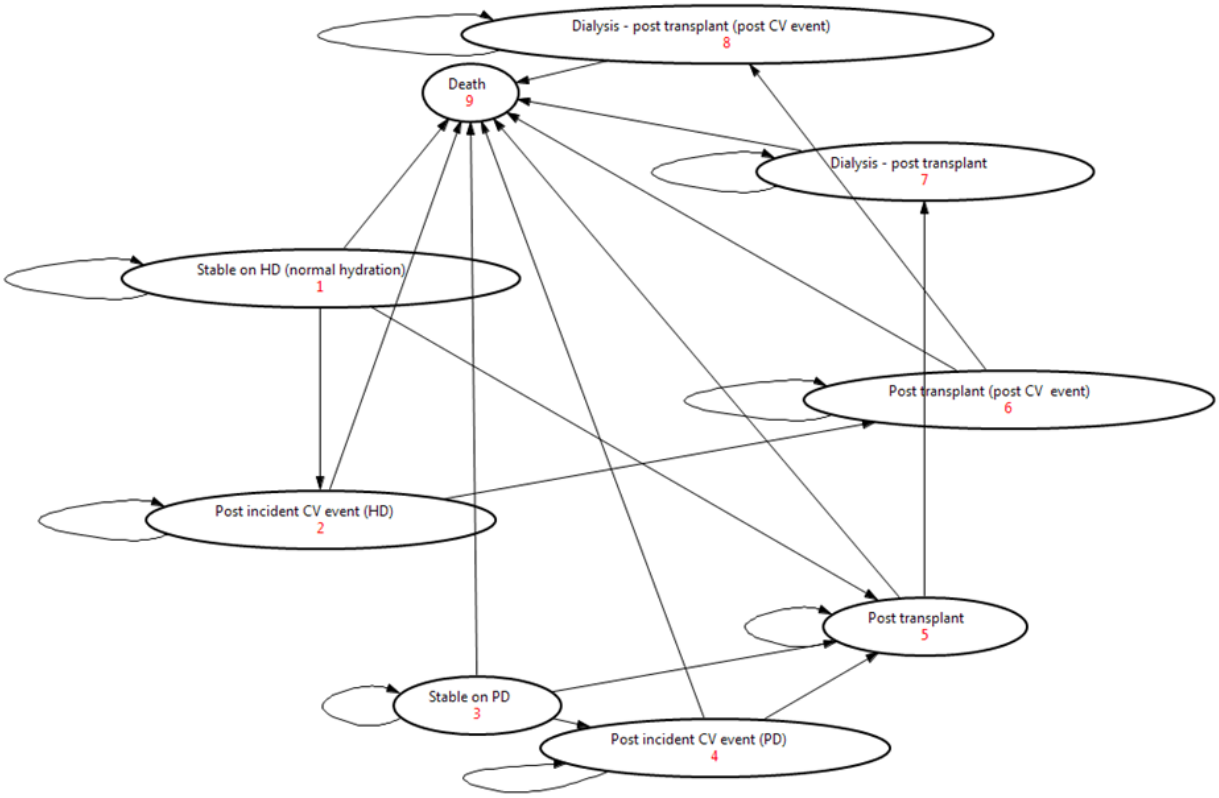
Model structure

The EAG developed a Markov model to simulate the effects of monitoring the fluid status of cohorts of people, using a multiple frequency bioimpedance device with standard assessment and standard assessment alone. The model took the perspective of NHS and personal social services. It was run as a cohort simulation for the patients in the 66-year old cohort in the base-case analyses over a lifetime time horizon of 30 years.

In the model, people start in a stable state on either haemodialysis or peritoneal dialysis and over time can either stay in this state or move to others when events (such as a kidney transplant, cardiovascular event or death) happen. These events can be in each cycle of the model, which is set as 3 months. Figure 2 shows all states in the model and how people can move between states over time (shown by the arrows). The characteristics of the cohort of patients modelled (for example, their age, the proportion of people

on haemodialysis or peritoneal dialysis, gender, and incidence of comorbidities) were based on the UK Renal Registry Report (2015), and are discussed in the diagnostics assessment report on page 54 onwards.

Figure 2 Schematic of model structure



The model also has an option to allow people in the 'stable' and 'post-CV event' dialysis states to be further classified as either severely overhydrated or normohydrated (based on their relative overhydration). This allowed scenarios to be run in the model in which mortality and hospitalisation rates were increased for dialysis patients who were overhydrated. No 'underhydrated' state was included because of a lack of evidence on the prevalence of underhydration in UK dialysis cohorts, the effect of underhydration on the risk of adverse events and quality of life, and the effectiveness of the BCM device in reducing the incidence of underhydration.

Model inputs

Parameter values used in the model were taken from several sources. These included data from focused reviews of the literature to identify baseline risks for mortality and hospitalisation, and also sources for cost and utility data, and the clinical-effectiveness review. Full details of the parameter values and sources can be found in the diagnostics assessment report from page 58 onwards.

Several possible outcomes that may be affected by using the BCM device were not included in base-case modelling because of a lack of evidence. These included changes in quality of life (independent of effects of hospitalisation and cardiovascular events), maintenance of residual renal function and effects on dialysis requirements (number and duration of sessions). Further details are given in the diagnostics assessment report on page 71 onwards.

The clinical-effectiveness review only found data on using the BCM, therefore only this device has been assessed in base-case analyses. Several scenarios were used to model the effect of BCM-guided fluid management on baseline model parameters. The treatment effects applied in each scenario are described below. The EAG's preferred approach was to use direct evidence on the effect of using the BCM device on final clinical outcomes in modelling. However, this was only possible for all-cause mortality. Several identified trials reported the effects of BCM-guided monitoring on surrogate endpoints, such as pulse wave velocity as a measure of arterial stiffness. The EAG carried out a further literature search to identify evidence that could be used to link changes in these surrogate endpoints to final health outcomes. Using this linked approach, estimated effects of BCM-guided monitoring on mortality and non-fatal cardiovascular events were calculated. Full details of the scenario analyses can be found in the diagnostics assessment report from page 67 onwards.

Scenario 1: A relative effect of 0.69 for all-cause mortality was applied to BCM-guided monitoring. This is based on the pooled hazard ratio (0.69; 95% CI 0.22 to 2.08) derived from clinical-outcome data in the clinical-effectiveness review. Although this is not statistically significant, the EAG applied a point estimate of 0.69 because the direction of the effect favoured reduced mortality with BCM-guided monitoring.

Scenario 2: An estimated effect of BCM-guided monitoring on the incidence of non-fatal cardiovascular events was added to scenario 1. The relative effect of BCM-guided monitoring on non-fatal cardiovascular events (hazard ratio 0.912; 95% CI 0.82 to 1.01) was derived by combining the pooled mean reduction in pulse wave velocity taken from the clinical-effectiveness review with data from a published observational study that reported the prognostic value of this outcome for cardiovascular events and mortality. Further details can be found in the diagnostics assessment report from page 68.

Scenario 3: Applied the same estimated effect of BCM-guided monitoring on the incidence of non-fatal cardiovascular events as scenario 2, but also applied this relative effect to all-cause mortality.

Scenario 4: Replicated scenario 3 but also included a reduction of costs for blood pressure medication when using the BCM. This reduction (£12.98 per year, based on assuming a 10% reduction in use) was estimated from data reported for a single RCT (Onofriescu et al. 2014).

Scenarios 5 and 6: In the final 2 scenarios, reported observational associations between overhydration status and mortality and all-cause hospitalisation were explored. Using data from Huan-Sheng et al. (2016), Scenario 5 assumed a 28% reduction in the proportion of people who are severely overhydrated (that is people with a relative overhydration of 15% or greater) in the BCM arm. This was applied by classifying people in dialysis states in the model as either severely overhydrated or normohydrated, which allowed mortality and hospitalisation rates to be adjusted upwards for

proportions of people in the dialysis cohorts who are estimated to be severely overhydrated. Scenario 6 was the same but assumed a reduction of 38%. Further details can be found in the diagnostics assessment report from page 66.

Table 2 gives a summary of the relative effects applied to different parameters in the base-case scenario analyses.

Table 2 Summary of effect estimates used in base-case scenario analyses

Scenario	Relative effect on all-cause mortality (HR; 95% CI)	Relative effect on hospitalisation for non-fatal CV (HR; 95% CI)	Effect on blood pressure medication costs (£ mean reduction)	Proportional reduction in severe overhydration
Scenario 1	0.69 (0.23 to 2.08)	1.00	0.00	N/A
Scenario 2	0.69 (0.23 to 2.08)	0.91 (0.82 to 1.01)	0.00	N/A
Scenario 3	0.91 (0.82 to 1.01)	0.91 (0.82 to 1.01)	0.00	N/A
Scenario 4	0.91 (0.82 to 1.01)	0.91 (0.82 to 1.01)	−12.98	N/A
Scenario 5	N/A	N/A	N/A	0.28
Scenario 6	N/A	N/A	N/A	0.38
Abbreviations: CI, confidence interval; CV, cardiovascular; HR, hazard ratio; N/A, not applicable.				

Costs

The model incorporates health service costs associated with maintenance dialysis, blood pressure medication, erythropoietin stimulating agents, all-cause inpatient hospitalisation, renal transplantation (including work-up, surgery and follow-up), post-transplantation immunosuppression and outpatient visits. Dialysis costs, per session (haemodialysis) or per day (peritoneal dialysis), were taken from NHS reference costs (2014-2015). For

haemodialysis, the average cost of £154 per haemodialysis session was calculated based on the cost per type of session, at home or at a unit, weighted by relative incidence. For peritoneal dialysis, the average cost per day of £69 was taken from the NHS reference costs. Full details can be found in the diagnostics assessment report on page 75.

Costs of bioimpedance monitoring included in modelling were purchase costs for devices (annuitised over 5 years), maintenance costs, staff costs related to using the device, training costs and device consumable costs (such as electrodes). The costs of the bioimpedance devices are shown in table 3.

Table 3 Costs of the multiple frequency bioimpedance devices

Bioimpedance device	Cost	Expected service life	Maintenance cost
BCM – Body Composition Monitor	£5,750	5 years	£250
BioScan 920-II	£4,950	5 years	£333[a]
InBody S10	£8,100	5 years	–[b]
MultiScan 5000	£7,600	5 years	£70[c]

[a] Assumes replacement or repair of cables every 2 years and an annual calibration check.

[b] No maintenance costs provided.

[c] Assumes a replacement set of leads annually.

Full details on the costs used in modelling can be found in the diagnostics assessment report on pages 75 to 85. All future costs and benefits included in modelling were discounted at a rate of 3.5% per annum.

Health-related quality of life and quality-adjusted life year decrements

Health state utility values for people on dialysis and post-renal transplant were identified through a focused search of the literature. Two systematic reviews were found that published EQ-5D data for UK patients (Wyld et al. 2012; Liem et al. 2008). Further searches did not identify any other studies reporting EQ-5D data for UK patients after 2010 (the end date for searches in the most recent systematic review). Short and longer-term utility multipliers associated

with cardiovascular events were calculated based on data from the Health Survey for England (2003 and 2006). Decreases in health state utilities resulting from hospitalisations were taken from the NICE guideline on peritoneal dialysis.

Details on the utilities used in modelling can be found in the diagnostics assessment report on pages 85 onwards.

Base-case results

For the purposes of decision-making, the incremental cost-effectiveness ratios (ICERs) per quality-adjusted life year (QALY) gained or lost will be considered. The following main assumptions were applied in the base-case analysis:

- Hydration status was assessed with a bioimpedance device every 3 months and, if needed, people had their target weight modified in line with the results.
- Any effect of BCM-guided monitoring on the length and frequency of dialysis sessions was assumed to be cost neutral.
- In the starting cohort of modelled patients, 87% were having haemodialysis and 13% were having peritoneal dialysis.
- The starting age of the cohort was 66 years
- Survival on haemodialysis and peritoneal dialysis was assumed to be equivalent, and patients did not switch between dialysis modes
- Fixed proportions of the cohort were on a waiting list for transplant, and waited a median of about 3 years, depending on survival. No transplants were done after the age of 75.
- It was assumed that 17.6% of all inpatient hospitalisations were because of cardiovascular events.
- Health state utility decrements were applied in the acute period for all hospitalisation events, and ongoing health state utility decrements were also applied after hospitalisation for a cardiovascular event.

- Effects of bioimpedance monitoring on all-cause mortality were applied for 10 years in the model.
- Effects of bioimpedance monitoring on cardiovascular-related or all-cause hospitalisation were applied over the lifetime of the cohort.

Six base-case scenarios were modelled, each differing in the assumed effects of BCM-guided monitoring, as described above in table 2. ICERs were calculated both with and without dialysis costs (table 4), because including BCM-guided monitoring in the model prolonged life expectancy, so dialysis was needed over a longer period which increased dialysis costs. The EAG commented that the high costs of dialysis treatment can affect the cost-effectiveness of technologies that prolong survival on dialysis. Sometimes, technologies that prolong survival on dialysis are not cost effective even at zero cost. The EAG also noted variation in practice in economic evaluations of end stage renal disease regarding whether the costs of dialysis are included in modelling. A full discussion of this issue can be found on pages 73 and 74 of the diagnostics assessment report.

When the cost of dialysis was included in modelling, ICERs resulting from using the BCM device compared with standard assessment alone were all above £58,000 per QALY gained. When excluding dialysis costs, scenarios which modelled the effect of BCM monitoring through reductions in the rate of mortality (scenario 1) and mortality plus cardiovascular events (scenarios 2 to 4) all had ICERs below £16,500 per QALY gained. When the effect of BCM-guided monitoring was modelled through effects on reducing the proportion of people who are severely overhydrated (scenarios 5 and 6), ICERs were higher. The ICER value was below £20,000 per QALY gained when BCM monitoring reduced the incidence of severe overhydration by 38% (scenario 6) but not when incidence was reduced by 28% (scenario 5).

Table 4 Deterministic cost-effectiveness scenarios for BCM-guided fluid management compared with standard practice (with and without dialysis costs)

Intervention	Including dialysis costs		Without dialysis costs	
	ICER (cost per QALY gained)	Net monetary benefit	ICER (cost per QALY gained)	Net monetary benefit
Scenario 1				
Standard assessment		−£104,077		£7,813
BCM	£62,524	−£128,341	£16,370	£9,884
Scenario 2				
Standard assessment		−£104,077		£7,813
BCM	£60,850	−£127,762	£15,430	£10,463
Scenario 3				
Standard assessment		−£104,077		£7,813
BCM	£59,146	−£109,962	£15,638	£8,469
Scenario 4				
Standard assessment		−£104,077		£7,813
BCM	£58,723	−£109,899	£15,215	£8,533
Scenario 5				
Standard assessment		−£162,039		−£47,046
BCM	£66,007	−£166,557	£21,201	−£48,497
Scenario 6				
Standard assessment		−£162,039		−£47,046
BCM	£64,151	−£167,999	£19,345	−£48,843
Abbreviations: BCM, BCM – Body Composition Monitor; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.				

The EAG commented that because of uncertainty in the current evidence base, all cost-effectiveness modelling could be speculative. Scenario 3 was used for further analysis because it seemed to be the most plausible for the effects of BCM monitoring (modelling a small effect on mortality and cardiovascular hospitalisation). Cumulative costs per patient monitored with and without the BCM device in scenario 3 are shown in table 5. Costs were higher for BCM-guided monitoring because people on average lived for longer, with dialysis costs making up most (74%) of the increase in cost.

Table 5 Cumulative per patient costs for scenario 3

	Standard care	BCM-guided care	Difference in BCM versus standard assessment
Cumulative inpatient hospital costs	£21,775	£22,404	£629
Cumulative dialysis costs	£111,890	118,432	£6,542
Cumulative medication costs	£10,792	£11,423	£631
Cumulative outpatient costs	£6,076	£6,431	£355
Cumulative acute transplant costs	£1,066	£1,101	£35
Cumulative post-transplant follow-up costs	£6,505	£6,709	£204
Bioimpedance testing costs	N/A	£497	£479
Total cumulative cost	£158,104	£166,997	£8,893
Abbreviations: BCM, BCM – Body Composition Monitor; N/A, not applicable.			

Analysis of alternative scenarios

The EAG also carried out several further scenario analyses, based on varying parameters in the base-case scenario 3 model. Results were generally reported without considering the costs of dialysis (unless otherwise stated) and in relation to the ICER produced in base-case scenario 3 when dialysis costs were excluded (£15,638 per QALY gained). This was done to show the sensitivity of the results when they are close to a maximum acceptable ICER of £20,000 to £30,000 per QALY gained. The results were as follows:

- Increasing the frequency of BCM monitoring to every month (from every 3 months) increased the ICER to £19,820 per QALY gained.
- Applying the estimated costs associated with monitoring in paediatric centres (which have a lower throughput of patients and consequently higher estimated costs of bioimpedance monitoring) to the modelled adult population increased ICERs to £20,331 (assuming testing every 3 months) or £23,649 per QALY gained (assuming testing every month).
- Assuming that BCM-guided fluid management resulted in a 2% improvement in health state utility over a patient's lifetime reduced the

ICER to £11,760 per QALY gained (£44,478 if dialysis costs were included). If this improvement was increased to 5%, the ICER reduced further to £8,571 per QALY gained (£32,419 if dialysis costs were included).

- If BCM-guided monitoring was assumed to result in a 10% reduction in lifetime dialysis costs, BCM-guided care dominated standard care (that is, it costs less but produces more QALYs). If a 5% reduction in lifetime dialysis costs was assumed, the ICER for BCM-guided care (including dialysis costs) was £19,761 per QALY gained (compared with £59,146 per QALY gained in the base-case analysis when including dialysis costs).
- If BCM-guided monitoring was assumed to have no effect on mortality (that is, the effects that were only as a result of changes in the incidence of non-fatal cardiovascular events), the ICER including the cost of dialysis was £21,519 per QALY gained (compared with £59,146 per QALY gained in base-case analysis).
- If BCM-guided monitoring was assumed to have no effect after 3 years, the ICER for BCM-guided monitoring increased to £22,647 per QALY gained.

Further scenario analyses produced little change in the base-case scenario ICERs, with ICER values (not including dialysis costs) of between £10,000 and £19,000 per QALY gained. Full details can be found in table 23 starting on page 102 of the diagnostics assessment report.

MultiScan 5000, BioScan 920-II, BioScan touch i8 and InBody S10

No clinical-effectiveness data were found for the MultiScan 5000, BioScan 920-II, BioScan touch i8 or InBody S10. These devices were therefore not included in base-case cost-effectiveness modelling. However, the EAG carried out scenario analyses which assumed that these devices reduced mortality and non-fatal cardiovascular events to the same extent as the BCM device in scenario 3 (but with different costs). The ICERs produced for these devices were very similar, being between £15,000 and £16,000 per QALY gained.

Subgroup analyses

The EAG also carried out analyses for subgroups of the dialysis population. They were grouped by comorbidity status (none or at least one), dialysis modality (haemodialysis or peritoneal dialysis), starting age of the cohort, whether a person was on a transplant list or not, and whether or not they were chronically overhydrated.

No large differences in cost effectiveness by subgroup were identified. ICERs for all subgroups stayed below £16,500 per QALY gained (when dialysis costs were not included), except for people listed for a transplant who had an ICER of £20,315 per QALY gained. Full details of the subgroup analyses can be found in the diagnostics assessment report on page 106 onwards.

Sensitivity analyses

Deterministic sensitivity analyses

One-way sensitivity analyses were carried out on the main model parameters for base-case scenario 3 (both with and without dialysis costs). When dialysis costs were included, adjusting the hazard ratio for all-cause mortality to 1.00 resulted in the most favourable ICER for BCM-guided monitoring, because these people have the same survival as those having standard monitoring, and therefore do not have higher dialysis costs. When dialysis costs are included, ICERs produced by varying model parameters within their specified ranges generally stayed above £30,000 per QALY gained.

When dialysis costs were not included, the ICERs stayed sensitive to varying all-cause mortality. However, the least favourable ICER occurs when the hazard ratio is equal to 1.00. Full details of the deterministic sensitivity analyses can be found in the diagnostics assessment report on page 99 onwards.

Probabilistic sensitivity analyses

The EAG carried out probabilistic sensitivity analyses for base-case scenarios 1, 3 and 4 (both with and without dialysis costs included). Results are shown in table 6. The probabilistic ICERs produced for all 3 base-case scenarios were similar to the deterministic ICERs (shown in table 4 above). If dialysis costs were included, the probability of BCM-guided monitoring being cost effective at a maximum acceptable ICER of £20,000 per QALY gained was 25% in scenario 1 and less than 6% in scenarios 3 and 4. However, if dialysis costs were excluded, BCM-guided monitoring was about 70% likely to be cost effective at this maximum acceptable ICER in all 3 scenarios.

The EAG warned that the uncertainty in the parameters produced by linking the effects of monitoring with the BCM device on arterial stiffness to mortality and non-fatal cardiovascular events (as in base-case scenarios 3 and 4) may not be fully captured in the probabilistic modelling.

Table 6 Probabilistic cost-effectiveness scenarios for BCM-guided fluid management compared with standard assessment (both with and without dialysis costs included)

Intervention	With dialysis costs		Without dialysis costs	
	ICER (cost per QALY gained)	**Probability of cost effectiveness at £20,000 per QALY gained**	**ICER (cost per QALY gained)**	**Probability of cost effectiveness at £20,000 per QALY gained**
Scenario 1				
Standard assessment		0.752		0.313
BCM	£62,563	0.248	£16,100	0.687
Scenario 3				
Standard assessment		0.944		0.299
BCM	£59,198	0.056	£15,430	0.701
Scenario 4				
Standard assessment		0.960		0.271
BCM	£57,652	0.040	£15,038	0.729
Abbreviations: BCM, BCM – Body Composition Monitor; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.				

Further details of the probabilistic analyses, including cost-effectiveness scatter plots and cost-effectiveness acceptability curves, can be found in the diagnostics assessment report from page 109.

3 Summary

Clinical effectiveness

Data identified in the clinical-effectiveness review did not show significant effects of BCM-guided fluid monitoring on clinical outcomes such as mortality or patient-reported adverse events. However, significant changes in several intermediate outcomes were shown. These included decreases in systolic blood pressure, arterial stiffness, absolute and relative overhydration (although changes were not significant for blood pressure and arterial stiffness if data from Onofriescu et al. 2012 was removed). No RCTs reported the effect of BCM-guided monitoring on residual renal function. However, 1 RCT suggested that it may have an adverse effect on people's ability to produce urine.

Several relevant ongoing trials were also identified. One of these is UK based and has a primary outcome of time to anuria (loss of urine output). Additional measured outcomes will include cardiovascular events, deaths and patient-reported outcomes, including quality of life.

Cost effectiveness

Several approaches were used by the EAG to model possible effects of BCM-guided monitoring. Because of a lack of data on the direct effects on clinical end outcomes, for some scenarios the EAG linked changes in intermediate outcomes (arterial stiffness, hydration status) to end outcomes using a linked evidence approach.

When dialysis costs were included in modelling, ICERs for BCM-guided fluid management ranged from £58,723 to £66,007 per QALY gained. These ICERs related to incremental costs that varied between £4,518 and £35,676, and corresponding incremental QALY gains that varied from 0.07 to 0.58. Most of the increased cost from using the BCM device was because of longer survival, and the greater dialysis cost this produces. When dialysis costs were excluded from the model, the base-case ICERs ranged from £15,215 to £21,201.

In further scenario and sensitivity analyses, when dialysis costs were included in modelling, removing the effect of BCM-guided monitoring on mortality (that is, setting the hazard ratio to 1.00) but keeping the effect on non-fatal hospitalisation events reduced the ICER to about £22,000 per QALY gained. The EAG commented that for BCM-guided monitoring to produce ICERs under £30,000 per QALY gained (when an effect on mortality was assumed and dialysis costs were included), it would also need to significantly reduce dialysis costs across the lifetime of patients, or have a constant percentage improvement in the health state utility of patients on dialysis.

When dialysis costs were removed from modelling, ICERs generated by using the BCM device stayed below £20,000 per QALY in most assessed scenarios.

4 Issues for consideration

Clinical effectiveness

None of the included RCTs were done in the UK and most studies did not give details of what standard clinical assessment of fluid status (in control arms of trials or alongside monitoring with the BCM device) comprised. If standard clinical practice for fluid assessment in the NHS differs from the trials, results may not be generalisable to NHS practice. Also, the frequency of BCM monitoring varied greatly in the RCTs, and may not accurately reflect frequency of use in NHS practice.

It is not clear if 2 of the included RCTs (Onofriescu et al. 2012 and 2014) reported outcomes from the same, or possibly overlapping, patient populations. Therefore the EAG carried out further analyses by removing data from Onofriescu et al. (2012) from meta-analyses. This decreased the estimated effect of BCM-guided monitoring on reducing systolic blood pressure and arterial stiffness to the extent that these reductions were no longer significant. There may also be overlap in the patient populations included in non-randomised studies O'Lone et al. (2014) and Oei et al. (2016).

No studies reporting the effectiveness of bioimpedance guided monitoring in people under 18 years were identified. In addition, most RCTs excluded patients with amputations, cardiac pacemakers and defibrillators – which may limit the generalisability of findings in the report to these groups.

Few of the subgroup analyses planned by the EAG could be carried out because of lack of data. These included analyses according to the type of dialysis for further clinical outcomes, by population (children under 5 years), by ethnicity and by other patient characteristics (such as people in whom the electrodes could not be positioned as recommended, people who could not get into the optimum position for measurements to be made, or people at extremes of body composition measurements).

Some limited subgroup comparisons were possible based on the modality of dialysis used (haemodialysis or peritoneal dialysis) for 2 outcomes: systolic blood pressure and absolute hydration. Only 1 out of the 6 identified RCTs assessed use of the BCM device in people on peritoneal dialysis, therefore limited data is available on the clinical effectiveness of BCM-guided monitoring in this group. Because of this, the EAG did not test for subgroup effects and compared the overall effect with the haemodialysis group effect (similar to a sensitivity analysis).

Cost effectiveness

There is uncertainty about the assumption made in modelling that BCM-guided monitoring is associated with reduced all-cause mortality. The pooled-effect estimate derived from the clinical-effectiveness review suggested that BCM-guided monitoring has no significant effect on this parameter. However a lower rate of mortality resulting from using the BCM device based on this pooled effect was assumed in base-case scenarios 1 and 2.

Base-case scenarios 2 to 6 include model parameters that were produced by extrapolating the effects of BCM-guided monitoring on surrogate endpoints (arterial stiffness or hydration status) using data from cross sectional observational studies. The assumptions made in linking the surrogate endpoints to effects on mortality and hospitalisation rates add additional uncertainty, which may not be fully captured in the probabilistic scenario analysis.

The ICERs for fluid management using the BCM device are largely driven by the assumption that it increases overall survival and so produces additional costs associated with dialysis during the period of extended survival. When dialysis costs were excluded, the ICERs for BCM-guided care for all 6 scenarios were below £21,300 per QALY gained. When dialysis costs were included, the ICER for BCM-guided fluid management was about £60,000 per QALY gained in all 6 base-case analyses. If dialysis costs are included, it is likely that BCM-guided monitoring would only be cost effective if:

- it produces a significant reduction in dialysis costs across the lifetime of patients
- it produces a constant percentage improvement in the health state utility of patients having dialysis or
- it has no effect on mortality (but reduces the incidence of non-fatal cardiovascular hospitalisation events).

No health-related quality-of-life estimates specific to reduced side effects of overhydration or underhydration were included in the model. It is possible that a reduction in intradialytic and interdialytic side effects, such as light headedness and cramping, may affect quality of life.

The effect of BCM-guided monitoring on the frequency and duration of dialysis sessions was not included in the model because of an absence of data, and it is assumed to have no effect (cost neutral). It is plausible that it may reduce the duration or number of sessions for some people, but these may increase for others.

The version of the model incorporating hydration states (used in base-case scenarios 5 and 6) only considered overhydration because no data were found to allow the effect of underhydration to be quantified. This could underestimate the benefits of BCM-guided fluid management if it can also reduce the proportion of patients that are over- and underhydrated. Alternatively, if BCM-guided monitoring reduces the number of patients who are overhydrated by increasing the incidence of underhydrated patients, the model could overestimate its benefits.

The effect of BCM-guided monitoring on residual renal function was also not included in the model, because of lack of data. If BCM-guided monitoring can help to preserve residual renal function, its benefits may be underestimated. Alternatively, it is possible that using BCM-guided fluid management could have an adverse effect. If its results are used to reach a lower target weight through high ultrafiltration volumes or rates, it could be associated with increased underhydration and more rapid loss of residual renal function.

No data were identified on the effectiveness of BCM-guided monitoring in people aged under 18 years and the EAG was unable to assess the cost effectiveness of the device in this group. The EAG commented that a different baseline model would be needed for people aged under 18 years, because of different population characteristics and because rates of renal transplant are

likely to be substantially different. However, the EAG produced estimates of ICERs for BCM-guided monitoring in adults using monitoring costs estimated for paediatric centres, combined with more frequent testing. The ICERs (not including the cost of dialysis) when applying these higher monitoring costs were either £20,331 (assuming testing every 3 months) or £23,649 per QALY gained (assuming testing every month).

No clinical-effectiveness data were identified for bioimpedance devices included in the assessment scope other than the BCM. The EAG estimated the cost effectiveness of using these other devices by assuming that their clinical effectiveness was the same as the BCM device and by using different costs associated with using these devices. Produced ICERs were similar for all devices (about £15,500 per QALY gained with dialysis costs excluded). However, there is no evidence on which to base the assumption of equivalent clinical effectiveness to BCM for these other devices.

As noted in the clinical-effectiveness section, removing the Onofriescu et al. (2012) data from meta-analysis reduced the estimated effect of BCM-guided monitoring on reducing arterial stiffness. Because the pooled estimate of arterial stiffness was used to estimate the relative treatment effects of the BCM in modelling (in base-case scenarios 2, 3 and 4), the EAG carried out revised cost-effectiveness analyses with BCM modelling assumed to have a smaller effect on hospitalisation for cardiovascular events and mortality (given in the addendum to the diagnostics assessment report). Similar ICERs were produced for revised base-case scenarios 2, 3 and 4 and also for most of the further revised sensitivity, subgroup and scenario analyses. However, there was greater uncertainty about the cost-effectiveness results in the revised analyses. When dialysis costs were included, the probability of BCM being cost effective increased from less than 6% to between 10% and 14% for scenarios 3 and 4. When dialysis costs were excluded, the probability of BCM being cost effective decreased for revised scenarios 3 and 4 (from about 70% to about 62%). This reflected the greater uncertainty in the effect of BCM-

guided monitoring on reducing arterial stiffness, and consequently the linked effect on all-cause mortality and hospitalisation for cardiovascular events.

5 Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

The incidence of chronic kidney disease and the need for dialysis increases with age, as does the presence of fluid overload in people on dialysis (Guo et al. 2013). Incidence rates for chronic kidney disease are greater in people of south Asian family origin (from India, Bangladesh, Sri Lanka and Pakistan), possibly because of higher rates of diabetes, and in people of African or Caribbean family origin, who may have increased rates of higher blood pressure (NHS Choices). Age and race are protected characteristics under the Equality Act 2010. Some people with chronic kidney disease may be protected under the disability provision of the Equality Act 2010. These potential equalities issues are related to the condition rather than of using the technology.

Identifying overhydration or underhydration using clinical assessment may be more difficult in people with extremes of body composition, for example people who are obese, so these people may particularly benefit from monitoring with bioimpedance devices. Normal ranges of lean or adipose tissue body composition may also differ between ethnicities, which may affect the interpretation of test results in practice, particularly when the tissue and fluid models used in the devices have been validated in non-representative populations. When using bioimpedance devices for monitoring people with amputations, estimated outputs of hydration parameters may need to be converted to take account of the amputation. Metal implants, such as replacement joints and vascular or cardiovascular stents, may also affect bioimpedance measurements. If it is not possible for electrodes to be placed

in recommended positions, possibly because of amputations or multiple open wounds, the electrodes may need to be positioned differently, for example, hand to hand or right hand to left foot. Care may be needed in interpreting these readings, which may be less accurate than values from the optimum placement of electrodes. Bioimpedance devices may not be able to be used for people with implanted electronic devices (for example, pacemakers) or, in the case of some devices, for pregnant women. The devices also may be less suitable for use in young children, particularly those under 2 years, because they may not be able to stay still long enough for measurements to be made.

6 Implementation

Local protocols will need to be developed to specify when and how often bioimpedance devices should be used to monitor fluid levels. A lack of clarity in how often devices should be used may prevent benefits from being fully realised.

Training in how to use devices may also be needed, especially because the devices will need to be integrated alongside current practice. In particular, issues may arise if bioimpedance devices and clinical assessment produce different estimates of the hydration status of an individual.

7 Authors

Thomas Walker
Topic Lead

Rebecca Albrow
Technical Adviser

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Appendix A: Sources of evidence considered in the preparation of the overview

A. The diagnostics assessment report for this assessment was prepared by Aberdeen Health Technology Assessment Group:

Scotland G, Cruickshank M, Jacobsen E, Cooper D, Fraser C, Shimonovich M, Marks A, Brazzelli M. Multiple frequency bioimpedance devices (BCM – Body Composition Monitor, BioScan 920-II, BioScan touch i8, InBody S10 and MultiScan 5000) for fluid management in people with chronic kidney disease having dialysis. Aberdeen HTA Group, Institute of Applied Health Sciences, University of Aberdeen, 2016.

B. The following organisations accepted the invitation to participate in this assessment as stakeholders. They were invited to attend the scoping workshop and to comment on the diagnostics assessment report.

Manufacturer(s) of technologies included in the final scope:

- Bodystat Ltd
- Derwent Healthcare Ltd
- Fresenius Medical Care
- Maltron International Ltd

Other commercial organisations:

- ImpediMed

Professional groups and patient/carer groups:

- British Association for Paediatric Nephrology
- British Kidney Patient Association
- Kidney Research UK
- Leeds Teaching Hospitals NHS Trust
- Polycystic Kidney Disease Charity
- Renal Association

- The Royal College Of Pathologists
- The Royal College Of Physicians

Research groups:

- None

Associated guideline groups:

- National Clinical Guidelines Centre

Others:

- Department of Health
- Healthcare Improvement Scotland
- Medicines and Healthcare products Regulatory Agency
- NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC)
- NHS England
- Welsh Government

Appendix B: Glossary of terms

Haemodialysis
A type of dialysis in which blood is removed from a person's body into an external machine which removes waste products and fluid, and then returns the blood to the body. Haemodialysis sessions typically last around 4 hours and are carried out several times a week.

Intradialytic hypotension
Abnormally low blood pressure during dialysis, usually resulting from too fast or inadequate removal of fluid.

Left ventricular hypertrophy
A thickening of the walls of the heart's left ventricle which can act as a surrogate marker for cardiovascular events.

Oedema
Swelling caused by an accumulation of fluid in a tissue. This can occur anywhere in the body, including the feet and ankles (peripheral oedema) or in the lungs (pulmonary oedema) which can cause breathlessness.

Peritoneal dialysis
A type of dialysis that uses the inside lining of the abdomen (the peritoneum) to remove waste products and excess fluid from the blood. Waste products and excess fluid are drawn out of a person's blood into dialysis fluid that is pumped into a person's peritoneal cavity through a fitted catheter. Used dialysis fluid is drained from the peritoneal cavity and replaced with fresh fluid several times a day. Alternatively, a machine can change dialysis fluid overnight as a person sleeps.