NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

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

Final scope

June 2016

1 Introduction

The Medical Technologies Advisory Committee identified the BCM - Body Composition Monitor as potentially suitable for evaluation by the Diagnostics Assessment Programme on the basis of a briefing note.

The final scope was informed by discussions at the scoping workshop held on 17 May 2016 and the assessment subgroup meeting held on 31 May 2016.

The technologies included in the scope for this assessment were identified and discussed with stakeholders and specialist committee members during scoping. NICE is aware that additional multiple frequency bioimpedance devices are available, however these devices are not portable and may also require people to stand during measurements. Clinical advice suggests that this makes them less suitable for use in people having dialysis and consequently they have not been included in the scope for this assessment.

A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE by manufacturers and experts, and on information available in the public domain. NICE has not carried out an independent evaluation of the descriptions.

2.1 Purpose of the medical technologies

Multiple frequency bioimpedance devices are used to monitor the hydration status of a person with chronic kidney disease who is receiving either haemodialysis or peritoneal dialysis treatment. The information provided by the technology can be used to guide how much fluid to remove during dialysis.

If too little or too much fluid is removed during dialysis this will lead to underhydration or fluid overload. Short-term complications of fluid overload include oedema of the hands, feet and face, and fluid retention in the lungs (pulmonary oedema), causing shortness of breath. In the short-term, underhydration can cause cramps, dizziness and tiredness. Long-term fluid imbalance can result in poor blood pressure control, leading to heart disease, further reductions in kidney function and increased mortality. Fluid overload in people receiving dialysis can also cause ventricular hypertrophy which increases the risk of heart attack, stroke and arrhythmia.

Multiple frequency bioimpedance devices aim to improve estimates of the amount of fluid to remove during dialysis, which may reduce complications associated with fluid overload or underhydration. Potential benefits of reduced fluid overload could include reduced use of antihypertensive medicine, reduced numbers of hypertensive episodes and reduced risk of cardiovascular complications and death. Potential benefits of reducing systematic underhydration could include greater preservation of renal function, reduced numbers of hypotensive episodes and a reduction in symptoms such as cramps and post-dialysis fatigue. Further benefits may include reduced hospital admission arising from fluid overload and underhydration, and improved quality of life for patients.

2.2 Product properties

2.2.1 BCM – Body Composition Monitor (Fresenius Medical Care)

The BCM – Body Composition Monitor is a portable device that uses bioimpedance spectroscopy and physiological tissue models to calculate an individual's fluid overload. The device displays a direct output of fluid overload volume based on estimating the amount of excess fluid in a person. The technology is comprised of a BCM – Body Composition Monitor unit (containing an output display screen) which is connected to disposable electrodes (for attachment to the body) via a cable. Fluid Management Tool software is also provided (for installation on a computer) for data analysis. In addition, the device can be used with external data storage devices

(PatientCards) which can transfer outputs from the BCM – Body Composition Monitor to a computer using a card reader. PatientCards can hold personal data (such as height, age and sex) and up to 20 measurements for an individual.

The device sends small, painless electrical signals through the body via electrodes placed on the hands and feet, which also measure the opposition to the flow of the electric current from body tissues. The BCM – Body Composition Monitor uses 50 frequencies between 5 and 1000 kHz (other bioimpedance devices can differ in the number and frequency of electrical signals used). The electrodes measure bioimpedance (obstruction to flow) to the alternating electrical current across the different frequencies. Built-in software uses these resulting values along with a patient's height and weight to calculate parameters relating to hydration, such as volumes of extracellular, intracellular and total body water, in addition to the ratio of extracellular to intracellular water volumes.

The software also calculates fluid overload using two physiological models validated for use with people having dialysis. The amount of extracellular water that should be present based on the identified amounts of lean and adipose tissue is calculated and compared to the measured volume of extracellular fluid (based on techniques published in Moissl et al. 2006 and Chamney et al. 2007). The resulting volume difference between predicted and actual extracellular fluid is used as a measure of a person's overhydration volume (the overhydration value), and is reported by the device in litres. The reported overhydration value can be either positive, where a person is estimated to be overhydrated, or negative, where a person is estimated to be underhydrated. As 1 litre of water weighs a kilogram, the overhydration value provided by the device can be subtracted from a person's current weight (or added if the overhydration value is negative) to identify their normohydration weight, that is the weight they would be if their body tissue was normally hydrated. This resulting value can be used by clinicians to assist their decisions regarding the amount of fluid to be removed during dialysis.

The company have suggested the device could be used from 1-3 times per week over the first month for people new to dialysis and then every 3-4 months thereafter, provided that a person's hydration state appears stable. The company state that there are no restrictions on the age of person that this device can be used on.

The accompanying software tool (the Fluid Management Tool) allows the plotting of parameter values (such as overhydration and lean tissue mass) over time. This software package also allows a hydration reference plot to be

produced which displays overhydration and blood pressure on a single graph compared to reference population values. The plot can be used to help a clinician determine whether hypertension is because of fluid overload or because of other causes, where hypertensive medication might be needed.

The BCM – Body Composition Monitor's output also contains further parameters such as total body water, intracellular water, extracellular water, lean tissue mass, body cell mass and adipose tissue mass (a full list is available from the company's website; accessed 28/04/16). These parameters can be used to evaluate nutritional status and help to identify malnutrition in people with chronic kidney disease who are on dialysis. Total body water volume can also be used in calculations to assess the adequacy of urea removal by dialysis.

2.2.2 MultiScan 5000 (Bodystat)

The MultiScan 5000 uses bioimpedance spectroscopy and measures bioimpedance across a spectrum of 50 frequencies (between 5 and 1000 kHz). The system consists of a bioelectrical impedance spectroscopy hardware unit which is connected by lead wires to disposable electrodes. Outputs are displayed on a colour touchscreen display. A calibrator unit and analytical software (BBIS Software) are also provided. Test results can be stored on the device (up to 1000 tests) or on a computer via a Wi-Fi or Bluetooth interface.

The device displays hydration measures, including an estimate of the volume of fluid excess or deficit in a person, which is displayed as the volume of overhydration in litres. This value is determined using models set out in published literature (Moissl et al. 2006 and Chamney et al. 2007). The value can be either positive, where a person is estimated to be overhydrated, or negative, where a person is estimated to be underhydrated. As 1 litre of water weighs a kilogram, the volume of overhydration provided by the device can be subtracted from a person's current weight (or added if the overhydration value is negative) to identify the weight they would be if their body tissue was normally hydrated. This value can be used, along with clinical assessment, in setting targets for fluid removal in dialysis.

The MultiScan 5000 also provides other hydration related parameters such as the volumes of total body water and intracellular and extracellular water, as well as the ratio of total body to extracellular water volumes. In addition to whole body measurements, bioimpedance can also be measured in different body segments using this device by attaching electrodes in different configurations on the body. Changes, or trends, over time in the ratio of total

to extracellular water in different body segments can then be monitored. Bioelectrical impedance vector analysis (BIVA) can also be carried out by the device.

The company suggest using the volume of overhydration output from this device for people aged 18-70 years old to assess hydration status. Outside of this age range, this value can be used to track relative changes over time. In addition, the ratio of total body to extracellular water calculated by the device (called the 'prediction marker') can be used as an additional marker to track hydration status over time in all age groups.

Additional parameters related to body composition are also measured or calculated. These include fat weight, lean weight, skeletal muscle mass and body cell mass. A full list of displayed results can be found on the product webpage (accessed 28/04/16). These parameters can be used to evaluate nutritional status and help to identify malnutrition in people with chronic kidney disease who are on dialysis.

2.2.3 BioScan 920-II and touch i8 (Maltron International)

BioScan 920-II analysers are multifrequency devices that measure bioimpedance at 5, 50, 100 and 200 kHz. The devices consist of an analyser unit that is connected via cables to electrodes for attachment to the body. Through attachment of electrodes in different configurations, measurements can be made in the whole body, thorax, trunk, legs and arms. Results can be viewed on a display screen or be downloaded to a computer for analysis using provided software. The device is able to store the results of 1000 completed tests.

Hydration status related outputs calculated by the device are dry weight (the calculated ideal post-dialysis weight of a person; in kg) and also the volumes of excess fluid or fluid deficit, that is the volumes that would need to be lost or gained, respectively, to achieve the dry weight (in litres). These results can be used, along with clinical assessment, in setting targets for fluid removal in dialysis. In addition, ratios of extracellular to intracellular water volumes are also produced, along with total body water volume and fat free mass hydration.

The BioScan 920-II device also provides additional parameters related to body composition. These include body cell mass, protein mass, fat mass and glycogen mass. A full list of displayed results can be found on the product webpage (accessed 28/04/16). These parameters can be used to evaluate

nutritional status and help to identify malnutrition in people with chronic kidney disease who are on dialysis.

Different versions of this device are available. The BioScan 920-II Standard is suggested for use with people aged 5-99 years. A version of this device (the BioScan 920-II-P) is also available for monitoring hydration status in preterm, neonatal and paediatric patients (for use from 23 weeks gestational age up to 18 years). A full list of the outputs calculated by the BioScan 920-II-P can be found on the product webpage (accessed 28/04/16).

The company have informed NICE that an updated version of the BioScan 920-II device, the BioScan touch i8, will be released during the course of this assessment. As with the BioScan 920-II, it is anticipated that there will be two versions of this device, one aimed at people aged 0-18 and one aimed at people aged 5-99. The device differs from the BioScan 920-II in having an updated user interface.

2.2.4 InBody S10 (InBody)

The InBody S10 model is a multifrequency bioimpedance device that measures bioimpedance across six different frequencies (1, 5, 50, 250, 500 and 1000 kHz). The device consists of an InBody S10 unit (containing a display monitor) which is connected via cables to electrodes for attachment to the body. Two types of electrode can be used with this device: disposable adhesive type electrodes and reusable touch type electrodes (which can be clipped to a person's hand and foot). Data can be transferred to a computer through use of USB ports (either via a USB storage device or a cable). Results can be obtained in pre-formatted results sheets, which can be transferred to a computer or printed out. In addition to whole body measurements, bioimpedance measurements can also be made in five segments of the body (right arm, left arm, trunk, right leg, left leg). The company recommend that the S10 device can be used for people aged 3-99 years.

Hydration related outputs from this device are calculated water volumes (extracellular water, intracellular water) and also a ratio of extracellular to total body water. These output parameters are provided along with a suggested standard range of values to facilitate identification of over- or underhydrated individuals. Dry weight can be calculated by accompanying software (Lookin'Body 120) which can calculate several suggested dry weight values for use depending on the presence of complications such as diabetes or hypoalbuminemia (which may alter extracellular fluid volumes). This result can

be used, along with clinical assessment, in setting targets for fluid removal in dialysis.

In addition to hydration related outputs, the InBody S10 also produces results related to body composition. These include body cell mass, basal metabolic rate, bone mineral content, skeletal muscle mass and fat free mass. A full list of outputs can be found on the product webpage (accessed 28/04/16). These parameters can be used to evaluate nutritional status and help to identify malnutrition in people with chronic kidney disease who are on dialysis.

3 Target condition

3.1 Chronic kidney disease and dialysis

The kidneys function to excrete certain waste products, excess water, acid and salts from the body. People with chronic kidney disease (CKD) have an irreversible and progressive decrease in kidney function, which is most commonly caused by diabetes and hypertension but can also be caused by glomerulonephritis, polycystic kidney disease and acute kidney injury. Chronic kidney disease can be categorised into 5 stages of severity, in accordance with NICE's guideline on chronic kidney disease. The stages are defined by the presence of markers of kidney damage and the glomerular filtration rate (an estimation of how much fluid is filtered from the blood by the kidneys every minute). In a small proportion of people chronic kidney disease progresses to the most severe stage (stage 5), at which point glomerular filtration rate has decreased to such an extent (<15 ml/min/1.73 m^2; approximately 15% of normal kidney function) that kidney failure occurs, and renal replacement therapy is required for survival. Renal replacement therapy comprises either transplantation or dialysis. Dialysis replicates many of the functions of a healthy kidney; for example, by filtering waste products and excess water from the blood.

Two modalities of dialysis are available: haemodialysis and peritoneal dialysis. NICE's guideline on peritoneal dialysis recommends that peritoneal dialysis should be considered the first choice of treatment modality for children 2 years old or younger, people with residual renal function and adults without significant associated comorbidities.

On 31 December 2014 there were 27,804 adults in the UK on dialysis. Of whom, 86.9% had haemodialysis (44.0% in satellite units, 38.6% in hospitals, 4.3% at home), 5.8% had continuous ambulatory peritoneal dialysis and 7.0% had automated peritoneal dialysis (UK Renal Registry 2015). In addition, 190 children and young people under the age of 18 years were on dialysis (103

haemodialysis and 87 peritoneal dialysis) (UK Renal Registry 2015). Reported 1 and 2 year survival for adult dialysis patients were 85.0% and 72.1% respectively. The highest reported cause of death in prevalent dialysis patients was cardiac disease (24% of deaths; UK Renal Registry 2015).

3.2 Fluid imbalance in dialysis users

In replacing normal renal function, dialysis needs to remove any excess fluid. Where haemodialysis is used this is fluid that has accumulated in the body since the last dialysis session. Removal of an appropriate volume of fluid is required to minimise complications caused by being either overhydrated or underhydrated. Determining when a person is 'overhydrated' or 'underhydrated' varies depending on the parameter used to determine fluid status, and also the cut-off points used to designate over- or underhydration, which differ between studies. When clinical assessment is used, fluid status is classified qualitatively. Individuals are classified as overhydrated or underhydrated if any corresponding symptoms are present and normohydrated (or 'euvolaemic') when they are absent.

(i) Overhydration

Overhydration (also known as 'hypervolemia') resulting from removal of too little water during dialysis can result in oedema, including pulmonary oedema resulting in breathlessness. Increased blood pressure can also result from retaining excess body fluid. Overhydration has also been associated with left ventricular hypertrophy, increased arterial stiffness and heart failure, in addition to increased rates of cardiovascular events and mortality. A negative association between higher diastolic blood pressure and residual renal function has also been reported (Jansen et al. 2002).

Complications associated with overhydration can be asymptomatic. For example, oedema may not be detectable until interstitial fluid volumes rise to approximately 30% above normal (Bozzetto et al. 2009). The use of blood pressure as a surrogate measure for fluid status is also complicated by additional factors (such as age and comorbidities) that can cause volume-independent hypertension.

(ii) Underhydration

Persistent underhydration (also known as 'hypovolemia') can result in cramps, nausea, dizziness, intradialytic hypotension and longer recovery time after dialysis. Intradialytic hypotension has further been associated with increases in cardiovascular events and mortality (Stefansson et al. 2014; Flythe et al.

2015). Depletion of fluid levels has also been linked to the loss of residual kidney function, and consequently a reduction in urine output. As with overhydration, underhydration can also occur without the appearance of symptoms.

3.3 Diagnostic and care pathway

Several guidelines relating to chronic kidney disease (CKD) and dialysis have been identified. These include NICE's guidelines on chronic kidney disease, peritoneal dialysis, anaemia management in chronic kidney disease and hyperphosphatemia management in chronic kidney disease. NICE technology appraisal guidance 48 provides recommendations on the setting for haemodialysis. A NICE guideline on renal replacement therapy is currently in development. The management of chronic kidney disease is further described in the NICE pathway on chronic kidney disease. In addition, guidelines have also been produced by the Renal Association, on Haemodialysis, Nutrition in CKD and Peritoneal Dialysis in CKD. The diagnosis and management of hypertension is described in the NICE pathway on hypertension and the Renal Association's Cardiovascular Disease in CKD guideline provides recommendations on managing hypertension in people on dialysis.

No guidelines have been identified that provide recommendations on monitoring the hydration status of people on either haemodialysis or peritoneal dialysis to guide how much fluid to remove during dialysis. Guidelines relating to measuring the 'dose' or 'adequacy' of dialysis have typically focused on easily measured markers such as urea and creatinine.

A national survey of fluid management practice in haemodialysis patients in the UK (which received responses from 61% of UK renal centres) reported that 22% of responding centres had an agreed fluid management policy and in 47% of centres management was carried out at the discretion of the individual clinician (Dasgupta et al. 2016).

3.3.1. Fluid monitoring

A central concept in dialysis management strategies is the setting of a 'dry' or 'target' weight (the term 'ideal weight' has also been used). This is often defined as how much a person should weigh at the end of a haemodialysis session or, for people who have peritoneal dialysis, how much they should weigh in the morning. Definitions of the term dry weight have included the lowest post-dialysis weight that can be tolerated before symptoms of underhydration develop or the post-dialysis weight at which a person won't develop symptoms of overhydration before the next dialysis session (Agarwal

and Weir 2010; Celik et al. 2011). While the terms dry and target weight are often used interchangeably in clinical practice and in published literature, hereafter the term 'target weight' will be used in this document.

Target weight will not necessarily be the same as a person's normally hydrated weight ('normohydrated weight'; the weight of a person with no fluid excess or deficit). Fluid will accumulate in between haemodialysis sessions (typically over 2-3 days) therefore target weights may be set to keep an individual within an acceptable range around their normally hydrated weight between dialysis sessions. In addition people may have different tolerances to being over- or underhydrated so target weight may be set, relative to the normally hydrated weight, to reflect this.

The comparison of a person's current and target weight will identify the amount of fluid to be removed during dialysis, to either get to the target weight or as close to it as is felt possible. Haemodialysis machines can be programmed to remove a specified volume of fluid (ultrafiltration volume) over a set period of time, or the frequency and length of sessions can be increased to remove greater amounts of fluid. For peritoneal dialysis, use of increased concentrations of dialysis fluid introduced to the abdomen, exchanged more frequently, will cause more fluid to be removed.

Target weight is usually determined by clinical assessment, typically by gradually reducing a patient's post-dialysis weight over successive dialysis sessions until it is as low as can be tolerated. This policy was identified by 53% of responding UK renal centres as best describing their policy for setting dry weight for haemodialysis patients (Dasgupta et al. 2016). Further reported policies included a compromise approach between reducing post-dialysis weight and maintaining urine volume (38% centres), and having stratified policies to take into account a person's cardiovascular function (19% centres).

Preserving residual renal function is an important consideration for fluid management strategies. The Renal Association's Haemodialysis guideline suggests that the management of haemodialysis patients should include dialysis strategies that preserve residual renal function (Guideline 5.9). In addition, guidelines concerning Peritoneal Dialysis in CKD (also from the Renal Association) recommend that strategies that preserve renal function should be used where possible, including the avoidance of episodes of underhydration (Guideline 4.5).

3.3.2. Clinical assessment

Assessment of fluid status to set, or adjust, target dialysis weight is usually based on clinical judgement and the identification of symptoms of over- or underhydration. Clinical parameters that are considered can include:

- Blood pressure
- Presence of oedema
- Changes in weight
- Residual renal function
- Any reported intradialytic or interdialytic symptoms of over- or underhydration (for example cramps, fatigue, diarrhoea, nausea, dizziness, fainting, breathlessness, decreased appetite, visual disturbances)
- Any pre-existing cardiovascular conditions.

In additional to these clinical parameters, healthcare practitioners may take further factors into account when setting target weight. These include any recent admission to hospital or if the person has a new fistula to enable vascular access for dialysis.

Dasgupta et al. (2016) reported on the methods used by renal centres for routine assessment of fluid status in haemodialysis patients. Clinical features taken into account were: interdialytic weight gain (87% centres), intradialytic hypotension (89% centres), pre-dialysis symptoms (60% centres), and post-dialysis symptoms (67% centres). Assessments used were: identifying peripheral oedema (96%), resting blood pressure (91%), auscultation of lung bases (76%), jugular venous pressure (69%), use of relative blood volume monitors (49% centres), postural blood pressure (47% centres) and use of Crit-Line monitors (27% centres). In addition, bioimpedance devices were used in 27% of responding centres (Dasgupta et al. 2016). Furthermore, 22% of surveyed renal centres routinely assessed the residual renal function of their haemodialysis patients. The assessment of creatinine clearance using interdialytic urine collection was the most used method, with the frequency of collection varying from monthly to every 6-12 months.

While the above figures relate to haemodialysis patients, similar methods and assessment criteria are used for people undergoing peritoneal dialysis treatment.

Dasgupta et al. (2016) also reported that in 42% centres routine assessments of fluid status are carried out by a dialysis nurse, with the remainder being conducted by consultant nephrologists, middle-grade doctors or trainees. In addition, a consultant nephrologist assessed patients in 58% of centres if there was concern about their symptoms or blood pressure.

3.3.3. Frequency of assessment

A survey of UK renal centres by Dasgupta et al. (2016) reported that 58% of centres reviewed the target weight of their haemodialysis patients once a month, 33% did this every 3 months and the remaining centres only assessed target weight when there was a clinical concern (Dasgupta et al. 2016).

The frequency of assessments to check fluid status and target weight in general varies widely. Experts suggested frequencies between every 1 to 6 months in current practice, commenting that the frequency of assessment is often increased for patients who don't have a stable weight or who have persisting symptoms of over- or underhydration. For children and young people, particularly if they are growing, the assessment frequency may need to be varied accordingly. Several experts also commented that assessment often only occurs if symptoms of over- or underhydration are reported. Opportunities to report symptoms (and have weight and blood pressure measured) for people who have their haemodialysis carried out at a hospital or satellite unit can occur at dialysis sessions which will happen several times a week. A survey of UK renal centres in 2014 reported that 95.4% of adult haemodialysis patients had a frequency of 3 dialysis sessions per week (UK Renal Registry 2015).

3.3.4. Reference standard for fluid overload

The measurement of the hydration related parameters produced by bioimpedance devices has been validated against gold standard measurements. For example total body water measurements have been validated against deuterium dilution and extracellular water measurements have been validated against bromide dilution. However no generally accepted gold standard exists for the measurement of fluid status, that is identifying if a person is over- or underhydrated and, if so, to what extent. Validation of overhydration measures have been made by using clinical assessment and ultrafiltration volume (Wabel et al. 2009). Other methods used to assess the volume status of people on dialysis have included lung ultrasound to evaluate extravascular lung water, measurement of inferior vena cava diameter and the measurement of brain natriuretic peptide (BNP) levels.

3.4 Patient issues and preferences

Haemodialysis, unless carried out at home, requires frequent visits to a hospital or satellite unit, typically three times a week for around 4 hours per visit. Any potential reduction in the required frequency of dialysis sessions will reduce travel requirements and the extent to which dialysis sessions affect work or leisure time.

A reduction in the incidence of symptoms associated with being over- or underhydrated will also improve quality of life for people on dialysis. For example, a decrease in intradialytic hypotension will reduce side-effects associated with having dialysis and potentially make longer sessions more tolerable. In addition, identification of overhydration as the cause of high blood pressure may also reduce the need to take antihypertensive medication.

People who are on dialysis need to monitor and restrict the amount of fluid that they drink. This is particularly the case for people who have haemodialysis because it may not be possible to remove several days' worth of excess fluid in a haemodialysis session if large amounts are drunk between sessions, but may also be an issue for people on peritoneal dialysis. Changes in diet may also be required, for example, to avoid salty, processed or spicy foods that can increase thirst or to improve glycaemic control. In addition, remaining within a recommended daily fluid allowance can be difficult, particularly during hot weather. The amount of fluid recommended per day depends, amongst other things, on the amount of urine produced; therefore people with greater residual renal function will be able to drink more.

Increased involvement of the patient in their fluid management could improve their understanding of their fluid status and consequently improve compliance with future fluid intake recommendations. This could lead to improved health outcomes by reducing the number of complications.

4 Comparator

The comparator to be used in this assessment is the use of clinical assessment (without the use of bioimpedance devices) to determine fluid status and set, or adjust, target weights for people with chronic kidney disease who are on dialysis. This may include the consideration of blood pressure measurements, changes in weight, the presence of oedema, assessment of residual renal function, any pre-existing cardiovascular conditions and also any reported symptoms of over- or underhydration (such as dizziness or nausea).

Clinical assessment does not directly measure fluid levels in the body to identify if a person is over- or underhydrated, but rather relies on the appearance of symptoms of these conditions. This approach could therefore miss individuals who are asymptomatic despite having an excess or deficit of body water. For example, symptoms such as oedema may not appear until individuals are substantially overhydrated and people with fluid overload do not always exhibit high blood pressure.

Additionally, clinical features are only surrogate markers for fluid overload and can therefore result from other, unrelated causes. This could lead to fluid levels being inappropriately adjusted. For example, a response to high blood pressure assumed to be caused by fluid overload (but actually caused by other factors) may be to remove increasing amounts of fluid during dialysis. This may lead to a person becoming underhydrated with loss of residual renal function.

5 Scope of the assessment

Table 1: Scope of the assessment

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. Where 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
Possible 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 over- 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 over- or underhydration • Changes of dialysis modality (from peritoneal dialysis to haemodialysis) because of fluid overload • Adherence with 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 arising 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.

6 Other issues for consideration

The lack of a gold standard for assessing hydration status, and the extent of over- and underhydration, makes it difficult to measure the accuracy of monitoring.

There is likely to be heterogeneity in studies on fluid management because there is considerable variation in how clinical assessment is used to determine fluid levels and set dialysis volumes in people undergoing dialysis. In addition, clinical assessment and dialysis protocols may vary in different countries so some studies may not be applicable to an NHS setting.

Where possible the economic modelling should include scenarios which consider the impact of different frequencies of monitoring with bioimpedance devices. For example, children may require more frequent monitoring during periods of growth.

Costs used in the economic modelling for haemodialysis may differ depending on where haemodialysis is carried out (at home or at a renal unit) and the grade of staff carrying out the monitoring.

No economic models have been identified relating to the assessment of fluid status in people with chronic kidney disease who are on dialysis.

7 Potential equality issues

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 (NICE guideline on peritoneal dialysis) as does the presence of fluid overload in people on dialysis (Guo et al. 2013). In addition, chronic kidney disease has greater incidence rates in people of south Asian family origin (from India, Bangladesh, Sri Lanka and Pakistan), potentially due to higher rates of diabetes, and 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 functions of the condition rather than of the use of the technology.

The detection of over- or underhydration using clinical assessment may be more difficult in people with extremes of body composition, for example people who are obese. This group may therefore benefit from the use of bioimpedance devices. In addition, normal ranges of lean or adipose tissue body composition may differ between ethnicities which may impact on the interpretation of test results in practice, particularly where the tissue and fluid models used in the devices have been validated in non-representative populations. When using bioimpedance devices for 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. In addition, if it is not possible for electrodes to be placed in recommended positions, potentially because of amputations or multiple open wounds, an alternative electrode configuration would need to be used; 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 derived from an optimum configuration of electrodes. The use of bioimpedance devices may not be possible for people with implanted electronic devices (for example, pacemakers) or, in the case of some devices, for pregnant women.

In addition, the devices may be less suitable for use in young children, particularly under 2 years, because they may not stay still long enough for measurements to be made.

8 Potential implementation issues

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 required; particularly as 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.

9 Authors

Thomas Walker
Topic Lead

Rebecca Albrow
Technical Adviser

June 2016

Appendix A Glossary of terms

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.

Appendix B Abbreviations

CKD

Chronic kidney disease

ECW

Extracellular water

kHz

Kilohertz

RRF

Residual renal function

TBW

Total body water

Appendix C References

Agarwal R and Weir MR (2010) Dry-Weight: A Concept Revisited in an Effort to Avoid Medication-Directed Approaches for Blood Pressure Control in Hemodialysis Patients. Clin J Am Soc Nephrol. 5(7): 1255–1260

Bozzetto S, Piccoli A and Montini G (2010) Bioelectrical impedance vector analysis to evaluate relative hydration status. Paediatric Nephrology 25; 329

Celik G, Kara I, Yilmaz, M and Apiliogullari S (2011) The Relationship between Bioimpedance Analysis, Haemodynamic Parameters of Haemodialysis, Biochemical Parameters and Dry Weight. The Journal of International Medical Research 39: 2421 – 2428

Chamney P, Wabel P, Moissl UM, Müller MJ, Bosy-Westphal A, Korth O and Fuller NJ (2007) A whole-body model to distinguish excess fluid from the hydration of major body tissues. Am J Clin Nutr; 85: 80-89

Dasgupta I, Farrington K, Davies SJ, Davenport A and Mitra S (2016) UK National Survey of Practice Patterns of Fluid Volume Management in Haemodialysis Patients: A Need for Evidence. Blood Purif 41:324-331

Flythe JE, Xue H, Lynch KE, Curhan GC and Brunelli SM (2015) Association of Mortality Risk with Various Definitions of Intradialytic Hypotension. JASN 26: 724-734

Guo Q, Yi C, Li J, Wu X, Yang X, Yu X (2013) Prevalence and Risk Factors of Fluid Overload in Southern Chinese Continuous Ambulatory Peritoneal Dialysis Patients. PLoS ONE 8(1): e53294

Lindley E, Devine Y, Hall L, Cullen M, Cuthbert S, Woodrow G and Lopot F (2005) A ward-based procedure for assessment of fluid status in peritoneal dialysis patients using bioimpedance spectroscopy. Peritoneal Dialysis International, Vol. 25 (2005), Supplement 3

Moissl U, Wabel P, Chamney PW, Bosaeus I, Levin NW, Bosy-Westphal A, Korth O, Müller MJ, Ellegård L, Malmros V, Kaitwatcharachai C, Kuhlmann MK, Zhu F, Fuller NJ (2006) Body fluid volume determination via body composition spectroscopy in health and disease. Physiol. Meas.; 27: 921-933

Keane DF and Lindley E (2015) Use of hand-to-hand measurements for body composition monitoring in patients with inaccessible or amputated feet. Journal of Renal Care 41: 28–32

Ronco C, Verger C, Crepaldi C, Pham J, De los Ríos T, Gauly A, Wabel P and Van Biesen W for the IPOD-PD Study Group (2015) Baseline hydration status in incident peritoneal dialysis patients: the initiative of patient outcomes in dialysis (IPOD-PD study). Nephrol. Dial. Transplant. First published online March 11, 2015 doi:10.1093/ndt/gfv013

Stefánsson BV, Brunelli SM, Cabrera C, Rosenbaum D, Anum E, Ramakrishnan K, Jensen DE and Stålhammar N (2014) Intradialytic Hypotension and Risk of Cardiovascular Disease. CJASN vol. 9 no. 12 2124-2132

*UK Renal Registry 2015, 18th Annual Report of the Renal Association, Fogarty D, Castledine C, Sinha MD, Fraser S, UK Renal Registry, Bristol, UK

* The data reported here have been supplied by the UK Renal Registry of the Renal Association. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the UK Renal Registry or the Renal Association.

Van Biesen W, Williams JD, Covic AC, Fan S, Claes K, Lichodziejewska-Niemierko M, et al. (2011) Fluid Status in Peritoneal Dialysis Patients: The European Body Composition Monitoring (EuroBCM) Study Cohort. PLoS ONE 6(2): e17148

Wabel P, Chamney P, Moissl U and Jirka T (2009) Importance of Whole-Body Bioimpedance Spectroscopy for the Management of Fluid Balance. Blood Purif 27:75-80

Wizemann V, Wabel P, Chamney P, Zaluska W, Moissl U, Rode C, Malecka-Masalska T and Marcelli C (2009) The mortality risk of overhydration in haemodialysis patients Nephrol. Dial. Transplant. 24 (5): 1574-1579.