NICE National Institute for Health and Care Excellence

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

Diagnostics Assessment Report (DAR) - Comments

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British Kidney Patients Association	1	3	Results	The comment 'The results of the meta-analyses conducted for this assessment showed that using the BCM - Body Composition Monitor, as compared with standard clinical methods, for fluid management in people with chronic kidney disease significantly reduced systolic blood pressure' is a significant development in management of dialysis patients in recent years and will be of great interest to patients. It therefore surprising that no discussion of potential opportunity to improve self-management is mentioned.	We have not further discussed these results because of the limitations of the current evidence base (i.e. majority of RCTs at unclear risk of bias and of relatively short duration). For the publication of this report in the NIHR Journals Library we will slightly revised the Discussion section of the Scientific Summary to reflect these limitations and the fact that the findings of this assessment are only tentative and should be interpreted with caution.
British Kidney Patients Association	2	11	Background	The role and skill of the healthcare professional in using other existing methods to assess fluid levels is disregarded and should be acknowledged. It is not perfect but is an essential part of the skills used in managing a dialysis patient. The potential for adverse events from underhydration could be partly offset by a skilled healthcare professional.	We agree that the quality of dialysis care depends on the experience and skills of the healthcare professionals who assess and manage patients' fluid levels. However, we have not found any specific information on this in the literature we have screened and assessed for this assessment.
British Kidney Patients Association	3	16	Conclusions	The summary does not mention benefits to quality of life or measures such as breathlessness (related to carrying too much fluid).	Whilst this is a hypothesised benefit of bioimpedance guided fluid management, there was a lack of randomised data on patient reported outcomes and health related quality of life.
British Kidney Patients Association	4			Cost estimates are based on use of device 4 times a year, whereas the former appraisal document states that it is recommended for use 12 times a year, which	The quarterly testing frequency was informed by members of the expert committee and by the information collected

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				would lead of course to a different total cost for comparison.	during the scoping phase of this assessment. To assess the sensitivity of this assumption, scenario analyses were conducted based on 12 tests per year (see Table 23 of DAR).
British Kidney Patients Association	5	85		Please state which tariff year is being used in cost models as a new tariff has been announced by NHS Improvement, which will apply from April 2017-March 2019	The 2014/2015 NHS reference costs were used, as the most up to data reference cost available at the time the analysis was undertaken. This will be clarified for final publication in the NIHR Journal Library. The NHS reference costs reflect average estimates of costs incurred by trusts delivering renal replacement therapy, rather than the prospectively agreed payments for services. For reassurance, we have assessed the impact of using the new agreed 2017 payment by results best practice tariffs in place of the NHS reference costs (assuming the same activity levels across the different approaches to dialysis). This has very little impact on the estimated annual costs of haemodialysis (£24,535 versus £23,998) but has a slightly larger impact on the estimated annual cost of PD (£19,843 versus £25,129). Updating the model to reference these alternative values, the base ICER for clinical effectiveness

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					scenario 3 only changes by ~£400 (from £59,146 to £58,739). For the PD subgroup alone, the ICER, including dialysis costs, comes to ~£43,991 per QALY gained.
Bodystat Ltd	6	16	2.2	Please amend wording from paragraph "Values for extracellular water, intracellular water, total body water, and volume of over/underhydration are obtained from the same physiological models as used in the BCM - Body Composition Monitor analysis." To read: "The values for extracellular water, intracellular water, total body water, and volume of over/underhydration are similar to those obtained from the physiological models used in the BCM - Body Composition Monitor analysis."	For the publication of this report in the NIHR Journals Library we will revise the sentence on page 19 as follows: "The values for extracellular water, intracellular water, total body water, and volume of over/underhydration are similar to those obtained from the physiological models used in the BCM - Body Composition Monitor analysis."
Fresenius Medical Care	7	14	2.2.	We suggest to underline the difference between Bioimpedance Spectroscopy (BIS) and Multi-frequency Bioimpedance Analysis (MF-BIA): Multi frequency devices (MF-BIA) measure from 3 to 8 frequencies (between 5-800 kHz), but these devices allow no accurate differentiation between ECW and ICW. MF-BIA uses empirical linear regression models to evaluate FFM, TBW, ICW and ECW that usually only apply to healthy subjects. Bioimpedance spectroscopy (BIS) uses physiological modelling and mixture equations (Cole–Cole plot and Hanai	For the publication of this report in the NIHR Journals Library we will revise the text on page 16 as follows: "Single frequency bioimpedance analysis uses only one single current (e.g. 50 kHz), multiple frequency bioimpedance analysis uses between three and eight currents of multiple frequencies (between 5 and 800 kHz) and bioimpedance spectroscopy uses a range of frequencies (5 to 1000 kHz).[29, 48] The main difference between multiple frequency bioimpedance

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				formulae) to first determine the electrical resistance of ECW and ICW and then calculate the volumes of these respective compartments. This is essential for identification of OH – the BCM – Body Composition Monitor uses the BIS technique and is validated in patient populations with an impaired fluid status. Extrapolation of results to other devices: The positive results from the studies performed with the BCM cannot be extrapolated to the other devices assessed in the diagnostic assessment reports. As the models and the output parameters are different between the different devices the results cannot be extrapolated. Also there is no evidence available for the clinical effectiveness of the non-BCM devices. There is also no study available that compares the results of the other devices with BCM to allow a generalization of the achieved results.	analysis and bioimpedance spectroscopy is that multiple frequency devices do not allow accurate differentiation between ECW and ICW. Multiple frequency bioimpedance analysis uses empirical linear regression models to evaluate FFM, TBW, ICW and ECW that usually only apply to healthy people. In contrast, bioimpedance spectroscopy uses physiological modelling and mixture equations (Cole-Cole plot and Hanai formulae) to first determine the electrical resistance of ECW and ICW and then calculate the volumes of the respective compartments, which is essential for identification of overhydration." See Comment 11 below.

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Fresenius Medical Care	8	67	4.2.	last sentence of 1st paragraph: ….of increasing the proportion that are ~~undehydrated~~ underhydrated, this model could potentially overestimate the benefits.	Amended as suggested.
Fresenius Medical Care	9	58	4.2 figure 13	Reposition the arrow: from 4 (post incident CV event (PD) to 6 (post transplant (post CV event) instead of 4 to 5 (Post transplant)	The diagram will be amended as suggested for final publication in the NIHR Journal Library. This amendment has identified a minor structural imprecision in the model, which we have corrected and we will provide an erratum to the DAR in due course. However, having checked through the impact of revising this in the deterministic analyses, it only changes the base case ICERs by £2 (scenario 3, Table 20-21) to £8 (Scenario 1, Table 20-21). The subgroup ICER most affected by this change relates to the subgroup analysis of PD patients (Table 24 of the EAG report). Here, the ICER changes by £24 when the transition state is revised, from £14,085 to £14,061. Impacts on further scenarios are also minimal.
Fresenius Medical Care	10	120	5.2	Limitations of the assessment:	We accept that bioimpedance monitoring may have potential benefits in pre-dialysis

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				The assessment protocol has included the bioimpedance technique to guide the fluid management in CKD patients having dialysis. Other applications of the biompedance technique, as guiding the fluid management in predialysis patients or measuring the nutritional status of patients has not been included in the assessment. This limitation of the assessment scope might result in an underestimation of the full diagnostic value of the bioimpedance technique in ESRD patients.	patients, and in helping to guide nutritional status. However, these applications were beyond the scope of this assessment.
Fresenius Medical Care	11	5	1	Page 5 chapter: Generalisability of the findings We would like to suggest a clearer statement that generalisability of the report is really limited because the assessment is only based on BCM studies. We suggest to include a statement as on page 121 (chapter limitations): “We were able to include only studies involving the BCM- Body Composition Monitor due to a lack published evidence of the effectiveness of the other specified bioimpedance devices. As the generalisability of the effects of bioimpdance devices has yet to be determined, we cannot generalise our findings across the devices beyond the BCM- Body Composition Monitor.	For the publication of this report in the NIHR Journals Library we will revise the text on page 5 as follows: “The included trials involved only the BCM - Body Composition Monitor due to the lack of published evidence on the effectiveness of the other multiple frequency bioimpedance devices. Therefore, the effects of the BCM - Body Composition Monitor cannot be generalised across other specified bioimpedance devices as the models and output parameters vary between devices. Furthermore, there are no studies which directly compare the effectiveness of the BCM - Body Composition Monitor with any of the other specified bioimpedance devices.”

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Fresenius Medical Care	12	5.2	120	Following our understanding as manufacturer of the BCM the ICER for bioimpedance guided fluid management should preferably not include dialysis costs in the model. The monitoring technique of the BCM was developed to improve the diagnostic strategies for the dialysis patients to improve hydration status, arterial stiffness and blood pressure and also the reduction of hospitalization costs and medication. For this targeted improvements caused by the device and the management strategy the BCM seems to be ~~s~~ cost effective – as shown in the report. The impact on ESRD itself was not intended and cannot be performed with a diagnostic device – therefore dialysis costs should be considered independently.	We accept that there are arguments for both inclusion and exclusion of dialysis costs in the cost-effectiveness analyses. For this reason we have provided results with and without dialysis costs.
Fresenius Medical Care	13	48	3.3	We would like to draw your attention to a study which showed in a large patient cohort (more than 35.000 patients) that correcting the overhydration (evaluated by BCM) is more important to reduce the mortality in dialysis patients than to correct the blood pressure and that overhydration is an independent mortality risk factor in dialysis patient with low, normal and high blood pressure. The manuscript has recently been submitted for publication.	Thank you for pointing out this recent manuscript and for providing a 'confidential' copy.

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				Title: EFFECT OF CHRONIC EXPOSURE TO FLUID OVERLOAD ON MORTALITY IN END STAGE KIDNEY DISEASE (ESKD) PATIENTS: a cohort study in a hemodialysis network in 26 countries Authors: Zoccali C, Moissl U, Chazot C, Mallamaci F, Tripepi G, Arkossy O, Wabel P, Stuard S. Submission 21-12-2016	
Fresenius Medical Care	14		General	Our company highly appreciated the enormous effort of the National Institute for Health and Care Excellence to develop this comprehensive assessment of the BCM technology on such a high scientific quality level. We really made an effort to include different departments and views within our company into an accurate and detailed review process. According to our actual experience the limited timeframe of 18 days (including the Christmas week) seems to be not sufficient to review a manuscript of 188 pages on a desirable quality level. For this reason we would encourage you to think about an extension of the stakeholder review period.	No response needed.
Fresenius Medical Care	15		General	A detailed de novo economic model for multiple frequency bioimpedance has been developed using the TreeAge Pro software. Having no practical experience with this software or with the selected semi-Markov model we had been confronted with a	No response needed.

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				great complexity to follow the details of the modelling procedure within the limited timeframe of the review.	