NICE National Institute for Health and Care Excellence

DIAGNOSTICS ASSESSMENT PROGRAMME

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

Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 23 March 2017

THEME: Additional evidence

Comment number	Name and organisation	Section number	Comment	NICE response
1	The BISTRO Study Group	Literature search.	There is a study undertaken – according to clinicaltrials.gov NCT02325856 Lim. P-S. Application of Bioimpedance Spectroscopy in Taiwan Dialysis Patients It is not clear where the data is published but one of us has seen this trial referred to with outcome data.	Thank you for your comment which the committee considered. The committee heard from the external assessment group that results from this study have been published in the following paper and were included in the diagnostics assessment report for this topic (see section 4.1 of the guidance document): Huan-Sheng C, Yeong-Chang C, Ming-Hsing H, Fan-Lieh T, Chu-Cheng L, Tsai-Kun W, et al. Application of bioimpedance spectroscopy in Asian dialysis patients (ABISAD-III): a randomized controlled trial for clinical outcomes. Int Urol Nephrol 2016;12:12.
2	The BISTRO Study Group	Literature search.	Again there is a trial Darlan M. Lara . 2010 NCT01104909. We believe that this was published as a PhD thesis – seen it referred to but not the actual data. Brazil.	Thank you for your comment which the committee considered.

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				The committee heard from the external assessment group that this PhD thesis assesses the use of the Maltron-BF906 device. The device is described as a single frequency device and is therefore outside the scope for this guidance, which assess the use of multiple frequency devices.
3	Fresenius Medical Care	4	In the last weeks an important paper was published in Kidney International – this paper analysies more than 8000 HD patients and analysis the mortality with respect to fluid overload, measured with the BCM - Impact of fluid status and inflammation and their interaction on survival: a study in an international hemodialysis patient cohort. [Dekker MJ, Marcelli D, Canaud BJ, Carioni P, Wang Y, Grassmann A, Konings CJ, Kotanko P, Leunissen KM, Levin NW, van der Sande FM, Ye X, Maheshwari V, Usvyat LA, Kooman JP; MONDO Initiative Kidney Int. 2017 Feb 13. pii: S0085-2538(16)30710-4. doi: 10.1016/j.kint.2016.12.008. [Epub ahead of print]] – it would be great if you could consider this paper in the report.	Thank you for your comment which the committee considered. The committee heard from the external assessment group that this paper provides evidence of an association between fluid status (as measured by the BCM device) and mortality. However, the paper does not provide data showing an effect of BCM guided fluid management on health outcomes when compared to fluid management without the device. The committee decided that no changes to the guidance were needed.

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4	Fresenius Medical Care	4.24	The analysis of the IPOD PD study data will be starting in this year – clinical trial number: NCT01285726 – it will bring important results concerning the fluid overload development in a large cohort of incident PD patients – it could be important to note this study in the report	Thank you for your comment which the committee considered. The committee heard from clinical experts that this is an observational cohort study of incident peritoneal dialysis patients, whose hydration state is assessed using the BCM device, and which is unlikely to provide data on an effect of BCM guided fluid management on health outcomes when compared to fluid management without the device. The committee concluded that no changes to the guidance were needed. NICE may review guidance before the expected review date when there is significant new evidence that it considers is likely to change the recommendations. NICE is keen to hear about any new evidence that becomes available before the review date (please send information to diagnostics@nice.org.uk). NICE will assess the likely impact of the new evidence on the recommendations and will

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				propose an update to the published guidance if required.
5	Fresenius Medical Care	4	Last week a new manuscript was accepted by the Journal of the American Society of Nephrology – academic in confidence – it will be published online in the next weeks – title: “Chronic Fluid Overload and Mortality in End Stage Renal Disease” – analysing the impact of fluid overload on mortality in > 34.000 incident HD patients from 26 countries – it would be great if you consider these important findings once the paper is published.	Thank you for your comment which the committee considered. The committee considered an academic in confidence copy of this paper and noted that an earlier version of this document had been provided by the stakeholder for consideration during the first committee meeting for this topic. The committee concluded that no changes to the guidance were needed.
6	Derwent Healthcare	1.1	They say they need more data to support the use of Bio-impedance BIA can be used to calculate the DW for Dialysis Patients. There has been many researches are being done with Multi-frequency BIA on Dialysis patients. By using InBody, the doctors are able to find out about body water balance, and also so that they can calculate the correct DW. If you refer to the research document A New Technique for Establishing Dry Weight in	Thank you for your comment which the committee considered. The committee heard from the external assessment group that the publication cited describes a method of estimating a person’s dry weight based on bioimpedance measurements. However the committee noted that in order to assess the clinical effectiveness of the included devices, evidence is needed that links the

			Haemodialysis Patient via Whole Body Bio impedance it shows a great example to on how the ecw was calculated and through this how the DW value was found.	measures of fluid status produced by the devices to health outcomes. The committee noted that these data were not available for the InBody S10 device (see section 5.3 of the guidance). Further, the committee noted that the included devices use different models to estimate how overhydrated or underhydrated a person is and that no data were available to determine the equivalence of these outputs between the devices included in the assessment (see section 5.3 of the guidance). The committee concluded that no changes to the guidance were needed.
7	Derwent Healthcare	5.2	5.2 requests more information to support S10. I've attached a zipfile that contains the relevant research documents so please refer to these documents.	Thank you for your comment which the committee considered. The committee considered the documents provided and heard from the external assessment group that none of the provided documents met the inclusion criteria for the diagnostics assessment

				report produced for this topic. In particular, the documents did not link the assessment of fluid status using the InBody S10 device with health outcomes. The committee concluded that no changes to the guidance were needed.

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THEME: Validation data in population subgroups

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8	Derwent Healthcare	5.2	Regarding the part in 5.2 that states "Also, validation data will be important for people with extremes of body composition, and across different ethnicities, because normal ranges of lean or adipose tissue body composition may differ between ethnicities." The ECW ratio that is used to calculate the DW is not only a standard made from Korean population, but it was on many different researches and these documents were based on many different races.	Thank you for your comment which the committee considered. Section 5.20 of the diagnostics guidance notes that the committee wished to encourage the companies to collect and publish data on both the validity of their device's underlying fluid model to calculate fluid overload and its associated clinical outcomes. Further the committee noted that validation data may be important for people with extremes of body composition, and across different ethnicities, because normal ranges of lean or adipose tissue body composition may differ between ethnicities. No data were found for the subgroups highlighted in the scope for this assessment.

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THEME: Differences between the technologies

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9	The BISTRO Study Group	3.7	The report states that the BodyStat uses the same physiological model to obtain values as the BCM. This is not correct. (At least this is the implication – 'based upon').	Thank you for your comment which the committee considered. Section 3.3 of the guidance document highlights that the models used by the BCM – Body Composition Monitor are adapted from techniques published by Chamney et al. (2007) and Moissl et al. (2006). The committee were aware that adaptations made to the models used by the BCM mean that the estimate of fluid overload it produces may not be comparable with those of other devices; this committee consideration is noted in section 5.3 of the guidance document.
10	The BISTRO Study Group	Various	The report fails to differentiate between BIS and multiple frequency BIA sufficiently. This may cause some confusion.	Thank you for your comment which the committee considered. The underlying technology used in each device is described in sections 3.2 to 3.7 of the guidance document where details on the number of frequencies at which the 3 included devices measure bioimpedance are given. Each

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				technology has been assessed individually and data from different devices have not been pooled; the distinction between BIS and BIA is therefore made on the basis of the technology name. Sections 4.2 and 4.3 of the guidance note that only data collected using the BCM device, which uses BIS, were found in the systematic review. The committee considered that in the absence of equivalence data, data from the BCM could not be extrapolated to the other BIS and BIA devices (see section 5.3 of the guidance document), therefore the clinical and cost effectiveness analyses relate to the BCM device only.

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THEME: General

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11	The BISTRO Study Group	General Comment	We welcome the guidance and its general support of the BISTRO trial which will hopefully provide more evidence on the clinical role for BI devices in supporting clinical management. It is helpful in supporting our view that there is true equipoise in the value of this technology. A particular strength of the assessment is the consideration of the bi-directional risk associated with fluid management which we believe to be important – i.e. excessive volume depletion to achieve surrogates (e.g. LV mass and blood pressure), as yet unproven, at the expense of excess ultrafiltration and premature loss of residual kidney function. From a wider contextual perspective, if BI technology is shown to support preservation of residual kidney function safely then this paves the way for safe introduction of incremental dialysis – which then would have very substantial cost benefit savings for the NHS as well as being more beneficial and acceptable to patients. It would be premature to do an economic analysis on this basis at this stage – but this would be the ultimate goal.	Thank you for your comment which the committee considered.

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THEME: General

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12	The BISTRO Study Group	Appendix 7	Top of the table the author Huan-Sheng is spelt incorrectly – written Huang	Thank you for your comment which the committee considered. The committee noted that this comment applies to the diagnostics assessment report for this topic, rather than the diagnostics consultation document.
13	Bodystat Ltd	General Comment	No Comments, although it should also be noted the recent increase in popularity of BIVA (Bioelectrical Impedance Vector Analysis) to monitor over-hydration in dialysis patients. Bodystat Quadscan 4000 & Multiscan 5000 use BIVA technology as well as spectroscopy to measure over-hydration.	Thank you for your comment which the committee considered. Section 3.7 of the guidance has been changed to highlight that the MultiScan 5000 can carry out BIVA.
14	Fresenius Medical Care	4.24	The BISTRO trial will bring very important results – especially in the range of dehydration. First data – still unpublished – shows an increased mortality and morbidity in the dehydrated population.	Thank you for your comment which the committee considered.