Bio-impedance spectroscopy added to a fluid management protocol does not improve preservation of residual kidney function in incident hemodialysis patients in a randomized controlled trial

OPEN

Simon J. Davies[1], David Coyle[2], Elizabeth J. Lindley[3], David Keane[4], John Belcher[1], Fergus J. Caskey[5], Indranil Dasgupta[6], Andrew Davenport[7], Ken Farrington[8], Sandip Mitra[9], Paula Ormandy[10], Martin Wilkie[11], Jamie MacDonald[12], Mandana Zanganeh[13], Lazaros Andronis[13], Ivonne Solis-Trapala[1] and Julius Sim[1]

[1]School of Medicine, Keele University, Keele, Staffordshire, UK; [2]NIHR Devices for Dignity, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [3]Renal Medicine, Leeds Teaching Hospitals NHS Trust, Leeds, UK; [4]CÚRAM SFI Research Centre for Medical Devices, University of Galway, Galway, Ireland; [5]Population Health Sciences, University of Bristol, Bristol, UK; [6]Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [7]UCL Department of Renal Medicine, Royal Free Hampstead NHS Trust, University College, London, UK; [8]Renal Medicine, East & North Hertfordshire NHS Trust, Hertfordshire, UK; [9]Manchester Academic Health Sciences Centre (MAHSC), University Hospital Manchester, Manchester, UK; [10]School of Health and Society, University of Salford, Manchester, UK; [11]Renal Medicine, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [12]Institute of Applied Human Physiology, Bangor University, Bangor, UK; and [13]Centre for Health Economics at Warwick, University of Warwick, Coventry, UK

Avoiding excessive dialysis-associated volume depletion may help preserve residual kidney function (RKF). To establish whether knowledge of the estimated normally hydrated weight from bioimpedance measurements (BI-NHW) when setting the post-hemodialysis target weight (TW) might mitigate rate of loss of RKF, we undertook an open label, randomized controlled trial in incident patients receiving HD, with clinicians and patients blinded to bioimpedance readings in controls. A total of 439 patients with over 500 ml urine/day or residual GFR exceeding 3 ml/min/1.73m^2 were recruited from 34 United Kingdom centers and randomized 1:1, stratified by center. Fluid assessments were made for up to 24 months using a standardized proforma in both groups, supplemented by availability of BI-NHW in the intervention group. Primary outcome was time to anuria, analyzed using competing-risk survival models adjusted for baseline characteristics, by intention to treat. Secondary outcomes included rate of RKF decline (mean urea and creatinine clearance), blood pressure and patient-reported outcomes. There were no group differences in cause-specific hazard rates of anuria (0.751; 95% confidence interval (0.459, 1.229)) or sub-distribution hazard rates (0.742 (0.453, 1.215)). RKF decline was markedly slower than anticipated, pooled linear rates in year 1: –0.178 (–0.196, –0.159)), year 2: –0.061 (–0.086, –0.036)) ml/min/1.73m^2/month. Blood pressure and patient-reported outcomes did not differ by group. The mean difference agreement between TW and BI-NHW was similar for both groups, Bioimpedance: –0.04 kg; Control: –0.25 kg. Thus, use of a standardized clinical protocol for fluid assessment when setting TW is associated with excellent preservation of RKF. Hence, bioimpedance measurements are not necessary to achieve this.

Kidney International (2023) ■, ■–■; https://doi.org/10.1016/j.kint.2023.05.016

KEYWORDS: anuria; bioimpedance spectroscopy; blood pressure; fluid status; patient-reported outcomes; residual kidney function

Most people starting dialysis have significant residual kidney function (RKF), and observational studies have consistently found that if this is preserved, it is associated with better survival and improved quality of life.[1–3] Despite this, there are few trials of interventions that might improve the preservation of RKF in hemodialysis (HD) patients, and where these have been undertaken, they are typically of fewer than 50 participants.[4–6] There is also plenty of evidence of inconsistency in the design and application of dialysis unit protocols to guide fluid management. This inconsistency was evident in a UK-wide survey of practices undertaken in preparation for the design of this study, where 50% of units claimed to use volume control to reduce dependence on antihypertensive medication.[7] The Dialysis

Correspondence: *Simon J. Davies, School of Medicine, Keele University, David Weatherall Building, Keele, Newcastle ST5 5BG, UK. E-mail: simonj.davies55@gmail.com*

Received 10 March 2023; revised 15 May 2023; accepted 18 May 2023

Lay Summary

Patients on hemodialysis benefit from keeping some of their own kidney function for as long as possible after starting dialysis. Removing too much fluid during dialysis, by setting a low target weight for the end of a dialysis session, could accelerate its rate of loss. We wanted to see how this could be affected by developing a standardized protocol for assessing fluid status in people new to dialysis and whether device called bioimpedance, which calculates the target weight independently, was better at guiding clinicians in avoiding setting target weights too low. A total of 437 people from 34 dialysis centers across the UK took part in the randomized trial for up to 2 years. Using bioimpedance did not result in better outcomes as clinicians were just as good in setting the target weight whether or not they used the device. We expected that approximately 25% would lose their own kidney function after 1 year. We found that this was much lower in both groups, such that <25% lost their kidney function by 2 years. There was good evidence that clinical staff engaged with patients' views when deciding whether to change the target weight. Safety, transplantation rates, and numbers of deaths were not affected. Bioimpedance does not improve on setting the target weight in the context of a standardized approach to fluid management. Applying a strategy that avoids excessive fluid removal is associated with better-than-expected preservation of kidney function.

Outcomes and Practice Patterns Study also found considerable variation in practices related to fluid management and that a protocol specifying the frequency of assessment was associated with better outcomes.[8]

Bioimpedance (BI) is frequently used in HD units to monitor fluid status and body composition. There is evidence that overhydration and loss of lean tissue mass, measured using BI, are associated with shorter survival[9–12] over and above other factors such as demography, comorbidity, inflammation, and blood pressure. What is less clear is whether BI has a role to play in guiding the adjustment of the postdialysis target weight (TW) when managing fluid status in HD. For example, reducing overhydration might help in controlling blood pressure but may risk intravascular volume depletion, putting RKF at risk.[13] In making recommendations for the use of BI, the National Institute for Health and Care Excellence in the UK considered that there was insufficient evidence to recommend its routine application.[14] This led the Health Technology Assessment Programme of the UK National Institute of Health and Care Research to develop a competitive funding call to evaluate the use of BI in guiding fluid management, including its cost-effectiveness, and, after wide consultation, the specified outcome of interest was RKF.[15]

One of the potential risks of accelerated loss of RKF in HD is the 3-times-weekly removal of fluid, which has the potential to cause circulatory volume depletion, reduced native kidney perfusion, and ensuing kidney damage.[16] In responding to the Health Technology Assessment call, we hypothesized that avoiding setting the TW below the estimated normally hydrated weight from BI (BI-NHW) where possible might limit the damage caused by excessive volume depletion, so helping to preserve RKF. To establish whether this use of the BI-NHW was associated with a lower rate of loss of RKF, we designed a pragmatic randomized controlled trial in which clinicians setting the TW were blinded to the BI data in the control group. We recognized that the imposition of a protocol that defines the timing of fluid assessments and includes the measurement of RKF and the use of a proforma to capture the assessment in detail is likely to modify standard practice. However, given that dialysis fluid assessments are an example of complex decision-making that should include patient preferences, this was felt to be essential. Here we report on the main findings of the trial, including an analysis of the integrity of the intervention.

METHODS

Trial design and participants

The trial protocol was published before the recruitment of participants.[17] Briefly, this was an open-label, longitudinal, randomized (1:1), multicenter UK-wide pragmatic trial of incident HD patients adopted onto the National Institute of Health and Care Research Clinical Research Portfolio (CPMS31766). Potential participants were adult HD patients within 3 months of commencing HD, identified using local processes and screened for eligibility. Inclusion criteria were broad but required evidence of RKF, defined as >500 ml of urine volume per day or a measured glomerular filtration rate (GFR) >3 ml/min per 1.73 m^2. Exclusion criteria were the inability to give consent or collect urine for RKF estimations and either high risk of death or expected transplantation within 6 months. Serious adverse events were monitored throughout the trial and categorized according to the Common Terminology Criteria for Adverse Events. The trial was sponsored by Keele University, UK, and registered before participant enrollment (ISCCTN number: 11342007). Study governance included independent steering and data monitoring committees and a patient-led (DC) advisory group, all receiving regular reports. The study had UK Integrated Research Ethics approval (206213), and all participants gave their written consent.

Intervention

Clinicians—doctors or nurses—whose usual role was to assess fluid status were trained in the use of the fluid assessment proforma (see Supplementary Slide Deck 1 in the Supplementary Material and protocol[17]) and asked to set the postdialysis TW so as to avoid excessive volume depletion, where possible. For the patients randomized to the intervention arm, the BI-NHW could be used in addition to clinical judgment. For patients in the control arm, the TW was set using clinical judgment only.

To achieve blinding, BI measurements (see below) were taken independently by research nurses in both groups, but the BI-NHW measurements were transferred to the proforma for patients in the intervention only. Otherwise, the proformas were identical. Protocol fluid assessments were made monthly for 3 months and then 3-monthly for up to the maximum follow-up period of 2 years, with scope for additional assessments if clinically required.

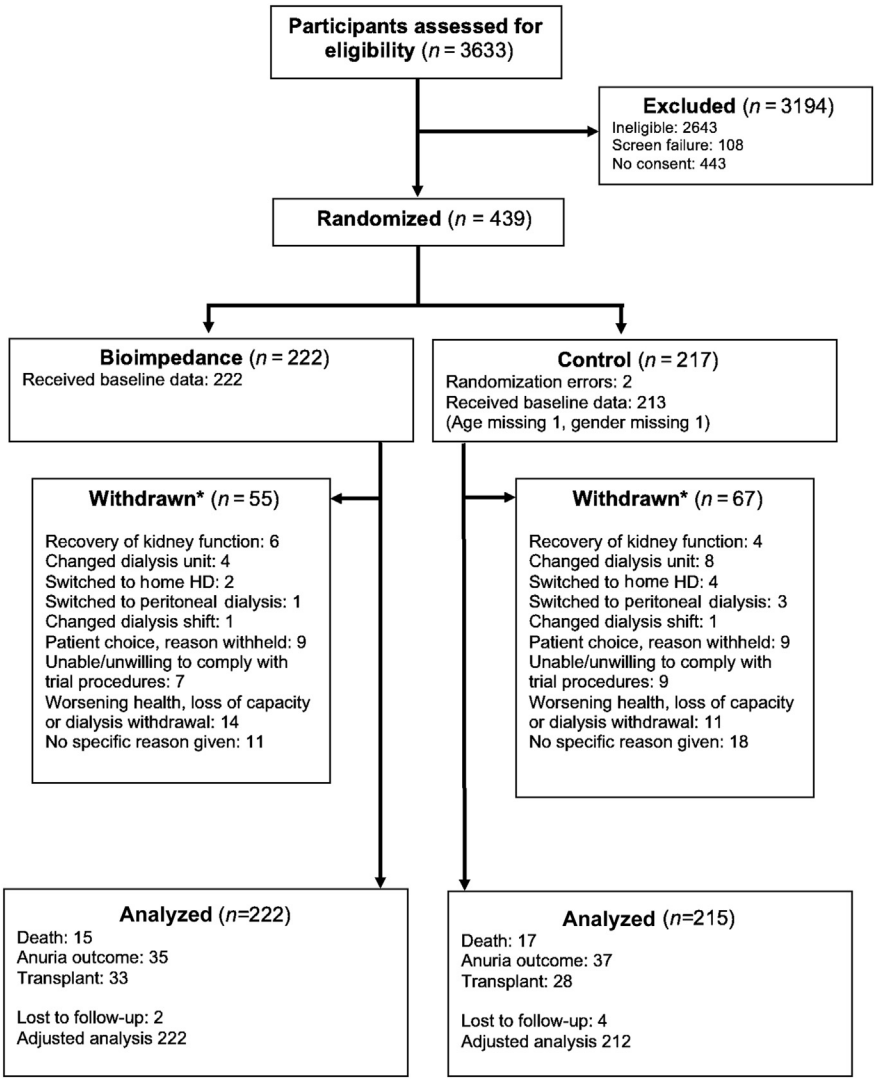


Figure 1 | CONSORT diagram. *Trial subjects did not have to give a reason for withdrawing from the study. HD, hemodialysis.

Bioimpedance

The trial funder specified an open approach to selection of the BI device. In an independent selection process, overseen by Kidney Research UK, 4 of 6 invited BI manufacturers submitted proposals that were judged according to their technical specification, patient interface, evidence base, ability to support the trial, and value for money. The Fresenius BCM was the clear preference. All centers were given formal training in the use of the BCM, repeated if necessary due to the change in personnel (see Supplementary Slide Deck 2 in the Supplementary Material). The BCM generates the BI-NHW by modeling what the weight would be if the tissues (muscle, fat, and interstitium) were normally hydrated.[18] Readings were taken ≤1 week before fluid assessments by an independent observer. Full BI data sets were downloaded onto unit computers, and throughout the trial, EJL and DK undertook regular blinded quality control assessments of submitted readings.

Outcomes

The main outcome of interest was RKF, assessed every 2 months and measured both as time to anuria (designated the primary outcome and defined as ≤100 ml/d or ≤200 ml of urine volume in the short interdialytic period, confirmed with a follow-up measure at 2 weeks) and as the rate of decline in measured GFR. The latter was calculated from an interdialytic urine collection and pre- and post-dialysate blood samples as the mean of the urea and creatinine clearances adjusted for body surface area using a "GFR calculator" (see Supplementary Slide Deck 3 in the Supplementary Material). Validation and audit of this approach, which enabled calculation when some of the blood samples were missing, have been published elsewhere.[19] Secondary outcomes included pre- and postdialysis blood pressure at the time of fluid assessment and patient-reported outcomes, of which those reported here include a generic health-related quality-of-life question: "how good is your health today?" (EQ-5D-5L visual analog scale: 0–100, rating worst to best health)[20] and dialysis-related symptoms (Integrated Palliative Care Outcome Scale-renal),[21] collected every 3 months.

Sample size

This was based on the primary outcome, time to anuria. We estimated, from published cohort studies[22–26] and data from one large

Table 1 | Baseline characteristics of the bioimpedance and control groups at randomization

Characteristic	Bioimpedance (n = 222)	Control (n = 213)[a]
Sex; male/female (% male)	157/65 (70.7)	149/63 (69.3)
HD modality: HD/HDF, n (%)	149 (67.1)/73 (32.9)	146 (68.5)/67 (31.5)
Age, yr, mean (SD)	60.06 (14.3)	62.7 (13.7)
Ethnicities, n (%)		
White	174 (78.4)	173 (81.2)
Black/Black British	6 (0.3)	0 (0)
Asian/Asian British	7 (0.3)	2 (0.4)
Other	35 (15.8)	38 (17.8)
Planned/unplanned start, n (%)	180 (81.1)/42 (18.9)	184 (86.4)/29 (13.6)
Access: fistula/graft/line, n (%)	115 (51.8)/4 (1.8)/103 (46.4)	116 (54.5)/3 (1.4)/94 (44.1)
Years since primary diagnosis, median (IQR)	4.3 (1.1–10.3)	3.1 (0.6–7.4)
Comorbidities, n (%)		
Malignancy	14 (6.3)	14 (6.6)
Ischemic heart disease	41 (18.4)	47 (22.1)
Peripheral vascular disease	19 (8.5)	33 (15.3)
Left ventricular dysfunction	31 (14.0)	25 (11.2)
Diabetes mellitus	107 (48.2)	91 (42.3)
Systemic collagen vascular disease	6 (2.7)	7 (3.3)
Comorbidity score, median (IQR)	1 (0–2)	1 (0–2)
Predialysis weight, kg, mean (SD)	86.9 (23.1)	82.7 (20.2)
Postdialysis weight, kg, mean (SD)	85.8 (22.7)	81.7 (20)
Normally hydrated weight, kg, mean (SD)	84.6 (23.2)	80.7 (20.2)
Predialysis blood pressure, mean (SD)		
Systolic	150.2 (23.3)	148.9 (22.9)
Diastolic	76.7 (14.3)	75.3 (15.4)
Postdialysis blood pressure, mean (SD)		
Systolic	148.2 (33.4)	146.9 (24.0)
Diastolic	75.7 (13.3)	75.9 (15.0)
Number (%) on diuretics	115 (51.8)	111 (51.6)
Number (%) on RAAS inhibition	61 (27.4)	49 (22.7)
Number (%) on calcium antagonists	103 (46.4)	117 (52)
Measured GFR, ml/min per 1.73 m^2, mean (SD)	5.03 (3.05)	4.44 (2.55)

GFR, glomerular filtration rate; HD, hemodialysis; HDF, hemodiafiltration; IQR, interquartile range; RAAS, renin angiotensin aldosterone system.
[a]Two of the 215 patients in the control groups did not have baseline data.

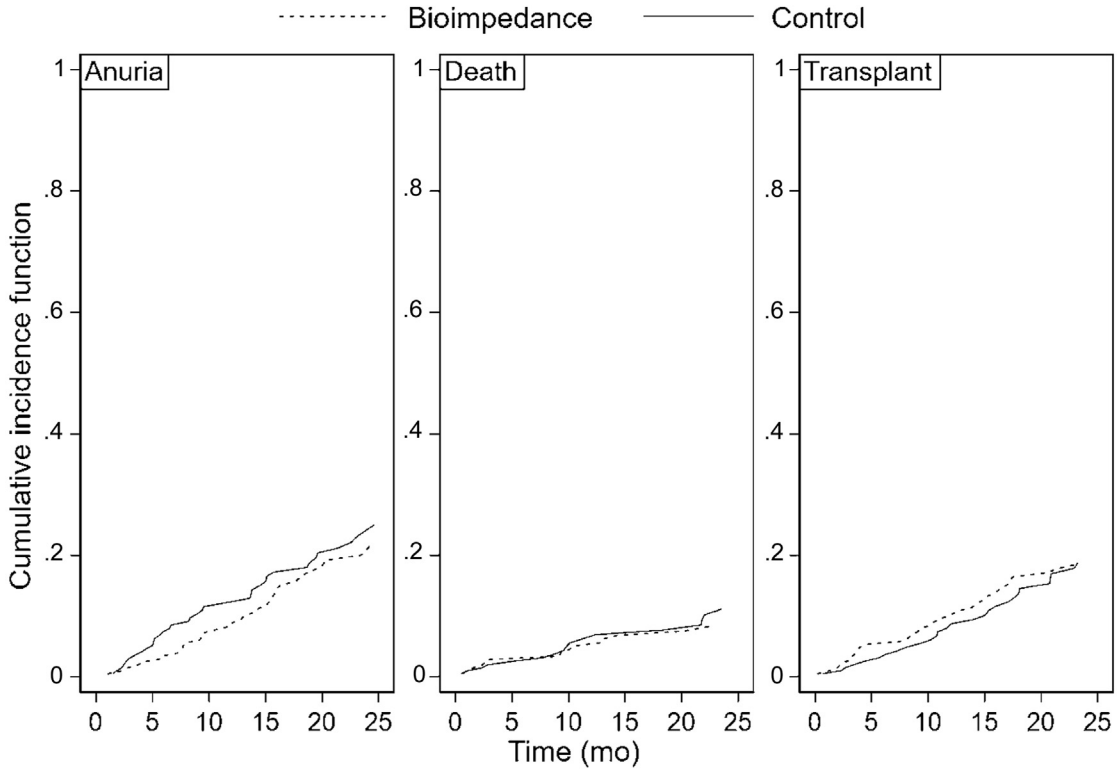
UK dialysis center, n = 615, that 30% (range: 25%–67%) of incident patients would be anuric by 10 months and that a clinically significant benefit would reduce this to 20%. Assuming 11% competing risks (death and transplantation data extrapolated from the 2013 UK Renal Registry report), an exponential decline in RKF, and proportional hazards, a total of 185 events (anuria) were required to have 90% power with 5% two-tailed significance to detect a hazard ratio (HR) of 0.62. This in turn required 516 patients to be randomized 1:1, allowing for a 5% loss to follow-up. We initially planned that all patients would have 12 months of follow-up, with approximately 50% having longer follow-up, up to a maximum of 2 years. However, to compensate for under-recruitment, follow-up was extended to 2 years for >90% of participants.

Randomization

Randomization was 1:1, stratified by center, using random permuted blocks of varying sizes from 2 to 8. Concealed allocation was via a secure centralized web-based, automated computer-generated randomization system provided by Keele University Clinical Trials Unit during office hours.

Statistical methods

The trial statistical analysis plan was signed off before study completion. Analyses were conducted on an intention-to-treat basis. Cox regression models were used to estimate cause-specific hazard functions, and competing-risks (i.e., death and transplantation) survival analysis to estimate subdistribution hazard functions of anuria, transplantation, and death. The parameters of interest were the cause-specific HR of anuria and the subdistribution HR of anuria (primary analysis), comparing the corresponding hazard rates of anuria between arms. Patients undergoing modality change or recovery of kidney function were censored at the point of treatment switch. The analysis was adjusted for baseline covariates likely affecting RKF, that is, age, race, self-reported biological sex, comorbidities (separately or using a validated scoring system), use of renin angiotensin aldosterone system blockade, calcium antagonists, and diuretics. The difference between groups in the rate of decline in RKF was analyzed using a random-effects segmented regression model to estimate the rate of change in GFR in each arm for years 1 and 2, with adjustment for baseline characteristics, as for the primary outcome variable. Blood pressure and patient-reported outcomes are reported using mean and SD or median and interquartile range for continuous variables and frequencies and percentages for categorical variables. To assess the integrity of the intervention, the difference between the TW and the BI-NHW was modeled for each fluid assessment using a multilevel mixed-effects model with multiple measurements from each individual nested within the 34 dialysis centers. Explanatory variables included randomization group, age, sex, comorbidity, and urine volume.



Event table

	Anuria						Death						Transplant					
Time	0	5	10	15	20	25	0	5	10	15	20	25	0	5	10	15	20	25
Control	0	5	14	21	31	35	0	6	8	13	13	15	0	11	16	24	30	33
Intervention	0	10	21	26	33	37	0	4	9	12	13	17	0	5	10	16	23	28

Number at risk

	Anuria						Death						Transplant					
Time	0	5	10	15	20	25	0	5	10	15	20	25	0	5	10	15	20	25
C	215	205	194	189	182	178	222	216	214	209	209	207	222	211	206	198	192	189
I	222	217	208	201	191	187	215	211	206	203	202	198	215	210	205	199	192	187

Figure 2| Cumulative incidence of anuria and the competing events, death, and transplantation (bioimpedance intervention group: dotted line; control group: solid line).

RESULTS

The study flow is summarized in the CONSORT diagram (Figure 1). Overall, 439 patients were recruited from 34 centers, an under-recruitment despite extending the planned recruitment period from 12 to 29 months (April 2017–October 2019), eventually curtailed after discussions with the funder. This slower-than-anticipated recruitment reflected logistical issues at the sites and not reluctance to participate. To compensate for under-recruitment, follow-up was extended to 2 years for >90% of participants. Five and a half months after closing to recruitment, the trial was interrupted by the COVID-19 pandemic, at which time all non-COVID–related clinical research in the UK was paused for 3 months. During this period, 193 (6.7%) fluid assessments were not recorded and 276 (8.1%) measurements of RKF were missed. Randomization led to well-balanced study arms according to baseline demography, comorbidity, and other characteristics, as shown in Table 1.

Table 2| Subdistribution (fine and gray) and cause-specific HRs for anuria, adjusted for prespecified baseline patient characteristics

Variable in the model	Cause-specific, HR (95% CI)	Subdistribution, HR (95% CI)
Bioimpedance (ref: control)	0.751 (0.459, 1.229)	0.742 (0.453, 1.215)
Age	0.987 (0.971, 1.005)	0.993 (0.977, 1.009)
Sex (ref: male)	1.239 (0.745, 2.063)	1.212 (0.741, 1.983)
Start (ref: planned)	1.282 (0.675, 2.436)	1.385 (0.709, 2.705)
Stoke Comorbidity Score	0.821 (0.645, 1.044)	0.852 (0.664, 1.093)
Ethnicity (ref: Asian/Asian British)		
Black or Black British	0.301 (0.033, 2.733)	0.396 (0.052, 3.041)
Other	0.604 (0.198, 1.849)	0.623 (0.226, 1.71)
White	0.272 (0.094, 0.787)	0.287 (0.111, 0.749)
RAAS inhibition (ref: not)	1.288 (0.774, 2.144)	1.321 (0.794, 2.201)
Calcium antagonist (ref: not)	1.195 (0.725, 1.969)	1.211 (0.741, 1.978)
Diuretic use (ref: no)	1.421 (0.867, 2.331)	1.346 (0.813, 2.226)

HR, hazard ratio; RAAS, renin angiotensin aldosterone system; ref, reference category.

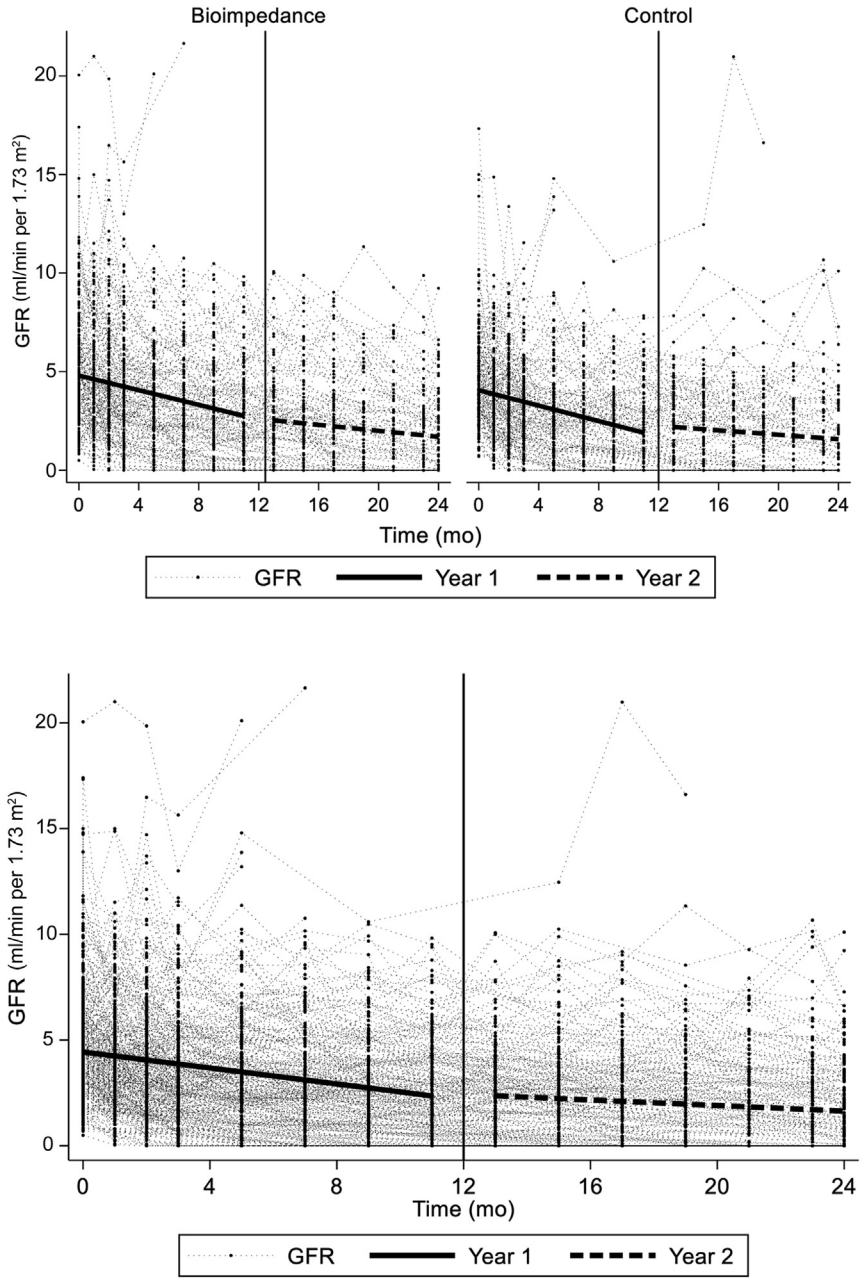


Figure 3 | Rate of decline in measured glomerular filtration rate (GFR; ml/min per 1.73 m^2) in years 1 and 2, by randomized group (upper panel) and pooled (lower panel).

Main outcomes of interest—time to anuria and rate of loss of residual kidney function

The primary outcome, hazard rate of anuria—adjusted for age, sex, ethnicity, comorbidity score, planned versus unplanned start and baseline use of calcium antagonists and renin angiotensin aldosterone system inhibition—did not differ significantly between the BI group and the control group ($P = 0.254$), with a cause-specific HR of 0.751 (95% confidence interval

Table 3 | Rate of decline of residual kidney function (measured GFR, ml/min per 1.73 m^2 per month), modeled with mixed-effects linear regression

	Slope estimates (95% CI)		
Year	Bioimpedance	Control	Pooled
1	−0.182 (−0.206, −0.157)	−0.173 (−0.199, −0.147)	−0.178 (−0.196, −0.159)
2	−0.083 (−0.117, −0.049)	−0.034 (−0.069, −0.001)	−0.061 (−0.086, −0.036)

CI, confidence interval; GFR, glomerular filtration rate.

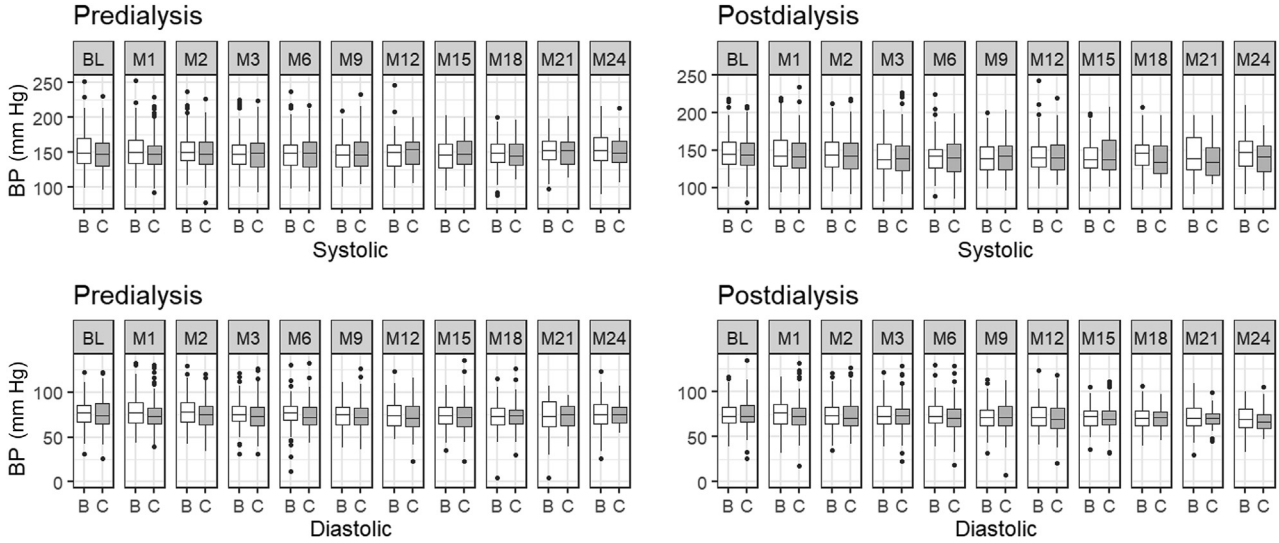


Figure 4| Longitudinal pre- and postdialysis systolic and diastolic blood pressures (BPs). Box plots displaying medians and interquartile ranges. B, bioimpedance; BL, baseline; C, control; M, month.

[CI]: 0.459, 1.229) and subdistribution HR of 0.742 (95% CI: 0.453, 1.215; see Figure 2; full details of the model are given in Table 2). The corresponding unadjusted hazard rates also did not differ significantly ($P = 0.426$), with a cause-specific HR of 0.829 (95% CI: 0.522, 1.316) and a subdistribution HR of 0.821 (95% CI: 0.519, 1.310). The corresponding unadjusted estimates for the competing risks were 0.776 (95% CI: 0.387, 1.555) and 0.793 (95% CI: 0.396, 1.588) for death and 1.036 (95% CI: 0.626, 1.714) and 1.078 (95% CI: 0.653, 1.781) for transplantation. Patients who withdrew from the study still contributed to the competing risks analysis. In the adjusted analysis, only 3 subjects in the control group (<1%) had missing data, so imputation was not used as this was unlikely to affect the parameter estimates.

The main secondary outcome, rate of decline in RKF (expressed as GFR), is shown in Figure 3 and Table 3. The baseline GFR was a little higher in the BI group than in the control group (5.03 vs. 4.44 ml/min per 1.73 m^2), but the gradient of the fall, whether adjusted or unadjusted, did not differ between study groups. The calculated linear rate of decline in RKF in the BI group for years 1 and 2 was –0.182 ml/min per 1.73 m^2 per month and –0.083 ml/min per 1.73 m^2 per month, respectively. The control group yielded slopes of –0.173 ml/min per 1.73 m^2 per month and –0.034 ml/min per 1.73 m^2 per month for years 1 and 2, respectively. Pooling treatment arms, the slopes were –0.178 ml/min per 1.73 m^2 per month and –0.061 ml/min per 1.73 m^2 per month, respectively. The linear mixed-effects model applied to GFR provided unbiased and efficient parameter estimates under a missing-at-random mechanism. Although this assumption is untestable, there were no apparent differential patterns of dropouts by treatment arm, suggesting that this assumption was plausible. Although the total percentage of dropouts was moderate (approximately 30%), the longitudinal analyses used all partial measurements efficiently.

Other secondary outcomes—blood pressure and dialysis-related symptoms

Mean blood pressure before and after dialysis at baseline and at each time point of the study follow-up did not differ between groups (Figure 4). There was a modest increase in the EQ-visual analog scale median rating at month 3, but otherwise this was unchanged throughout. Symptoms during dialysis including cramps, dizziness, palpitations, low blood pressure related, and shortness of breath were relatively uncommon and did not differ between groups (Table 4). The dialysis recovery time (see Figure 5) was quite variable and tended to worsen as the trial progressed, but again did not differ between groups.

Integrity of the intervention

It was important to determine how effective clinicians were in setting the TW in both the BI group and the control group. Of the total 2675 fluid assessments undertaken, complete data sets were available in 2501, 169 more in the BI group (n = 1335) than in controls (n = 1166), reflecting additional measurements as allowed in the protocol. The mean difference between the TW and the BI-NHW was minimal, BI: –0.038 kg (SD 2.7); control: –0.25 kg (SD 2.6). Furthermore, in both groups where decisions were made to increase or decrease the TW, patients were typically 1.6 kg below or 2.0 kg above their TW in the BI group and 1.4 kg below or 0.9 kg above TW in the control group (see Supplementary Table S1). There were no between-group longitudinal differences in either the TW – (BI-NHW), the TW and the actual postdialysis weight, or the intradialytic fluid removal (difference between pre- and postdialysis weight; see Supplementary Figures S1–S3). A multilevel analysis of the difference between target and BI-NHW found no significant difference between the study arms, with within-patient variance accounting for 45.0% (95% CI: 40.2%, 50.7%) and within-

Table 4 | Patient-reported outcomes: Euro-Qual EQ-5D-5L VAS reporting overall health rating and dialysis-related symptoms

Measure	Baseline		Month 3		Month 6		Month 9		Month 12		Month 15		Month 18		Month 21		Month 24	
	B	C	B	C	B	C	B	C	B	C	B	C	B	C	B	C	B	C
n	196	193	154	156	127	123	109	93	104	87	77	66	70	53	60	42	68	51
EQ-VAS[a]	59 (40–75)	60 (45–75)	65 (50–80)	65 (50–80)	60 (50–80)	59 (40–75)	60 (40–76)	60 (45–75)	60 (50–80)	60 (45–75)	60 (45–75)	60 (40–80)	60 (40–80)	60 (45–80)	60 (40–80)	59 (40–85)	60 (40–80)	59 (40–80)
Recovery time (%)																		
Within minutes	30	36	28	31	30	26	31	25	29	32	19	22	23	21	22	23	16	26
By bedtime or worse	49	36	53	49	54	51	58	49	55	48	60	50	53	51	49	48	58	63
Cramps[a]	1 (0–3)	1 (0–4)	2 (1–5)	1 (0–4)	2 (0–5)	2 (0.5–4)	2 (0–5)	2 (0–5)	2 (0–4)	2 (0.5–4)	2 (1–4)	1.5 (1–4)	2 (0–4.75)	2 (1–5)	2 (0–3)	2 (1–5)	2 (1–5)	2 (0–4)
Dizziness[a]	1 (0–4)	0.5 (0–2)	1 (0–3)	0 (0–3)	1 (0–3)	0 (0–3)	1 (0–3)	0 (0–3)	1 (0–3)	1 (0–3)	0 (0–3)	1 (0–3)	1 (0–2)	1 (0–2)	1 (0–2)	0 (0–2)	1 (0–2)	2 (0–3.5)
Palpitations[a]	0 (0–1)	0 (0–0)	0 (0–1)	0 (0–1)	0 (0–2)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0.5)	0 (0–1)	0 (0–1)	0 (0–1)
Low BP symptoms[a]	0 (0–3)	0 (0–2)	1 (0–3)	1 (0–3)	1 (0–4)	1 (0–3)	1 (0–3.75)	1 (0–4)	1 (0–3)	1 (0–3)	1 (0–3)	1 (0–4)	1 (0–3)	1 (0–4.5)	1 (0–3)	1 (0–4)	1 (0–3)	1 (0–5)
Short of breath[a]	0 (0–1)	0 (0–1)	0 (0–2)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–2)	0 (0–0.75)	0 (0–2)	0 (0–1)	0 (0–1)	0 (0–3)	0 (0–2)

B, bioimpedance; BP, blood pressure; C, control; EQ-5D-5L, EuroQual-5 Dimension-5 Level standardized measure of health-related quality of life; EQ-VAS, the EQ-5D-5L visual analog scale for the generic question "How good is your health today?"
[a]For these variables, 0 = never, 1–2 = occasionally, 3–5 = sometimes.
Data shown are median (interquartile range) except for recovery time (%).

center variance just 2.3% (95% CI: 0.5%, 5.3%) of the total residual variance (see Table 5). Significant within-subject factors included age, sex, and most recent urine volume. Finally, the proforma requested documentation of patients' preferences when deciding on changing the TW, and it is clear that there was a high level of agreement between clinicians and patients (Table 6).

Adverse events

Overall, there were 400 serious adverse events reported during the course of the trial: 203 in the BI participants and 197 in the control participants. These were dominated by admission to hospital, 159 versus 150, respectively, with 27 events in both groups considered life-changing and 15 deaths in the BI group versus 17 in the control group (3 sudden deaths in each group). There were 34 episodes of pulmonary edema, equally distributed. For further details, see Supplementary Table S2.

DISCUSSION

Our trial found that adding the BI-derived BI-NHW to a standardized fluid management protocol, in which clinicians were asked to set a TW to avoid volume depletion, did not result in better preservation of RKF. The reasons for this may be several, but of notable importance are that RKF was much better preserved than previous studies would suggest, and that the estimation of the BI-NHW by clinicians was just as good in the control group as in the BI-directed group. Given the good preservation of RFK, it might be argued that Bio-impedance Spectroscopy To maintain Renal Output (BISTRO) provides important observational evidence that the avoidance of excessive volume depletion is a safe approach to fluid management in patients with RKF.

Despite the importance of preserved RKF to people on dialysis, routine measurement is uncommon[27] and there are relatively few clinical trials of interventions that might lead to its better preservation. In retrospect, when designing the trial, we overestimated the rate of RKF loss despite the fact that observational studies and trials published both before and since would generally support our estimates. The Dialysis Morbidity and Mortality Study, which collected follow-up RKF between 8 and 18 months of dialysis initiation, documented that 69% of HD patients had become anuric.[22] The Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) found that, in the incident HD cohort, GFR fell from 6 to 2 ml/min per 1.73 m^2 by 12 months, that is, −4 ml, compared with a pooled reduction of −2.15 (95% CI: −1.93, −2.36) observed in the first year of BISTRO, a greater drop than we observed over the full 24 months.[23] The Frequent Hemodialysis Network also observed much more rapid declines in urine volume and measured GFR. In the nocturnal trial, 72% had RKF at baseline, and by 12 months, albeit starting at a lower measured GFR (3.4 ml/min), 40% of those on conventional dialysis were anuric, 70% in the frequent nocturnal group. In the Daily Dialysis Trial, 50% of those with RKF in the conventional group were anuric at 12 months.[28] More recently the Dialysis Outcomes and Practice

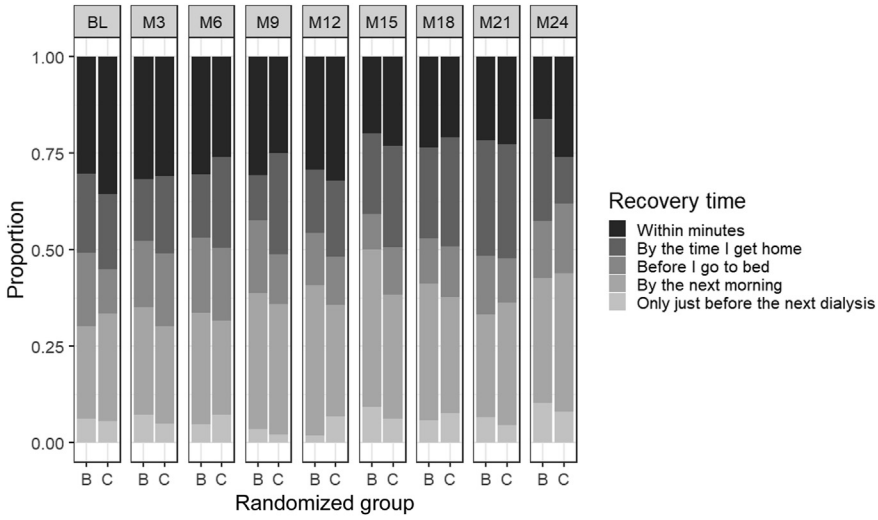


Figure 5 | Postdialysis recovery time by month. B, bioimpedance; C, control; M, month.

Patterns Study (phase 5) collected self-reported urine volume from HD patients. Of the 60% starting dialysis with a urine volume of >500 ml (as in our trial), 20% had become anuric by 10 months and 40% by 24 months.[29] Much smaller trials, included in a meta-analysis of the effects of hemodiafiltration on the rate of RKF decline, reported faster annualized rates of decline than we observed (typically >2.8 ml/min per 1.73 m^2), but did not report time to anuria.[4,5] In one trial investigating the effects of irbesartan on RKF in 82 prevalent HD patients, GFR fell by 1.75 ml/min per 1.73 m^2 over 1 year, compared with the overall average annualized loss of 1.46 ml/min per 1.73 m^2 in BISTRO.[30]

Our reason for selecting time to anuria over the rate of RKF decline as our primary outcome was the large impact this has on patients, confirmed by our patient advisory group, and its association with disproportionally worse outcomes in NECOSAD. We were also influenced by the findings of the balANZ trial, which studied the effects of a biocompatible dialysis fluid on RKF in peritoneal dialysis patients.[31] The balANZ trial found a significant effect on time to anuria that did not translate into a significant difference in the rate of RKF decline. As with our trial, balANZ observed a faster rate of RKF decline in the first 12 months compared with the second, with mean values of −0.28 and −0.10 ml/min per 1.73 m^2 per month in the control group and −0.22 and −0.09 in the intervention group, respectively. These are not slower than the rates we observed in BISTRO: year 1: −0.178 and year 2: −0.061 (see Table 3). Similar proportions developed anuria: 13% over 2 years in balANZ compared with 16% in BISTRO. Previously some, but not all, comparisons of the rate of loss of RKF on HD and peritoneal dialysis have suggested that this is faster for HD. BISTRO suggests that this gap can be narrowed.

One possible explanation of the relatively low rate of decline in RKF is the use in both groups of a protocol that included routine fluid assessments, regular measurements of RKF, and a standardized proforma that encouraged clinicians to take a systematic approach when setting the TW. Clinicians were trained to use this, and the close agreement between BI-NHW and TW in both groups, combined with the analysis showing almost no center-level variation in its application, strongly suggests that this was applied consistently. There was also excellent agreement in both study arms between the TW and the actual postdialysis weight, indicating a high degree of compliance when compared with other reports.[32] As in many medical activities, the use of a consistent approach prompted by a checklist is likely to influence quality,[33] and it is relevant that having a fluid assessment protocol in place was associated with better outcomes in the Dialysis Outcomes and Practice Patterns Study study.[8] It is likely that this structured approach will be of benefit, given that setting the TW is a good example of complex decision-making. Of note, our fluid assessment proforma recognized that patients often have a clear preference as to the setting of their TW, which should represent a negotiation using a shared decision-making approach.[34] In prompting clinicians to report this preference, which was done in two-thirds of the fluid assessments undertaken, it was clear that in the large majority of cases, there was good agreement between patient preferences and clinical decisions.

Table 5 | Multilevel mixed-effects model to determine factors associated with the difference between the set target weight and the BI derived normally hydrated weight (kg) for all fluid assessments

Covariate	Coefficient	95% CI	*P* value
Bioimpedance (ref: control)	0.108	−0.282, 0.498	0.586
Age (per yr)	0.016	0.002, 0.030	0.030
Sex (ref: male)	−0.577	−1.004, −0.150	0.008
Urine volume (per L)	0.030	0.016, 0.044	<0.001
Comorbidity score (per unit)	0.101	−0.080, 0.282	0.273
Study visit (in order)	−0.016	−0.031, −0.0007	0.040

CI, confidence interval; ref, reference category.

Table 6 | Relationship between patient preferences and the decision to change (increase or decrease) or not change the TW at the fluid assessments

Randomization group	Patient preference	TW increased (%)	No change in TW (%)	TW decreased (%)
Bioimpedance	Feels better at higher TW and wishes to increase	52.0	2.6	2.2
	Feels OK at current TW not wanting to change	15.0	65.8	18.7
	Feels better at lower TW wants to decrease	1.4	3.0	36.0
	Preference not documented	31.6	28.5	43.0
Control	Feels better at higher TW and wishes to increase	59.6	2.9	1.5
	Feels OK at current TW not wanting to change	14.1	66.2	24.2
	Feels better at lower TW wants to decrease	0.004	2.1	37.4
	Preference not documented	25.0	28.8	36.9

TW, target weight.

Most importantly, however, BISTRO provides reassuring observational evidence that application of a treatment strategy that avoids excessive volume depletion is associated with well-preserved RKF and its benefits, for example, relatively low interdialytic fluid gains and thus fewer requirements for high ultrafiltration rates, which in excess are both associated with worse outcomes.[11,32,35] It also represents a clear change in the strategy reported in our pretrial survey of fluid management practices in UK dialysis units.[7]

Another explanation for the relatively low rate of RKF loss could be the effect of selective enrollment of individuals into clinical trials. We endeavored to make the inclusion criteria pragmatic and inclusive so as to make our findings as generalizable as possible. BISTRO recruited from almost half of all UK centers, and, when compared with all new incident patients commencing dialysis in 2019 reported to the UK Renal Registry,[36] they were only a little younger (62 vs. 64 years), with a similar but higher proportion of White (79% vs. 75%) and male subjects (70% vs. 64.5%), a higher proportion of participants with diabetes (44% vs. 30.4%), and very similar proportions of unplanned starts (16% vs. 16.4%).

Not surprisingly, given the lack of effect on RKF, there were no differences by group in pre- and postdialysis blood pressure readings or patient-reported outcomes. It is notable, however, that symptoms associated with volume status were relatively low when compared with other reports, and this might reflect the good preservation of RKF.[37] Interdialytic fluid gains and need for fluid removal during dialysis were modest. A more comprehensive analysis of quality of life is currently underway as part of a full health economic assessment that will be published separately.

Our trial has several limitations. We were not able to recruit to the initial target within the funding period, and despite a funded extension and our attempt to compensate for this by extending the follow-up period, this did not make up the number of required anuria events. However, it is also clear that the under-recruitment was less important in achieving sufficient event numbers than the lower-than-anticipated decline in RKF. In fact, a significantly larger trial would be required to demonstrate a benefit from using BI-NHW given the negligible difference in the setting of the TW between the study groups. This observation reflects a growing number of trials that have been unable to demonstrate the benefit of technologies, including BI[14,38,39] and lung ultrasound,[40] in directing the management of fluid status. This is especially the case in participants with RKF.[41–43] Unfortunately, our trial was interrupted by COVID, which led to some loss of data collection and fluid assessments (<10%). It is a testimony to the engagement of our trial sites and management team that the trial did not have to be stopped completely and all the primary outcome data were collected. Finally, it should be noted that there was a significant dropout rate in the trial.

In conclusion, BI does not add value to fluid assessments designed to preserve RKF in incident HD patients, and TW set using a standardized clinical approach to setting the TW agreed closely with the BI estimates of the BI-NHW. This would suggest that a standardized approach to clinical fluid assessment should be considered the basis of routine practice. BISTRO provides clear evidence that preservation of RKF can be achieved over a significant period of time in incident HD patients, and we have validated a simpler method of estimating this from routine blood and urine collections.[19] Further studies of interventions designed to preserve RKF are now needed, and BISTRO provides valuable information that will inform their design.

DISCLOSURE

All the authors declared no competing interests.

DATA STATEMENT

The trial data are available to investigators under the conditions of a data sharing agreement. This will include group- and individual-level fully anonymized data. Applications should be made to the corresponding author.

ACKNOWLEDGMENTS

Previous presentation in abstract form: The results of this trial were presented at the ERA-EDTA meeting in Paris, 2022 at the late breaking trials session.

Funding

The study was supported by the National Institute for Health and Care Research Health Technology Assessment Programme under assigned grant number 14/216/01. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Health Technology Assessment Programme, National Institute of Health and Care Research, NHS, or the Department of Health. DK is currently supported by a Research Centre grant from Science Foundation Ireland (grant number RC/2073_P2 [CÚRAM]).

Trial management
Keele University Clinical Trials Unit—especially Nancy Fernandes Da Silva, Vicki Harper, Andrea Cherrington, Sarah Bathers, and Louise Phillips-Darby.

Patient advisory group
David Coyle (chair), Liam Howorth, Cassie Brzoza, Pauline Obi, and Michael Winfrow.

Trial steering committee
Richard Fluck (chair), James Wason, Elaine Davies, James Mason, Katherine Crompton, Nicola Heron, Melina Dritsaki, Brett Dowds, and Liz Pryde.

Independent data monitoring committee
Richard Haynes (chair), Simon Bond, and Russell Roberts.

Participating sites (principal investigators)
Julie Wessels, University Hospitals of North Midlands, Stoke-on-Trent, UK; Arfi Khwaja, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; Indranil Dasgupta, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; Andrew Davenport, Royal Free Hampstead NHS Trust, London, UK; Enric Vilar, East and North Hertfordshire NHS Trust, Stevenage, UK; Sandip Mitra, Manchester University NHS Foundation Trust, Manchester, UK; Albert Power, North Bristol NHS Trust, Bristol, UK; David Meredith, Royal Devon and Exeter NHS Foundation Trust, Exeter, UK; Michael Schulz, Royal Liverpool and Broadgreen Hospitals NHS Trust, Liverpool, UK; Michael Bedford, East Kent Hospitals University NHS Trust, Canterbury, UK; Kieran McCafferty, Barts Health NHS Trust, London, UK; Punit Yadav, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; Sally Pugh, Gloucestershire Hospital NHS Foundation Trust, Gloucester, UK; Stewart Lambie, NHS Highland, Raigmore, Scotland, UK; Beng So, Lancashire Teaching Hospitals, Preston, UK; James Burton, University Hospitals of Leicester NHS Trust, Leicester, UK; Janet Hegarty, Salford Royal NHS Foundation Trust, Salford, UK; Timothy Shipley, South Tees NHS Trust, Middlesbrough, UK; Neal Morgan, Southern Health and Social Care Trust, Newry, Northern Ireland, UK; Linda Bisset, Nottingham University Hospitals NHS Trust, Nottingham, UK; Thomas Connor, Oxford University Hospital NHS Trust, Oxford, UK; James Chess, Abertawe Bro Morgannwg University Health Board, Swansea, Wales, UK; Colin Jones, York Teaching Hospital NHS Foundation Trust, York, UK; Azra Nache, Aintree University Hospital NHS Foundation Trust, Aintree, UK; Rajan Patel, NHS Greater Glasgow and Clyde, Glasgow, Scotland, UK; Neill Duncan, Imperial College Healthcare NHS Trust, London, UK; Johann Nicholas, Shrewsbury and Telford Hospital NHS Trust, Shrewsbury, UK; Sharlene Greenwood, King's College Hospital NHS Foundation Trust, London, UK; Kanwaljit Sandhu, The Royal Wolverhampton NHS Trust, Wolverhampton, UK; Subash Somolanka, Epsom and St Helier University Hospitals NHS Trust, UK; Kate Shiell, NHS Fife, Kirkaldy, Scotland, UK; Stephanie Bolton, Northern Health and Social Care Trust, Antrim, Northern Ireland, UK; and Abdulfattah Alejmi, Betsi Cadwalader University Health Board, Bangor, Wales, UK.

AUTHOR CONTRIBUTIONS
All authors were responsible for trial protocol development, review and interpretation of findings, and finalization of the manuscript. SJD was Chief Investigator with overall responsibility for trial delivery. DC was a patient co-investigator, lead for patient and public involvement, and a member of the trial management group. EJL and DK were co-lead on the development and delivery of bioimpedance technology training during the trial and quality control of bioimpedance and residual kidney function data. JM from Bangor University provided expertise in body composition and delivery of bioimpedance training. PO led on nurse participation, feasibility of data collection, and patient collaboration techniques using social media. FJC was an advisor on data capture by UK Renal Registry and Data Linkage. ID was a lead on patient recruitment and safety. SJD, AD, MW, and KF were co-investigators and had expertise on hemodialysis. MZ and LA were responsible for the analysis of patient-reported outcome measures, quality-of-life measures, and health economics. JB, IS-T, and JS were responsible for statistical analysis.

SUPPLEMENTARY MATERIAL
Supplementary File (Word)

Supplementary Table S1. Difference between target weight (TW) and normally hydrated weight (NHW) at fluid assessments is shown for all fluid assessments and separately according to the decision to either increase or decrease the target.

Supplementary Table S2. Serious adverse events as categorized by the body system according to the Common Terminology Criteria for Adverse Events (CTCAE) classification.

Supplementary Figure S1. *Assessment of intervention:* longitudinal difference between the postdialysis target weight set by clinicians and the normally hydrated weight determined from bioimpedance.

Supplementary Figure S2. *Assessment of intervention:* longitudinal difference between the target postdialysis weight set by clinicians and the actual postdialysis weight.

Supplementary Figure S3. *Assessment of intervention:* longitudinal difference between the post- and predialysis weight (equivalent to fluid removal).

Supplementary File (PDF)

Supplementary Slide Deck 1. BCM training for HD MDT.

Supplementary Slide Deck 2. BCM training for Research nurses taking readings.

Supplementary Slide Deck 3. Carrying out urine collections.

REFERENCES
1. Termorshuizen F, Dekker FW, van Manen JG, et al. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. *J Am Soc Nephrol*. 2004;15:1061–1070.
2. Obi Y, Rhee CM, Mathew AT, et al. Residual kidney function decline and mortality in incident hemodialysis patients. *J Am Soc Nephrol*. 2016;27:3758–3768.
3. Merkus MP, Jager KJ, Dekker FW, et al. Quality of life in patients on chronic dialysis: self-assessment 3 months after the start of treatment. The Necosad Study Group. *Am J Kidney Dis*. 1997;29:584–592.
4. Schiffl H, Lang SM, Fischer R. Ultrapure dialysis fluid slows loss of residual renal function in new dialysis patients. *Nephrol Dial Transplant*. 2002;17:1814–1818.
5. Lu W, Ren C, Han X, et al. The protective effect of different dialysis types on residual renal function in patients with maintenance hemodialysis: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97:e12325.
6. Lang SM, Bergner A, Töpfer M, Schiffl H. Preservation of residual renal function in dialysis patients: effects of dialysis-technique-related factors. *Perit Dial Int*. 2001;21:52–57.
7. Dasgupta I, Farrington K, Davies SJ, et al. UK national survey of practice patterns of fluid volume management in haemodialysis patients: a need for evidence. *Blood Purif*. 2016;41:324–331.
8. Dasgupta I, Thomas GN, Clarke J, et al. Associations between hemodialysis facility practices to manage fluid volume and intradialytic hypotension and patient outcomes. *Clin J Am Soc Nephrol*. 2019;14:385–393.
9. Tabinor M, Elphick E, Dudson M, et al. Bioimpedance-defined overhydration predicts survival in end stage kidney failure (ESKF): systematic review and subgroup meta-analysis. *Sci Rep*. 2018;8:4441.

10. Dekker MJE, Marcelli D, Canaud B, et al. Unraveling the relationship between mortality, hyponatremia, inflammation and malnutrition in hemodialysis patients: results from the international MONDO initiative. *Eur J Clin Nutr*. 2016;70:779–784.
11. Hecking M, Moissl U, Genser B, et al. Greater fluid overload and lower interdialytic weight gain are independently associated with mortality in a large international hemodialysis population. *Nephrol Dial Transplant*. 2018;33:1832–1842.
12. Zoccali C, Moissl U, Chazot C, et al. Chronic fluid overload and mortality in ESRD. *J Am Soc Nephrol*. 2017;28:2491–2497.
13. Onofriescu M, Mardare NG, Segall L, et al. Randomized trial of bioelectrical impedance analysis versus clinical criteria for guiding ultrafiltration in hemodialysis patients: effects on blood pressure, hydration status, and arterial stiffness. *Int Urol Nephrol*. 2012;44:583–591.
14. National Institute for Health and Care Excellence. Multiple frequency bioimpedance devices to guide fluid management in people with chronic kidney disease having dialysis. Published June 21, 2017. Accessed June 8, 2023. https://www.nice.org.uk/guidance/dg29
15. National Institute for Health Research. HTA no 14/216. Bioimpedance guided fluid management in dialysis patients. Accessed June 8, 2023. https://njl-admin.nihr.ac.uk/document/download/2023261
16. Marants R, Qirjazi E, Grant CJ, et al. Renal perfusion during hemodialysis: intradialytic blood flow decline and effects of dialysate cooling. *J Am Soc Nephrol*. 2019;30:1086–1095.
17. Davies SJ, Caskey FJ, Coyle D, et al. Rationale and design of BISTRO: a randomized controlled trial to determine whether bioimpedance spectroscopy-guided fluid management maintains residual kidney function in incident haemodialysis patients. *BMC Nephrol*. 2017;18:138.
18. Chamney PW, Wabel P, Moissl UM, et al. A whole-body model to distinguish excess fluid from the hydration of major body tissues. *Am J Clin Nutr*. 2007;85:80–89.
19. Lindley E, Keane D, Belcher J, et al. Monitoring residual kidney function in haemodialysis patients using timed urine collections: validation of the use of estimated blood results to calculate GFR. *Physiol Meas*. 2022;43:ac80e8.
20. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20:1727–1736.
21. Davison SN, Klarenbach S, Manns B, et al. Patient-reported outcome measures in the care of in-centre hemodialysis patients. *J Patient Rep Outcomes*. 2021;5(suppl 2):93.
22. Moist LM, Port FK, Orzol SM, et al. Predictors of loss of residual renal function among new dialysis patients. *J Am Soc Nephrol*. 2000;11:556–564.
23. Jansen MAM, Hart AAM, Korevaar JC, et al. Predictors of the rate of decline of residual renal function in incident dialysis patients. *Kidney Int*. 2002;62:1046–1053.
24. McKane W, Chandna SM, Tattersall JE, et al. Identical decline of residual renal function in high-flux biocompatible hemodialysis and CAPD. *Kidney Int*. 2002;61:256–265.
25. Lin Y-F, Huang J-W, Wu M-S, et al. Comparison of residual renal function in patients undergoing twice-weekly versus three-times-weekly haemodialysis. *Nephrology (Carlton)*. 2009;14:59–64.
26. Fernández-Lucas M, Teruel-Briones JL, Gomis-Couto A, et al. Maintaining residual renal function in patients on haemodialysis: 5-year experience using a progressively increasing dialysis regimen. *Nefrologia*. 2012;32:767–776.
27. Flythe JE, Chang TI, Gallagher MP, et al. Blood pressure and volume management in dialysis: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int*. 2020;97:861–876.
28. Daugirdas JT, Greene T, Rocco MV, et al. Effect of frequent hemodialysis on residual kidney function. *Kidney Int*. 2013;83:949–958.
29. Hecking M, McCullough KP, Port FK, et al. Self-reported urine volume in hemodialysis patients: predictors and mortality outcomes in the International Dialysis Outcomes and Practice Patterns Study (DOPPS). *Am J Kidney Dis*. 2019;74:425–428.
30. Kjaergaard KD, Peters CD, Jespersen B, et al. Angiotensin blockade and progressive loss of kidney function in hemodialysis patients: a randomized controlled trial. *Am J Kidney Dis*. 2014;64:892–901.
31. Johnson DW, Brown FG, Clarke M, et al. Effects of biocompatible versus standard fluid on peritoneal dialysis outcomes. *J Am Soc Nephrol*. 2012;23:1097–1107.
32. Flythe JE, Kshirsagar AV, Falk RJ, Brunelli SM. Associations of posthemodialysis weights above and below target weight with all-cause and cardiovascular mortality. *Clin J Am Soc Nephrol*. 2015;10:808–816.
33. Wolff AM, Taylor SA, McCabe JF. Using checklists and reminders in clinical pathways to improve hospital inpatient care. *Med J Aust*. 2004;181:428–431.
34. Elwyn G, Durand MA, Song J, et al. A three-talk model for shared decision making: Multistage consultation process. *BMJ*. 2017;359:j4891.
35. Flythe JE, Curhan GC, Brunelli SM. Disentangling the ultrafiltration rate-mortality association: the respective roles of session length and weight gain. *Clin J Am Soc Nephrol*. 2013;8:1151–1161.
36. UK Renal Registry. (2021) UK Renal Registry 23rd Annual Report—data to 31/12/2019. Accessed June 8, 2023. renal.org/audit-research/annual-report
37. Rayner HC, Zepel L, Fuller DS, et al. Recovery time, quality of life, and mortality in hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Am J Kidney Dis*. 2014;64:86–94.
38. Covic A, Ciumanghel A-I, Siriopol D, et al. Value of bioimpedance analysis estimated "dry weight" in maintenance dialysis patients: a systematic review and meta-analysis. *Int Urol Nephrol*. 2017;49:2231–2245.
39. Tabinor M, Davies SJ. The use of bioimpedance spectroscopy to guide fluid management in patients receiving dialysis. *Curr Opin Nephrol Hypertens*. 2018;27:406–412.
40. Zoccali C, Torino C, Mallamaci F, et al. A randomized multicenter trial on a lung ultrasound–guided treatment strategy in patients on chronic hemodialysis with high cardiovascular risk. *Kidney Int*. 2021;100:1325–1333.
41. Tan BK, Yu Z, Fang W, et al. Longitudinal bioimpedance vector plots add little value to fluid management of peritoneal dialysis patients. *Kidney Int*. 2016;89:487–497.
42. Oh KH, Baek SH, Joo KW, et al. Does routine bioimpedance-guided fluid management provide additional benefit to non-anuric peritoneal dialysis patients? Results from compass clinical trial. *Perit Dial Int*. 2018;38:131–138.
43. Davies SJ. The elusive promise of bioimpedance in fluid management of patients undergoing dialysis. *Clin J Am Soc Nephrol*. 2020;15:597–599.