

# Meta-Analysis of Randomized Controlled Trials Using Tool-Assisted Target Weight Adjustments in Chronic Dialysis Patients



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**Introduction:** Technological adjuncts have been developed to improve the accuracy of fluid removal goals in maintenance dialysis recipients. We aimed to determine whether the introduction of these tools has been shown to impact clinical outcomes.

**Methods:** We performed a systematic review and meta-analysis of randomized controlled trials that compared fluid management guided by technological adjuncts to standard care in hemodialysis and peritoneal dialysis. The primary outcome was all-cause mortality. Secondary outcomes were cardiovascular events, hospitalizations, intradialytic hypotension, blood pressure, symptoms, antihypertensive medications, and left ventricular mass index.

**Results:** Of the 2940 citations retrieved, we identified a total of 12 eligible trials comprising 2406 participants. In the 10 studies ( $n = 2111$ ) with data on mortality, the use of adjunct technologies was not associated with a reduction of mortality (rate ratio [RR]: 0.92; confidence interval [CI]: 0.57–1.51;  $I^2 = 36\%$ ). The intervention conferred a reduction in systolic arterial pressure (mean difference:  $-3.14$ ; CI:  $-5.89$  to  $-0.38$ ;  $I^2 = 39\%$ ) but did not affect other outcomes. In a subgroup analysis, bioimpedance was associated with a reduced risk of hospitalization (RR: 0.68; CI: 0.46–0.99;  $I^2 = 55\%$ ). The risk of bias was high or unclear in most studies and the quality of evidence was judged to be low.

**Conclusions:** Among maintenance dialysis recipients, technological adjuncts for fluid management did not improve survival. Trials mostly investigated the use of bioimpedance, whereas the evidence for use of other technologies remain very scarce. Future adequately powered trials should assess a broader array of promising technologies using meaningful clinical outcomes over a prolonged follow-up duration.

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KEYWORDS: bioimpedance; blood volume monitoring; dialysis; fluid overload; lung ultrasound

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Despite considerable technological advances over the past 30 years, mortality among maintenance dialysis recipients remains unacceptably high.<sup>1</sup> Although partially attributable to classic cardiovascular risk factors that are commonly found in patients with chronic kidney disease, “nontraditional” risk factors unique to dialysis recipients could predispose this population to adverse outcomes. Chronic fluid overload leading to hypertension and myocardial hypertrophy is considered an important mediator of adverse outcomes in dialysis recipients and

experts in the field have recently advocated a greater focus on a patient's vital status in the hopes of improving clinical outcomes.<sup>2–4</sup>

Target weight, one of the most fundamental components of any dialysis prescription, is traditionally determined by the synthesis of patient-reported symptomatology and physical examination. However, reliance on conventional physical signs, such as peripheral edema,<sup>5</sup> pulmonary auscultation,<sup>6</sup> and blood pressure,<sup>7</sup> may not accurately characterize a patient's volume status.

The inadequacy of traditional approaches to volume assessment has stimulated the study of novel diagnostic tools aimed at complementing or supplanting the current standard of care. These include intradialytic blood volume monitoring,<sup>8</sup> bioimpedance,<sup>9</sup> natriuretic

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peptide measurement,<sup>10</sup> and point-of-care ultrasound of the lung<sup>11</sup> and inferior vena cava.<sup>12</sup> We conducted a systematic review and meta-analysis of randomized controlled trials involving dialysis recipients to determine whether the integration of these tools into clinical practice affects meaningful clinical outcomes. We hypothesized that the addition of novel technologies to inform target weight determination and ultrafiltration volume would reduce mortality in maintenance dialysis recipients compared with traditional clinical evaluation alone.

## METHODS

Our study was performed in concordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Protocols<sup>13</sup> and a Measurement Tool to Assess systematic Reviews guidelines.<sup>14</sup> This study was registered in the International Prospective Register of Systematic Reviews database (ID: CRD42018081228) before data extraction and analysis.<sup>15</sup>

### Study Eligibility

We considered all randomized controlled trials enrolling patients treated with maintenance hemodialysis or peritoneal dialysis for end-stage kidney disease and that tested 1 or more adjunct tool(s) to guide target weight and/or ultrafiltration goals. We focused on the following methods of assessment: bioimpedance, blood volume monitoring, ultrasound of the inferior vena cava, lung ultrasound, measurements of natriuretic peptides and chest radiograph. Eligible trials had to have a comparator group in which target weight was based on usual care (i.e., the clinical evaluation of the attending clinician). We only considered trials with a follow-up duration of at least 3 months. Studies with a crossover design were eligible, but only data from the first treatment phase were to be included. Cluster randomized controlled trials, in which the unit of randomization was a group of dialysis recipients or an entire dialysis center, were not eligible. All available reports, including conference abstracts, were considered. When we suspected multiple reports including the same participants, the authors were contacted to clarify this issue and determine which data were to be extracted based on the number of participants and the outcomes reported in each document.

To be eligible for inclusion, trials had to report at least 1 of the following outcomes: all-cause mortality (primary outcome); the rate of cardiovascular events, all-cause hospitalizations, episodes of intradialytic hypotension; patient-reported symptoms; changes in blood pressure and/or the number of prescribed antihypertensive medications; or left ventricular mass index.

### Search Strategy

We searched MEDLINE (PubMed), EMBASE (Ovid), and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to November 2018 for eligible studies. Three sets of terms were used to identify research reports. First, for the population of interest, the terms were selected to identify all studies involving patients on any modality of dialysis. Second, for the intervention, one set of terms was created for each technology type and were separated by an OR Boolean operator to identify reports with at least one type of technology mentioned in the abstract. Finally, for the type of study design, validated filters with high sensitivity were used to identify randomized trials.<sup>16</sup> Complete details of the search strategy are presented in [Supplementary Table S1](#) in [Supplementary Appendix S1](#). When only a published conference abstract was found through the previously described strategy or when a trial not included in the systematic database search was referenced within the full text of included studies, manual searching through MEDLINE, EMBASE, CENTRAL, Google Scholar, ResearchGate, on individual journal websites, and via direct contact with the authors was performed to determine if the full article was published or available in pre-print status.

### Study Selection and Data Extraction

At least 2 investigators independently examined each title and abstract. After an initial screen of potentially eligible citations, full texts were reviewed to determine eligibility. The choice of eligible studies was compared between the investigators and a third reviewer was available to resolve any discrepancy.

Data extraction from the included studies was performed independently by 2 investigators using standardized forms. Studies published in languages other than English or French were translated before assessment. The items extracted are presented in detail in [Supplementary Table S2](#) in [Supplementary Appendix S2](#). When missing or incomplete information on mortality was identified, the corresponding author was contacted via e-mail to provide clarification (*at least 2 attempts were made before declaring the receipt of no response*). During data extraction, some assumptions were made when incomplete information was present and are presented in detail in [Supplementary Appendix S2, Section 2.1](#).

### Assessment of the Risk of Bias in Individual Studies

The risk of bias in the selected studies was assessed using the Cochrane Collaboration tool.<sup>16</sup> The domains most vulnerable to bias in studies that considered mortality as an outcome were the presence or absence of random sequence generation, allocation concealment,

completeness of outcome data, imbalance in baseline characteristics or inappropriate administration of the intervention. The evaluation was performed independently by at least 2 reviewers and in case of disagreement, the final rating was discussed with another investigator.

### Summary Measures and Synthesis of Results

For the measure of treatment effect for all-cause mortality, results were expressed as rate ratios (RR) and pooled using a random-effect model in a Mantel-Haenszel analysis. For outcomes reported as counts such as rates of an event that can occur multiple times in single patient, results were reported as rate ratios and the results were pooled using a random-effect model in an inverse of variance analysis. For outcomes reported on a continuous scale, the mean differences were used and pooled using a random-effect model in an inverse of variance analysis. All effect measures are presented with a 95% CI. Additional methodological details are available in [Supplementary Appendix S2, Section 2.2](#).

Heterogeneity was assessed using the  $I^2$  test and values above 50% were considered to represent substantial heterogeneity. The following subgroup analyses were planned *a priori*: (i) dialysis modality, (ii) type of technology studied, (iii) follow-up duration (less than or equal to a year vs. more than a year), (iv) inclusion of incident dialysis recipients only (<6 months) versus studies without this restriction, (v) trials including patients with preexisting cardiovascular disease only versus no restriction, and (vi) study sponsorship (peer-review funding vs. industry-sponsored). We also performed sensitivity analyses by evaluating the effect of removing studies with a high risk of bias and for which the full peer-reviewed report was not available. We also conducted 2 *post hoc* sensitivity analyses. First, we removed studies for which only a conference abstract was available. Second, we performed an additional subgroup analysis for the study design: protocolized (fluid management based on prespecified rules/algorithms) or pragmatic (fluid management based on clinical judgment). To assess reporting bias, visual inspection of a funnel plot was performed.

The cumulative evidence supporting the effect of the various interventions on the primary and secondary outcomes was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.<sup>17</sup>

## RESULTS

### Search Results and Study Characteristics

Of the 2940 reports identified through our search strategy and manual search, 12 unique trials (10 full reports,<sup>18–26</sup> 1 published conference abstract,<sup>27</sup> and 1

full report in pre-print version obtained directly from the authors<sup>28</sup>) were found to be eligible. These comprised 2406 participants (1197 who received the intervention and 1209 controls). The search process is depicted in [Figure 1](#). [Table 1](#)<sup>18–30</sup> shows the characteristics of the studies, including 10 trials investigating the measurement of bioimpedance,<sup>19–24,26–29</sup> 1 trial investigating the use of blood volume monitoring,<sup>18</sup> and 1 trial investigating the combined use of lung ultrasound and bioimpedance.<sup>25</sup> No eligible randomized control trials investigated the use of inferior vena cava ultrasound, natriuretic peptides, or chest radiograph. Five studies comprised only peritoneal dialysis patients,<sup>19,23,27–29</sup> whereas 7 were conducted among maintenance hemodialysis patients.<sup>18,20–22,24,25,30</sup> The median intervention period was 12 months, with 2 studies<sup>21,25</sup> having a follow-up period of more than 12 months.

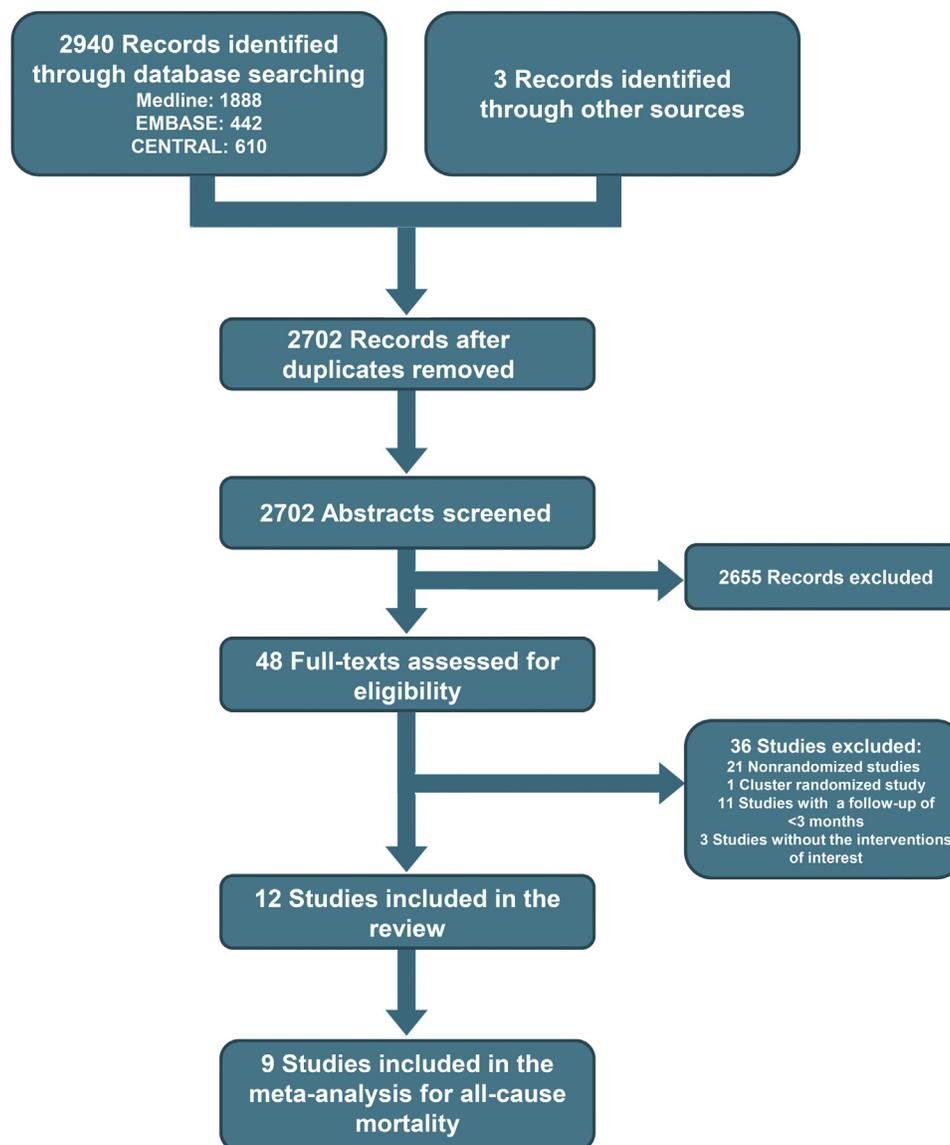
### Primary Outcome: Mortality

For 2111 patients enrolled in the 10 trials with available mortality data,<sup>18,21–25,27</sup> the use of adjunct technologies to adjust target weight did not affect mortality (pooled RR: 0.92, CI: 0.57–1.51,  $I^2$ : 36%; [Figure 2](#)). However, there was an increase in the risk of mortality ( $P = 0.04$ ) in the only study involving blood volume monitoring (RR: 2.58; CI: 1.11–6.02) as compared with the absence of a significant effect in trials using bioimpedance alone (RR: 0.71; CI: 0.43–1.17;  $I^2$ : 0%) or combined with lung ultrasound (RR: 1.03; CI: 0.56–1.89). No mortality difference was found in further subgroup analyses by dialysis modality, duration of follow-up, source of funding, risk of bias or study design ([Supplementary Appendix S3, Section 3.1](#)). A sensitivity analysis excluding 2 studies for which the full peer-review report was not available<sup>27,28</sup> did not significantly modify the overall result (RR: 1.06; CI: 0.62–1.78;  $I^2$ : 39%).

### Secondary Outcomes

Results of the meta-analysis for secondary outcomes are presented in [Table 2](#). The use of adjunct technologies to adjust target weight mediated a reduction in systolic arterial blood pressure (mean difference:  $-3.14$  mm Hg; CI:  $-5.89$  to  $-0.38$ ;  $I^2$ : 39%;  $n = 1289$ , 8 studies). No significant differences between subgroups were found ([Supplementary Appendix S3, Section 3.6](#)). A sensitivity analysis revealed that all statistical heterogeneity was explained by one study for which the peer-reviewed full text was not available ([Supplementary Appendix S3, Section 3.6](#)).<sup>28</sup>

Overall, the use of adjunct technologies did not affect the risk of cardiovascular events, all-cause hospitalization, intradialytic hypotension, intradialytic



**Figure 1.** Flow diagram of included studies.

symptoms, diastolic blood pressure, or measurements of the left ventricular mass index. Significant statistical heterogeneity was found in the results for cardiovascular events, all-cause hospitalizations, intradialytic hypotension, symptoms during dialysis, diastolic blood pressure and left ventricular mass index measurements.

In subgroup analysis, there was an increased risk of hospitalization with blood volume guided fluid management (RR: 1.39; CI: 1.09–1.78;  $n = 443$ , 1 study) and a reduction in hospitalizations among patients who received bioimpedance-based fluid management (RR: 0.68; CI: 0.46–0.99;  $I^2: 55\%$ ;  $n = 831$ , 4 studies). Furthermore, a decreased risk of hospitalization was observed in studies involving peritoneal dialysis recipients (RR: 0.61; CI: 0.42–0.87;  $I^2: 0\%$ , 2 studies) which was significantly different from the result observed in studies involving hemodialysis recipients (RR: 1.05; CI: 0.77–1.44;  $I^2: 69\%$ ).

The effect of technologic adjuncts on the rate of cardiovascular events, diastolic blood pressure and left ventricular mass index did not differ according to dialysis modality, funding source and follow-up duration (Supplementary Appendix S3, Sections 3.6 and 3.7). Subgroup analyses could not be performed for the rate of symptoms during dialysis and antihypertensive medication use because fewer than 3 studies reported these secondary outcomes (Supplementary Appendix S3, Sections 3.5, 3.8, and 3.9).<sup>22,27</sup>

Secondary outcomes from some studies could not be included in the meta-analysis because of the format of presentation for the data in question. For example, one study<sup>22</sup> reported the use of antihypertensive medications as a dichotomous outcome (RR: 0.52; CI: 0.22–1.22), whereas another defined it as a change over the intervention period.<sup>28</sup> In another study,<sup>21</sup> intradialytic hypotension was reported as a mean of episodes per

**Table 1.** Characteristics of included trials

Source/registration	Participants	n	Age (mean, SD)	Setting	Technology used	Intervention	Primary outcomes	Duration	Funding
Reddan <i>et al.</i> 2005 <sup>18</sup> (not registered)	Adult patients on hemodialysis ( $\geq 2$ mo)	443	59 $\pm$ 15	10 centers, United States and Canada	Blood volume monitoring using Crit-Line during dialysis (Hema Metrics)	Ultrafiltration rate adjusted every 30 min according to change in relative plasma volume during dialysis	All-cause hospitalizations	6 mo	Industry
Luo <i>et al.</i> 2011 <sup>19</sup> (not registered)	Adult patients on peritoneal dialysis ( $\geq 3$ mo)	160	60 $\pm$ 15	1 center, China	Bioimpedance every 6 wk or less using BCM (Fresenius Medical Care)	Target weight adjusted by the attending clinician using all available information (nonprotocolized)	Change in overhydration	3 mo	Academic implication of the industry (third author)
Onofriescu <i>et al.</i> 2012 <sup>20</sup> (not registered)	Adult patients on hemodialysis ( $\geq 3$ mo)	135	52 $\pm$ 13	1 center, Romania	Bioimpedance every 3 mo using BCM (Fresenius Medical Care)	Target weight set according to absolute fluid overload before dialysis. Changes allowed if intra-dialytic complications occurred	Blood pressure control, pulse-wave velocity and hydration status	12 mo	Industry
Hur <i>et al.</i> 2013 <sup>22</sup> (NCT00974857)	Adult patients on hemodialysis ( $\geq 3$ mo)	156	52 $\pm$ 12	2 centers, Turkey	Bioimpedance twice monthly using BCM (Fresenius Medical Care)	Target weight set according to TAFO. TAFO = $\frac{\text{Fluid overload}_{\text{Pre}} - \text{Interdialytic weight gain}}{2}$	Change in left ventricular mass index	12 mo	Industry
Onofriescu <i>et al.</i> 2014 <sup>21</sup> (NCT01828658)	Adult patients on hemodialysis ( $\geq 3$ mo)	131	53 $\pm$ 13	1 center, Romania	Bioimpedance every 3 mo using BCM (Fresenius Medical Care)	Target weight gradually adjusted to achieve normohydration ( $-1.1$ to $+1.1$ liter)	All-cause mortality	2.5 yr	Academic
Tian <i>et al.</i> 2015 <sup>27</sup> (NCT02000128)	Peritoneal dialysis patients with fluid overload	240	50 $\pm$ 15	1 center, China	Bioimpedance analysis (frequency of measurements not specified)	Fluid management guided by bioimpedance. No other details available	All-cause mortality	12 mo	Not specified
Tan <i>et al.</i> 2016 <sup>23</sup> (NCT00801112)	Adult patients on peritoneal dialysis	308	56 $\pm$ 14	4 centers, United Kingdom and China	Bioimpedance (vector plot analysis) every 3 mo using BI 101 ASE (Akern, Italy)	Target weight adjusted by the attending clinician using all available information (nonprotocolized)	Change in bioimpedance measurements	12 mo	Academic
Huan-Sheng <i>et al.</i> 2016 <sup>24</sup> (NCT02325856)	Adult patients on hemodialysis ( $\geq 3$ mo)	298	62 $\pm$ 12	6 centers, Taiwan	Bioimpedance every month using BCM (Fresenius Medical Care)	Target weight adjustments guided by postdialysis fluid overload: (absolute fluid overload before dialysis – net ultrafiltration)	All-cause hospitalizations	12 mo	Industry
Siriopol <i>et al.</i> 2017 <sup>25</sup> (NCT01815762)	Adult patients on hemodialysis ( $\geq 3$ mo) at low cardiovascular risk	250	59 $\pm$ 14	2 centers, Romania	B-line score on ultrasound assessment once a week when B-line score $>15$ and every month when B-line score $<15$ Bioimpedance performed if clinical symptoms of hypovolemia	Target weight adjustment to reduce B-line score to $<15$ . Increase of target weight when clinical symptoms develop if absolute fluid overload $<1.1$ liter	Composite: all-cause mortality or first cardiovascular event	24 mo	Academic
Paunic <i>et al.</i> 2018 <sup>26,30</sup> (not registered)	Hemodialysis patients	83	57 $\pm$ 12	1 center, Serbia	Bioimpedance using BCM (Fresenius medical care) every mo and frequency increased to every wk if OH $> 15\%$ or symptoms	Target weight was adjusted according to bioimpedance findings and clinical judgment. Changes of target weight of 0.1 to 0.5 kg/wk to obtain average weekly relative OH $\leq 15\%$	Change in echocardiographic parameters Arterial blood pressure	9 mo	Industry
Oh <i>et al.</i> 2018 <sup>29</sup> (NCT01887262)	Peritoneal dialysis patients with preserved diuresis ( $>500$ ml/24 h)	137	52 $\pm$ 13	5 centers, South Korea	Bioimpedance using BCM (Fresenius medical care) twice per month	Target weight adjusted to obtain a OH within 1 liter of normal range	Change in glomerular filtration rate (mean of the creatinine and urea clearance normalized to body surface area)	12 mo	Industry
Brimble <i>et al.</i> <sup>28</sup> (NCT010459800)	Peritoneal dialysis patients	65	61.6 $\pm$ 12.6	6 centers, Ontario, Canada	Bioimpedance using Quadscan 4000 (Bodystat) by the vector graph method assessed every 2 mo	Interventions targeted overhydration including successive strategies of dietary sodium restriction and intensification of diuretic use, introduction of icodextrin, and use of higher-strength glucose solutions without a prespecified algorithm	Change in left ventricular mass	12 mo	Mixed (industry + academic)

BCM, body composition monitor; OH, overhydration; TAFO, time-averaged fluid overload.

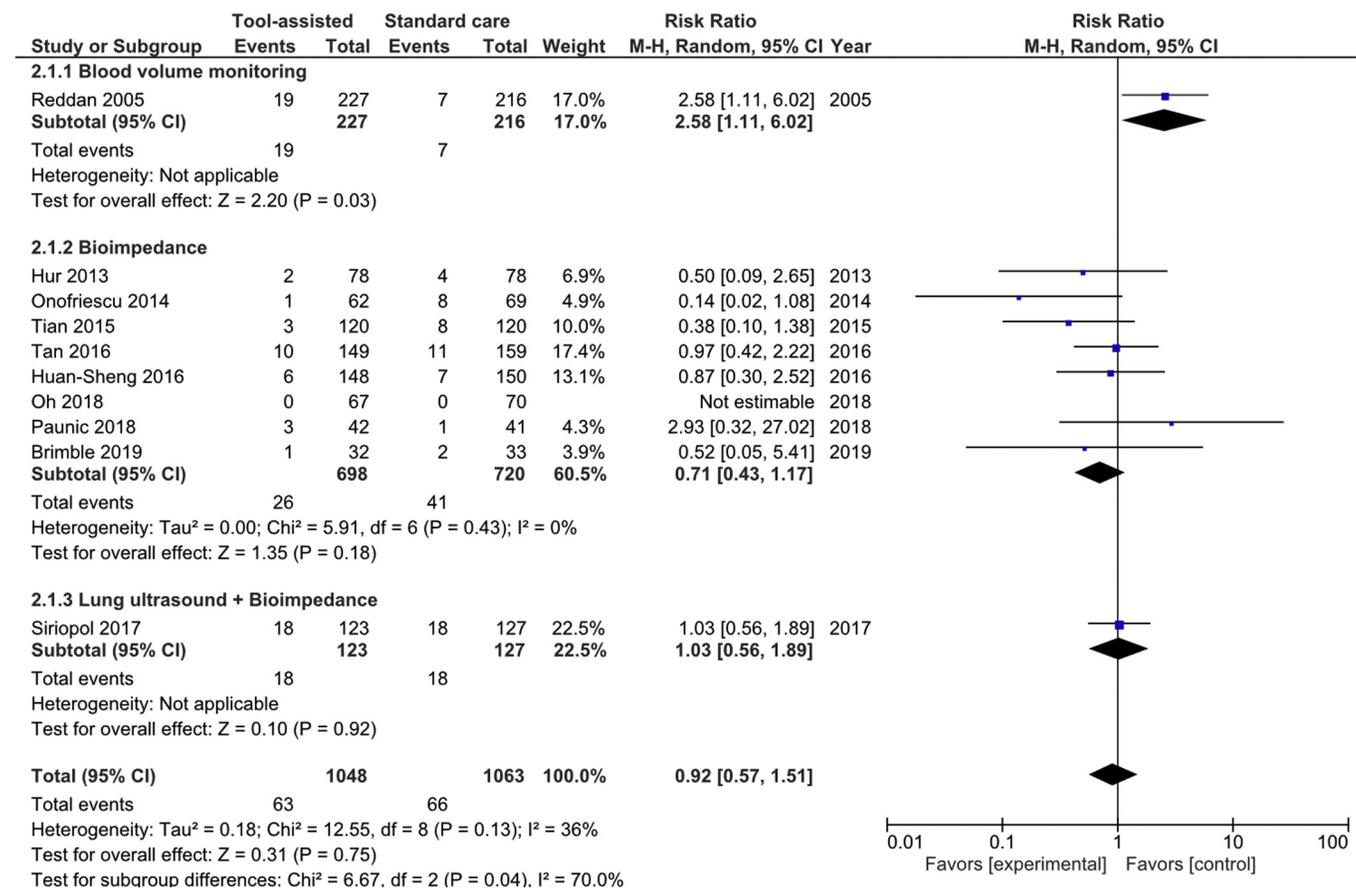


Figure 2. All-cause mortality and technology-assisted target weight adjustment. CI, confidence interval; M-H, Mantel-Haenszel.

patients (mean difference: -0.48 events/patients; CI: -2.37 to 1.41). Finally, in one report, adverse events including hospitalizations and cardiovascular events were reported as dichotomous outcomes at the end of an unequal follow-up period that was extended after the 12-month intervention period.<sup>28</sup>

### Risk of Bias Assessment

For trials that examined all-cause mortality, 3 were considered at high risk for incomplete outcome assessment (attrition bias).<sup>23,24,28</sup> In these studies, the high loss to follow-up (approximately 10%) was particularly concerning because the low incidence of

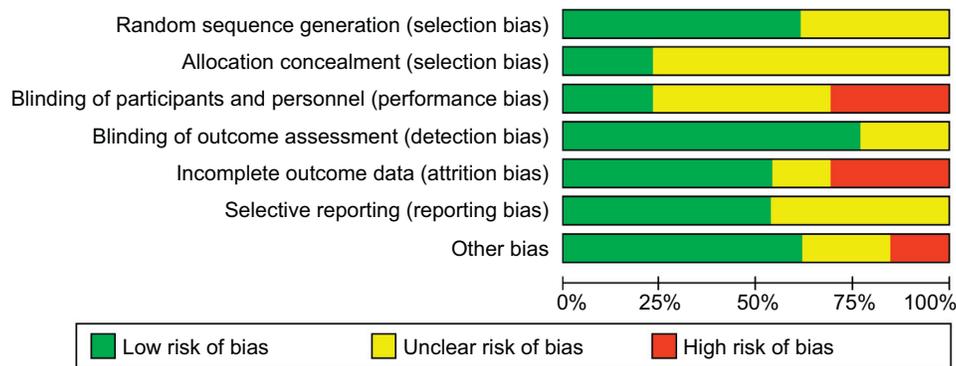
mortality combined with the inclusion of patients with missing outcome data could have substantially altered the results.<sup>23,24,28</sup>

The inadequate description of random sequence generation<sup>19,22,23,27,30</sup> and/or allocation concealment<sup>19-22,24,25,27,30</sup> was a further concern in several trials. Finally, 1 study was considered to be at very high risk of bias as it was stopped prematurely at half of the planned follow-up duration for unclear reasons.<sup>19</sup> The risk of bias in the studies included in the review is presented in Figure 3 and details are presented in Supplementary Figure S4.1 in Supplementary Appendix S4.

Table 2. Summary of findings for secondary outcomes

Outcomes	No. of studies	References	No. of patients			Effect estimate (95% CI)	I <sup>2</sup> (%)	Strength of evidence <sup>a</sup>
			Total	Intervention	Control			
Cardiovascular events	4	22, 24, 25, 29	811	402	409	RR 0.78 (0.45-1.33)	46	Very low
All-cause hospitalization	6	18, 22, 24, 25, 27, 29	1254	629	625	RR 0.88 (0.63-1.21)	76	Very low
Intradialytic hypotension	3	22, 24, 25	704	349	355	RR 1.01 (0.91-1.12)	77	Moderate
Symptoms during hemodialysis	2	24, 25	548	270	278	RR 1.12 (0.89-1.41)	96	Very low
Systolic blood pressure (mm Hg)	8	19-24, 28-30	1152	667	681	MD -3.14 (-5.89 to -0.38)	39	Moderate
Diastolic blood pressure (mm Hg)	6	19, 20, 22, 23, 28, 29	966	479	487	MD -1.17 (-3.97 to 1.63)	69	Moderate
Left ventricular mass index (g/m <sup>2</sup> )	5	22, 26-29	635	319	316	MD -13.6 (-29.7 to 2.48)	89	Low

CI, confidence interval; MD, mean difference; RR, rate ratio.  
<sup>a</sup>See Table S6.2 in Supplementary Appendix S6 for details.



**Figure 3.** Risk of bias in the included studies.

### Publication Bias and Quality of Evidence

Publication bias was assessed using a funnel plot (Supplementary Figure S5.1 in Supplementary Appendix S5) and no obvious asymmetry was found. The quality of evidence with respect to the all-cause mortality outcome was evaluated using the GRADE methodology.<sup>31</sup> Methodologic limitations were noted as described previously in the Risk of Bias Assessment section. The small number of studies combined with the low number of deaths in most of the included studies led to the imprecision of the effect estimate with wide CIs. For the previously mentioned reasons, the quality of the body of evidence for mortality was considered low. Further details about the evaluation of the quality of the body of evidence are presented in Supplementary Tables S6.1 and S6.2 in Supplementary Appendix S6.

## DISCUSSION

In this systematic review and meta-analysis, we found that the integration of technological adjuncts into the fluid management of patients with end-stage kidney disease did not affect mortality. The introduction of tool-assisted fluid management led to a small reduction in systolic arterial blood. The use of bioimpedance to guide target weight was associated with a decreased rate of hospitalization. The body of evidence available for the use of technologies other than bioimpedance was very scarce or inexistent.

Although each of the technologies had the common goal of optimizing fluid status, the principles underlying their use differ. Blood volume monitoring is based on the principle that the rate of change in the hematocrit represents the adequacy of intravascular refilling from the expanded interstitial space. An excessive drop in relative blood volume may signify slow refilling and this can imply that the optimal dry weight has been reached.<sup>8</sup> Bioimpedance provides a quantification of extracellular water, which should be

higher in fluid overloaded patients compared with a healthy population. The data emanating from bioimpedance measurements provides explicit quantitation of the deviation of the patient's present status from his or her ideal body water content, thereby providing concrete guidance for the ultrafiltration prescription. Finally, lung ultrasound is based on the semi-quantitative measurement of extravascular lung water content as a marker of pulmonary congestion from fluid overload. Fluid overload measured by bioimpedance and increased extravascular lung water detected by ultrasound have both been associated with increased mortality in dialysis recipients.<sup>32,33</sup> However, it remains unclear if and how clinicians should respond to results emanating from these evaluations.

The interest in technological adjuncts of volume assessment in dialysis recipients has grown on the premise that their adoption will improve fluid status and improve patient-relevant outcomes. In particular, blood volume monitoring devices are now integrated into the software and on-screen output of several contemporary hemodialysis machines. However, clinicians should not assume that the ready availability of these data will necessarily translate into improved patient care. Careful evaluation of how these data are interpreted and applied in usual care is vital before broad adoption.<sup>34,35</sup> Furthermore, although a compelling epidemiological association exists between fluid overload and adverse clinical outcomes,<sup>36,37</sup> it is unclear whether an aggressive approach aimed at achieving euvolemia will translate into meaningful benefits for patients and whether these benefits outweigh the risks, such as intradialytic hypotension.<sup>38</sup> In addition, as the consequences of fluid overload can progressively develop over a long period of time in patients with chronic kidney disease, it is likely that the benefits of any technology-driven fluid balance strategy would only become apparent with sustained use. Consequently, trials with a short duration of follow-up might not be adequate to provide a definitive

conclusion. It is notable that the only trial reporting a favorable difference in survival analysis with bioimpedance use had a longer follow-up duration and deaths did not occur until the 20th month of follow-up.<sup>21</sup>

To our knowledge, this is the first meta-analysis to comprehensively evaluate an array of technological adjuncts for volume assessment in dialysis recipients. Two meta-analyses that focused on the impact of using bioimpedance in dialysis recipients found no reduction of all-cause mortality or other clinical outcomes.<sup>39,40</sup> Both of these meta-analyses included a smaller number of randomized controlled trials and thus fewer patients, which compromised their statistical power to detect an effect on important outcomes, such as mortality. Other strengths of our meta-analysis include a broad search strategy including searching multiple databases and hand-searching, the use of an *a priori* protocol, and registered in the PROSPERO database.<sup>13,16,31</sup>

There are key limitations that merit consideration. First and foremost, most of the data available to be combined came from bioimpedance studies with very few studies investigating the use of other technologies. Furthermore, the wide CI surrounding the reported effect estimates suggests that this meta-analysis may still be underpowered to detect a clinically meaningful reduction in the risk of death and other key outcomes. In addition, the analysis of cardiovascular and intradialytic events was limited by the low number of trials reporting those outcomes. Although systolic blood pressure reduction was demonstrated, the relevance of predialysis measurements, as compared with ambulatory measurements, in dialysis recipients has been questioned.<sup>41</sup> Second, although the overarching therapeutic principle underlying the trials was the same, the methodology and measurements used to adjust target weight or ultrafiltration prescription varied widely from study to study, potentially resulting in significant clinical heterogeneity. It is important to note that several subgroup analyses could not be performed because of a lack of trials aimed at specific subgroups. For example, whether the effect of the intervention is different in patients with significant residual kidney function, dialysis vintage, or preexisting heart failure could not be investigated.

In conclusion, among recipients of maintenance dialysis, existing data on technological adjuncts to guide volume management did not demonstrate an impact on mortality. Completed trials suggest that integration of these tools into practice may improve blood pressure control and bioimpedance may lower the need for hospitalization. However, completed studies have been limited by small size, nonuniform

translation of findings into practice, short follow-up duration, and substantial risk of bias. Although these tools hold promise, we believe that more rigorous and sustained evaluation of these technologies is needed before their widespread adoption.

## DISCLOSURE

RW has received unrestricted research grants from Baxter and served as a consultant to Baxter. AYD is a speaker for CAE Healthcare and Masimo. All the other authors declared no competing interests.

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## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

**Appendix S1.** Search strategy.

**Appendix S2.** Details on data extraction.

**Appendix S3.** Forest plot for subgroup analysis and secondary outcomes.

**Appendix S4.** Risk of bias assessment.

**Appendix S5.** Assessment of publication bias.

**Appendix S6.** Quality of the body of evidence assessment.

**Supplementary References.**

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