Clinical Practice Guideline: Management of blood pressure in adults, children and young people on dialysis

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Authors:

Dr Tim Doulton
Consultant Nephrologist, East Kent Hospitals University NHS Foundation Trust

Dr Mariyam Adam
Renal Registrar, Liverpool University Hospitals NHS Foundation Trust

Ms Katie Durman
Renal Dietitian, Barts Health NHS Trust

Dr Stan L-M Fan
Consultant Nephrologist, William Harvey Research Institute, Queen Mary University of London

Dr Anna Forbes
Renal Registrar, University Hospital Lewisham

Mr Ed Jenkinson
Haemodialysis patient & lay representative

Ms Charlotte Mallindine
Renal Pharmacist, East and North Hertfordshire NHS Trust

Dr Kieran McCafferty
Consultant Nephrologist, Barts Health NHS Trust

Prof Manish D Sinha
Consultant Paediatric Nephrologist, Evelina London Children's Hospital

Dr Douglas J Stewart
Consultant Paediatric Nephrologist, NHS Greater Glasgow and Clyde

Dr Pauline Swift
Consultant Nephrologist, Epsom and St Helier University Hospitals NHS Trust

Prof Indranil Dasgupta – Chair
Consultant Nephrologist, Heartlands Hospital, Birmingham

Literature sources and search terms

The review process for this guideline was in accordance with the PRISMA statement (9). Several databases were searched (including PubMed, EMBASE, Ovid MEDLINE, Cochrane and CINAHL) to obtain articles that met eligibility for the literature review. Articles included were those with a publication date from 1st January 2000 to 31st December 2022 published in the English language. Full details of the PICO search tool, with all included databases and search strategies, are available in Appendix B.

Inclusion and exclusion criteria

Detailed inclusion criteria, according to the PICO search tool, are available in Appendix B. Exclusion criteria were studies relating to: (i) acute haemodialysis, (ii) acute peritoneal dialysis, (iii) continuous veno-venous haemofiltration and other acute kidney replacement modalities, and (iv) non-systemic hypertension in any specialised vascular bed (e.g. pulmonary, intracranial).

Study selection

All articles identified from the literature search were allocated to a predefined topic group by lead authors AF and TD. The seven topic groups were developed along the main themes highlighted previously. Within each topic group, articles were screened by at least two authors. Any discrepancies in whether an article met inclusion criteria were dealt with by mutual agreement between the authors allocated to that topic group, and TD or ID if consensus could not be met. Authors for each topic group are listed in Appendix B.

Data extraction and quality appraisal

For articles where there was a consensus opinion on inclusion, data extracted were: study aim, study design, method of BP assessment, follow-up period, sample size, population (country and kidney replacement therapy modality), primary analysis, and major results. These data are summarised in the Evidence Tables (Appendix C) and findings were used to support the rationale for the recommendations of this guideline. The recommendations and supporting rationale were reviewed by all authors and by key stakeholders prior to publication of the guidelines.

Evidence grading

We followed the principles set out in the UK Kidney Association's "Clinical Practice Guideline Development Manual" and grade evidence according to a two-tier grading system (see Table 1.1). We use the term "recommend" within the guideline text where Recommendations are based on Grade 1 evidence, and the term "suggest" for those based on Grade 2 evidence. We also made ungraded 'Research recommendations', which help define ongoing areas of clinical uncertainty, and we offer 'Audit measures', to define how to demonstrate effective implementation of recommendations.

Conflicts of Interest Statement

All authors made declarations of interest in line with the policy in the UK Kidney Association Clinical Practice Guidelines Development Manual. Further details can be obtained on request from The UK Kidney Association.

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Introduction

The UK adult population receiving dialysis continues to increase. Between 2020-2021, the annual increase was 1.5%, compared with 2-2.5% seen prior to the COVID-19 pandemic. The average age of adults receiving dialysis is older (66.1 years for HD and 63.3 years for PD) with a longer duration of therapy required (median duration 3.2 years) when compared with published registry data from 2010 [1, 2].

Cardiovascular (CV) disease remains one of the most significant causes of mortality in adults receiving dialysis, with an incidence of over 20%, and death from a primary CV disease cause is more likely in those less than 65 years of age [2]. In children and young people (CYP) with end stage kidney disease (ESKD), similar trends are seen, with the current childhood dialysis population in the UK being the largest on record. CYP are waiting longer than before to receive a kidney transplant and CV disease remains the most common cause of morbidity and mortality for those receiving dialysis [2, 3].

Hypertension is one of the commonest modifiable causes of CV disease in adults receiving dialysis [4-7]. In CYP on maintenance dialysis too, hypertension is the strongest risk factor for left ventricular hypertrophy (LVH), the most evaluated surrogate marker of CV abnormality in this population (8). Data from adults on long term dialysis additionally highlight increased CV risk from lower blood pressure (BP) and declining BP over time [4, 5].

This guideline has been developed with a focus on BP management, acknowledging the central role of body fluid status in adults and CYP receiving dialysis [6, 7]. Existing guidance does not focus on the systematic evaluation of the evidence base for BP management in dialysis-dependent adults and CYP and, as such, highlights the need for specific guidelines [1, 6].

The authors of this report include a broad range of healthcare professionals with experience in kidney disease, including dietitians, pharmacists and both adult and paediatric kidney doctors, as well as a patient representative, who have worked together to review the evidence for management of BP in adults and CYP who are receiving dialysis for ESKD.

The main themes in this document include evaluation of the published evidence for: (i) measurement of BP; (ii) BP targets; (iii) lifestyle modifications; (iv) dialysis prescription modifications; (v) antihypertensive management to aid with BP control; (vi) dry weight optimisation in adults, and (vii) CYP receiving dialysis. Our overall aim with this guidance is to ensure a consistent and standardised approach to the management of BP in patients receiving dialysis across the UK, whilst striving to improve quality of care and reduce disparities in outcomes.

Table 1.1: UK Kidney Association's grading system for recommendations' strength and evidence quality

Level of evidence	Evidence quality
• Grade 1 recommendation is a strong recommendation to do (or not do) something, where the benefits clearly outweigh the risks (or vice versa) for most, if not all, patients (i.e. "recommendations"). • Grade 2 recommendation is a weaker recommendation, where the risks and benefits are more closely balanced or are more uncertain (i.e. "suggestions").	• Grade A evidence means high-quality evidence that comes from consistent results from well-performed randomised controlled trials, or overwhelming evidence of some other sort. • Grade B evidence means moderate-quality evidence from randomised trials that suffer from serious flaws in conduct, inconsistency, indirectness, imprecise estimates, reporting bias, or some combination of these limitations, or from other study designs with special strength. • Grade C evidence means low-quality evidence from observational studies, or from controlled trials with several very serious limitations. • Grade D evidence is based only on case studies or expert opinion.

Summary of clinical practice guidelines

Measurement of blood pressure

1. We recommend interdialytic ambulatory blood pressure monitoring (ABPM) as the gold standard to diagnose hypertension in people on haemodialysis. (1C)
2. We suggest using either home blood pressure measurement (HBPM) or standardised out-of-dialysis unit clinic BP measurement to monitor BP and guide treatment for in-centre haemodialysis. (2C)
3. We suggest clinicians use routine dialysis unit BP measurements to inform safety of delivering haemodialysis rather than to inform hypertension management decisions, because of the imprecision of routine dialysis unit BP measurement compared to standardised out-of-dialysis-unit BP measurement and interdialytic ABPM. (2C)
4. We suggest using either HBPM or standardised clinic BP measurements to monitor BP and guide treatment in patients receiving home-based dialysis (home haemodialysis and peritoneal dialysis). (2C)

Blood pressure targets

5. We suggest, for those on haemodialysis where *non-standardised* in-centre BP measurements are used, aiming for:
    a. pre-dialysis systolic BP between 140 and 165 mmHg (2B) and pre-dialysis diastolic BP between 60 and 100 mmHg. (2C)

   b. post-dialysis systolic BP between 120 and 140 mmHg and post-dialysis diastolic BP of ≥70 mmHg (2C)
6. We suggest aiming for the lower end of the systolic BP ranges in recommendation 5a, unless this results in an increased frequency of intradialytic hypotension (IDH) and/or in those with a prior history of frequent IDH (2D)
7. We suggest that factors such as age and comorbidities may be used to determine an individual patient's target BP range. For younger people or those with fewer co-morbidities, a *lower* systolic BP range than suggested in recommendation 5a can be considered. (2C)
8. We suggest that clinic BP should be <140/90 in people on peritoneal dialysis. (2C)

Lifestyle modification

9. We recommend salt reduction to a maximum intake of 5 g daily. (1B)
10. We suggest that fluid restriction, together with salt reduction, should be advised. Fluid restriction should be individualized considering urine output, fluid gains between dialysis and ultrafiltration. (2D)
11. We suggest that exercise should be considered as a strategy to reduce BP in those receiving haemodialysis. (2D)
12. We suggest that a combination of aerobic and resistance exercise at least 3 times per week of moderate to vigorous intensity, either during or in between dialysis, would be most likely to reduce BP in haemodialysis patients. (2B)
13. We suggest that haemodialysis units consider adoption of strategies to support patient adherence to lifestyle changes. (2D)

Dialysis and Dialysate

14. We suggest that extended dialysis hours should be considered for individuals who fail to achieve adequate BP control or experience IDH during the standard thrice weekly dialysis if the resources are available. (2A)
15. We suggest that lowering dialysate temperature can reduce incidence of IDH in patients prone to this condition. (2A)
16. We suggest that online haemodiafiltration (HDF) could be trialled in patients experiencing symptomatic IDH to improve CV tolerance of treatment. (2B)
17. We suggest that HDF should only be considered once alternative causes for IDH have been addressed and where patients have failed to respond to other methods. (2C)
18. We suggest that HDF should *not* be used as a treatment strategy to control BP in patients who are hypertensive. (2C)
19. We recommend that bicarbonate-based dialysate should be used rather than acetate-based solutions to reduce IDH risk. (1B)
20. We suggest that low magnesium dialysate concentrations (≤0.25mmol/L) be avoided, particularly if dialysate calcium is 1.25mmol/L, in patients at risk of IDH. (2D)
21. Icodextrin can be a useful tool to control BP when used in conjunction with effective setting and probing of target weight in people who are on peritoneal dialysis. (2D)

Dry weight optimization

22. We suggest that patients on dialysis (both haemo- and peritoneal dialysis) should avoid significant over or underhydration. (2A)
23. We suggest that dialysis patients should be assessed regularly in a systematic manner for fluid volume status to guide alterations to their dry/target weight and ultrafiltration volume. (2C)
24. Multiple technologies are available to aid fluid volume management in dialysis patients including continuous blood volume monitoring, inferior venacaval diameter measurement, lung ultrasound and bioimpedance spectroscopy. There is inadequate evidence to recommend one method as superior to another or clinical assessment of fluid volume status. (2C)

Medication

25. We recommend BP lowering medication to reduce all-cause and CV mortality in adult dialysis patients. (1B)
26. We suggest β-blockers (βBs) as first line and calcium channel blockers (CCBs) as second line BP lowering medication in adults on haemodialysis, based upon BP lowering efficacy. (2B)
27. We suggest ACE inhibitors (ACEi) as third line BP lowering medication in adults on haemodialysis, based upon BP lowering efficacy and enhanced risk of hypotension and discontinuation compared to βBs and CCBs. (2B)
28. We suggest ACEis or angiotensin receptor blockers (ARBs) as first line BP lowering medication in people on peritoneal dialysis, based upon evidence that these classes of antihypertensive may slow loss of residual kidney function. (2B)
29. We suggest mineralocorticoid receptor antagonists (MRAs), combined with careful monitoring of plasma potassium levels, may be considered in those with difficult to control BP. (2B)
30. We suggest advising people on haemodialysis *against* the practice of omitting BP lowering medications prior to dialysis sessions. For those in whom BP lowering medication is implicated as contributing to IDH we suggest advising consistent evening dosing instead. (2D)
31. We suggest that, where β-blockers are used, those with low dialysability are generally preferred in those receiving haemodialysis. (2C)
32. We suggest that use of BP lowering medication with prolonged half-lives (e.g. atenolol, amlodipine, lisinopril or enalapril) in people on haemodialysis could be considered in those who are non-adherent to medication when combined with dosing at the end of the dialysis session. (2D)
33. We suggest that L-carnitine and/or oral midodrine may be considered as part of a multi-faceted approach to management of IDH although data supporting usage is limited. (2C)

Children & Young People (CYP)

We suggest the following:

34. When measuring BP in CYP on dialysis, the clinical setting and assessment method should be standardised. (2C)
35. The best accepted practice for diagnosing hypertension in CYP on dialysis is with 24-hour ABPM. This should be performed at least annually once children reach a height of 120 cm. (2B)
36. If ABPM is not feasible, standardised in-centre BP measurements and/or home BP monitoring (HBPM), should be used to assess BP control. (2D)

37. For CYP receiving in-centre haemodialysis, BP should be monitored at every dialysis session (including pre-, intra- and post-dialysis measurements), to aid with assessment of required fluid removal. This should be done in conjunction with weight measurement and clinical evaluation of fluid status. (2C)
38. For CYP on dialysis, BP should be targeted to <90th percentile for age, height and sex on non-dialysis days. (2D)
39. There is inadequate evidence to provide target BP ranges for HBPM in CYP on dialysis although this method may be used as an adjunct to in-centre measurements. (2D)
40. For CYP on dialysis, baseline and annual echocardiography should be performed to assess for morphological left ventricular changes that may indicate hypertension-mediated organ damage. (2C)
41. For CYP with elevated BP on dialysis, salt intake should not exceed the age-related upper limit of recommended daily intake (RDI) although nutritional requirements should be regularly reviewed by dietetic colleagues. (2B)
42. Antihypertensive medications should be considered if BP remains uncontrolled despite lifestyle interventions (e.g. fluid and salt restriction) and optimised fluid removal, particularly in the context of underlying target organ damage. (2C)
43. When prescribing antihypertensive medications for CYP on dialysis, there is insufficient evidence to support the first-line use of any specific single agent or drug class. Both patient-specific factors, including the pharmacokinetics and dialysability of a drug (*Appendix D*), should be considered with the support of pharmacist colleagues. (2D)

Practice Points

1. We recognise that there may be circumstances in which a clinician and/or patient prefers to base BP management decisions on out-of-office (HBPM or ABPM) or standardized clinic BP readings. Whilst we have not suggested a target BP range based on HBPM due to a paucity of evidence, we note that observational studies utilising HBPM or standardised clinic BP readings generally demonstrate a linear relationship between BP and adverse outcomes, and that a systolic BP approximately ≤130 mmHg appears to be associated with lowest risk of all-cause and/or CV mortality.

Rationale for clinical practice guidelines

Measurement of blood pressure

There is no universal agreement on the measurements that should be used to diagnose hypertension and monitor BP in people on dialysis, even though they have their BP checked more frequently than any other group of patients. There is absence of randomised control trial (RCT) data comparing various BP monitoring techniques and their effects on long-term outcomes. However, there are emerging themes from the current research that must be incorporated into clinical practice for people receiving haemodialysis. The evidence is even more scarce in people receiving peritoneal dialysis. Therefore, recommendations made here are based on either very low-grade evidence or expert opinion.

Diagnosis

For the minority of patients who may not already have hypertension diagnosed prior to starting dialysis, we recommend using ABPM as gold-standard to diagnose hypertension. Fagugli *et al.* compared 48-hour ABPM that included a dialysis day and found that 24-hour APBM either on interdialytic period or dialysis day is not different from 48-hour ABPM. Prevalence of hypertension diagnosed in this study (SBP >140 mmHg) was 80% compared to 61.7% diagnosed by predialysis SBP of >140 mmHg [10].

For people on haemodialysis, BP measured outside the dialysis unit has more prognostic value [4, 11] and both studies suggest ambulatory BP is more closely associated with the risk of all-cause mortality than home BP. Alborzi *et al.* studied this in a cohort of 150 people on haemodialysis and found that every increase in SBP by 22.3 or DBP by 13.8 mmHg was associated with 50% increase in mortality, whereas home BP was associated with 35-40% elevation in risk [11]. There was no association seen with dialysis unit SBP or DBP. Agarwal *et al.* report similar findings in a larger cohort of a similar population and demonstrated an increased risk of all-cause mortality with increasing SBP using both ABPM and HBPM but not with dialysis unit BP [4].

There is very limited data on using HBPM to diagnose hypertension in dialysis patients. Agarwal found one week averaged systolic BP of 150 mmHg or post-dialysis standardized BP of 122 mmHg has both high sensitivity and specificity to predict hypertension diagnosed by ABPM [12].

Monitoring

Routine pre- and post-dialysis BP are poor estimates of average BP measured by ABPM. In a meta-analysis of 692 haemodialysis patients, SD of the difference of the pooled observations between ambulatory SBP and pre-dialysis SBP was 16.7 mmHg with wide limits of agreement of 41.7 mmHg to −25.2 mmHg [13]. In addition to inaccuracy, dialysis unit BP doesn't have any prognostic value as demonstrated in a cohort of 326 maintenance haemodialysis patients, where a strong relationship was observed for mortality over an average of 32 months with increasing quartiles of BP measured by 44 hr ABPM and HBPM but not for dialysis unit BP [4]. Therefore, we suggest that dialysis unit BP should only be used to guide safety of dialysis sessions rather than to inform long-term management of elevated BP and CV risk. This raises an important question as to which other measurements might be more appropriate to use for long term management of hypertension in people on dialysis.

As outlined above ABPM seems to have most evidence and is used in studies as a gold standard for comparison of BP measurement methodologies. It is, however, not feasible to use ABPM routinely on patients, whereas HBPM and standardised clinic BP measurement are two alternatives. There is evidence that out-of-unit BP measurements including standardised clinic BP [14] and HBPM and ABPM [4] show a linear relationship to mortality. Further, there is a linear relationship between out-of-unit BP readings and CV risk [14].

There are some studies using HBPM to guide long term management of hypertension and these show that it is feasible, safe and acceptable to people on dialysis [15] and it more closely reflects changes in interdialytic ABPM when compared to standardised pre- and post-dialysis BP measured in-centre [16]. A small RCT of 96 people on haemodialysis showed that treatment decisions based on HBPM resulted in

better BP control as determined by ABPM as the gold standard, compared to routine pre-dialysis BP [17]. Although these differences in BP control did not translate into lower left ventricular mass index in the HBPM cohort, follow-up was short at 6 months. The frequency of HBPM measurements differs between studies. However most suggest twice a day BP monitoring for 4 consecutive days [18, 19]. Perhaps more importantly, however, it is not yet clear what the target BP should be when utilising home BP readings in people on dialysis.

Dialysis unit BP measurements are an inaccurate estimate of interdialytic BP [13]. While every effort should be made to standardise BP measurement in the dialysis unit, it will be logistically challenging to implement in routine care. Furthermore, there is no evidence to guide what the target BP should be for standardised pre- and post-dialysis BP measurements. On the other hand, there is evidence that HBPM is more accurate [12, 16] and better predicts CV events and mortality [4, 11]. Therefore, a focus for future research should be how we can incorporate HBPM and standardised out-of-unit BP measurements into clinical practice.

The table below summarises advantages and disadvantages of different BP readings available for dialysis patients.

Relative merits and demerits of different BP measurement techniques in haemodialysis patients

Prognostic accuracy + - Ease of utilisation - +

BP measurement technique	Advantages	Disadvantages
Ambulatory monitoring (ABPM)	▪ Good reproducibility ▪ Good prognostic accuracy **Gold Standard**	▪ Low patient acceptability ▪ Expensive, ▪ Complex to utilise in routine practice
Home monitoring (HBPM)	▪ Reproducible ▪ Good prognostic accuracy ▪ Widely available ▪ Relatively inexpensive ▪ Empowers patients	▪ Need motivated patients ▪ Noncompliance ▪ Needs training
Standardised out-of-centre	▪ Linear relationship with outcomes ▪ Easy to utilise in practice	▪ Clinic attendance on anon-HD day ▪ Prognostic accuracy lower than ABPM and HBPM
Standardised peri-dialytic	▪ More accurate than routine BP ▪ Better prognostic value than routine BP - especially post-HD	▪ Time constraint ▪ Difficult to utilisein a busy dialysis unit
Routine peri-dialytic	▪ Readily available	▪ Imprecise ▪ Confounded by various healthcare and patient related factors ▪ 'U' or 'J' shaped relationship with outcomes ▪ Poor reproducibility

Blood Pressure Targets

Numerous observational studies have described a 'U' or 'J' shaped relationship between pre-dialysis systolic BP and outcomes in people on haemodialysis where only low and, usually, very high BPs are associated with excess all-cause or CV mortality. Such studies have typically utilised 'usual' non-standardised BP measurements and there is poor agreement between 'usual' BP readings and those taken in standardised conditions [20]. Besides a likelihood that ascertainment of 'usual' BP readings doesn't adhere to best practice [21] other factors account for the 'U' or 'J' shaped relationship which contrasts with the linear relationship between BP and adverse outcomes seen in the general

hypertensive population and in haemodialysis patients where other measurement methods (standardised, HBPM, or ABPM) are utilised. For example, in the CRIC study standardised BP (mean of 3 seated BP measurements) taken away from the dialysis unit is linearly related to mortality, whereas pre-dialysis measurements retain a U-shaped association within the same cohort of patients [22]. There are likely to be several explanations for these discrepant relationships, not least that pre-dialysis BP reflects an individual's physiological ability to tolerate volume loading. Importantly, people on haemodialysis differ from the general hypertensive population in another important regard: a tendency to suffer IDH which affects ~30% of dialysis sessions. Accumulating evidence suggests that IDH and ultrafiltration volumes are independently predictive of myocardial stunning which, in turn, is predictive of left ventricular systolic dysfunction and myocardial fibrosis [23], vascular access thrombosis [24] and mortality [25].

A single feasibility and safety study randomised 126 hypertensive haemodialysis patients to a "standard" BP target range of 155-165 mmHg or an "intensive" range of 110 to 140 mmHg, measured in a *standardised* manner in the immediate pre-dialysis period [26]. Of seven pre-specified feasibility objectives [27], two were achieved (mean separation of BP between arms by >10 mmHg; 75% participants providing minimum required number of standardised unit BP measurements), two were not achieved (IDH in intensive arm not >20% higher than standard arm; ≥66% of required HBPM/ABPM measurements) and three were not reported. Additionally, 55% of the 281 participants that consented did not progress to randomization, predominantly due to not achieving SBP 155 mmHg despite back-titration of medications (n=65, 23% of those consented) or participant-initiated withdrawal (45, 17%). Nonetheless the authors judged that a full scale RCT would be feasible, presumably with modifications. Importantly, and despite not being powered for definitive conclusions, a number of safety signals emerged around intensive BP lowering: those in the intensive arm experienced a non-significant three-fold increase in vascular access thrombosis (incidence rate ratio, IRR 3.09) and an IRR of 1.61 for hospitalisation.

Besides this study, the remaining data to guide BP targets is predominantly derived from observational cohort studies utilising non-standardised pre- and post-dialysis BP measurements described above. These studies fairly consistently show worse outcomes where pre-haemodialysis BP is below ~140 mmHg. A facility-level analysis of DOPPS data designed to minimise effects of unmeasured patient-level confounding found lowest mortality in those with a pre-haemodialysis BP of 130 to 159 mmHg [28]. Other studies have found lowest risk of CV events with a pre-haemodialysis systolic BP range of 140 to 170 mmHg (5); lowest risk for all-cause mortality at 165 mmHg and for CV mortality at 157 mmHg [29] and lowest risk for all-cause mortality at 152 mmHg and CV events at 143 mmHg [30]. Considering the totality of data available, we suggest for haemodialysis units or individual clinicians wishing to base BP targets on pre-haemodialysis measurements, that a systolic BP range of approximately 140 to 165 mmHg appears to be associated with the fewest short- and long-term adverse outcomes.

Data on pre-dialysis diastolic and post-dialysis BP are more limited. In the Robinson study, facility-level pre-dialysis DBP between 60 and 99 mmHg and post-dialysis SBP between 120 and 139 mmHg were associated with lowest mortality [31]. The same analysis identified post-dialysis DBP <70 mmHg to be associated with increased mortality with no corresponding upper limit. Hannedouche did not find a pre-dialysis DBP level that was indicative of minimal risk for all-cause mortality. For CV mortality, a DBP of 90 mmHg was found to be associated with lowest CV mortality, although 95% confidence intervals

for hazard ratio were wide, and depart from 1.0 at a DBP of approximately 70 mmHg [29]. Post-dialysis BP readings were not analysed.

Limited observational data suggest that demographic characteristics such as age [32], co-morbidities including diabetes [33], atrial fibrillation and heart failure [34] and biomarkers, e.g. troponin I and NT-proBNP [35], influence the nature of the relationship between BP and outcomes, such that in younger patients without co-morbidity and normal biomarkers only higher SBP tends to be associated with adverse outcomes, leading us to suggest that aiming for lower BP targets may be acceptable in this population.

Studies using HBPM, ABPM and standardised clinic BP readings generally demonstrate a positive linear relationship between BP and outcomes [4, 5, 11]. For example, a study of 326 predominantly African American haemodialysis patients dialysing in Indiana, US found an average home SBP of 120-130 mmHg to be associated with lowest all-cause mortality [4]. Similarly the CRIC study investigators found in 377 haemodialysis patients that, compared to those with a standardised SBP <128 mmHg, adjusted HR for CV events was 2.14 (95% CI 1.17 to 3.9) and 2.9 (95% CI 1.55 to 5.42) for those with SBP 128 to 145 and >145 mmHg respectively (5). A similar relationship was demonstrated in a recent Brazilian study in 2,672 haemodialysis patients, where BP was measured in the inter-dialytic period albeit probably not in a standardized manner. Compared to a reference SBP of ≥ 171 mmHg, incidence of CV events was reduced in those with SBP 101-110 (HR 0.65, 95% CI 0.46-0.90), 111-120 (HR 0.66, CI 0.49-0.89), 121-130 (HR 0.75, CI 0.57-0.98), and 131-140 mmHg (HR 0.76, CI 0.6-0.97) [36].

However, it is important to recognise important limitations of these studies. Firstly, they were conducted in small, often single-centre, populations that are unrepresentative of the wider UK dialysis population; and, secondly, some excluded participants with important CV co-morbidities such as atrial fibrillation [4, 11]. In a European study using ABPM in 344 haemodialysis patients, a *U-shaped* relationship between ambulatory SBP and CV and all-cause mortality was observed in the whole study cohort, whereas when ~30% with either atrial fibrillation or heart failure were excluded a positive linear relationship between BP and outcomes was observed [34]. These contradictory findings emphasize the inherent difficulties in using observational data to guide clinical practice even when using 'gold-standard' BP measurement methodologies, and the need for well-designed interventional trials to define appropriate BP targets in those on dialysis.

In the peritoneal dialysis population there are few data to guide BP targets with the ISPD recommended target of <140/90 mmHg being extrapolated from the general and CKD population [37]. One large prospective cohort study undertaken in China found a U-shaped relationship between usual clinic SBP – presumably non-standardized – and all-cause and CV mortality, with an SBP range of 119-141 being associated with lowest hazard ratio for adverse outcomes [38]. An analysis of UK Renal Registry data in peritoneal dialysis suggested that higher BP is associated with reduced mortality in the first 12 months following commencement of renal replacement therapy (RRT), except in the subgroup listed for transplantation within six months of starting RRT [39]. Assuming, as the authors suggest, that early transplant listing is a proxy for minimal comorbidity, it is suggested that we should aim for lower BP targets in less comorbid peritoneal dialysis patients although no specific BP targets are identified by this study.

Lifestyle modification

Salt intake

Volume expansion, net positive sodium balance, renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system activation contribute to high BP in people on dialysis [40]. Lifestyle interventions that attenuate these effects may have some impact on BP control.

Volume expansion by salt and water is thought to be a major contributor to hypertension in people on dialysis [41, 42]. Higher dietary sodium intake is independently associated with greater mortality in people on haemodialysis [43]. Reduction in salt intake lowers BP in the general population, in hypertensives of all ethnicities, in people with and without diabetes and in people with chronic kidney disease (CKD) [44-48]. A low salt diet may be particularly beneficial in people on dialysis because they are largely dependent on the dialysis process to remove excess sodium and water. Studies in the 1990s explored dietary salt reduction together with dialysis interventions to achieve optimal dry weight and BP control [49-51]. The studies reported to date, however, are poorly designed, uncontrolled and underpowered to show a BP difference following dietary interventions. A meta-analysis of randomized controlled trials in 91 haemodialysis patients has shown that a mean difference in salt intake of 5 g/day was associated with a reduction in BP of 8/4 mmHg (95% CI 4.8 to 12/2.2 to 6.6) [52]. A subsequent systematic review and meta-analysis of salt reduction in all stages of CKD included 5 studies in haemodialysis patients and found reducing salt intake reduced systolic BP by 6.32 mmHg (95% CI -11.04 to -1.60) and diastolic BP by 3.46 mm Hg (95% CI -6.39 to -0.54) [53].

Fluid restriction

Volume overload is a risk factor for mortality amongst dialysis patients [54]. Efforts to achieve ideal target weight are discussed in other sections of this guideline, some of which will involve salt and water restriction, increased ultrafiltration and longer dialysis times to facilitate achieving euvolaemia. There is an acceptance that fluid restriction requires concomitant salt intake reduction, but evidence for fluid restriction alone lacks any contemporary evidence base [55].

Other dietary approaches

There is good evidence in the general population that a diet high in fruits and vegetables such as the Dietary Approaches to Stop Hypertension (DASH) diet can help to lower BP [46, 56]. However, trials in people on dialysis are lacking. An observational cross-sectional study in 2022 assessed the diets of 583 individuals on haemodialysis and categorized according to adherence to the DASH diet [57]. Higher adherence to the DASH diet was associated with lower serum potassium levels, although no difference in BP was observed between the groups (personal communication with author). This study allays concerns that a DASH diet may lead to hyperkalaemia and paves the way for further research.

Several authors have investigated diets rich in polyphenols. A systematic review of three trials found a reduction in DBP but not SBP [58]. Another small study has reported a reduction in SBP and DBP with pomegranate juice [59]. Due the small number of trials with low numbers the evidence is not strong enough to make a recommendation.

Although there is a lack of evidence in the dialysis population, we suggest that other lifestyle measures to control BP are adopted including maintenance of ideal body weight, excessive intake of alcohol, coffee and caffeine rich foods and drinks should be discouraged as per advice for the general population with hypertension. We also suggest that specialist renal dietitians are best placed to provide dietary advice to those on dialysis. Patients on dialysis have complex dietary requirements and renal dietitians can provide individualized, holistic advice.

Exercise

A number of systematic reviews and meta-analyses have considered whether exercise reduces BP in dialysis. Most studies have focused on intra-dialytic exercise.

In a 2019 meta-analysis of intradialytic exercise trials that included BP as an outcome, there was a significant reduction in SBP of 4.87 mmHg (95% CI -9.2 to -0.5, p=0.03) and DBP of 4.11 mmHg (95% CI -6.5 to -1.72, p=0.0007) [60]. In another meta-analysis of intradialytic exercise, the effect of aerobic exercise and combined exercise (aerobic and strength) were analysed separately. The authors found a significant reduction in SBP of 10.07 mmHg (95% CI --16.36 to –3.78) with aerobic exercise and a reduction in DBP of 5.76 mmHg (95% CI -2.7 to -8.83) with combined exercise, but there was no reduction in SBP with combined exercise or DBP with aerobic exercise [61].

Other meta-analyses have explored the effects of all types of exercise, intradialytic exercise, exercise on non-dialysis days, aerobic and combined strength and aerobic, on BP in dialysis populations. One included 16 studies of at least 8 weeks and found that only combined training reduced BP. SBP was reduced by 9 mmHg (95% CI -13 to -4) and DBP by 5 mmHg (95% CI -6 to -3) [62]. The other considered whether the intensity of exercise was important. Moderate to vigorous exercise was found to be most effective at reducing SBP by 8.8 mmHg (95% CI -17 to -1.6) and DBP by 4.9 mmHg (95% CI –9.9 to –0.4) [63]. Both meta-analyses suggest that combined training was the most effective.

The most comprehensive report on exercise in dialysis populations is a 2022 Cochrane systematic review of RCTs and quasi-RCTs of any structured exercise programs of eight weeks or more in adults undergoing maintenance dialysis compared to no exercise or sham exercise [64]. The authors report uncertainty as to whether exercise training reduces the risk of death and no studies reported CV events. They found that exercise training was likely to improve functional capacity and depressive symptoms with some degree of certainty. The effects of exercise on BP were analysed in smaller meta-analyses, which considered different types of exercise regimens separately. There was a significant reduction in SBP 8.69 mmHg (95% CI -13.69 to -3.69) and DBP 4.45 mmHg (95% CI -5.98 to -2.91)- with combined exercise, but authors consider the results are of very low certainty due to the high risk of bias, the short duration of the interventions and follow-up and the low number of participants in the included studies. There was no significant reduction in BP with aerobic exercise alone. We are unable to make any recommendations for exercise reducing BP in PD patients due to the lack of evidence.

Self-care engagement

Achieving BP targets is notoriously difficult for a combination of reasons. Some small studies have reported recently that explore the impact of interventions on adherence to diet, fluid and BP

medications [65]. An educative nursing intervention in 118 participants recruited from 6 haemodialysis units in the USA found that BP education sessions, with home BP monitoring twice daily, diarising salt and fluid intake weekly for a 12-week period vs. standard care with BP monitoring and medication adjustment by health care providers on a weekly basis in the haemodialysis unit significantly decreased both SBP and DBP in the treatment group. Another non-controlled study has reported a greater likelihood of reduction in SBP in a cohort of 58 haemodialysis patients, who received counselling from a pharmacist on adherence to BP medications [66]. We considered that these studies are not sufficient to make a recommendation on the role of supportive care interventions in BP management of dialysis patients, but measures to support adherence to treatment goals is possibly an area for further research.

Dialysis and Dialysate

Studies of extended duration of haemodialysis (beyond the conventional 3 to 5 hours three times a week) generally support improved BP control and or reduced BP medication burden, with inconsistent findings on left ventricular mass measurements [67-70].

More recently, however, extended duration HD has been shown to be associated with lower mortality. This is true whether the haemodialysis session is extended, or the frequency of haemodialysis is increased [71, 72]. The Frequent Hemodialysis Network (FHN) Daily Trial reported that 2 months of a frequent haemodialysis regimen lowered pre-dialysis SBP by 7.7 mm Hg (95% CI: −11.9 to −3.5) and DBP by 3.9 mm Hg (95% CI −6.5 to −1.3) [73] whilst the FHN Nocturnal Trial reported a reduction in systolic SBP from baseline of 7.9 ± 18.4 mm Hg in the nocturnal cohort at 12 months [74]. Short daily and nocturnal schedules also reduce the per-session probability of IDH by between 20 and 68%, while wellbeing and shorter recovery times are observed in those having extended hours HD, possibly mediated through a combination of optimizing sodium and volume status or enhanced solute clearance [70, 74].

Whilst there is good evidence to support extending haemodialysis for improved BP control, either by longer sessional hours or increased frequency of sessions, universal adoption of practice is unlikely due to the high cost of providing this service. The NightLife study is ongoing and will evaluate the cost and clinical effectiveness, including effect on BP, of thrice-weekly extended in-centre nocturnal haemodialysis versus daytime haemodialysis [75].

It has also been reported that HDF, compared to haemodialysis, improves cardiovascular stability during treatment sessions and that it reduces the frequency of IDH [76-78]. These findings, however, are not consistent across all studies. Two meta-analyses on this topic have reached differing conclusions on the intervention effect on IDH, but neither study reports a significant effect on BP outcomes [79, 80]. These inconsistent findings may be explained by failure to achieve sufficient convective volumes, different haemodialysis modalities (low-flux vs high-flux) and HDF techniques, participant demographics and access type. With the view that there was still clinical equipoise as to the potential benefits of high dose HDF compared to conventional high-flux haemodialysis, the CONVINCE and H4RT trials were conceived to address the issue. CONVINCE has recently reported on the primary outcome; a reduction in death from any cause in the HDF group (hazard ratio, 0.77; 95% CI, 0.65 to 0.93), although risk of death from CVD was similar in HDF and high-flux haemodialysis treatment arms [81]. At

present, there remains insufficient evidence to recommend the widespread implementation of HDF on the grounds of cardiovascular benefit. H4RT trial outcome data is awaited [82].

Active BP lowering in haemodialysis patients can lead to increased frequency of IDH. Large observational studies have demonstrated an association between frequency of IDH and mortality [83-85]. It is therefore prudent that steps are taken to minimize IDH especially in IDH prone patients. Comparative studies have shown that haemodialysis tolerance, which includes IDH, is better when using bicarbonate rather than acetate dialysate [70, 71]. However, we note that in an RCT [85] there appeared to be a dissociation between IDH reduction (reduced with temperature lowering) and mortality (no effect).

Different strategies for changing dialysate temperature have been studied including biofeedback and different degrees of temperature lowering. A systematic review [86] of 11 RCTs concluded that lowering dialysate temperature reduced the rate of IDH by 70% (95% CI 49% to 89%). However, more recent studies including a multi-centre RCT enrolling 73 patients for 12 months [87] and a cluster randomised study [88] did not demonstrate an advantage of setting dialysate temperature -0.5°C below body temperature vs. 37°C. On other hand, a recent large observational study using the Fresenius NephroCare Eclid database [85] did show that in case-mix, facility-level adjusted incident haemodialysis patients, a 0.5°C reduction in dialysate temperature was associated with a 33% risk reduction of IDH. It is possible that patient selection (patients at high risk of IDH [85] vs. patients at lower risk of IDH [87, 88]) accounts for the different outcomes.

Results of studies examining effect of changing dialysate sodium concentration on BP and IDH have been conflicting and covered in recent systematic reviews [89, 90]. Whilst studies have shown that lowering dialysate sodium reduces pre-dialysis mean arterial pressure (MAP) by 3.6 mmHg (95% CI -5.7 to -1.7) and post-dialysis MAP by 3.3 mmHg (95% CI -1.7 to -4.8) [91-94], there is also weak evidence that lowering dialysate sodium may increase rate of IDH in IDH-prone patients [91, 92]. The effect of varying dialysate sodium (sodium profiling) during a dialysis session has also been examined. Different profiles of sodium reduction were the subject of a meta-analysis [95]. Stepwise rather than linear reduction of sodium concentrations was found to reduce IDH. A single centre RCT [96] also confirmed that profiling reduced IDH although, contrary to the meta-analysis, the authors reduced dialysate sodium concentrations linearly. This study demonstrated similar benefit on IDH by dialysate cooling but the benefits were not additive. Given the theoretical risk of "sodium loading" leading to increased dialytic weight gain, we do not feel there is enough evidence to recommend sodium profiling. This was decision has been supported by DOPPS cohort study showing that routine use of sodium profiling was associated with higher all-cause mortality [31]. Sodium profiling may have a role in IDH prone patients but there is insufficient evidence to recommend as routine care.

The correction of chronic metabolic acidosis is an important goal of dialysis and dialysate bicarbonate should be optimised for mineral bone disorder and nutrition. However, acid-base balance might have an acute effect on BP and therefore IDH. We acknowledge that DOPPS [97] have suggested a reduction of the dialysate bicarbonate concentration can be considered for patients with significant peri- and post-dialysis alkalaemia with frequent IDH unresponsive to classical management protocols. However, we considered that the evidence based on three studies was weak [98-100].

There are few studies examining the effect of adjusting dialysate magnesium [101, 102] on BP and IDH. A single study of 14 patients [101] suggests that low dialysate concentration of magnesium (0.25mmol/L) be avoided with dialysate calcium concentration of 1.25mmol/L due to increased risk of IDH. We considered that the evidence base too weak to make a recommendation. A study has examined the effect of dialysate calcium concentration on IDH risk (99) but we suggest that dialysate calcium should be adjusted in accordance for optimal management of mineral bone disorder.

There is evidence that long intraperitoneal dwells of 7.5% icodextrin can achieve greater ultrafiltration than 2.27% glucose dwells [103]. Sodium removal in peritoneal dialysis is dependent on convection so it is to be expected that using icodextrin can improve fluid status [104] and hence help to attain dry weight in people on peritoneal dialysis.

Dry weight optimization

Optimum fluid volume management in people on dialysis is important for both patient experience and outcomes. Both volume overload and depletion are associated with poor outcomes [105-109]. Therefore, accurate 'dry' or 'target' weight assessment is critically important. The clinical assessment of target weight is based on symptoms, skin turgor, peripheral oedema, jugular venous pressure, BP measurement and lung auscultation. It is often a 'guesstimate'. Several technologies are now available to aid fluid volume assessment including blood volume monitoring, inferior vena caval diameter measurement, lung ultrasound scan and bio-impedance spectroscopy (BIS).

A large, international, observational study and small single centre RCTs suggest that protocolised clinical assessment of volume status in people on haemodialysis may be associated with better clinical and patient reported outcomes [31, 110, 111]. This is further supported by the recently published BISTRO trial demonstrating that standardised clinical assessment of fluid volume status is equivalent to standardised clinical assessment augmented by BIS in maintaining residual kidney function in people on haemodialysis [112].

Of the technologies available to assist fluid volume management, BIS is most extensively studied. However, when compared with routine clinical assessment of target weight, none of these technologies have provided consistent benefit in terms of clinical outcomes [106, 113-131]. These include two recently published, well-conducted, RCTs (LUST [132]and BISTRO [112]). Furthermore, some of these found increased adverse patient reported outcomes in the technology assisted fluid management group.

Hypertension is a common consequence of fluid overload in dialysis patients. Several observational studies and small trials demonstrate improvement in BP control in both people on peritoneal and haemodialysis [110, 114, 117, 120, 123, 124, 131, 133]. However, there are also other studies that fail to show the BP lowering effect of active fluid volume management. Importantly, the BISTRO trial did not demonstrate difference in BP control between protocolised fluid volume management compared with BIS added to protocolised fluid volume management in people on haemodialysis [112]. Therefore, there is lack of consistent and firm evidence to support any strong recommendations for fluid volume management to control BP in dialysis patients.

Medication

BP lowering with medication has been demonstrated to reduce all-cause and CV mortality in people on dialysis [134]. The pooled reduction in BP was -4.5/-2.3 mmHg and relative risk (RR) of CV events, CV mortality and all-cause mortality were 0.71, 0.71 and 0.8 respectively. Eight RCTs were included in this meta-analysis of which 7 were in haemodialysis populations and only 4 explicitly included participants with elevated BP. Therefore, there is little direct evidence of effects of BP lowering medication on outcomes in people on peritoneal dialysis. BP-lowering medications used in the intervention arm of included trials was heterogenous: ARBs in three, ACEi in two, βBs in two and CCBs in one. A further meta-analysis published at the same time was not included in our evidence synthesis since it included the same original publications, did not provide a pooled estimate of BP reduction, but it did reach very similar conclusions regarding event rates [135].

We identified three RCTs of BP lowering medication in dialysis patients with a primary or secondary outcome relevant to our search criteria that have been published since this 2009 meta-analyses [136-138]. These three trials were not included in the network meta-analysis described below as these were all 'treat to target' trials. One of these trials compared ACEi vs. non-renin-angiotensin system inhibition (RASi) and a second compared ARB vs. non-RAS. Both trials achieved similar BPs in intervention and comparator arms as per their respective designs, but found no difference in their respective primary composites end-point of CV mortality, non-fatal stroke or myocardial infarction (plus heart failure admission in the first trial) [137, 138]. A third trial compared a βB to ACEi in predominantly African-American haemodialysis patients [136]. Despite a 'treat to target' design with a goal home BP of ≤140/90 mmHg, in post-hoc analysis there was a slightly lower home BP (p=0.037) in the atenolol arm; on 44-hr ABPM, there was numerically lower BP in the atenolol arm (-3.6/3 mmHg). This trial was terminated early due to an excess of CV events in the ACEi group, with no difference found in primary outcome of change in left ventricular mass index.

We were unable to draw firm conclusions regarding choice of antihypertensive drug class in dialysis patients due to lack of consistent evidence of reduction in all-cause, CV mortality or other relevant endpoints favouring any particular class. We have therefore based several of our suggestions on the findings of a recent network meta-analysis that assessed comparative BP lowering efficacy of antihypertensive medications in people on haemodialysis [139]. Mineralocorticoid receptor antagonists (MRAs) and βBs were most effective at reducing systolic BP (SBP), compared to both placebo (MRAs: -10.8 mmHg; βBs: -8.7 mmHg) and other classes (e.g. MRAs -6.4 mmHg vs. ACEi and βBs -4.4 mmHg vs. ACEi). CCBs and ACEi lowered BP compared to placebo by -4.6 mmHg and -4.3 mmHg respectively. Additionally, the βB vs. placebo comparison provided a high confidence rating for effect estimate whereas other comparisons in this meta-analysis varied from moderate (e.g. CCB and ACEi vs. placebo; CCB and βB vs. ACEi) to low or very low confidence ratings.

Hypotension and discontinuation due to adverse effects were more common with ACEi (RR for hypotension and discontinuation were 6.62 and 1.77 vs. control). For these reasons, and in the absence of a clear cardioprotective class effect of RAS blockade in dialysis patients, we have suggested use of ACEi as third line in those on haemodialysis. In those on peritoneal dialysis there is evidence from small RCTs that ACEi or ARBs preserve residual renal function and urine output compared to control groups, despite similar reductions in BP over 12 to 24 months [140, 141] with a mean difference in GFR compared to controls of +0.93 mL/min/1.73 m^2 (95% CI 0.11-1.75) for ACEi and +1.11

mL/min/1.73 m^2 (95% CI 0.38-1.83) for ARB in pooled analyses [142, 143], leading us to suggest these classes as first line antihypertensives in people on peritoneal dialysis.

Although MRAs are most efficacious at lowering SBP, higher rates of discontinuation due to adverse effects (RR 3.35) were observed for this class, with a numerically increased risk for hyperkalaemia (RR 1.63, 95% CI 0.75 to 3.57). Additionally, the confidence rating for the effect estimate of MRA vs. comparators, including placebo, was either low or very low. Finally, although three meta-analyses [144-146] confirm BP-lowering efficacy of MRAs and impressive reductions in pooled estimates of CV and all-cause mortality (RR around 0.4 for all-cause mortality), concerns exist around the quality of some of the original trials of MRAs. Two large global RCTs of MRAs in haemodialysis populations (ACHIEVE and ACCOMPLISH) are expected to complete recruitment shortly, and these are anticipated to define the efficacy and safety of MRAs with greater confidence. For these reasons, and until publication of ACHIEVE and ACCOMPLISH studies, we recommend that MRAs are considered for use only in those dialysis patients with more problematic hypertension.

Alpha-blockers (αBs), ARBs and renin inhibitors were not found to lower BP more than placebo, although confidence intervals for the former two classes were wide (-6.7 mmHg, 95% CI -14.1 to 0.7 for αB vs. placebo; -3.0 mmHg, 95% CI -8.7 to 2.6 for ARB vs placebo) and only indirect comparison between αBs with placebo was available. Discontinuation due to adverse effects was also higher for ARBs (RR 1.57).

There are significant differences between antihypertensives in the extent to which they are removed by dialysis (see *Appendix D*). Theoretically, choice of antihypertensives based on dialysability may affect BP lowering efficacy, enhance BP variability and, in the case of drugs that reduce cardiac events by other mechanisms e.g. antiarrhythmic effects of βBs, dialysability may confer more a immediate effect on risk of CV events. There exists some lower quality evidence to support this hypothesis: a large propensity-matched retrospective cohort study from a Canadian haemodialysis population (n=6588) found increased risk of all-cause (RR 1.4) and CV (RR 1.2) mortality in those receiving high (atenolol, acebutolol, metoprolol) vs. low dialysability (bisoprolol, propanolol) βBs [147]. Conversely, in non-adherent patients, it may be helpful to administer antihypertensives under direct supervision at the end of a dialysis session, particularly if using highly dialysed antihypertensives (e.g. atenolol, lisinopril, enalapril) that have prolonged half-lives in people on haemodialysis. Given the continuous nature of peritoneal dialysis, and paucity of relevant evidence in this population, we do not make any recommendations about in-class choice of BP lowering medication in those on peritoneal dialysis.

Anecdotal evidence suggests that dialysis patients may omit prescribed antihypertensives prior to haemodialysis sessions, either on advice of healthcare professionals or by their own decision [148]. We were unable to find evidence to support this practice. However, it is reasonable to assume that, where a person takes one or more antihypertensive medications early in the morning on 4 days of the week and 6 or more hours later than this on the remaining 3 days, this may increase BP variability. Observational studies have established increased short- and long-term BP variability as independent predictors of all-cause and CV mortality and major adverse CV events in people on haemodialysis [149]. Considering that the TIME study found that evening dosing of antihypertensive medication did not differ from morning dosing in terms of major CV outcomes in the general population [150], we suggest that clinicians discourage omission of antihypertensives prior to dialysis sessions and instead encourage consistent night-time dosing of antihypertensive medication in those patients for whom

such medication is thought to be contributory to IDH. We acknowledge that the efficacy of this approach should be tested in a clinical trial.

We found limited evidence to support pharmacological approaches to management of IDH. Evidence to support the use of midodrine is inconclusive. A meta-analysis, published in 2004, included 10 studies with 117 participants and reported nadir BP 13.3/5.9 mmHg higher in those receiving midodrine, but no consistent benefit in terms of symptom reduction [151]. All included studies had significant methodological flaws (e.g. none were of parallel group design) and were subjective to substantial risk of bias. A retrospective cohort study of 3083 patients, albeit not necessarily with confirmed IDH and subject to confounding by indication, found an adjusted incidence rate ratio of 1.37, 1.31 and 1.41 for all-cause mortality, all-cause hospitalization and hospitalization for CV causes respectively for those prescribed midodrine vs. controls [30].

Evidence to support use of L-carnitine supplementation is similarly inconclusive. A recent meta-analysis (8 studies, 224 participants) of 6 to 24 weeks duration using either cross-over or parallel group design [152]. Of the included studies, only two were judged to be at low overall risk of bias. Compared to controls, participants allocated to L-carnitine supplementation had a pooled odds ratio for incidence of IDH of 0.26 (95% CI 0.1-0.72). Subgroup analysis suggested that only oral, as opposed to intravenous, supplementation was effective and that a minimum weekly dose of 4,200 mg is required. Conversely, a recent Cochrane review (3 RCTs, 128 participants) found insufficient evidence that L-carnitine prevented IDH (RR 0.76, 95% CI 0.34-1.69; low certainty evidence) [153].

Children and Young People (CYP)

Hypertension (defined as SBP and DBP ≥95th percentile for age, height and sex) is highly prevalent in CYP on dialysis [154-156]. However, lack of BP measurement standardisation for CYP on dialysis makes interpretation of values difficult. Details regarding standardisation of BP measurement are available from clinical practice guidelines [157, 158]. Although there is lack of data demonstrating an association between hypertension in CYP on dialysis and increased incidence of CV events or mortality, several studies have reported correlation with proxy markers of CV morbidity, such as LVH and carotid intima media thickness (cIMT) [8, 159-161]. Improved BP control in children on haemodialysis, with BP maintained <90th percentile, has been demonstrated to reduce left ventricular mass (LVM) [160]. As such, echocardiography should be conducted at regular intervals to screen for serial morphological changes.

Current evidence for the management of BP in CYP with CKD *not* on dialysis is to lower MAP to ≤50th percentile to slow CKD progression [158, 162] and to reverse adverse cardiac remodelling [163]. For patients on dialysis, particularly those with residual urine output, targeting BP to this level increases the risk of extreme BP variability and IDH. IDH is defined by the Paediatric Continuous Renal Replacement Therapy (PCRRT) working group as SBP <5th percentile for age along with the presence of clinical symptoms [164]. As for adults, episodes of IDH in CYP affect dialysis adequacy, increase the risk of myocardial stunning, and may lead to long-term adverse clinical outcomes [164, 165]. For this reason, targeting BP to ≤50th percentile in CYP on dialysis is not generally recommended. Consensus recommendations for minimising the risk of IDH in CYP were published in 2019 [164].

ABPM is considered the gold standard for measuring BP in CYP, including those on dialysis [18, 166]. However, normative data do not exist for those <120 cm in height or <5 years of age. Furthermore, achieving compliance in younger patients may not be possible. Compared with in-centre haemodialysis measurements, ABPM enhances the predictability for identifying BP as a risk factor for target organ damage [167, 168]. Our suggestion is that an ABPM monitor should be fitted at the end of a mid-week haemodialysis session to allow for standardisation of measurement. Data on the use of HBPM are lacking in CYP on dialysis, but it may be a useful adjunct alongside ABPM to provide measurements that are less affected by the white coat phenomenon (for both patients on haemodialysis and peritoneal dialysis), by pre-dialysis fluid overload, and by BP fluctuations secondary to acute fluid removal.

This guideline suggests targeting BP to <90th percentile for age, height and sex as a measure of minimising long-term risk of hypertension-mediated organ damage. However, our recommendations remain weak as data are not available to suggest that accepting or targeting higher BP values, such as in the range of the 90th-95th percentiles, confers worse prognosis in CYP on dialysis. The evidence base for recommendations in CYP on peritoneal dialysis are even weaker owing to a lack of published research in this area. One small study, involving 87 children, demonstrated improved preservation of residual kidney function in patients on peritoneal dialysis when SBP and DBP were maintained ≤95th percentile [169].

Within the confines of our literature search, no RCTs analysing CYP on dialysis in groups according to BP target were identified. The current evidence related to BP control in CYP is derived from several studies that have looked at BP as either a primary or secondary outcome measure following:

- Commencement of antihypertensive therapies [170, 171]
- Implementation of a blood volume monitoring algorithm to guide ultrafiltration [172, 173]
- Implementation of a haematocrit-guided ultrafiltration algorithm to guide ultrafiltration [174]
- Implementation of a bioimpedance analysis algorithm to guide ultrafiltration [175]
- Assessment of interdialytic weight gain (IDWG) and categorisation into groups according to percentage increase in IDWG [176, 177]
- Commencement of HDF compared with standard haemodialysis [178, 179]

Guidance on the upper limit of recommended daily intake (RDI) for salt is provided by the 2008 KDOQI Guideline for Nutrition in Children with CKD [180]. Age-related RDI ranges are: 3.8 grams (1-3 years); 4.8 grams (4-8 years); 5.6 grams (9-13 years); 5.8 grams (14-18 years). This guidance is supported by studies in adults demonstrating that limiting salt intake in hypertensive dialysis patients allows for optimised volume status and BP control [50, 181, 182]. A meta-analysis of paediatric trials demonstrated that salt reduction of 42% was associated with a significant reduction in both SBP and DBP in hypertensive CYP without CKD [183]. One study identified a positive simplified sodium balance (i.e. the difference between daily sodium intake and daily urinary sodium losses) to be an independent predictor of IDWG in CYP on both haemodialysis and peritoneal dialysis, although there was no correlation with SBP and DBP standard deviation scores [184]. However, salt intake remains important for growth in CYP on dialysis, particularly for those who are polyuric [185] and where dialysis prescription and modality may increase sodium removal and put the patient at risk of hyponatraemia [186]. The support of dietetic colleagues is therefore vital to develop an individualised approach for each patient.

No single antihypertensive agent, or drug class, has been demonstrated to be more effective, or have an improved safety profile, in CYP on dialysis. Data on antihypertensive therapies remain limited to those with CKD stages 2-4. Prospective analysis of 478 CYP enrolled in the Chronic Kidney Disease in Children (CKiD) study demonstrated renin-angiotensin system (RAS) antagonists were associated with reduced odds of developing LVH compared with other antihypertensive agents, although this did not reach statistical significance [187]. Data from the International Pediatric Peritoneal Dialysis Network (IPPN) registry showed lower incidence of LVH in those on RAS antagonists [159]. Alongside its antihypertensive effect, ramipiril has been demonstrated to improve serum levels of inflammatory mediators and biomarkers of endothelial dysfunction compared with placebo in CYP on dialysis [171]. A clinical practice questionnaire, conducted in the US, demonstrated that dihydropyridine-CCBs and angiotensin converting enzyme inhibitors (ACEis) were the most commonly prescribed antihypertensives in CYP on both haemodialysis and peritoneal dialysis [188]. In terms of the mechanism of action, RAS antagonists are likely to be of limited benefit in anephric patients. Although there is a theoretical risk of reduced urinary excretion of potassium, or potassium accumulation in those with anuria, adult data suggest that RAS antagonists in those on maintenance haemodialysis are not associated with an increased incidence of hyperkalaemia [189]. As per the adult pharmacological recommendations in this guideline, we suggest a consistent evening dosing schedule for antihypertensives where they are implicated as a contributory factor to the development of IDH and when dialysis sessions are delivered during the day. Additionally, pharmacokinetic profiles need to be considered when determining dosing schedules as drugs that are readily dialysed by either haemodialysis and peritoneal dialysis may be unsuitable or may need to be administered after dialysis sessions rather than before.

Summary of audit measures

1. Proportion of adult dialysis patients having ABPM for diagnosis of *de novo* hypertension.
2. Proportion of adult dialysis patients using HBPM or standardized out-of-dialysis unit BP measurements to monitor treatment of hypertension.
3. Proportion of adult dialysis patients who have received advice and support to reduce salt intake to <5 g/day.
4. Proportion of haemodialysis sessions where patients (adults and CYP) experience symptomatic IDH as defined by The UK Kidney Association [164, 190].
5. Proportion of patients (adults and CYP) who have routine (e.g. minimum 3 monthly) assessment of dry weight.
6. Proportion of hypertensive adult haemodialysis patients prescribed β-blockers.
7. Proportion of hypertensive adult peritoneal dialysis patients prescribed ACEis or ARBs
8. Proportion of CYP on dialysis undergoing annual ABPM assessment.
9. Proportion of hypertensive CYP with LVH.
10. Proportion of CYP on dialysis on antihypertensive medications and, in those taking antihypertensives, the number of agents used.

Summary of research recommendations

1. Pragmatic RCT comparing management of hypertension using routine (including 'usual' dialysis unit BP in in-centre haemodialysis patients) BP, HBPM and ABPM in dialysis patients.
2. Pragmatic RCT in both haemodialysis and peritoneal dialysis to determine optimal BP target ranges, preferably utilising standardised office BP or home BP monitoring as the primary method for measuring BP
3. RCT of multiple lifestyle interventions (including dietary salt and fluid reduction, exercise and psychosocial support for medication adherence) on BP and symptomatic IDH in people on dialysis.
4. An implementation or hybrid effectiveness-implementation study of protocolised fluid volume management to improve CV outcomes in people receiving haemodialysis.
5. RCT to determine whether routine evening/night-time dosing of antihypertensive medication reduces incidence of symptomatic intra-dialytic hypotension.
6. RCT to determine effectiveness of midodrine and/or L-carnitine in preventing symptomatic IDH and reducing hospitalizations, and whether these treatments are well tolerated and safe.
7. RCT in CYP on dialysis to determine whether those in whom BP is targeted to <90th centile have a lower risk of LVH compared with those in whom BP is permitted ≥90th centile.
8. Study in CYP on dialysis to determine whether HBPM values correlate with data from ABPM assessment.

Lay summary

Background

High blood pressure (BP) is very common in people with end stage kidney disease (ESKD) on dialysis. It is a risk factor for heart disease, which is the most common cause of death in people on dialysis. Managing high BP in people on dialysis is not always straightforward because of a lack of good quality research evidence on how and when to measure BP, what target BP to aim for, and how to best use different strategies to control BP with diet, exercise, dialysis techniques and medications.

How did we develop these guidelines?

These guidelines were developed by a broad group of experienced kidney care professionals. They went through existing research evidence to give guidance on how best to manage BP in people on dialysis. The guidelines group was divided into different topic areas. The recommendations and suggestions made by these groups are summarized below.

The topic areas were:

- How to measure BP
- What BP we should be aiming for
- Lifestyle measures and medications to help with BP control
- Modifications to dialysis and dialysate fluid

- Assessment of dry weight
- Considerations that apply to children and young people (CYP)

How should we measure blood pressure and what blood pressure should we be aiming for in adults on dialysis?

We found limited good quality information to tell us which BP measurement should be used in people on dialysis. Most research studies in haemodialysis patients have used *'usual' pre- and post-dialysis readings* taken in the dialysis unit. These are often not very accurate. Also, both high and low 'usual' BP readings are associated with bad outcomes. This makes it difficult for kidney professionals to know how far we can safely lower BP. Finally, 'usual' pre- and post-dialysis readings are not good at predicting long term risks associated with high BP.

We suggest that usual BP readings should be used primarily to ensure safe delivery of haemodialysis. We encourage kidney care professionals to consider other ways of measuring BP in dialysis patients to help with long-term risks heart disease, stroke, etc. However, because usual pre- and post-dialysis readings are the most used readings in UK units, we make some suggestions about what these 'usual' readings should be.

These are:

- Aim for a pre-dialysis systolic (upper) reading of between 140 and 165 mmHg.
- For patients whose BP is stable during dialysis try to aim for the lower end of this range.
- For those with few or no other medical conditions, and in younger people, aiming for a BP lower than 140 may be appropriate.

Ambulatory blood pressure monitoring (ABPM) is the most accurate method for measuring BP. The downside of ABPM is that it involves wearing a monitor for 24 or 48 hours. Many people find this inconvenient. Because of difficulties associated with ABPM, we suggest that it is mainly used to diagnose high BP in adults on dialysis.

Home blood pressure monitoring (HBPM) – measurement by patients or carers of BP at home – is thought to be more accurate than usual readings for longer term BP management. However, some people may find taking readings burdensome. For those that use HBPM, we have suggested that we should aim for an average BP under 130 mmHg.

The alternative to HBPM may be to make sure BP is carefully measured in a standardized way within HD units and clinics, as recommended by international guidelines groups such as KDIGO. However, standardized measurements take more time and would be difficult to do regularly in busy HD units. We suggest that standardized BP readings could be carried out in an outpatient clinic.

What lifestyle measures help control BP?

We recommend that dialysis patients restrict their salt intake to no more than 5 grams (less than a level teaspoon full) per day. Renal dieticians can assist patients in how to calculate the salt content of

various foods. There are benefits from taking regular exercise and we suggest that exercise is adopted wherever possible.

How may modifications of dialysis and dialysate fluid help?

Changing the type and duration of dialysis treatment or changing the composition of dialysis fluid may help to improve BP control. We suggest that those with high BP, increasing the duration of haemodialysis and using icodextrin (Extraneal) solution in peritoneal dialysis patients may help fluid management and BP control.

For those suffering from low BP during dialysis (intradialytic hypotension or IDH), lowering dialysis fluid temperature, frequent short dialysis, nighttime dialysis or home haemodialysis may be helpful. After ruling out other causes of IDH, a period of haemodialfiltration (HDF) may be tried. HDF combines haemodialysis with filtration, which allows the removal and replacement of fluid.

How should dry weight be determined?

Dialysis patients who have too much (overloaded) or too little fluid (dehydrated) in their circulation have worse outcomes. So it is important for dialysis staff to correctly assess each patient's 'fluid status'. The weight at which a patient has the correct amount of fluid in their body and they feel comfortable is called 'target weight' or 'dry weight'. Keeping someone around their dry weight can help control BP and, in people on haemodialysis, reduce large BP changes and help avoid episodes of feeling unwell during dialysis.

It is not easy to determine exactly how overloaded or dehydrated a person is, and there are several ways to help dialysis staff in doing this. Clinical examination is most often used. There are several devices which may help to assess dry weight correctly. It is not clear whether one device or technique is better than others or better than clinical examination to do this.

We suggest that dialysis patients should be examined regularly to determine volume status. This information can then be used to decide a patient's dry weight. This guides dialysis staff to know how much and how quickly fluid can be removed or added during dialysis sessions.

What medications help with blood pressure on dialysis?

Many people having dialysis will require BP lowering medications. The pros and cons of the various types of medications are beyond the scope of this summary. In brief, we suggest beta-blockers (e.g. bisoprolol) as first choice medication in haemodialysis patients, followed by calcium channel blockers (e.g. amlodipine). ACE inhibitors (e.g. ramipril) are recommended as first choice medication in those on peritoneal dialysis.

People on dialysis may be on medicines to manage BP that are not mentioned in this guideline. This does not mean they should not be used but it may be because there is little information from research studies. If you have any concerns about your medicines, then do not stop them. Instead, please talk to your kidney doctor, GP, kidney pharmacist or a member of the kidney team.

What is particularly important in Children & Young People (CYP)?

High BP is common in CYP on dialysis, and this can lead to long term changes to the heart. Unlike in the adult population, we do not have clear information from research that high BP directly leads to an increased risk of death from heart disease. Studies helping us to understand what the ideal BP should be for CYP on dialysis are very few. This makes it difficult to make any firm recommendations regarding suitable BP targets in this age group.

Normal BP in CYP varies by age, height and sex. Measurements are compared against existing groups of children of the same age, height and sex. To avoid large drops in BP during dialysis, it is suggested that BP should be kept near the 90th percentile of CYP of the same weight, height and sex.

The best way to monitor BP in CYP on dialysis requires more research. ABPM is very reliable in CYP and this should be performed at least once a year in all CYP on dialysis, once a minimum height of 120 cm has been reached. However, ABPM is not always practical and will need to be performed alongside measurements taken in the hospital and/or at home. As in adults receiving haemodialysis in hospital, BP should be checked before, during, and after each dialysis session, with regular physical examination to ensure correct estimation of dry weight.

Salt in the diet should be reduced to specific amounts recommended for age. Kidney dietitians can provide support with this. If lifestyle changes, such as being very careful with fluid and salt intake, are unsuccessful in controlling BP then doctors and nurses may consider giving medications to lower BP. This is particularly important if there is any evidence of damage to specific organs in the body due to high BP. When choosing which medication to use, there is not enough information to indicate that any one type of BP medication is better than another. Doctors and nurses need to think about the specific patient and how the drug works in their body.

Appendix A: Topic group membership

BP Measurement: Mariyam Adam, Indranil Dasgupta

Blood pressure targets: Indranil Dasgupta, Douglas Stewart, Kieran McCafferty, Tim Doulton

Lifestyle modification: Katie Durman, Pauline Swift

Dry weight: Kieran McCafferty, Manish Sinha, Indranil Dasgupta, Ed Jenkinson

Dialysis and dialysate: Anna Forbes, Pauline Swift, Stan Fan

Medication: Tim Doulton, Charlotte Mallindine

Children & young people: Manish Sinha, Douglas Stewart

Lay representative: Ed Jenkinson

Appendix B: PICOS for literature search, search strategies & PRISMA flowchart

PICOS

Eligibility Criteria:

Population: Adults, children and young people receiving dialysis (haemodialysis, haemodiafiltration and peritoneal dialysis) for end stage renal disease

Intervention:

- Any intervention intended to reduce blood pressure (BP), to include but not limited to: blood pressure lowering medication; target/dry weight reduction or optimization; dialysis prescription, including ultrafiltration volumes, ultrafiltration rate; diet, including salt restriction; exercise or other lifestyle intervention; self-management techniques.
- Any intervention intended to mitigate intradialytic hypotension (IDH) or other hypotensive episodes, including low temperature dialysis, ultrafiltration profiling, dialysate sodium concentration and profiling, midodrine use.

Comparison: Any trial that compares one or more interventions intended to reduce BP and/or to mitigate IDH or other hypotensive episodes in people receiving dialysis, including trials that compare an intervention with placebo or standard of care.

Outcomes: All-cause mortality; CV events (including, but not limited to, myocardial infarction, unstable angina, stroke/TIA, admission for heart failure, PVD events); BP reductions; IDH; vascular access thrombosis; post-dialysis recovery time; injurious falls, fractures; hospitalization for any cause; medication adherence; patient reported outcomes; residual renal function; intra-dialytic weight gain; left ventricular hypertrophy, carotid intima media thickness, aortic pulse wave velocity.

Studies: Clinical trials; Meta-analyses; Systematic reviews; Trial protocols; Conference proceedings/abstracts; Unpublished literature / grey literature

In the knowledge that clinical trials on this topic are limited, we will also include: observational and qualitative studies that have population and/or outcomes as described above, and where the primary focus of the study is at least one of:

- BP measurement techniques
- Relationship between BP and outcomes above
- Patient and/or carer perspectives, experience, knowledge in relation to strategies to manage BP

Exclusion Criteria:

The search strategy will eliminate studies solely focusing on:

- Acute haemodialysis
- Acute peritoneal dialysis
- Continuous veno-venous haemofiltration (CVVHF) and other acute renal replacement modalities
- Hypertension in any specialised vascular bed (e.g. pulmonary, intracranial)

Search Strategies

PubMed

((("end stage" OR chronic) AND (kidney OR renal) AND (disease OR failure))

AND

(dialysis OR haemodialysis OR haemodiafiltration OR "peritoneal dialysis"))

AND

((hypertension OR hypotension OR "blood pressure" AND (medication OR reduc* OR optimiz* OR optimis* OR lower* OR (ultrafiltration AND (volum* OR rate)) OR diet OR (salt AND (reduction OR restriction OR limiting)) OR exercise OR lifestyle OR self-management)) OR ("intradialytic hypotension" OR IDH OR "hypotensive episod*" OR "low temperature dialysis" OR "ultrafiltration profiling" OR ("dialysate sodium" AND (concentrat* OR profil*)) OR midodrine))

AND

("all cause mortality" OR cardiovascular OR "myocardial infarction" OR "unstable angina" OR stroke OR TIA OR "heart failure" OR PVD OR "vascular access thrombosis" OR "post-dialysis recovery time" OR fall* OR hospitalisation OR hospitalization OR adherence OR "patient reported outcom*" OR PROM OR "residual renal function" OR "intra-dialytic weight gain" OR "left ventricular hypertrophy" OR "carotid intima media thickness" OR "aortic pulse wave velocity")

Filters: Clinical Study, Clinical Trial, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Controlled Clinical Trial, Evaluation Study, Meta-Analysis, Multicenter Study, Observational Study, Pragmatic Clinical Trial, Randomized Controlled Trial, Review, Systematic Review, from 1/1/2000 to 31/12/2022

Embase

1 exp end stage renal disease/
2 (("end stage" or chronic) and (kidney or renal) and (disease or failure)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
3 1 or 2
4 exp dialysis/
5 exp hemodialys/
6 (dialysis or haemodialysis or haemodiafiltration or (peritoneal and dialysis)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
7 4 or 5 or 6
8 exp hypotension/ or exp hypertension/

9 (blood pressure and (medication or reduc$ or optimiz$ or optimis$ or lower$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
10 (ultrafiltration and (volum$ or rate)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
11 (diet or (salt and (reduction or restriction or limiting))).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
12 (exercise or lifestyle or self-management).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
13 (intradialytic hypotension or IDH or hypotensive episod* or low temperature dialysis or ultrafiltration profiling or (dialysate sodium and (concentrat$ or profil$)) or midodrine).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
14 9 or 10 or 11 or 12 or 13
15 8 and 14
16 (all cause mortality or cardiovascular or myocardial infarction or unstable angina or stroke or TIA or heart failure or PVD or vascular access thrombosis or post-dialysis recovery time or fall$ or hospitalisation or hospitalization or adherence or patient reported outcom$ or PROM or residual renal function or intra-dialytic weight gain or left ventricular hypertrophy or carotid intima media thickness or aortic pulse wave velocity).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
17 3 and 7 and 15 and 16
18 limit 17 to yr="2000 -Current"
19 ("randomi$ed controlled trial" or RCT or "controlled clinical trial" or "systematic review" or "meta-analysis").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
20 exp randomized controlled trial/
21 exp meta analysis/
22 exp "systematic review"/
23 19 or 20 or 21 or 22
24 18 and 23

Cochrane

#1 MeSH descriptor: [Kidney Failure, Chronic] explode all trees
#2 ("end stage" or chronic) and (kidney or renal) and (disease or failure):ti,ab,kw
#3 #1 OR #2
#4 MeSH descriptor: [Dialysis] explode all trees
#5 MeSH descriptor: [Renal Dialysis] explode all trees
#6 dialysis or haemodialysis or haemodiafiltration or (peritoneal and dialysis):ti,ab,kw

#7 #4 OR #5 OR #6
#8 MeSH descriptor: [Hypotension] explode all trees
#9 blood pressure and (medication or reduc$ or optimiz$ or optimis$ or lower$):ti,ab,kw
#10 ultrafiltration and (volum$ or rate):ti,ab,kw
#11 diet or (salt and (reduction or restriction or limiting)):ti,ab,kw
#12 (exercise or lifestyle or self-management):ti,ab,kw
#13 (intradialytic hypotension or IDH or hypotensive episod* or low temperature dialysis or ultrafiltration profiling or (dialysate sodium and (concentrat$ or profil$)) or midodrine):ti,ab,kw
#14 #9 OR #10 OR #11 OR #12 OR #13
#15 #8 AND #14
#16 (all-cause mortality or cardiovascular or myocardial infarction or unstable angina or stroke or TIA or heart failure or PVD or vascular access thrombosis or post-dialysis recovery time or fall$ or hospitalisation or hospitalization or adherence or patient reported outcom$ or PROM or residual renal function or intra-dialytic weight gain or left ventricular hypertrophy or carotid intima media thickness or aortic pulse wave velocity):ti,ab,kw
#17 #3 AND #7 AND #15 AND #16 with Publication Year from 2000 to 2022, in Trials

CINAHL

S1 (MH "Kidney Failure, Chronic+")
S2 (kidney OR renal) AND (end stage OR chronic) AND (failure OR disease OR injury)
S3 S1 OR S2
S4 (MH "Hemodialysis+") OR (MH "Dialysis+")
S5 dialysis OR haemodialysis OR haemodiafiltration OR “peritoneal dialysis”
S6 S4 OR S5
S7 ((“blood pressure” AND (medication OR reduc* OR optimiz* OR optimis* OR lower* OR (ultrafiltration AND (volum* OR rate)) OR diet OR (salt AND (reduction OR restriction OR limiting)) OR exercise OR lifestyle OR self- management)) OR (“intradialytic hypotension” OR IDH OR “hypotensive episod*” OR “low temperature dialysis” OR “ultrafiltration profiling” OR (“dialysate sodium” AND (concentrat* OR profil*)) OR midodrine))
S8 (MH "Hypotension")
S9 S7 OR S8
S10 (“all cause mortality” OR cardiovascular OR “myocardial infarction” OR “unstable angina” OR stroke OR TIA OR “heart failure” OR PVD OR “vascular access thrombosis” OR “post- dialysis recovery time” OR fall* OR hospitalisation OR hospitalization OR adherence OR “patient reported outcom*” OR PROM OR “residual renal function” OR “intra- dialytic weight gain” OR “left ventricular hypertrophy” OR “carotid intima media thickness” OR “aortic pulse wave velocity”)
S11 S3 AND S6 AND S9 AND S10, Limiters - Published Date: 20020101-20221231

Medline

1 exp Renal Insufficiency, Chronic/
2 (("end stage" or chronic) and (kidney or renal) and (disease or failure)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept

word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

3 1 or 2

4 exp Dialysis/

5 exp Renal Dialysis/

6 (dialysis or haemodialysis or haemodiafiltration or (peritoneal and dialysis)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

7 4 or 5 or 6

8 exp Hypotension/

9 (blood pressure and (medication or reduc$ or optimiz$ or optimis$ or lower$)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

10 (ultrafiltration and (volum$ or rate)).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

11 (diet or (salt and (reduction or restricting or limiting))).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

12 (exercise or lifestyle or self-management).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

13 (intradialytic hypotension or IDH or hypotensive episod$ or low temperature dialysis or ultrafiltration profiling or (dialysate sodium and (concentrat$ or profil$)) or midodrine).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

14 9 or 10 or 11 or 12 or 13

15 8 and 14

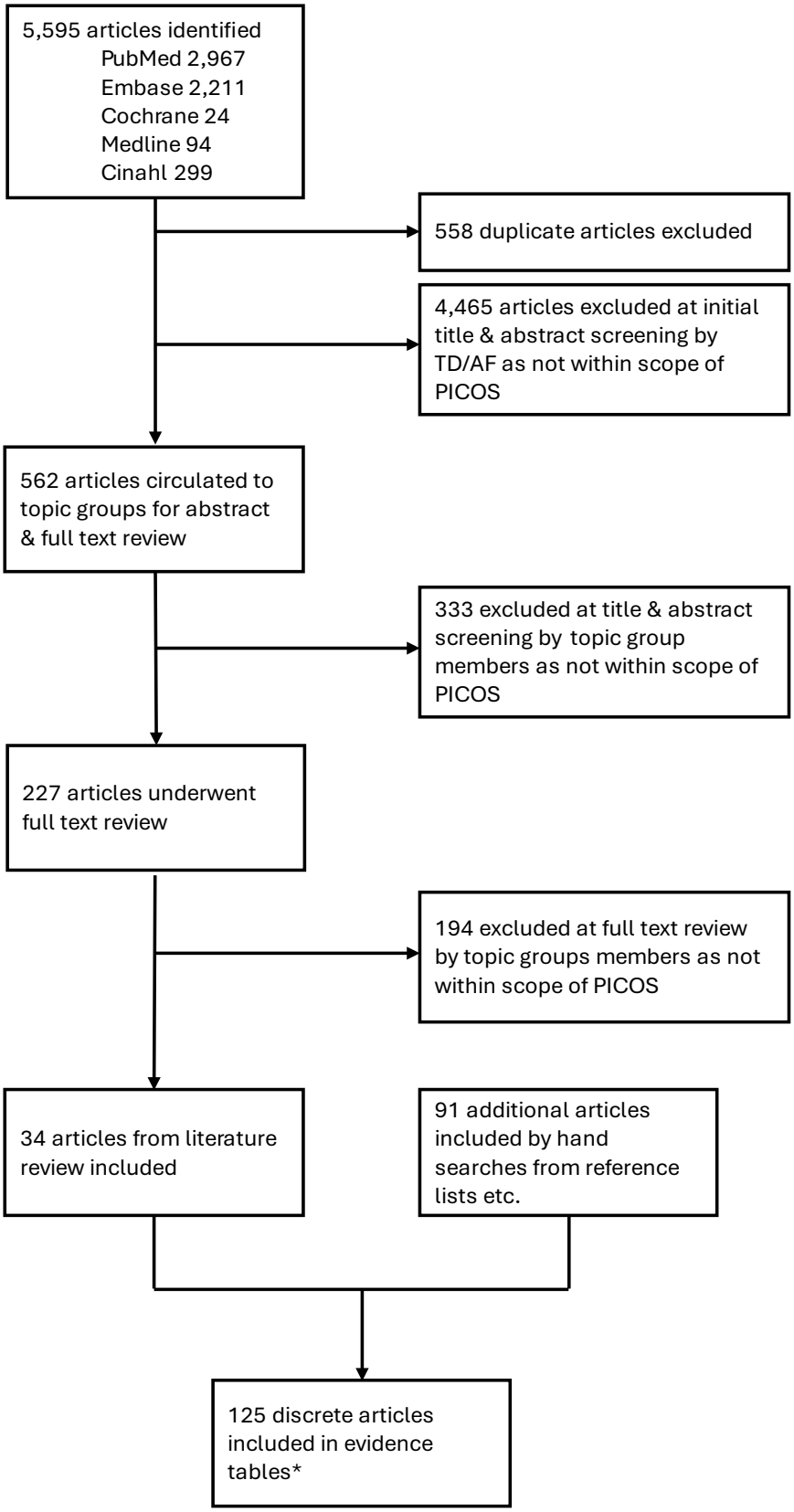
16 (all cause mortality or cardiovascular or myocardial infarction or unstable angina or stroke or TIA or heart failure or PVD or vascular access thrombosis or post-dialysis recovery time or fall$ or hospitalisation or hospitalization or adherence or patient reported outcom$ or PROM or residual renal function or intra-dialytic weight gain or left ventricular hypertrophy or carotid intima media thickness or aortic pulse wave velocity).mp. [mp=title, book title, abstract, original title, name of

substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

17 3 and 7 and 15 and 16

18 limit 17 to yr="2000 - Current"

PRISMA flowchart



*includes 3 articles that appear in both BP measurement and BP targets sections

Appendix C: Evidence tables

1st author Year of publication Reference	Aim of the study	Study design Method of BP measurement Follow-up period	Number Population (Country, RRT modality)	Primary analysis	Results/Conclusion
BP Measurement					
Agarwal, 2006 (13)	Determine the magnitude of the difference and the variability in the difference between BP that is recorded in the dialysis environment, before and after the dialysis procedure, and ABPM that is performed simultaneously in the haemodialysis population.	Meta-Analysis (1992-2003) ABPM – measured 24-48 hr duration some including dialysis session itself Dialysis unit BP – 7 studies used standard BP monitoring and rest 'routine' BP Some averaged over few weeks- months and some were single point measurements	692 Countries of studies not reported HD	Differences between the dialysis unit BP, i.e., predialysis systolic (SBP) and diastolic (DBP), and postdialysis SBP and DBP and the corresponding ABPM BP (SBP or DBP) were calculated	Dialysis unit blood pressures have poor agreement with ABPM. Unable to calculate a pooled estimate using standard meta-analytic methods due to significant heterogeneity between studies. SD of the difference of the pooled observations between systolic ABP and predialysis SBP was 16.7 mmHg with limits of agreement of 41.7 mmHg to −25.2 mmHg. Predialysis diastolic BP overestimated the ABP with wide agreement limits (23.7 to -18.9 mmHg). Postdialysis BP underestimated average ABP with wide agreement limits for both postdialysis systolic BP (33.1 to -36.3 mmHg) and diastolic BP (19.3 to -23.9 mmHg).
Agarwal, 2006 (12)	To assess the relationship between BP recordings obtained in the dialysis unit by routine and standardized methods; home BP recordings obtained	Cohort study ABPM – 44 hr interdialytic BP Dialysis unit – Routine and standardised BP	104 Indiana University, Indianapolis, US Predominantly black (75%)	Sensitivity and specificity of haemodialysis unit BP, Home BP in diagnosing hypertension compared with ambulatory blood pressure monitoring	Routine dialysis unit BP measurements have marginal performance in the diagnosis of hypertension Only home BP and post-dialysis standardised BP had an acceptable sensitivity and specificity. One week averaged systolic home BP of 150 mmHg or post-dialysis standardized BP of 122 mmHg has both high

	by the patients; and the reference standard of 44-h interdialytic ambulatory BP recordings.	measurements averaged for 2 weeks Home BP – 3x daily for one week	HD		sensitivity and specificity to predict hypertension assessed by ambulatory BP monitoring
Agarwal, 2009 [16]	Evaluate the relationship of concurrent reduction in home BP, predialysis BP and postdialysis BP compared to the gold standard of interdialytic ambulatory BP measurements – Prespecified goal of DRIP Trial	RCT (DRIP) ABPM- 44 hr interdialytic BP Dialysis unit BP- Routine dialysis unit BP – mean of 3 dialysis sessions Home BP- 3 x daily for 1 week	150 Indiana University, Indianapolis, US Predominantly black HD 8 weeks	Changes from baseline in home, predialysis BP and postdialysis BP were compared to interdialytic 44-hour ambulatory BP at 4 weeks and 8 weeks.	The changes in response to nonpharmacological intervention in haemodialysis patients with hypertension can be most reliably detected by 44-hour interdialytic ambulatory BP monitoring as early as after 4 weeks Predialysis SBP is not as sensitive as ambulatory BP in detecting this change but post dialysis BP can detect a change although may not persist over time in interdialytic period Home BP can reliably detect changes in BP at 8 weeks but may not detect changes at 4 weeks Ambulatory and home BP were more reproducible, i.e. they had greater test-re- test reliability compared to predialysis and postdialysis BP.
Agarwal, 2010 [4]	To compare mortality for haemodialysis patients with dialysis unit BP, ambulatory BP and Home BP monitoring to see if one offers more prognostic value than others	Cohort study ABPM – 44 hr interdialytic BP Dialysis unit – Routine and standardised BP measurements averaged for 2 weeks	326 Indiana University, Indianapolis, US Predominantly black (75%)	All-cause mortality for different blood pressure measurements	A significant relationship between increasing levels of systolic blood pressure and all cause mortality was seen with home and ambulatory blood pressure. Dialysis unit BP recordings were of no prognostic importance. Systolic ambulatory BP associated with least mortality was between 110–120 mmHg. The “best” systolic home BP was between 120–130 mmHg.

		Home BP – 3x daily for one week	HD Mean duration - 32 months		
Agarwal, 2014 [18]	discuss the diagnosis, epidemiology, and management of hypertension among dialysis patients	Review Article	n/a		Home BP better than pre and post dialysis BP readings BP measurements to be made twice daily (on waking up in the morning and just before going to sleep) after a midweek dialysis for 4 days
Alborzi, 2007 [11]	Evaluate the presence, strength, and shape of the relationship among BP that are measured using various modalities (home, ambulatory, and dialysis unit) and cardio- vascular and all-cause mortality in HD patients.	Prospective Cohort study	150 Indiana University, Indianapolis, US Predominantly black (75%) HD 24 months	All cause mortality for ambulatory, Home BP, HD unit pre and post dialysis routine and standard BP	Measurements in the dialysis unit for SBP and DBP were not predictive of total mortality although postdialysis SBP was associated with an increase in cardiovascular mortality. Ambulatory BP was associated with a nearly 50% higher death rate for a 1-SD or 22.3/13.8-mmHg increment in SBP/DBP. In comparison, home BP was associated with a 35 to 40% elevation in risk for death. BP in different measurement groups divided in to four quartiles. BP measurements in 2nd quartile were associated with lowest mortality and BP in 4th quartile of ABPM (>140) was associated with significantly high mortality compared to first quartile.
Bansal, 2015 [22]	1- Delineate the shapes and strengths of the association of SBP with mortality at	Cohort (CRIC)	n=1705 n=403 n=326	All cause mortality compared to SBP in CKD 5, Dialysis unit BP and	A U-shaped association between dialysis-unit SBP and mortality was observed among those who started haemodialysis.

	eGFR <30 mL/min/1.73 m2 (but not on dialysis) and 2- to compare the association between dialysis-unit SBP versus out-of-dialysis-unit SBP with mortality among the participants who progressed to ESRD and initiated haemodialysis.	EGFR <30 – Standardised BP in CRIC study visit Dialysis unit BP- average of 4 sessions BP measured at the start of HD session Out-of-unit BP- standardised BP measured in CRIC study visit after initiation of HD	Multi-Centre, US CKD 4 and 5 and HD	out of office SBP in incident HD patients.	A linear association between out-of-dialysis-unit SBP and mortality (hazard ratio, 1.26 [95% confidence interval, 1.14-1.40] per every 10 mm Hg increase).
Bansal, 2021 [15]	Randomised to home BP vs predialysis BP to guide BP management (target <140 in each group)	Pilot RCT Home BP 2 readings every 2 weeks (mid week intradialytic day am and pm) Dialysis unit BP- Predialysis BP from over 2 weeks (average of 6 sessions)	50 University of Washington and the University of California, San Francisco – US HD 4 months	feasibility, adherence, safety and tolerability of home BP measurement	Demonstrated feasibility and high adherence to home BP measurement and treatment in haemodialysis patients and there were no safety concerns. Home SBP was on average 4.6mmHg lower than dialysis unit BP at baseline. Secondary outcomes Pre-dialysis SBP was similar in the two arms at baseline, and started to separate by week 6 with SBP becoming lower among those randomized to pre-dialysis BP treatment arm, which was sustained through the last several weeks of the intervention – Dry weight adjustment was the most common intervention. No significant discordance between home BP and 44-hour ABPM at baseline in terms of classifying blood pressure as being above or below 140 mmHg
Cohen, 2014 [19]		Review	n/a		Home BP readings more closely associated with ABPM Home BP readings more reproducible from one week to next BP measured 2x /day for 4 days following midweek dialysis session

Da Silva, 2009 [17]	Whether antihypertensive treatment using home BP or predialysis BP can improve BP control in HD patients	RCT Home BP – 2 x day measurements for 7 days Predialysis BP- average of 9 consecutive HD sessions routine pre dialysis BP ABPM- 24 hr monitoring after midweek HD session	97 Single Centre, Brazil HD 6 months	BP control pre and post intervention using ABPM between intervention groups And changes in LV mass between groups	Patients HBPM (home BP monitoring) had better BP control after 6 months No change in LV mass between groups Patients in intervention group (HBPM) had their BP medications adjusted monthly using HBPM readings. Patients in the intervention group has significant reduction in their BP control pre and post intervention as measured by ABPM (BP 144 ± 14 mmHg and 135 ± 12 mmHg P<0.05 respectively). Additionally, a significant number of patients also developed a dipping BP pattern during sleep after 6 months (11.7% versus 38.2%, P < 0.05). There was also a significant reduction in predialysis SBP between the beginning and end of the study (157 ± 25 mmHg versus 147 ± 18 mmHg; P < 0.05) in HBPM group. Echocardiographic measures – no significant difference in any of the parameters between both groups
Fagugli, 2009 [10]	Examine the differences between prediaysis BP, inter-HD (iHD) or HD day 24 h ABPM, with 48 h ABPM, to predict BP burden and hypertension.	Cohort study ABPM – 48 hour BP including a midweek dialysis day and off day Prediaylysis BP- routine measurements measured at each dialysis unit- Mean readings from 1 month	163 Regional Hospital of Perugia, Italy HD	Difference between 48 hour ABPM and predialysis BP, iHD or HD day 24 hour ABPM	Predialysis BP overestimated BP values in relation to 48 h ABPM, both in the case of SBP and DBP (systolic 48 h ABPM = 139.6 1 20.2 mmHg and predialysis SBP = 142.8 1 17.2 mmHg, P < 0.01; diastolic 48 h ABPM = 76.6 1 10.8 mmHg and predialysis DBP = 79.5 1 9.1 mmHg, P < 0.01) Systolic and diastolic ABPM of 24 h recorded during iHD day were significantly higher than those recorded during HD day (SBP: 141.2 1 20.8 vs 137.9 1 20.9 mmHg, P < 0.01; DBP: 77.1 1 11.1 vs 76.1 1 10.9 mmHg, P < 0.01). ABPM of 24 h, iHD or HD day, was not different from 48 h ABPM Prevalence of BP levels in the range of hypertension was reported to be 80.5% when BP measurements were performed using 48 h ABPM, without any difference if

					ABPM was performed on off-dialysis day (81.2%) or on HD day (73.4%). The prevalence of BP levels in the range of hypertension was significantly lower if predialysis BP was used. (61.7%, c2 = 13.28; P < 0.001)
BP targets					
Agarwal, 2010 [4]	To evaluate the presence, strength, and shape of the relationship between BP measured using different modalities (HBPM, ABPM, dialysis unit) and all-cause mortality among HD patients	Prospective cohort (1) HBPM: 3x/day for 1 week using validated device (2) ABPM: 44 hours starting after 1st or mid-week HD session (3) HD unit measurements: average of 6 'usual' (i.e. non-standardized) pre- and post-HD readings Median FU 2.4 years	326 United States HD (N.B. Majority were African American & those with chronic AF were excluded)	Association between BP and all-cause mortality	(1) W-shaped relationship between ambulatory and home SBP and all-cause mortality, including following adjustment for CV risk factors (age, gender, ethnicity, DM, pre-existing CV disease, dialysis vintage) (2) Ranges of SBP associated with lowest mortality risk were 110-120 mmHg for ambulatory BP and 120-130 for home BP (3) No relationship between DBP and outcomes No relationship between HD unit 'usual' BP readings and outcomes
Alborzi, 2007 [11]	To evaluate the presence, strength, and shape of relationship between BP using various modalities (HBPM, ABPM and dialysis unit 'usual' and standardized) and CV and ACM in HD patients	Prospective cohort (1) HBPM: 3x/day for 1 week using validated device (2) ABPM: 44 hours starting after 1st or mid-week HD session (3) HD unit 'usual': average of 6 'usual' (i.e. non-standardized) pre- and post-HD readings (4) HD unit: 'standardized': 3	150 United States HD (Similar population to Agarwal 2010; those with chronic AF were excluded)	Association between BP and all-cause mortality A 'secondary focus' was associated between BP and CV death	(1) Linear relationship between increasing home (p=0.05 for trend) and ambulatory (p=0.011) BP expressed as quartiles and ACM (2) No relationship between usual or standardized HD unit measurements and ACM Only 4th quartile of ambulatory BP (SBP >145 mmHg) was associated with significantly higher mortality compared to 1st (reference) quartile (<113.5 mmHg), HR 2.52 (95% CI 1.03 to 6.19). No quartile of home BP was significantly different to the referent.

		readings pre- & post-HD taken by research nurse after 5 mins rest; averaged over 6 HD sessions Median FU 2 years			
Bansal, 2015 [22]	To compare association between SBP and mortality between (1) HD unit BP readings; and (2) BP readings taken outside of HD unit	Prospective cohort (1) Non-standardized pre-HD BP (mean of 1 weeks readings) (2) Standardized out-of-unit SBP (mean of 3 resting seated readings) Mean FU 2.72 years (cohort 1) & 2.83 years (cohort 2)	403 (HD unit SBP m'ment) 326 (Out-of-unit SBP m'ment) United States HD	Association between SBP and mortality	(1) Non-linear (U-shaped) association between HD-unit SBP and mortality Linear association between out-of-HD unit SBP and mortality – mortality increases by HR 1.26 (95% CI 1.13-1.39) per 10 mmHg increase in SBP
Bansal, 2017 [5]	To compare association between SBP, DBP and PP and CV events between (1) HD unit BP readings; and (2) BP readings taken outside of HD unit	Prospective cohort (1) Non-standardized pre-HD BP (mean of 1 week readings) (2) Standardized out-of-unit SBP (mean of 3 resting seated readings) Mean FU 2.72 years	377 United States HD	Association between SBP and CV events	(1) Non-linear (U-shaped) association between HD-unit SBP and risk of CV events, with nadir between 150 and 170 mmHg (2) Linear direct association between out-of-HD unit SBP and CV events; fully adjusted HR for CV events was 2.14 (95% CI 1.17-3.90) for SBP ≥128 mmHg compared to SBP ≤112 mmHg (HR for 113-127 mmHg was 1.33, 95% CI 0.71-2.5)
De Lima, 2023 [36]	To clarify the value of BP, measured at the interdialytic period, as a predictor of outcomes in an HD population	Retrospective cohort Average of 2 BP readings recorded using a calibrated aneroid sphygmomanometer, with the patient in a	2,672 Brazil HD	Association between BP and (i) all-cause mortality (ii) CV events	(1) Compared with the reference category of SBP ≥ 171 mmHg, the incidence of CV events was reduced in those with SBP 101-110 (HR 0.65, 95% CI 0.46-0.90), 111-120 (HR 0.66, CI 0.49-0.89), 121-130 (HR 0.75, CI 0.57-0.98), and 131-140 mmHg (HR 0.76, CI 0.6-0.97) When analysed by percentiles of BP, SBP 130 mmHg was associated with reduced risk of CV events (HR 0.75, CI 0.64-

		seated position, taken mid-week, between 2 consecutive dialysis sessions. Median FU 2.58 years			0.88, p=0.001) but not reduced mortality (HR 0.89, CI 0.78-1.01, p=0.077) compared to reference 170 mmHg.
Hannedouche, 2016 [29]	To analyse associations between pre-dialysis SBP, DBP, and PP with all-cause mortality, CV mortality, and nonfatal CV endpoints	Prospective cohort Usual (non-standardized) pre-HD supine BP Median FU 1.5 years	9,333 France HD	Association between pre-HD SBP, DBP, PP and all-cause mortality, CV mortality & non-fatal CV events	Non-linear (U-shaped) association between SBP and all-cause mortality and both SBP and DBP and CV mortality Lowest HR for all-cause mortality was 165 mmHg (no lower limit for DBP as L-shaped relationship) For CV mortality, nadir risk was found at 157/90 mmHg In time varying component adjusted Cox model SBP had predictive power for stroke HR 1.15 (95% CI 1.07-1.23) for each 10 mmHg increase Analysis by presence/absence of prior CV disease, use of antihypertensive medication or whether prevalent or incident patient doesn't change nature of relationship
Hara, 2018 [191]	To clarify the association between pre-dialysis BP and mortality and morbidity in HD patients; in addition, to explore BP at which the outcomes risk was at its lowest	Prospective cohort Usual (non-standardized) pre-HD supine BP at baseline FU for 4 years	3,436 Japan HD	Association between pre-HD SBP & DBP and all-cause & CV mortality	SBP of 152 mmHg and DBP of 68 mmHg were associated with lowest risk of all-cause mortality SBP of 143 mmHg was associated with lowest risk of CV events
Jhee, 2018 [32]	To investigate the optimal BP target and the effect of confounding factors on outcomes in patients undergoing prevalent dialysis	Prospective cohort Pre-dialysis sitting BP (unclear whether standardized or not) Median FU 4.5 years	2,299 Korea HD (59.9%) & PD (40.1%)	Association between pre-dialysis SBP and all-cause mortality	Non-linear (U-shaped) association between SBP and all-cause mortality in HD patients; similar, non-significant, association observed in PD patients SBP <110 and ≥170 mmHg associated with increased risk of all-cause mortality (SBP <110 mmHg: HR 1.68, 95% CI 1.14-2.49; SBP ≥170 mmHg: HR 1.63, 95% CI 1.1-2.42)

Mayer, 2018 [34]	To investigate the nonlinear association between ambulatory BP and mortality in an HD cohort.	Prospective cohort ABPM applied over 24 period starting prior to a mid-week HD session FU 3.13 years	344 Germany HD	Association between ambulatory SBP and all-cause and CV mortality	Non-linear (U-shaped) association between SBP & PP and all-cause & CV mortality When analysed by presence (30.5% of whole cohort) or absence of AF and/or heart failure, a negative linear association between both SBP and PP with ACM and CV mortality was found. Conversely, a positive linear association between SBP and PP and ACM and CV mortality was observed in those without CV co-morbidity.
Miskulin, 2018 [26]	To assess feasibility of an RCT in HD patients randomised to a standardized pre-dialysis SBP of 110–140 mmHg (intensive arm) or 155–165 mmHg (standard arm).	Pilot randomized control Standardized pre-HD BP "in accordance with AHA guidelines" FU for 365 days	126 United States HD	Primary outcome: assess feasibility of study. Secondary outcome: assess change in LVM.	The incidence rate ratios for intensive vs standard arm were 1.18 (0.40 to 3.33), 1.61 (0.87 to 2.97), and 3.09 (0.96 to 8.78) for major adverse cardiovascular events, hospitalisations, and vascular access thrombosis, respectively. The intensive and standard arms had similar median changes in LVM of −0.84 (−17.1 to 10.0) g and 1.4 (−11.6 to 10.4) g, respectively.
Myers, 2010 [33]	To examine whether age, race, and diabetes status affect the association between pre-dialysis SBP and mortality	Retrospective cohort Usual (non-standardized) pre-dialysis BP Median FU 1.5 years	16,283 United States HD	Association between pre-dialysis BP and PP and all-cause mortality	1) In those >50 years old, SBP <140 (and not SBP >160) mmHg was associated with increased mortality; conversely, in those <50 years old, only SBP >160 (and not SBP <140) mmHg was associated with increased mortality. Higher mortality in those with diabetes (vs. those without) was restricted to those who also had SBP <140 mmHg; in those with SBP >140 mmHg, the association with mortality was not influenced by diabetes status.
Park, 2013 [192]		Retrospective cohort Usual (non-standardized) pre- and post-HD BP, averaged over all sessions (~39) in a quarter Median FU 2.2 years	113,255 United States HD	Association between ΔSBP & DBP during HD and all-cause mortality	Non-linear (U-shaped) association between ΔSBP (& DBP) and ACM & CV mortality, including after adjustment for case-mix and malnutrition-cachexia syndrome: -30 and >0 mmHg associated w increased mortality; nadir risk/greatest survival associated with -14/-6 mmHg (HR 0.92, 95% CI 0.91-0.93; 0.93, 0.91-0.94 for ΔSBP & DBP respectively). Relationship persists at all levels of pre-HD BP, except <120 mmHg (FIG 3)

					Relationship not modified by UF volume (as % of doy weight) or HD session time (FIG 4)
Robinson, 2012 [28]	Analysis of association between pre-HD SBP and mortality by Cox regression adjusted for patient & facility-level characteristics, as a means to lessen potential bias due to unmeasured confounders affecting SBP and mortality.	Retrospective cohort (using DOPPS data) Usual (non-standardized) pre-HD BP (median of 1 weeks data in DOPPS wave 1 & 2; most recent [single] reading in DOPPS wave 3) Mean FU 1.7 years	24,525 Multiple countries HD	Retrospective facility & patient level analysis of BP levels & association with all-cause mortality	In fully adjusted multivariable models: At patient level: compared to reference category of 130-139 mmHg, all-cause mortality increased for 110-119 mmHg (HR 1.14, CI 1.01-1.28), 120-129 mmHg (HR 1.11, CI 1-1.23) and decreased for SBP 150-159 mmHg (HR 0.9, CI 0.91-0.99) At facility level: Compared to 130-159 mmHg, all-cause mortality increased for 110-129mmHg (HR 1.13, CI 1.05-1.21) and ≥160 (HR 1.16, CI 1.1-1.23) For post-HD BP lowest risk is (facility level) 120-139 mmHg (see figure 7B)
Shafi, 2014 [35]	To test the hypothesis that stratification by serum biomarker (BM) levels may change the association between predialysis SBP and outcomes in HD patients	Prospective cohort Usual (non-standardized) pre-HD sitting BP Median FU 3.1 years	446 United States HD	Relationship between pre-HD BP and all-cause & CV mortality and CV events, stratified by levels of BMs cardian troponin I and NT-proBNP	High BM levels associated with worse survival at 2.4 years (vs 3.5 yrs in low BM group). Those in high BM group had more overt CV disease (atherosclerotic and heart failure). In low BM group, there was linear increase in all-cause with pre-HD SBP >140 mmHg; no evidence of increase in all-cause mortality at low BP. HR for all-cause mortality was 1.07 (95% CI 1.01-1.14) for each 10 mmHg rise increase in SBP. In high BM group, no relationship between SBP and all-cause mortality existed at high or low BP
Xie, 2020 [38]	To explore an optimal target of BP for the PD patient population	Prospective cohort Usual clinic BP (no detail given) averaged over the first 3 months after the initiation of PD; median number of BP measurements contributed by each	7,335 China PD	Relationship between BP (as detailed) and (i) all-cause mortality (ii) CV mortality	Non-linear (U-shaped) relationship between SBP and all-cause and CV mortality (1) Compared to reference SBP tertile of 119-141 mmHg, HR for all-cause mortality was 1.38 (95% CI 1.12-1.69) for SBP <119 mmHg and 1.2 (CI 1.07-1.35) for BP >141 mmHg For same tertiles, HR for CV mortality were 1.4 (CI 1.02-1.93) and 1.3 (CI 1.08-1.56)

		patient was 4 [interquartile range 3–4] Median FU 2.98 years			
Lifestyle modification					
Argilés 2004 [41]	To assess the participation of interdialytic body weight gain variations in the seasonal profile of blood pressure	Prospective observational trial Routine systolic and diastolic blood pressure while in a supine position on dialysis Observation for 7 years and 6 months; mean follow up time 42.6 ± 3.4 months	99 stable satellite HD patients France HD	The effect of interdialytic body weight gain variations in the seasonal profile of blood pressure	Blood pressure varied throughout the year, following a cyclic pattern. Systolic and diastolic blood pressures were strongly correlated with interdialytic body weight gain (r= 0.925; P < 0.0001 and r= 0.888; P= 0.0001, respectively)
Bernier-Jean, 2022 [64]	To assess the benefits and safety of regular structured exercise training in adults undergoing dialysis on patient-important outcomes. To define the optimal prescription of exercise in adults undergoing dialysis.	Cochrane review. 21 studies included which reported on BP. Included studies of intra and interdialytic exercise No details on method of BP measurement. Follow-up 8 weeks to 2 years for all studies, follow up for just the studies looking at BP is not stated.	21 studies, 324 participants. Authors from Australia, studies included from a variety of countries. HD	A subset of studies analysed the effect of aerobic and combined (aerobic and resistance) exercise on SBP and DBP	SBP: It is uncertain whether aerobic exercise reduced SBP due to low certainty of the evidence MD -3.99mm Hg, 95% CI -9.78 to 1.80; I^2 = 45%; very low certainty evidence. There is very uncertain evidence that combined exercise effect SBP MD -8.69 mm Hg, 95% CI -13.69 to -3.69; I^2 = 57%; very low certainty evidence) Note the heterogeneity was resolved after one study was excluded DBP: The authors conclude It is uncertain whether aerobic exercised reduces DBP, the pooled results show a mean increase in DBP with exercise MD 0.72 mm Hg, 95% CI -2.24 to 3.69; I^2 = 31%, very low certainty evidence. Evidence is very uncertain whether combined exercise reduces DBP MD -4.45 mm Hg, 95% CI -5.98 to -2.91; I^2 = 0%; very low certainty evidence. The quality of the evidence was very low due to the high risk of bias, the short duration of the interventions and follow-up and low number of participants.

Barati Boldaji, 2020 [59]	The effect of pomegranate juice on cardiometabolic risk factors, biomarkers of oxidative stress and inflammation in hemodialysis patients	Randomized cross over trial. Blood pressure was measured in pre-dialysis state twice with an interval of at least 5 min using a digital barometer (Microlife BP A200 AFIB). The mean of two measurements was used. Follow up: 8 weeks	41 HD patients. 100mls pomegranate juice after HD x 3 per week for 8 weeks. 4 week wash out and then 8 weeks no juice. Country: Iran HD patients	The effect of pomegranate juice on total antioxidant capacity and malondialdehyde were the primary outcomes with interleukin-6 as the secondary outcome. Blood pressure along with serum lipid levels were also reported	Decrease in SBP MD -6.97 (-4.88 to -9.05) P<001 and DBP MD-6.88 (-9.08 to -4.68) p <00.1 overall mean BP changes: 137/97 to 128/90
Chazot, 1995 [49]	To determine if long HD sessions have an effect on inter dialytic BP	Observational study Inter-dialytic ABPM Single session	91 France Stable HD patients receiving 3x8hrd per week HD as standard	Linear regression to determine if there was a correlation between HD hours and inter-dialytic ABPM	The Mean BP was inversely correlated with the treatment duration, but not with inter-dialysis weight gain.
Cole NI, 2019 [52]	To determine the effect of dietary salt reduction on blood pressure in individuals receiving dialysis	Systematic review and meta-analysis of randomised controlled trials (RCTs)	Four RCTs (91 participants) met inclusion criteria UK HD patients	Primary outcome was change in systolic and diastolic blood pressure	Dietary salt reduction was associated with an 8.4 mmHg reduction in systolic blood pressure (95% CI 4.8-12.0, I2 = 0%), and a 4.4 mmHg reduction in diastolic blood pressure (95% CI 2.2-6.6, I^2 = 0%).

Daud, 2021 [66]	Does counselling by home pharmacy care improve medication adherence and blood pressure	Controlled trial, participants randomized based on HD schedule. Average of 2 BP measurements in the morning and average of 2 BP measurements in the afternoon taken at home for 7 days in week 1 and 6 Follow- up 6 weeks	58 hypertensive HD patients in Indonesia	Intervention group were counselled by pharmacist once a week at home, weeks 2-5 of trial. BP measured daily for first 7 days and then compared with BP measured in weeks 2 and 6.	Results reported as % of patients with a reduction in SBP and DBP in the control and intervention groups. Treatment group: 86% experienced reduction in SBP and 69% in DBP. Compared with control 17% reduction in SBP and 10% in DBP. Magnitude of reduction was not reported or mean reduction. Young population aged 39-59, 57% high school graduates – could not be extrapolated to other groups.
Ferrari, 2020 [61]	To assess the impact of different types of Intradialytic training (IDT) on clinical outcomes and functional parameters in ESRD patients undergoing HD.	Systematic review and metanalysis No details of method of BP measurement. Follow up was 1 day to 12 months for all the 50 studies included. No details are given on the follow up of the studies which look at BP	10 studies included looked at the effect of aerobic exercise on BP, 2 studies looked at the effect of combined exercise on BP (actual numbers of patients not given) Authors from Brazil, studies included from a variety of countries. HD	Primary outcomes were a range of clinical and functional parameters including BP m	Aerobic IDT reduced SBP MD − 10.07 mmHg (-16.35 to -3.78) I^2 44% p= 0.002. but there was a large heterogenicity. Combined training reduced DBP MD − 5.76 mmHg (-8.83 to -2.7) I^2 0% p 0.0002. There was a non-significant reduction in SBP -4.33 mmHg (-9.75 to 1.08 p=0.12 This trial only looked at intradialytic exercise. Only 2 studies in combined exercise analysis.

Kauric-Klein, 2017 [65]	Examined the effects of an educative, self-regulation intervention on blood pressure self-efficacy, self-care outcomes, and blood pressure control in adults receiving haemodialysis.	Randomised controlled trial Follow-up 12 weeks. BP was measured pre-dialysis and average weekly systolic and diastolic pressure was calculated	118 HD patient from 6 HD units in Detroit USA. With high BP and on HD for >6 months. 86% African Americans	BP education sessions 2x 15 min sessions, 12 wks of individual counselling. Participants kept: BP log, Na checklist, fluid log, an 11 item BP self-efficacy scale was undertaken at baseline and 12 weeks.	No overall improvement in BP self-efficacy scores. No overall improvement in BP. BP self-efficacy scores were related to lower average diastolic BPs at baseline (r = −.21, p < .001) and at 12 weeks (r = −.318, p < .001) Poor adherence to some aspects only 11% of Na logs were completed.
Marx, 2017 [58]	To investigate if polyphenol rich interventions can improve cardiovascular risk markers in HD patient	systematic review and meta-analysis no details on methods to assess BP fup 30 days to 12 months	A subset of 3 studies, 115 participants looked at the effect of polyphenols on blood pressure. HD patients Australia (authors) Studies included from Germany, Israel, USA HD	Primary analysis were lipid profile, inflammation, oxidative stress and blood pressure	Improvement in DBP (MD −5.62 mmHg (95% CI −8.47, −2.78); I^2 = 2%; p = 0.0001; but not SBP (MD mmHg −10.02 (95% CI −21.39, 1.35); I^2 = 66%; p = 0.08;
Mc Causland, 2012 [43]	To determine the effect of dietary sodium intake on blood pressure and mortality	A post-hoc analysis of 1770 patients in the HEMO Study with available dietary, clinical, and laboratory information. Median follow-up time was 2.1 years	1770 patients 772 were men, 1113 black, and 786 diabetic, with a mean	Linear regression modelling to determine the effect of dietary sodium intake on blood pressure and mortality	No indices were associated with the pre-dialysis systolic blood pressure. Higher baseline dietary sodium and the ratio of sodium to calorie or potassium were each independently associated with greater all-cause mortality.

			age of 58 years and a median dietary sodium intake of 2080 mg/day HD patients in the HEMO study		Higher reported dietary sodium intake was independently associated with greater mortality among prevalent haemodialysis patients. Randomized trials will be necessary to determine whether dietary sodium restriction improves survival.
McMahon, 2021 (53)	To determine the effect of two or more levels of salt intake on outcomes in people with any stage of CKD	Systematic review and meta-analysis of RCTs of salt reduction in CKD Subgroup analysis in dialysis patients (5 studies, 149 participants) Where more than one BP measurement was reported, 24-hour ambulatory BP was used preferentially in analyses and clinic-assessed BP was used preferentially over self-assessed BP measurements.	149 in relevant sub-group analysis Canada HD	Effect of salt reduction death and cardiovascular death and CKD progression Secondary outcomes include effect of salt reduction on blood pressure Subgroup analysis of salt reduction on BP in dialysis patients	In dialysis patients, reducing salt intake reduced both systolic (Analysis 1.2.2 (5 studies, 149 participants): MD -6.32 mm Hg, 95% CI -11.04 to -1.60; I^2 = 0%) and diastolic BP (Analysis 1.3.2 (5 studies, 149 participants): MD -3.46 mm Hg, 95% CI -6.39 to -0.54; I^2 = 0%).
Ozkahya, 1998 (51)	To determine the effect of persistent strict volume control by ultrafiltration alone on LVH	Uncontrolled retrospective observational study	15 Turkey	The effect of ultrafiltration on BP control and LVMI	Mean pre-dialysis BP values of the study group were 139±20/83±11 mmHg at the beginning and 116± 12/73±7 mmHg at the end of observation period. Corresponding post-dialysis values were 126±8/75± 10 mmHg and 105±7/65±3 mmHg respectively

		BP mean of three consecutive pre-dialysis recordings Follow-up period mean 37±15 months	HD patients with a previous echocardiographic assessment in the preceding 1.5 years		The reduction in BP was achieved by diet and fluid advice and ultrafiltation and was associated with a reduction in LVMI from 175±60 to 105±11 g/m2.
Pu, 2019 [60]	To assess the efficacy and safety of intradialytic exercise for haemodialysis patients	systematic review and meta-analysis. No details on method of BP measurement. Follow-up: at least 7 weeks	27 RCTs involving 1215 subjects. 7 of these trials, 287 subjects compared BP of those who exercised for a min of 7 weeks with control (no exercise). Cycling was the exercise in the trials which looked at BP. Authors from China, studies included from a	Primary outcomes were dialysis adequacy, VO2 peak, QOL, depression and adverse event. There were a number of secondary outcomes including blood pressure at rest	Intradialytic exercise (cycling) reduces SBP (MD −4.87, 95% CI −9.20 to –0.55, p=0.03) and DBP (MD −4.11, 95% CI −6.50 to –1.72, p=0.0007). no increase in intradialytic hypotension

			variety of countries. HD		
Scapini, 2019 (193)	A systematic review to investigate if aerobic, resistance and combined exercise training improve aerobic capacity, arterial blood pressure and haemodialysis efficiency in people requiring haemodialysis. Is one exercise training modality better than the others?	Systematic review and metanalysis of trials of inter and intra dialytic exercise. Systolic and diastolic arterial pressures at rest. 12wks – 12 months	16 studies included total of 496 participants. Authors from Brazil, Studies included from variety of countries. HD	Primary outcomes were aerobic capacity, arterial blood pressure at rest and haemodialysis efficiency	Combined training significantly reduced systolic (−9 mmHg, 95% CI −13 to −4) and diastolic (−5 mmHg, 95% CI −6 to −3) blood pressure compared to control Combined training (aerobic and resistance) was found to lower blood pressure but not aerobic alone.
Song, 2022 (63)	To determine the most effective exercise intensity and modality for improvements in physical function, blood pressure control, dialysis adequacy, and health-related quality of life for haemodialysis patients	Bayesian network meta-analysis and systematic review No details on method of BP measurement. Follow up of 8 to 40 weeks for the 46 studies included, No details for the follow up just those studies which looked at BP	HD, 46 studies, 1893 participants 21 studies looked at the effect of exercise modality and 19 exercise intensity on BP. Authors from China, studies included from a variety of countries.	The 6 minute walk test, Kt/V, systolic and diastolic blood pressure and the short-form 36 health questionnaire (physical and mental health scores compared separately)	No exercise modality significantly reduced SBP or DBP more than the control group. Moderate–vigorous exercise significantly reduced SBP(MD = −8.7, 95% CI = −17 to −1.6, I^2 = 70.8%) and DBP (MD = −4.9, 95% CI = −9.9 to −0.35, I^2 = 74.2%) than the control group

			HD		
Dialysis and dialysate					
Akdag, 2015 [91]	To determine the effect of reducing dialysate sodium from 140 to 137mmol/L for 6 months vs control	Double blinded, single centre RCT,	46	Ambulatory BP measurements over 24 hours	Patients randomised to low dialysis sodium showed reduced systolic ambulatory BP readings (P<0.05) which was not found in the control group. IDWG was found to be significantly decreased in the low-sodium dialysate group after 6 months (P<0.001).
Basile, 2016 [89]	To review the effect of different dialysate sodium concentration on pre-dialysis BP and IDH	Systematic review	23	Pre-dialysis BP and interdialytic weight gain	Patients treated with higher dialysate sodium had higher IDWG and no difference in BP.
Causland, 2022 [92]	To determine the effect of dialysate sodium 138 vs 142mmol/L in hospitalised maintenance HD patients	Double blind, single centre RCT in hospitalised HD patients	139	Average decline in systolic BP after HD and rate of IDH	No significant differences in systolic BP decline between the 2 groups (23 ± 16 versus 26 ± 16 mmHg, P=0.57). The proportion of total sessions complicated by IDH was similar in the higher dialysate sodium group, compared with the lower dialysate sodium group (OR 0.72, 95% CI 0.36 to 1.44, P = 0.35).
Culleton, 2007 [67]	To determine the effect of frequent nocturnal HD on left ventricular mass	Prospective, two-centre, parallel-group RCT BP assessed by dialysis machine's automated BP cuff immediately post-dialysis 6 months follow up	52	Change in left ventricular mass and change in BP	Frequent nocturnal haemodialysis improved left ventricular mass, mean left ventricular mass difference between groups (15.3 g, 95% CI 1.0 to 29.6 g, P = 0.04) and improved BP control. Antihypertensive medication use was reduced or discontinued in 16 of 26 patients randomised to nocturnal haemodialysis and only 3 of 25 patients randomised to conventional haemodialysis (P <0.001). Despite the reduction in use of antihypertensive medications in the nocturnal haemodialysis group, 6-month systolic BP decreased in patients randomised to nocturnal haemodialysis by 7 mm Hg and increased in patients randomised to conventional haemodialysis by 4 mm Hg (mean difference 11 mm Hg, 95% CI −2 to 24 mm Hg).
Dasgupta, 2019 [31]	To examine the association between facility practises	Observational study of facility practises on patient outcomes	10,250	IDH and mortality	Routine use of lower dialysate temperature was associated with lower cardiovascular mortality (HR 0.76, 99% CI, 0.58 to 0.98). Routine use of sodium modelling/profiling to limit

	related to fluid volume management and IDH & mortality				or prevent intradialytic hypotension was associated with higher all-cause mortality (HR 1.36, 99% CI, 1.14 to 1.63)
Davenport, 2006 (94)	The impact of HD centres using predominantly 136 vs 140mmol/L dialysate sodium	Observational study of dialysis practise	469	IDWG, proportion of patients receiving antihypertensive agents, number of classes of antihypertensive agents and symptomatic IDH	Patients dialysing in centres with lower dialysate sodium had lower IDWG without increased IDH and had lower proportion taking antihypertensive agents and fewer multiple classes of drugs.
Del Giorno, 2020 (102)	To determine the effect of using dialysate magnesium of 0.5 vs 0.75mmol/L over 2 weeks	RCT cross over, open label	39	Vascular stiffness and haemodynamic profile	Subjects did not have any difference in IDH rate when using higher dialysate magnesium vs lower dialysate magnesium (RR 1.10, 95% CI 0.90 to 1.34).
Dunlop, 2019 (90)	A review effect of different dialysate sodium on pre-dialysis BP and IDH	Cochrane review	12 studies	Pre-dialysis BP, IDH and interdialytic weight gain	"Low" sodium dialysate reduced IDWG (10 studies: mean difference -0.35kg, 95% CI -0.18 to -0.51), reduced pre-dialysis MAP (4 studies: mean difference -3.58mmHg, 95%CI -5.46 to -1.69) but increased IDH events (9 studies: RR 1.56, 95% CI 1.17 to 2.07)
Dunne, 2017 (95)	To compare the effect of stepwise vs linear reduction in sodium during HD	Meta-analysis of RCT involving sodium profiling techniques in chronic HD	10 articles	Rate of IDH	Stepwise reduction in dialysate sodium during HD session associated with reduced IDH episodes but linear sodium profiling had no effect on IDH
Ebrahimi, 2017 (96)	To determine the effect of temperature (35 vs 37C) and dialysate sodium (138mmol/L vs linear profiling from 150 to 138mmol/L)	RCT 2x2 design, cross over	80	IDH	Rate of IDH was significantly affect by both temperature and sodium profiling
Fagugli, 2001 (68)	Effect of short daily HD vs standard HD on BP control and left ventricular mass	Randomised two-period cross over study	12	Change in BP and LV mass	A significant reduction in 24-hour BP during short daily HD was reported (systolic BP DHD, 128 +/- 11.6 mm Hg; SHD, 148 +/- 19.2 mm Hg; P < 0.01; diastolic BP: DHD, 67 +/- 8.3 mm Hg; SHD, 73 +/- 5.4 mm Hg; P = 0.01). The decrease in BP was accompanied by the withdrawal of antihypertensive therapy in 7 of 8 patients during DHD (P < 0.01)

Gabbuti, 2003 (100)	To determine the effect of using dialysate bicarbonate (26 vs 32mmol/L) over 6 weeks treatment	RCT cross over trial	26	BP, heart rate, IDH	Subjects had increased rate of IDH (5.55 vs 1.7%, P<0.05) and more saline or hypertonic glucose infusions (20.9 vs 13.7% of the dialysis sessions, P<0.05) when receiving high dialysate bicarbonate.
Gabutti, 2009 (99)	To determine the effect of using dialysate bicarbonate (26 vs 35mmol/L) and calcium (1.25mmol/L vs 1.50mol/L) at 3 weeks of treatment	RCT cross over study	21	Pulse wave analyser, bioimpedance and BNP	An increase in systolic and diastolic BP was observed using either a high calcium (+5.6 and +2.5 mmHg, respectively) or a low bicarbonate (+4.7 and +1.7 mmHg, respectively) concentration
Inrig, 2015 (93)	To examine the effect of high dialysate sodium (serum sodium +5mmol/L) vs low dialysate sodium (serum sodium – 5mmol/L)	Participant blinded, investigator unblinded randomised cross over	16	Intradialytic changes in serum Endothelin-1, nitrite levels and BP	The average systolic BP throughout all haemodialysis treatments in the week treated with low dialysate sodium concentrations was lower than the week treated with high dialysate sodium concentrations; parameter estimate, 29.9mmHg (95% CI, 213.3 to 26.4, P < 0.001).
Jardine, 2017 (69)	To evaluate the effect of increasing weekly haemodialysis hours on quality of life over 12 months compared with standard haemodialysis	RCT, multicentre of in centre and home HD patients	200	The primary outcome was change in quality of life Secondary outcomes included medication usage and change in left ventricular mass index	Change in EQ-5D score at study end did not differ between groups BP did not differ between groups at study end. Extended hours were associated with fewer BP-lowering agents In a sub-study with 95 patients, there was no difference in left ventricular mass index (mean difference, −6.0, 95% CI −14.8 to 2.7 g/m2, P=0.18)
Kyriazis, 2004 (101)	To determine the effect of changing dialysate magnesium and calcium on BP (performed as 2 studies)	RCT cross over	8 + 14	IDH and intradialytic BP	The dialysis solution containing 0.25 mmol/L magnesium and 1.25 mmol/L calcium had the highest rate of IDH, and increasing dialysate magnesium to 0.75mmol/L had lower IDH when dialysate calcium was 1.25mmol/L
Lin, 2001 (76)	To assess the advantages in the	Partially randomised patient preference	111	Haemodynamic parameters including	Maximum drop of systolic BP, episodes of symptomatic hypotension and mean saline infusion volumes during

	biochemical, haemodynamic, and clinical effects in uremic patients treated with different frequencies of online-HDF (thrice, twice, once per week) and high-flux HD.			maximum drop of systolic BP, episodes of symptomatic hypotension and mean saline infusion volumes during dialysis	dialysis were reduced when frequencies of on-line HDF were increased.
Maduell, 2013 [77]	To compare the effect of on-line HDF with conventional HD on all-cause mortality, cardiovascular mortality, all-cause hospitalization, and treatment tolerability	Multi-centre RCT	906	Treatment tolerability	The incidence of intradialysis symptoms was affected by treatment assignment. There were 679.2 intradialysis hypotension episodes per 100 patient-years in the OL-HDF group versus 937.7 episodes per 100 patient-years in the haemodialysis group (rate ratio 0.72, 95% CI, 0.68 to 0.77, P<0.001)
Manji, 2021 [194]	To determine the effect of Low sodium dialysate (137mmol/L) vs standard (140mmol/L) dialysate sodium	RCT cross over	41	IDWG and pre-dialysis BP	Results of 6 weeks cross over trial of chronic HD patients receiving twice a week dialysis showed no difference in IDWG or BP.
Morena, 2017 [78]	To explore the potential benefits of using on-line HDF versus optimal high-flux HD in elderly ESKD patients.	RCT	381	Intradialytic tolerance	No difference in adverse events, which included asymptomatic and symptomatic IDH between the groups. Exploratory analysis which considered the dialysis session as the statistical unit (rather than the patient), suggested that online HDF was associated with fewer episodes of asymptomatic IDH, but there was no difference in symptomatic hypotension between the two treatment groups. After 24 months of-follow-up there were no significant differences in BP.
Mustafa, 2016 [86]	To determine if lowering dialysate temperature	Systematic review	484	Rate of IDH	Reduced temperature dialysis reduced IDH by 70% (95% CI 49% - 89%)

	improves outcomes for HD patients				
MyTemp, 2022 [88]	To determine the effect of dialysate temperature set at 36.5C vs 0.5-0.9C below body temperature	Open label, cluster multi-centre RCT	15,413	Composite end point of Cardiovascular mortality or hospital admissions from MI, ischaemic stroke or heart failure	No difference in composite end-point after 4 year follow up; cooler dialysate vs standard (adjusted HR 1.00, 95% CI 0.89 to 1.11).
Nistor, 2015 [79]	To compare convective (HF, HDF, or AFB) with diffusive (HD) dialysis modalities on clinical outcomes (mortality, major cardiovascular events, hospitalisation and treatment-related adverse events) in men and women with ESKD.	Meta-analysis of RCTs	4,039	Treatment-related adverse events	No difference in the number of dialysis sessions with hypotension (mean difference, -4.05, 95% CI, -15.39 to 7.3), pre-dialysis systolic BP (mean difference, 1.19, 95% CI -1.46 to 3.84) or pre-dialysis diastolic BP (mean difference, -0.25, 95% CI -1.06 to 0.56). HDF was associated with a lower maximal drop in BP and reduced the rate of hypotension during dialysis compared with HD.
Odudu, 2015 [87]	To determine the effect of dialysate temperature set at 37C vs -0.5C below body temperature	Multi-centre, open-label RCT	73	Cardiac magnetic resonance imaging	Pre-dialysis mean arterial BP showed no statistically significant difference between groups over 12 months
Smith, 2017 [195]	To determine whether recovery time and adverse events during treatments differs between HD and HDF.	Randomised cross over trial	100	Recovery time in minutes Incidence of adverse events during treatments	There was no overall difference in recovery time between treatments (medians for HDF vs HD of 47.5 [IQR, 0-240] vs 30 [IQR, 0-210] minutes, respectively, P = 0.9). HDF was associated with an increased frequency of IDH. Symptomatic IDH occurred in 5.3% of HD treatments compared to 8% of HDF sessions (relative risk 1.52, 95% CI 1.2 to 1.9). However, 80% of IDH episodes were mild and successfully managed with temporary discontinuation of ultrafiltration.

Stefansson, 2014 [83]	To determine prevalence of IDH and association with cardiovascular events and mortality	USRDS Observational study	39,497	IDH according to interdialytic weight gain and association between IDH and CV outcomes and mortality	IDH strongly associated with cardiovascular morbidity and mortality.
Tentori, 2013 [97]	To determine the association between facility practises related to dialysate bicarbonate and IDH & mortality	Observational study of facility practises on patient outcomes	17,031	mortality	Dialysate bicarbonate concentration was positively associated with mortality. Adjusted HR 1.08 per 4 mEq/L higher, 95% CI 1.01 to 1.15 and adjusted HR 1.07 (95% CI, 0.97 to 1.19) for dialysate bicarbonate ≥38 vs. 33–37 mEq/L.
Tsujimoto, 2019 [196]	To review the effect of dialysate temperature on IDH	Cochrane review	25 studies	IDH	Very low evidence that fixed reduction of dialysate temperature improves IDH rate (8 studies, RR 0.52, 95% CI 0.34 to 0.80)
Viegas, 2017 [98]	To determine the effect of using dialysate bicarbonate 34 vs 30mmol/L for 9 months	RCT	93	IDH and IDWG	High bicarbonate vs low bicarbonate had no effect on IDH (28.0 vs. 27.4 episodes per 1000 sessions, P=0.906).
Wang, 2014 [80]	To compare the effect of convective modalities of dialysis (HDF and HF) versus standard HD	Meta-analysis of RCTs	1,259	Episodes of symptomatic hypotension	HDF reduced symptomatic hypotension compared to conventional HD (relative risk 0.49, 95% CI, 0.28 to 0.86). No significant difference in end of treatment BP between treatment groups (weighted mean difference 2.69 mm Hg, 95% CI 0.98 to 4.40).
Yu, 2018 [84]	To determine risk factors and prognosis of IDH in HD patients	Single centre observational	293	Risk factors associated with IDH and Mortality	IDH is an independent risk factor for long-term mortality in HD patients
Zoccali, 2023 [85]	To determine if cold HD prevents IDH and mortality	Observational, incident HD patients.	8,071	IDH and mortality after case-mix at facility level adjustment	A 0.5 degree reduction in dialysate temperature was associated with reduced IDH (OR 0.67, 95% CI 0.63 to 0.72), but no effect on mortality (HR 1.01, 95% CI 0.88 to 1.16)
Dry weight					
Agarwal, 2009 [110]	To assess the participation of interdialytic body weight gain variations in the seasonal profile of blood pressure	Prospective observational trial Routine systolic and diastolic blood pressure	99 stable satellite HD patients France	The effect of interdialytic body weight gain variations in the seasonal profile of blood pressure	Blood pressure varied throughout the year, following a cyclic pattern. Systolic and diastolic blood pressures were strongly correlated with interdialytic body weight gain (r= 0.925; P < 0.0001 and r= 0.888; P= 0.0001, respectively)

		while in a supine position on dialysis Observation for 7 years and 6 months; mean follow up time 42.6 ± 3.4 months	HD		
Agarwal, 2016 (111)	To evaluate the effect of lowering home BP on change in symptoms	Sub analysis of RCT Follow up 1 year BP measurement: Mid-week 44hr ambulatory blood pressure monitoring	133 Single centre USA HD	Correlation between fall in BP from baseline and improved uraemic ($P<0.05$) and cardiovascular ($P<0.001$) symptoms without an increase ($P=0.047$) in dialysis related symptoms	Reducing BP is association with improvement of symptoms including those unrelated to volume excess.
Dasgupta, 2019 (31)	Evaluate the association between haemodialysis unit practices related to fluid volume and all cause mortality	Retrospective cohort study Follow up 3 years Method of BP measurement: Non standardised	10,250 International (DOPPS database) HD	10 faculty practices as reported by dialysis unit medical directors were associated with all cause and CV mortality	After multivariate adjustment the following reported practices were associated with improved outcomes. Having a protocol specifying how often to assess dry weight was associated with lower all-cause (HR, 0.78; 99% CI], 0.64 to 0.94) and cardiovascular mortality (HR, 0.72; 99% CI, 0.55 to 0.95). Routine orthostatic BP measurement to assess dry weight was associated with lower all-cause hospitalization (HR, 0.86; 99% CI, 0.77 to 0.97) and cardiovascular events (HR, 0.85; 99% CI, 0.73 to 0.98). Routine use of lower dialysate temperature to limit or prevent intradialytic hypotension was associated with lower cardiovascular mortality (HR, 0.76; 99% CI, 0.58 to 0.98). Routine use of an online volume indicator to assess dry weight was associated with higher all-cause hospitalization (HR, 1.19; 99% CI, 1.02 to 1.38). Routine use of sodium profiling to limit or prevent intradialytic hypotension was associated with higher all-cause mortality (HR, 1.36; 99% CI, 1.14 to 1.63), cardiovascular mortality (HR, 1.34; 99% CI, 1.04 to 1.73), and cardiovascular events (HR, 1.21; 99% CI, 1.03 to 1.43).

					Conclusion: haemodialysis facility practices are associated with different patient outcomes. The results emphasize the importance of regular and careful clinical assessment of target weight and fluid balance.
Davies, 2023 [112]	To determine whether bioimpedance guided target dry weight assessment preserves residual renal function	Prospective randomised open label trial Follow up 24 months Method of BP measurement: Median of weekly systolic/diastolic BPs taken as per routine care.	439 uric (>500ml) Multicentre UK HD	Primary outcome was time to anuria Secondary end points: rate of residual renal function decline blood pressure and patient-reported outcomes	Compared to standard care, the addition of bioimpedance knowledge did not lead to a preservation of RRF (HR 0.751 ;95% CI 0.459-1.229, p=0.254). No significant difference in any secondary end points between groups. Conclusion: bioimpedance is not useful above routine care in targeting dry weight to preserve RRF.
Dekker, 2018 [106]	Evaluate the association between pre-dialysis fluid status and pre-SBP on 1 year all-cause mortality	Retrospective cohort study Follow up 1 year Blood pressure was measured prior to the start of dialysis in the clinic in seated position using an oscillometric method.	8,883 International multicentre (MONDO database) HD	Association of pre dialysis fluid status classified as overloaded (>+1.1 to +2.5 L) or fluid deplete (<-1.1L) using BCM versus normovolaemia and pre dialysis systolic blood pressure status measured using *non-standardised* in-centre BP measurements classified as low (<110mmHg) normotensive 110-140mmHg) versus >140)	In normotensive patients both pre-dialysis fluid overload [adjusted HR 1.57 (95% CI 1.21–2.04)] and fluid deplete [adjusted HR 1.95 (95% CI 1.08–3.51)] were associated with increased mortality risk. In euvolemic patients, low pre-SBP <110 mmHg was associated with better survival [adjusted HR 0.46 (95% CI 0.23– 0.91)] Conclusion: Patients with SBP<140 who are euvolemic a have reduced mortality.
Flythe, 2015 [105]	Evaluate the associations of post-dialysis weights above and below the prescribed target weight and outcomes	Prospective cohort study Blood pressure was machine-measured in the seated position Follow up: until death/censored median FU 2.1 years	10,785 Multicentre USA HD	Association of 'HD target weight' miss defined as either 2kg above or 2kg below in >30% of dialysis treatments versus those who were on target)	Above target weight miss n=1549 (versus not) was associated with greater all-cause mortality (adjusted hazard ratio, 1.28; 95% confidence interval, 1.15 to 1.43) and cardiovascular mortality (adjusted HR, 1.26; 95% CI, 1.07 to 1.50) Below target weight miss (n=682) in at least 30% of treatments (versus not) was associated with

				with all cause and cardiovascular mortality.	greater all-cause mortality (adjusted hazard ratio, 1.22; 95% confidence interval, 1.05 to 1.40) and cardiovascular mortality (adjusted HR, 1.56; 95% CI, 1.26 to 1.93). Conclusion: Maintenance of euvolemia is associated with reduced mortality
Huan-Sheng, 2016 [116]	Comparison of BCM measured protocolised dry weight targets with clinically determined dry weight on outcomes of all cause hospitalisation, fluid overload, CV events, hypertension and IDH events	Prospective randomized controlled trial 1 year follow up BP measured recumbent after 10min rest	298 Taiwan Single centre HD	Primary: all-cause hospitalization rate. Secondary: acute fluid overload, CV- related events, hypertension (systolic >150mm/hg) and intra-dialysis events	BCM versus clinical exam did not lead to a difference in hospitalisation, symptoms, or mortality. Average change in weight between baseline and 1 year was no different between groups. No difference in systolic BP between groups. Lower incidence of fluid overload or CV events (0.50 (0.26–0.94 p=0.03) In conclusion: little/no difference between BCM derived dry weight targets and clinically determined dry weight
Hur, 2013 [117]	Comparison of BCM targeted dry weight with clinically determined dry weight on LV mass index	Prospective, randomized, and controlled study. 1 year follow up BP measured pre post dialysis, method not described	156 Multi Centre Turkey HD	regression of left ventricular mass index during a 1-year follow-up. Improvement in blood pressure and left atrial volume were the main secondary outcomes.	LV mass fell in BCM versus control (95% CI, 19.2 to 1.17 g/m^2; *P* 0.04) BCM group lost more weight than control 0.5 L (95% CI, 0.8 to 0.2; *P* 0.001 Bigger fall in pre-dialysis systolic (-4.5mm/hg; 95% CI -8.9 to 0.1 p=0.04) and diastolic (-2.6mmHg 95% CI -4.8 to -0.3.p = 0.02) between baseline and 1 year in the BCM versus control group. Similar results were seen in diastolic BP measurements with a 6.6mmhg (p=0.005) and 3.7mm/hg (p=0.002) greater fall in post HD systolic and diastolic BP respectively between BCM and control.

					LA volume fell in BCM group (1.7ml/m2,p=0.03) but not in control group. No difference in adverse events Conclusions: BCM may help control BP and echo parameters better than clinical examination.
Hecking, 2018 (109)	Evaluate the relationship between fluid overload and intradialytic weight gain on all cause mortality	Retrospective cohort study Median follow up 491 days BP measurement method not described	38,614 Multicentre International HD	Association of pre and post dialysis relative fluid overload defined as the ratio between absolute fluid overload and extracellular fluid ratio measured using BCM on mortality in an incident HD cohort, in addition IDWG was assessed as an additional exposure over a median of 491 days.	When compared with the second quartile of pre or post dialysis volume overload those patients in the 3rd and 4th quartile of fluid overload had a higher mortality (3rd Quartile Pre HR1.75; 95%CI= 1.59-1.92) 3rd Quartile post HR1.2; 95% CI 1.11-1.3) 4th quartile Pre (HR 1.75 95% CI 1.59-1.92) 4thquartile Post (HR 1.74; 95% CI 1.6-1.9) The lowest quartile of IDWG was associated with highest mortally with the authors suggesting a confounding factor of decreased nutritional intake. Conclusion: both pre HD and post HD volume overload is associated with increased mortality across a range of IDWG.
Leung, 2017 (119)	Outcome of blood volume monitoring guided ultrafiltration versus standard of care.	Randomised single blind crossover trial in HD patients with frequent symptomatic IDH BP measurement method not described Follow up 22 weeks	32 Multicentre Canada HD	Primary end point: the rate of symptomatic IDH. Secondary end points: Proportion of sessions with symptomatic and non-symptomatic IDH, volume status, Troponin, BNP.	Compared to usual care, BVM biofeedback did not alter rate of IDH (p=0.29), nor any of the secondary end points. Conclusion: in IDH prone HD patients blood volume monitoring is no better than clinical care.
Loutradis, 2019 (133)	The effect of dry-weight reduction guided by lung ultrasound on ambulatory blood pressure in	Randomised open label parallel group trial in clinically euvolemic HD patients. BP measurement method 48h ambulatory BP	71 Multi centre Greece	Primary outcome: the difference between groups in the change of 48-hour SBP between baseline and 8-week.	Compared to regular care the lung US group had a fall target weight of -0.71 compared to an increase weight in the standard care group of +0.51 (p<0.001) from baseline to week 8. The Lung US group had a greater fall in 48h ambulatory BP between baseline and week 8:

	haemodialysis patients	Pre- and post- dialysis BPs were recorded with a validated oscillometric device with the patient sitting for at least 5 minutes. Follow up 8 weeks	HD	Secondary outcomes changes in 48-hour DBP and other inter- dialytic and intradialytic BP variables	between group difference of 5.9mmHg p=0.03 for systolic and between group difference of 3.3mmHg p=0.03 for diastolic. Similarly, intradialytic BP, 44-hour BP, and daytime or night systolic/diastolic BP during both days of the interdialytic interval were significantly reduced in the active group but remained unchanged in the control group. There was no difference in adverse events between the groups. Conclusion: lung-ultrasound-guided strategy for dry-weight reduction can effectively and safely reduce ambulatory BP levels in haemodialysis patients
Luo, 2011 [120]	Comparison between bioimpedance versus standard care in management of fluid status.	Randomised single blind study BP measurement: single reading seated after 5 min resting BP Follow up 12 weeks	160 CAPD Single centre (China)	Volume status measured using bioimpedance	BCM guided weight reduction lead to less overhydration, lower ICW, lower systolic BP (all p<0.05 compared to standard care. BCM guided fluid management in addition to clinical examination is superior to clinical examination alone in CAPD patients.
McIntyre, 2003 [121]	Evaluation of the use of blood volume monitoring biofeedback on tolerability and volume status in a HD cohort	Non randomised prospective crossover interventional trial. Follow up 3 weeks BP measurement method not described	15 Single Centre (UK) HD	End points: Patients tolerability Intradialytic weight gains, and dialysis adequacy.	BVM reduced frequency of hypotension (p<0.001), symptomatic hypotension (p<0.001), requirement of saline infusions (p<0.001) and IDWG (p=0.009) and increased urea kinetics (11% higher equilibrated Kt/V P<0.01). Conclusion: BVM improved tolerability, reduced fluid gains and increased adequacy in a group of stable HD patients.
Nesrallah, 2008 [122]	Evaluation of the use of blood volume monitoring biofeedback on volume status in a HD cohort	Randomised open label prospective trial of BVM versus standard care in volume expanded HD patients to reduce extracellular fluid volume. Follow up 6 months BP method: standing and seated positions before and after HD.	60 Single centre Canada HD	The primary endpoint: change in ECFV. exploratory end points: frequency of IDH, interdialytic weight gain, and changes in serum Na	BVM biofeedback did not lead to a significant difference in extracellular fluid, blood pressure, IDWG, dialysis adequacy but was associated with a reduction in IDH (p=0.014) compared to standard care. BVM biofeedback was not superior to clinical care in volume management in volume expanded HD patients, but may lead to reduced IDH.

Onofriescu, 2012 [123]	Evaluation of the use of bioimpedance versus standard care to guide UF management in a cohort of HD patients	Prospective randomised open label trail of bioimpedance versus standard care in ultrafiltration management BP measurement: The average of three consecutive HD sessions BP was taken after 10 minutes of recumbence using mercury sphygmomanometer. Follow up 12 months	135 Single centre (Romania) HD	Primary end point not clearly stated. Endpoints included: BP, pulse wave velocity, NT pro BNP	At 12 months the BCM group had a lower systolic and diastolic BP compared to baseline though no documentation of antihypertensive regimen. PWV fell in BCM group, and rose in usual care group. No defence in volume status in either group between baseline and 12 months. Between group comparison not performed so unclear if BCM made any difference and study limited by lack of medication use.
Onofriescu, 2015 [108]	Evaluate the associations between pre-dialysis overhydration on all-cause mortality and cardiovascular events	Prospective cohort study BP measurement: ten minutes of recumbence, using a sphygmomanometer. Follow up : median 66.2 months	221 Single centre Romania HD	Association of relative fluid overload defined as the ratio between absolute fluid overload and extracellular fluid ratio measured using BCM on mortality	After multivariate analysis those who had 15% relative fluid overload had increased mortality (HR = 1.87, 95%CI =1.12–3.13) and cardiovascular events (2.31, 95%CI = 1.42–3.77. Conclusion: volume overloaded associated with increased mortality
Patel, 2019 [124]	Evaluation of impact of bioimpedance guided UF compared to routine care on blood pressure control, antihypertensive use and IDH.	Prospective parallel group open label randomised trial. Follow up 6 months. Patients randomised to knowledge of bioimpedance result versus standard care to guide ultrafiltration and target weight.	50 Multi centre India HD	Primary end points blood pressure control, intradialytic complication secondary: anti-hypertensive drug burden.	Blood pressure: no significant difference in systolic, diastolic or MAP at 6 months between groups. No difference in the change in the systolic or diastolic pressure between baseline and 6 months between groups. Weight: no difference in weight between groups at baseline or 6 months. Fewer dialysis episodes of IDH (p=0.003), cramps (p=0.048) and dizziness (p=0.012) in the BIS group.

		BP measurement: pre/during and post HD, method not specified.			No difference change in weight between groups. Medication use: BIS guided UF did not make a difference in amount of antihypertensives used at 6 months, but did demonstrated a bigger change in the amount of antihypertensive use between baseline and 6 months (p=0.008). Conclusion: Bioimpedance guided UF management is not superior to routine care in target weight, or absolute blood pressure parameters. However it may reduce patients symptoms and may allow a reduction in antihypertensive medication use.
Santoro, 2002 [126]	Does blood volume biofeedback improve dialysis tolerance in hypotension proone HD patients	Prospective, randomized, crossover study Follow up duration 4 months Randomised patients into blood volume biofeedback versus usual care. BP measured pre and post dialysis supine and standing. No additional specified methods.	36 Multicentre Italy HD	Primary end point: difference in acute hypotension episodes between groups	Patients using blood volume biofeedback has a 30% lower (p=0.004) IDH events, and 10% reduction in inter dialysis symptoms (p<0.001) compared to standard care with no change in weight, Kt/v or pre HD BP. BVM in hypotension prone HD patients may improve patients symptoms on dialysis.
Selby, 2006 [127]	Does biofeedback versus usual care haemodialysis improve cardiac function	Prospective open label randomised crossover study. Male HD patients 'prone to hypotension' were assigned to either 2 weeks of usual care or 2 weeks of blood volume monitoring biofeedback dialysis followed by crossover. Follow up 4 weeks.	8 Single centre UK HD	Primary end point: change in LV regional wall motion abnormalities (RWMA).	Biofeedback dialysis led to higher intra dialysis systolic and diastolic pressure, significantly fewer RWMA (OR 0.6 CI 0.39-0.91) and fewer new RWMA at peak stress (p=0.02).

		BP measurement: pre/during and post HD, method not specified.			
Siriopol, 2017 [128]	Evaluation of dry weight assessment using lung US and bioimpedance versus standa rd care	Prospective parallel group open label RCT. BP measurement: method not specified. Follow up 24 months	250 Multicentre Romania HD	Primary end point: All composite of cause mortality and first CV event	Compared to standard care lung uss and bioimpedance guided dry weight did not alter mortality of CV events. Standard care lead to greater dyspnoea but less cramps. LUS–bioimpedance-guided dry weight adjustment is not superior to standard care.
Yoon, 2019 [129]	Evaluation of Bioimpedance spectroscopy-guided fluid management in peritoneal dialysis patients with residual kidney function	Prospective parallel group open label randomised controlled trial BP measurement: method not specified. Median follow up 36 months	201 Multicentre South Korea PD	Primary end point: RRF at 12 months And CV events at 36 months	No significant difference between groups in terms of volume status, RRF, BP, weight, CV events. Bioimpedance no better than standard of care.
Zoccali, 2021 [132]	Evalution of lung ultrasound guided volume management strategy on MACE	Prospective open label parallel group randomised controlled trial Mean follow up duration 1.49 years Pre- and post- dialysis BPs were recorded with a validated oscillometric device with the patient sitting for at least 5 minutes.	367 International multicentre HD	Primary end point: death, non fatal MI, decompensated heart failure.	Compared to usual care, lung us guided volume target, did not alter MACE, echo parameters, hospitalisations or patient reported outcomes. There was no significant difference in blood pressure, IDGW or target weight between groups. Lung US does not appear to be superior to standard care in assessing target weight.
Zoccali, 2017 [107]	Evaluate the associations between chronic overhydration and all cause mortality	Retrospective cohort study BP measurement method: not stated Follow-up 1 year	39, 556 International multicentre HD	In an incident dialysis population the association of fluid overload (defined as the ratio between absolute fluid overload and extracellular fluid ratio measured using BCM	Baseline fluid overload was associated with increased mortality across categories of pre systolic blood pressure measurement. (<130 mmHg: HR, 1.51; 95% CI, 1.38 to 1.65; 130–160 mmHg: HR, 1.25; 95% CI, 1.16 to 1.36; >160 mmHg: HR, 1.30; 95% CI, 1.19 to 1.42; all *P*<0.001).

				with >15% in men and >13% in women classed as fluid overloaded) 1 year on mortality.	1 year cumulative fluid overload predicted a higher death risk across pre systolic BP categories (<130 mmHg: HR, 1.94; 95% CI, 1.68 to 2.23; 130–160 mmHg: HR, 1.51; 95% CI, 1.35 to 1.69; >160 mmHg: HR, 1.62; 95% CI, 1.39 to 1.90). Both baseline overhydration and 1 year cumulative overhydration associated with increased mortality.
Medication					
Agarwal, 2014 (136)	Atenolol vs Lisinopril 3x week post HD on LVMI in hypertensive HD patients with LVH	Randomised controlled study using random permuted block design Baseline ambulatory BP then home BP 12 months	200 USA HD	Change in LVMI	This trial was terminated early due to an excess of CV events in the ACEi group (incidence rate ratio 2.36, 95% CI 1.36 to 4.23), with no difference found in primary outcome. Despite a 'treat to target' design with a goal home BP of ≤140/90 mmHg, in post-hoc analysis there was a slightly lower home BP (p=0.037) in the atenolol arm; on 44-hr ABPM, there was numerically lower BP in the atenolol arm (-3.6/3 mmHg). Such differences in BP, however, were probably too small to fully account for the observed differences in the secondary outcome, given the relatively small number of participants.
Brunelli, 2018 (30)	Effect of Midodrine on outcomes in HD patients with IDH	Retrospective cohort study In-centre BP Up to 15 months	3083 USA HD	ACM, CV hospitalizations	Midodrine use compared to non-use was associated with higher rates of death (adjusted incidence rate ratio 1.37, 95% CI 1.15–1.62), all-cause hospitalization: 1.31, 1.19–1.43 and CV hospitalization: 1.41, 1.17–1.71. Midodrine use tended to be associated with lower pre-dialysis SBP, lower nadir SBP, greater fall in SBP during HD, and a greater proportion of treatments affected by IDH. Included patients were not confirmed IDH suffers.
Chewcharat, 2022 (152)	L-carnitine vs control in HD patients with dialysis related hypotension	Meta- analysis 6-24 weeks BP method uncertain	224 8 RCTs USA, Mexico, UK, India, Iran, Japan, Canada, Italy HD	Incidence of dialysis related hypotension	Compared to control group, L-carnitine reduced the incidence of dialysis-related hypotension among haemodialysis patients (pooled OR = 0.26, 95% CI [0.10–0.72], p = 0.01, I^2 = 76.0%). Subgroup analysis on the route of supplementation revealed that only oral but not intravenous L-carnitine significantly reduced dialysis-related hypotension. The dose > 4,200 mg/week and duration of at least 12 weeks appeared to prevent dialysis-related hypotension.

Gou, 2022 [144]	Effects on mortality & CV of MRAs in dialysis patients vs control	Meta-analysis BP method uncertain 2 weeks – 36 months	1630 16 RCTs Multicentre HD & PD	ACM, CVM, LV ejection fraction, LVMI, BP, serum K+	Pooled analysis of 8 trials (n=1205) demonstrated that MRA may significantly reduce the risk of ACM: OR 0.42 (95% CI 0.27-0.66, p<0.01). Pooled analysis of 7 trials (n=988) showed MRAs may significantly reduce CVM: OR 0.43 (CI 0.25-0.74, p<0.01). SBP was significantly decreased by MRAs (mean difference -7.4 mmHg (CI -10.6 to -4.2 mmHg, p<0.01)) as well as DBP (mean diff -4.6 mmHg (CI -9.1 to -0.1 mmHg, p=0.04)) K+: mean difference 0.06 mmol/L (CI 0.03 to 0.15, p=0.22)
Heerspink, 2009 [134]	Effect of lowering BP in dialysis patients	Meta-analysis BP measurement uncertain	1679 Multicentre 8 RCTs (7 RCT HD 1 RCT PD)	BP reduction CVM, ACM	Meta-analysis demonstrated BP lowering medication vs control reduced BP, pooled reduction in BP -4.5/-2.3 mmHg (No CIs given), was associated with lower risk of CV events, RR 0.71 (95% CI 0.44-0.92, p=0.009), reduced relative risk of ACM, RR 0.8 (CI 0.66-0.96, p=0.014) and CV mortality: 0.71 (CI 0.5-0.99, p=0.044). Two trials studied bBs, two ACEi, three ARBs and one CCBs.
Iseki, 2013 [137]	Olmesartan vs. 'other' antihypertensive, not including ACEi or ARB in hypertensive haemodialysis patients	RCT Mean follow up 3.5 years Incentre BP measurements	469 Japan HD	Composite of CVM, (non-fatal stroke or MI and coronary revasculization), all cause death	This was a 'treat to target' design trial and mean BP was found to be 0.9/0.0mmHg lower in the Olmesartan group than control but not significant. 28.9% of Olmesartan group and 28.6% of control group had primary composite endpoints [hazard ratio (HR) in the olmesartan group 1.00, 95% confidence interval (CI) 0.71–1.40, P = 0.99]. All-cause deaths occurred in 38 patients (16.2%) in the olmesartan group and 39 (16.7%) in the control group (HR, 0.97; 95% CI, 0.62–1.52, P = 0.91).
Li, 2003 [140]	Effects of Ramipril on residual renal function in PD patients	Randomised, open-label, controlled trial 12 months BP measurements uncertain	60 Hong Kong PD	Preservation of residual renal function	Patients were randomly assigned to ramipril or no treatment. Target BP <135/80mmHg. Residual GFR declined in both groups over 12 months but it declined by 2.07 ± 1.12mL/min per 1.73m^2 in the ramipril group compared to 3.00 ± 1.86 mL/min per 1.73m^2 in the control group (P=0.03). The average decline in residual GFR was 0.93 mL/min per 1.73m^2 (95% CI, 0.09 to 1.78 mL/min per 1.73m^2) less in patients receiving ramipril than in control patients.

Li, 2020 [149]	Blood pressure variability (BPV) and outcomes in HD patients	Meta-analysis BP measurements mainly clinic predialysis readings but 3 studies used ABPM 0.5 to 14 years	31,841 15 studies 8 studies North America /Europe, 7 studies from Asia HD	ACM, CVM, CV event (CHD, MU, HF or stroke)	The meta-analysis observed that increased BPV is associated with a higher risk of cardiovascular and mortality outcomes in HD patients. A 1-SD increase in systolic BP variability was associated with an 18% higher risk of ACM (HR=1.18; 95% CI1.11-1.26, I^2=53.8%). The HR for CV mortality was 1.23 (95% CI 1.10-1.37, I^2=7.2%). For diastolic BP variability a 1-SD increase in DBPV was associated with an 14% higher risk of ACM (HR=1.14; 95% CI 1.05-1.23, I^2=0.00%). The HR for CV mortality was 1.14 (95% CI 0.94-1.38, I^2=0.00%).
Liu, 2017 [142]	Effect of ACEi and ARBs on CV events & residual renal fuction in dialysis patients vs other active treatment or placebo	Meta-analysis of RCTs 1 to 3.5 years BP measurements uncertain	1,856 11 RCTs Multicentre (4 from Japan) PD & HD	Major CV events, changes in GFR and drug related adverse events.	Effect of ACEi/ARBs on residual renal function studied in 1 HD trial and 4 PD. ACEI/ARB therapy significantly slowed the rate of decline in both residual renal function (MD 0.93 mL/min/1.73 m2, 0.38 to 1.47 mL/min/1.73 m2) and urine volume (MD 167 ml, 95% CI 21 ml to 357 ml). No significant difference was found in respect to frequency of MI, stroke, CV death and ACM. ARB therapy reduced the risk of heart failure events by 33% (RR 0.67, 95% CI 0.47 to 0. 93). No increased risk of side effects in patients receiving ACEi/ARBs.
Liu, 2022 [145]	Safety & efficacy of Spironolactone in patients on dialysis	Meta-analysis 2 weeks to 3 years BP measurements uncertain	1,258 15 RCTs Multicentre 8 RCT in HD patients, 3 in PD and 2 in both	ACM, CVD, hyperkalaemia gynaecomastia	This meta-analysis found that spironolactone significantly decreased ACM (OR 0.42 (95% CI 0.28-0.62, p<0.0001)) and CVD (OR 0.54 (CI 0.45-0.85, p<0.008)). It was shown that patients on spironolactone had significantly higher potassium levels compared to controls (mean difference 0.22 mmol/L (CI 0.12 to 0.31, p<0.0001)) although the incidence of hyperkalaemia showed no significant difference between the two groups (RR 1.21 (CI 0.83-1.77, P=0.31)).

					Changes in BP was a secondary outcome and pooled analysis in 10 trials showed a decrease in SBP (mean difference -4.61 mmHg (CI -10.78 to 1.56 mmHg, p=0.14)) and in DBP (mean diff -0.12 mmHg (CI -3.54 to 0.27 mmHg, p=0.94)).
Nishioka, 2022 (153)	Review of Carnitine supplementation in people requiring dialysis	Systematic review 2-4 months	128 3 trials	IDH	IDH RR 0.76 (0.34-1.69. Low certainty.
Prakash, 2004 (151)	Safety & efficacy of Midodrine in IDH	Systematic review BP measurements incentre	117 10 studies (not all RCTs) HD Multicentre	Post-HD BP Nadir BP Symptoms Saline usage	Six studies reported improvements in symptoms, one study reported no improvements and the other three did not report on symptoms. Pooled analysis showed an increase in post BP (mean difference: +12.4/7.3 mmHg (CI 7.1-17.6/3.7-10.9)) and an increase in nadir BP (mean difference: +13.3/5.9 mmHg (CI 8.6-18/2.7-9.1)). None of the included studies used a parallel group RCT design with the majority being pre/post intervention studies (7/10) and majority were unblinded to allocation.
Quach, 2016 (146)	Safety & efficacy of MRAs in patients on HD or PD with or without HF	Meta-analysis 0.5 – 36 months BP measurements variable	829 5 in HD, 4 in PD MRA vs. placebo (n=7) or SoC (n=2) Multicentre	ACM, CVM, hyperkalaemia, BP	This meta-analysis included RCT evaluating MRAs in dialysis (8 trials spironolactone, 1 trial eplerenone). Compared to controls, the RR of CVM for patients treated with MRAs was RR 0.34 (95% CI 0.15-0.75, p=0.008) and ACM: RR 0.4 (95% CI 0.23-0.69, p=0.001). Hyperkalaemia was significantly associated with MRA use, RR 3.05 (CI 1.2-7.71, p=0.04) although there was a wide range of definitions from >5 to >6.5 mm/L used. Due to differences in BP reporting methods, meta-analysis of BP could not be completed. However decreases in pre-dialysis SBP ranged from 1.7-11mmHg and from 2-5.2mmHg in control patients. In the 2 trials that reported hypotensive episodes there was no difference between MRA and placebo groups.

					Studies included were small and low quality.
Ruggenenti, 2021 [138]	Effect of Ramipril vs non RAASi on CV events in HD patients with hypertension &/or LVH	RCT Up to 42 months BP measurement incentre	269 Italy HD	Composite CV death, MI, stroke	Patients were randomised to ramipril or non RAASi titrated to maximum tolerated dose. At comparable BP control (treat to target design trial), 16% of ramipril group and 19% non RAASi group reached primary endpoints (HR 0.93 (CI 0.52 to 1.64, p=.8)). Hypotensive episodes were more frequent in the ramipril group vs controls (41% vs 12%)
Shaman, 2020 [139]	Most effective & safest BP lowering agents in dialysis patients	Network meta-analysis BP measurements uncertain	4283 40 RCTs (32 HD, 4 PD, 4 both) Multicentre	SBP reduction	This meta-analysis showed that ACEi, βB, CCB, MRAs all lowered SBP to greater extent than placebo; MRAs -10.8 mmHg (CI -14.8 to -6.7), βB -8.7 mmHg (CI -10.9 to -6.4), CCB -4.6 mmHg (-7 to -2.2), ACEi -4.3 mmHg (-7.2 to -1.5). However ARB, αBs, renin inhibitors did not lower BP more than placebo (-6.7 mmHg, CI -14.1 to 0.7 for αB vs. placebo; -3.0 mmHg, CI -8.7 to 2.6 for ARB vs placebo). βB vs. placebo comparison provided a high confidence rating for effect estimate whereas other comparisons in this meta-analysis varied from moderate (e.g. CCB and ACEi vs. placebo; CCB and βB vs. ACEi) to low or very low confidence ratings. MRA and βB were shown to lower BP more than ACEi (MRA -6.4mmHg, CI -11.4 to -1.4; βB -4.4 mmHg, CI -7.4 to -1.3) and also ARBs, CCBs, renin inhibitors. ACEi & ARB usage was associated with increased risk of hypotension compared to control (RR 6.62, CI 1.48 to 29.54 for ACEi; RR 1.53, CI 0.94 to 2.48 for ARB). Discontinuation due to adverse effects were more likely with MRA, ACEi, ARB (RR 3.35, CI 1.32 to 8.49 for MRA; RR 1.77, CI 1.09 to 2.87 for ACEi; RR 1.57, CI 0.96 to 2.57 for ARB)

					No differences between classes were observed in respect to hyperkalaemia risks. However MRAs increased K 0.32 mmol/L (CI 0.15-0.49) compared to controls.
Suzuki, 2008 [197]	Effect of ARBs vs non-ARBs on cardiovascular disease events in HD patients with hypertension	RCT Pre-dialysis BP 36 months	386 HD Japan	Composite of CVM, (CV death, non-fatal stroke/MI, HF, CABG, PCI)	Patients were randomly assigned to open label ARB or non ARB. ARB choice was at the discretion of prescriber. For primary end points, event free survival was significantly greater in the ARB group (P=0.001), 49% RRR (CI 0.33-0.79, p=0.002). **This reduction is driven largely by fewer fatal and non-fatal HF events.** BP did not differ significantly between the 2 groups at 12, 24 and 36 months. IDH developed in 38 patients on ARBs and 36 in the non ARB group (P=0.9)
Weir, 2015 [147]	High vs low dialyzability βBs & mortality rates in HD patients over 66 years	Retrospective cohort, propensity-matched 180 days	6588 HD Canada	Mortality in following 180 days	Patients over 66 years old on HD who were initiated on βBs were divided into a high dialysability group ie initiated on atenolol, acebutolol or propranolol (n=3294) or a low dialysability group initiated on bisoprolol or propranolol (n= 3294) An increased relative risk of all-cause mortality of 1.4 (95% CI 1.1 to 1.8) and cardiovascular mortality of 1.2 (95% CI 1 to 1.5) was found in those receiving high vs. low dialysability βBs.
Zhang, 2014 [143]	Review of ACEi & ARBs for preserving residual renal function in PD patients	Open-label studies	257 6 trials	Review to evaluate the benefits and harms of ACEis and ARBs for preserving residual kidney function in PD patients.	Small studies have shown a benefit in preserving renal function with ARBs Long-term use (≥ 12 months) of an ARB showed significant benefit of preserving residual kidney function in CAPD patients (MD 1.11 mL/min/1.73 m^2, 95% CI 0.38 to 1.83), but no significant benefit when an ARB were used short-term (≤ six months). Long-term use (>12 months) of ARBs and ACEi vs other antihypertensives were associated with preserving renal

					function in CAPD patients and there was no significant difference between ACEi and ARBs. There was no significant difference in BP with ARBs vs other antihypertensives.
Children & Young People					
Ateya, 2022 [171]	To assess the effect of ramipril vs. placebo on markers of endothelial dysfunction in hypertensive CYP on HD	Double-blind randomised controlled trial Method not specified 16 weeks	135 Egypt / HD	Assessment of markers of endothelial dysfunction (ADMA; hs-CRP, IL-6 and TNF-a)	In the ramipril group, there was an observed reduction in markers of endothelial dysfunction and safe and effective lowering of BP occurred (secondary analysis). Median between group differences for SBP and DBP were −12.0 mmHg (95% CI −18.0 to −9.5) and −9.0 mmHg (95% CI −12.0 to −4.5) respectively (p=<0.001)
De Zan, 2021 [179]	To assess BP trends and changes in BP over 1 year in children on conventional HD vs. HDF	Parallel-arm retrospective observational 24-h ABPM in midweek interdialytic interval and manual pre-dialysis BP 1 year	133 (78 on HD and 55 on HDF) Europe and Canada (multicentre) / HD	Assessment of 24-h MAP-SDS, pre-dialysis manual BP, prevalence of hypertension, and change in BP status at baseline and 1 year. Agreement between 24-h MAP-SDS and pre-dialysis manual BP was also analysed.	Despite equivalent dialysis dose, those on HD experienced a significantly sustained increase in BP over 1 year compared to stable BP seen in those on HDF (MAP-SDS increase of +0.98 [p < 0.0001] in the HD group vs. +0.15 [p = 0.23] in the HDF group. Poor agreement was found between manual and 24-h values.
Fadel, 2014 [173]	To assess the benefit of non-invasive monitoring of haematocrit (NIVH) in determining dry weight and determining the effect on intra-dialytic morbid events (IME) which included hypotension, light headedness, nausea, vomiting and/or	Prospective observational Pre- and post-dialysis BP; method not specified 3 months	15 Egypt / HD	Assessment of IME with and without a NIVM-guided UF protocol	There was no significant difference in pre-HD systolic, post-HD systolic, or mean BP (p >0.1 for all) before and after the implementation of the NIVM-guided UF protocol

	cramps) requiring intervention				
Karava, 2018 (177)	To assess markers of cardiovascular morbidity in CYP on HD with normal BP	Retrospective observational 24-h ABPM Median duration 10.4 months	19 France / HD	Assessment of IDWG and its effect on cIMT, LVMI, and PWV	High IDWG was associated with increased cIMT. Median SBP and DBP values were not significantly different between groups (i.e. IDWG <4% vs. ≥4%)
Mitsnefes, 2005 (3)	To determine the prevalence of hypertension and assess risk factors for elevated BP for CYP on dialysis	Retrospective cohort Method not specified Median duration 1 year (up to 5 years)	3743 North and Central America (multicentre) / HD and PD	Assessment of BP over a 5-year period of HD using data from the NAPRTCS database	Normotensive CYP at baseline experienced a significant increase in BP over the first year of HD, whereas hypertensive CYP experienced a significant decrease in BP (D indexed SBP, -0.081 ± 0.005; p ≤0.001; D indexed DBP, -0.116 ± 0.007; p ≤0.001). BP did not change significantly after the first year of dialysis (51% had uncontrolled hypertension after the first year). Baseline hypertensive status and use of antihypertensive agents were risk factors for subsequent hypertension in logistic regression analysis
Özçakar, 2006 (168)	To compare office vs 24-h ABPM values in patients receiving PD (for >2 months) and to assess correlation between BP values and LVH	Prospective observational Office BP taken manually off dialysis 5 months	25 (9 on ≥1 antihypertensive agent) Turkey / PD	Assessment of office BP and 24-h ABPM and correlation with echocardiographic findings associated with LVH	Mean 24-h SBP was higher than office SBP. Systolic hypertension was diagnosed in 32% using office SBP values vs. 56% for mean daytime SBP. There was a significant correlation between LVMI and office BP measurements and all ABPM parameters (excluding SBP and DBP dipping)
Paglialonga, 2012 (175)	To assess the usefulness of bioimpedance analysis (BIA) in estimating dry weight in CYP on HD	Retrospective cohort Pre- and post-dialysis BP; method not specified Median duration 5.5 years (non-BIA group) and 4.4 years (BIA group)	31 Italy / HD	Assessment of LVMI and incidence of pulmonary oedema	LVMI was reduced in the BIA group. There was no difference in BP, or number of antihypertensive agents used, per patient with or without use of BIA (secondary analysis)

Paglialonga, 2015 [176]	To assess median IDWG in CYP on HD, and explore correlation with various markers, including morphological LV changes	Retrospective observational Pre-dialysis automated Median duration 1.7 years	16 Italy / HD	Assessment of various factors including LVMI, % change in LVMI, % of symptomatic dialysis sessions, and median pre-dialysis SBP and DBP	Significant correlation was found between IDWG and LVMI. Those with IDWG <4% were at lower risk of LVH and had lower median DBP (vs. those in the IDWG >4% group (0.24 vs 1.72, p=0.04)
Paglialonga at al, 2023 Pediatr Nephrol DOI: 10.1007/s00467-023-05932-y	To assess an interdialytic simplified sodium balance (sNaB) model in CYP on maintenance dialysis, and explore correlation with BP and IDWG	Prospective observational 24-h ABPM or office BP Median duration 1 year	41 European (multicentre) / HD and PD	Assessment of SBP and DBP standard deviation scores (SDS) according to age, and interdialytic weight gain (IDWG).	sNaB was the strongest predictor of IDWG in multivariate analysis (β=0.63; p=0.005). Neither SBP SDS nor DBP SDS correlated with sNaB.
Patel et al, 2007 [174]	To evaluate the effects of introducing an algorithm for non-invasive monitoring of haematocrit on BP control and LVM on CYP on HD	Prospective observational 24-h ABPM 6 months	16 USA / HD	Assessment of the difference in weight, BP, number of antihypertensive medications, 24-h ABPM findings, echocardiographic findings, and UF-associated symptoms between baseline and 6 months	An improvement in ABPM index for both daytime SBP and DBP was observed (p=0.05 for both) despite no significant change in achieved post-HD weight or estimated dry weight
Roszkowska-Blaim, 2015 [169]	To evaluate the effect of hypertension and antihypertensive therapies on residual renal function (RRF) in those on PD, and to determine the optimum target BP	Retrospective observational Manual BP 12 months	87 Poland / PD	Analysis of BP, presence and control of HTN, use of antihypertensive medications, and RRF (expressed as daily diuresis) and residual GFR (rGFR) at baseline and 12 months.	In children with uncontrolled HTN, relative daily diuresis loss was higher compared to those with SBP/DBP <95th percentile. In multivariate analysis, relative rGFR decline showed an inversely relationship with SBP percentile (β=0.21, p=0.045)

	centile to maintain RRF				
Shroff, 2019 [178]	To compare the effect of HDF vs. HD on various factors including BP control	Prospective cohort 24-h ABPM in midweek interdialytic interval 12 months	177 Europe and Canada (multicentre) / HD	Assessment of BP control, cIMT, height SD score, b2-microglobulin, PTH, patient-reported symptoms, and post-dialysis recovery time	HDF was associated with better MAP SD score compared with HD (at both baseline and 12 months; p <0.001 for both), but there was no significant change in MAP SD score between baseline and 12 months for those on HDF
Srisuwan, 2015 [172]	Comparison of blood volume monitoring vs. clinical assessment to guide ultrafiltration to adjust dry weight in CYP on HD	Prospective cohort Pre-, intra- and post-dialysis; automated 8 weeks	10 Thailand / HD	Assessment of the difference between dry weight and post dialysis body weight between use of blood volume monitoring (BVM) and clinical assessment	BVM led to lower dry weight estimation than clinical assessment. There was no difference in pre-dialysis BP and/or intradialytic hypotension episodes between groups (secondary analysis)
Ulinski, 2006 [160]	To assess LV mass LVM during an observational period whilst receiving regular HD	Retrospective observational Pre-dialysis BP; method not specified Median duration 16.3 months	17 France / HD	LVM measurement 3-6 monthly with BP measurement 1 week before and 1 week after each echocardiographic assessment	SBP and DBP decreased over the observational period (p <0.001 for both) and correlated with a reduction in LVM in multivariate analysis

Appendix D: Dialysability of blood pressure lowering medication

	Dialysed in HDF/High Flux	Dialysed in PD	Half life (hrs)	Half life in ESRF (hrs)
Beta Blockers				
Atenolol	Dialysed	Not dialysed	6-7	15-35
Bisoprolol	Dialysed	Not dialysed	9-12	18-24
Carvedilol	Not Dialysed	Unlikely	6-10	Unchanged
Labetalol	Unknown	Not dialysed	4-8	Unchanged
Metoprolol	Dialysed	Not dialysed	1-9	Unchanged
Propranolol	Unknown	Not dialysed	2-6	Unchanged
Calcium Channel Blockers				
Amlodipine	Unlikely	Not dialysed	35-50	50
Diltiazem	Not dialysed	Not dialysed	2-11; SR 5-8	Unchanged
Felodipine	Not dialysed	Not dialysed	24	Unchanged
Lacidipine	Unknown	Unknown	13-19	Unknown
Lercanidipine	Unknown	Unlikely	8-10	Increased
Nicardipine	Unknown	Unlikely	8.6	Unchanged
Nifedipine	Unknown	Not dialysed	1.4-11 (depends on formulation)	Unchanged
Verapamil	Unknown	Not dialysed	4.5-12	Increased
ACE inhibitors				
Captopril	Dialysed	Not Dialysed	2-3	21-32
Enalapril	Dialysed	Dialysed	11	34-60
Fosinapril	Unlikely	Not Dialysed	11.5-14	14-32
Lisinopril	Dialysed	Unknown	12	40-50
Perindopril	Dialysed	Unknown	1	27
Quinapril	Dialysed	Not Dialysed	1	12-14
Ramipril	Dialysed	Unknown	13-17	Increased
MRAs				
Eplerenone	Unknown	Unknown	3-6	Unknown
Spironolactone	Unknown	Not dialysed	1.3-1.4	Unchanged
ARBs				
Azilsartan	Not dialysed	Not dialysed	11	15-18
Candesartan	Not dialysed	Unlikely	9	18
Irebesartan	Unknown	Not dialysed	11-15	Unchanged
Losartan	Not dialysed	Not dialysed	1.5-2.5	4-6
Olmesartan	Unlikely	Not dialysed	10-15	36
Telmisartan	Unknown	Not dialysed	24	Unchanged
Valsartan	Unknown	Not dialysed	5-9	Unchanged

Appendix E: References

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