

## Table of Contents

Ultrasound-Guided Haemodynamic Profiling in Haemodialysis Patients.....	2
Introduction.....	2
Study Objectives and Analytic Structure .....	3
Schedule of Assessments (Adapted SPIRIT Figure) .....	4
Methodology.....	6
Study Design and Setting .....	6
Participants .....	8
Ultrasound Assessment Protocol.....	8
Quality Assurance, Interpretability, and Data Completeness .....	9
Outcomes and Data Collection .....	10
Clinician Questionnaire and Disclosure Procedure .....	11
Statistical Analysis Plan.....	12
Objective 1 — Descriptive Characterisation .....	13
Objective 2 — Ultrasound Profile and Intradialytic Hypotension: Within-Patient Analyses (Primary Inferential Aim).....	14
Objective 3 — Clinician-Reported Management Impact (Exploratory) .....	16
Objective 4 — Longitudinal Clinical Outcomes (Exploratory) .....	16
Missing Data.....	16
Table 2. Prespecified Ultrasound Variables and Clinical Covariates .....	17
Sample Size Calculation.....	18
Data Management.....	20
Ethical and Safety Considerations.....	20
References .....	22

# Ultrasound-Guided Haemodynamic Profiling in Haemodialysis Patients

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## Introduction

Patients with end-stage renal disease on haemodialysis (HD) face a delicate balance in fluid management. Haemodynamic instability during HD, particularly intradialytic hypotension (IDH), is a frequent and serious complication of chronic HD.<sup>1</sup> IDH occurs in 8–40% of sessions and is associated with distress, repeated end-organ ischaemia, vascular access thrombosis, cardiovascular events and increased all-cause mortality.<sup>1</sup> Conversely, chronic fluid overload between dialysis sessions contributes to hypertension, heart failure and pulmonary oedema, and likewise correlates with worse patient outcomes.<sup>2</sup> Achieving and maintaining an optimal “dry weight” is therefore crucial, as both excessive fluid removal and volume expansion can precipitate adverse events.<sup>2</sup> However, accurately assessing volume status and perfusion in HD patients remains challenging. Traditional methods — including clinical examination, blood pressure trends, weight changes and chest X-rays — have significant limitations in sensitivity and specificity for impending instability.<sup>2</sup> As a result, clinicians often lack real-time, objective measures to guide ultrafiltration to prevent IDH or fluid overload.

**Rationale for an Integrated Ultrasound Approach:** Advances in point-of-care ultrasonography offer a potential solution by directly visualising cardiovascular and volume status. Cardiac ultrasound (echocardiography) can evaluate cardiac function and filling pressures; notably, a high pre-dialysis septal E/e' ratio (reflecting elevated left ventricular filling pressure) has been identified as an independent predictor of IDH in patients with preserved ejection fraction.<sup>3</sup> Lung ultrasound allows bedside detection of extravascular lung water via B-lines — vertical artefacts that increase in pulmonary oedema. Lung ultrasound B-line scores have shown accurate correlation with invasively measured extravascular lung water index, providing a non-invasive gauge of pulmonary congestion.<sup>4</sup> Venous ultrasound, using the Venous Excess Ultrasound (VEXUS) framework, assesses systemic venous congestion by combining the inferior vena cava (IVC) diameter and collapsibility with Doppler waveforms of abdominal veins (typically hepatic and portal veins).<sup>5</sup> The composite VEXUS score grades the severity of venous congestion: for example, a dilated IVC (>2 cm) plus abnormal hepatic and portal vein flow patterns can indicate severe congestion.<sup>5</sup> This technique focuses on organ venous pressure as a marker of

congestion, rather than volume alone, aligning with the emerging concept of a patient's "fluid tolerance" — how well they can tolerate fluid removal without organ perfusion compromise.<sup>6</sup> By integrating cardiac, pulmonary, and venous ultrasound findings, clinicians can obtain a holistic haemodynamic profile at the bedside. Such a multi-organ point-of-care ultrasound approach may better identify patients at risk of IDH (for example, those with limited cardiac reserve or high venous pressures) and guide safe ultrafiltration, compared to one-dimensional measures like blood pressure or weight change.

**Existing Evidence and Gaps:** Early studies support the feasibility and potential utility of ultrasound-guided haemodynamic assessment in dialysis patients, though significant gaps remain. Chen et al. (2021) demonstrated that dynamic echo measurements (specifically E/e' ratios) during HD can stratify IDH risk.<sup>3</sup> Several small prospective studies have applied VEXUS and lung ultrasound in the HD setting. Leyba et al. reported from a multicentre cohort that large-volume fluid removal via HD produces measurable improvements in VEXUS grade and lung ultrasound B-line count pre- to post-dialysis, highlighting that these ultrasound metrics do capture volume changes.<sup>7</sup> In the ACUVEX study (Wong et al., 2024), serial VEXUS scans and lung ultrasounds were performed during HD: only about 15% of patients showed significant venous congestion (elevated VEXUS scores) at baseline, and those patients uniformly experienced a reduction in VEXUS score after ultrafiltration.<sup>8</sup> Notably, all individuals with an elevated VEXUS in that study had bi-ventricular systolic dysfunction, suggesting that VEXUS-positive congestion in HD patients may be closely linked with underlying cardiac failure rather than volume overload alone.<sup>8</sup> Tonelli et al. (2024) further observed that among VEXUS parameters, the portal vein Doppler pulsatility was the most sensitive to volume removal — portal flow pulsatility significantly normalised after a single dialysis session, whereas IVC diameter and hepatic vein changes were more modest.<sup>9</sup> This finding supports portal vein Doppler as a rapid indicator of decongestion in HD patients, echoing other reports that portal vein indices can reflect acute haemodynamic shifts in this population. On the other hand, some data underscore the need for caution and further research. Aslaner et al. (2024) studied maintenance HD patients presenting to the Emergency Department and found that a composite VEXUS score had limited predictive value for urgent dialysis requirement due to volume overload — only the portal vein Doppler showed a modest ability to predict emergency HD, with sensitivity ~61%.<sup>10</sup> This suggests that while ultrasound congestion markers are promising, they are not yet foolproof in clinical decision-making. More broadly, the integration of multi-organ ultrasound in dialysis care is still in its infancy. No consensus protocol exists, and prospective outcome-oriented data are lacking.<sup>2</sup> A recent comprehensive review concluded that modern tools like lung ultrasound, focused echocardiography, and VEXUS show great promise for optimising fluid management in dialysis patients, but called for further studies to standardise their use and determine impact on hard outcomes.<sup>2</sup>

## Study Objectives and Analytic Structure

**Study Objective:** We propose a single-centre prospective observational cohort study to evaluate an ultrasound-guided haemodynamic profiling strategy in chronic HD patients. The parent cohort will provide serial, integrated assessments of cardiac function, lung water, and venous congestion at quarterly intervals and generate a dataset from which several pre-planned analytic objectives will be addressed.

**Analytic structure.** This protocol defines one parent cohort serving four pre-specified analytic objectives, each with its own primary estimand, outcome set, and analysis plan. Not all objectives have the same evidentiary status: Objectives 1 and 2 are the primary analytical aims and are powered for confirmatory inference within the constraints of the sample; Objectives 3 and 4 are explicitly exploratory.

- **Objective 1 — Descriptive characterisation of ultrasound-derived haemodynamic profiles.** *Estimand:* The magnitude and variability of pre- and post-dialysis ultrasound parameters (cardiac, lung, VEXUS) across sessions and over time, including within-session changes with ultrafiltration and between-session trajectories. *Status:* Primary descriptive aim.
- **Objective 2 — Ultrasound profile and intradialytic hypotension: within-patient analyses.** *Estimand:* The primary estimand is the within-patient association between pre-dialysis ultrasound parameters and same-session IDH, estimated via an embedded case-crossover design restricted to scheduled profiled sessions, with each patient serving as their own control. A secondary estimand extends the case-crossover to include event-triggered IDH sessions captured during routine care, framed as an association and phenotyping analysis. A further secondary estimand is the population-averaged association between pre-dialysis ultrasound parameters and session-level IDH, estimated via generalised linear mixed models. *Status:* Primary inferential aim.
- **Objective 3 — Clinician-reported management impact of ultrasound disclosure.** *Estimand:* The proportion of scheduled profiled sessions in which post-session disclosure of ultrasound findings would have changed the treating physician’s intended management. *Status:* Exploratory (descriptive).
- **Objective 4 — Longitudinal clinical outcomes.** *Estimand:* The association between serial ultrasound trajectories and time-to-event outcomes (hospitalisation, cardiovascular events, mortality). *Status:* Exploratory and hypothesis-generating, with expected event counts insufficient for confirmatory analysis.

Each analytic objective may generate separate publications. The pre-specification of objectives, estimands, and evidentiary status is intended to prevent post-hoc selection from a broad exploratory dataset and to allow reviewers to evaluate each objective on its own terms.

## Schedule of Assessments (Adapted SPIRIT Figure)

**Table 1. Participant timeline and schedule of study procedures.**

Procedure	Screening/ Enrolment	Baseline (Visit 1)	Month 3 (Visit 2)	Month 6 (Visit 3)	Month 9 (Visit 4)	Event-triggered (ad hoc)
Informed consent	X					
Eligibility screening	X					

Procedure	Screening/ Enrolment	Baseline (Visit 1)	Month 3 (Visit 2)	Month 6 (Visit 3)	Month 9 (Visit 4)	Event-triggered (ad hoc)	
Baseline demographics / comorbidities		X					
Pre-dialysis POCUS (cardiac, LUS, VEXUS)		X	X	X	X		
Post-dialysis POCUS (cardiac, LUS, VEXUS)		X	X	X	X	(if feasible)	
Peri-event POCUS (during/after IDH)						X <sup>a</sup>	
Clinician pre-disclosure questionnaire		X	X	X	X	(if feasible)	
Ultrasound disclosure to treating physician		X <sup>b</sup>	X <sup>b</sup>	X <sup>b</sup>	X <sup>b</sup>	X <sup>b</sup>	
Clinician post-disclosure questionnaire		X	X	X	X	(if feasible)	
Session-level clinical data (CRF) <sup>c</sup>		X	X	X	X	X	
IDH event documentation by nursing staff		X	X	X	X	X	
Intradialytic BP monitoring (routine)		X	X	X	X	X	
Laboratory values (routine clinical)		X	X	X	X		
Clinical outcome tracking (hospitalisations, CV events, mortality)			Continuous follow-up				

<sup>a</sup> Event-triggered POCUS performed when clinically feasible and safe during or immediately after an IDH episode, suspected fluid overload, or suspected underestimated dry weight. IDH-triggered scans with complete timing/intervention metadata are eligible for the secondary Objective 2 case-crossover analysis. <sup>b</sup> Disclosure occurs only after the dialysis session is complete and all intradialytic outcome data have been recorded; exception: findings meeting the emergency disclosure criteria (see Ethical and Safety Considerations) are communicated immediately. <sup>c</sup> Session-level CRF includes: interdialytic weight gain, pre-dialysis BP and heart rate, antihypertensive medications on day of dialysis, prescribed UF volume and rate, dialysate composition (Na, Ca, temperature), session duration, intercurrent illness or hospitalisation, and medication changes since preceding session. For event-triggered IDH scans: exact time from IDH onset to scan, BP at event onset and at scanning, and acute interventions (UF reduction/interruption, saline, repositioning) before imaging.

## Methodology

### Study Design and Setting

This is a single-centre, prospective observational cohort study of adult patients undergoing maintenance haemodialysis. We plan to enrol approximately 60 patients from our outpatient HD unit. Each participant will undergo serial ultrasound assessments before and after a dialysis session at 3-month intervals over the study period (at baseline, 3, 6, and 9 months), as detailed in Table 1. Recruitment is planned to start in May 2026, with participant follow-up lasting 12 months and overall study completion anticipated on 01/10/2027.

To capture both peak volume load and more steady-state conditions, participants will be allocated at enrolment to have their scheduled study ultrasound performed either during the first dialysis session after the long interdialytic interval (2/5 of participants) or during a mid-/late-week session (3/5 of participants). This allocation will be prespecified and kept consistent for each participant across all scheduled follow-up timepoints. Session type (post-long interdialytic interval vs mid-/late-week) will be recorded for every visit.

**Embedded case-crossover substudy (Objective 2).** An embedded within-patient case-crossover design will compare pre-dialysis ultrasound parameters at sessions where IDH occurs with the same patient's sessions where IDH does not occur. The primary case-crossover analysis is restricted to scheduled profiled sessions, thereby ensuring that all ultrasound measurements are obtained before the dialysis session begins and that the estimand retains a predictive interpretation. Because control sessions are drawn from the same patient's own scheduled profiled sessions that were free of IDH, all time-invariant between-patient confounders (age, sex, comorbidities, dialysis vintage, vascular access type) are eliminated by design. Control sessions will be matched where feasible on session type (post-long interdialytic interval vs mid-/late-week). The exact timing of each session will be recorded and reported, and the interval between case and control sessions will be considered in sensitivity analyses.

A secondary case-crossover analysis will extend the case pool to include event-triggered IDH sessions captured during routine care when ultrasound is performed during or immediately after the episode and the prespecified timing and intervention metadata are available (see Table 1). Because some eligible cases in this extended analysis will be captured peri-event rather than pre-dialysis, the secondary estimand is an association and phenotyping estimand rather than a purely predictive one. This distinction will be stated explicitly when reporting secondary results.

Key time-varying confounders that differ between sessions and are not inherently controlled by the within-patient design — including interdialytic weight gain, antihypertensive medication use on the day of dialysis, recent medication changes, pre-dialysis blood pressure, prescribed ultrafiltration volume, and any intercurrent illness or hospitalisation — will be systematically recorded on the case report form for both case and control sessions and included as covariates in the analysis. For event-triggered IDH case sessions used in the secondary analysis, additional metadata will include the exact time from IDH onset to scan, blood pressure at event onset and at scanning, and whether

ultrafiltration reduction/interruption, saline administration, repositioning, or other acute interventions occurred before imaging. These variables will be incorporated into sensitivity analyses to distinguish the ultrasound phenotype of the untreated event from the post-intervention phenotype. The exchangeability assumption underpinning the case-crossover design (i.e. that a patient's control session ultrasound findings represent their expected baseline in the absence of the triggering event) will be assessed empirically using serial measurements from participants who remain event-free throughout the study to characterise the within-patient variability of ultrasound parameters over time.

**Event-triggered substudy.** In addition to the scheduled quarterly assessments, when clinically feasible and safe, an ultrasound examination will be performed during or immediately after an episode of intradialytic hypotension, suspected clinically significant fluid overload, or suspected underestimated dry weight. Event-triggered scans performed for IDH will be eligible for the secondary Objective 2 case-crossover analysis if the prespecified timing and intervention variables are captured. Event-triggered scans performed for suspected fluid overload or underestimated dry weight, and any IDH-triggered scans not meeting the secondary Objective 2 analytical criteria, will be reported descriptively within Objective 1. The timing and clinical context of each event-triggered scan will be recorded.

**Clinician-impact substudy (Objective 3).** For each scheduled profiled session, the treating physician in charge will complete a brief structured questionnaire before disclosure of the study ultrasound findings. This pre-disclosure section will record the physician's intended management for that session (for example ultrafiltration target, intended dry-weight adjustment, perceived congestion or underfilling profile, anticipated risk of intradialytic hypotension, and any planned adaptation of the dialysis prescription). To prevent contamination of the primary IDH outcome, disclosure of the ultrasound findings will occur only after the dialysis session is complete and all intradialytic outcome data (blood pressure recordings, IDH events, nursing interventions, session completion status) have been recorded, except when findings meet the emergency disclosure criteria defined below. Once outcome data are secured, a second post-disclosure section of the questionnaire will capture whether the findings provided clinically relevant new information and whether, had they been available in real time, they would have changed the prescription or wider management. The questionnaire thus assesses hypothetical clinician-reported impact, not actual management change during the index session.

When feasible, a similar impact questionnaire may also be completed during event-triggered sessions, though these will not contribute to the primary Objective 3 analysis.

**Observational design.** This study remains primarily observational. No study-mandated therapeutic algorithm will be applied, and the study team will

The study will not recommend or require any change in dialysis prescription on the basis of ultrasound findings. The questionnaire and disclosure procedure are intended to assess clinician-reported potential impact on decision-making rather than to direct care. Any subsequent clinical action after disclosure will remain entirely at the discretion of the treating physician as part of usual care. Standard care will otherwise proceed unchanged.

## Participants

**Inclusion criteria** are: (1) adults (age  $\geq 18$  years) on thrice-weekly chronic haemodialysis for end-stage renal disease, (2) receiving treatment at our centre, and (3) able and willing to provide informed consent. We will include patients with a range of volume status and comorbidity profiles to ensure generalisability (including those with heart failure, diabetes, etc., as long as they meet other criteria).

**Exclusion criteria** are kept minimal given the observational nature. We will exclude individuals who cannot safely undergo ultrasound procedures or follow the protocol (e.g. patients with an open chest wound or severe skin infection at probe sites, which is highly unlikely; or those with cognitive inability to consent without a legal representative). Patients with persistent arrhythmias and/or valvular disease will not be excluded a priori to preserve generalisability. Rhythm/valvular pathology at the time of the scan will be reported. Measurements that are not interpretable or applicable in the presence of these diseases will be flagged accordingly. These patients will be included in the main cohort analyses with prespecified stratified and sensitivity analyses. We will exclude pregnant women for prudence, and prisoners or other vulnerable populations who cannot freely consent. Patients on peritoneal dialysis are not eligible, as the study focuses on HD. If a participant receives a kidney transplant or transfers care during the study, their active participation will end at that point (data up to that time will be included).

We will recruit patients by approaching them during their routine dialysis sessions; information sheets and consent forms will be provided, and ample opportunity given to ask questions. Written informed consent will be obtained from all participants prior to any study-specific procedures.

## Ultrasound Assessment Protocol

Each study ultrasound will be performed by a trained operator (a nephrologist with certification in point-of-care ultrasonography) using a portable ultrasound device in the dialysis unit. Scheduled exams will take place immediately before the assigned HD session (per prespecified allocation) and repeated at the end of the same session. The comprehensive assessment includes three domains:

**Cardiac ultrasound.** We will perform focused transthoracic echocardiography to evaluate cardiac function and haemodynamics. Key parameters will include qualitative left ventricular ejection fraction (visual estimate or Simpson's biplane if image quality permits), left ventricular thickness, velocity time integrals and cardiac output estimation. Additional markers of diastolic function will include the mitral inflow E wave to mitral annular e' velocity ratio ( $E/e'$ ), atrial volume, pulmonary veins Doppler (if possible) and mitral inflow E wave over the mitral inflow A wave ( $E/A$ ). These parameters will be recorded conditional on the predefined quality and interpretability criteria. Diastolic left atrium pressure estimation will be guided by a standardised algorithm (ASE recommendation for the evaluation of left ventricular diastolic function).<sup>11</sup> Right heart evaluation will consist of inferior vena cava (IVC) diameter and collapsibility at end-expiration vs. inspiration assessment. Basic right ventricular function (TAPSE,  $S'$ ) and the presence of pericardial effusion will be noted as well. Last, a quick evaluation of systolic pulmonary pressure

through tricuspid valve regurgitation (TRV) will also be made when interpretable. In case of arrhythmias, the Doppler measurements will be averaged over ten consecutive beats.

**Lung ultrasound.** A standard lung ultrasound exam will survey multiple zones on both sides (8-zone validated protocol) for B-lines. B-lines are comet-tail artefacts indicating extravascular lung water; we will count the number of B-lines in each zone and derive a total B-line score. The presence of alveolar-interstitial syndrome will be defined by multiple ( $\geq 3$ ) B-lines per lung zone or confluent B-lines. Changes in B-line count pre- to post-dialysis will be recorded, as reduction in B-lines is expected with effective fluid removal from the lungs.<sup>7</sup> We will also document pleural effusions if detected.

**Venous congestion ultrasound (modified VEXUS score).** We will evaluate systemic venous congestion using a modified VEXUS protocol. This involves examining: (a) IVC diameter (already measured in the cardiac portion) and its collapsibility; (b) hepatic vein Doppler waveform via subcostal right upper quadrant view (pulsed-wave Doppler in the middle hepatic vein), characterised as normal triphasic, dampened, or with systolic flow reversal — a severely abnormal hepatic vein flow (e.g. S<D or frank S reversal) indicates high right atrial pressure transmission; (c) portal vein Doppler via a right mid-abdominal approach, measuring the pulsatility of portal vein flow — a pulsatility fraction >50% (flow velocity variation >50%) is considered abnormal (sign of elevated right-sided pressures causing pulsatile portal flow). Renal parenchymal vein Doppler is intentionally omitted for practicality and because many HD patients have small kidneys that make reliable Doppler tracing challenging.

Our VEXUS scoring will thus be based on the three elements above (IVC, hepatic, portal). We will assign a VEXUS grade 0 (no congestion), 1 (mild), 2 (moderate), or 3 (severe) using criteria similar to those published by Beaubien-Souligny et al.<sup>5</sup> In brief, an IVC >2.0 cm that is poorly collapsible combined with progressively abnormal hepatic/portal flows increases the grade. These ultrasound measurements for VEXUS will be obtained in the supine position before HD and repeated after HD to observe changes. All scans will be saved and later reviewed by a second blinded reviewer to ensure consistency in grading.

### Quality Assurance, Interpretability, and Data Completeness

For each examination, overall ultrasound quality and domain-specific quality (cardiac, venous congestion/VEXUS, and lung ultrasound) will be graded. The main limiting factors (e.g. poor acoustic windows, obesity/body habitus, COPD/emphysema, inability to position, arrhythmia, tachycardia, Doppler alignment, valvular disease, other) will also be recorded. Measures will be interpreted under prespecified, consensus-based quality criteria and according to international ultrasonography guidelines. All scans will be stored for later review.

**Taxonomy of incomplete data.** In multi-organ point-of-care ultrasound, it is anticipated that some measurements will be unavailable at certain sessions. The reasons for unavailability are not interchangeable and will be classified into four categories: (1) *not applicable* — the measurement is structurally inapplicable to the patient (e.g. Doppler parameters requiring sinus rhythm in a patient with persistent atrial fibrillation; this is not “missing” and will not be imputed); (2) *not interpretable* — the measurement was

attempted but the image or signal quality was insufficient for reliable interpretation despite adequate effort (e.g. poor transthoracic acoustic window due to body habitus, hyperinflation, or prior surgery; this represents a structural limitation and will not be imputed); (3) *not obtained* — the measurement could in principle have been obtained but was not attempted due to time constraints, operator availability, or logistical reasons (this is genuinely missing data and is a candidate for imputation under appropriate assumptions); (4) *obtained but quality-limited* — the measurement was obtained and recorded but flagged as marginal quality (these values will be included in the primary analysis with prespecified sensitivity analyses excluding them). The reason category will be recorded for every unavailable parameter at every session.

Because systematic inability to obtain a given domain is unlikely to be missing at random — patients with poor cardiac windows are more likely to have obesity, chronic lung disease, prior thoracic or cardiac surgery, or body habitus characteristics that may independently affect haemodynamic tolerance — partial-protocol data represent a potential source of informative missingness. To address this, several prespecified sensitivity analyses will be conducted: (1) a complete-domain analysis restricted to sessions with fully interpretable cardiac, VEXUS, and lung ultrasound data; (2) comparison of baseline characteristics, comorbidity burden, and outcome rates between patients with complete versus partial protocols, to characterise the direction and magnitude of any selection effect; and (3) domain-specific analyses in which each ultrasound component (cardiac, VEXUS, lung) is evaluated independently using all sessions for which that domain was interpretable, thereby maximising sample size per domain. The proportion, pattern, and reason category of incomplete data will be reported transparently.

## Outcomes and Data Collection

Outcomes are organised by analytic objective.

**Objective 1 — Descriptive characterisation.** Pre- and post-dialysis values of all ultrasound parameters listed in Table 2; within-session changes (pre-to-post); between-session trajectories across quarterly assessments; within-patient variability summaries.

**Objective 2 — Ultrasound profile and intradialytic hypotension: within-patient analyses (primary outcome).** Two definitions of IDH will be applied to every profiled session and reported separately. The primary definition is a decrease in systolic BP  $\geq 20$  mmHg from the pre-dialysis baseline with accompanying symptoms or nursing intervention required, consistent with the KDOQI definition. This symptomatic definition is used for Objective 2 case ascertainment because it enables real-time identification of IDH case sessions during both scheduled and event-triggered capture. The secondary definition is a nadir systolic blood pressure  $< 90$  mmHg at any point during the session (or  $< 100$  mmHg if pre-dialysis SBP  $\geq 160$  mmHg), the nadir-based definition shown by Flythe et al.<sup>15</sup> to have the most consistent association with mortality across multiple cohorts; this definition will be applied retrospectively from routine intradialytic blood pressure recordings. Sensitivity analyses will examine the impact of the IDH definition on all Objective 2 results. The primary Objective 2 analysis uses only scheduled profiled sessions (case-crossover with predictive estimand). The secondary case-crossover extends the case

pool to include event-triggered IDH sessions (association/phenotyping estimand). Additional intradialytic outcomes include premature session termination, delivered dialysis dose reduction due to intolerance, ultrafiltration reduction and/or interruption, and saline administration.

**Objective 3 — Clinician-reported impact (exploratory).** For each scheduled profiled session, whether post-session disclosure of the ultrasound findings would have changed the treating physician's intended management, analysed as a binary variable (change vs no change) and descriptively by domain of change. The physician's rating of clinical relevance and confidence in the management decision will also be captured.

**Objective 4 — Longitudinal clinical outcomes (exploratory).** All-cause hospitalisations, particularly those related to cardiovascular causes or fluid overload; cardiovascular events (acute coronary syndromes, heart failure exacerbations, strokes, arrhythmias); and all-cause mortality. These outcomes will be tracked from medical records over the study duration (anticipated 12 months). Given the expected small number of events (approximately 9–12 deaths), all Objective 4 analyses are explicitly exploratory and hypothesis-generating.

**Session-level data.** For each scheduled ultrasound time-point, concurrent data will be collected on blood pressure, heart rate, weight change, and dialysis details (ultrafiltration volume, duration, sodium modelling, dialysate temperature, etc.). During each session's evaluation, patient symptoms (dyspnoea score, cramps, dizziness) and blood pressure will also be recorded. Intradialytic hypotension episodes will be carefully documented by dialysis staff per usual practice. Session type (post-long interdialytic interval vs mid-/late-week) will be recorded for each profiled visit. For both event-triggered and scheduled sessions, a dedicated case report form section will capture key time-varying factors as detailed in Table 1. For event-triggered IDH scans, the exact timing of the scan relative to IDH onset and to any acute therapeutic intervention will be recorded.

### Clinician Questionnaire and Disclosure Procedure

For each scheduled ultrasound time-point, the treating physician responsible for the session will initially remain blinded to the study ultrasound findings. Before the session begins, the physician will complete a short questionnaire recording the intended management for that session. The questionnaire will be closely aligned with real-world dialysis decisions and will include, at minimum, the planned ultrafiltration target, intended change in dry weight, the physician's assessment of the patient's predominant haemodynamic or volume profile, anticipated risk of intradialytic hypotension, and any intended adaptation of the dialysis prescription.

The questionnaire will not collect the physician's name, e-mail address, initials, stamp number or any other nominative physician identifier. Responses will be analysed at session/patient level only and will not be reported by individual physician.

After the dialysis session is complete and all intradialytic outcome data have been recorded (including blood pressure readings, IDH events, nursing interventions, saline administration, ultrafiltration modifications, and session completion status), the ultrasound

findings from the study examination will be disclosed to the physician. A second section of the questionnaire will then record whether the findings were considered clinically relevant, whether they would have changed the intended management, which specific aspects of management would have been modified (e.g. ultrafiltration target, dry-weight strategy, session duration, sodium or temperature prescription, additional investigations), and whether the findings increased confidence in the prescription. This post-session disclosure design ensures that the primary IDH outcome is uncontaminated by knowledge of ultrasound findings.

**Exception: emergency disclosure.** The post-session disclosure rule is overridden when the pre-dialysis ultrasound reveals prespecified findings of immediate clinical concern, as defined in the Ethical and Safety Considerations section below.

## Statistical Analysis Plan

Quantitative analysis will be organised by analytic objective and will proceed through prespecified stages within each. All analyses will be performed in R (version  $\geq 4.3$ ). The statistical analysis plan follows the DEBATE-SAP framework for observational studies<sup>16</sup> and was finalised before any study data were examined. All planned analyses, including their designation as primary, secondary, or exploratory, were decided a priori; any post-hoc analyses will be clearly labelled as such in the final report.

**Analysis populations.** Three analysis populations are defined. The full analysis set includes all enrolled participants who undergo at least one scheduled ultrasound assessment. The per-protocol set includes participants who complete all four quarterly assessments with interpretable data in at least one ultrasound domain. The event-triggered set includes all participants who contribute at least one case-control pair in the embedded case-crossover substudy. Primary analyses will be conducted on the full analysis set. Prespecified sensitivity analyses will include repetition on the per-protocol set to assess the impact of incomplete follow-up, on the complete-domain set (sessions with all three ultrasound domains interpretable) to evaluate partial-protocol bias, and under alternative IDH definitions as described above. The analysis population used for each sensitivity analysis will be reported explicitly.

**Multiplicity and analytic hierarchy.** The primary analysis (Objective 2: primary scheduled-session case-crossover) will use a two-sided  $\alpha$  of 0.05. Secondary analyses (Objective 1: within-session comparisons and variability characterisation; Objective 2: extended case-crossover and scheduled-session prognostic modelling) will apply false discovery rate control (Benjamini-Hochberg) within families of related tests. Exploratory analyses (Objective 3: clinician impact; Objective 4: longitudinal hard outcomes; all subgroup analyses) will report exact p-values with effect sizes and confidence intervals without formal multiplicity correction, and will use language such as “hypothesis-generating” and “warrants confirmation.” Pre-registration of this analysis plan will be completed before data analysis begins.

**Confounder adjustment strategy.** Based on the clinical causal structure, the following variables are prespecified as potential confounders for adjustment in all multivariable models: age, sex, diabetes status, dialysis vintage, vascular access type, pre-dialysis systolic

blood pressure, interdialytic weight gain, prescribed ultrafiltration volume, and session type (post-long interdialytic interval vs mid-/late-week). Additional session-level covariates (antihypertensive use on the day of dialysis, dialysate sodium and temperature) will be included in session-level analyses. Confounder selection is driven by clinical causal reasoning and pre-specification, not by observed imbalance in the baseline table. The confounder set is fixed regardless of the magnitude of standardised mean differences between groups.

**Prespecified variables.** The ultrasound outcome variables, clinical covariates, and derived variables used across all analytical stages are listed in Table 2.

### Objective 1 — Descriptive Characterisation

**Stage 1a — IDH patterns.** At the session level, the overall IDH rate will be reported as  $n(\text{IDH sessions})/N(\text{total sessions})$  with a 95% confidence interval accounting for within-patient clustering (from a generalised linear mixed model intercept-only model). At the patient level, each patient's IDH proportion across their sessions will be computed and reported as mean  $\pm$  SD and median (IQR). Patients will be classified as having “frequent IDH” if  $\geq 30\%$  of their sessions are affected, consistent with the threshold used in recent literature and shown to be associated with mortality. A histogram of patient-level IDH proportions will be presented. The intraclass correlation coefficient (ICC) for IDH across sessions within patients will be reported, as it directly informs the effective sample size for all downstream analyses.

Ultrasound parameters will be summarised according to their distributional properties: continuous variables as mean  $\pm$  SD or median (IQR) depending on normality assessed by Shapiro–Wilk testing, and ordinal variables (e.g. VEXUS grade) as frequency and percentage per category. Baseline characteristics will be presented in a descriptive table stratified by IDH frequency group (frequent vs infrequent). Between-group balance will be assessed using standardised mean differences (SMDs) rather than p-values;<sup>17,22</sup> an SMD exceeding 0.1 will be reported as indicating potentially meaningful imbalance but will not be used to determine which confounders are adjusted for, as the confounder set is pre-specified based on clinical causal reasoning.

**Stage 1b — Within-session pre- versus post-dialysis comparisons.** Univariate paired comparisons will be performed for each ultrasound outcome variable listed in Table 2. The choice between parametric and non-parametric tests will depend on the distribution of within-session differences assessed by Shapiro–Wilk testing; ordinal variables will use the Wilcoxon signed-rank test. For dichotomised thresholds, McNemar's test will be applied. For the multivariate framework, a multivariate linear mixed model will be fitted, specifying separate sub-models for each ultrasound outcome with appropriate distributional families and estimating residual cross-outcome correlations. Session-level and patient-level covariates from Table 2 will be included to examine their influence on pre-to-post changes. This approach is preferred over repeated-measures MANOVA, which requires multivariate normality, complete data, and cannot accommodate ordinal outcomes. Exploratory visual analyses will include: (1) spaghetti plots of individual pre-to-post trajectories coloured by clinical subgroup; (2) forest plots of subgroup-specific pre–post effect estimates with 95%

CIs; (3) interaction plots showing predicted mean change as a function of ultrafiltration volume stratified by comorbidity; and (4) stratified correlation heatmaps of pre-to-post change scores.

**Stage 1c — Between-session variability.** Within-patient trajectories of each ultrasound parameter (Table 2) across the quarterly assessments will be modelled using linear mixed models with random intercepts and random slopes per patient. The ICC will be reported for relative reliability; modified Bland–Altman analyses using within-subject standard deviations will assess absolute agreement. To investigate whether within-patient variability of ultrasound parameters is itself associated with IDH frequency, mixed-effects location-scale (MELS) models<sup>18</sup> will be fitted as a prespecified secondary analysis. MELS models jointly model both the mean response and the within-person variance as functions of covariates, allowing each patient their own intrinsic variability level. The within-patient variance sub-model will include session-level covariates from Table 2 as potential mediators of increased variability. The application of MELS models to session-to-session ultrasound variability represents a novel extension of the cardiovascular risk-factor variability paradigm to point-of-care ultrasound in this setting; no published study has applied this approach to serial POCUS data in haemodialysis. With only four quarterly observations per patient, per-patient variance estimates will be imprecise; the MELS model addresses this by borrowing strength across the 60 patients through shared distributional parameters, but individual-level variance estimates should be interpreted cautiously.

**Stage 1d — Dimension reduction.** Multilevel principal component analysis will be applied to the ultrasound outcome variables (Table 2) to decompose the total covariance into between-patient and within-patient components. Patient-level means and within-patient standard deviations of PC scores will be computed as summary measures of individual ultrasound profile stability. Uniform Manifold Approximation and Projection (UMAP) will be used for exploratory visualisation of patient clusters but will not replace PCA in formal models.

**Peri-event descriptive analyses.** Ultrasound findings from event-triggered scans (during or immediately after IDH, suspected fluid overload, or suspected underestimated dry weight) will be reported descriptively. These will include comparison of peri-event ultrasound profiles with the same patient’s most recent scheduled pre-dialysis scan, with the aim of characterising the ultrasound phenotype of haemodynamic decompensation. These analyses are descriptive and do not contribute to the primary Objective 2 case-crossover.

## **Objective 2 — Ultrasound Profile and Intradialytic Hypotension: Within-Patient Analyses (Primary Inferential Aim)**

**Primary analysis: scheduled-session case-crossover.** The primary Objective 2 analysis will use conditional logistic regression stratified by patient to compare pre-dialysis ultrasound parameters at scheduled profiled sessions where IDH occurs (cases) versus the same patient’s scheduled profiled sessions where IDH does not occur (controls). This restriction to scheduled pre-dialysis scans ensures that all ultrasound measurements are obtained before the dialysis session begins and that the estimand retains a genuine

predictive interpretation: does the pre-dialysis ultrasound profile predict same-session IDH? Time-varying confounders from Table 2 will be included as covariates. Power derives from discordant case-control pairs rather than total cohort size. Given the expected number of scheduled-session IDH events (approximately 22–36 across 216–240 sessions depending on the definition used), the candidate predictor set for the primary case-crossover analysis will be limited to 2–3 pre-dialysis ultrasound variables selected a priori on clinical grounds. The number of discordant pairs, the number of unique patients contributing case sessions, and the total number of IDH events will be reported.

**Secondary analysis: extended case-crossover with event-triggered cases.** A secondary case-crossover analysis will extend the case pool to include event-triggered IDH sessions captured during routine care, in addition to all scheduled IDH sessions. Controls remain the patient's own stable scheduled profiled sessions. Because event-triggered cases are captured peri-event (during or immediately after IDH), this extended analysis is explicitly framed as an association and phenotyping analysis rather than prediction. To preserve interpretability, the secondary case-crossover model will use the same 2–3 prespecified ultrasound variables as the primary analysis. Prespecified sensitivity analyses will include: (a) stratification by scan timing (pre-dialysis scheduled vs peri-event); (b) restriction to event-triggered cases scanned within 15 minutes of IDH onset. The number of scheduled versus event-triggered IDH cases and the distribution of scan-to-event intervals will be reported.

**Scheduled-session prognostic modelling (secondary).** A generalised linear mixed model with a logit link and a random intercept per patient will estimate the association between pre-dialysis ultrasound parameters measured during scheduled profiled sessions and same-session IDH. This analysis is deliberately restricted to scheduled pre-dialysis scans so that it retains a genuine prognostic interpretation. Candidate predictors will be limited to 5–6 variables to maintain adequate events per variable. Where variable selection is required, elastic net regularisation will be applied within the GLMM framework; bootstrap confidence intervals (resampling whole patients, not individual sessions) will be reported for all model coefficients. With the expected number of scheduled-session IDH events, the events-per-variable ratio remains modest, and this analysis is therefore framed as exploratory prognostic signal detection rather than formal model development. Penalised estimation (ridge or elastic net) will be used throughout to reduce overfitting. If derived profile scores from Stage 1d are incorporated, the dimension-reduction step will be refit within each training fold and held-out patients will be projected into the training-derived component space in order to avoid information leakage.

**Internal validation.** Internal validation of the scheduled-session prognostic analysis, if developed, will use leave-one-patient-out cross-validation (LOPOCV). Performance metrics will include cluster-corrected AUC with bootstrap confidence intervals, calibration slope, and calibration plots. Reporting will follow TRIPOD<sup>19,20</sup> and TRIPOD-Cluster guidelines. The exploratory nature of the prognostic analysis and the limited events-per-variable ratio will be stated explicitly. No external validation is planned; this analysis is intended as signal detection to inform the design of a larger confirmatory cohort.

### Objective 3 — Clinician-Reported Management Impact (Exploratory)

The proportion of scheduled profiled sessions in which the treating physician reported that ultrasound disclosure would have changed management will be reported with a 95% confidence interval accounting for within-physician clustering. Changes will be tabulated by domain (ultrafiltration target, dry-weight strategy, dialysis session adaptation, antihypertensive management, need for additional session, further diagnostic work-up). The physician's rating of clinical relevance and confidence change will be summarised descriptively. No multivariable modelling of the clinician-impact outcome is planned; this substudy is descriptive. The Objective 3 questionnaire data will not be combined with the Objective 2 quantitative analyses.

### Objective 4 — Longitudinal Clinical Outcomes (Exploratory)

For time-to-event outcomes (hospitalisations, cardiovascular events, mortality), joint models for longitudinal and survival data<sup>21</sup> will be used as the primary analysis, simultaneously modelling the ultrasound trajectory and the hazard of the event. Given the expected small number of deaths (approximately 9–12 over 12 months), survival analyses are explicitly framed as exploratory and hypothesis-generating, limited to 1–2 ultrasound predictors per model. As a prespecified sensitivity analysis, a two-stage approach will also be conducted: mixed models will first characterise each patient's ultrasound trajectory, and the resulting summary measures will be entered as predictors in standard Cox proportional hazards models. Competing risks from kidney transplantation will be handled using cause-specific hazard and Fine–Gray subdistribution hazard models. Hospitalisation analyses, which are expected to have substantially more events, will use recurrent-event (Andersen–Gill) models and may support 3–4 predictors.

### Missing Data

The primary analysis will use all available data under a missing-at-random assumption, with domain-specific analyses as described in the quality assurance section above. Only data classified as “not obtained” (category 3 in the taxonomy above) are candidates for imputation. Data classified as “not applicable” or “not interpretable” (categories 1 and 2) represent structural limitations and will not be imputed; these will be handled through domain-specific analyses that use all sessions for which each domain was interpretable. For multivariable models requiring multiple ultrasound domains simultaneously, multiple imputation by chained equations will be performed using at least 20 imputed datasets pooled with Rubin's rules, restricted to parameters with a “not obtained” reason for missingness. A sensitivity analysis under plausible missing-not-at-random assumptions will use a  $\delta$ -adjustment approach for domains where informative missingness is clinically plausible (e.g. cardiac parameters missing due to body habitus that independently affects haemodynamic tolerance). Complete-case analysis will also be reported. If more than 40% of observations on any domain are unavailable, that domain will be treated as secondary or exploratory for multivariable analyses.

**Table 2. Prespecified Ultrasound Variables and Clinical Covariates**

<b>Variable</b>	<b>Type</b>	<b>Domain / Role</b>	<b>Timing</b>
<i>Ultrasound outcome variables (measured pre- and post-dialysis)</i>			
Mitral E velocity	Continuous	Diastolic function	Pre + Post
Mitral A velocity	Continuous	Diastolic function	Pre + Post
E-wave deceleration time	Continuous	Diastolic function	Pre + Post
Septal e' velocity	Continuous	Diastolic function	Pre + Post
Lateral e' velocity	Continuous	Diastolic function	Pre + Post
LA volume	Continuous	Diastolic function	Pre + Post (optional)
LVOT VTI	Continuous	Systolic / haemodynamic	Pre + Post
LV systolic function	Ordinal (4- level)	Systolic / haemodynamic	Pre + Post
Heart rate	Continuous	Systolic / haemodynamic	Pre + Post
TAPSE	Continuous	Right heart	Pre + Post
Tricuspid S'	Continuous	Right heart	Pre + Post
Estimated RAP	Continuous	Right heart	Pre + Post
IVC diameter	Continuous	VEXUS	Pre + Post
IVC collapsibility	Continuous	VEXUS	Pre + Post
Hepatic vein Doppler	Ordinal (3- level)	VEXUS	Pre + Post
Portal vein pulsatility	Ordinal (3- level)	VEXUS	Pre + Post
Total B-line count	Count	Lung	Pre + Post
Pericardial effusion	Ordinal (4- level)	Cardiac (descriptive)	Pre + Post
<i>Session-level clinical covariates (time-varying)</i>			
Rhythm at scan	Categorical	Effect modifier	Per session
UF target / delivered volume	Continuous	Covariate	Per session
Interdialytic weight gain	Continuous	Covariate	Per session
Pre-dialysis systolic BP	Continuous	Covariate	Per session
Session type (1st of week vs other)	Binary	Covariate	Per session
Dialysate Na / Ca / temperature	Continuous	Covariate	Per session

<b>Variable</b>	<b>Type</b>	<b>Domain / Role</b>	<b>Timing</b>
Session duration	Continuous	Covariate	Per session
Pleural effusion	Ordinal	Covariate	Pre + Post
<i>Patient-level covariates (baseline)</i>			
Age, sex	Continuous / binary	Confounder	Baseline
Dialysis vintage	Continuous	Confounder	Baseline
Vascular access type	Categorical	Confounder	Baseline
Residual diuresis (yes/no + volume)	Binary + continuous	Confounder	Baseline
ESRD aetiology	Categorical	Confounder	Baseline
Dialysis modality (HD vs HDF)	Binary	Confounder	Baseline
Diabetes	Binary	Confounder / modifier	Baseline
Hypertension	Binary	Confounder	Baseline
Coronary artery disease	Binary	Confounder	Baseline
Heart failure + phenotype	Categorical	Confounder / modifier	Baseline
COPD	Binary	Confounder / modifier	Baseline
Baseline LVEF (prior TTE)	Continuous	Baseline structural	Baseline
IVS / PW thickness	Continuous	Baseline structural	Baseline
ACE inhibitor or ARB use	Binary	Confounder	Baseline
Beta-blocker use	Binary	Confounder	Baseline
Diuretic use	Binary	Confounder	Baseline
Serum albumin	Continuous	Confounder	Baseline
Haemoglobin	Continuous	Confounder	Baseline
<i>Derived variables (reported but not entered as separate model terms)</i>			
E/A, E/e' (septal and average), stroke volume, cardiac output, PASP, LAVI, PV S/D, VEXUS grade, diastolic dysfunction grade			

## Sample Size Calculation

This is an exploratory single-centre prospective observational cohort study. The planned sample size of 60 patients was chosen primarily on the basis of feasibility within the

recruiting haemodialysis unit and the expected precision for the main scheduled-session outcome, rather than on a formal comparison between predefined intervention groups. Each participant will undergo ultrasound profiling at approximately 3-month intervals (baseline, 3, 6 and 9 months), yielding about 240 scheduled profiled sessions if follow-up is complete; allowing for around 10% missed visits, incomplete assessments or withdrawal, approximately 216 scheduled sessions are expected to remain available for analysis.

Given the primary analytical focus is the occurrence of intradialytic hypotension or intolerance during these scheduled profiled sessions, and because the study aims mainly to estimate event rates and explore associations between ultrasound findings and haemodynamic instability, a precision-based approach was used for sample-size justification rather than a conventional between-group power calculation.<sup>12</sup> In the haemodialysis literature, intradialytic hypotension is common, but reported session-level frequencies vary substantially depending on the definition used; a recent systematic review and meta-analysis found prevalence estimates around 10.1% using the EBPG definition and 11.6% using a nadir systolic blood pressure <90 mmHg definition, while emphasising wide heterogeneity across studies and definitions.<sup>13</sup>

Using a planning assumption of an overall scheduled-session intradialytic hypotension rate of 10%, 240 scheduled sessions would yield approximately 24 events and 216 sessions would yield approximately 22 events. Because repeated sessions from the same patient are not statistically independent, a simple design-effect correction was applied to account for within-patient clustering;<sup>14</sup> under the standard formula  $DE = 1 + (m - 1) \times ICC$ , with  $m = 4$  scheduled sessions per patient and a plausible within-patient intraclass correlation coefficient range of 0.10 to 0.20, the design effect ranges from 1.3 to 1.6, corresponding to an effective sample size of approximately 135 to 166 if 216 sessions remain after attrition. Under these assumptions, the estimated 95% confidence interval half-width around a 10% intradialytic hypotension proportion is approximately 4.6% to 4.8% for 240 and 216 sessions respectively.

**Sample size adequacy by analytic objective.** For Objective 1 (descriptive characterisation), the sample provides adequate precision for estimating ultrasound parameter distributions and within-session changes. For Objective 2, the primary scheduled-session case-crossover derives power from discordant within-patient pairs rather than total events; under the expected number of scheduled-session IDH events (approximately 22–36), the primary analysis supports 2–3 predictors. The secondary extended case-crossover is expected to include additional event-triggered IDH sessions, strengthening the within-patient analysis, though the capture rate depends on operator availability and cannot be precisely forecast. The secondary scheduled-session prognostic GLMM remains exploratory and supports at most 2–3 predictors in unpenalised models or 5–6 with penalised estimation. For Objective 3 (clinician impact), the ~240 questionnaire observations provide adequate precision for estimating the proportion of sessions with management impact. For Objective 4 (hard outcomes), the expected ~9–12 deaths support at most 1 predictor in a survival model; these analyses are hypothesis-generating only.

Because the prevalence of ultrasound-defined haemodynamic profiles is not known a priori and is not controlled by the investigators, a formal sample-size calculation based on

comparing intradialytic hypotension rates between predefined profile groups would require speculative assumptions about both the distribution of profiles and the magnitude of between-profile differences. The analytic ambition of each objective has been calibrated to the expected information content of this dataset.

## Data Management

All ultrasound findings and non-nominative clinician questionnaire responses will be recorded and stored in a secure database. Each patient's research data will be coded with a study ID. Direct identifiers, including the patient's name, initials, hospital number/ID Erasme, national registry number and full date of birth, will not be included in the analysis dataset or exported for statistical analysis. A separate code-identification list linking the study ID to the participant identity will be maintained locally and stored separately in a secure, access-restricted, password-protected file. Access to this password-protected code-identification list will be limited to the Principal Investigator, Dr Thomas Baudoux, and the Head of Department, Dr Alain Le Moine. Age at inclusion will be used in the analysis dataset instead of full date of birth. Digital ultrasound images/clips will be pseudonymised before study archiving and stored on secure hospital servers for off-line analysis and quality control. The pseudonymised data and essential study documents will be retained for 20 years after study completion, unless a longer legal or institutional requirement applies. We will periodically assess inter-observer reliability of key measures by having a second expert sonographer re-read a sample of scans.

## Ethical and Safety Considerations

The study involves minimal risk. Ultrasound is a non-invasive, painless imaging modality considered to be very safe. The ultrasound exam may cause mild inconvenience (e.g. lying still for a few extra minutes before and after HD), but does not interfere with the dialysis treatment itself. There is no contrast or drug given. The additional clinician questionnaire introduces only minimal extra workload for the treating physician and no material additional burden for participants.

Funding and cost coverage. The study-specific ultrasound examinations will be performed by the study investigators using existing departmental equipment and will be covered by the sponsor / Department of Nephrology of HUB Hôpital Erasme. They will not be billed to participants or to their insurer. No external industrial funding is planned for these examinations. Participation does not require additional study visits or additional travel outside routine haemodialysis care; therefore no travel reimbursement or financial compensation is planned.

**Disclosure policy and emergency disclosure.** As described above, disclosure of the ultrasound findings to the treating physician occurs after the dialysis session is complete and all intradialytic outcome data have been recorded. This post-session timing ensures that the primary IDH outcome is not influenced by knowledge of the ultrasound profile. However, a mandatory exception applies when pre-dialysis ultrasound reveals findings of immediate clinical concern. The following prespecified findings require immediate communication to the treating physician, regardless of session timing:

- (a) pericardial effusion with echocardiographic signs of tamponade physiology (right atrial or ventricular diastolic collapse, exaggerated respiratory variation in mitral inflow);
- (b) new or previously unknown severe left ventricular systolic dysfunction (estimated LVEF <30%);
- (c) large pleural effusion with signs of respiratory compromise;
- (d) findings suggestive of acute right heart failure not previously documented (severe RV dilatation, D-shaped septum, new severe tricuspid regurgitation).

When emergency disclosure occurs, the event will be recorded in the study database, including the finding disclosed, the timing of disclosure, and any resulting clinical action. Sessions with emergency disclosure will be excluded from the primary Objective 2 case-crossover analysis and handled in a prespecified sensitivity analysis that includes all sessions regardless of disclosure timing. The number and nature of emergency disclosures will be reported.

The study team will not instruct any prescription change on the basis of the study examination outside the emergency disclosure criteria above; any action taken after routine or emergency disclosure will remain within the treating physician's usual clinical discretion. Because the protocol is non-interventional, we do not anticipate any direct harm from participation. All participants will receive standard HD care as prescribed by their physicians.

This study protocol has been designed in accordance with the Declaration of Helsinki. Approval from the local Research Ethics Committee will be obtained before study initiation. Each patient will provide written informed consent after a full explanation of the study procedures and objectives. Participants will be free to withdraw at any time without any effect on their medical care. Collected data will be kept confidential and used solely for research purposes. Results will be anonymised in any publications.

In summary, 60 HD patients will undergo comprehensive ultrasound profiling every three months (pre- and post-dialysis), with tracking of their clinical course. The parent cohort supports four pre-specified analytic objectives addressing descriptive characterisation, IDH prediction and phenotyping, clinician-reported impact, and exploratory longitudinal outcomes. A brief clinician questionnaire completed before the session and disclosed after session completion will additionally allow assessment of whether the haemodynamic profile would influence prescribing and broader management decisions. This methodology will allow us to observe temporal trends in haemodynamic parameters and evaluate their relationship with patient outcomes. By integrating cardiac, lung, and venous ultrasound measures, our study seeks to generate evidence on the utility of routine point-of-care ultrasound in guiding fluid management in haemodialysis. We anticipate that the findings will inform larger studies or interventional trials in the future. The ultimate goal is to improve haemodynamic stability and reduce adverse events in haemodialysis through better monitoring tools.

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## Administrative sign-off

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