# Pilot-scale, single-arm, observational study to assess the utility of a machine learning algorithm to assess fluid status in haemodialysis patients

## Haemodialysis Outcomes & Patient Empowerment study 03 (HOPE-03)

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# Table of Contents

# Protocol Summary

| | |
|---|---|
| Product | Machine learning algorithm to assess fluid status |
| www.clinicaltrials.gov identifier | |
| Protocol title | Pilot-scale, single-arm, observational study to assess the utility of a machine learning algorithm to assess fluid status in haemodialysis patients |
| Principal investigator | Prof. C. O'Seaghdha, Beaumont Hospital, Beaumont Road, Dublin D09 V2N0, Ireland |
| Number of study sites | 1: Beaumont Hospital dialysis centre. |
| Study objectives | To determine the validity and reproducibility of a machine learning algorithm that assesses fluid status compared with bioimpedance and clinical dry weight estimation in ambulatory haemodialysis patients. |
| Methodology | Open, prospective, single-arm observational |
| Number of subjects | Total treated: 20 |
| Diagnosis | End Stage Kidney Disease requiring regular ongoing ambulatory haemodialysis |
| Main criteria for inclusion | Age ≥18 years, demonstrated understanding of study processes, written informed consent |
| Test product/intervention | Fluid status estimation model |
| Comparator product/intervention | None |
| Duration of observation | 8 weeks/patient |
| Primary endpoint(s) | Fluid status predicted by machine learning algorithm compared to bioimpedance data |
| Secondary endpoint(s) | Symptoms, adverse events. |
| Interim analysis | None planned |

| | |
|---|---|
| Statistical methods | Descriptive tables or figures will be prepared. Within-patient comparison of fluid status data as determined by different methodologies. |

# Flow charts

## Flow chart 1 Assessments during observation period

| | study observation period (8 weeks) | | | |
|---|---|---|---|---|
| | **Baseline visit** | **At each dialysis session** | **Week 2 Week 4 Week 6** | **Week 8 (end)** |
| Informed consent | X | | | |
| Demographic data (include dialysis & medicines history) | X | | | |
| Vital signs, body weight, routine hemodialysis measurements in-clinic[A] | X | X | X | X |
| Assess fluid status with bioimpedance[B] | X | | X | X |
| Estimate fluid status using machine learning algorithm[C] | X | X | X | X |
| Record symptoms related to fluid status[D] | X | | X | X |
| Record adverse events[E] | | X | X | X |
| End of study | | | | X |

[A] Routine measurements (at each hemodialysis session) include total fluid removal, interdialytic weight gain (IDWG), proportion of haemodialysis sessions in which IDWG is ≤ 4%, pre-dialysis and post-dialysis weight, pre-dialysis, intradialytic and post dialysis BP and pulse rate.

[B] Fluid status will be assessed by bioimpedance measurements immediately before start of haemodialysis.

[C] The machine learning model is a software program which examines the demographic data, recent vital signs, body weight and hemodialysis measures to predict a patient's fluid status.

[D] Symptoms related to fluid status will be recorded before haemodialysis.

[E] For example, requirement for nursing intervention such as stopping dialysis or administering fluid bolus. Adverse events include, but are not limited to muscle cramps, symptomatic hypotension, access-related complications, hypertension-related symptoms, congestive heart failure, pulmonary edema, requirement for additional unscheduled dialysis, or need for hospitalisation and changes in number and type(s) of BP medications.

# List of figures and tables



# List of abbreviations and terms

| | |
|---|---|
| BP | blood pressure |
| BVM | blood volume monitoring |
| CV | cardiovascular |
| DTIF | Disruptive Technologies Innovation Fund |
| ECW | extracellular water |
| HOPE | Haemodialysis Outcomes & Patient Empowerment |
| IDWG | interdialytic weight gain (fluid weight gain between dialysis sessions) |
| L | litre |
| OH | overhydration |
| PND | paroxysmal nocturnal dyspnea |

# 1. Introduction

## 1.1 Medical background

End stage kidney disease is defined by kidney failure severe enough to require some form of renal replacement therapy. This replacement has three forms, kidney transplant, haemodialysis and peritoneal dialysis. Haemodialysis is the most common form of replacement therapy and usually entails three sessions of dialysis per week on alternate days starting either on Monday or Tuesday. The period between dialysis sessions is known as the interdialytic period and as dialysis is delivered on alternate days there is one interdialytic period per week that is longer than the other. In order to maintain extracellular fluid balance and to prevent high blood pressure, haemodialysis sessions focus on removing the fluid that was gained between dialysis sessions.

Haemodialysis patients experience high rates of mortality, driven largely by an exceptionally high rate of cardiovascular (CV)-related mortality, which exceeds that of the general population by 10-to 20-fold [1, 2]. High levels of both interdialytic weight gain and rate of fluid removal during dialysis have been linked with increased mortality, particularly during the longer interdialytic period [1]. It is postulated that the haemodynamic effects of high fluid removal rates during dialysis may result in cardiovascular morbidity and mortality. Similarly, volume depletion induced by excessive ultrafiltration is associated with myocardial stunning, cerebrovascular events and mortality [3,4].

However, at present no method exists that can consistently refine volume status and provide patients with feedback to allow adjustments to their fluid intake. Current standards used to assess volume are either poorly predictive of fluid status, cumbersome to use, or lack an adequate patient interface [1].

The advent of the electronic health record has given us access to large quantities of patient data, which are ideal for data analytics and machine learning [2, 3]. Dialysis datasets contain large amounts of heterogeneous clinical data collected at thrice weekly intervals, creating the ideal environment to form individualised predictive algorithms. Machine learning methods have been applied to guide complex decision making within the dialysis unit [4, 5, 6], and in the prediction of

volume-related adverse events, such as intradialytic hypotension [7] and dry weight.

Volume assessment is arguably an ideal task for machine learning. Each method regularly used to assess volume, such as blood pressure (BP), and the relative blood volume slope, has partial predictive power in assessing fluid status [8,9]. Machine learning has the ability to synthesise multiple variables with partial predictive power in order to improve prediction accuracy. Several prototype models for dry weight assessment exist [10, 11, 12] but to date, only one of these models has been assessed in a prospective clinical trial [10].

We have created a prototype machine learning model based upon the data of 100,000 dialysis patients collected over 1 year from an anonymised database provided by Fresenius.

This study will evaluate if this machine-learning model for assessing fluid status is acceptable and usable for managing fluid volume in haemodialysis patients, while also assessing validity and reproducibility against validated measurements.

As the machine learning model for assessing fluid status was trained and tested on retrospective data, there is sufficient justification in testing the performance plus acceptability and usability of the model in a controlled observational setting in a prospective study. To date, this approach has not been explored in haemodialysis patients.

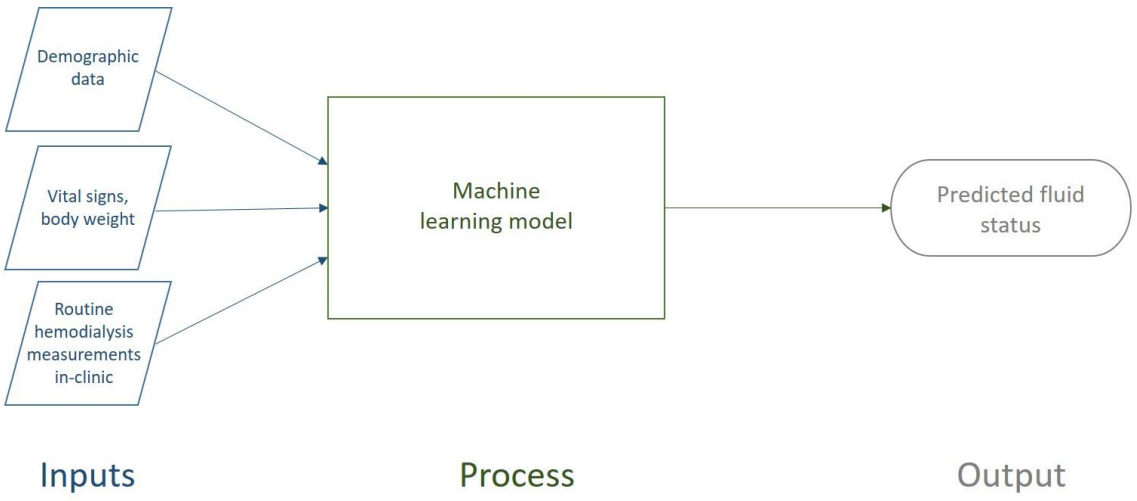
This is a pilot-scale study to assess if this approach has merit and could be tested and developed further.

## 1.2 Product profile

The machine learning model is a software program designed to assess fluid status in patients with end stage renal disease. It was developed on a large retrospective global dataset of anonymised dialysis patient data. The machine-learning model software program was designed to predict fluid status using patient demographic information and data from their recent dialysis sessions. This machine-learning model software program was trained using standard algorithm approaches on the global dialysis dataset.

In this prospective pilot study, the machine-learning model will be run every two weeks for each patient on their recently recorded information to estimate their fluid status. The inputs for the machine-learning model include demographic data (include dialysis & medicines history), vital signs, body weight and routine hemodialysis measurements in-clinic for the patient. The output from the machine-learning model is the predicted fluid status individualised for the patient. An illustration of the inputs and output for the machine-learning model is shown in Figure 1.2: 1 below.

Figure 1.2: 1 Diagram of machine learning model




The study team will complete all tasks required to run and assess the machine-learning model. (No action is required by the patient in running or assessing the machine-learning model.) The machine-learning predicted fluid status will not be used to adjust the patient's treatment regimen and the patient will not be informed of the machine-learning predicted fluid status.

# 2. Rationale, objectives and benefit-risk assessment

## 2.1 Rationale for performing the study

This study will evaluate if a machine learning model to estimate fluid status is acceptable and usable for managing fluid volume in haemodialysis patients, and will also evaluate validity and reproducibility against validated measurements.

This is a pilot-scale study to assess if this approach has merit and could be tested and developed further.

As the machine-learning model for estimating fluid status was trained and tested on retrospective data, there is sufficient justification in testing the performance plus acceptability and usability of the model in a controlled observational setting.

## 2.2 Study objectives

The objective of this pilot-scale study is to assess how the machine learning estimation model functions when used in a range of haemodialysis patients of varying age, gender, body habitus and volume status.

The primary objective is to determine the validity and reproducibility of the machine learning estimation model in haemodialysis patients. (The goal is to determine if the machine learning estimation model can provide actionable insights to better manage fluid overload in the interdialytic period.)

Haemodialysis parameters will be assessed as usual during the study and will include:

- total fluid removal (each haemodialysis session)
- interdialytic weight gain (IDWG)
- proportion of haemodialysis sessions in which IDWG is ≤ 4%.
- pre-dialysis weight
- post-dialysis weight
- Pre-, intra- and post-dialysis BP
- pulse rate
- dialysis access pressures
- dialysis flow rate and blood flow rate
- dialysis temperature
- routine haemodialysis monthly haematology (e.g. haemoglobin) and blood chemistry [renal profile (e.g. sodium, potassium), bone profile (e.g. calcium, phosphate)] data
- number and type(s) of BP medications
- requirement for nursing interventions (e.g. stopping dialysis or administering fluid bolus)
- adverse events requiring or prolonging hospitalisation

- requirement for additional unscheduled dialysis

Fluid status estimated by the machine learning estimation model will be compared with bioimpedance findings.

Patient-reported symptoms related to haemodialysis and their underlying medical condition will be recorded before haemodialysis. Adverse events and unscheduled interventions will be recorded. The effect of symptoms, adverse events and interventions on the performance of the model will be evaluated.

### 2.3 Benefit-risk assessment

This study is designed to contribute to the development of a multivariate algorithm to help haemodialysis patients monitor and manage their fluid intake. The machine learning estimation model will be used to estimate fluid removal requirements during multiple haemodialysis sessions. The estimated values will be compared with actual values to assess the validity of the machine learning estimation model.

The machine learning estimation model will not be used to adjust the patient's haemodialysis treatment regimen during this study. The machine learning estimation model does not provide feedback to the patient. It is not expected that the study or the machine learning estimation model will create any additional risks for the haemodialysis patients in this study.

All patients will receive optimal haemodialysis during the study. In addition, the on-call nephrology registrar at Beaumont hospital will be available to handle any medical enquiries from patients enrolled in the study.

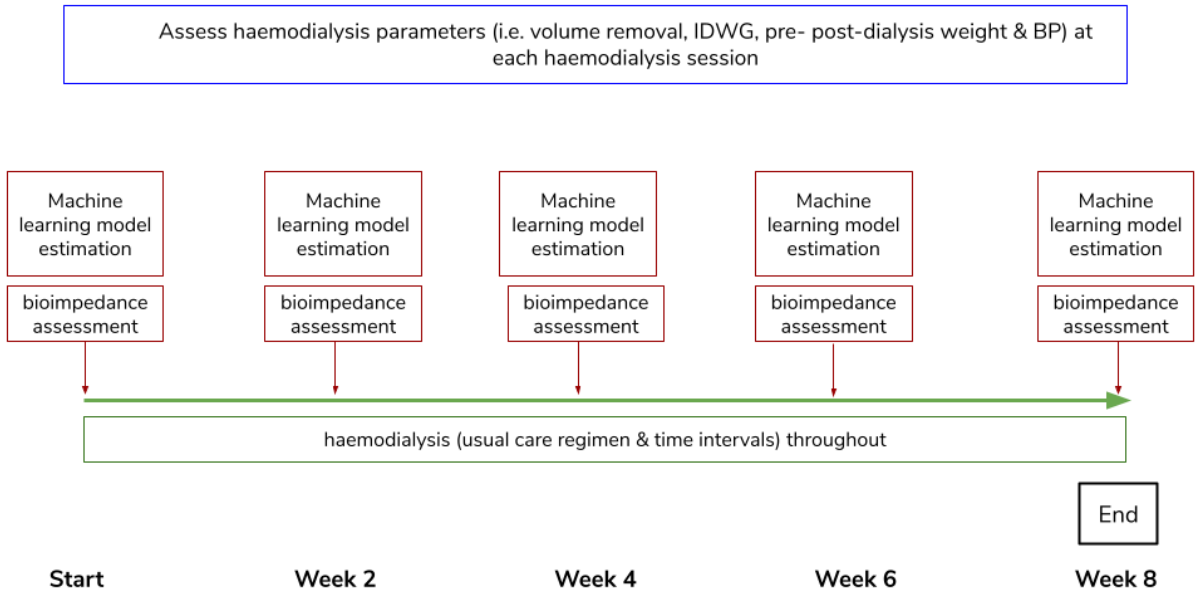
## 3. Description of design and study population

### 3.1 Overall design and plan

Prospective, open-label run-in observation period (8 weeks). (See Figure 3.1: 1 for diagram of design.)

The study will not make any changes to the usual haemodialysis schedule for the patients.

## Figure 3.1: 1 Diagram of study design




### 3.1.1 Administrative structure of study

This is a single centre study at the Beaumont Hospital, a tertiary care centre for nephrology in Dublin, Ireland.

Fresenius supplied an anonymized dataset which was used to create the machine learning model to estimate fluid status which is being evaluated in this study. Fresenius did not have any input into the design of this study.

The study is being conducted as part of the Haemodialysis Outcomes & Patient Empowerment (HOPE) project supported by the Disruptive Technology Innovation Fund of Ireland (DTIF). The HOPE project is a collaboration between the Royal College of Surgeons in Ireland, Beaumont Hospital, patientMpower Ltd., 60 Merrion Square South, Dublin D02 KX26 and Sixty (registered as Design to Value Ltd.), Innishannon, Co. Cork. The objective of HOPE is to develop artificial intelligence-enabled software to improve determination and maintenance of fluid balance in haemodialysis patients with a long-term goal of increasing the proportion of patients receiving dialysis at home. This study is a

collaboration between all partners in HOPE and the data and outcomes will be shared with all partners. The study is funded by the DTIF.

The protocol was designed by Dr. Conall O'Seaghdha (Principal Investigator), Dr. Vicki Sandys (both of Beaumont Hospital, Dublin 9, Ireland), Dr. Donal Sexton, St. James' Hospital, James Street, Dublin D08 NHY1, Ireland and patientMpower Ltd., 60 Merrion Square South, Dublin D02 KX26, Ireland.

The study sponsor is the Royal College of Surgeons in Ireland, 123 St. Stephen's Green, Dublin D02 YN77, Ireland.

patientMpower will be the Data Processor (on behalf of the HOPE project partners) for data collected in this study.

## 3.2 Discussion of study design, including choice of control group

This is a pilot-scale, prospective, open-label, single-arm observational study.

All patients will be allocated to the same observation sequence.

Patients will follow their usual haemodialysis regimen throughout the study.

Clinical assessments (e.g. IDWG, BP, pulse rate, ultrafiltration volume, symptoms) will be assessed at each dialysis visit.

The study design will allow assessment of the validity and reproducibility of data provided by the machine learning fluid status estimation model in haemodialysis patients. These data will be compared against other validated methods of volume assessment (haemodialysis machine and bioimpedance data) and with observed symptoms in patients across a range of age, genders and volume status.

The study will also allow evaluation of the utility and acceptability of the machine learning fluid status estimation estimation model in a haemodialysis patient population. This will be assessed from the healthcare professional perspective.

## 3.3 Selection of study population

### 3.3.1 Main diagnosis for study entry

Require maintenance haemodialysis in an ambulatory care setting.

Patients with a range of baseline fluid status will be considered for enrollment.

### 3.3.2 Inclusion criteria

Aged at least 18 years

Demonstrates understanding of the study requirements.

Willing to give written informed consent.

### 3.3.3 Exclusion criteria

Conditions precluding accurate use of bioimpedance (e.g. limb amputations, severe malnourishment, pregnancy, cardiac resynchronisation devices, pacemakers).

Significant confusion or any concomitant medical condition, which would limit the ability of the patient to record symptoms or other parameters.

### 3.3.4 Removal of patients from therapy or assessments

#### 3.3.4.1 Removal of individual patients

Patients are free to withdraw from the study at any time without any impact on their ongoing medical care.

The investigator may withdraw a patient from the study at any time if they believe that further participation in the study is not in the best interests of the patients.

#### 3.3.4.2 Discontinuation of the trial

The study may be terminated early if recruitment is significantly behind schedule or if for any other reason, it is unlikely that the study can be completed.

# 4. Study observational intervention

All patients will continue to receive their usual haemodialysis regimen throughout the study as prescribed by their healthcare professionals.

## 4.1 Observational intervention to be assessed

### 4.1.1 Identity of observational intervention and comparator(s)

The machine learning estimation model is a software program to assess fluid level that was developed on a large retrospective dataset of anonymised dialysis patient data. The machine-learning model processes recent information for the dialysis session and the patient to predict their fluid status. The recent information includes demographic data (including dialysis & medicines history), vital signs, body weight and their routine hemodialysis measurements in-clinic. The patient will not be involved in running or assessing the machine-learning model software program. The machine-learning model predicted fluid status will not be used to assess the patient's dialysis regimen and no information on the machine-learning model predicted fluid status will be provided to the patient.

There is no comparator intervention.

### 4.1.2 Method of assigning patients to observational groups

All patients who give informed consent and enter the study will be allocated to the same observation sequence.

### 4.1.3 Blinding and procedures for unblinding

The study is open-label.

## 4.2 Concomitant therapy, restrictions and rescue treatment

### 4.2.1 Rescue medication, emergency procedures and other treatment

If any patient or their healthcare professional has a concern the renal registrar on call at Beaumont Hospital will respond to calls out of hours and at weekends.

Any exacerbations of the patient's underlying medical condition(s) should be treated according to standard procedures.

Any other adverse events should be treated according to standard procedures.

### 4.2.2 Restrictions

There are no restrictions on concomitant treatment. All concomitant treatments as prescribed by the patients' healthcare professionals are allowed. Patients will continue to take all medicines and other treatments as prescribed by their healthcare professionals. As per the co-interventions protocol (Appendix 10.1), all nephrologists working at Beaumont Hospital will be asked not to alter the patients' usual fluid balance management during the study.

The study does not mandate any additional restrictions on diet or life-style. Patients will continue to follow all instructions on diet, exercise and lifestyle as directed by their healthcare professionals.

## 4.3 Treatment adherence

Patients will be asked to follow all study-specific instructions as directed by their healthcare professionals.

# 5 Variables and their assessment

## 5.1 Efficacy

### 5.1.1 Efficacy endpoints

#### 5.1.1.1 Primary endpoint

The primary endpoint will be to determine the validity and reproducibility of the machine learning model to estimate dry weight in assessing fluid removal requirements in haemodialysis patients. This will be evaluated by comparing validated monitoring techniques such as bioimpedance.

The primary endpoint variables include:

- volume status as measured by bioimpedance pre-dialysis.

- volume overload as defined by bioimpedance: overhydration (OH)/extracellular water (ECW) > 15% (corresponding to 2.5L)
- normohydration defined as: ECW -7 to + 7% (corresponding to -1.1L to + 1.1L)

#### 5.1.1.2 Secondary endpoints

The secondary endpoints are:

- to evaluate the performance of the machine learning model in assessing fluid status compared to clinical estimation of dry weight.
- to evaluate the effect of patient symptoms, adverse events and dialysis data (including relative plasma volume) on the performance of the machine learning model.

Patient symptoms (before haemodialysis) will be recorded and before haemodialysis [at baseline, weeks 2, 4, 6 and at week 8 (end of study)].

Symptoms of hypovolaemia:

- thirst directly after haemodialysis
- symptomatic hypotension, on change of position
- symptomatic hypotension
- nausea and vomiting
- muscle cramps
- limpness/ tiredness between dialysis sessions
- dizziness between dialysis sessions

Symptoms of hypervolaemia

- chronic coughing (new)
- dyspnea on exertion
- dyspnea at rest; 1 pillow
- dyspnea at rest: 2 pillow
- dyspnea at rest: 3 pillows
- pretibial oedema
- paroxysmal nocturnal dyspnea (PND)

Haemodialysis parameters will be assessed and will include:

- total fluid removal (each haemodialysis session)
- IDWG

- proportion of haemodialysis sessions in which IDWG is ≤ 4%.
- pre-dialysis and post-dialysis weight
- pre-dialysis, intradialytic and post dialysis BP
- pulse rate
- number and type(s) of BP medications
- dialysis access pressures
- dialysis flow rate and blood flow rate
- dialysis temperature
- routine haemodialysis monthly haematology (e.g. haemoglobin) and blood chemistry [renal profile (e.g. sodium, potassium), bone profile (e.g. calcium, phosphate)] data

### 5.1.2 Assessment of efficacy

The primary and secondary endpoint data will be listed and tabulated or displayed graphically.

The primary endpoint will be to evaluate the validity and reproducibility of the machine learning algorithm in estimating fluid status when compared to bioimpedance data. The primary endpoint will be assessed by comparison of the fluid status output of the algorithm versus the fluid status determined by bioimpedance.

## 5.2 Safety

It is not anticipated that any safety issues will arise from use of the dry weight estimation model or bioimpedance assessment. Issues regarding abnormal BP readings will be addressed by the nephrology department at Beaumont Hospital.

Adverse events will be recorded and assessed. Adverse events include, but are not limited to:

- muscle cramps, symptomatic hypotension, access-related complications, hypertension-related symptoms, congestive heart failure, pulmonary edema, requirement for additional unscheduled dialysis, or need for hospitalisation
- requirement for nursing intervention such as stopping dialysis or administering fluid bolus

Any adverse events observed with medical treatments should be reported to the manufacturers or suppliers of those treatments.

### 5.3 Other variables

Demographic data [e.g. date of birth, gender, medical cause of haemodialysis, time since first ever dialysis, vascular access route for haemodialysis, medication(s) prescribed for hypertension].

### 5.4 Appropriateness of measurements

The primary efficacy endpoint variables are measurements which are important and accepted measures of fluid status and renal function in haemodialysis patients.

## 6 Investigational plan

Patients who participate in the study will follow their usual haemodialysis regimen for approximately eight weeks. The machine learning estimation model will be used to estimate fluid status of patients during the study. In addition to usual care, participating patients will have fluid status measured by bioimpedance on five occasions.

### 6.1 Visit schedule

The total observation period will be approximately eight weeks. It is anticipated that patients will attend the clinic for haemodialysis three times per week on average. No additional patient visits are required for this study.

### 6.2. Patient recruitment process

Approximately 300 patients attend for dialysis under the governance of Beaumont Hospital. Eligible individuals will be invited to participate. It is estimated that twenty (20) people will be enrolled in this study.

The study centre will publicise the study to their potential patient population. When potential patients who are interested in the study attend for a usual care haemodialysis visit, the research staff will discuss the study (face-to-face) with

the patient. If the person wishes to participate, they will give written informed consent. The patient will receive a paper and electronic copy of the patient information document.

The study observation period can start after written informed consent.

## 6.3 Details of trial procedures

The trial procedures at each visit are summarized in the flow chart on page 6.

### 6.3.1 Baseline clinic visit (start of study)

At a planned usual care haemodialysis visit, the study centre research team will discuss the study with the patient and confirm the patient's understanding of the study processes and their willingness to participate. The patient information document will be given to the patient. The patient will have the opportunity to ask questions on the study processes and will be asked to give their written informed consent before any study-specific procedures.

Demographic data, vital signs, medical history and concomitant therapy for renal and other relevant conditions will be recorded.

At the baseline visit and at each haemodialysis visit during the study the following usual care parameters will be assessed and recorded:

- total fluid removal (each haemodialysis session)
- IDWG
- proportion of haemodialysis sessions in which IDWG is ≤ 4%.
- pre-dialysis and post-dialysis weight
- pre-dialysis, intradialytic and post-dialysis BP
- pulse rate
- dialysis access pressures
- dialysis flow rate and blood flow rate
- dialysis temperature
- requirement for additional nursing intervention (e.g.stopping dialysis, administering fluid bolus)
- adverse events related to the patient’s underlying condition (e.g. access-related complications, hypertension-related symptoms, congestive heart failure, pulmonary edema)

- requirement for additional unscheduled dialysis, or need for hospitalisation
- number and type(s) of BP medications

In addition, fluid status will be assessed by bioimpedance immediately before haemodialysis.

Patient symptoms related to volume status (questions described above in section 5.1.1.2) will be recorded before haemodialysis.

The research team will estimate fluid status using the machine learning estimation model.

### 6.3.2 Haemodialysis visits during study observation period

The patient will attend for haemodialysis as required for an observation period of approximately three weeks.

The measurements related to haemodialysis described in section 6.3.1 (usual care haemodialysis parameters) will be recorded at each haemodialysis visit during the study observation period.

### 6.3.3 Week 2, Week 4 and Week 6 clinic visits

The measurements related to haemodialysis described in section 6.3.1 (usual care haemodialysis parameters) will be recorded.

Symptoms (related to fluid status) will be assessed before haemodialysis.

In addition, fluid status will be assessed by bioimpedance immediately before haemodialysis.

The research team will estimate fluid status using the machine learning estimation model.

### 6.3.4 Week 8 visit (end of study)

The measurements related to haemodialysis described in section 6.3.1 (usual care haemodialysis parameters) will be recorded.

Symptoms (related to fluid status) will be assessed before haemodialysis.

In addition, fluid status will be assessed by bioimpedance immediately before haemodialysis.

The research team will estimate fluid status using the machine learning estimation model.

The study procedures are concluded at this visit.

# 7. Statistical methods

This a pilot-scale study to determine the validity and utility of the machine learning estimation model to assess fluid status model in haemodialysis patients.

## 7.1 Statistical design and model

This is a prospective, open-label, single-arm observational study.

All patients will attend for haemodialysis according to their usual regimen during the study.

## 7.2 Null and alternative hypotheses

Not relevant.

## 7.3 Planned analyses

Results will be collected and summarized for descriptive statistical display.

### 7.3.1 Primary analyses

The objective of this pilot-scale study is to assess how the machine learning estimation model functions when used in a range of haemodialysis patients of varying age, gender, body habitus and volume status.

The primary endpoint will be assessed by comparison of the fluid status determined using the machine learning estimation model with those observed via bioimpedance and haemodialysis machine data.

### 7.3.2 Secondary analyses

Patient-reported symptoms related to haemodialysis and their underlying medical condition will be recorded before haemodialysis. Symptom data will be assessed and compared with fluid status data.

An additional objective of this observational study is to assess the acceptability and utility of the dry weight estimation model (from the healthcare professional perspective).

### 7.3.3 Safety analyses

Patient-reported symptoms and adverse events will be tabulated and displayed.

### 7.3.4 Interim analyses

None planned.

### 7.3.5 Health economic analyses

Any additional healthcare resource utilisation (e.g. additional unplanned haemodialysis sessions, hospitalisation) will be tabulated and displayed.

## 7.4 Handling of missing data

No imputations of missing data will be made.

## 7.5. Randomisation

Not relevant. All patients will be allocated to the same observation sequence.

## 7.6 Determination of sample size

This is a pilot-scale study. The sample size (n = 20) was chosen arbitrarily.

# 8. Informed consent, data quality and storage

## 8.1 Study approval, patient information and informed consent

The study will be approved by the relevant ethics committee(s) for the participating centre.

The study will be discussed with each patient and they will be provided with a written document describing the study conditions and procedures.

All patients will give written informed consent before enrollment and any study-specific procedures.

## 8.2 Data quality assurance

All endpoint data will be stored on a central database for analysis. The data as reported by the patients will not be queried before descriptive statistical analysis tables are prepared.

## 8.3 Records

### 8.3.1 Source documents

The original electronic data and relevant medical records will be the source documents.

### 8.3.2 Direct access to source data and documents

The research team will ensure that all data entered to the central database is a true record of events. Source data verification will not be performed.

### 8.3.3 Storage of records

Medical data relating to patient care will be stored in the medical records according to the usual procedures of the treatment site(s).

The endpoint data, haemodialysis parameters (including bioimpedance data) and symptoms data will be stored on a central database managed by patientMpower Ltd. These data will be pseudonymised and will be shared with all partners in the HOPE project i.e. Beaumont Hospital research team, Design to Value Ltd. and patientMpower Ltd.

### 8.4 Statement of confidentiality

Patients will only be identified by a unique identification number on the study database (i.e. data will be pseudonymised). All data will be treated as confidential. Each patient's data will be linked to their unique identification number.

### 8.5 Completion of trial

The trial will be complete when 20 patients have completed the 8-week observation period.

If it appears to be unlikely that the target number of patients can be achieved (e.g. because of slow recruitment) a lower target will be set (after discussion and agreement with the investigator).

### 8.6 Protocol violations

All data will be analysed on an intention-to-treat basis without regard to protocol violations.

### 8.7 Compensation available in the event of study-related injury

It is not anticipated that any study-related injury will occur.

## 9. References

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# 10. Appendices

## Appendix 10.1 Cointerventions protocol

All nephrologists working at Beaumont Hospital will be asked not to alter the patients' usual fluid balance management during the study