Pilot Randomised Controlled Trial of Personalised Goal Directed Therapy after Living Donor Kidney Transplant.

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# Proposal

## Title

Pilot Randomised Controlled Trial of Personalised Goal Directed Therapy after Living Donor Kidney Transplant.

## Universal Trial Number

U1111-1280-3038

## Investigators details

**Dr Karthik Venkataraman**

Renal Advanced Trainee, Central and Northern Adelaide Renal and Transplantation Service

Role: Primary investigator

Email: Karthik.venkataraman@sa.gov.au

Duties: Draft of protocol, design of data capture database, write up of results

**Dr Michael Collins**

Senior Nephrologist, Central Adelaide Local Health Network

Role: Associate Investigator

Email: Michael.collins@sa.gov.au

Duties: Trial design, assistance with statistics and randomisation protocol, recruitment of participants

**Professor Toby Coates**

Senior Nephrologist, Central Adelaide Local Health Network. Professor of Medicine, University of Adelaide. Director of Kidney and Islet Transplantation, Central Adelaide Local Health Network

Role: Associate investigator

Email: toby.coates@sa.gov.au

Duties: Trial design, recruitment of participants, collaboration between units.

## Introduction

End stage kidney disease (ESKD) represents a public health concern, both nationally and internationally. ESKD is either managed supportively, with dialysis or transplantation. Kidney transplantation improves survival and quality of life, when compared to either haemodialysis or peritoneal dialysis, at significantly lower cost(1, 2). Graft function post operatively impacts long term graft survival(3). Delayed graft function (DGF), is defined by the requirement for dialysis due to poor kidney function after transplantation and is associated with a reduction in graft survival(4). In addition to DGF, slow graft function, which is variably defined in the literature, has also been associated with adverse graft outcomes(3). Post operative hypotension is thought to be factor contributing to DGF. However, the magnitude of the effect of post transplantation hypotension has been poorly characterised. In addition, the mechanisms to monitor volume status, a key driver of blood pressure, post transplantation is not known(5).

More broadly, post-operative hypotension after major non-cardiac surgery is a common, clinically significant problem. It is thought to contribute to both post operative death and strokes(6) and post operative myocardial infarction(7). Additionally, intraoperative hypotension has been linked to acute kidney injury in non-cardiac, non-transplant surgery(8). This peri-operative hypotension has been hypothesised to lead to poorer graft outcomes in the kidney transplantation cohort, however this has not been definitively shown(9).

## Anticipated Start and Finish Dates

Start: 1 September 2022

Finish: 31 December 2023

## Aim

The aim of this study is to assess the feasibility, efficacy and safety of a protocolised, post-operative management plan to detect and treat post-transplant hypotension.

1.5.1 Hypothesis: a protocolised post-operative recovery model after renal transplantation will decrease incidence and duration of postoperative hypotension.

## Study design

This study will be a single centre, open-label pilot randomised control trial, implementing a protocolised post-operative management strategy, to be administered by nursing and medical staff. The intervention arm will consist of post-operative management strategy with frequent haemodynamic assessments by medical staff, combined with a protocolised approach to of escalating therapy, using fluids, vasopressors, or both in combination. The intervention protocol, including post-operative is available in Appendix 2.

The control arm will be the current standard of care protocol, which is detailed in Appendix 1.

This trial will be used to assess the feasibility of undertaking a larger study to determine the effect of minimising post operative hypotension in improving longer term graft outcomes. The primary feasibility outcomes will be recruitment rates and adherence to protocol.

### Participants

All living donor kidney transplant recipients within the Central and Northern Adelaide Renal and Transplantation Service (CNARTS), scheduled between July 2022 and June 2023, will be given an opportunity to participate and offered enrolment. We expect approximately 20 to 25 living donor transplants during the proposed study period.

#### Inclusion and Exclusion criteria

Inclusion Criteria

* Adult (18 years of age or older) patients undergoing living donor kidney transplantation, who are able to provide written consent.

Exclusion Criteria

Patient requiring peri-operative plasma exchange for either high Angiotensin II Receptor Type 1 antibodies or pre-formed Human Leukocyte Antigen (HLA) antibodies. These patients may require post operative plasma exchange, which may not be able to be delivered in a timely fashion to the intervention arm with current levels of resourcing.

### Methodology

#### Recruitment

Patients will initially be approached regarding enrolment in the study in the final week assessment, scheduled as a part of the standard pre-transplant assessment. Eligible recipients will be given a verbal briefing and a written information sheet by the trial team. Patients that consent to participating in the trial will be required to sign a consent form. The information sheet and consent form are appended in Appendix 3 and Appendix 4 respectively.

#### Randomisation

Participants with be randomised in a 1:1 ratio to either standard of care post-operative management (control) or the protocolised post-transplant recovery model (intervention). The randomisation sequence will be generated externally by a statistical consultant using permuted block randomisation, with variable block sizes. Allocations will be concealed using opaque envelopes. Participants while be stratified based on hypertension, defined as the use of one or more antihypertensive agents.

Randomisation will occur at the time of induction. This will result in blinding of the participant, as well as the anaesthetic and surgical team intra-operatively. The on-site investigators, and post operative care staff will be unblinded throughout. Due to the nature of the study, all involved parties will be unblinded post operatively.

#### Study protocol

Patients enrolled into this prospective study will be reviewed by study team the day prior to operation. Patients with End Stage Kidney Disease on renal replacement therapy will undergo dialysis as directed by the transplant team.

##### Control Arm

Patients in the control arm will receive current standard of care, as per the Central Adelaide Local Health Network Renal Transplant: Post-Operative Management protocol (CNARTS-PRC03932).

Personnel involved in care will be

* Renal speciality nurse – rostered to 1:1 patient care as “nursing special” for 24 hours post transplantation
* Renal resident medical officer – Basic Physician Trainee, employed by the Royal Adelaide Hospital, on site 24 hours.
* Renal registrar – Renal Advanced Trainee, employed by Central and Northern Adelaide Renal and Transplantation Service, on call 24 hours.
* Transplant nephrologist - employed by Central and Northern Adelaide Renal and Transplantation Service, on call 24 hours.
* Other consulting clinicians as required.

##### Intervention Arm

Patients in the intervention arm will be admitted post operatively into the Advanced Recovery Room within the Royal Adelaide Hospital, for monitoring overnight. The parameters that will be monitored will include a variety of haemodynamic measures, such as blood pressure, central venous pressure and mean arterial pressure. In addition, novel haemodynamic monitoring using the ClearSight™ and FloTrac™ devices (Edwards Lifescience™) will enable capture of more advanced haemodynamic monitoring such as cardiac index and pulse pressure variation. Markers of end organ perfusion such as capillary refill time, urine output and serum haemoglobin and lactate will also be used in the multimodal haemodynamic assessment. Interpretation of the urine output trend, haemoglobin trend and lactate trend will rely on clinical judgement. A more detailed intervention protocol and assessment algorithm is available in Appendix 2 and 5.

The entirety of the intervention will be delivered under the direct supervision of the personnel below.

Personnel involved in care will be

* Renal speciality nurse – rostered to 1:1 patient care as “nursing special” for 24 hours post transplantation
* Advanced Recovery nurse – will assist with haemodynamic monitoring and use of vasopressors
* Renal resident medical officer – on site 24 hours
* Advanced recovery RMO – will assist with clinical reviews
* Renal registrar – on call 24 hours
* Anaesthetist– on call 24 hours
* Transplant nephrologist - on call 24 hours
* Other consulting clinicians as required.

### Data collection and Analysis

Data will be collected into a dedicated database using the RedCAP® tool. Demographic data will be collected to assess trends. Intraoperative data, such as volume of intraoperative fluids, vasopressor use and periods of hypotension will be recorded.

Post-operative data collected will include episodes of hypotension, duration of hypotension, urine output in the first 24 hours, admissions to the Intensive Care Unit (ICU) and adverse graft outcomes; a) delayed graft function, b) arterial or venous thromboses and c) requirement for biopsy within the first week.

## Outcomes

As this is a pilot study, there will be separate end points for feasibility, safety and efficacy

### Feasibility end-point

* Rate of enrolment into the study, measured against all living donor kidney transplant performed at the Royal Adelaide Hospital.

### Safety end-point

* Adverse event reporting – defined as harm resulted to a person receiving healthcare and stratified using the Severity Assessment Codes

### Primary efficacy outcomes

* Difference between average 24 hour mean arterial pressure – calculated by comparing the area under the curve of mean arterial pressure over time.

### Secondary outcomes

* Incidence of hypotension – defined by either systolic blood pressure (SBP) under 100mmHg OR mean arterial pressure (MAP) of under 65mmHg
* Duration of hypotension – Measured in 30-minute blocks. Defined as a 30-minute period during which the SBP was below 100 mmHg or MAP under 65mmHg
* Incidence of slow graft function – defined by a creatinine reduction ratio, which is defined as 1 - the creatinine at post-operative day 2 divided by the pre-operative creatinine, of less than 0.3 (30%) but not requiring dialysis
* Adverse graft outcomes – composite outcome of graft thrombosis, graft loss within 30 days, urine leak, urinary tract obstruction and rejection
* Wound complications requiring intervention
* Vasopressor use – defined by the amount of vasopressor use in the first 24-hour post operatively, measured in mg. Metaraminol with be the preferred vasopressor use.
* Urine output volume within the first 24 hours
* Length of stay – From elective admission to hospital until discharge from hospital
* Number of ICU admissions – defined by admission to the intensive care unit within 48 hours post operatively.

## Predicted sample size and Statistical analysis

We intend to recruit for 12 months, and predict that we will be able to recruit 20-25 patients, at a rate of approximately 2 patients per month. Ability to recruit participants will be feasibility end point.

Frequencies, expressed as percentages, will be reported for categorical variables.

The measures of central tendencies will be calculated for continuous demographic data; reported as mean and standard deviations for normally distributed variables and median and interquartile range for non-normally distributed data.

The difference between groups will be assessed using either t test or Wilcoxon rank sum test for continuous variables and chi-squared test for categorical variables.

The primary efficacy end point, namely the difference in mean 24-hour blood pressure between the control and intervention groups will be compared using generalised estimating equations.

## Confidentiality, Data storage and security

Study data will only be available to members of the investigating team. All data collected will be recorded and stored as per the standards contained in the Australian Code for Responsible Conduct of Research(10) and the National Standard on Ethical Conduct in Human Research(11). Data will be entered into an electronic database hosted on SA health servers under password protection. Data analysis will be performed on a password protected computer and will be de-identified for this process. Electronic Data will be kept confidentially for five years following the study and then securely destroyed by the primary investigator.

## Dissemination of findings

The findings from this study will be used internally by CNARTS to inform further quality assurance and improvement measures. We hope to present the results of the study in the form of presentations, conference abstracts and publication in scientific journals. The results of the study will be made available to the CNARTS Clinical Research Group, as well as the CNARTS Transplant Management Group

## Funding

Funding will be sought to purchase consumables. This is likely to amount to approximately $2400. Funding will be sought from Hospital Research Fund or relevant subsidiary, such as Kidney, Diabetes & Transplant Research Australia .

## Special considerations

Nil special considerations sought

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# Appendices

## Appendix 1: Standard of care protocol

This protocol is adapted from the Central Adelaide Local Health Network Renal Transplant: Post-Operative Management protocol (CNARTS-PRC03932)

* **Immediately and on return to ward, with recovery nurse, check the following:**
	+ Sedation level and oxygen therapy
	+ Recovery vital signs
	+ Central venous catheter (Ensure CVC position has been confirmed with C-XRAY before accessing it)
	+ Analgesia: PCA effectiveness, pain score and sedation score
	+ Precise Fluid Balance (blood loss in OT/recovery, Urine output, wound drainage output, intra-op and recovery fluid input)
	+ Current fluid replacement regimen and order
	+ All medications have been signed for in the worklist manager and entered in Intake/Output flowsheets on Electronic Medical Record
	+ Wound and wound drainage
	+ Patency of dialysis vascular access
	+ Family notified
* **Observations frequency:**
* **Vital signs:**
* **Please refer always to Renal Transplant Team Post-Op Parameters & Notify Medical officer if Measurements are outside acceptable limits.**
	+ Report TEMP 37.5C or above at all times during admission
	+ half hourly vital signs for the first 4 hours
	+ if stable 1 hourly for 4 hours
	+ hourly observations for 4 hours, Review if stable
	+ 6 hours observations until discharge
	+ 1 hourly urine measure with IV fluid replacement as prescribed
		- BD weight (0600 & 1600)
		- 1 hourly wound drain output observations for the first 24hours post-op, drainage bag to be measured and emptied at 10:00 hrs and charted on EMAR Input/Output Flowsheets
	+ 1 hourly transplant wound site observations for the first 24 hours post-op
	+ AVF patency Check with vital signs
	+ CVC observations (site, patency & dressing)
	+ 1/24 blood glucose monitoring if patient is on an insulin infusion. Adjust insluin doses according to insulin infusion protocol and Renal Transplant team orders.
* **PCA Observations:**
	+ As per PCA protocol and Acute Pain Service Team
* **Urine Output and Elimination:**
	+ Monitor urine output hourly for the first 24hrs post-op and while IVT replacement still running, Report blood clots or any sudden decrease in urine output immediately to the Renal Transplant team.
	+ Constipation management: administer aperients to prevent constipation post-surgery
* **Fluid Balance Chart:**
	+ Document fluid intake, IV hydration, wound drain output and urine output accurately on Sunrise Intake/Output flowsheets
	+ Report significant fluid imbalances to the Renal transplant team
* **Fluid Replacement Regime and IV Orders:**
	+ IVT replacement as per Renal Transplant team (Use blood warmer if urine output greater than 500mls/hr). Usually input determined by hourly output + 30ml to cover insensible losses.
* **ERAS Protocol:**
* **Please follow ERAS protocol, Sign and document each shift until Discharge**
* **Patient Education:**
	+ Medications action, dosage, side effects and importance of taking them as prescribed
	+ Signs and symptoms of infection
	+ Pharmacist
	+ Dietitian
	+ Transplant Nurse
	+ Post-discharge daily transplant clinic
	+ For all diabetic and new onset post-transplant diabetic patients: Please encourage self-management of blood glucose monitoring and insulin self-administration
	+ Diabetes Educator referral

## Appendix 2: Intervention protocol + Proposed post-operative checklist

### Intervention protocol

#### Frequency of observations

Haemodynamic monitoring

* Continuous cardiac monitoring
* Continuous CVP monitoring
* Blood pressure monitoring
	+ Continuous MAP monitoring via Clearsight device
	+ 30 minutely BP for first 4 hours.
	+ If stable, 1 hourly BP for 4 hours after that
	+ If stable, 4 hourly BP until discharge from ARRC

Fluid monitoring

* 1 hourly urine output monitoring
* IV fluid therapy as dictated by medical order
* Drain output monitoring hourly, drainage bag to be emptied at 1000hrs

Other observation

* Blood glucose monitoring as per Renal Transplant: Post-operative Management
* Patient controlled analgesia observation as per protocol

#### Maintenance fluid therapy

IVT replacement as per Renal Transplant team (Use blood warmer if urine output greater than 500mls/hr). Usually input determined by hourly output + 30ml to cover insensible losses.

### Protocolised post-operative targets

|  |  |  |  |
| --- | --- | --- | --- |
| System | Goal Checklist  | Goal achieved  | Management plan |
| Basic haemodynamic assessment | Systolic blood pressure > 100MAP > 70 |  Y  N Y  N |  |
| Advanced haemodynamic assessment | Stroke Volume Variation < 13%Haemoglobin trend acceptable |  Y  N Y  N |  |
| Graft perfusion measures | Urine Output acceptable |  Y  N |  |
| End organ perfusion measures | Lactate trend acceptable (If arterial line in situ)Capillary refill time acceptable |  Y  N Y  N |  |

### Demographics table

|  |
| --- |
| Age at transplant, median (IQR) |
| Sex |
| Aboriginal or Torres Strait Islander |
|  Yes/No |
| Primary renal disease |
|  (Sub Types listed + other) |
| Diabetes |
| Coronary disease |
| Cerebrovascular disease |
| Peripheral vascular disease |
| Hypertension |
| Ideal body weight |
| Induction immunosuppression |
| Body Mass Index |
| Total ischaemic time |
| Warm ischaemic time |
| Human Leukocyte Antigen Mismatches |
| Panel Reactive Antigens  |
| Donor Age |
| Donor Gender |
| Dialysis modality |
|  Haemodialysis Peritoneal dialysis Pre-emptive transplantation |

## Appendix 3: Participant Information Sheet

**Introduction**

You are invited to participate in a study assessing the utility of an advanced recovery model, with more intensive monitoring after your living donor kidney transplant operation.

**What is the purpose of the study?**

The care of your new kidney, in the first 24 hours of the operation, is very important. Parameters such as your blood pressure, the amount of fluid we give you and the amount of urine you make all have an impact on how well your new transplant kidney works in the immediate post operative period. Optimisation of these parameters may have an impact on the long-term function of your graft.

This is a pilot study looking at different way that you can be monitored after your kidney transplant. The study would aim to compare our current protocol against additional methods of monitoring your blood pressure and fluid status, to see if this leads to better outcomes.

**What does the study involve?**

This study is a randomised trial. If you agreed to participate, you will be randomised to 1 of 2 post operative care models.

One model is the current standard Royal Adelaide Hospital post transplantation management protocol, which will involve you being managed on the kidney ward (ward 7F) with a team of kidney doctors and nurses after time spent in recovery.

The second model will involve you being admitted to a specialised advanced recovery area for 24 hours after your kidney transplant. You will have regular observations and occasional blood tests. The study may require the placement of an arterial line, which is a line that can be used for intensive blood pressure monitoring and blood taking without the need for additional venepuncture. After the operation, you will be monitored carefully by a team consisting of kidney doctors, recovery nurses and kidney nurses trained in post-transplant care. After 24 hours, you will move to the kidney ward.

**Who is undertaking the research?**

The research study is being conducted by a team of researchers that are part of the Clinical Research Group within CNARTS (listed below).

**Dr Karthik Venkataraman**

Renal Advanced Trainee, Central and Northern Adelaide Renal and Transplantation Service

Email: Karthik.venkataraman@sa.gov.au

**Dr Michael Collins**

Senior Nephrologist, Central Adelaide Local Health Network

Email: Michael.collins@sa.gov.au

**Professor Toby Coates**

Senior Nephrologist, Central Adelaide Local Health Network. Professor of Medicine, University of Adelaide. Director of Kidney and Islet Transplantation, Central Adelaide Local Health Network

Email: toby.coates@sa.gov.au

**5. What changes will be made to my care if I decide to enter the study?**

If you are allocated into the control arm, your care will be the same high level of care we provide to all transplant recipients. This would involve close monitoring in a ward based environment.

If you are allocated to the treatment arm, your clinical care will take place in the Advanced Recovery Room, on level 4 of the Royal Adelaide Hospital, and will included extra monitoring, with the possible addition of extra blood testing. You may have an arterial line placed in your wrist. You may receive medications to increase your blood pressure if it drops too low. It should be noted that this medication is current standard of care and you may receive it even if you don’t enrol in the study, should your blood pressure drop after the kidney transplant.

**6. What if I choose not to enter the study?**

This is a research project and you do not have to be involved. If you choose not to participate, your medical care will not be affected in any way.

**7. What if I enter the study and then change my mind?**

You may withdraw from the study at any time.

**8. What are the benefits of the study for me?**

The aim of the project is to improve the care of patient undergoing kidney transplantation. As a part of this study, you may be more intensely monitored in the first 24 hours than standard of care.

**9. What benefits will the study have to the community?**

We hope that this project will improve our understanding of low blood pressure on kidney function immediately after transplantation and will allow us to improve the care of all patients undergoing kidney transplantation.

**10. Will I be inconvenienced in any way by being in the study?**

You may be inconvenienced by having an arterial line placed in your arm, usually in your wrist. You may be inconvenienced by the frequency of observations.

**11. Are there any foreseeable risks associated with being in the study?**

The study will increase the intensity of monitoring after your kidney transplant. While this is likely to have an overall benefit to you, it may cause inconvenience. The risks of arterial line placement include risk of injury to the radial artery, an artery in the risk. Importantly, this may impact on your ability to have an arteriovenous fistula for dialysis in the future

**12. Who will have access to my responses?**

The information collected in this study will only be available to the clinical research team involved with this study. You will not be identifiable within the analysis of the group data. De-identified data will used by the University of Adelaide study investigators. Your data may be used in research that arises from this study but your individual details will not be transferred.

**13. How with the data be stored?**

All paper based data collected will be stored securely within CNARTS, and only able to be accessed by the study team. Electronic data will be stored on a secure SA Health database and will only be able to be access by trial investigators and authorised users. Data will be stored for a period of five years from the date of publication.

**14. Can anyone else access the data?**

In addition to the processes described above, data may otherwise be discoverable through processes of law or for assessing compliance with research procedures.

**15. What if I want to access my responses?**

You have the right to access the information collected and stored by researchers about you. You have the right to request that any information with which you disagree be corrected.

**16. Who can I contact if I have concerns?**

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) incorporating all updates. This statement has been developed to protect the interests of people who agree to participate in human research studies.

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any medical problems which be related to your involvement in the project, you can contact the principal study doctor via email Karthik.venkataraman@sa.gov.au or mobile 0430495079.

The study has been approved by the Central Adelaide Local Health Network Human Research Ethics Committee. If you wish to speak to someone not directly involved in the study about your rights as a volunteer, or about the conduct of the study, you may also contact the CALHN HREC Chairperson, on 7117 2229.

## Appendix 4: Patient Consent Form

**Consent Form**

|  |  |
| --- | --- |
| **Title** | Pilot Randomised Controlled Trial of Personalised Goal Directed Therapy after Living Donor Kidney Transplant. |
| **Protocol Number** | TBA |
| **Project Sponsor** | TBA |
| **Principal Investigator** | Dr Karthik Venkataraman |
| **Associate Investigator(s)** | Dr Michael Collins, Prof. Toby Coates |
| **Location** | Royal Adelaide Hospital |

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to the Central Adelaide Local Health Network concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

|  |
| --- |
|  |
|  | Name of Participant (please print) |  |  |  |  |
|  |
|  | Signature |  |  Date |  |  |
|  |

|  |
| --- |
|  |
|  | Name of Witness\* to Participant’s Signature (please print) |  |  |
|  |
|  | Signature |  |  Date |  |  |
|  |

\* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

|  |
| --- |
|  |
|  | Name of Study Doctor/Senior Researcher† (please print) |  |  |
|  |  |
|  | Signature |  |  Date |  |  |
|  |

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

## Appendix 5: Intervention flowchart



## Appendix 6: Data dictionary

### Data dictionary

|  |  |  |
| --- | --- | --- |
| Data field | Description/ Definition | Mechanism of measurement |
| Demographic data | See Table below (subsection 2.2.2) |  |
| Preoperative blood pressure (mmHg) | Blood pressure taken the day of transplantation prior to induction immunosuppression and anaesthesia | Non-invasive blood pressure, recorded on electronic medical record (EMR) |
| Preoperative weight (kg) | Weight recorded the day of transplantation prior to induction immunosuppression, dialysis and anaesthesia | Scale on wards |
| Intraoperative vasopressor requirement Metaraminol (mg)Noradrenaline (microg)Adrenaline (microg)Dobutamine (microg)Vasopressin (units) | Amount of vasopressor used from time of induction of anaesthetic until entry to recovery room | As recorded on anaesthetic chart, available on EMR |
| Intraoperative fluid volume (mL) | Amount of intravenous fluid delivered from time of induction of anaesthetic until entry to recovery room | As recorded on anaesthetic chart, available on EMR |
| Postoperative maintenance intravenous fluids (mL) | Amount of intravenous fluid delivered from entry to recovery room until 24 hours postoperatively. |  |
| Total bolus intravenous fluids (mL) | Amount of intravenous fluid delivered in response to hypotension. Measured from entry to recovery room until 24 hours postoperatively. | To be considered bolus fluid, therapy must be labelled as bolus fluid in EMR or designated as bolus fluid within a medical or nursing noted on EMR.  |
| Additional fluids (mL) | Amount of oral fluid delivered AND amount of fluid used in intravenous medications administration from entry to recovery room until 24 hours postoperatively. | As recorded on EMR |
| Total urine output (mL) | Amount of urine recorded from entry to recovery room until 24 hours postoperatively. | Measured from indwelling urinary catheter out, recorded on EMR. |
| Total ultrafiltration (mL) | Amount of fluid removed on dialysis if required post operatively | Measured from by fluid removed  |
| ICU admission | Admission to the intensive care unit within the Royal Adelaide Hospital  |  |

## Appendix 7: Template for intervention description and reporting checklist

|  |  |
| --- | --- |
| **TIDieR Checklist** | **Section number** |
| Title | First page, Heading 1.1  |
| Why | Heading 1.3, 1.5  |
| What- materials | Heading 1.6, Heading 1.6.2.3.2 |
| What – procedures | Heading 1.6.2.3.2, Appendix 2, Appendix 5 |
| Who | Heading 1.6.2.3.1, Heading 1.6.2.3.2 |
| How | Heading 1.6 |
| Where | Heading 1.6.2.3.2 |
| When | Heading 1.6.2.3.2 |
| Tailoring  | Appendix 5 |
| Modification | Not applicable  |
| How well – Planned | Not planned given directly observed intervention |
| How well - Actual | Not applicable |