ARISE FLUIDS

Australasian Resuscitation In Sepsis Evaluation: FLUid or vasopressors In emergency Department Sepsis

Health Economics Analysis Plan

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THIS STUDY IS ENDORSED BY THE AUSTRALIAN AND NEW ZEALAND INTENSIVE CARE SOCIETY CLINICAL TRIALS GROUP (ANZICS CTG) AND THE AUSTRALASIAN COLLEGE FOR EMERGENCY MEDICINE CLINICAL TRIALS NETWORK (ACEM CTN)

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ABBREVIATIONS

AE	Adverse event
ANZIC-RC	Australian and New Zealand Intensive Care Research Centre
ANZICS CTG	Australian and New Zealand Intensive Care Society Clinical Trials Group
APACHE II	Acute Physiologic Assessment and Chronic Health Evaluation II
ARISE	Australasian Resuscitation In Sepsis Evaluation
ARISE FLUIDS	Australasian Resuscitation In Sepsis Evaluation: FLUid or vasopressors In emergency Department Sepsis
CEAC	Cost-effectiveness Acceptability Curve
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CI	Confidence interval
DAOH-D90	Days alive and out of hospital to day 90
ED	Emergency department
EQ-5D-5L	EuroQol- 5 Dimension- 5 Levels
FFP	Fresh Frozen Plasma
GDP	Gross Domestic Product
GLM	Generalised Linear Model
HDEC	Health and Disability Ethics Committee (New Zealand)
HEAP	Health Economics Analysis Plan
HREC	Human Research Ethics Committee
HRQoL	Health-Related Quality of Life
ICU	Intensive Care Unit
ICER	Incremental Cost-Effectiveness Ratio
ICUR	Incremental Cost-Utility Ratio
IQR	Interquartile range
IV	Intravenous
MAP	Mean arterial pressure
MRFF	Medical Research Future Fund
NMB	Net Monetary Benefit
NZD	New Zealand Dollar
QALY	Quality-adjusted life-year
SAP	Statistical Analysis Plan
SOFA	Sequential organ failure assessment score
SSC	Surviving Sepsis Campaign
USD	United States Dollar
WB	Whole blood
WHODAS	World Health Organization Disability Assessment Schedule

TABLE OF CONTENTS

Investigators and Personnel 2
Abbreviations 4
1. Administrative Information 6
2. BACKGROUND AND RATIONALE 6
3. OVERALL STUDY DESIGN 7
3.2 Inclusion criteria 8
3.3 Exclusion criteria 8
5. OBJECTIVES 8
6. Economic Evaluation 8
6.1. Data Variables 9
6.2. Health Outcomes 10
6.3. Health Resource Use and Costs 10
6.4. Cost-effectiveness analyses 17
6.5. Sensitivity analyses 18
6.6. Subgroup analyses 18
7. Presentation of Results 19
8. Ethical Approval 20
9. Funding 20
10. PUBLICATION POLICY 20
11. REFERENCES 21
12. Appendix 1: Post-discharge Assumptions 24
12.1 Hospital Readmissions Extending Beyond Day 90 24
12.2 Rehabilitation Stays Extending Beyond Day 90 24
12.3 Long-Term Care Facility Residence 25
12.4 Discharge Occurring Close to Day 90 25
12.5 Missing Discharge Destination at Day 90 25
13. Appendix 2: Table of Changes 26
14. Appendix 3: Case Report Forms 27

1. ADMINISTRATIVE INFORMATION

This Health Economics Analysis Plan (HEAP) outlines the planned cost-effectiveness analysis of the Australasian Resuscitation In Sepsis Evaluation: FLUid or vasopressors In emergency Department Sepsis (ARISE FLUIDS) randomised controlled trial. The trial compares two haemodynamic resuscitation strategies in patients with early septic shock: a restricted-fluid and early-vasopressor strategy versus a liberal-fluid and later-vasopressor strategy. It should be read in conjunction with the ARISE FLUIDS trial protocol and Statistical Analysis Plan (SAP), which provides detailed information on the objectives, design, outcomes, data management, and statistical considerations. (1, 2)

2. BACKGROUND AND RATIONALE

Sepsis is a major global health problem and a leading cause of critical illness, mortality, and healthcare expenditure.(3) It is estimated to affect over 50 million people worldwide each year and accounts for approximately 11% of all intensive care unit (ICU) admissions in Australia and New Zealand.(4, 5) Despite improvements in recognition and early management, mortality from septic shock remains close to 20%, and many survivors experience long-term physical, cognitive, and psychological impairments that contribute to reduced quality of life and ongoing health service use.(5, 6) The overall cost of sepsis care is substantial, with a significant proportion of expenditure occurring in the acute hospital phase due to prolonged ICU and ward stays, complex organ support, and post-discharge rehabilitation needs. In Australia, the estimated cost per episode of sepsis requiring ICU admission exceeds AUD $39,000, with costs largely driven by ICU length of stay, organ support, and post-discharge care.(7)

Haemodynamic resuscitation is a cornerstone of early sepsis management, aimed at restoring tissue perfusion and oxygen delivery. Traditionally, international guidelines, including the Surviving Sepsis Campaign, recommend the administration of at least 30 mL/kg of intravenous (IV) crystalloid within the first three hours of presentation for patients with hypotension or elevated lactate.(8) However, these recommendations are based largely on expert consensus rather than evidence from high-quality randomised clinical trials. Emerging data suggest that liberal fluid administration may lead to harm through tissue oedema, endothelial injury, and worsening organ dysfunction.(9, 10) Conversely, initiating vasopressor therapy earlier, with less fluid loading, may restore perfusion more rapidly and reduce fluid overload, but requires greater monitoring and may increase the need for ICU-level care.(11)

The ARISE FLUIDS trial was developed to address this uncertainty. ARISE FLUIDS is a multi-centre, randomised clinical trial comparing two haemodynamic resuscitation strategies in patients presenting to the emergency department (ED) with septic shock: a restricted fluid and early vasopressor strategy versus a liberal fluid and later vasopressor strategy.(1, 12) The trial has enrolled 1,000 participants. Follow-up for the primary outcome is expected to be complete in February 2026 with longer-term follow-up expected to be complete in November 2026. The primary outcome is days alive and out of hospital to day 90 (DAOH-D90), a patient-centred endpoint that captures both survival and duration of hospitalisation.(13-15) Secondary outcomes include mortality, length of stay in the

emergency department, ICU and hospital, duration of organ support, and longer-term functional outcomes and quality of life.

From a health economics perspective, the two resuscitation strategies are expected to have distinct cost profiles and potentially different outcomes. A restrictive approach may reduce fluid expenditure, ICU length of stay, and downstream complications associated with fluid overload, while early vasopressor use may increase short-term costs related to drug therapy, monitoring, and staffing intensity.(9, 10, 16-18) Understanding these trade-offs is essential for determining whether a restrictive or liberal fluid approach represents better value for money within the Australian and New Zealand health systems.

The economic evaluation conducted alongside ARISE FLUIDS will therefore estimate and compare the healthcare resource utilisation, costs and cost-utility of the two resuscitation strategies. By integrating clinical and economic outcomes, the analysis will provide decision-makers with evidence to guide policy, funding, and guideline development for the management of septic shock in emergency settings.

3. OVERALL STUDY DESIGN

The ARISE FLUIDS trial is a multi-centre, open-label, randomised controlled trial conducted in emergency departments across Australia, New Zealand, and the Republic of Ireland. The ARISE FLUIDS trial protocol and SAP have been published.(1, 12) In brief, eligible patients presenting to the emergency department with suspected or confirmed sepsis and shock are randomised to receive one of two early haemodynamic resuscitation strategies: a restricted fluid and early vasopressor strategy, or a liberal fluid and later vasopressor strategy. Randomisation occurs in a 1:1 ratio, stratified by site at enrolment, to ensure balance between treatment groups.

The protocol specified that eligible participants would receive the allocated resuscitation strategy for a minimum of 6 hours and up to 24 hours post-randomisation, after which further management will follow standard local practice.(1) The trial recruited 1,000 participants from emergency departments in metropolitan and regional hospitals in Australia, New Zealand and the Republic of Ireland. Participants will be followed to day 90 for the primary outcome and to 6 and 12 months for longer-term mortality, disability, and health-related quality of life, where data are available.

The primary outcome for the trial is DAOH-D90, defined as the number of days within the first 90 days post-randomisation that the participant is alive and not hospitalised.(13-15) This measure integrates survival, duration of hospital stay, and readmissions to reflect overall recovery. Secondary outcomes include all-cause mortality at 28- and 90- days, days alive and at home within the first 90-days, duration of ICU and hospital stay, ventilator-free, vasopressor-free and renal replacement therapy-free days to day 28, and health-related quality of life and disability at 6 and 12 months.(1, 2)

3.2 Inclusion criteria

Patients will be eligible if ALL of the following criteria are met while in the ED:

1. Clinically suspected infection
2. Systolic blood pressure (SBP) <90 mm Hg or mean arterial pressure (MAP) <65 mm Hg, despite a ≥1000ml cumulative total bolus of IV fluid administered over a maximum of 60 minutes; including pre-hospital boluses
3. Arterial or venous blood lactate >2.0 mmol/L
4. At least one dose of an IV antimicrobial has been commenced

3.3 Exclusion criteria

Patients will be excluded if ANY of the following apply:

1. Age < 18 years
2. Confirmed or suspected pregnancy
3. Transferred from another acute care facility
4. Hypotension suspected to be due to a non-sepsis cause
5. >2L total IV fluid administered (including prehospital fluids but excluding drugs and flushes)
6. More than 6 hours has elapsed since presentation to the ED or more than 2 hours has elapsed since last inclusion criterion has been met
7. Treating clinician considers that one or both of the treatment regimens are not suitable for the patient or the study protocol cannot be delivered e.g. limitation of care, requirement for immediate surgery
8. Death is considered imminent or inevitable
9. Underlying disease that makes survival to 90 days unlikely
10. Inability to follow patient up to day-90 e.g. unstable accommodation, overseas visitor
11. Previously enrolled in the ARISE FLUIDS study

5. OBJECTIVES

The objective of this study is to assess the cost-effectiveness of a restricted-fluid and early-vasopressor strategy compared with a liberal-fluid and later-vasopressor strategy for the resuscitation of patients with early septic shock in the Emergency Department.

6. ECONOMIC EVALUATION

An economic evaluation will be conducted alongside the ARISE FLUIDS randomised controlled trial to compare the cost-effectiveness of a restricted-fluid, early-vasopressor strategy with a liberal-fluid, later-vasopressor strategy in patients presenting to the ED with early septic shock. The analysis will follow intention-to-treat principles and adopt a public healthcare provider perspective representing the Australian and New Zealand health systems.

A within-trial cost-utility analysis will be undertaken over a 12-month time horizon. The primary economic outcome will be cost per quality-adjusted life year (QALY) gained and cost per life-year saved at 12 months. The analysis will incorporate survival, long-term mortality and health-related quality of life, and healthcare resource utilisation from randomisation to 12 months or death, whichever occurs first.

All costs will be valued in 2024 AUD and NZD, adjusted using each country's health price indices. Where required for publication in international journals, results will also be expressed in USD or Euros, converted using World Bank purchasing-power-parity (PPP) factors. Discounting will not be applied, as all analyses are within 12 months. Findings will be reported in accordance with the 2022 Consolidated Health Economic Evaluation Reporting Standards (CHEERS).(19)

6.1. Data Variables

Data collected during the ARISE FLUIDS trial through the case report forms (CRFs) and may be used for this economic evaluation will include:

1. **Socio-demographic characteristics:**
   Age; sex; weight and country of enrolment
2. **Baseline clinical characteristics:**
   Suspected or confirmed infection source (e.g., respiratory, abdominal, urinary); presence of comorbidities (cardiac, renal, hepatic, malignancy, diabetes); illness severity scores including Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) where available; baseline MAP; lactate concentration; and mechanical ventilation status at randomisation; volume of IV fluids and vasopressor use prior to randomisation
3. **Intervention-related variables:**
   Total volume and type of intravenous (IV) fluids administered from emergency department presentation to 24 hours post-randomisation; time to and duration of vasopressor infusion; type, duration and dose of vasopressors; central or peripheral line use.
4. **Organ support and adjunctive therapies:**
   Duration of invasive and non-invasive mechanical ventilation; extracorporeal membrane oxygenation (ECMO); renal replacement therapy (RRT); and use of blood products and vasopressors.
5. **Hospitalisation details:**
   Date and time of emergency department presentation, ICU admission and discharge, and hospital discharge; discharge destination (home, rehabilitation, long-term care, or transfer to another hospital).
6. **Clinical outcomes:**
   Survival status at ICU discharge, hospital discharge, day 90, 6- and 12-months; date of death; and days alive and out of hospital to day 90 (DAOH-D90) as a clinical outcome.
7. **Post-hospitalisation details:**
   Dates of admission and discharge for subsequent readmissions to acute hospitals, long-term care facility, or rehabilitation centre up to 12-months post randomisation.

8. **Follow-up data:**
   Mortality, health related quality of life measured using EuroQol- 5 Dimension- 5 Levels (EQ-5D-5L) and disability measured using World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) at 6 and 12 months.

All variables necessary to quantify healthcare resource utilisation are captured in the ARISE FLUIDS CRFs. Data management and quality control procedures will follow the main trial SAP.(2)

6.2. Health Outcomes

The primary health outcome for this economic evaluation is quality adjusted life years (QALYs) at 12 months. QALYs will be derived from EQ-5D-5L utility values measured at 6- and 12 months.

EQ-5D-5L responses will be converted to utility values using Australian national value sets.(20) Utility scores typically range from values less than 0 (health states considered worse than death) to 1 (full health), with a value of 0 representing death. QALYs will be estimated using an area-under-the-curve (AUC) approach, combining utility scores with survival data and assuming linear interpolation between observed assessment points. Participants who died while in hospital or before a scheduled follow-up assessment will be assigned a utility value of zero from the date of death onwards. Consistent with previous economic evaluations in critically ill populations, participants will be assumed to have a baseline utility value of zero at randomisation.(21-24)

WHODAS 2.0 data will be used to support exploratory secondary analyses estimating cost per death and disability avoided, at 6- and 12 months. Disability is defined into categories using prespecified WHODAS 2.0 percentage thresholds. (25, 26) These categories comprised no disability (0–4.5%), mild disability (4.5–24.5%), moderate disability (24.5–49.5%), severe disability (49.5–95.5%), and complete disability (95.5–100%). These analyses will complement QALY-based results by providing additional insight into functional recovery and longer-term morbidity following septic shock.

6.3. Health Resource Use and Costs

Healthcare resource use will be quantified for each trial arm using patient-level data collected through the ARISE FLUIDS CRFs and trial database. Resource utilisation will be measured from randomisation to 12 months or death, whichever occurs first. The analysis will be undertaken from the health-care provider perspective (Australian and New Zealand public health systems).

The following resource categories will be included:

- **Emergency Department:** ED presentation.
- **Intensive Care Unit:** ICU admission and discharge dates/times to determine ICU length of stay; and organ supports.
- **Ward/Inpatient Care:** number of non-ICU hospital days following ICU discharge or direct ward admission.
- **Intervention-related resources**: total volume and type of intravenous (IV) fluids administered and the duration of vasopressor infusion.

- **Organ Support:** duration of invasive or non-invasive mechanical ventilation, renal replacement therapy (RRT), the type and volume of blood products transfused and extracorporeal membrane oxygenation (ECMO).
- **Post-Discharge Care**: Hospital readmissions, rehabilitation, and long-term care.

Detailed information on the type and number of blood product units administered will be available from a subset of participating sites. This will be used to estimate blood product type and number based on the volume of blood received by each patient. Unit costs will be sourced from national pricing schedules and applied consistently across all participants.

For participants who remain in a rehabilitation facility, or long-term care facility at day 90, length of stay beyond day 90 was not collected and assumptions will be made as outlined below. Participants residing in a rehabilitation facility or long-term care facility at day 90 will be assumed to remain in that setting until death or end of follow-up, whichever occurs first. Worked examples of these assumptions (e.g. partial readmission episodes overlapping day 90) are provided in Appendix 1.

Resource use will be costed by multiplying the quantity of each item by their respective unit costs. Unit costs will be based on publicly available Australian and New Zealand cost weights and inflated to 2024 AUD and NZD, respectively. Australian unit costs will be inflated using the Australian Institute of Health and Welfare (AIHW) health price index, while New Zealand unit costs will be adjusted using the consumer price index. Costs may be converted to USD or Euros using Purchasing Power Parity (PPP) adjustments for international publication. As the maximum analytic horizon is 12 months, no discounting will be applied.

As only one participant was enrolled from the Republic of Ireland, Australian unit costs will be applied to this participant.

ICU and ward bed-day costs are anticipated to contribute the largest proportion of total expenditure, reflecting the intensity and duration of critical care in septic shock. Fluid, vasopressor, and organ-support costs will be itemised separately to demonstrate differences between the two resuscitation strategies. Adverse-event costs will not be costed separately, as they are expected to be captured through increased organ supports or extended length of stay.

Table 1. Unit costs applied to measured healthcare resource use in the ARISE FLUIDS trial

Country	Cost item	Unit cost (local currency)	Cost year	Inflation rate from the cost year to 2024	PPP conversion factor (World Bank)	Cost per unit, (2024 USD, base year)	Source
Australia	Emergency Department presentation per visit	AUD $2,212 per visit	2023	1.05	1.26	USD $1,836.46 per visit	Based on AECC code E1810Z (Septicaemia) Source: Independent Health and Aged Care Pricing Authority. National Hospital Cost Data Collection (NHCDC) Public Sector 2022–23 https://www.ihacpa.gov.au/resources/national-hospital-cost-data-collection-nhcdc-public-sector-2022-23
	ICU stay per bed-day	AUD $5,760 per bed-day, or by the number of organ supports: 0 – AUD $4,103.30 per bed-day 1 – AUD $4,396.76 per bed-day 2 – AUD $6,068.94 per bed-day 3 – AUD $6,865.82 per bed-day 4 – AUD $7,908.09 per bed-day	2024	1.00	1.26	USD $4,571.43 per bed-day or by the number of organ supports: 0 – USD $3,256.59 per bed-day 1 – USD $3,489.49 per bed-day 2 – USD $4,816.62 per bed-day 3 – USD $5,449.07 per bed-day 4 – USD $6,276.26 per bed-day	Estimated using the national ICU cost rate of AUD $240 per hour, multiplied by 24 hours. Source: Independent Health and Aged Care Pricing Authority. National Pricing Model Technical Specifications 2023-24 https://www.ihacpa.gov.au/resources/national-pricing-model-technical-specifications-2023-24 Organ support categories derived from the National Cost Collection 2023-24 reported by the National Health Service in England. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection

Country	Cost item	Unit cost (local currency)	Cost year	Inflation rate from the cost year to 2024	PPP conversion factor (World Bank)	Cost per unit, (2024 USD, base year)	Source
	Hospitalisation (medical ward) per bed-day	AUD $2,249.63 per bed day	2023	1.05	1.26	USD $1,867.71 per bed-day	Based on AR-DRG codes T60 A-C (Sepsis, septic shock and systematic infection). Source: Independent Health and Aged Care Pricing Authority. National Hospital Cost Data Collection (NHCDC) Public Sector 2022–23 https://www.ihacpa.gov.au/resources/national-hospital-cost-data-collection-nhcdc-public-sector-2022-23
	Long-term care per bed-day	AUD $280.01 per bed-day	2014	1.00	1.26	USD $222.23 per bed-day	Source: Schedule of Subsidies and Supplements for Aged Care (Schedule from 1 October 2024) https://www.health.gov.au/resources/publications/schedule-of-subsidies-and-supplements-for-aged-care-before-1-november-2025
	Rehabilitation per bed-day	AUD $1,476.71 per bed-day	2023	1.05	1.26	USD $1,226.00 per bed-day	Based on AN-SNAP v5 code 599A Source: Independent Health and Aged Care Pricing Authority. National Hospital Cost Data Collection (NHCDC) Public Sector 2022–23 https://www.ihacpa.gov.au/resources/national-hospital-cost-data-collection-nhcdc-public-sector-2022-23

Country	Cost item	Unit cost (local currency)	Cost year	Inflation rate from the cost year to 2024	PPP conversion factor (World Bank)	Cost per unit, (2024 USD, base year)	Source
	Blood transfusions per unit:						National Blood Authority. Annual Report 2022-23. https://www.blood.gov.au/sites/default/files/documents/2024-10/NBA0912%20%E2%80%93%20NBA%20Annual%20Report%202023%E2%80%9324%20WCAG%20accessible.pdf
	Red blood cells	AUD $375.00	2024	1	1.26	USD $297.62	Whole blood (WB) red cells leucodepleted
	Platelets	AUD $403.35	2024	1	1.26	USD $320.12	Average cost of WB platelet pool leucodepleted and apheresis platelet leucodepleted
	Clinical Fresh Frozen Plasma (FFP)	AUD $188.00	2024	1	1.26	USD $149.21	Average of WB clinical FFP and apheresis clinical FFP
	Cryoprecipitate	AUD $253.75	2024	1	1.26	USD $201.39	Average of WB cryoprecipitate and apheresis cryoprecipitate
New Zealand	Emergency Department presentation per visit	NZD $370.00 per visit	2018	1.20	0.74	USD $598.69 per visit	PHARMAC Cost Resource Manual, Version 3. https://pharmac.govt.nz/medicine-funding-and-supply/the-funding-process/policies-manuals-and-processes/economic-analysis/cost-resource-manual/
	ICU stay per bed-day	NZD $5,500.00 per bed-day	2017	1.21	0.74	USD $8,981.58 per bed-day	

Country	Cost item	Unit cost (local currency)	Cost year	Inflation rate from the cost year to 2024	PPP conversion factor (World Bank)	Cost per unit, (2024 USD, base year)	Source
	ICU stay per bed-day by the number of organ supports	0 – NZD $4,760.33 per bed-day 1 – NZD $5,100.77 per bed-day 2 – NZD $7,040.71 per bed-day 3 – NZD $7,965.19 per bed-day 4 – NZD $9,174.35 per bed-day	2024	1.21	0.74	0 – USD $6,398.29 per bed-day 1 – USD $6,855.88 per bed-day 2 – USD $9,463.32 per bed-day 3 – USD $10,705.90 per bed-day 4 – USD $12,331.11 per bed-day	Organ support categories derived from the National Cost Collection 2023-24 reported by the National Health Service in England. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection
	Hospitalisation (medical ward) per bed-day	NZD $1,200.00 per bed-day	2017	1.21	0.74	USD $1,959.62 per bed-day	PHARMAC Cost Resource Manual, Version 3. https://pharmac.govt.nz/medicine-funding-and-supply/the-funding-process/policies-manuals-and-processes/economic-analysis/cost-resource-manual/
	Long-term care per bed-day	NZD $130.00 per bed-day	2018	1.20	0.74	USD $210.35 per bed-day	
	Rehabilitation per bed-day	NZD $1,334.10 per bed-day	2023	1.06	0.74	USD $1,895.61 per bed-day	WIESNZ23 (FY 2022/23) // NZDRG70 codes: Z60Z https://www.tewhatuora.govt.nz/for-health-professionals/data-and-statistics/nz-health-statistics/data-references

Country	Cost item	Unit cost (local currency)	Cost year	Inflation rate from the cost year to 2024	PPP conversion factor (World Bank)	Cost per unit, (2024 USD, base year)	Source
	Blood transfusions per unit						New Zealand Blood Service Product Price Schedule 2022 - 2023 https://redbook.streamliners.co.nz/NZBS%20Price%20List%20for%202022-23.pdf
	Red blood cells	NZD $343.96	2023	1.06	0.74	USD $488.73	WB leucocyte depleted (Product code 01480)
	Platelets	NZD $1,000.65	2023	1.06	0.74	USD $1,421.81	Platelet apheresis leucocyte depleted (Product code 12110 – 12112)
	FFP	NZD $259.64	2023	1.06	0.74	USD $368.92	Average cost of plasma fresh frozen apheresis - leucocyte depleted and FFP leucocyte depleted (Product code 18170 – 18175 and 18280 – 18191)
	Cryoprecipitate	NZD $487.49	2023	1.06	0.74	USD $692.67	Cryoprecipitate apheresis high fibrinogen leucocyte depleted (Product code 11090)

6.4. Cost-effectiveness analyses

The economic evaluation will compare the costs associated with the restricted-fluid and early-vasopressor strategy with the liberal-fluid and later-vasopressor strategy in patients with early septic shock. Analyses will adopt a health-care provider perspective representing the Australian and New Zealand public health systems.

The primary economic analysis will be a within-trial-cost-utility analysis conducted over a 12-month time horizon using quality-adjusted life-years (QALYs) as the primary health outcome measure. This analysis will incorporate survival, health-related quality of life, and healthcare resource utilisation from randomisation to 12 months or death, whichever occurs first.

The primary measure of cost-effectiveness will be the incremental cost per quality-adjusted life-year (QALY) gained. Secondary economic outcomes will include the incremental cost per life-year gained and incremental cost per death and disability avoided at 12-months. QALYs will be derived from health-related quality-of-life (HRQoL) data collected using the EQ-5D-5L instrument at 6 and 12 months as outlined in 6.2 above. The 12-month analysis will incorporate post-discharge resource use and prespecified assumptions described in Appendix 1.

All analyses will follow the intention-to-treat principle. Descriptive analyses will first summarise mean (SD) and median (IQR) costs and outcomes by treatment group. Between-group differences in mean per-patient costs will then be estimated using generalised linear models (GLMs) with appropriate link and distribution families to account for skewed cost data. Models will adjust for baseline covariates consistent with the main statistical analysis plan (age, sex, baseline lactate, infection source, mechanical ventilation status, site, and country).

Incremental results will be presented as:

- **Incremental cost-effectiveness ratio (ICER):** the cost per additional life-year saved at 12 months.
- **Incremental cost-utility ratio (ICUR):** the cost per QALY gained at 12 months.
- **Incremental net monetary benefit (INMB):** the monetary value of health gains minus the additional costs, expressed at a willingness-to-pay (WTP) threshold of AUD 50 000 per QALY.

Secondary economic outcomes will include cost per death and disability avoided at 12 months. These analyses will use survival data and WHODAS 2.0 disability categories and are intended to complement the primary QALY-based results.

Uncertainty and missing data

Uncertainty around incremental costs and effects will be quantified using non-parametric bootstrapping with resampling at the participant level. Bootstrapped estimates will be used to construct 95% confidence intervals and displayed on cost-effectiveness planes, with corresponding cost-effectiveness acceptability curves (CEACs) illustrating the probability that the restricted-fluid and early-vasopressor strategy is cost-effective across a range of WTP thresholds.

Where appropriate, missing cost and outcome data will be handled using single imputation nested in bootstrapping.(27) Imputation models will incorporate baseline characteristics,

treatment allocation, and observed outcomes. Incremental cost and outcome estimates will then be calculated within each imputed bootstrap sample, and the overall mean and 95% confidence intervals will be derived from the bootstrap distribution. This approach allows the resulting confidence intervals to reflect both sampling variability and uncertainty associated with missing data. Results from the imputed analyses will be compared with complete-case analyses to assess the impact of missingness on study findings.

All statistical analyses will be conducted using R Statistical Software and/or Stata.

6.5. Sensitivity analyses

Sensitivity analyses will be undertaken to assess the robustness of the cost-effectiveness results. A probabilistic sensitivity analysis will be performed using non-parametric bootstrapping to quantify uncertainty around incremental costs and outcomes. Bootstrapped results will be plotted on cost-effectiveness planes, and a CEAC will illustrate the probability that the restricted-fluid and early-vasopressor strategy is cost-effective across a range of willingness-to-pay (WTP) thresholds.

Non-parametric bootstrapping will use at least 1,000 replications (and up to 10,000 if computationally feasible) for the primary QALY-based cost-utility analysis. Where missing cost and/or outcome data are imputed, uncertainty will be propagated by combining multiple imputation and bootstrapping using an approach consistent with published recommendations (e.g., “bootstrap-then-impute” or “impute-then-bootstrap” workflows as appropriate), with results pooled across imputations using Rubin’s rules.(27)

Deterministic (one-way) sensitivity analyses will examine the effect of varying key assumptions and input parameters. These will include the use of alternative unit-cost inputs, variation in daily ICU and ward costs (± 20 %), exclusion of participants with extreme total costs, and separate application of Australian and New Zealand cost bases.

Sensitivity analyses will explicitly test the impact of prespecified post-discharge assumptions described in Appendix 1, including assumptions regarding length of stay beyond day 90, rehabilitation duration, long-term care residence, and handling of incomplete post-discharge follow-up over the 12-month time horizon.

The combined results of all analyses will provide an assessment of the stability, direction and reliability of the primary cost-effectiveness findings.

6.6. Subgroup analyses

To explore potential differences in cost and effectiveness between patient groups, several subgroup analyses will follow the ARISE FLUIDS SAP.

Pre-specified subgroups will include:

- Country of enrolment: Australia vs New Zealand.
- Age: <65 years vs ≥65 years;
- Sex: male vs female;
- Baseline lactate: <3 mmol/L vs ≥3 mmol/L;

- Illness severity: APACHE II <15 vs ≥15;
- Source of infection: respiratory, urinary, or other;
- Fluid volume administered prior to randomisation.

Exploratory subgroups will include:

- Timing of vasopressor initiation: ≤3 hours vs >3 hours from presentation;
- Mechanical ventilation: intubated vs not intubated at randomisation
- COVID-19 infection status.

Subgroup analyses will only be conducted for the 12-month cost-utility (QALYs) outcome. For each subgroup, differences in costs, QALYs, and INMB will be assessed, and where appropriate, treatment-by-subgroup interaction terms will be tested within regression models. Incremental cost-effectiveness estimates will be summarised for each subgroup and illustrated with cost-effectiveness planes to show uncertainty. Because the trial is not powered to detect subgroup interactions, results will be interpreted descriptively and considered exploratory.

7. PRESENTATION OF RESULTS

Findings will be summarised for the overall trial population and stratified by country (Australia and New Zealand). All data will be de-identified prior to analysis, and no site- or participant-specific identifiers will be reported.

Results will be presented for the within-trial economic evaluation reporting QALYs over a 12-month time horizon.

Key outcomes to be presented include:

- Mean total and component costs per participant (AUD and NZD),
- Incremental cost and effectiveness differences between treatment arms,
- Incremental cost-effectiveness ratios (ICERs) and INMB, and
- CEACs showing probability of cost-effectiveness at varying willingness-to-pay thresholds.

Descriptive tables will summarise healthcare resource use and the main cost drivers (e.g., ICU and ward bed-days, vasopressor duration, ventilation, and renal replacement therapy). Figures will display cost distributions, cost-effectiveness planes, and CEACs to illustrate uncertainty.

All results will be presented with 95% confidence intervals or bootstrapped uncertainty intervals, as appropriate. Figures will use consistent colour schemes and axis scaling to enable direct visual comparison between treatment groups and outcomes.

The following tables and figures will be produced for the within-trial 12-month cost-utility analysis:

Table 1	Baseline characteristics of study participants by treatment group (restricted-fluid and early-vasopressor vs liberal-fluid and later-vasopressor strategies).

Table 2.	Healthcare resource utilisation and total costs by treatment group to 12 months.
Table 3.	Summary of 12-month incremental cost-effectiveness results (mean costs, life-years, QALYs, ICERs, ICURs, and NMB).
Figure 1.	Cost-effectiveness plane (cost per life-year saved, 12-months).
Figure 2.	Cost-effectiveness plane (cost per QALY gained, 12-months).
Figure 3.	Cost-effectiveness acceptability curves (probability of cost-effectiveness across WTP thresholds, 12 months).
Supplementary Table 1.	Unit costs (AUD and NZD) applied to measured resource use.
Supplementary Table 2.	Comparison of baseline characteristics between participants with and without missing economic data.
Supplementary Table 3.	Subgroup analyses of mean costs, QALYs, and cost-effectiveness by key patient groups

8. ETHICAL APPROVAL

The ARISE FLUIDS trial, including the pre-specified economic evaluation, received approval from Australian Human Research Ethics Committees (HRECs) (2020/ETH02874), New Zealand Health and Disability Ethics Committees (HDECs) (21/NTB/40) and Republic of Ireland Health Research Consent Declaration Committee (HRCDC) (23-008-AF1), with local governance authorisation at each site. Given the emergency nature of septic shock, enrolment occurred without prior consent under approved waiver-of-consent procedures. Consent processes were implemented in accordance with local jurisdiction requirements, using either an opt-out-approach or a written consent to continue obtained from participants or their representatives as soon as practicable.

9. FUNDING

This investigator-initiated study is funded by the Australian Government's Medical Research Future Fund (MRFF) and New Zealand Health Research Council (22/409). The study is supported by the Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), Monash University. Funding for the global health economics component is included within the overall trial grant. AMH is supported by an NHMRC Investigator Grant (GNT2008447).

10.PUBLICATION POLICY

Findings from the economic evaluation will be published in a peer-reviewed journal. Additional manuscripts or conference presentations may focus on health economic methods, key cost drivers, or cross-country comparisons (Australia vs New Zealand).

All publications will comply with the ANZIC-RC authorship and publication policy and acknowledge MRFF (APP1200084) funding support. The final economic dataset and analysis code will be archived securely at ANZIC-RC and made available to collaborating investigators upon request, consistent with Monash University and MRFF data-sharing guidelines.

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12. APPENDIX 1: POST-DISCHARGE ASSUMPTIONS

This appendix outlines the prespecified assumptions used to estimate post-discharge healthcare resource utilisation for the 12-month economic evaluation for the ARISE FLUIDS trial. These assumptions are required to extend cost and outcome estimation beyond the 90-day follow-up point where episodes of care are ongoing or where post-discharge resource use is incompletely observed. These assumptions are intended to ensure consistency, transparency, and reproducibility of cost estimates and will be applied uniformly across treatment groups in the 12-month cost-utility and cost-effectiveness analyses.

General Principles

1. All assumptions will be applied equally to both treatment arms and only within the 12-month economic evaluation.
2. Where possible, assumptions will be informed by observed trial data.
3. In the absence of complete trial data, assumptions will be informed by published Australian and New Zealand literature describing post-ICU hospitalisation, rehabilitation, and long-term care following critical illness.
4. Conservative assumptions will be used to minimise the risk of bias in favour of either intervention.
5. The impact of these assumptions will be explored in pre-specified sensitivity analyses.

12.1 Hospital Readmissions Extending Beyond Day 90

If a participant is readmitted to hospital prior to day 90 but remains hospitalised at the day-90 follow-up point, the total length of the readmission episode will be estimated using the mean readmission length of stay observed among participants with completed readmission episodes within the trial.

Worked Example A1

Participant discharged from index hospital on Day 70

Hospital readmission on Day 80

Participant remains hospitalised at Day 90 (10 observed days)

Mean readmission length of stay in trial cohort = 20 days

Assumption applied:

An additional 10 hospital bed-days will be assigned beyond Day 90, resulting in a total readmission length of stay of 20 days.

12.2 Rehabilitation Stays Extending Beyond Day 90

For participants admitted to an inpatient rehabilitation facility prior to day 90 and not discharged by day 90, rehabilitation length of stay will be estimated using the mean rehabilitation length of stay observed among participants with completed rehabilitation episodes. Where trial data are insufficient, published national benchmarks will be used.

Worked Example B1

Participant discharged from acute hospital on Day 65

Admitted to inpatient rehabilitation on Day 65

Still in rehabilitation at Day 90 (25 observed days)

Mean rehabilitation length of stay = 35 days

Assumption applied:

An additional 10 rehabilitation bed-days will be assigned beyond Day 90, resulting in a total rehabilitation stay of 35 days.

12.3 Long-Term Care Facility Residence

Participants residing in a long-term care facility (e.g. nursing home or residential aged-care facility) at Day 90 will be assumed to remain in that setting until death or end of the 12-month follow-up, whichever occurs first.

This assumption reflects the chronic nature of long-term care placement following critical illness and is consistent with prior Australasian trial-based economic evaluations.(28)

12.4 Discharge Occurring Close to Day 90

If the estimated mean length of stay for a post-discharge care episode implies discharge immediately after Day 90, discharge will be assumed to occur on Day 91 for costing purposes.

Worked Example D1

Participant admitted to rehabilitation on Day 78

Mean rehabilitation length of stay = 12 days

Expected discharge Day = 90

Assumption applied:

Discharge will be assumed to occur on Day 91, and no rehabilitation costs beyond Day 90 will be included.

12.5 Missing Discharge Destination at Day 90

If discharge destination at Day 90 is missing, participants will be assumed to remain in their most recently documented care location (acute hospital, rehabilitation facility, or long-term care facility). This location will be carried forward until the next documented transition, death, or the end of follow-up, with duration of stay estimated using the prespecified assumptions outlined in Sections 12.1–12.4, as applicable.

13. APPENDIX 2: TABLE OF CHANGES

Section/Area	Current Version #	New Version #	Reason for Change	Implications
6.3 Health Resource Use and Costs	1.0	1.1	The New Zealand rehabilitation unit cost previously listed as to be confirmed has now been replaced with the calculated unit cost derived using WIESNZ23 (FY 2022-23) cost weights.	This update removes the placeholder value and ensures that all cost inputs used in the economic evaluation are fully specified and reproducible.
6.3 Health Resource Use and Costs	1.1	1.2	Corrected transcription errors in cost figures.	Corrections are presentational only and do not alter the intended cost values or methods of the economic evaluation.
9. Funding	1.1	1.2	Updated the funding statement to include funding New Zealand Health Research Council.	Clarification only; no implications for the planned health economic analysis.

14. APPENDIX 3: CASE REPORT FORMS

ARISE FLUIDS Study
FORM
Randomisation

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1. Patient Demographics

1.1 Patient Initials ☐☐☐ *FML or F - L*

1.2 Date of Birth ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)
NZ Sites: leave day blank & enter only month and year

1.3 Sex ☐ Male ☐ Female

1.4 Date & time of ED triage presentation ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

1.5 Date & time LAST inclusion criterion met See instructions on page 2 ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

1.6 Patient weight *Actual or estimated* ☐☐☐ Kg

2. Inclusion Criteria: *Must answer YES to ALL for patient to be eligible – Must meet these criteria in the ED*

2.1	Clinically suspected infection	☐ No	☐ Yes
2.2	Systolic blood pressure (SBP) <90 mm Hg OR mean arterial pressure (MAP) <65 mm Hg, despite a ≥ 1000 ml cumulative total bolus of IV fluid administered over a maximum of 60 min, including pre-hospital boluses	☐ No	☐ Yes
2.3	Arterial or venous blood lactate >2.0 mmol/L	☐ No	☐ Yes
2.4	At least one dose of an IV antimicrobial has been commenced	☐ No	☐ Yes

3. Exclusion Criteria: *Must answer NO to each question for patient to be eligible*

3.1	Age < 18 years	☐ No	☐ Yes
3.2	Confirmed or suspected pregnancy	☐ No	☐ Yes
3.3	Transferred from another acute care facility	☐ No	☐ Yes
3.4	Hypotension suspected to be due to a non-sepsis cause	☐ No	☐ Yes
3.5	>2L total IV fluid administered (including pre-hospital **bolus fluids** but excludes drugs and flushes)	☐ No	☐ Yes
3.6	More than 6 hours has elapsed since presentation to the ED or more than 2 hours has elapsed since last inclusion criterion has been met	☐ No	☐ Yes
3.7	Treating clinician considers that one or both of the treatment regimens are not suitable for the patient OR the study protocol cannot be delivered e.g. limitation of care, requirement for immediate surgery	☐ No	☐ Yes
3.7.1	Specify reason: _____		
3.8	Death is imminent or inevitable	☐ No	☐ Yes
3.9	Underlying disease that makes survival to 90 days unlikely	☐ No	☐ Yes
3.10	Inability to follow patient up to day-90 e.g. unstable accommodation, overseas visitor	☐ No	☐ Yes
3.11	Previously enrolled in this study	☐ No	☐ Yes
3.12	Other, specify: _____	☐ No	☐ Yes

If patient is eligible (meets all Inclusion Criteria but has no Exclusion Criteria) randomise & complete page 2
If patient is NOT eligible, please enter information into online Screening Log

ARISE FLUIDS Form Randomisation V1.1 Page 1 of 2

ARISE FLUIDS Study
FORM
Randomisation

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4. Randomisation Details - *Automatically populated by database upon randomisation*

4.1 Patient study number ☐☐☐ – ☐☐☐☐
3 Digit SITE number *4 Digit PATIENT number*

4.2 Date and time of randomisation ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐
dd mmm yyyy hours minutes

4.3 Randomised to
☐ **Vasopressors arm**: Restricted fluids and early vasopressors
☐ **Fluids arm:** Larger fluid volume and later vasopressors, if required

LAST inclusion criteria met data point instructions

Date and time LAST inclusion criterion met: ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐
dd mmm yyyy hours minutes

To determine the 'LAST inclusion criteria met', complete the following information. This is the last date & time from the below information.

First blood pressure criteria met:

The blood pressure criteria must have been met after at least 1000ml cumulative total bolus of IV fluid administered over a maximum of 60 minutes. This fluid includes pre-hospital boluses given in the ambulance.

Patient may have met the SBP and/or the MAP criteria. Enter the blood pressure criteria they met first. The reading may be from either a non-invasive blood pressure cuff (NIBP) or an accurate arterial line.

NOTE: they can only meet both the SBP & MAP criteria if they are on the same BP measurement. This must be the first SBP or MAP to be low and meet the inclusion criteria after receiving 1L of fluid resuscitation. The BP may drop further after meeting the inclusion criteria – collect the first SBP &/or MAP only which may not be the lowest.

Systolic Blood Pressure < 90 mm Hg ☐ No ☐ Yes → If YES, SBP ☐☐ mm Hg

And/or

Mean Arterial Pressure < 65 mm Hg ☐ No ☐ Yes → If YES, MAP ☐☐ mm Hg

Date & time **first blood pressure** (SBP &/or MAP) criteria met ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐
dd mmm yyyy hours minutes

First lactate criteria met:

Enter the first blood lactate level which is >2.0 mmol/L.. E.g. 2.1 mmol/L. This may be a lactate from an arterial or venous sample.

If there are more than one lactate result >2.0 mmol/L then enter the first result and the date and time this sample was taken.

Arterial or venous lactate ☐☐.☐ mmol/L

Date & time first Lactate criteria met sample taken: ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐
dd mmm yyyy hours minutes

Antimicrobial criteria met:

Date & time 1st dose of IV antimicrobial commenced ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐
dd mmm yyyy hours minutes

ARISE FLUIDS Form Randomisation V1.1 Page 2 of 2

ARISE FLUIDS Study
FORM 1
Eligibility & Baseline

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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1.1 Eligibility Data — *Indicate the inclusion criteria data met by the patient prior to randomisation*

1.1.1 Date and time of ED triage presentation ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

First Blood pressure criteria met:

1.1.2 Systolic Blood Pressure < 90 mm Hg ☐ No ☐ Yes → If YES, 1.1.2.1 SBP ☐☐ mm Hg

And/or

1.1.3 Mean Arterial Pressure < 65 mm Hg ☐ No ☐ Yes → If YES, 1.1.3.1 MAP ☐☐ mm Hg

1.1.4 Date & time **first blood pressure** (SBP &/or MAP) criteria met ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

Lactate criteria met:

1.1.5 Arterial or venous lactate ☐☐.☐ mmol/L

1.1.5.1 Date & time lactate criteria first met ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

Antimicrobial criteria met:

1.1.6 Date & time 1st dose of IV antimicrobial commenced ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

1.1.7 Date & time last inclusion criteria met ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

1.2 Patient Demographics

1.2.1 Date of Birth ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) NZ Sites: leave **day** blank & enter only **month** and **year**

1.2.2 Sex ☐ Male ☐ Female

1.2.3 Weight ☐☐☐ kg

1.2.4 Usual residence ☐ Home ☐ Long term care facility

1.2.5 Functional status ☐ Independent with all ADLs ☐ Requires help with at least one ADL

1.2.6 Ethnicity NZ Sites only
☐ European ☐ Asian
☐ Maori ☐ Middle East/Latin American/African
☐ Pacific Peoples ☐ Other ethnicity

1.3. Patient Co-morbidities

1.3.1 Does the patient have any of the following pre-existing comorbidities ☐ No ☐ Yes Indicate ALL that apply

☐ Myocardial infarction
☐ Congestive cardiac failure
☐ Peripheral vascular disease
☐ Cerebrovascular disease
☐ Dementia
☐ Chronic obstructive pulmonary disease
☐ Peptic ulcer disease
☐ Kidney disease
☐ Connective tissue disease
☐ Hemiplegia or paraplegia
☐ Liver disease → ☐ Mild ☐ Moderate-severe
☐ Diabetes → ☐ Moderate ☐ End organ damage
MOD = on medication
☐ Solid tumour
☐ Leukaemia/Lymphoma
☐ Metastatic solid tumour
☐ AIDS

ARISE FLUIDS Study
FORM 1
Eligibility & Baseline

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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1.4 Vital Signs — *closest to but prior to randomisation*

1.4.1	Core temperature	☐☐.☐ °C	☐ Not available	
1.4.2	Heart rate	☐☐☐ bpm	☐ Not available	
1.4.3	SBP	☐☐☐ mm Hg	☐ Not available	
1.4.4	DBP	☐☐☐ mm Hg	☐ Not available	
1.4.5	Respiratory rate	☐☐ Breaths per min	☐ Not available	
1.4.6	Non-sedated GCS	☐☐	☐ Not available	
1.4.7	SpO_2	☐☐☐ %	☐ Not available	
1.4.7.1	FiO_2	☐.☐☐	☐ Not available	Complete FiO^2 only if SpO^2 available. FiO^2 must correspond to oxygen pt was on for SpO^2

1.5 Baseline SOFA & APACHE II Scores — worst parameters during the 24 hours *prior to randomisation*

1.5.1	SOFA Respiratory	☐	☐ Not available
1.5.2	SOFA Cardiovascular	☐	☐ Not available
1.5.3	SOFA Liver	☐	☐ Not available
1.5.4	SOFA Renal	☐	☐ Not available
1.5.5	SOFA Coagulation	☐	☐ Not available
1.5.6	APACHE II Score	☐☐	

1.6 Laboratory Values — *closest to but prior to randomisation*

1.6.1	Creatinine	☐☐☐ umol/L	OR	☐.☐☐ mg/dL	☐ Not available	
1.6.2	Bilirubin	☐☐.☐ umol/L			☐ Not available	
1.6.3	Lactate	☐☐.☐ mmol/L			☐ Not available	
1.6.4	Haemoglobin	☐☐☐ g/L			☐ Not available	
1.6.5	WCC	☐☐.☐ X 10^9/L			☐ Not available	
1.6.6	Platelet count	☐☐☐ X 10^9/L			☐ Not available	
1.6.7	pH	☐.☐☐			☐ Not available	

ARISE FLUIDS Study
FORM 1
Eligibility & Baseline

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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1.7 IV Fluid Therapy

- Include pre-hospital & ED bolus fluids & blood products
- DO NOT include fluids for medication delivery e.g. midazolam, noradrenaline, drugs and flushes

1.7.1 Total volume of IV fluid administered to the time final eligibility criterion met ☐☐☐☐☐ mls

1.7.2 Total volume of IV fluid administered from the time final eligibility criterion met until randomisation ☐☐☐☐☐ mls

End of Form

OFFICIAL

ARISE FLUIDS Study
FORM 2
Hourly Data T0-T6

Patient Study No: ☐☐☐ – ☐☐☐

Patient Initials: ☐☐☐

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2.0 Hourly Data Completion

Please select all time points for which data is available	☐ T1 data available	☐ T2 data available	☐ T3 data available	☐ T4 data available	☐ T5 data available	☐ T6 data available

2. IV Fluid Therapy T0-T6

NOTE: T1 is from randomisation until end of 1st full hour i.e. R = 0910 h, T1 = 1100 h	T1 ☐☐:00 (hours / minutes)	T2 ☐☐:00 (hours / minutes)	T3 ☐☐:00 (hours / minutes)	T4 ☐☐:00 (hours / minutes)	T5 ☐☐:00 (hours / minutes)	T6 ☐☐:00 (hours / minutes)
Did the patient receive IV fluids this hour?	2.1.1 ☐ No ☐ Yes If YES, Complete below	2.2.1 ☐ No ☐ Yes If YES, Complete below	2.3.1 ☐ No ☐ Yes If YES, Complete below	2.4.1 ☐ No ☐ Yes If YES, Complete below	2.5.1 ☐ No ☐ Yes If YES, Complete below	2.6.1 ☐ No ☐ Yes If YES, Complete below
Did the patient receive IV crystalloid this hour?	2.1.2 ☐ No ☐ Yes If YES, 2.1.2.1 ☐☐☐☐☐ mls	2.2.2 ☐ No ☐ Yes If YES, 2.2.2.1 ☐☐☐☐☐ mls	2.3.2 ☐ No ☐ Yes If YES, 2.3.2.1 ☐☐☐☐☐ mls	2.4.2 ☐ No ☐ Yes If YES, 2.4.2.1 ☐☐☐☐☐ mls	2.5.2 ☐ No ☐ Yes If YES, 2.5.2.1 ☐☐☐☐☐ mls	2.6.2 ☐ No ☐ Yes If YES, 2.2.6.2 ☐☐☐☐☐ mls
Did the patient receive IV colloid this hour?	2.1.3 ☐ No ☐ Yes If YES, 2.1.3.1 ☐☐☐☐☐ mls	2.2.3 ☐ No ☐ Yes If YES, 2.2.3.1 ☐☐☐☐☐ mls	2.3.3 ☐ No ☐ Yes If YES, 2.3.3.1 ☐☐☐☐☐ mls	2.4.3 ☐ No ☐ Yes If YES, 2.4.3.1 ☐☐☐☐☐ mls	2.5.3 ☐ No ☐ Yes If YES, 2.5.3.1 ☐☐☐☐☐ mls	2.6.3 ☐ No ☐ Yes If YES, 2.6.3.1 ☐☐☐☐☐ mls
Did the patient receive IV blood products this hour?	2.1.4 ☐ No ☐ Yes If YES, 2.1.4.1 ☐☐☐☐☐ mls	2.2.4 ☐ No ☐ Yes If YES, 2.2.4.1 ☐☐☐☐☐ mls	2.3.4 ☐ No ☐ Yes If YES, 2.3.4.1 ☐☐☐☐☐ mls	2.4.4 ☐ No ☐ Yes If YES, 2.4.4.1 ☐☐☐☐☐ mls	2.5.4 ☐ No ☐ Yes If YES, 2.5.4.1 ☐☐☐☐☐ mls	2.6.4 ☐ No ☐ Yes If YES, 2.6.4.1 ☐☐☐☐☐ mls

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ARISE FLUIDS Study
FORM 3
Six Hourly Data (T6, T12, T18, T24)

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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3.0 Six Hourly Data Completion

Please select all time points for which data is available	☐ No data available ☐ T6 data available ☐ T12 data available ☐ T18 data available ☐ T24 data available

3.1 Vital Signs

	Data at T6: 6 hours post-randomisation (± 1 hour)		Data at T12: 12 hours post-randomisation (± 2 hours)	
Core Temperature	3.1.1.1 ☐☐.☐ °C	☐ Not available	3.1.2.1 ☐☐.☐ °C	☐ Not available
Heart Rate	3.1.1.2 ☐☐☐ bpm	☐ Not available	3.1.2.2 ☐☐☐ bpm	☐ Not available
MAP	3.1.1.3 ☐☐☐ mm Hg	☐ Not available	3.1.2.3 ☐☐☐ mm Hg	☐ Not available
Respiratory Rate	3.1.1.4 ☐☐ Breaths per min	☐ Not available	3.1.2.4 ☐☐ Breaths per min	☐ Not available
SpO_2	3.1.1.5 ☐☐☐ %	☐ Not available	3.1.2.5 ☐☐☐ %	☐ Not available
	Data at T18: 18 hours post-randomisation (± 2 hours)		**Data at T24: 24 hours post-randomisation (± 4 hours)**	
Core Temperature	3.1.3.1 ☐☐.☐ °C	☐ Not available	3.1.4.1 ☐☐.☐ °C	☐ Not available
Heart Rate	3.1.3.2 ☐☐☐ bpm	☐ Not available	3.1.4.2 ☐☐☐ bpm	☐ Not available
MAP	3.1.3.3 ☐☐☐ mm Hg	☐ Not available	3.1.4.3 ☐☐☐ mm Hg	☐ Not available
Respiratory Rate	3.1.3.4 ☐☐ Breaths per min	☐ Not available	3.1.4.4 ☐☐ Breaths per min	☐ Not available
SpO_2	3.1.3.5 ☐☐☐ %	☐ Not available	3.1.4.5 ☐☐☐ %	☐ Not available

ARISE FLUIDS Study
FORM 3
Six Hourly Data (T6, T12, T18, T24)

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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3.2 Vasopressors infusion

	Data at T6: 6 hours post-randomisation	Data at T12: 12 hours post-randomisation
Was the patient on **noradrenaline** at this time point?	3.2.1.1 ☐ No ☐ Yes 3.2.1.1.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min	3.2.2.1 ☐ No ☐ Yes 3.2.2.1.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min
Was the patient on **adrenaline** at this time point?	3.2.1.2 ☐ No ☐ Yes 3.2.1.2.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min	3.2.2.2 ☐ No ☐ Yes 3.2.2.2.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min
Was the patient on **vasopressin** at this time point?	3.2.1.3 ☐ No ☐ Yes 3.2.1.3.1 ☐☐.☐☐ IU/hr	3.2.2.3 ☐ No ☐ Yes 3.2.2.3.1 ☐☐.☐☐ IU/hr
Was the patient on **metaraminol** at this time point?	3.2.1.4 ☐ No ☐ Yes 3.2.1.4.1 ☐☐☐ mg/hr	3.2.2.4 ☐ No ☐ Yes 3.2.2.4.1 ☐☐☐ mg/hr
Was the patient on **phenylephrine** at this time point?	3.2.1.5 ☐ No ☐ Yes 3.2.1.5.1 ☐☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min	3.2.2.5 ☐ No ☐ Yes 3.2.2.5.1 ☐☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min
Was the patient on **ANOTHER vasopressor infusion** at this time point?	3.2.1.6 ☐ No ☐ Yes 3.2.1.6.1 ☐☐☐ mls/hr 3.2.1.6.2 Name: ☐☐☐☐☐☐☐☐☐☐ 3.2.1.6.3 Concentration ☐☐.☐☐ ☐ mg ☐ mcg ☐ IU / ☐☐☐ mL	3.2.2.6 ☐ No ☐ Yes 3.2.2.6.1 ☐☐☐ mls/hr 3.2.2.6.2 Name: ☐☐☐☐☐☐☐☐☐☐ 3.2.2.6.3 Concentration ☐☐.☐☐ ☐ mg ☐ mcg ☐ IU / ☐☐☐ mL

	Data at T18: 18 hours post-randomisation	Data at T24: 24 hours post-randomisation
Was the patient on **noradrenaline** at this time point?	3.2.3.1 ☐ No ☐ Yes 3.2.3.1.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min	3.2.4.1 ☐ No ☐ Yes 3.2.4.1.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min
Was the patient on **adrenaline** at this time point?	3.2.3.2 ☐ No ☐ Yes 3.2.3.2.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min	3.2.4.2 ☐ No ☐ Yes 3.2.4.2.1 ☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min
Was the patient on **vasopressin** at this time point?	3.2.3.3 ☐ No ☐ Yes 3.2.3.3.1 ☐☐.☐☐ IU/hr	3.2.4.3 ☐ No ☐ Yes 3.2.4.3.1 ☐☐.☐☐ IU/hr
Was the patient on **metaraminol** at this time point?	3.2.3.4 ☐ No ☐ Yes 3.2.3.4.1 ☐☐☐ mg/hr	3.2.4.4 ☐ No ☐ Yes 3.2.4.4.1 ☐☐☐ mg/hr
Was the patient on **phenylephrine** at this time point?	3.2.3.5 ☐ No ☐ Yes 3.2.3.5.1 ☐☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min	3.2.4.5 ☐ No ☐ Yes 3.2.4.5.1 ☐☐☐.☐☐ ☐ mcg/min ☐ mcg/kg/min
Was the patient on **ANOTHER vasopressor infusion** at this time point?	3.2.3.6 ☐ No ☐ Yes 3.2.3.6.1 ☐☐☐ mls/hr 3.2.3.6.2 Name: ☐☐☐☐☐☐☐☐☐☐ 3.2.3.6.3 Concentration ☐☐.☐☐ ☐ mg ☐ mcg ☐ IU / ☐☐☐ mL	3.2.4.6 ☐ No ☐ Yes 3.2.4.6.1 ☐☐☐ mls/hr 3.2.4.6.2 Name: ☐☐☐☐☐☐☐☐☐☐ 3.2.4.6.3 Concentration ☐☐.☐☐ ☐ mg ☐ mcg ☐ IU / ☐☐☐ mL

ARISE FLUIDS Study
FORM 3
Six Hourly Data (T6, T12, T18, T24)

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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3.3 Laboratory Data

	Data at T6: 6 hours post-randomisation (± 1 hour)			Data at T12: 12hours post-randomisation (± 2 hours)		
Haemoglobin	3.3.1.1	☐☐☐ g/L	☐ Not available	3.3.2.1	☐☐☐ g/L	☐ Not available
Lactate	3.3.1.2	☐☐.☐ mmol/L	☐ Not available	3.3.2.2	☐☐.☐ mmol/L	☐ Not available
PaO2	3.3.1.3	☐☐☐ mm Hg	☐ Not available	3.3.2.3	☐☐☐ mm Hg	☐ Not available
PaCO2	3.3.1.4	☐☐☐ mm Hg	☐ Not available	3.3.2.4	☐☐☐ mm Hg	☐ Not available
pH	3.3.1.5	☐.☐☐	☐ Not available	3.3.2.5	☐.☐☐	☐ Not available
Bicarbonate⁻	3.3.1.6	☐☐ mmol/L	☐ Not available	3.3.2.6	☐☐ mmol/L	☐ Not available
FiO2	3.3.1.7	☐.☐☐	☐ Not available	3.3.2.7	☐.☐☐	☐ Not available
	Data at T18: 18 hours post-randomisation (± 2 hours)			Data at T24: 24 hours post-randomisation (± 4 hours)		
Haemoglobin	3.3.3.1	☐☐☐ g/L	☐ Not available	3.3.4.1	☐☐☐ g/L	☐ Not available
Lactate	3.3.3.2	☐☐.☐ mmol/L	☐ Not available	3.3.4.2	☐☐.☐ mmol/L	☐ Not available
PaO2	3.3.3.3	☐☐☐ mm Hg	☐ Not available	3.3.4.3	☐☐☐ mm Hg	☐ Not available
PaCO2	3.3.3.4	☐☐☐ mm Hg	☐ Not available	3.3.4.4	☐☐☐ mm Hg	☐ Not available
pH	3.3.3.5	☐.☐☐	☐ Not available	3.3.4.5	☐.☐☐	☐ Not available
Bicarbonate	3.3.3.6	☐☐ mmol/L	☐ Not available	3.3.4.6	☐☐ mmol/L	☐ Not available
FiO2	3.3.3.7	☐.☐☐	☐ Not available	3.3.4.7	☐.☐☐	☐ Not available

ARISE FLUIDS Study
FORM 3
Six Hourly Data (T6, T12, T18, T24)

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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3.4 Fluids

	T6 Data: 0-6 hours post-randomisation	T12 Data: Fluids 6-12 hours post-randomisation
Did the patient receive **IV fluids** within this period?		3.4.1.1 ☐ No ☐ Yes
Did the patient receive **IV crystalloid** within this period?		If YES, 3.4.1.2 ☐ No ☐ Yes 3.4.1.2.1 ☐☐☐☐☐ mls
Did the patient receive **IV colloid** within this period?		3.4.1.3 ☐ No ☐ Yes 3.4.1.3.1 ☐☐☐☐☐ mls
Did the patient receive **IV blood products** within this period?		3.4.1.4 ☐ No ☐ Yes 3.4.1.4.1 ☐☐☐☐☐ mls

	T18 Data: Fluids 12-18 hours post-randomisation	T24 Data: Fluids 18-24 hours post-randomisation
Did the patient receive **IV fluids** within this period?	3.4.2.1 ☐ No ☐ Yes	3.4.3.1 ☐ No ☐ Yes
Did the patient receive **IV crystalloid** within this period?	If YES, 3.4.2.2 ☐ No ☐ Yes 3.4.2.2.1 ☐☐☐☐☐ mls	If YES, 3.4.3.2 ☐ No ☐ Yes 3.4.3.2.1 ☐☐☐☐☐ mls
Did the patient receive **IV colloid** within this period?	3.4.2.3 ☐ No ☐ Yes 3.4.2.3.1 ☐☐☐☐☐ mls	3.4.3.3 ☐ No ☐ Yes 3.4.3.3.1 ☐☐☐☐☐ mls
Did the patient receive **IV blood products** within this period?	3.4.2.4 ☐ No ☐ Yes 3.4.2.4.1 ☐☐☐☐☐ mls	3.4.3.4 ☐ No ☐ Yes 3.4.3.4.1 ☐☐☐☐☐ mls

ARISE FLUIDS Form 3 Six Hourly Data V1

Page 4 of 4

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ARISE FLUIDS Study
FORM 4
Microbial Data

Patient Study No: ☐☐☐ – ☐☐☐

Patient Initials: ☐☐☐

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4.1 Positive Culture — *within 72 hours of ED presentation*

4.1.1 Did the patient have any positive cultures taken within 72 hours of ED presentation? ☐ No ☐ Yes

If YES, **4.1.1.1** Date and time of collection of the 1st positive culture: ☐☐ / ☐☐☐ / ☐☐☐☐ ☐☐ : ☐☐
(dd / mmm / yyyy / hours / minutes)

4.1.1.2 Indicate the 1st positive culture sample type/site:

- ☐ Respiratory
- ☐ Blood
- ☐ Urine
- ☐ Soft tissue
- ☐ Bone/joint
- ☐ Other sterile site

4.1.1.3 Indicate ALL the positive cultures organisms:

- ☐ Gram positive
- ☐ Gram negative
- ☐ Viral
- ☐ Fungal
- ☐ Parasitic
- ☐ Other

4.1.2 Did the patient have a 2nd positive cultures taken within 72 hours of ED presentation for a different organism? ☐ No ☐ Yes

If YES, **4.1.2.1** Date and time of the 2nd positive culture collected: ☐☐ / ☐☐☐ / ☐☐☐☐ ☐☐ : ☐☐
(dd / mmm / yyyy / hours / minutes)

4.1.2.2 Indicate the positive cultures sample type/site:

- ☐ Respiratory
- ☐ Blood
- ☐ Urine
- ☐ Soft tissue
- ☐ Bone/joint
- ☐ Other sterile site

4.1.2.3 Indicate ALL the positive cultures organisms:

- ☐ Gram positive
- ☐ Gram negative
- ☐ Viral
- ☐ Fungal
- ☐ Parasitic
- ☐ Other

4.1.3 Did the patient have a 3rd positive cultures taken within 72 hours of ED presentation for a different organism? ☐ No ☐ Yes

If YES, **4.1.3.1** Date and time of the 3rd positive culture collected: ☐☐ / ☐☐☐ / ☐☐☐☐ ☐☐ : ☐☐
(dd / mmm / yyyy / hours / minutes)

4.1.3.2 Indicate the positive cultures sample type/site:

- ☐ Respiratory
- ☐ Blood
- ☐ Urine
- ☐ Soft tissue
- ☐ Bone/joint
- ☐ Other sterile site

4.1.3.3 Indicate ALL the positive cultures organisms:

- ☐ Gram positive
- ☐ Gram negative
- ☐ Viral
- ☐ Fungal
- ☐ Parasitic
- ☐ Other

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ARISE FLUIDS Study
FORM 4
Microbial Data

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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4.2 Site of Sepsis

4.2.1. Principal Investigator's assessment of the primary site of infection that was responsible for the septic shock admission:

NOTE: This assessment must be performed at resolution of septic shock or death, whichever occurs first

- ☐ Pulmonary
- ☐ Primary Blood Stream e.g. malaria
- ☐ Urinary Tract
- ☐ Skin and Soft Tissue
- ☐ Intra-abdominal
- ☐ Central Nervous System
- ☐ No clear source/Unknown
- ☐ OTHER, 4.2.2 Specify: _____

4.3 Antimicrobial Appropriateness

4.3.1 In the Principal Investigator's opinion, was the first antimicrobial therapy administered appropriate for the treatment of the infection ?

- ☐ No
- ☐ Yes
- ☐ Unknown

4.3.2 In the Principal Investigator's opinion, was the antimicrobial therapy administered in the first 72 hours from ED admission appropriate for the treatment of the infection ?

- ☐ No
- ☐ Yes
- ☐ Unknown

4.4 COVID Status

4.4.1 Is this episode of illness considered to be due to acute COVID-19 infection (confirmed by SARS-CoV2 PCR or serological test)?

- ☐ No
- ☐ Yes

End of Form

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ARISE FLUIDS Study
FORM 5
Antimicrobial Data

Patient Study No: ☐☐☐ – ☐☐☐

Patient Initials: ☐☐☐

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5.1 Antimicrobial Data- *Enter all IV antimicrobials administered from ED presentation to T72 hours*

5.1.1 Antimicrobial therapy group	5.1.2 Date & time 1st dose commenced
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes
☐ 1. ☐ 3. ☐ 5. ☐ 7. ☐ 9. ☐ 2. ☐ 4. ☐ 6. ☐ 8.	☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ dd mmm yyyy hours minutes

Numbered antimicrobial list for indication at **5.1.1**

1. **Penicillins include**: amoxycillin/ampicillin; amoxicillin/clavulanate, dicloxacillin, flucloxacillin, penicillin, piperacillin/tazobactam;
2. **Cephalosporins include:** ceftazidime, cefazolin, cefepime, cefotaxime, ceftriaxone, cefuroxime, cephalexin, cephalothin;
3. **Macrolides include:** azithromycin, erythromycin, roxithromycin;
4. **Aminoglycosides include:** amikacin, gentamicin,
5. **Carbapenems include:** meropenem
6. **Fluoroquinolones includes:** ciprofloxacin, moxifloxacin;
7. **Glycopeptides include:** vancomycin;
8. **Nitroimidazoles include:** metronidazole;
9. **Other includes:** amphotericin B, acyclovir, aztreonam, chloramphenicol, linezolid, sulfamethoxazole/trimethoprim;

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6.1 Invasive Mechanical Ventilation – IMV – *During this hospital admission*

6.1.1 Did the patient receive **Invasive Mechanical Ventilation**? ☐ No ☐ Yes

6.1.1.1 IMV start date and time: dd / mmm / yyyy hours : minutes

6.1.1.2 IMV stop date and time: dd / mmm / yyyy hours : minutes

6.1.2 Did the patient have another episode of **IMV**? ☐ No ☐ Yes

6.1.2.1 IMV start date and time: dd / mmm / yyyy hours : minutes

6.1.2.2 IMV stop date and time: dd / mmm / yyyy hours : minutes

6.1.3 Did the patient have another episode of **IMV**? ☐ No ☐ Yes

6.1.3.1 IMV start date and time: dd / mmm / yyyy hours : minutes

6.1.3.2 IMV stop date and time: dd / mmm / yyyy hours : minutes

6.1.4 Did the patient have another episode of **IMV**? ☐ No ☐ Yes

6.1.4.1 IMV start date and time: dd / mmm / yyyy hours : minutes

6.1.4.2 IMV stop date and time: dd / mmm / yyyy hours : minutes

6.2 Non-Invasive Ventilation – NIV – *During this hospital admission*

6.2.1 Did the patient receive **Non-Invasive Ventilation**? ☐ No ☐ Yes

6.2.1.1 NIV start date and time: dd / mmm / yyyy hours : minutes

6.2.1.2 NIV stop date and time: dd / mmm / yyyy hours : minutes

6.2.2 Did the patient have another episode of **NIV**? ☐ No ☐ Yes

6.2.2.1 NIV start date and time: dd / mmm / yyyy hours : minutes

6.2.2.2 NIV stop date and time: dd / mmm / yyyy hours : minutes

6.2.3 Did the patient have another episode of **NIV**? ☐ No ☐ Yes

6.2.3.1 NIV start date and time: dd / mmm / yyyy hours : minutes

6.2.3.2 NIV stop date and time: dd / mmm / yyyy hours : minutes

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ARISE FLUIDS Study
FORM 6
Treatment & Outcomes

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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6.3 Acute Renal Replacement Therapy – RRT – *During this hospital admission*

6.3.1 Worst post-randomisation creatinine (from randomisation until ED Discharge if went to the ward, OR up to day 7or ICU discharge, whichever occurs first, if went to ICU) ☐☐☐ umol/L OR ☐.☐☐ mg/dL

6.3.2 Did the patient have an episode of acute **RRT**? ☐ No ☐ Yes

6.3.2.1 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.3.2.2 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.3.3 Did the patient have another episode of **RRT**? ☐ No ☐ Yes

6.3.3.1 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.3.3.2 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.3.4 Did the patient have another episode of **RRT**? ☐ No ☐ Yes

6.3.4.1 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.3.4.2 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.4 Extra-Corporeal Membrane Oxygenation – ECMO – *During this hospital admission*

6.4.1 Did the patient have an episode of **ECMO**? ☐ No ☐ Yes

6.4.1.1 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.4.1.2 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.4.2 Did the patient have another episode **ECMO**? ☐ No ☐ Yes

6.4.2.1 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.4.2.2 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5 Vasopressor infusions – *During this hospital admission*

6.5.1 Did the patient receive vasopressor support? ☐ No ☐ Yes

6.5.1.1 Which vasopressor did the patient receive?

- ☐ Noradrenaline
- ☐ Adrenaline
- ☐ Vasopressin
- ☐ Metaraminol
- ☐ Phenylephrine
- ☐ Other

If OTHER, 6.5.2.1.1 specify: ☐

6.5.1.2 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.1.3 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

ARISE FLUIDS Study
FORM 6
Treatment & Outcomes

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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6.5 Vasopressor infusions – *During this hospital admission*

6.5.2 Did the patient receive another vasopressor or another episode of vasopressor infusion support? ☐ No ☐ Yes

6.5.2.1 Which vasopressor did the patient receive?
☐ Noradrenaline ☐ Phenylephrine
☐ Adrenaline ☐ Other
☐ Vasopressin If OTHER, 6.5.2.1.1 specify: ☐☐☐☐☐☐☐☐☐☐
☐ Metaraminol

6.5.2.2 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.2.3 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.3 Did the patient receive another vasopressor or another episode of vasopressor infusion support? ☐ No ☐ Yes

6.5.3.1 Which vasopressor did the patient receive?
☐ Noradrenaline ☐ Phenylephrine
☐ Adrenaline ☐ Other
☐ Vasopressin If OTHER, 6.5.3.1.1 specify: ☐☐☐☐☐☐☐☐☐☐
☐ Metaraminol

6.5.3.2 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.3.3 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.4 Did the patient receive another vasopressor or another episode of vasopressor infusion support? ☐ No ☐ Yes

6.5.4.1 Which vasopressor did the patient receive?
☐ Noradrenaline ☐ Phenylephrine
☐ Adrenaline ☐ Other
☐ Vasopressin If OTHER, 6.5.4.1.1 specify: ☐☐☐☐☐☐☐☐☐☐
☐ Metaraminol

6.5.4.2 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.4.3 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.5 Did the patient receive another vasopressor or another episode of vasopressor infusion support? ☐ No ☐ Yes

6.5.5.1 Which vasopressor did the patient receive?
☐ Noradrenaline ☐ Phenylephrine
☐ Adrenaline ☐ Other
☐ Vasopressin If OTHER, 6.5.5.1.1 specify: ☐☐☐☐☐☐☐☐☐☐
☐ Metaraminol

6.5.5.2 Start date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

6.5.5.3 Stop date and time: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ (hours:minutes)

ARISE FLUIDS Study
FORM 6
Treatment & Outcomes

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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6.6 Study Treatment Arms – Vascular Access & Complications — Up to T24 hours

6.6.1 Did the patient receive **vasopressor infusion via a peripheral line from T0 to T24?** ☐ No ☐ Yes

If Yes **6.6.1.1** Date and time of start of vasopressor infusion via peripheral line: ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

If Yes **6.6.1.2** Did the patient have a complication related to the administration of vasopressors via peripheral line: ☐ No ☐ Yes

If Yes **6.6.1.2.1** Tissue necrosis ☐ No ☐ Yes

6.6.1.2.2 Date of tissue necrosis ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

6.6.1.3.1 Other: ☐ No ☐ Yes **6.7.1.3.2** Specify: ☐

6.6.1.3.3 Date of OTHER complication ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

6.6.2 Did the patient have a **central venous line/ PICC line inserted from T0 to T24?** ☐ No ☐ Yes

If Yes **6.6.2.1** Date and time of CVC/PICC insertion: ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

If Yes **6.6.2.1.1** Did the patient receive a vasopressor infusion via CVC/PICC line from T0 to T24? ☐ No ☐ Yes

If Yes **6.6.2.1.2** Date & time vasopressor via CVC/ PICC started from T0 to T24: ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

6.6.2.2 Did the patient have CVC/PICC complication related to the study intervention? ☐ No ☐ Yes

If Yes **6.6.2.2.1** Pneumothorax ☐ No ☐ Yes

6.6.2.2.2 Date of & time Pneumothorax ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

6.6.2.2.3 Arterial puncture ☐ No ☐ Yes

6.6.2.2.4 Date of & time arterial puncture ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

6.6.2.2.5 CVC/PICC related infection ☐ No ☐ Yes

6.6.2.2.6 Date of & time infection ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

6.6.2.2.7 CVC/PICC related thrombosis ☐ No ☐ Yes

6.6.2.2.8 Date of & time CVC thrombosis ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

6.6.2.2.9 Other: ☐ No ☐ Yes **6.7.2.2.9.1** Specify: ☐

6.6.2.2.10 Date & time of OTHER complication ☐☐/☐☐☐/☐☐☐☐ ☐☐:☐☐ (dd / mmm / yyyy hours:minutes)

ARISE FLUIDS Study
FORM 6
Treatment & Outcomes

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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6.6 Study Treatment Arms: Vascular Access & Complications

6.6.3 Did the patient have Acute Pulmonary Oedema (**APO) related to study intervention**? ☐ No ☐ Yes

If Yes **6.6.3.1** Date and time of 1st episode of APO: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

6.6.4 Did the patient have **ischaemic complications which are related to the study intervention**? ☐ No ☐ Yes

If Yes **6.6.4.1** Ischaemic bowel ☐ No ☐ Yes

6.6.4.1.1 Date & time of ischaemic bowel ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

6.6.4.2 Ischaemic digits ☐ No ☐ Yes

6.6.4.2.1 Date & time of ischaemic digits ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

6.6.4.3 Cardiac ischaemia ☐ No ☐ Yes

6.6.4.3.1 Date & time of cardiac ischaemia ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

6.6.4.4 Other: ☐ No ☐ Yes **6.6.4.4.1** Specify: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

6.6.4.4.2 Date and time: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

6.7 Concomitant Therapy – *During this hospital admission*

6.7.1 Did the patient receive IV **steroids** for admission diagnosis of septic shock? ☐ No ☐ Yes

6.7.1.1 Date and time of commencement: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

6.7.2 Did the patient have **surgery/procedure** for the presumed/known source of infection? ☐ No ☐ Yes

6.7.2.1 Date and time of 1st surgery or procedure: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

ARISE FLUIDS Study
FORM 6
Treatment & Outcomes

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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6.8 Daily Fluid Balance – *Day 1 – Day 7 or until ICU discharge, whichever occurs first*

6.8.1	D1 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available
6.8.2	D2 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available
6.8.3	D3 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available
6.8.4	D4 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available
6.8.5	D5 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available
6.8.6	D6 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available
6.8.7	D7 daily fluid balance:	☐ +	☐ -	☐☐☐☐☐ mls	☐	Not available

End of Form

ARISE FLUIDS Study
FORM 7
Consent

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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7.1 Study Consent

7.1.1 Was consent obtained or HREC / IRB approval obtained to use data for this patient?
☐ No → If NO, skip to Q 7.2
☐ Yes → If YES, continue below

7.1.1.1 What model of consent was used for this patient?
☐ Opt-out consent → Go to 7.1.2
☐ Consent to continue → Go to 7.1.3

If **Opt-out** consent was used for this patient to be enrolled into the study:

7.1.2 Was written study information/brochure provided? ☐ No ☐ Yes

If YES, 7.1.2.1 provided to: ☐ Patient — 7.1.2.1.1 Date provided: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)
Tick all that apply
☐ Person responsible — 7.1.2.1.2 Date provided: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

If NO, 7.1.2.2 reason:
☐ Patient died before study information/brochure could be given
☐ Other, 7.1.2.2.1 ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

If **Consent to continue** was used for this patient to be enrolled into the study:

7.1.3 Was consent to continue obtained? ☐ No ☐ Yes

If YES, 7.1.3.1 obtained from :
☐ Patient — 7.1.3.1.1 Date obtained: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)
Tick all that apply
☐ Person responsible — 7.1.3.1.2 Date obtained: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

If NO, 7.1.3.2 reason:
☐ Patient died before consent could be obtained, permission to use data obtained from ethics committee — 7.1.3.2.1 ☐ Pending ☐ Received
☐ Other, 7.1.3.2.2 ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

7.2 Withdrawal/Opt out from Study

7.2.1 Was consent withdrawn, refused or opted-out?
☐ No
☐ Yes → If **YES**, continue below

7.2.2 Who withdrew/opted-out of consent?
☐ Person responsible
☐ Patient

7.2.3 Date of withdrawal, refusal or opt-out ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

7.2.4 Can data be used?
☐ All data can be used for this patient
☐ Data can be used up until date of withdrawal for this patient
☐ No data can be used for this patient

7.2.5 Can Day 90, 6 and 12 month phone call be completed? ☐ No ☐ Yes

End of form

ARISE FLUIDS Form 7 Consent V1 Page 1 of 1

ARISE FLUIDS Study
FORM 8
Discharge Data

Patient Study No: ___ – ___
Patient Initials: ___

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8.1 ED Discharge

8.1.1 ED discharge date and time — dd / mmm / yyyy hours : minutes

8.1.2 ED discharge status ☐ Alive ☐ Deceased

NOTE: if deceased, discharge details are date of time of death

If ALIVE, 8.1.2.1 ED discharge destination

- ☐ ED short stay unit
- ☐ General ward
- ☐ ICU/HDU
- ☐ OT/Radiology then to ward
- ☐ OT/Radiology then to ICU/HDU
- ☐ Transfer to another hospital
- ☐ Home

8.2 ICU Admission and Discharge

8.2.1 Was the patient admitted to ICU? ☐ No ☐ Yes

If YES, 8.2.1.1 ICU admission date and time — dd / mmm / yyyy hours : minutes

8.2.1.2 ICU discharge date and time — dd / mmm / yyyy hours : minutes

8.2.1.3 ICU discharge status ☐ Alive ☐ Deceased

NOTE: if deceased, discharge details are date & time of death

If ALIVE, 8.2.1.3.1 Was the patient discharged to the hospital ward? ☐ No ☐ Yes

8.3 ICU Readmission

8.3.1 Was the patient readmitted to ICU during this hospital admission? ☐ No ☐ Yes

8.3.1.1 First ICU readmission date and time — dd / mmm / yyyy hours : minutes

8.3.1.2 Date and time of ICU discharge — dd / mmm / yyyy hours : minutes

8.3.2.1 Second ICU readmission date and time — dd / mmm / yyyy hours : minutes

8.3.2.2 Date and time of ICU discharge — dd / mmm / yyyy hours : minutes

ARISE FLUIDS Study
FORM 8
Discharge Data

Patient Study No: ___ – ___
Patient Initials: ___

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8.4 Hospital Discharge

8.4.1 Hospital discharge date and time: dd / mmm / yyyy hours : minutes

8.4.2 Hospital discharge status: ☐ Alive ☐ Deceased

NOTE: if deceased, discharge details are date of time of death

If ALIVE, 8.4.2.1 Hospital discharge destination

- ☐ Other hospital ICU
- ☐ Other acute care hospital– not ICU
- ☐ Rehabilitation facility
- ☐ Long term care facility
- ☐ Home

If DECEASED, 8.4.2.2 Cause of death

- ☐ Neurological
- ☐ Arrhythmia
- ☐ Cardiac Shock
- ☐ Septic Shock
- ☐ Hypovolaemic Shock
- ☐ Multi-System Organ Failure
- ☐ Hypoxic Respiratory Failure
- ☐ Metabolic
- ☐ Other

End of form

ARISE FLUIDS Study
FORM 9
Day 90 Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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Day 90 Follow Up-CRF Instructions

- This data forms an important part of the composite primary outcome and therefore particular attention is required.
- If the patient is deceased at D90, then you do NOT need to collect data at Q 9.2 onwards.
- To qualify as an admission to a care facility the admission must have been an overnight stay. Weekend or day leave from a care facility does NOT qualify as a discharge and readmission.
- Ascertain Q 9.2 information from participant/NOK. The 'Patient diary/information collection sheet' given to them should assist this. This information will then be checked against hospital database or verified by email/contact with care facility.

9.1 Day 90 Follow Up

9.1.1 Date Day 90 follow up completed: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

9.1.2 Survival status at day 90:
☐ Alive ☐ Deceased
☐ Lost to follow Up ☐ Declined follow up

If DECEASED,

9.1.2.1 Date of death: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

9.1.2.2 Primary cause of death:
☐ Neurological
☐ Arrhythmia
☐ Cardiac Shock
☐ Septic Shock
☐ Hypovolaemic Shock
☐ Multi-System Organ Failure
☐ Hypoxic Respiratory Failure
☐ Metabolic
☐ Other

9.2 Readmissions/Admissions– *from hospital discharge up to Day 90*

9.2.1 Was the data collected from the patient/NOK of admissions to care facilities after initial hospital discharge? ☐ No ☐ Yes

If NO, **9.2.1.1** Reason why: ☐ Lost to phone/Email contact ☐ Declined follow up

9.2.2 Was the patient admitted to a care facility after index hospital discharge? ☐ No ☐ Yes

If YES, **9.2.2.1** Type of care facility:
☐ Acute care facility
☐ Rehabilitation facility
☐ Long term care facility

9.2.2.2 First readmission/admission date ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

9.2.2.3 Date of discharge ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐ Not discharged at D90

ARISE FLUIDS Study
FORM 9
Day 90 Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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9.2 Readmissions/Admissions– *from hospital discharge up to Day 90*

9.2.3 Was the patient admitted to another care facility after index hospital discharge? ☐ No ☐ Yes

If YES, **9.2.3.1** Type of care facility:
☐ Acute care facility
☐ Rehabilitation facility
☐ Long term care facility

9.2.3.2 Second readmission/admission date ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

9.2.3.3 Date of discharge ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐ Not discharged at D90

9.2.4 Was the patient admitted to another care facility after index hospital discharge? ☐ No ☐ Yes

If YES, **9.2.4.1** Type of care facility:
☐ Acute care facility
☐ Rehabilitation facility
☐ Long term care facility

9.2.4.2 Third readmission/admission date and time ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

9.2.4.3 Date and time of discharge ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐ Not discharged at D90

9.2.5 Was the patient admitted to another care facility after index hospital discharge? ☐ No ☐ Yes

If YES, **9.2.5.1** Type of care facility:
☐ Acute care facility
☐ Rehabilitation facility
☐ Long term care facility

9.2.5.2 Fourth readmission date and time ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

9.2.5.3 Date and time of discharge ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐ Not discharged at D90

9.2.6 Was the patient admitted to another care facility after index hospital discharge? ☐ No ☐ Yes

If YES, **9.2.6.1** Type of care facility:
☐ Acute care facility
☐ Rehabilitation facility
☐ Long term care facility

ARISE FLUIDS Study
FORM 9
Day 90 Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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9.2 Readmissions/Admissions– *from hospital discharge up to Day 90*

9.2.6.2 Fifth readmission/admission date and time ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

9.2.6.3 Date and time of discharge ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐ Not discharged at D90

End of form

ARISE FLUIDS Study
FORM 10
Day 180 Follow Up

Site Study No: ___ ___ ___ – ___ ___ ___
Patient Initials: ___ ___ ___

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10.1 Day 180 Follow Up

10.1.1 Date Day 180 follow up completed: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (dd / mmm / yyyy)

10.1.2 Survival status at day 180:

☐ Alive ☐ Deceased

☐ Lost to follow up ☐ Declined follow up

If DECEASED,

10.1.2.1 Date of death: ___ ___ / ___ ___ ___ / ___ ___ ___ ___ (dd / mmm / yyyy)

10.1.2.2 Primary cause of death:

☐ Neurological
☐ Arrhythmia
☐ Cardiac Shock
☐ Septic Shock
☐ Hypovolaemic Shock
☐ Multi-System Organ Failure
☐ Hypoxic Respiratory Failure
☐ Metabolic
☐ Other

10.2 EQ-5D-5L

10.2.1 Was the EQ-5D-5L completed?

☐ No → **10.2.1.1** Reason why:
- ☐ Deceased
- ☐ Declined
- ☐ Lost to follow up

☐ Yes

10.2.2 Completed by: ☐ Patient ☐ Proxy

10.2.3 **Mobility**

☐ I have no problems in walking about
☐ I have slight problems in walking about
☐ I have moderate problems in walking about
☐ I have severe problems in walking about
☐ I am unable to walk about

ARISE FLUIDS Study
FORM 10
Day 180 Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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10.2 EQ-5D-5L

10.2.4 Self-Care

- ☐ I have no problems washing or dressing myself
- ☐ I have slight problems washing or dressing myself
- ☐ I have moderate problems washing or dressing myself
- ☐ I have severe problems washing or dressing myself
- ☐ I am unable to wash or dress myself

10.2.5 Usual Activities (e.g. work, study, housework, family or leisure activities)

- ☐ I have no problems doing my usual activities
- ☐ I have slight problems doing my usual activities
- ☐ I have moderate problems doing my usual activities
- ☐ I have severe problems doing my usual activities
- ☐ I am unable to do my usual activities

10.2.6 Pain / Discomfort

- ☐ I have no pain or discomfort
- ☐ I have slight pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have severe pain or discomfort
- ☐ I have extreme pain or discomfort

10.2.7 Anxiety / Depression

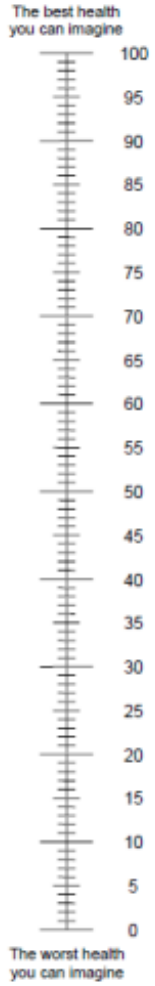
- ☐ I am not anxious or depressed
- ☐ I am slightly anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am severely anxious or depressed
- ☐ I am extremely anxious or depressed

10.2.8 We would like to know how good or bad the patient's health is TODAY.

- The scale is numbered from 0 to 100.
- 100 means the best health that can be imagined.
- 0 means the worst health that can be imagined.
- Mark an X on the scale to indicate how the patient's health is TODAY.
- Now, please write the number marked on the scale in the box below.

Score: ☐☐☐

Health State Scale



ARISE FLUIDS Study
FORM 10
Day 180 Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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10.3 WHODAS 2.0

10.3.1 Was the WHODAS completed? ☐ No → **10.3.1.1** Reason why: ☐ Deceased ☐ Declined ☐ Lost to follow up
☐ Yes

10.3.2 Completed by: ☐ Patient ☐ Proxy

In the past 30 days, how much difficulty did the you/patient have in: *Select one only for each question*

		None	Mild	Moderate	Severe	Extreme or cannot do
10.3.3	Standing for long periods such as 30 minutes					
10.3.4	Taking care of your household responsibilities					
10.3.5	Learning a new task, for example, learning how to get to a new place					
10.3.6	How much of a problem did you have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can					
10.3.7	How much have you been emotionally affected by your health problems					

In the past 30 days, how much difficulty did you/the patient have in: *Select one only for each question*

		None	Mild	Moderate	Severe	Extreme or cannot do
10.3.8	Concentrating on doing something for ten minutes					
10.3.9	Walking a long distance such as a kilometre [or equivalent]					
10.3.10	Washing your whole body					
10.3.11	Getting dressed					
10.3.12	Dealing with people you do not know					
10.3.13	Maintaining a friendship					
10.3.14	Your day-to-day work/school					

10.3.15	Overall, in the past 30 days, how many days were these difficulties present?	☐☐ Days
10.3.16	In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?	☐☐ Days
10.3.17	In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any	☐☐ Days

End of form

ARISE FLUIDS Study
FORM 11
12 Month Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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11.1 12 Month Follow Up

11.1.1 Date 12 month follow up completed: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

11.1.2 Survival status at 12 months

☐ Alive ☐ Deceased

☐ Lost to follow Up ☐ Declined follow up

If DECEASED,

11.1.2.1 Date of death: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

11.1.2.2 Primary cause of death:

☐ Neurological
☐ Arrhythmia
☐ Cardiac Shock
☐ Septic Shock
☐ Hypovolaemic Shock
☐ Multi-System Organ Failure
☐ Hypoxic Respiratory Failure
☐ Metabolic
☐ Other

11.2 EQ5D-5L

11.2.1 Was the EQ5D-5L completed?

☐ No → **11.2.1.1** Reason why:
- ☐ Deceased
- ☐ Declined
- ☐ Lost to follow up

☐ Yes

11.2.2 Completed by: ☐ Patient ☐ Proxy

11.2.3 **Mobility**

- ☐ I have no problems in walking about
- ☐ I have slight problems in walking about
- ☐ I have moderate problems in walking about
- ☐ I have severe problems in walking about
- ☐ I am unable to walk about

ARISE FLUIDS Study
FORM 11
12 Month Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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11.2 EQ5D-5L

11.2.4 Self-Care

- ☐ I have no problems washing or dressing myself
- ☐ I have slight problems washing or dressing myself
- ☐ I have moderate problems washing or dressing myself
- ☐ I have severe problems washing or dressing myself
- ☐ I am unable to wash or dress myself

11.2.5 Usual Activities (e.g. work, study, housework, family or leisure activities)

- ☐ I have no problems doing my usual activities
- ☐ I have slight problems doing my usual activities
- ☐ I have moderate problems doing my usual activities
- ☐ I have severe problems doing my usual activities
- ☐ I am unable to do my usual activities

11.2.6 Pain / Discomfort

- ☐ I have no pain or discomfort
- ☐ I have slight pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have severe pain or discomfort
- ☐ I have extreme pain or discomfort

11.2.7 Anxiety / Depression

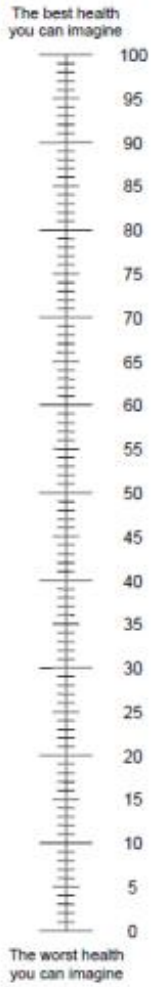
- ☐ I am not anxious or depressed
- ☐ I am slightly anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am severely anxious or depressed
- ☐ I am extremely anxious or depressed

11.2.8 We would like to know how good or bad the patient's health is TODAY.

- The scale is numbered from 0 to 100.
- 100 means the best health that can be imagined.
- 0 means the worst health can be imagined.
- Mark an X on the scale to indicate how the patient's health is TODAY.
- Now, please write the number marked on the scale in the box below.

Score: ☐☐☐

Health State Scale



ARISE FLUIDS Study
FORM 11
12 Month Follow Up

Site Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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11.3 WHODAS 2.0

11.3.1 Was the WHODAS completed?

☐ No → **9.2.1.1** Reason why:
- ☐ Deceased
- ☐ Declined
- ☐ Lost to follow up

☐ Yes

11.3.2 Completed by:

☐ Patient ☐ Proxy

In the past 30 days, how much difficulty did you have in: *(Select one only for each question)*

		None	Mild	Moderate	Severe	Extreme or cannot do
11.3.3	Standing for long periods such as 30 minutes					
11.3.4	Taking care of your household responsibilities					
11.3.5	Learning a new task, for example, learning how to get to a new place					
11.3.6	How much of a problem did you have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can					
11.3.7	How much have you been emotionally affected by your health problems					

In the past 30 days, how much difficulty did you have in: *(Select one only for each question)*

		None	Mild	Moderate	Severe	Extreme or cannot do
11.3.8	Concentrating on doing something for ten minutes					
11.3.9	Walking a long distance such as a kilometre [or equivalent]					
11.3.10	Washing your whole body					
11.3.11	Getting dressed					
11.3.12	Dealing with people you do not know					
11.3.13	Maintaining a friendship					
11.3.14	Your day-to-day work/school					

11.3.15	Overall, in the past 30 days, how many days were these difficulties present?	☐☐ Days
11.3.16	In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?	☐☐ Days
11.3.17	In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?	☐☐ Days

End of form

OFFICIAL

ARISE FLUIDS Study
FORM 12
Adverse Events

Patient Study No: ☐☐☐ – ☐☐☐

Patient Initials: ☐☐☐

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12. Adverse Events

	12.1 Event: NOTE: Do NOT include as AEs events which are collected as study outcomes on FORM 7	12.2 AE Onset Date	12.3 Severity	12.4 Action taken	12.5 Outcome	12.6 Relationship to study protocol	12.7 AE resolution date (If AE persisting/unresolved or outcome unknown, leave blank)
a)		dd / mmm / yyyy					dd / mmm / yyyy
b)		dd / mmm / yyyy					dd / mmm / yyyy
c)		dd / mmm / yyyy					dd / mmm / yyyy
d)		dd / mmm / yyyy					dd / mmm / yyyy
e)		dd / mmm / yyyy					dd / mmm / yyyy
f)		dd / mmm / yyyy					dd / mmm / yyyy
g)		dd / mmm / yyyy					dd / mmm / yyyy
h)		dd / mmm / yyyy					dd / mmm / yyyy

Severity: **1** = Mild; **2** = Moderate; **3** = Severe

Action: **1** = None: vasopressor arm continued unchanged; **2** = Vasopressor arm stopped/modified; **3** = None: fluids arm continued unchanged; **4** = Fluids arm stopped/modified; **5** = None: Outside the intervention period

Outcome: **1** = Unknown / LTFU; **2** = Unresolved- end of study/or at death; **3** = Resolved; **4** = Resolved with sequelae

Relationship: **1** = Not related; **2** = Unlikely; **3** = Possible; **4** = Probable; **5** = Definitely

OFFICIAL

OFFICIAL

ARISE FLUIDS Study
FORM 13
SAE

Patient Study No: ☐☐☐ – ☐☐☐

Patient Initials: ☐☐☐

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13.1 Demographics

13.1.1 Date of birth ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) NZ Sites: leave day blank & enter only month and year

13.1.2 Sex ☐ Male ☐ Female

13.2 Event Details

13.2.1 Follow up type: ☐ Initial ☐ Final

13.2.2 Event Diagnosis

13.2.3 Event Type

☐ Death
☐ Life threatening
☐ Prolongation of hospitalisation
☐ Permanently disabling
☐ Congenital anomaly
☐ Medically important

13.2.4 Event description and treatment:

13.2.5 Randomisation date and time: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes)

13.2.6 Event onset date & time: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (hours : minutes) Time estimated ☐

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ARISE FLUIDS Study
FORM 13
SAE

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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Event Details – *Continued*

13.2.7 Event Outcome

- ☐ Unknown / Lost to follow up
- ☐ Unresolved at end of study or death
- ☐ Resolved → If YES, 13.2.7.1 Event resolution: ☐☐ / ☐☐☐ / ☐☐☐☐ (dd / mmm / yyyy)
- ☐ Resolved with sequelae → If YES, 13.2.7.2 Specify: ☐
- ☐ Death → If YES, 13.2.7.3 Death date and time: ☐☐ / ☐☐☐ / ☐☐☐☐ ☐☐ : ☐☐ (dd / mmm / yyyy hours : minute)

13.2.7.4 Cause of death: ☐

13.2.8 Action taken with study protocol

- ☐ None: vasopressor arm continued unchanged
- ☐ Vasopressor arm stopped/modified
- ☐ None: Fluids arm continued unchanged
- ☐ Fluids arm stopped/modified
- ☐ None: Outside the intervention period

13.3 Event information to be determined by Principal Investigator or delegated investigator

13.3.1 Relationship of event to study treatment as determined by the PI or Investigator

- ☐ Not related
- ☐ Unlikely
- ☐ Possible
- ☐ Probably
- ☐ Definitely

End of Form

ARISE Fluid Study
FORM 14
Protocol Deviation

Patient Study No: ___ – ___
Patient Initials: ___

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14.1 Protocol Deviation Details

14.1.1 Date and time: dd / mmm / yyyy hh : mm

14.2.1 *Please specify protocol deviation details below: (choose one only)*

☐ Patient randomised but not eligible:
If checked, select reason not eligible.

- ☐ Inclusion criteria NOT met:
  Check ALL that apply
  - ☐ SBP <90 mm Hg or MAP <65 mm Hg despite a ≥1000 ml cumulative total bolus if IV fluid administered over a max of 60 min (incl. pre-hospital boluses)
  - ☐ Arterial or venous lactate > 2.0 mmol/L
  - ☐ At least one dose of an IV antimicrobial has been commenced at randomisation
- ☐ Exclusion criteria met:
  Check ALL that apply
  - ☐ Age <18 years
  - ☐ Confirmed or suspected pregnancy
  - ☐ Transferred from another acute care facility
  - ☐ Hypotension suspected to be due to a non-sepsis cause
  - ☐ > 2 L total IV fluid administered (incl. pre-hospital fluids but excl. drugs & flushes)
  - ☐ > 6 hrs since ED presentation OR >2 hrs since inclusion criteria met
  - ☐ Treating clinician considers that one or both of the treatment regimens are not suitable OR the protocol cannot be delivered
  - ☐ Death is considered imminent or inevitable
  - ☐ Underlying disease that makes survival to 90 days unlikely
  - ☐ Inability to follow patient up to day 90 e.g. unstable accommodation, overseas
  - ☐ Previous enrolment in this study

☐ Fluid arm: one or more boluses of 500 mls or more not administered for hypotension and/or hypoperfusion

☐ Vasopressors arm: Vasopressors not commenced for hypotension and/or hypoperfusion

☐ Vasopressors arm: Fluid boluses administered without specified indication as per study protocol e.g. persistent hypotension/hypoperfusion

☐ Vasopressors arm: One or more fluid boluses >250 ml/hr administered

☐ OTHER, If OTHER, Specify

ARISE Fluid Study
FORM 14
Protocol Deviation

Patient Study No: ☐☐☐ – ☐☐☐
Patient Initials: ☐☐☐

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Protocol Deviation Details

14.3 Reason for protocol deviation:

14.4 What were the consequences or action taken due to protocol deviation?

End of form