

# Randomised comparison of fluid resuscitation with human albumin solution or normal saline among critically ill patients

<b>Submission date</b> 19/09/2002	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 19/09/2002	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 08/11/2022	<b>Condition category</b> Signs and Symptoms	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

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### Contact details

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## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

### ClinicalTrials.gov number

Nil known

## Secondary identifying numbers

153711

# Study information

## Scientific Title

Randomised comparison of fluid resuscitation with human albumin solution or normal saline among critically ill patients

## Acronym

SAFE Study (Saline versus Albumin Fluid Evaluation)

## Study objectives

When 4% albumin is compared to 0.9% sodium chloride (normal saline) for intravascular fluid resuscitation in patients in the Intensive Care Unit (ICU) there is no difference in 28-day all-cause mortality.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Ethics approval at Royal North Shore Hospital (affiliated with the University of Sydney and the Institute for International Health) was issued on 27 November 2000 (protocol ref: 0010-173M). Each participating institution also received ethics approval.

## Study design

Randomised controlled trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

## Health condition(s) or problem(s) studied

Critically ill patients requiring intravenous fluid resuscitation

## Interventions

The study treatment will be randomly allocated with stratification within the ICU and across the study population for patients admitted for trauma causes or non-trauma causes. Administration of the study treatments will be double blinded. Each eligible participant will be randomised to receive either 4% human albumin or 0.9% sodium chloride.

Co-sponsor for this trial:

Australian and New Zealand Intensive Care Society Clinical Trials Group

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Contact person: Professor Simon Finfer (sfinfer@george.org.au)

## **Intervention Type**

Drug

## **Phase**

Not Specified

## **Drug/device/biological/vaccine name(s)**

Human albumin solution or normal saline

## **Primary outcome measure**

Death from all causes at 28 days after randomisation

## **Secondary outcome measures**

1. Survival time during the first 28 days
2. The proportion of patients with one, two, three, four and five new organ failures (defined as documented change in cardiovascular, respiratory, renal, haematologic or hepatic component of the Sepsis-related Organ Failure [SOFA] score from zero, one or two at base-line to three or four during ICU stay)
3. Duration of mechanical ventilation
4. Duration of renal replacement therapy
5. Duration of ICU and hospital stay

## **Overall study start date**

01/01/2003

## **Completion date**

31/12/2004

# **Eligibility**

## **Key inclusion criteria**

Patients are eligible for inclusion in the study if ALL the following requirements are met:

1. Fluid resuscitation is required for intravascular fluid depletion that is in addition to intravenous fluid that is required for nutrition or to replace ongoing insensible losses, urinary losses, ongoing losses from other sites (e.g., fistula losses from the gastrointestinal tract, urinary losses from diabetes insipidus, cerebral salt wasting syndrome or the polyuric phase of acute

renal failure) or to restore normonatraemia

2. The ICU clinician considers that both 4% human albumin solution and 0.9% sodium chloride are equally appropriate for the patient and that no specific indication or contraindication for either exists

3. The requirement for fluid resuscitation must be supported by AT LEAST ONE of the following clinical signs:

- a. Heart rate greater than 90 beats/min
- b. Systolic Blood Pressure (SBP) less than 100 mmHg or Mean Arterial Pressure (MAP) less than 75 mmHg or a 40 mmHg decrease in SBP or MAP from the baseline recording
- c. Central venous pressure less than 10 mmHg
- d. Pulmonary artery wedge pressure less than 12 mmHg
- e. Respiratory variation in systolic or mean arterial blood pressure of greater than 5 mmHg
- f. Capillary refill time greater than one second
- g. Urine output less than 0.5 ml/kg for one hour

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Sex**

Not Specified

### **Target number of participants**

7000

### **Key exclusion criteria**

Patients are excluded from the study if one or more of the following are present:

1. A known previous adverse reaction to human albumin solution
2. Any known religious objection to the administration of human blood products (for example if patient is a Jehovahs Witness)
3. A requirement for the patient to receive plasmapheresis during this ICU admission
4. An admission to the ICU following cardiac surgery
5. An admission to the ICU for the treatment of body burn
6. An admission to the ICU following liver transplantation surgery
7. Age less than 18 years
8. Brain death or brain death that is likely to be diagnosed within in the next 24 hours of fluid resuscitation being required
9. If the patient is moribund and expected to die within the next 24 hours - defined as having a treatment limitation order in place that exceeds a not for resuscitation order and that indicates the treating clinicians are not committed to full supportive care
10. If the patient has previously been enrolled and has completed follow up in the SAFE study
11. If the patient has previously received fluid resuscitation that was prescribed within the study ICU and during this current ICU admission
12. If the patient has been transferred to the study ICU from a non-study ICU and received a fluid bolus or fluid resuscitation for the treatment of volume depletion in that non-study ICU

### **Date of first enrolment**

01/01/2003

**Date of final enrolment**

31/12/2004

**Locations****Countries of recruitment**

Australia

New Zealand

**Study participating centre**

The George Institute for International Health

Sydney

Australia

NSW 2021

**Sponsor information****Organisation**

The George Institute for International Health (Australia)

**Sponsor details**

c/o Professor Simon Finfer

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207 Kent Street

Sydney

Australia

NSW 2021

**Sponsor type**

Research organisation

**Website**

<http://www.thegeorgeinstitute.org>

**ROR**

<https://ror.org/023331s46>

**Funder(s)****Funder type**

Hospital/treatment centre

**Funder Name**

Funding has been from several organisations (listed in alphabetical order):

**Funder Name**

Auckland Hospital (New Zealand)

**Funder Name**

Commonwealth Department of Health and Aged Care (Australia)

**Funder Name**

CSL Limited, Melbourne (Australia)

**Funder Name**

Middlemore Hospital, Auckland (New Zealand)

**Funder Name**

National Health and Medical Research Council (Australia) - three year project grant (ref: 153711)

**Funder Name**

National Health Research Council (New Zealand) (ref: 01/386)

**Funder Name**

New South Wales Health Department

**Funder Name**

Northern Territory Health Services (Australia) - grant from the Australian Health Care Agreement 1998 - 2003 Quality Improvement and Enhancement Funds

**Funder Name**

Queensland Health Services Department (Australia)

**Funder Name**

Royal Hobart Hospital, Tasmania (Australia)

**Funder Name**

South Australia Department of Human Services (Australia)

**Funder Name**

Victoria Department of Human Services (Australia)

**Funder Name**

Western Australia Health Department (Australia)

**Funder Name**

The SAFE study was initiated and designed by the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Australian and Red Cross Blood Service. The study design, protocol and procedures have been finalised in collaboration with the Institute for International Health, independently of the aforementioned funding bodies. The data will be collected, analysed and published independent of the funding bodies and a copy of the final report will be distributed to them on completion of the study.

## Results and Publications

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan**

Not provided at time of registration

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		18/11/2006		Yes	No
<a href="#">Results article</a>		30/08/2007		Yes	No