

Participant initials: Participant ID: 

### INCLUSION CRITERIA

<i>Participants will be excluded if <b>ANY</b> of the following are No:</i>	<b>YES</b>	<b>NO</b>
Aged 18 years or above	<input type="checkbox"/>	<input type="checkbox"/>
Being treated on an ICU	<input type="checkbox"/>	<input type="checkbox"/>
Septic shock according to internationally accepted definitions*	<input type="checkbox"/>	<input type="checkbox"/>
Heart rate $\geq 95$ bpm (at the time of randomisation)	<input type="checkbox"/>	<input type="checkbox"/>
Receiving vasopressor support to maintain a target blood pressure for $\geq 24$ hours	<input type="checkbox"/>	<input type="checkbox"/>
Are being treated with noradrenaline at a rate $\geq 0.1$ mcg/kg/min	<input type="checkbox"/>	<input type="checkbox"/>

## \*Sepsis -3 definitions:

- confirmed or suspected infection requiring antibiotic therapy
- new organ dysfunction, as evidenced by an increase in SOFA score  $\geq 2$
- a blood lactate  $> 2$  mmol/l at any point during shock resuscitation
- vasopressor therapy to maintain mean arterial pressure (MAP)  $\geq 65$  mmHg

In particular the presence of a blood lactate  $> 2$  mmol/l is only necessary for the diagnosis of septic shock and is NOT necessary for randomisation 24 hours later.

### EXCLUSION CRITERIA

<i>Participants will be excluded if <b>ANY</b> of the following are Yes:</i>	<b>YES</b>	<b>NO</b>
Tachycardia as a result of pain, discomfort from medical devices (including endotracheal tubes), during interventions or other patient distress	<input type="checkbox"/>	<input type="checkbox"/>
Any form of vasodilatory shock that is not caused by sepsis	<input type="checkbox"/>	<input type="checkbox"/>
Noradrenaline infusion $< 0.1$ mcg/kg/min	<input type="checkbox"/>	<input type="checkbox"/>
$> 72$ hours after start of vasopressor therapy	<input type="checkbox"/>	<input type="checkbox"/>
$< 12$ hours since noadrenaline to treat a medical condition other than septic shock stopped	<input type="checkbox"/>	<input type="checkbox"/>
Having pre-existing severe cardiac dysfunction (NYHA grade 4 or more)	<input type="checkbox"/>	<input type="checkbox"/>
Having pre-existing severe pulmonary hypertension (mean PA pressures $> 55$ mmHg)	<input type="checkbox"/>	<input type="checkbox"/>
Acute severe bronchospasm (due to asthma or COPD)	<input type="checkbox"/>	<input type="checkbox"/>
Untreated second or third degree heart block	<input type="checkbox"/>	<input type="checkbox"/>
Untreated phaeochromocytoma	<input type="checkbox"/>	<input type="checkbox"/>
Prinzmetal's angina	<input type="checkbox"/>	<input type="checkbox"/>
A past history of ischaemic stroke or transient ischaemic attack (TIA) or untreated severe carotid stenosis	<input type="checkbox"/>	<input type="checkbox"/>
Advanced liver disease with Child-Pugh Score of $\geq B$	<input type="checkbox"/>	<input type="checkbox"/>
Known sensitivity to beta-blockers	<input type="checkbox"/>	<input type="checkbox"/>
Patient / legal representative unwilling to provide written informed consent	<input type="checkbox"/>	<input type="checkbox"/>
Known to be pregnant	<input type="checkbox"/>	<input type="checkbox"/>
Terminal illness other than septic shock with a life expectancy $< 28$ days	<input type="checkbox"/>	<input type="checkbox"/>
Participants who have been administered an investigational medicinal product for another research trial in the past 30 days	<input type="checkbox"/>	<input type="checkbox"/>
Patients in whom the clinical team feel are about to finish their noradrenaline therapy	<input type="checkbox"/>	<input type="checkbox"/>
Decision of withdrawal of care is in place or imminently anticipated	<input type="checkbox"/>	<input type="checkbox"/>
Receiving extracorporeal membrane oxygenation (ECMO) treatment	<input type="checkbox"/>	<input type="checkbox"/>

'I confirm that this patient is eligible for enrolment in this trial'

Form completed by ( <i>print name</i> ):	Signature (approved investigator only):	Date:
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