

# Can lactate testing improve maternal sepsis identification? A multi-country, test accuracy study

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<b>Registration date</b> 21/03/2022	<b>Overall study status</b> Ongoing	<input checked="" type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 24/09/2024	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Maternal sepsis is a severe bacterial infection, usually of the uterus (womb), which can occur in pregnant women or more commonly, in the days following childbirth.

Maternal sepsis can develop in pregnant women and women who have recently experienced pregnancy and is a life-threatening condition that develops as a result of an infection which develops during pregnancy, childbirth, post-abortion, or the post-partum period. The results of the WHO Global Maternal Sepsis Study (GLOSS) suggest infection contributes to up to half of all maternal deaths and is also a major cause of maternal morbidity. Leaving many who survive sepsis with life-changing effects, such as post-traumatic stress disorder (PTSD), chronic pain and fatigue, and persistent problems or disability. Failure to rapidly recognise and treat maternal sepsis is a common factor identified in those women who die.

Research in high income countries has shown that groups of key treatments given together at the same time can help reduce poor outcomes and deaths from sepsis. These groups of treatments collectively referred to as care bundles and usually consist of small sets of evidence-based, interventions that together result in significantly improved outcomes compared to when they are implemented individually. Care bundles have been a cornerstone of sepsis improvement initiatives in high-income settings and shown to reduce mortality in adult, high income populations.

Measurement of blood lactate forms a key part of sepsis management and risk stratification in current international guidelines from both National Institute for Healthcare Excellence (NICE) in the United Kingdom (UK) and the Surviving Sepsis Campaign. However, these guidelines were developed for non-pregnant populations in high income countries. In the substantially different population of pregnant women, in low-resource settings, it is anticipated that the test may perform differently. Additionally, pregnancy itself induces profound cardiovascular, physical and immunological changes that affect baseline physiology and the response to infection. The infections in pregnancy causing sepsis are also different to those in a typical adult medical population, and the co-morbidities are also different.

We propose in this study to investigate if a lactate measurement has an incremental benefit over conventional maternal vital sign assessment in the diagnosis of sepsis and identification of women at risk of severe morbidity or mortality in low resource settings. We will determine the diagnostic and prognostic accuracy of venous lactate measurement in the maternity populations, in low resource settings, which is unknown. If lactate testing in this population then this has the potential to improve maternal sepsis outcomes.

**Who can participate?**

Women aged 16 years or above who are pregnant or within 6 weeks of the end of the pregnancy with a suspected or confirmed infection requiring in-patient care

**What does the study involve?**

Participants will provide two blood samples whilst they are hospital inpatients. Research Staff will visit women at their bedside to collect information until they are sent home

**What are the possible benefits and risks of participating?**

We hope that the results from the study will help women in the future when doctors are making decisions about treatment. All women who agree to participate in the study will have other bloods taken by their doctor to monitor their infection. These are done on day 0 and day 1 and may be of benefit as they are not always available as an option in Low-income settings. The results will be provided to staff to support the best treatment for participants. The only results not shared are the extra samples taken to measure Lactate. The risks to participants of providing two blood samples are very low, however, any blood samples taken can result in some localised bruising.

**Where is the study run from?**

Malawi Liverpool Wellcome (Malawi)

**When is the study starting and how long is it expected to run for?**

January 2021 to September 2025

**Who is funding the study?**

UKRI Global Maternal and Neonatal Health 2019 (UK)

**Who is the main contact?**

Sonia Whyte, [swhyte@liverpool.ac.uk](mailto:swhyte@liverpool.ac.uk)

Prof. David Lissauer, [david.lissauer@liverpool.ac.uk](mailto:david.lissauer@liverpool.ac.uk)

**Study website**

<https://lctc.org.uk/Research>

## Contact information

**Type(s)**

Public

**Contact name**

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Scientific

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**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number****ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

UoL001655

**Study information**

Scientific Title

Using lactate testing to improve maternal sepsis identification: a multi-country test accuracy study: LACTate in mATernal sEpsis

## **Acronym**

LACTATE

## **Study objectives**

To determine the diagnostic accuracy of maternal venous lactate measurement in addition to maternal vital sign thresholds, in maternal sepsis in low-resource health facility settings in Malawi, Uganda and Pakistan

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

1. Approved 25/02/2022, Aga Khan University Ethics Review Committee, ref: 2022-7066-20701
2. Approved 10/03/2022, National Institutes of Health Health Research Institute National Bioethics Committee (NBC) (Health Research Institute, Shahrah-e-Jamhuriat, Off Constitution Avenue, Sector G-5/2, Islamabad, Pakistan; +92 (0)51 9224325, 9216793; nbcpakistan@nih.org.pk), ref: No.4-87/NBC-744/22/1647
3. Approved 26/04/2022, University of Liverpool Central University Research Ethics Committee D, ref: 10737
4. Approved 21/02/2023, Aga Khan University Ethics Review Committee, ref: 2023-7066-24108
5. Approved 21/03/2023, National Institutes of Health Health Research Institute National Bioethics Committee (NBC) (Health Research Institute, Shahrah-e-Jamhuriat, Off Constitution Avenue, Sector G-5/2, Islamabad, Pakistan; +92 (0)51 9224325, 9216793; nbcpakistan@nih.org.pk), ref: No.4-87/NBC-744/23/1478
6. Approved 16/03/2022, College of Medicine Research and Ethics Committee (COMREC) University of Malawi, ref: P.01/22/3553
7. Approved 15/11/2022, Mbale Regional Referral Hospital Research and Ethics Committee (MRRH-REC) (Ministry of Health Mbale Regional Hospital, PO Box 921, Mbale — Uganda; +256 (0) 39 3280584; +256 (0)41 4671162; mrrhrec@gmail.com), ref: BUFHTS-2022-23
8. Approved 03/11/2022, Busitema University Faculty of Health Sciences REC, ref: BUFHS-2022-23
9. Approved 12/12/2022, Uganda National Council for Science and Technology (UNCST), ref: HS2589ES
10. Approved 30/01/2023, University of Liverpool Central University Research Ethics Committee D, ref: 10737

## **Study design**

Prospective multi-site phase III test accuracy study

## **Primary study design**

Observational

## **Secondary study design**

Test accuracy

## **Study setting(s)**

Hospital

## **Study type(s)**

Screening

## **Participant information sheet**

Not available in web format. Please use contact details to request a country specific information sheet.

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

Maternal sepsis

## **Interventions**

Day 0: We will obtain consent from individuals who meet the inclusion criteria to participate. After which we will collect the participants' medical and obstetric history; details about the current or most recent pregnancy; Vital signs such as blood pressure, pulse, temperature, oxygen levels, urine output. We will collect one extra blood sample (ideally at the same time as routine samples) approximately 2.5ml to test for lactate. The sample is sent to the Laboratory for processing and the results blinded to clinical staff.

Day 1: Approximately 24 hours later the second blood sample will be taken for lactate along with other routine bloods. We will also take some vital signs, collect information about the pregnancy including any delivery or birth outcomes and record the result of any other blood tests conducted by the clinical team. The second lactate sample will be sent to the laboratory for processing.

Day 2 to Day 14: We will collect vital signs and information about the pregnancy including any delivery or birth outcomes. We will also collect near miss and death details as they occur.

Study End: The study ends when the woman is discharged, dies, or on Day 14, no further follow up information is collected.

## **Intervention Type**

Other

## **Primary outcome measure**

Maternal sepsis will be assessed using venous lactate measurement in addition to maternal vital sign thresholds at two time points following inclusion: Day 0 (blood sample 1) and Day 1 (blood sample 2) taken 22 -36 hours after sample 1.

## **Secondary outcome measures**

1. Immediate diagnostic value of lactate testing by comparing the baseline index test with baseline reference standard. Maternal venous blood lactate will be measured at baseline using the blood sample collected (day 0) at the same timepoint that maternal sepsis will be assessed.
2. Short-term predictive value of lactate testing, by comparing the baseline index test with 24-hour reference standard, in those without sepsis at baseline. Maternal venous blood lactate will be measured at baseline (day 0 blood sample ), and in those without sepsis at baseline the index test will be assessed against the reference standard at day 1.
3. Severe morbidity and mortality from infection. This will be assessed daily until day 14 or discharge or death if sooner: Day 0-14.
4. Pregnancy status (pregnant or post-delivery/post miscarriage/post-abortion) and country of recruitment

## **Overall study start date**

01/01/2021

**Completion date**

30/09/2025

## Eligibility

**Key inclusion criteria**

1. Be pregnant or within 6 weeks of the end of the pregnancy.
2. Women with a suspected or confirmed infection requiring in-patient care:
  - 2.1. Any suspected or confirmed infection with or without organ-dysfunction.
  - 2.2. Any clinical signs suggestive of infection (e.g., fever).
  - 2.3. Request for any bodily fluid culture (blood, urine, cerebrospinal fluid, etc.) or swab specimens (nasopharyngeal, oropharyngeal, vaginal, endocervical) for the diagnosis of suspected infection (not routine sampling e.g., routine COVID-19 screening).
  - 2.4. Non-prophylactic use of antibiotics or other antimicrobial drugs at admission or during hospital stay.
  - 2.5. Any procedure for treatment of a suspected infection (e.g., wound exploration, evacuation of the uterus, laparotomy, etc.)
  - 2.6. Any unexplained organ-dysfunction (i.e., organ dysfunction not attributable to an underlying cause).
3. Estimated age  $\geq 16$  years.
4. Willing to provide a signed (and witnessed, if applicable) informed consent form.
5. Willing to be contacted, if necessary.
6. Willing to have additional blood samples taken.

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

16 Years

**Sex**

Female

**Target number of participants**

500

**Total final enrolment**

567

**Key exclusion criteria**

1. Women in active labour or within 2 hours of delivery are excluded as lactate is expected to be elevated by labour and childbirth.
2. Women with any non-severe, localised, or chronic infection (TB, HIV) or colonization (GBS)
3. Women undergoing only treatment with prophylactic antibiotics (for procedures, GBS)

**Date of first enrolment**

20/07/2022

**Date of final enrolment**

22/06/2023

## **Locations**

**Countries of recruitment**

Malawi

Pakistan

Uganda

**Study participating centre****Queen Elizabeth Hospital**

Chipatala Avenue

Box 95

Blantyre

Malawi

-

**Study participating centre****Mbale regional referral Hospital**

Pallisa road

P.O Box 921

Mbale City

Uganda

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**Study participating centre****Liaquat University of Medical and Health Sciences (LUMHS)**

Department Unit 2

Hyderabad

Pakistan

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## **Sponsor information**

**Organisation**

University of Liverpool

**Sponsor details**

Clinical Research, Sponsorship and Governance Manager Clinical Directorate  
4th Floor Thompson Yates Building  
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England  
United Kingdom  
L69 3GB  
+44 7717 863747  
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**Sponsor type**

University/education

**Website**

<https://www.liverpool.ac.uk/intranet/research-support-office/research-contracts/>

**ROR**

<https://ror.org/04xs57h96>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

UKRI Global Maternal and Neonatal Health 2019

## **Results and Publications**

**Publication and dissemination plan**

The results from different participating sites will be analysed together and published as soon as possible, always maintaining participant confidentiality. The Uniform Requirements for Manuscripts Submitted to Biomedical Journals (<http://www.icmje.org/>) will be respected. The study registration number will be attached to any publications resulting and members of the TOC will be acknowledged. Any publications arising from this research will be reviewed internally by the TMG and peer reviewed by journals prior to publication.

**Intention to publish date**

30/09/2026

**Individual participant data (IPD) sharing plan**

At the end of the study, after the primary results have been published, and the separate country teams have completed any desired secondary analysis of country specific data, the anonymised individual participant data (IPD) and associated documentation (e.g., protocol, statistical analysis plan, annotated blank CRF) will be prepared to be shared with external researchers. All requests



for access to the IPD will be reviewed by an internal committee at the Liverpool Clinical Trials Center (LCTC) and discussed with the Chief Investigator in accordance with the LCTC policy on data sharing.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Statistical Analysis Plan</a>	version 1.0	07/02/2023	10/03/2023	No	No
<a href="#">Statistical Analysis Plan</a>	version 2.0	14/06/2023	04/09/2023	No	No