# Bedside diagnosis of neonatal sepsis by detection of Serum Amyloid A.


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## INTRODUCTION

### SEPSIS: A MAJOR GLOBAL CONCERN

Sepsis is the body's overwhelming response to an infection, if not treated it can lead to multi-organ failure, shock and death.

- 47 – 50 million sepsis cases per annum [1]
- 11 million deaths per year
  - ➢ 1 death every 2.8 seconds
- Sepsis survivors often face lifelong consequences
- Lack of awareness = lack of diagnosis
- Sepsis disproportionately affects vulnerable populations
  - ➢ Neonates, pregnant or recently pregnant women, older persons and immunocompromised individuals

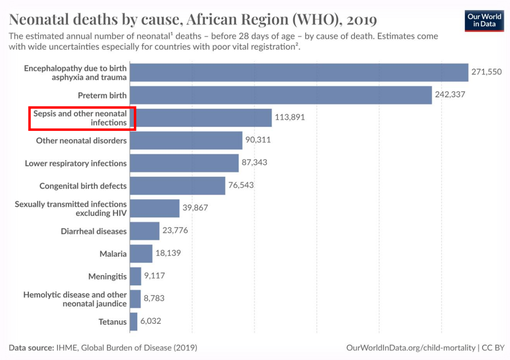
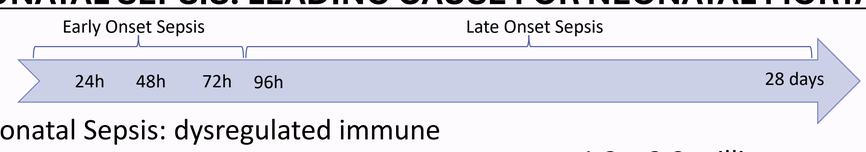



**Figure 1.** Neonatal deaths by cause, in African Region (WHO) in 2019.

### NEONATAL SEPSIS: LEADING CAUSE FOR NEONATAL MORTALITY




- Neonatal Sepsis: dysregulated immune reaction to a pathogen within the first month of life.
- Difficulty in diagnosis of neonatal sepsis lies in non-specific symptoms, lack of specific biomarkers and suitable and accurate diagnostic systems. Resulting in high sepsis-associated death rates:
  - ➢ 225,000 – 700,000 deaths per year [1]
- 1.3 – 3.9 million new cases reported annually
- LMICs have the highest burden of neonatal sepsis.
- **Uganda has the highest rate of neonatal mortality**
  - ➢ **17 neonatal sepsis-related deaths per day**

## Neonatal Sepsis Study: Materials and Methods

### Our Goal

**To improve neonatal sepsis detection and reduce neonatal mortality in line with UN SDG 3.2 objectives.** As part of a SFI funded challenge: We propose the implementation of a (i) reliable, (ii) easy to use, (iii) patient-compatible and (iv) patient-side **SAA-detecting Lateral flow test (LFT): NeoSep-SAA**

- Early diagnosis of neonatal sepsis using the NeoSep-SAA will enable clinical decision-making to begin treatment
- In the case of negative test results, it will minimise unnecessary antibiotic use

### Serum Amyloid A

- Serum Amyloid A (SAA) is a well-characterised protein biomarker of sepsis-associated inflammation.
- Elevated blood SAA levels have been proven to be sensitive and specific for confirming infection in neonates.[2,3,4]
- A recent study has shown that SAA detection is superior to all other biomarkers (n = 15) for the detection of neonatal sepsis.[5]

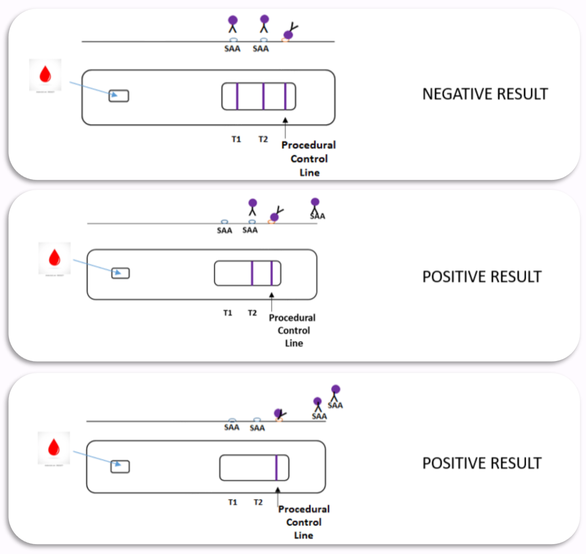



**Figure 2.** NeoSep SAA test schematic showing **POSITIVE/**POSITIVE (1 or 2 lines) and **NEGATIVE** (3 lines) results.

### NeoSep-SAA detects SAA in blood

- The SAA-LFT is a competitive semi-quantitative immunoassay based on the inhibition by SAA in test specimens of gold nanoparticle-labelled IgG [anti-human SAA] interaction with recombinant human SAA printed onto nitrocellulose membranes.
- A positive result (elevated or high SAA in a human blood sample) prevents line formation on the test membrane, whereas a negative result is observed when normal SAA levels do not prevent gold nanoparticle-labelled IgG [anti-human SAA] interaction with recombinant human SAA and results in line appearance.

### Clinical Evaluation Studies

- 1500+ NeoSep-SAA tests shipped from Ireland to Uganda
- **Familiarisation study**: 450 adult samples and 50 neonatal samples
  - ✓ Test familiarisation and user training
  - ✓ Confirming test functionality patient-side
- **Neonatal sepsis study**: 955 neonatal samples
  Highly powered study based on G*Powered calculations
  - Healthy controls and clinically suspected-sepsis neonatal samples from hospital and non-clinical settings
  - ✓ NeoSep-SAA performance analysed against the commonly used C-Reactive Protein test.

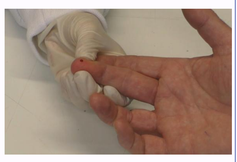


**Figure 3.** 5µl of blood


**Figure 4.** Neonatal sepsis study locations

## Neonatal Sepsis Study: Results

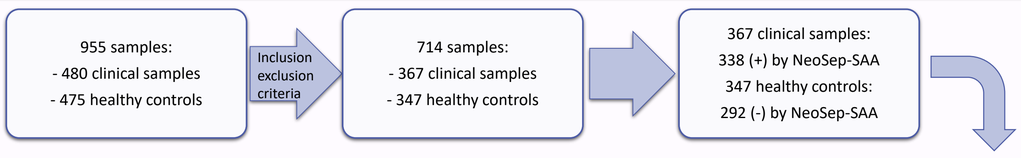



**Table 1.** NeoSep-SAA performance in terms of sensitivity, specificity, PPV and NPV.

| | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|
| | % | % | % | % | % |
| **NeoSep-SAA** | 92 | 73 | 78 | 90 | 83 |

- **High sensitivity = NeoSep-SAA correctly detects infection / sepsis in neonates** [6]
- High NPV = rules out sepsis. Can facilitate decision to hold off antibiotic administration
- Out-performed CRP test in sepsis detection, CRP, an established biomarker of infection, presented with a sensitivity of only 32% (27%, 37%)[6]
- Less painful and less invasive than currently available diagnostics:
  - Blood culture, CRP, complete blood count
  - Parents are satisfied with heel-prick blood sampling (5 µl) - little pain and distress to neonates
- Applicable in remote settings: NeoSep-SAA performance was evaluated in non-clinical settings with none or limited laboratory facilities

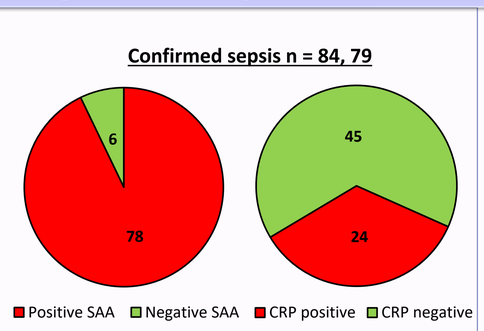



**Figure 5.** NeoSep-SAA in use on-site

**Figure 6.** NeoSep-SAA in use bedside

### Stakeholder Feedback

37 interviews were conducted with stakeholders in Uganda

Hospital managers [Interviewee 21] : "I think will be welcome, and us management would actually encourage it, as long as the supplier has guaranteed us availability."

Lab technicians [Interviewee 14] : "it seems like it will be fitting in our environment and situation… a bedside or point of care kind of test, which would really be very helpful"

Nurses & Midwives [Interviewee 17] : "… if I was to be asked, "what you prefer?" I prefer this…these babies they have one traumatising them... This is very simple, just a small drop of blood"

Doctors [Interviewee 16] : "… like in this outpatient setting, it's really easy because you can screen [and], if they're actually sick you can send them to the hospital earlier."

❖ Healthcare staff affirm the ease-of-use and satisfaction with the low-invasive nature, rapidness and useability of the test and support the adoption of the NeoSep-SAA into routine neonatal testing in aid of neonatal sepsis detection.

## Discussion

- ➢ NeoSep-SAA is a reliable test that will fulfil an essential gap in the ability to detect sepsis in neonates in LMICs, especially where limited resources hinder neonatal care. [6]
- ➢ NeoSep-SAA could enable early diagnosis of neonatal sepsis, prompting timely treatment.
- ➢ NeoSep-SAA can facilitate evidence-based decision-making, by providing rapid onsite test results, suitable for first responder use or non-clinical settings.

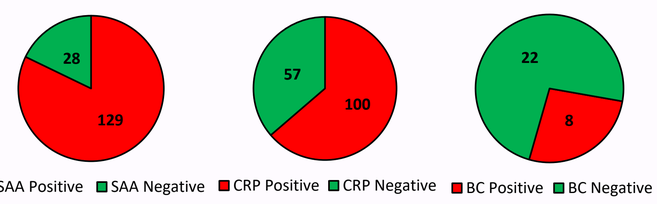
## Current Work

**1. Neonatal antibiotic response study (n = 930)**

- Using NeoSep-SAA to monitor response to antibiotic therapy in neonatal sepsis.
- C-Reactive Protein test (CRP) and Blood cultures (BC) as comparator tests.

**Provisional Results:**

**Confirmed sepsis n = 157**




**2. Maternal sepsis study (n = 930)**

- Using NeoSep-SAA to detect maternal sepsis, with CRP and BC tests as comparators.
- ✓ 3000+ NeoSep-SAA tests have been deployed to 6 hospitals in Uganda as of May 2025.

## Conclusions

- NeoSep-SAA is a functional, bedside, rapid test with high sensitivity, diagnostic accuracy and sufficient specificity and would provide critical assistance in neonatal sepsis diagnosis, particularly in low-resource environments. Early diagnosis will subsequently enable prompt treatment, improving sepsis outcomes.
- Positive feedback from stakeholders support and encourage the integration of the NeoSep-SAA into the Ugandan healthcare system. Additional clinical evaluations are being carried out for further evidence.
- **This study demonstrated that the performance of NeoSep-SAA has proved more satisfactory than the comparator, C-Reactive Protein test, based on statistical analysis, and by contextual appropriateness and is preferred over blood cultures due to its rapidness, ease of use and non-invasiveness.**[6]

## References & Acknowledgements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