Paper Title:

Evaluation of the feasibility of the FAST-M maternal sepsis intervention in Pakistan, a protocol

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Abstract

Background: Maternal sepsis is a life-threatening condition, defined by organ dysfunction caused by infection during pregnancy, childbirth and the postpartum period. It is estimated to account for between one tenth and half of all maternal deaths globally. An international stake-holder group, including the World Health Organization, developed a maternal sepsis management bundle called "FAST-M" for resource limited settings through a synthesis of evidence and international consensus. The FAST-M treatment bundle consists of five components: **F**luids, **A**ntibiotics, **S**ource identification and control, assessment of the need to **T**ransport or Transfer to a higher level of care and ongoing **M**onitoring (of the mother and neonate). This study aims to adapt the FAST-M intervention and evaluate its feasibility in Pakistan.

Methods: The proposed study is a mixed method, with a before and after design. The study will be conducted in two phases at Liaquat University of Medical and Health Sciences, Hyderabad. In the first phase, we will adapt the bundle care tools for the local context and assess in what circumstances different components of the intervention are likely to be effective, by conducting interviews and a focus group discussion (the Adaptation Phase). In the second phase, we will evaluate the feasibility of the FAST-M intervention (the Feasibility Assessment Phase).

Discussion: The utilisation of bundles can facilitate recognition and timely management of maternal sepsis. There is a need to adapt, integrate and optimise a bundled care approach in low-resource settings in Pakistan to minimise the burden of maternal morbidities and mortalities due to sepsis.

Keywords: FAST-M intervention, maternal sepsis, Pakistan, qualitative study, sepsis bundle, care bundle, complex intervention, low-resource setting, feasibility study, maternal deaths.

Background

Pregnancy and childbirth-related complications are a major public health concern [1]. Every day approximately 830 women die from preventable causes related to pregnancy and childbirth and almost one-third of these occur in South Asia [2]. Physiological and immunological variations during pregnancy and the postpartum period predispose women to risks of these complications [3]. About 60% of maternal deaths occur during delivery and postpartum period [4]. Most of the maternal deaths occur within 24 to 72 hours of delivery where postpartum hemorrhage, eclampsia and maternal sepsis are the leading causes of maternal mortality [5].

The World Health Organization estimates suggests that globally, maternal sepsis accounts for about one tenth of the maternal deaths around the time of childbirth and is the third most common cause of maternal mortality [7]. Whilst the maternal mortality related to sepsis has decreased considerably in high income countries accounting for 2.1% of the total maternal deaths, the numbers are still high in the lower income countries accounting for up to 15.1% of maternal deaths annually [8]. However, more recent WHO estimates that were focused specifically on understanding better the contribution of maternal infection to adverse outcomes suggested that up to half of all maternal deaths were actually infection related [9]. A substantial proportion of the improvements in maternal outcomes in high income countries was attributed to the prevention and appropriate treatment of maternal sepsis [10].

Early warning scores, modules of educational material in routine healthcare settings and the bundled approach to sepsis management in high income countries have been effective in reducing maternal mortalities and morbidities [10]. A more rapid completion of a 3-hour bundle of sepsis care and rapid administration of antibiotics were found to be associated with lower risk-

adjusted in-hospital mortality ($p < 0.001$) [11]. Despite the improvement of sepsis care in high income countries, there is still lack of maternal sepsis-care bundle specific to the maternal population of low-resource settings [12].

The development of a maternal sepsis treatment bundle has been identified as an international "Priority Action" [13]. In collaboration with the WHO Maternal Sepsis Initiative, a Delphi approach was adopted to select contributory components to a maternal sepsis treatment bundle in low-resource settings [14]. The components selected were: **F**luids, **A**ntibiotics, **S**ource identification and control, assessment of the need to **T**ransport/Transfer to a higher level of care and ongoing **M**onitoring (of the mother and neonate). The treatment bundle was named "FAST-M" as a memorable acronym for both communication and awareness-raising [14].

The FAST-M intervention was implemented in districts of Malawi to evaluate the feasibility of early identification and management of maternal sepsis, and demonstrated significant improvements in maternal sepsis care [15]. The components included a 1) Maternal Early Obstetric Warning System (MEOWS) chart and FAST-M decision tool, 2) FAST-M treatment bundle and 3) The FAST-M implementation programme which consisted of the following: training programme, sepsis champions, task shifting, performance dashboards and data feedback to promote systems level change [15].

The FAST-M intervention has the capacity to strengthen maternal sepsis care as demonstrated in Malawi. We therefore aim to evaluate implementation of the FAST-M intervention to assess improvement in maternal sepsis care in low-resource setting of Pakistan.

Study Aim

This study aims to determine whether it is feasible to introduce a complex intervention (including a bundled approach) for maternal sepsis care in low resource setting of Pakistan; and to describe the facilitators and barriers to its implementation.

Study Objectives

- To adapt FAST-M bundle care tools (MEOWS chart, decision tool and treatment bundle) to the context in Pakistan
- We will also investigate how to optimally implement the approach in Pakistan's low resource hospital
- To understand the barriers and facilitators to these approaches in these settings
- Assess whether the use of the FAST-M intervention is feasible in the local healthcare system and improves sepsis care.
- Prepare the FAST-M intervention for a large-scale intervention trial.

Methods

Study setting

The study will be conducted at Liaquat University of Medical Health Sciences (LUMHS), which is a public sector tertiary hospital located in Hyderabad district of Pakistan. The hospital has a total of 3000 beds and 35 departments which serves a large number of mostly underprivileged populations. The hospital provides 24 hours' emergency cover to patients coming from nearby urban and rural areas. LUMHS has three Obstetrics and Gynecology units.

The current data from the facility shows that a total of approximately 11205 patients were admitted in OBGYN units from the period of January to August 2021; and the maternal mortality rate was recorded as 159/11205 (1.4%). Out of these 159 deaths, 45 were due to confirmed maternal sepsis (28.3%). These indicators direct that there is a need of a robust system to early detect and manage maternal sepsis cases in the hospital.

Study design

The study will use a mix-method design and will be conducted in two phases.

Phase 1-Adaptation of FAST-M intervention (Qualitative)

For a FAST-M bundle to be effective in Pakistan, it is necessary to identify how best to implement the FAST-M bundle in the context of local settings. In order to adapt this intervention, a systematic method will be taken to understand the nature of existing practices and an appropriate system for characterising the intervention and its components that can make use of this understanding. This constitute phase 1 of the study.

This formative research (phase 1) will adopt a qualitative research design involving focus group discussion (FGD) and key-informant interviews (KIIs) and a purposive sampling approach. The aim of group discussion and interviews will be to engage health practitioners, government officials and other key stakeholders to understand the behavior of existing practices in the study setting for maternal sepsis care, to finalize the FAST-M tools for the context of Pakistan, and to identify various facilitators and barriers that may influence implementation of the FAST-M intervention. The FGD and KIIs will be conducted using interview guides developed through the use of the Consolidated Framework for Implementation Research (CFIR) [16].

Consolidated Framework for Implementation Research (CFIR)

The CFIR is a commonly used framework to facilitate implementation research design, evaluate and implement evidence-based interventions, and comprises five major domains: 1) Intervention characteristics, 2) Outer setting, 3) Inner setting, 4) Characteristics of individuals, and 5) Process of implementation. It is categorized as a determinant framework with the objective to understand and explain factors (individual or organization) which influence implementation outcomes [16]. CFIR has been used in a wide range of studies because this flexible framework can be tailored to different settings across multiple contexts [17]. We aim to use the tailored CFIR framework to assess critical barriers and facilitators to implementation that need to be addressed at multiple levels if the FAST-M bundle is to be successfully optimized, and adopted in health care practices in Pakistan (Appendix-1).

The interview guides (Appendix-2) for KIIs and the FGD have been developed using five major domains of CFIR to identify existing practices for sepsis management. These guides will also identify the facilitators and barriers to implementation of FAST-M intervention in the study setting. The identification of existing practices for maternal sepsis care and facilitators and barriers in phase 1 will then form the basis of feasibility testing of FAST-M intervention in phase 2.

Inclusion criteria for KIIs and the FGD

- HCPs including physicians, nursing staff, healthcare administrators who are associated with maternal sepsis care and management
- HCPs who have worked at the study site for last six months

Sample size

15 to 20 semi-structured key informant interviews are planned in the qualitative phase of the study until data saturation is reached. One focus group will be conducted before initiation of the study to adapt the tools and identify implementation approaches; and a second will be conducted at the end of the study as a summative evaluation of the study to identify perceptions about success of implementation. Therefore, two focus group discussions (before and after implementation) will be conducted with 8-10 health care providers in each discussion.

Data collection and management

A semi-structured interview guide has been developed to explore healthcare professionals' views and attitudes towards FAST-M intervention and its implementation at their facility. Before beginning the interview, the qualitative researchers will describe the FAST-M bundle components and the patient referral pathway demonstrating the algorithm and summary for utilization of FAST-M bundle care tools (Appendix-3).

A free flow of discussion among participants will be encouraged, using probes from these discussions to obtain healthcare professionals' perceptions about the feasibility of the FAST-M intervention. Interviews will be conducted face-to-face in Urdu and English according to the participants' preference, and will be audio recorded following consent from study participants. Interviews and focus group discussion will be conducted by experienced study team members who are also trained qualitative researchers. Detailed field notes will be also taken during each interview to capture non-verbal language and cues.

All data will be kept confidential for seven years on password-protected computers and/or locked filing cabinets only accessible to members of the research team. During transcription, audio-

recordings will be referenced only with an identification number for anonymity of participants, with all identifying information removed before using the software analysis tool.

COVID-19- Standard Operating Procedures (SOPs)

In view of current of current COVID-19 pandemic situation, all project related activities will comply with standard operating procedures (SOPs). The following measures will be taken related to this study: 1) All research staff will be provided with appropriate masks, sanitizers, and/or other applicable Personal protective equipment (PPE) to the field staff; 2) Daily mandatory screening for COVID-19 symptoms of all project staff; 3) KIIs and FGDs will be conducted with social distancing (6 feet) with all vaccinated participants wearing face coverings.

Analysis plan

Qualitative data gained through individual interviews and FGDs will be audio recorded, transcribed and analysed using an inductive approach to determine the facilitators and barriers for implementation of the intervention and will be summarized according to CFIR domains. This will help to understand the important contextual features that are helping or hindering the operationalization of the FAST-M intervention.

The analysis will be an ongoing iterative process during phase 1 of this study. The research team will conduct multiple reviews of the transcripts and tapes to familiarize themselves with the data and identify initial themes that will be reflexive and interactive. Analysis will begin as soon as the first interview is completed in phase 1 and will be continued concurrently with data collection to help determine when new information is no longer being generated from interviews.

Although, we identified the CFIR as the appropriate framework, additional codes may emerge during the familiarization process to develop a thematic framework from experiences of

participants. The codes, categories and themes will be developed using NVivo version 10 (QSR International, Pty Ltd) software.

An audit trail will be used to document our decision-making process. Sections of the transcripts will be charted, organized by CFIR domains, and then re-framed to better reflect descriptions from participants. The primary team will review the codes and associated themes multiple times to check for potential biases, to ensure they are reflecting participants' words and meanings, and improve the credibility of their interpretation of the interviews. Initial findings will be shared with a group of participants to help with interpretation and generate meaning from the data.

The facilitators and hindering factors will be identified through phase 1 of the work. The FAST-M bundle care tools (MEOWS chart, decision tool and treatment bundle) will be modified through construal gained from interviews and discussion with health care providers.

Phase 2- Intervention phase

Following phase 1, intervention phase will be implemented for the feasibility testing.

Study population

During the intervention phase, patients will be assessed by a healthcare practitioner on decision to initiate screening for potential maternal sepsis that will be based on the following inclusion criteria:

- Women who are pregnant or within 6 weeks of miscarriage, termination of pregnancy or delivery
- Abnormal maternal observations triggered on the inpatient MEOWS chart
- Healthcare practitioner concern regarding potential maternal infection

- Fetal tachycardia greater than or equal to160 beats per minute

Sample size

For enrollment of sepsis cases, we will power to a primary process outcome of "sepsis management compliance". This is defined as "the proportion of patients admitted with features of sepsis who receive appropriate monitoring (full set of vital sign measurements on admission) and antibiotics within 1 hour (if required)." This means the notes of all patients with suspected or confirmed sepsis will be reviewed and their data would be collected using study Case Report Forms (CRFs).

Assuming baseline compliance is less than 10%, grounded on observations from FAST-M study in Malawi, to detect an increase in compliance to 20%, with an alpha of 0.05, we will require the observation of 199 participants in each phase to achieve a power of 80%. This is adequate precision to allow important increases to be estimated. Allowing for loss to follow-up and missing / laboratory results, we consider an initial sample size of 400 as appropriate to allow the study to have adequate power to detect an increase in compliance. This number of cases will be feasible to collect within 6 months, based on current rate of sepsis from hospital records of anticipated site. The flow of participants through the study is presented in Appendix-4.

Study period

This feasibility study is anticipated to run for seven months. This includes a baseline assessment period of two months, and training programme planned to schedule at completion of baseline phase before commencing intervention phase of four months.

The intervention phase will be introduced after training all health care provides involved in management of maternal sepsis at the study site. At the start of the intervention phase, FAST-M

bundle care tools will be introduced including MEOWS chart, FAST-M decision tool, and FAST-M treatment bundle. Appendix -5 provides the summary of enrollment, intervention and assessment

Modified early obstetric warning score

MEOWS stands for modified early obstetric warning score (MEOWS) to identify suspected maternal sepsis patients. This tool helps in identifying any early warning scores used to track the physiological parameters of an individual over time onto a chart, with guidance thresholds to trigger clinical action of they become abnormal [18]. The MEOWS chart used during implementation of the FAST-M intervention in the districts of Malawi will be adapted in context of Pakistan for the purpose of this feasibility study [15].

The use of obstetric early warning systems (OEWS) in UK maternity units was recommended in the 2007 Confidential Enquiry into Maternal and Child Health (CEMACH) report as an adjunct to reducing maternal morbidity and mortality. [19] MEOWS consisted of scores of respiratory rate, oxygen saturation, temperature, heart rate, blood pressure, assessment of urine, including for proteinuria, color of amniotic fluid, neurological response, pain score, assessment of lochia, and an overall assessment of whether the woman appears well [19]. Clinical action is triggered by a single parameter exceeding a red threshold or any two parameters exceeding a yellow threshold. MEOWs chart have been widely adopted in the UK and internationally [20].

To complete the MEOWS chart, the healthcare providers involved in the study will be trained to record patient observations (heart rate, respiratory rate, blood pressure, conscious level, urine output and temperature) and fetal heart rate (if applicable) from medical records. These observations will be charted on a MEOWS chart in the inpatient setting.

Decision tool

Abnormal observations (indicated by a single red or two yellow thresholds) will trigger a review by an attending doctor or nurse. This will be agreed locally prior to study commencement. These patients will then be screened for potential sepsis using the FAST-M decision tool. In addition to abnormal maternal observations, cases of suspected sepsis will also be identified using the FAST-M patient pathway when prompted by attending clinician concern regarding potential maternal sepsis or an increased fetal heart rate greater than or equal to160 beats per minute.

Patients will be defined as having or are at a higher risk of having sepsis, who will trigger a red flag on the decision tool and will be commenced immediately on the FAST-M treatment bundle pathway. These patients will receive a review from a doctor/nurse as soon as possible, with the bundle initiated within one hour. Those patients who trigger two yellow flags on the decision tool and have or at a higher risk of having sepsis require a review from a doctor/nurse within three hours. All suspected cases will remain in observation for possible development of red flags. Half-hourly (if red trigger) or hourly (if two yellow triggers) observations will be made in the first instance, until otherwise specified by an attending clinical decision maker. Those patients without at least one red or two yellow flags will be considered to have a low risk of sepsis and will be managed according to local guidelines by the screening healthcare practitioner.

FAST-M treatment bundle

Patients managed with the FAST-M treatment bundle will have their treatment recorded on the FAST-M treatment bundle form including documentation of actions completed and any reasons for not completing certain component of the bundle.

The FAST-M treatment bundle consists of the timely consideration of all the following:

- Fluids
- Antibiotics
- Source identification and control
- Assessment of the need to Transport / Transfer to a high level of care
- Ongoing Monitoring (of the mother and neonate)

Co-interventions for implementation of intervention

Training Programme

Multiple full day training sessions by the study team will be delivered to healthcare practitioners working for maternal care and sepsis management at the study site. The interactive sessions will be offered in English and Urdu languages for each healthcare practitioner to understand the processes completely. Any requirement for supplementary educational material such as posters and a study booklet will be determined during the implementation programme via feedback from front line clinical staff and stakeholders on facilitators and barriers to use of the tools. This will be done using qualitative interviews and focus groups discussion.

The training and implementation programme is likely to consist of:

- Background information on maternal sepsis, including risk factors, signs and symptoms and the potential consequences if untreated
- Use of the MEOWS chart to track and trigger the recognition of deteriorating patients
- Use of the FAST-M decision tool to recognise and screen for potential study participants at risk of maternal sepsis
- Use of the FAST-M treatment tool to initiate the bundle components
- Guidance around implementing the individual components of the FAST-M bundle
- Use of feedback tools (run chart and dashboard) and approaches the team can use to work together to improve compliance and outcomes

Post training, an impact survey will be made to measure the extent to which skills and knowledge learned in the program have translated into improved behavior among participants who attended the training program.

Clinical champions

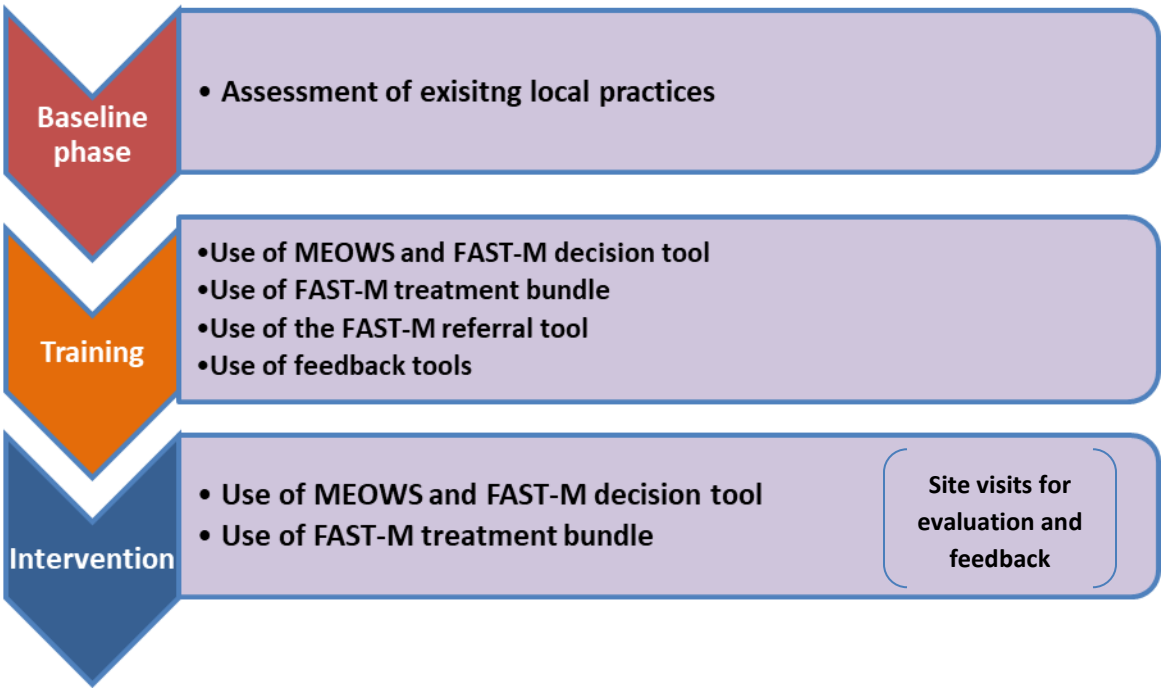
The local clinical champions and team leaders will be identified and trained to take a lead at study sites from different units where study will be implemented, and will remain engaged throughout the implementation process. The overarching goal of each champion will be to encourage engagement and compliance with the FAST-M bundle. To achieve this goal, champions at each site will be engaged in a number of key activities: disseminating knowledge, advocating, navigating boundaries, facilitating consensus, arranging meetings with stakeholders,

tracking quality indicators and developing organizational communication strategies and relationships.

Ongoing improvement approaches

Ongoing improvement practices at different units of the study site will be carried out by clinical champions of the respective units. The improvement strategies include: 1) weekly/biweekly training of health care providers on FAST-M tools, 2) display of run charts, dashboards in units to demonstrate rate of maternal sepsis and outcomes of maternal sepsis cases over-time, and 3) meeting with stakeholders for communicating needs and requirements for implementation of the FAST-M intervention. Appendix-6 shows the summary of ongoing improvement approaches planned to implement for FAST-M implementation

An overview of the implementation of the complex intervention is illustrated in the figure below;



Data collection and management

During the intervention phase, data will be collected by a member of the research team who will not be part of the clinical team. Data will be collected using CRFs on various outcomes; structural, clinical, organizational and any adverse events.

If the patient requires a transfer as part of the FAST-M treatment bundle to any other health facility due to shortage of beds or other resources, the data collector will continue to follow up the patient's clinical outcomes. The data collection team will keep their study site updated on their performance using this data, and will visually display it on run charts and dashboards and work on strategies to improve performance. The data will be maintained in an investigator file to be secured in a locked cabinet. Information recorded on the data collection sheet will be recorded in a database located on a secure server.

Analysis plan

Quantitative analyses will be done to assess numerous outcomes; process, organizational, clinical, structural and adverse events with quantitative comparisons made between before and after implementation of the bundle. Quantitative data will be analysed using percentages, means, medians interquartile ranges and 95% confidence intervals and the change identified over time. Binary outcomes will be analysed using logistic regression and continuous measures by linear regression.

A mixed methods approach will be used to explore the implementation of the intervention. In this approach both quantitative and qualitative data collection methods will be used, and then integrated to draw conclusions. A sequential exploratory design will be used to collect qualitative

data for adaption of the FAST-M bundle care tools and will be applied to make these tools contextual based. This will be then followed by the implementation of contextual based modified FAST-M tools at the study setting. This mixed-methods study will help in exploring the perspectives and adaptation of FAST-M intervention in phase 1 and evidence of its feasibility in phase 2 of the study. This will allow us to assess practicality of implementation in order to build a robust and successful full-scale trial for future.

Main outcome measurements

We will explore a range of outcomes measurement for maternal sepsis care. Primary process include 1) the proportion of patients admitted with features of sepsis who received appropriate monitoring (full set of vital sign measurements on admission recorded on MEOWS chart) 2) the proportion of women with suspected maternal sepsis received antibiotics within 1 hour (if required), 3) the proportion of women with suspected maternal sepsis receiving the FAST-M treatment bundle (including each bundle component) within 1 hour of identification of sepsis. Secondary outcomes will include: 1) the proportion of women with suspected maternal sepsis referred to clinical decision maker on the basis of abnormal vital signs records; and 2) the proportion of women with suspected maternal sepsis receiving a clinical review by a senior clinical decision maker following their diagnosis.

Potential Harms

Fluid resuscitation in patients with sepsis if not managed appropriately can precipitate volume overload and subsequent pulmonary edema. This is a particular concern in patients with preeclampsia. Clear teaching and guidance regarding fluid resuscitation will be provided during the training programme. When fluid resuscitating patients with suspected maternal sepsis, the

decision regarding the rate of fluid administration will be made by the responsible clinician based on clinical examination findings and ongoing monitoring.

Discussion

Overall, bundle care tools have the potential to enhance improvements in sepsis care [11]. However, the implementation challenges posed by these bundles should be examined, especially in low-resource settings.

The FAST-M maternal sepsis intervention has the potential to be used as an integrated strategy for early recognition and management of maternal sepsis in low resource health settings.

This mixed-method study will establish whether it is feasible to implement the FAST-M bundle for early identification and management of maternal sepsis in Pakistan. A large multi-country interventional trial is anticipated to ascertain the effectiveness of the bundle to improve maternal sepsis care and outcomes in low and middle income countries. The long-term vision is that the intervention will then be trialled in other settings across Pakistan. The study findings will be disseminated to clinicians and key stakeholders to formulate appropriate bundle care tools for sepsis care. This will help reduce the high rate of maternal mortalities caused by sepsis.

Abbreviations

CFIR: Consolidated Framework for Implementation Research; FAST-M: Fluids, Antibiotics, Source control, assessment of the need to Transport/Transfer to a higher level of care and ongoing Monitoring (of the mother and neonate);FGD: Focus Group Discussion ; HCPs: Health Care Providers; KIIs: Key Informant Interviews; LMIC: Low Middle Income Countries;

LUMHS: Liaquat University of Medical Health Sciences; MEOWS: Maternal Early Obstetric Warning Signs; SSC: Surviving Sepsis Campaign

Declarations

Ethics approval and consent to participate

Ethical approval for this study was obtained from the LUMHS hospital [REC/-886, 4-87], Aga Khan University Ethical Review Committee [2019-2061-7102] and National Bioethics Committee [515/20/]. Participants will be asked to provide written consent to indicate their willingness to participate. Voluntary participation and the right to ask any questions and to decline participation at any time will be emphasized during the data collection.

Consent for publication

Written consent for publication will be obtained from all study participants.

Availability of data and materials

All data developed for this intervention is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SI, DL, RB & LS conceptualized the design of the study and creation of data collection tools. DL, AC, RB, JS, CD provided feedback on the first draft. SI & BK edited and wrote the final draft. The authors read and approved the final manuscript.

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Appendix 1: **CFIR framework adapted from Damschroder LJ et al. for classification of outcomes**

Domains	Constructs
One: Intervention Characteristic	Intervention Source Evidence Strength and quality Relative Advantage Adaptability Trialability Complexity Design Quality and packaging Cost
Two: Outer Setting	Patient Needs and Resources Cosmopolitanism Peer Pressure External Policies and Incentives
Three: Inner Setting	Structural characteristics Networks & Communication Culture Implementation Climate Tension for change Compatibility Relative priority Organizational incentives and rewards Goals and feedback Learning climate Readiness for implementation Leadership engagement Available resources Access to knowledge and information
Four: Characteristics of Individuals	Knowledge and Beliefs about the intervention Self-efficacy Individual stage of change Individual identification with organization Other personal Attributes
Five: Process	Planning Engaging Opinion leaders Formally appointed internal implementation leaders Champions External change agents Executing Reflecting and evaluating

Appendix 2: Interview Guide

Interview Guide

1. Intervention Characteristics

1. What do you know about the intervention or its implementation?
2. How different is this intervention from your existing practices?
3. What kind of information or evidence are you aware of that shows whether or not the intervention will work in your setting?
4. What kinds of changes or alterations do you think you will need to make to the intervention so it will work effectively in your setting?
    - Do you think you will be able to make these changes? Why or why not?
5. What is your perception of the bundling of the intervention for implementation and quality of the supporting materials? Prompts: format, design, user-friendly. Duration, scope, intricacy and number of steps

2. Outer Setting

6. How do you think the individuals served by your organization will respond to the intervention?
7. What barriers will the individuals served by your organization face to participating in the intervention?
8. What kind of local, state, or national performance measures, policies, regulations, or guidelines might be important in influencing how this intervention can be implemented?

3. Inner Setting

9. Can you describe how the intervention will be integrated into current processes?
10. What are your current guidelines to assess and manage patients with maternal sepsis? Probes: tool, framework or guidelines for maternal sepsis, lactate test
11. What is your knowledge about importance of lactate test and what is your current practice about lactate testing? Probes: implications for lactate test, guidelines for lactate test
12. What is your current patient to doctor and patient to nurse's ratio in your setting?

13. Explain the role of doctors and nurses in management of maternal sepsis in your organization. Which cadre is responsible for care and at what level of care? Probes: nurses, doctors, technicians and other health care cadres

14. Other than human resources, what resources are utilized in management of maternal sepsis in your hospital?

15. Do you expect to have sufficient resources to implement and administer the intervention?

    - [If no] What resources will not be available? Probes: human resource, equipments, critical units etc

16. Do you feel the training planned for you will prepare you to carry out the roles and responsibilities expected of you? - What are the positive aspects of planned training? What is missing?

4. Characteristics of Individuals

17. How do you feel about the intervention being used in your setting?
18. Do you think the intervention will be effective in your setting? Why or why not?

5. Process

19. Who will lead implementation of the intervention?
20. Are there people in your organization who are likely to champion (go above and beyond what might be expected) the intervention?

    Prompts: Position of these champions have in your organization?

21. How do you think they will help with implementation?

Appendix 3- FAST-M bundle care tools and patient algorithm

MODIFIED EARLY OBSTETRIC WARNING CHART (MEOWS CHART)

FAST-M

Contact clinical decision maker if patient triggers **ONE RED** or **TWO YELLOW** flags at any one time.

Patient		Patient ID		DOB/Age	

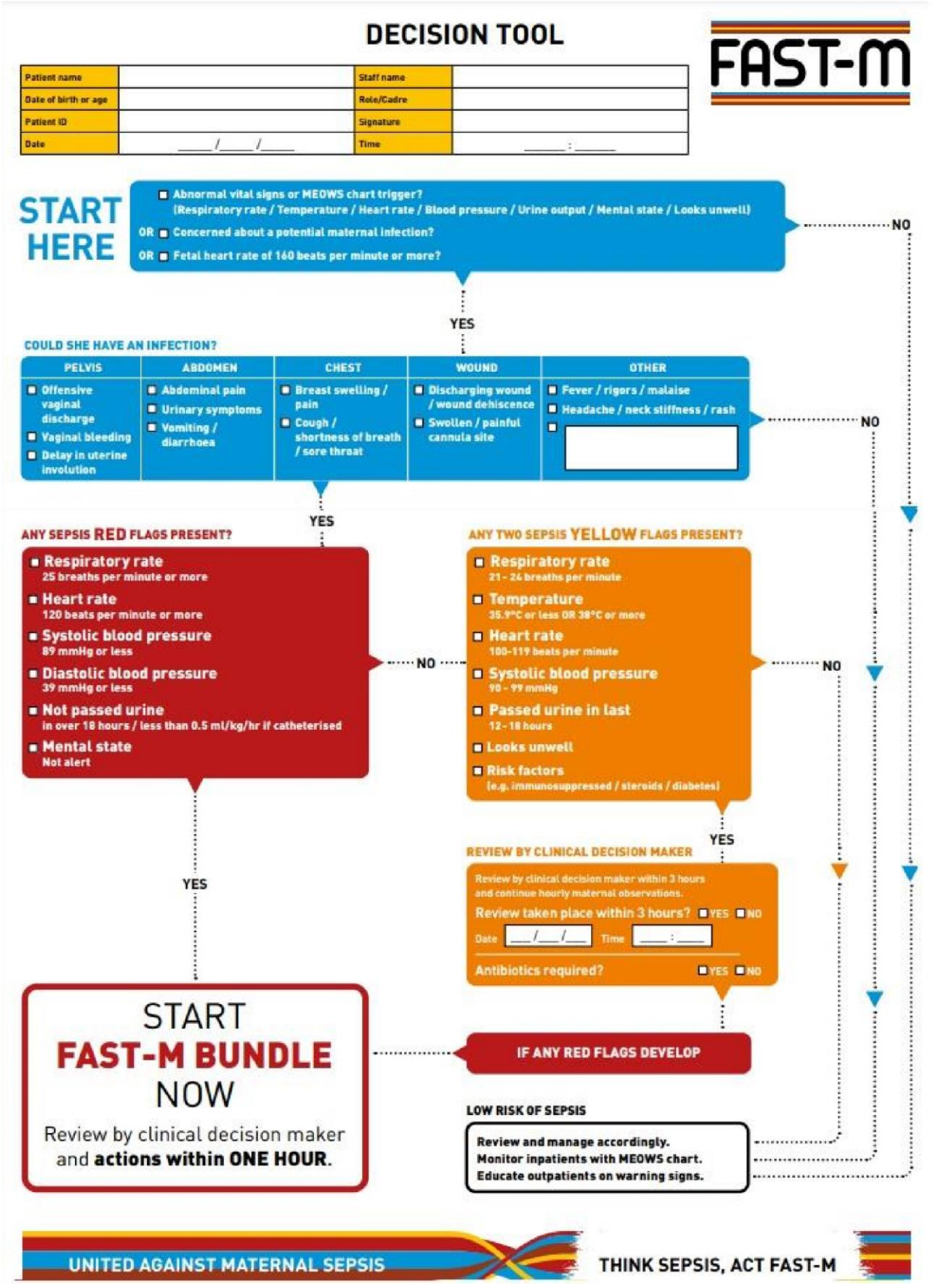
WRITE **VALUES** IN BOXES PROVIDED

			Date													
			Time													
			Initials													
Respiratory rate (breaths per minute)	25 or more	RED														
	21 - 24	YELLOW														
	11 - 20	NORMAL														
	10 or less	RED														
Temperature (°C)	38 or more	YELLOW														
	36.0 to 37.9	NORMAL														
	35.9 or less	YELLOW														
Heart rate (beats per minute)	120 or more	RED														
	100 - 119	YELLOW														
	50 - 99	NORMAL														
	40 - 49	YELLOW														
	39 or less	RED														
Systolic blood pressure (mmHg)	160 or more	RED														
	140 -159	YELLOW														
	100 -139	NORMAL														
	90 - 99	YELLOW														
	89 or less	RED														
Diastolic blood pressure (mmHg)	110 or more	RED														
	90 -109	YELLOW														
	40 - 89	NORMAL														
	39 or less	RED														
Urine output Hours since patient passed urine (tick box)	12 hours or less	NORMAL														
	12 - 18 hours	YELLOW														
	18 hours or more OR less than 0.5 ml/kg/hour	RED														
Mental State (tick box)	Alert	NORMAL														
	Not Alert	RED														
Looks unwell (tick box)	No	NORMAL														
	Yes	YELLOW														
TOTAL YELLOW FLAGS																
TOTAL RED FLAGS																
ACTION TAKEN (IF REQUIRED) Yes (Y) / No (N)																

ACT NOW if patient triggers ONE RED or TWO YELLOW flags at any time. Escalate to clinical decision maker and start FAST-M decision tool.

UNITED AGAINST MATERNAL SEPSIS

THINK SEPSIS, ACT FAST-M


DECISION TOOL
FAST-M
Patient name
Staff name
Date of birth or age
Role/Cadre
Patient ID
Signature
Date
Time
START HERE
Abnormal vital signs or MEOWS chart trigger?
(Respiratory rate / Temperature / Heart rate / Blood pressure / Urine output / Mental state / Looks unwell)
OR Concerned about a potential maternal infection?
OR Fetal heart rate of 160 beats per minute or more?
NO
YES
COULD SHE HAVE AN INFECTION?
PELVIS
Offensive vaginal discharge
Vaginal bleeding
Delay in uterine involution
ABDOMEN
Abdominal pain
Urinary symptoms
Vomiting / diarrhoea
CHEST
Breast swelling / pain
Cough / shortness of breath / sore throat
WOUND
Discharging wound / wound dehiscence
Swollen / painful cannula site
OTHER
Fever / rigors / malaise
Headache / neck stiffness / rash
NO
YES
ANY SEPSIS RED FLAGS PRESENT?
Respiratory rate
25 breaths per minute or more
Heart rate
120 beats per minute or more
Systolic blood pressure
89 mmHg or less
Diastolic blood pressure
39 mmHg or less
Not passed urine
in over 18 hours / less than 0.5 ml/kg/hr if catheterised
Mental state
Not alert
NO
ANY TWO SEPSIS YELLOW FLAGS PRESENT?
Respiratory rate
21 - 24 breaths per minute
Temperature
35.9°C or less OR 38°C or more
Heart rate
100-119 beats per minute
Systolic blood pressure
90 - 99 mmHg
Passed urine in last
12 - 18 hours
Looks unwell
Risk factors
(e.g. immunosuppressed / steroids / diabetes)
NO
YES
REVIEW BY CLINICAL DECISION MAKER
Review by clinical decision maker within 3 hours and continue hourly maternal observations.
Review taken place within 3 hours? YES NO
Date ___/___/___ Time ___:___
Antibiotics required? YES NO
YES
START
FAST-M BUNDLE
NOW
Review by clinical decision maker and actions within ONE HOUR.
IF ANY RED FLAGS DEVELOP
LOW RISK OF SEPSIS
Review and manage accordingly.
Monitor inpatients with MEOWS chart.
Educate outpatients on warning signs.
UNITED AGAINST MATERNAL SEPSIS
THINK SEPSIS, ACT FAST-M

TREATMENT BUNDLE

FAST-M

REMEMBER TO COMPLETE THESE ACTIONS WITHIN ONE HOUR

Patient name		Staff name	
D.O.B or age		Role/Cadre	
Patient ID		Signature	

Date & time of red flag observation	__/__/__ __:__	Date & time bundle started	__/__/__ __:__	Date & time of review by clinical decision maker	__/__/__ __:__

F — FLUIDS (caution in pre-eclampsia, severe anaemia and pulmonary oedema)

Date	__/__/__	Time fluids initiated	____:____	Initials	
Details / reason not completed					

Give 500 ml crystalloid immediately. Repeat 500 ml boluses to a maximum of 30 ml/kg if hypotension persists.

A — ANTIBIOTICS

Date	__/__/__	Time started	____:____	Initials	
Details / reason not completed					

See antibiotic guidelines below

S — SOURCE – identify and treat the source of infection

Date	__/__/__	Time considered	____:____	Initials	
Details / reason not completed					

See source identification and treatment boxes below

T — TRANSPORT (to higher level hospital or location within hospital, if required)

Date & time transport considered	__/__/__ __:__	Initials		Transport Required	☐ YES ☐ NO
Date & time transport requested	__/__/__ __:__	Initials		☐ N/A	
Date & time patient left facility	__/__/__ __:__	Initials			
Destination					
Reason for any delay					

M — MONITORING (start MEOWS chart if not already started. Repeat observations every 30 minutes until otherwise decided by clinical decision maker)

Date & time monitoring commenced	__/__/__ ____:____	Details / reason not completed
Maternal / fetal monitoring should include	• Respiratory rate • Temperature • Heart rate • Blood pressure • Urine output • Mental state • Fetal heart rate	
Neonatal monitoring and review commenced	☐ YES ☐ NO ☐ N/A	

ANTIBIOTIC GUIDELINES

Insert local guidance here

Immediate treatment for Maternal Sepsis:

- Ceftriaxone 2 g IV once daily (if no IV access this can be given as 2 IM injections of 1 g in different sites).
- If possible intra-abdominal source add Metronidazole 500 mg IV three times daily or 400 mg PO three times daily.

If above antibiotic regime is not available then give:

- Chloramphenicol 1 g IV/IM four times daily plus Gentamycin 240 mg IV/IM once daily.

If maternal infection source is known, or as soon as it is identified:

- Use specific treatment based on Malawi Standard Treatment Guidelines.

IDENTIFY THE SOURCE

Consider

• Clinical history	• Blood cultures	• Sputum sample
• Clinical examination	• HIV and Malaria testing	• Imaging (abdominal, chest)
• Blood tests (if available) (FBC, U&Es, LFTs, CRP, clotting)	• Urine sample	• Lumbar puncture
	• Swabs (wound, vagina, throat)	• Other _____

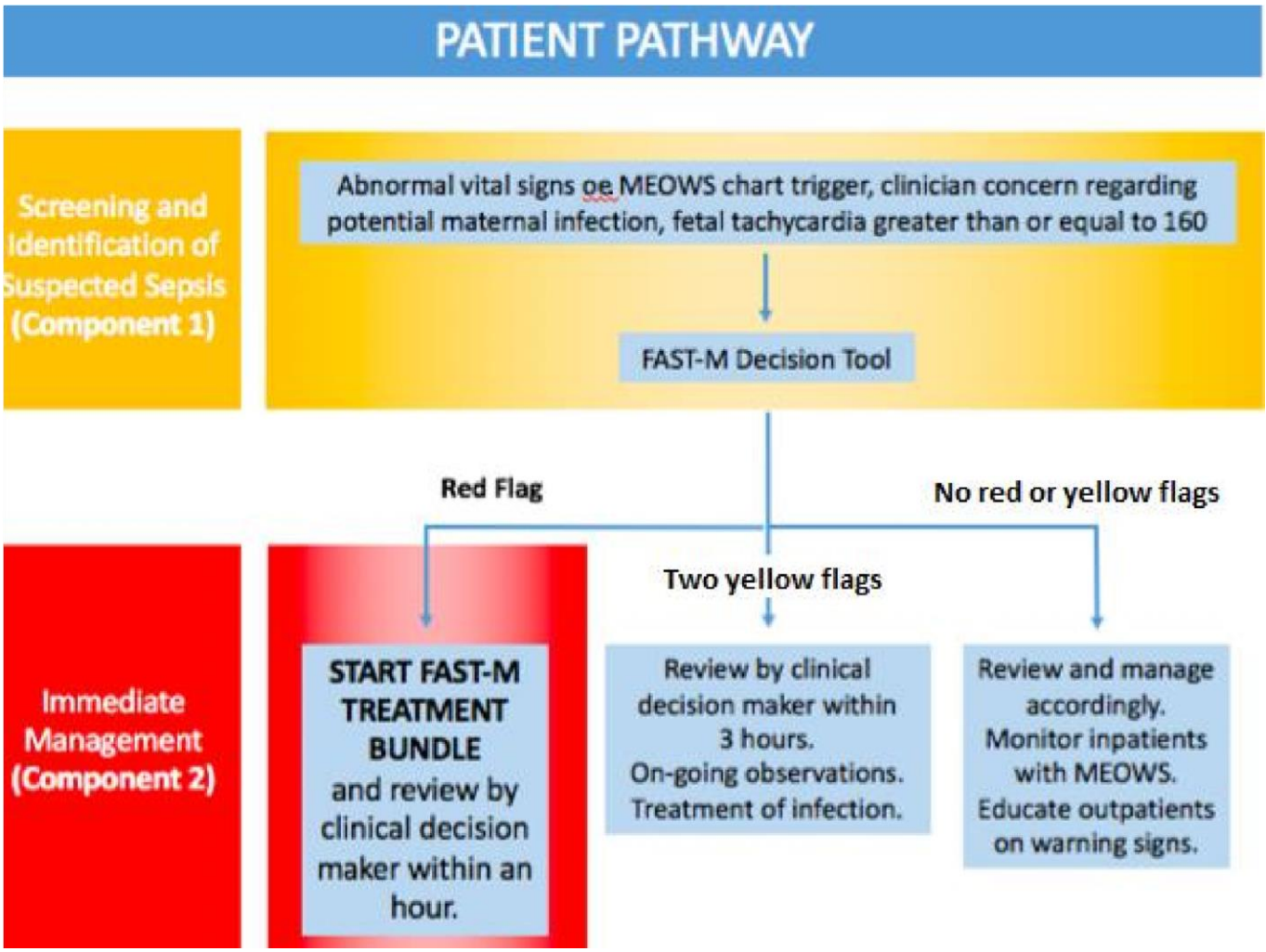
REMOVE / TREAT THE SOURCE

Consider

• Malaria treatment	• Removal of infected cannula / line
• Consider delivery of baby	• Hysterectomy
• Removal of retained products of conception	• Targeted antibiotics once source known
• Debridement of wound / drainage of collection	

UNITED AGAINST MATERNAL SEPSIS

THINK SEPSIS, ACT FAST-M


PATIENT PATHWAY
Screening and identification of Suspected Sepsis (Component 1)
Abnormal vital signs oe MEOWS chart trigger, clinician concern regarding potential maternal infection, fetal tachycardia greater than or equal to 160
FAST-M Decision Tool
Red Flag
No red or yellow flags
Two yellow flags
Immediate Management (Component 2)
START FAST-M TREATMENT BUNDLE and review by clinical decision maker within an hour.
Review by clinical decision maker within 3 hours. On-going observations. Treatment of infection.
Review and manage accordingly. Monitor inpatients with MEOWS. Educate outpatients on warning signs.

Appendix 4: Figure 1.

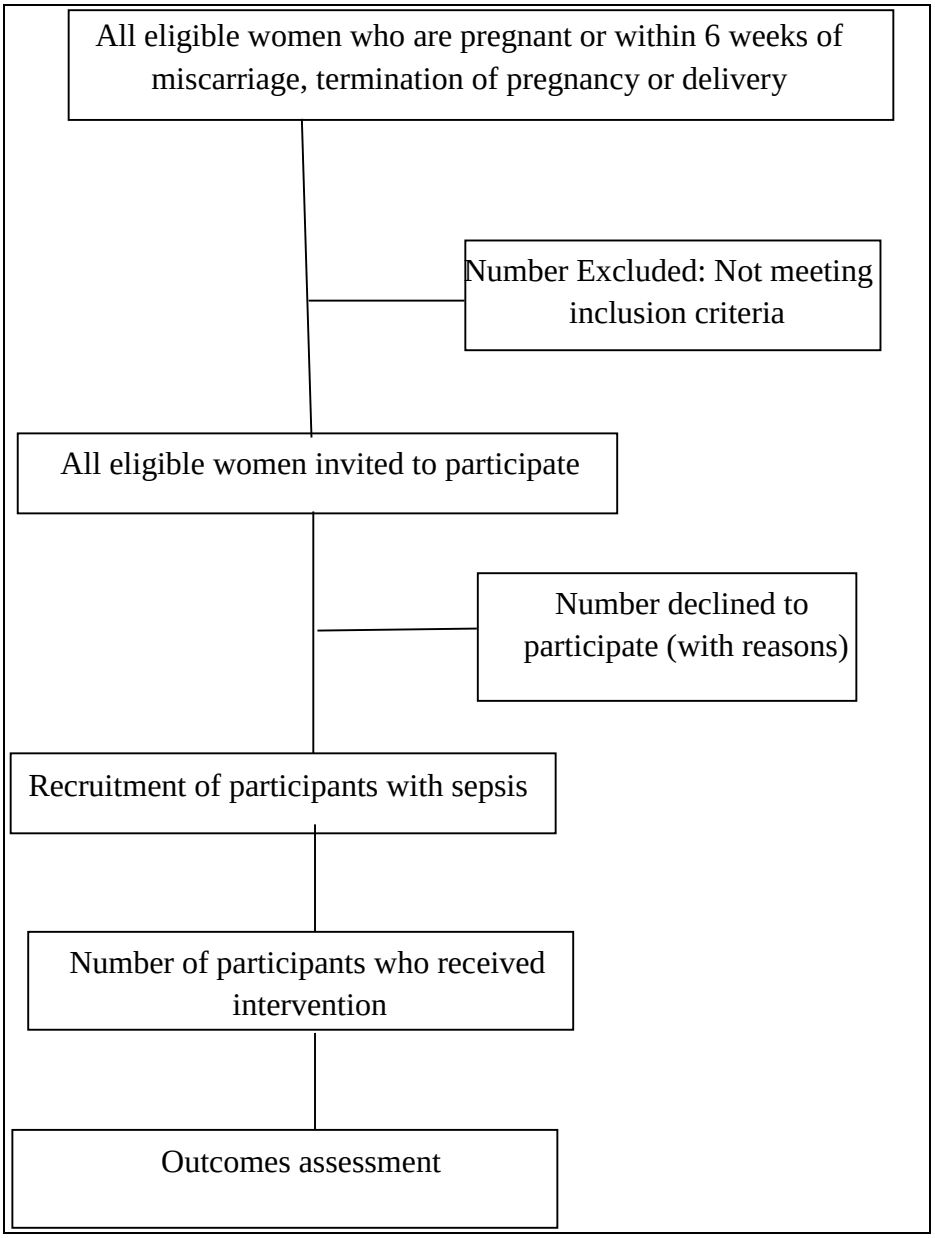


Fig. 1. Flow of participants through the study

Appendix 5: Figure 2

	STUDY PERIOD			
	Enrolment	**Allocation**	**Post-allocation**	**Close-out**
TIMEPOINT	$-t_1$	**0**	t_1	t_2
ENROLMENT:				
Eligibility screen	X			
Informed consent	X			
Baseline data collection	X			
Allocation		X		
INTERVENTION:				
Feasibility of FASTM bundle care tool			⟷	
ASSESSMENTS:				
/proportion of inpatients receiving a full set of vital signs on admission/			X	
/proportion of women with suspected maternal sepsis receiving the full FAST-M bundle/			X	X
/proportion of women with suspected maternal sepsis escalated to senior healthcare practitioners on the basis of abnormal vital signs/			X	X

Fig. 2. Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) figure of enrolment, interventions and assessments

Appendix 6

Approaches	Planned Strategies
Facility level approaches	Site leadership by project champion,
	Formation of local sepsis committee
	Formal site launch
Individual level approaches	Multi-disciplinary, scenario-based local training
	Coaching by local project champion
	Aide-memoires, posters
	Paper-based tools (MEOWS chart, decision tool, treatment tool)
	Task sharing of vital sign measurement
Ongoing improvement approaches	Site based performance dashboards and run charts
	Local problem solving: led by sepsis committee (ongoing quality improvement, ownership, local adaptations, engagement, learning climate and sustainability)

Table 1. Summarised FAST-M implementation approach