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Electronic clinical decision support for acute fever management

Submission date
03/10/2023

Recruitment status
No longer recruiting

Registration date
17/10/2023

Overall study status
Completed

Last Edited
27/05/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute febrile illness (AFI) is a common reason for patient presentations to primary healthcare providers, such as primary healthcare centres (PHCs), in rural South and Southeast Asia. Malaria was previously a common cause of acute fever. However, the drastic reduction in malaria incidence due, in part, to the established use of malaria rapid diagnostic tests, means that presumptive treatment for malaria in such patients is no longer appropriate. Compounding this issue is that of poor clinical and laboratory diagnostic capacity because of low healthcare worker skills and the isolation of healthcare facilities. These factors lead to sub-optimal clinical decision-making, resulting in issues such as over-prescription of empirical antibiotic therapy and missed identification of patients needing higher-level care. In addition to the impact on the quality of patient care, over-prescription of antibiotics also drives antimicrobial resistance (AMR), a problem which is especially urgent in this region. Improving the management of acute fever by upskilling healthcare workers to treat more than just malaria also has the benefit of ensuring the success of malaria eradication programmes by maintaining confidence in primary healthcare services, as malaria treatment is dependent on patients continuing to seek care. In this study, rural primary health centres (PHCs) in Battambang province, Cambodia have been clustered together and then randomly assigned to different experimental groups to evaluate the impact of an electronic decision support tool on antibiotic prescribing for patients who present with acute fever.

Who can participate?
Patients aged 1 year and over who have an unscheduled presentation at the participating PHCs for acute care

What does the study involve?
The tool, named EDAM (short for 'Electronic clinical Decision support for Acute fever Management') integrates symptoms, vital sign measurements (including pulse oximetry), and two point-of-care diagnostic tests (malaria and C-reactive protein) into an algorithm deployable as a mobile app on Android devices. The study is powered by site, and the randomisation will be done at site level i.e., such that each site will have 15 control and 15 intervention clusters, rather than considering all clusters in the three sites together before randomisation. A cluster is defined as one PHC and control PHCs will continue with the current standard of care. This study

has been motivated by the appetite among experts, policymakers, and healthcare workers in PHCs for algorithmic management of AFI incorporating point-of-care tests which have the potential to change management, as documented in a series of stakeholder analyses conducted across the region and as described in the literature. In addition to antibiotic prescribing, various secondary outcomes will also be assessed (see above). This study will leverage the infrastructure of the South and Southeast Asian Community-based Trials Network (SEACTN) which, since 2021, has been running a large-scale observational study aiming to define the regional epidemiology of AFI in primary care (SEACTN Rural Febrile Illness (RFI) Project Work Package A).

To date, no such electronic clinical decision support tool tailored to rural South and Southeast Asian primary care settings has been developed or assessed under real-world conditions. The results of this study will, therefore, provide crucial information for digital health practitioners, public health policymakers, and researchers to help refine further iterations of EDAM and inform the development of other electronic decision support tools for semi-skilled primary health workers in this region.

What are the possible benefits and risks of participating?
Currently, given the low clinical diagnostic and management skill levels of rural primary healthcare workers in the study sites, hospital referral and antibiotic prescribing are poorly targeted. This leads to potential inappropriate referral and burdening of secondary care, inappropriate antibiotic prescribing such as to patients in whom antibiotics are not indicated or the prescription of an antibiotic not appropriate to the clinical syndrome, and non-identification of patients whose care should be escalated and/or to whom antibiotics should be prescribed. Furthermore, unnecessary use of antibiotics exposes patients to the risk of adverse effects and is known to increase the risk of subsequent acquisition of resistant infections, as well as destruction of the microbiome with a host of associated adverse outcomes. EDAM addresses all these issues in an easy-to-use, tablet-based app, and this study will provide information on its effectiveness in streamlining patient management, including better antibiotic stewardship which will reduce the prevalence of antibiotic-resistant bacteria in the population, and preserving antibiotics for treating serious bacterial infections. There will be no other direct benefits to participants for taking part in this study.

The risks of participation are low. Firstly, the measurement of oxygen saturation using pulse oximetry is now considered the ‘fifth vital sign’ and is recommended by the WHO when possible in rural LMIC primary care settings, therefore its use is not controversial. Secondly, symptom- and vital sign-based diagnostic algorithms, such as the Integrated Management of Childhood Illness guideline, are also widely used in clinical practice. Lastly, MORU has previously conducted a large clinical trial on CRP-guided treatment in patients with AFI with extensive patient follow-up, demonstrating that it is effective in reducing antibiotic prescribing and did not adversely affect patient outcomes. A decision support tool integrating all three would, therefore, not be expected to pose a risk to patient safety. Healthcare workers in the intervention arm are also able to use their discretion if they do not agree with the management recommended by EDAM. Additionally, as an extra safeguard, they will be trained to provide safety-netting to all patients they recruit. As such, no major risks of harm from participating in this implementation study are foreseen, although there may be possible mild discomfort while taking finger-prick blood for malaria and CRP rapid tests. The potential risks of using confidential data will be minimised by anonymisation.

Where is the study run from?
Mahidol Oxford Tropical Medicine Research Unit (Thailand)

When is the study starting and how long is it expected to run for?
November 2022 to April 2025

Who is funding the study?
1. The Wellcome Trust (UK)
2. The Australasian Society for Infectious Diseases (Australia)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
HCR23008

Study information

Scientific Title
Evaluation of an electronic clinical decision support algorithm to improve rural primary care management of acute febrile illness

Acronym
EDAM

Study objectives
Can an electronic clinical decision support tool which integrates clinical features, pulse oximetry, and malaria and C-reactive protein (CRP) rapid tests into an algorithm (the EDAM app) improve routine clinical management of patients with acute febrile illness?

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 02/10/2023, Oxford Tropical Research Ethics Committee (OxTREC) (Research Services, University of Oxford, Boundary Brook House, Churchill Drive, Headington, Oxford, OX3 7GB, United Kingdom; +44 (0)1865(2)82585; oxtrec@admin.ox.ac.uk), ref: 550-23

2. approved 29/12/2023, Cambodian National Ethics Committee for Health Research (National Institute of Public Health, Lot 80, 289 Samdach Penn Nouth St, Phnom Penh, 120408, Cambodia; +855 (0)12528789; nouthsarida@gmail.com), ref: 395-NECHR

Study design
Pragmatic cluster-randomized controlled trial with two study arms

Primary study design
Interventional

Study type(s)
Diagnostic, Treatment, Safety

Health condition(s) or problem(s) studied
Acute febrile illness

Interventions
Current interventions as of 05/06/2024:

This is a pragmatic, cluster-randomized controlled trial with two study arms each comprised of 15 clusters located in Battambang province, Cambodia. A cluster is defined as a primary health centre (PHC).

The intervention is the use of the EDAM app. PHCs at each site will be randomly allocated into two study arms using a computer-generated procedure:
• Arm 1: EDAM app-guided clinical management arm (N = 15 PHCs)
• Arm 2: control (standard care) arm (N = 15 PHCs)
Intervention arm PHCs will be provided with the full version of the app capable of executing functions required for the study (screening, recruitment, and data collection) in addition to the clinical decision support algorithm. Control arm PHCs will have a simplified version that does not contain the clinical decision support algorithm but is able to perform the other functions.

Previous interventions:

This is a pragmatic, cluster-randomized controlled trial with two study arms. There will be three study sites, each comprised of 30 clusters, located in Bangladesh, Cambodia, and Myanmar. A cluster is defined as a primary health centre (PHC).

The intervention is the use of the EDAM app. PHCs at each site will be randomly allocated into two study arms using a computer-generated procedure:
• Arm 1: EDAM app-guided clinical management arm (N = 15 PHCs)
• Arm 2: control (standard care) arm (N = 15 PHCs)
Intervention arm PHCs will be provided with the full version of the app capable of executing functions required for the study (screening, recruitment, and data collection) in addition to the clinical decision support algorithm. Control arm PHCs will have a simplified version that does not contain the clinical decision support algorithm but is able to perform the other functions.

Intervention Type
Other

Primary outcome(s)
Proportion of patients with acute fever aged ≥1 year who are prescribed antibiotics in the two study arms measured using data collected in the EDAM app by the end of the study

Key secondary outcome(s))
Current secondary outcome measures as of 04/10/2024:

1. The proportion of patients with full recovery at 7 and 14 days in intervention and control PHCs.
2. The proportion of patients referred to hospital at presentation in intervention and control PHCs.
3. The proportion of patients in intervention PHCs whose management followed the EDAM recommendations.
4. The proportion of patients with unplanned re-presentations to any healthcare facility at 7 and 14 days (if not fully recovered by 7 days) in intervention and control PHCs.
5. The proportion of patients prescribed antibiotics by a healthcare provider or who independently purchased antibiotics during the follow-up period, as determined by self-report, in intervention and control PHCs.
6. The proportion of patients with severe clinical outcomes (death or hospitalization) at 7 and 14 days (if not fully recovered by 7 days) in intervention and control PHCs, not including those referred to hospital at presentation.
7. The proportion of patients prescribed an antibiotic in intervention PHCs by CRP level (<10 mg /L, between 10 and 80mg/L, >80 mg/L)
8. The usability and acceptability of EDAM for healthcare workers (a separate ethical approval application will be made for this work).
9. The cost-effectiveness of EDAM compared to routine care.

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Previous secondary outcome measures:

The following secondary outcome measures use data collected in the EDAM app, except where measures are defined:
1. Proportion of patients with full recovery at 7 and 14 days in the two study arms
2. Proportion of patients referred to hospital at presentation in the two study arms
3. Proportion of patients in the intervention arm whose management followed the EDAM

recommendations
4. Proportion of patients with unplanned re-presentations at 7 and 14 days (if not fully recovered by 7 days) in the two study arms; for patients who re-present, proportion prescribed antibiotics
5. Proportion of patients with severe clinical outcomes (death or hospitalization) at 7 and 14 days (if not fully recovered by 7 days) in the two study arms, not including those referred to hospital at presentation.
6. Proportion of patients prescribed an antibiotic in the intervention arm with:
6.1. CRP less than 10 mg/L
6.2. CRP more than or equal to 10mg/L, less than or equal to 80mg/L
6.3. CRP more than 80mg/L
7. Measure of usability and acceptability measured using structured interviews conducted with the healthcare workers in the intervention arm at the end of the study to determine whether EDAM is usable and useful and whether they support its continued use (a separate ethical approval application will be made for this work).
8. Measure of cost-effectiveness measured using study records by the end of the study: A cost-effectiveness analysis will be carried out to assess the budget implications of introducing EDAM

Completion date
28/04/2025

Eligibility

Key inclusion criteria
1. Age ≥1 year
2. Unscheduled presentation for acute care
3. Documented fever (≥37.5°C axillary) or hypothermia (<35.5°C) or history of fever in the last 24 hours

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
1 years

Sex
All

Total final enrolment
4752

Key exclusion criteria
1. Onset of illness ≤14 days
2. Presenting due to accident or trauma

3. Presenting ≤3 days after routine immunizations
4. Presenting within the follow-up period

Date of first enrolment
27/05/2024

Date of final enrolment
13/01/2025

Locations

Countries of recruitment
Cambodia

Study participating centre
Ta Sanh Health Centre
Samlout District, Battambang Province
Cambodia
Cambodia
020907

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research council

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Australasian Society for Infectious Diseases

Alternative Name(s)
Australasian Society for Infectious Diseases (ASID) Limited, Australasian Society for Infectious Diseases Limited, ASID

Funding Body Type
Government organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Australia

Results and Publications

Individual participant data (IPD) sharing plan
Electronic data will not be modifiable by the healthcare worker after submission to the server. The database and all electronic data will be backed up daily, with weekly off-site storage. In accordance with MORU Standard Operating Procedures (SOPs), de-identified electronic data will be stored indefinitely on the central server, while paper records will be preserved for five years. Anonymised stored data may be shared with other researchers for future use according to the terms defined in the MORU data-sharing policy (https://www.tropmedres.ac/units/moru-bangkok/bioethics-engagement/data-sharing/moru-tropical-network-policy-on-sharing-data-and-other-outputs).

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		18/10/2024	21/10/2024	Yes	No
Protocol file	version 2.0	13/02/2024	05/06/2024	No	No
Statistical Analysis Plan	version 1.0		27/05/2025	No	No