ISRCTN71392921 https://doi.org/10.1186/ISRCTN71392921

Innovative monitoring in paediatrics in low-resource settings: an aid to save lives?

Submission date
29/03/2022

Recruitment status
No longer recruiting

Registration date
25/04/2022

Overall study status
Completed

Last Edited
09/04/2025

Condition category
Signs and Symptoms

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The number of children dying in African hospitals remains too high. A large part may be prevented if children can be observed more closely allowing timely life-saving treatments. Continuous monitoring of vital signs such as heart rate and oxygen saturation is applied for this reason in high-income countries but these techniques have not been adapted for low resource settings. New techniques allow not only to detect but also to predict deterioration, these include new vital signs sensors, bedside blood tests (biomarkers), and artificial intelligence /machine learning.

The study aims to a) develop algorithms using vital signs to predict deterioration (critical illness) by applying a vital signs monitor system (IMPALA) developed for use in African hospitals, and b) test if biomarkers can help to predict critical illness alongside vital signs.
The overall aim of the entire IMPALA project is to adjust a monitoring system for use in children in a low-resource setting by making it affordable, user-friendly, robust, and integrating a validated algorithm to detect critical illness allowing early detection and treatment. The primary aim is to reduce amendable in-hospital deaths in children living in low-resource settings.

Who can participate?
Children aged 28 days to 60 months that will be admitted to the high dependency wards

What does the study involve?
This clinical observational study will gather the data required to develop the predictive algorithms that will be incorporated into the IMPALA system. These data will consist of vital signs (e.g. blood pressure, heart rate, and respiratory rate) of 1,000 children admitted to the high dependency unit of two hospitals in Malawi (Queen Elizabeth Central Hospital and Zomba Central Hospital). In addition, small blood samples will be collected for bedside detection of biomarkers (RNA or protein) that may predict critical illness and sociodemographic data of the patients will be collected. These data and/or data on the biomarker will optionally be used to strengthen the predictive power of the predictive algorithms.

What are the possible benefits and risks of participating?
Potential benefits:

If an abnormality in routine vital signs is noted while the participant is being observed for the study, a doctor or clinical officer will be informed and the participant will be assisted accordingly. Participant conditions will be measured all the time, and if any problem is detected early, early treatment will be administered.
Potential risks:
There are no potential risks associated with the monitoring system based on previous experience in the Netherlands and Malawi
The child might find the monitoring discomforting
The blood and nasals mucus will be taken using routine care approaches and will carry the usual risks associated with these techniques

Where is the study run from?
Kamuzu University of Health Sciences (KUHeS) (Malawi)

When is the study starting and how long is it expected to run for?
March 2022 to July 2023

Who is funding the study?
European & Developing Countries Clinical Trials Partnership (Netherlands)

Who is the main contact?
William Nkhono, wnkhono@kuhes.ac.mw

Contact information

Type(s)
Principal investigator

Contact name
Dr Job Calis

ORCID ID
https://orcid.org/0000-0001-6522-1347

Contact details
Amsterdam Center Global Child Health - AIGHD
Amsterdam University Medical Centers (NL)
Amsterdam
Netherlands
Private bag 360
+31 616154964
job.calis@gmail.com

Type(s)
Principal investigator

Contact name
Dr Jenala Njirammadzi

Contact details

Kamuzu University of Health Sciences (KUHeS)
Blantyre
Malawi
Private bag 360
+265 (0)999282885
Jnjirammadzi@kuhes.ac.mw

Type(s)
Scientific

Contact name
Dr Josephine Langton

Contact details
Department of Paediatrics and Child Health
KUHeS
Blantyre
Malawi
PBag 360
+265-9-93630543
joelangton@doctors.org.uk

Type(s)
Scientific

Contact name
Dr James Makina

Contact details
Department of Paediatrics and Child health - MOH
Blantyre
Malawi
-
+265 (0)881068899
jhmakina01@hotmail.com

Type(s)
Scientific

Contact name
Dr Jessica Chikwana

Contact details
Department of Paediatrics and Child Health - MoH & Zomba Central Hospital
Zomba
Malawi
-
+265 (0)999303951
jesschikwana22@gmail.com

Type(s)

Scientific

Contact name
Dr Glory Mzembe

Contact details
Training and Research Unit of Excellence (TRUE)
Zomba
Malawi
-
+265 (0)997373789
gmzembe@cartafrica.org

Type(s)
Scientific

Contact name
Mrs Jacquline Msefula

Contact details
Kamuzu University of Health Sciences (KUHeS)
Blantyre
Malawi
-
+265 (0)998110962
Jmsefula@kuhes.ac.mw

Type(s)
Scientific

Contact name
Prof Michael Levin

Contact details
Imperial College London
London
United Kingdom
-
+44 7967700750
m.levin@imperial.ac.uk

Type(s)
Scientific

Contact name
Mr William Nkhono

Contact details
Kamuzu University of Health Sciences (KUHeS)
Blantyre
Malawi

-
+265 (0)993204898
wnkhono@kuhes.ac.mw

Type(s)
Scientific

Contact name
Prof Mark Hoogendoorn

Contact details
Amsterdam Institute for Global Health & Development
Vrije University of Amsterdam
Amsterdam
Netherlands
1081 HV
+31 (0)205987772
m.hoogendoorn@vu.nl

Type(s)
Scientific

Contact name
Dr Maria José Villalobos Quesada

Contact details
Senior scientist - bioinformatics, networks and bioethics
National eHealth Living Lab – Leiden University Medical Center
Leiden
Netherlands
-
+31 (0)642697065
M.J.Villalobos_Quesada@lumc.nl

Type(s)
Scientific

Contact name
Dr Alick Vweza

Contact details
Biomedical engineer
Malawi University of Business and Applied Sciences (MUBAS)
Blantyre
Malawi
-
+265 (0)991199899
avweza@mubas.ac.mw

Type(s)
Scientific

Contact name
Mr Bart Bierling

Contact details
Biomedical engineer and founder of the social enterprise GOAL3
Amsterdam
Netherlands
-
+31 (0)640687620 / +265 (0)997867890
bart.bierling@goal3.org

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
RIA2020I-3294

Study information

Scientific Title
Innovative Monitoring in Paediatrics in Low-resource settings: In search of machine learning algorithms using vital signs and biomarkers

Acronym
IMPALA

Study objectives
To predict critical illness in Malawian children using vital signs monitoring and applying machine learning to detect, train and test a predictive algorithm.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/05/2022, College of Medicine Research & Ethics Committee (COMREC) (Kamuzu University of Health Sciences, Private Bag 360, Chichiri, Blantyre 3, Malawi; +2651874377; comrec@medcol.mw), ref: P.02/22/3575

Study design
Observational cross sectional

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Early detection and prevention of critical illness in children in high dependence unit (HDU) in Malawian hospitals

Interventions
This is a clinical observational study aimed at the identification of predictors of critical illness in children using vital signs, clinical information, and point-of-care (POC) biomarkers at Queen Elizabeth Central Hospital (QECH) and Zomba Central Hospital (ZCH)

Participants will be connected to a vital signs monitoring device/sensors(sticker and the clip) upon giving informed consent and admission to the high dependency unit (HDU). The vital signs will be monitored at regular intervals throughout the patient's admission duration. The instruments are non-invasive and will remain outside of the body and will not cause any pain to the participant. The monitor will be used until the participant gets better and can move to a normal hospital ward or when the participant does not require constant monitoring anymore. The clinical team will decide if the patient does not require monitoring.

In addition to the continuous monitoring, nurses will gather routine 6 daily vital signs including temperature, Blantyre Coma Score, capillary refill time, pulses, limb temperature and pallor as well as clinical observations. A daily weight will be taken. As most of these data are routinely collected for clinical purposes we will enter these on the e-CRF and the hospital charts to minimise the impact on the patients.

Study samples will be collected on study enrolment after informed consent. A repeat sample will be collected in children with the critical illness event sepsis. On enrolment (admission to the high dependency area) we will collect:
1. 1-2 ml for blood culture and malaria microscopy (if not yet collected in the prior 24 hrs)
2. 1-2 ml venous blood sample in an EDTA tube for biomarker testing and storage
3. A nasal swab for detection of respiratory viruses using PCR
4. 2-10 ml urine using a urine collection bag for dipstick testing and storage

If during the study the clinical team decides to collect a new blood culture and/or start or change antibiotics, the study nurse will ask the clinical team to draw an additional 2 ml for:
1. 1-2 ml venous blood sample in an EDTA tube for biomarker testing and storage
2. Malaria microscopy (if not yet ordered by the clinical team)

The study nurse will further collect a new nasal swab for detection of respiratory viruses using PCR and 2-10 ml urine using a urine collection bag for dipstick testing and storage. Children will not be pricked extra for these samples. All the above samples will only be collected if we can combine collection sampling with that of the clinical team. We do not expect to follow up with any of the participants after they have been discharged from the hospital.

Intervention Type
Other

Primary outcome(s)
Critical Illness events are measured every 4 hours by the clinical hospital nurse:
1. Respiratory - Start or increase respiratory support: oxygen or CPAP, (Non)Invasive ventilation: bag & mask ventilation or intubation, start or increase of bronchodilator support
2. Circulatory - Transfusion of blood (products), Intravenous fluid bolus of 10ml/kg or more, start or increase of continuous/intermittent inotropic support (IV/IM adrenalin), cardio-pulmonary

resuscitation (CPR): resuscitation setting involving chest compressions
3. Neurological - Decrease in Blantyre Coma Score of 1 point or more, Convulsions requiring anticonvulsants
4. Other
4.1. Sepsis: clinical suspicion of sepsis that has led to the collection of new blood culture and/or starts or change in antibiotic treatment
4.2. Start anti-malarial treatment
4.3. Objectified hypoglycaemia requiring correction (IV or enteral)
4.4. Unplanned admission to the (P)ICU
4.5. Unplanned surgical procedure (including chest drains)
4.6. Death

Key secondary outcome(s))
1. To assess the contribution of adding sociodemographic data to the predictive power of the algorithms.
2. To assess the potential added role of a predefined set of biomarkers in a predictive algorithm to detect critical illness. These markers will be including POC testing of two RNA transcription markers (FAM89A and IFI44L), C-Reactive protein and further analysis including previously described markers.
3. Design separate predictive models for critical illness in a better-resourced centre (Blantyre) as compared to a less-resourced centre (Zomba) which may more closely resemble most sub-Saharan hospital settings and assess the accuracy of these models.
4. Design separate predictive models for critical illness in infants (aged between 28 days and 12 months) and older children (12 to 60 months) and assess the accuracy of these models.
5. Make predictive models using conventional statistical approaches to compare the accuracy (sensitivity, specificity, false-positive and negative ratios, and area under the curve) of our model (s) against models published in the literature or identified in a retrospective dataset.

Completion date
31/07/2023

Eligibility

Key inclusion criteria
Children aged 28 days – 60 months that will be admitted to the high dependency bays

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
28 days

Upper age limit
60 months

Sex
All

Total final enrolment
793

Key exclusion criteria
1. Children outside the age range
2. Children not admitted to the high dependency bays/ward
3. Children in which monitoring is technically not possible
4. No informed consent was given on admission

Date of first enrolment
01/07/2022

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
Malawi

Study participating centre
Kamuzu University of Health Sciences (KUHeS)
Private Bag 360
Blantyre
Malawi
-

Study participating centre
Training Research Unit of Excellence
1 Kufa Road
Mandala
Blantyre
Malawi
-

Sponsor information

Organisation
Stichting Amsterdam Institute for Global Health and Development (AIGHD)

Funder(s)

Funder type
Government

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European & Developing Countries Clinical Trials Partnership (EDCTP), The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
Clinical data generated during this study is considered highly sensitive data. Sharing data within the consortium activities will be carried out according to the consortium agreement, which will consider the conditions established by the GDPR. If considered necessary, a DTA will be signed.

The monitoring system is being developed by a non-profit organisation (Goal3), which is part of the consortium. It will be established if an embargo period for sharing data is necessary and if the monitoring system, software and algorithm will be subjected to IP rights.

Informed consent will include the choice to consent to sharing data beyond the project with restricted access, for secondary purposes, and only when certain conditions are met. We do not plan to restrict the use of data depending on the nature of the requester (public or private), or objectives (for-profit or non-profit). Access will be granted according to the conditions established in the consortium agreement and by a data access committee.

IPD sharing plan summary
Stored in publicly available repository, Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Basic results			09/04/2025	No	No
Participant information sheet	version 1.0	01/02/2022	25/04/2022	No	Yes
Protocol file	version 1.0	31/12/2021	25/04/2022	No	No
Statistical Analysis Plan	version 1.0	28/03/2022	25/04/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes