Grand Challenges ICODA webinar series

Privacy Enhancing Technologies (PETs): The use of Trusted Research Environments in global health research

Neil Postlethwaite
Technical Director, ICODA

Joseph Ouma
Senior Programmer, periCOVID study

Dr Carl Marincowitz
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Convened by

Agenda

Overview of Trusted Research Environments

Neil Postlethwaite
Technical Director International COVID-19 Data Alliance (ICODA) / HDR Global

- Overview of Privacy-Enhancing Technologies (PETs)
- Background on ICODA
- Introduction to the Five Safes
- The ICODA Workbench as our Trusted Research Environment

Trusted Research Environments in practice

Joseph Ouma
Senior Programmer for the periCOVID study, Makarere University Johns Hopkins University (MUJHU), Uganda

Dr Carl Marincowitz
Principal Investigator of the PRIEST Study for Low and Middle-Income Countries, Sheffield University, UK

- Brief overview of research project
- Experience using TREs in project

Q/A

Privacy-Enhancing Technologies

Traditional PETs:

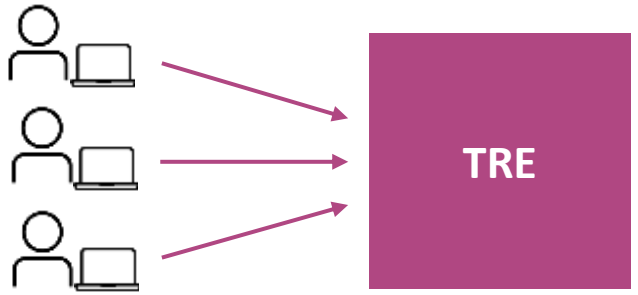
- Encryption in transit and at rest
- De-identification techniques

Emerging PETs:

- **Trusted Research Environments**
- Federated analytics
- Differential privacy
- Multi-party computation
- Homomorphic encryption

Reference: https://cdeiuk.github.io/pets-adoption-guide/what-are-pets

Enables researchers to **collaborate**, **link data**, **run analyses**, and **share code and results** within a secure environment.

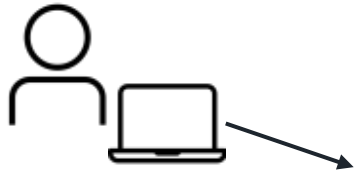


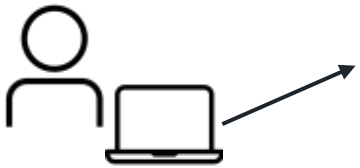
Researchers

Other names:

- Trusted Execution Environments (TEE)
- Virtual Research Environment (VRE)
- Digital Research Environments (DRE)
- Secure Research Environment (SRE)
- Secure Data Environment (SDE)

Benefits of Trusted Research Environments





Researchers

Trusted Research Environment TRE

Secure airlocked environment: Users are authenticated with access based on roles and permissions. Outputs are quarantined before release

Configurable tools and services: Analysis tools can be added and configured. Federated queries offer connection to other TREs

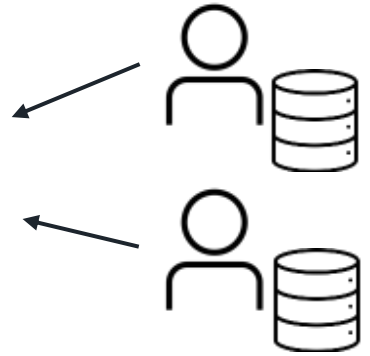
Enhanced collaboration: Shared workspaces allow users to work collaboratively on research projects

Single, secure data storage: Custodians can store and manage data within the TRE

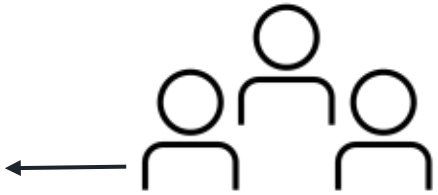
Secure remote access: Accessible to accredited users remotely, allowing project teams to work globally

Scalable compute power: Processing power is provided by TRE servers and not individual user's machines, and can be scaled based on demand

Enhanced Trustworthiness: Data is stored securely, providing reassurance to public that their sensitive data is managed correctly



Data custodians



Public, patient, practitioners

Convened by HDRUK Health Data Research UK

International COVID-19 Data Alliance (ICODA)

The **International COVID-19 Data Alliance (ICODA)** was convened by HDR UK in mid 2020 to focus on a rapid response the COVID-19 pandemic, using data science approaches and leave a lasting infrastructure, processes and learnings

ICODA is trying to add distinctive value to other data platforms in three key ways:

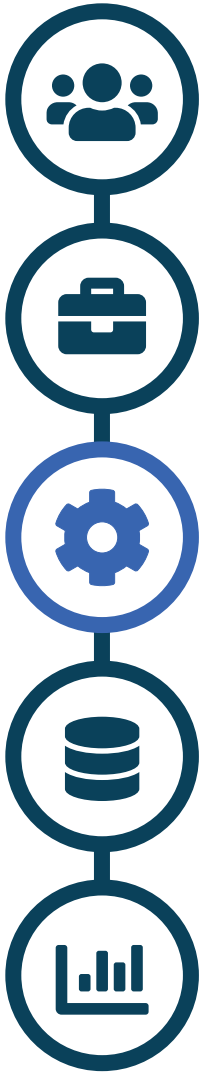
1. **Improving discoverability:** working with multiple data providers to make "meta data" available for researchers to search and find datasets
2. **Providing a secure analysis platform**: relevant data from multiple sources can be brought together on the ICODA Workbench, a secure Trusted Research Environment for researchers to address specific research questions.
3. **Facilitating federated access:** where it is not possible to transfer data, providing a federated approach to allow researchers to send analysis to the data (rather than moving data to the researcher) in one or more different locations.

PET

PET

We prioritise the importance of demonstrating **trustworthy data stewardship** and making data FAIR – findable, accessible, interoperable, reusable

Introduction to Five Safes



Safe People
Researchers are trained and authorised to use data safely

Safe Projects
Research projects are approved by data owners and for the public good

Safe Settings
A Trusted Research Environment provides a secure environment within which to perform research

Safe Data
Data is curated to protect any confidentiality concerns

Safe Outputs
Screened and approved outputs that are non-disclosive

The ICODA Workbench

Allows researchers to access data in a trusted research environment with the opportunity to work on important research questions

Provided by Aridhia Informatics

Data Access

- Invited researchers register
- Login via 2 Factor Authentication
- Permits global access

Tooling

- Collaborative workspaces with open source tooling (R, Python, SQL)
- Bring your own data, code and 3rd party software or tools
- Specialised clinical research tools available from ICODA partners

Compute

- Web based tools or clustered virtual machines (Windows, Linux, GPU)
- Scalable cloud computing

Global Portfolio of Driver Projects

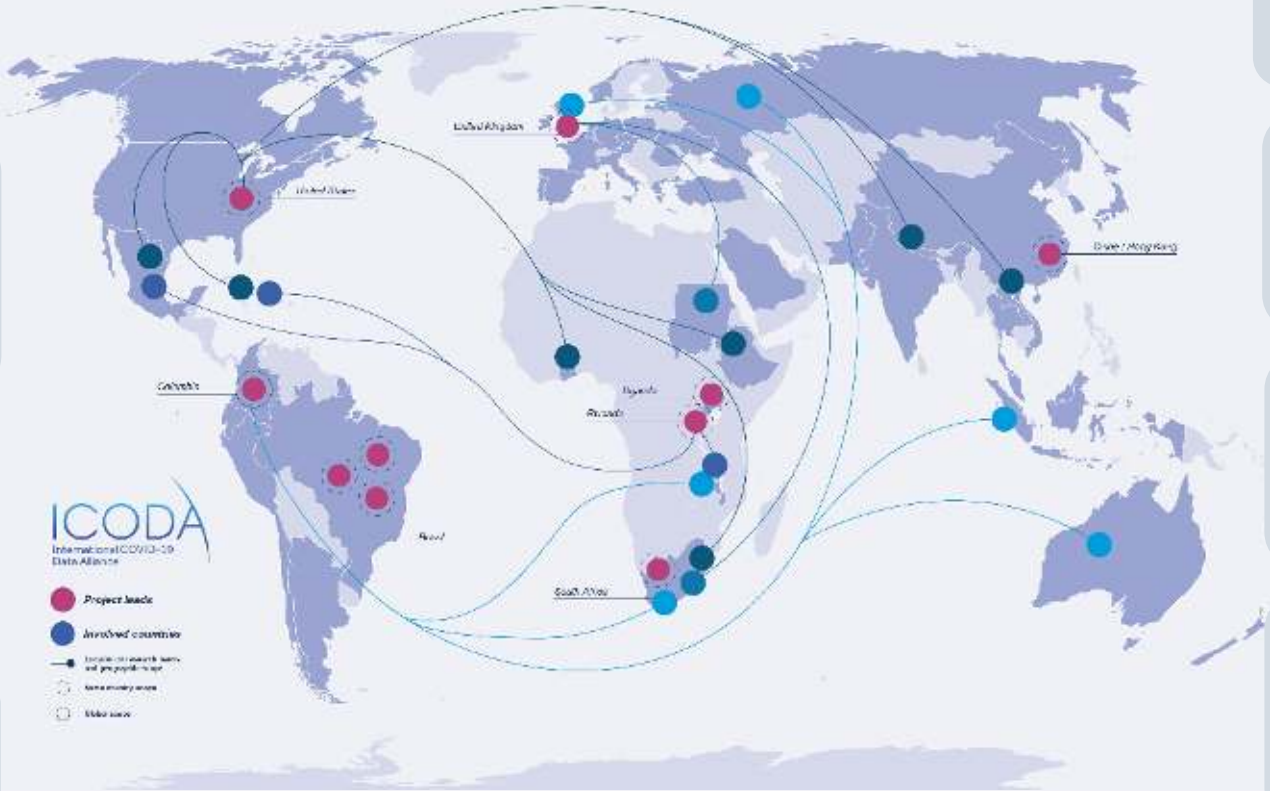
All working within ICODA's Workbench PET

DP1-EFCT
Duke University, Certara, Cytel, BMGF, NMD Group
Evaluating the efficacy and` safety of COVID-19 treatments

DP2-iPOP
University of Edinburgh, University of Manitoba, Murdoch Children's Research Institute, University of New South Wales + iPOP Consortium
International Perinatal Outcomes in Pandemic (iPOP)

DP-PRIEST
University of Sheffield & Cape Town
Pandemic Respiratory Infection Emergency System Triage (PRIEST) Study for Low and Middle-Income Countries

DP-EFFECT
Fiocruz, Brazil
Effectiveness of COVID-19 Vaccination in Brazil Using Mobile Data



https://icoda-research.org/research/driver-projects/

DP-REHCORD
Harvard T.H. Chan School of Public Health
Impact of COVID-19 on Health Service Delivery and Institutional Mortality: A Multi Country Consortium

DP-ISARIC
Universidad de La Sabana in Colombia
Data Descriptor, Reference Coding, and Characterization of the Systemic Complications of Critical Care Patients Included in the ISARIC COVID-19 Dataset

DP-IROC
MRC/UVRI & LSHTM Uganda Research Unit and Makarere University
Incidence and risk factors for COVID-19 amongst pregnant and lactating women and their infants in Uganda

DP-ACCORD
Western Cape Government Health Department and the University of Cape Town
Addressing Critical Covid-19 Questions Through Research Using Linked Population Data

DP-PIH-CovCo
Partners in Health of Haiti, Malawi, Mexico, and Rwanda
The Impact of COVID-19 on Chronic Care Patients' Health Care Utilization and Health Outcomes in Haiti, Malawi, Mexico and Rwanda

DP-IDS-COVID 19
Fiocruz, Brazil
Evaluating Effects of Social Inequalities on the COVID-19 Pandemic in a Low- and Middle Income Country

DP-RASUP
Fiocruz, Brazil
Routine Assessment of Infections, Prevention, and Control of SARS-CoV-2 on Unequal Populations

DP-CHAIN
City University of Hong Kong
Characterizing COVID-19 Transmission Chains for Precision Mitigation Using Epidemiological Survey Data

Trusted Research Environments in practice

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Senior Programmer, periCOVID study
Makarere University Johns Hopkins University (MUJHU), Uganda

Dr Carl Marincowitz
Principal Investigator, PRIEST Study for Low and Middle-Income Countries
Sheffield University, UK

ICODA International COVID-19 Data Alliance
aridhia
Bill & Melinda Gates foundation
Minderoo Foundation
Convened by HDRUK Health Data Research UK

IROC:
Incidence and Risk factors for COVID-19 among pregnant and lactating women and their infants in Uganda

Joseph Ouma, IROC team, Uganda

HDR-UK Ref Number: 2021.0096

Project period: 5th July 2021 to 4th October 2022

Outline

- Project team
- IROC, Goals and Objectives
- Data, Progress and Achievements
- Experiences using the workbench
  - Benefits
  - Challenges

Core team

- **Prof Kirsty Le Daore**, Principle Investigator. MRC/UVRI & LSHTM Uganda Research Unit and Makerere University John's Hopkins University Research Collaboration (MUJHU), Uganda.
- **Joseph Ouma,** Senior Data Manager/Biostatistician, Makerere University John's Hopkins University Research Collaboration (MUJHU), Uganda.
- **Dr Lauren Hookham,** Program manager peri-COVID study, in Uganda
- **Gordon Rokundo,** Data Manager, Makerere University John's Hopkins University Research Collaboration (MUJHU), Uganda.
- **Mary Kyohere,** Program manager, Makerere University John's Hopkins University Research Collaboration (MUJHU), Uganda.
- **Prof Philippa Musoke,** Executive Director, Makerere University John's Hopkins University Research Collaboration (MUJHU), Uganda

Collaborations and partnerships

- **Makerere University John's Hopkins University Research Collaboration (MUJHU), Uganda.**
- MRC/UVRI & LSHTM Uganda Research Unit
- Kawempe National Referral Hospital, Uganda
- Division of Health information, MoH, Uganda
- Department of MNCH, MoH, Uganda
- **The International COVID-19 Data Alliance (ICODA)**

The gap

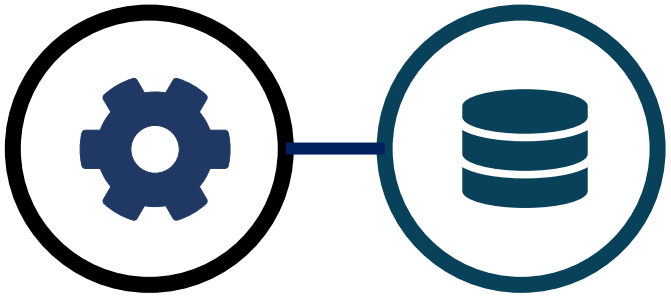
- Real time data collection, analysis, reporting and **USE to rapidly support changes to guidelines and care** are critical
- Electronic Health Records (EHR) address a number of challenges**, providing a platform that supports clinical care, real-time data collection, data analysis, reporting and disease surveillance.**

Goal and objectives of IROC

To determine risk factors for adverse pregnancy and neonatal outcomes during the COVID 19 pandemic using the EHR;

1. **Develop a risk factor model for indirect and direct effects** of the pandemic on MNCH services in Uganda;
2. **Identify at risk populations** who would benefit from vaccination catch up programmes;
3. **Formulate guidance on infection prevention and control** during pregnancy and in the postpartum period;
4. **Develop a Ministry of Health COVID19 Dashboard for MNCH data for this and future pandemics**

Setting and data



- **Kawempe National Referral Hospital (KNRH)**, provides MNCH services to **>30,000 women** annually
- UgandaEMR, an electronic medical records system is used to capture patient level service delivery data based on MoH HMIS tools
- Data on women accessing **Antenatal, Delivery and postnatal services at** KNRH for Jan 2020 – Oct 2021 used for the study**.**
  - Outcomes - death (maternal, neonatal, infant<6 months), prematurity, stillbirth, miscarriage, gestational diabetes, antepartum & postpartum hemorrhage
  - Other variables – Maternal demographics (age, level of education, marital status, area of residence –rural/urban) and parity, gravidity, gestational age.
- Data on Government initiated restrictions- showing lockdown timelines from the CoVID19 Dashboard, Ministry of Health

Progress and achievements

- Stakeholder engagement meetings with MoH and KNRH staff were held:
  - Guided dashboard development,
  - selected indicators for dashboard,
  - built excitement and acceptability and
  - initiated use case as well as ongoing commitment
- Risk factor model and at risk population identified
  - manuscript to be submitted for publication by end of September 2022
- Abstract on data visualization accepted for poster presentation at the conference in Cape town South Africa

- Visualization dashboard complete shared with KNRH

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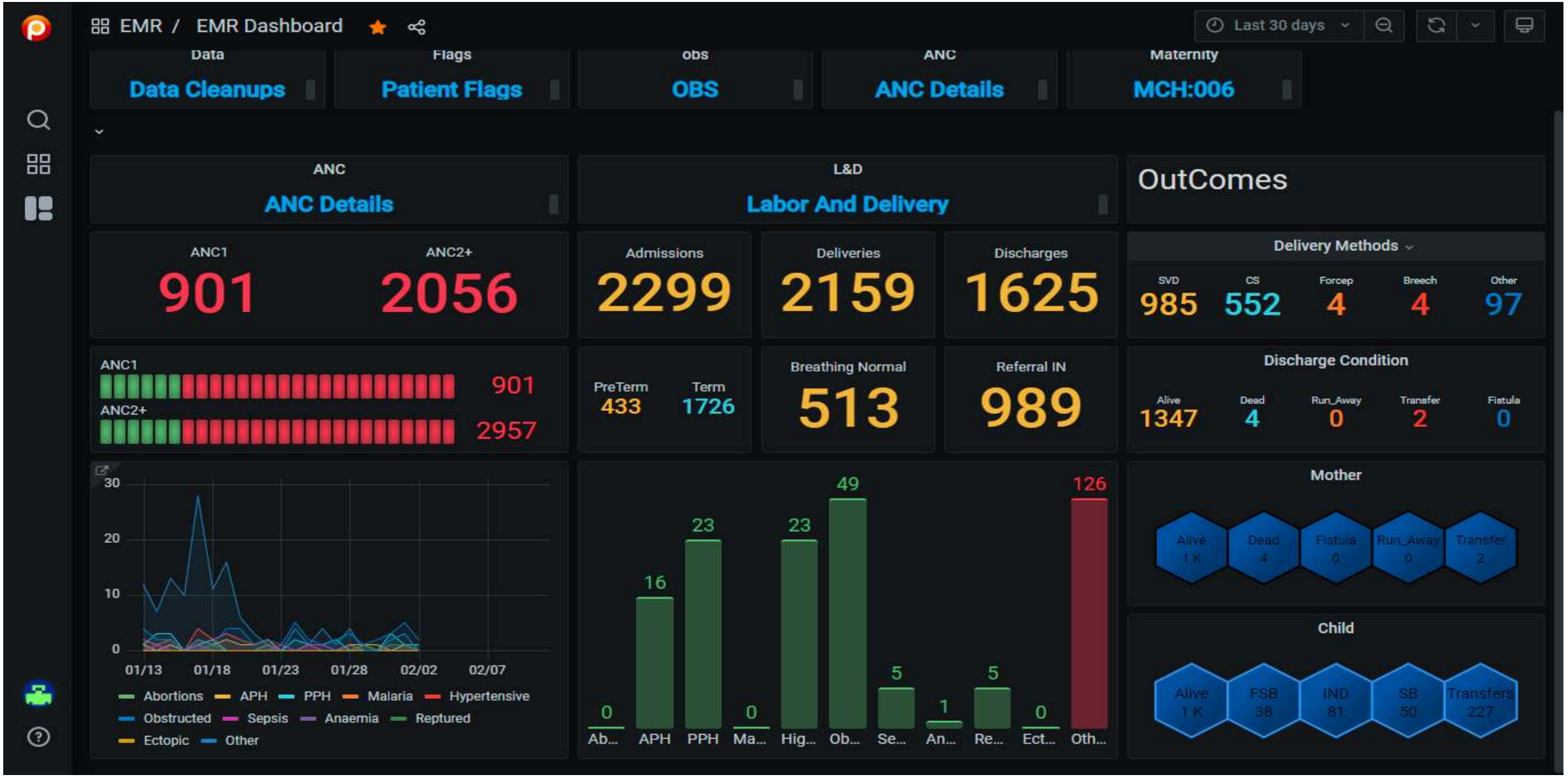
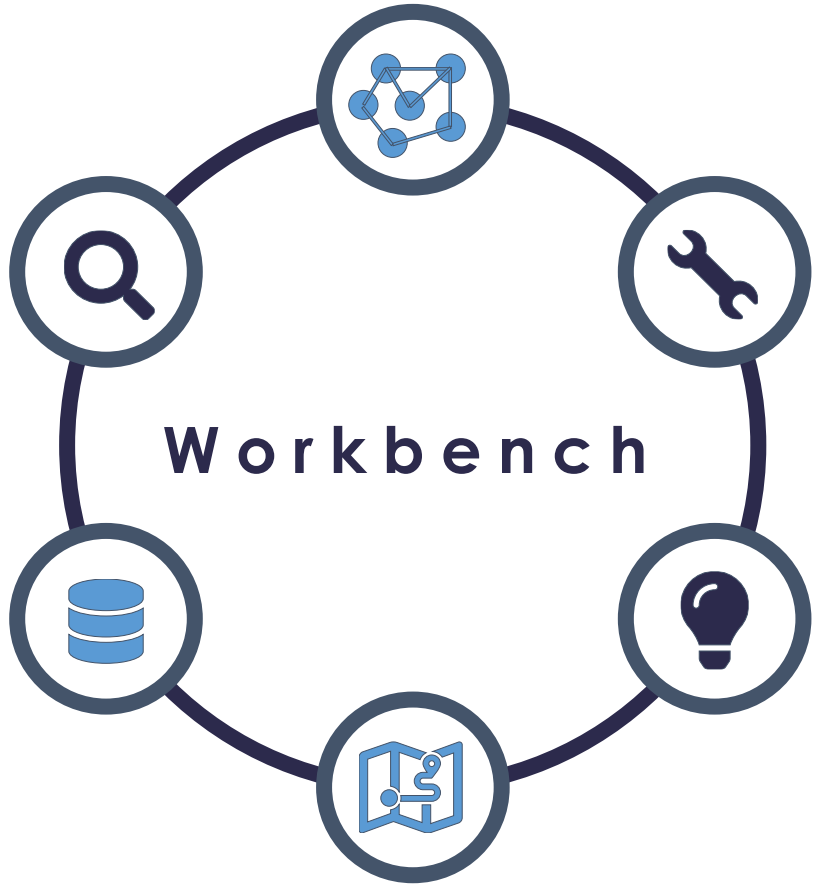
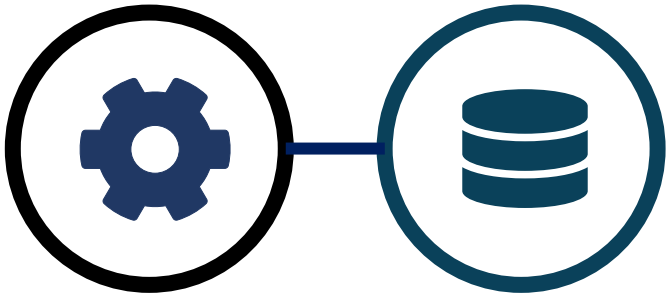


Workbench onboarding and preparations

- Training and signing up on Synapse
  - Team were introduced to Synapse environment, available tools to share, organize and promote research work and outputs.
- Data Processing Agreement (DPA) for data sharing and processing were completed
- Training on mandatory ICODA workbench courses and modules completed.
- User accreditation and granting access to study, IROC, workspaces on the workbench.



IROC data in the workbench



- Large dataset >49,700 antenatal and >51,680 Labour and delivery attendance beyond the workbench data table editor specifications of 100x10,000.
- Windows VM was deployed to the workspace
  - Interactive sessions held with the workbench team to inform expansion of workbench space and utility
- R Markdown modules made available via the virtual machine
  - through interactive sessions, IROC team were shown how to use them for data analysis

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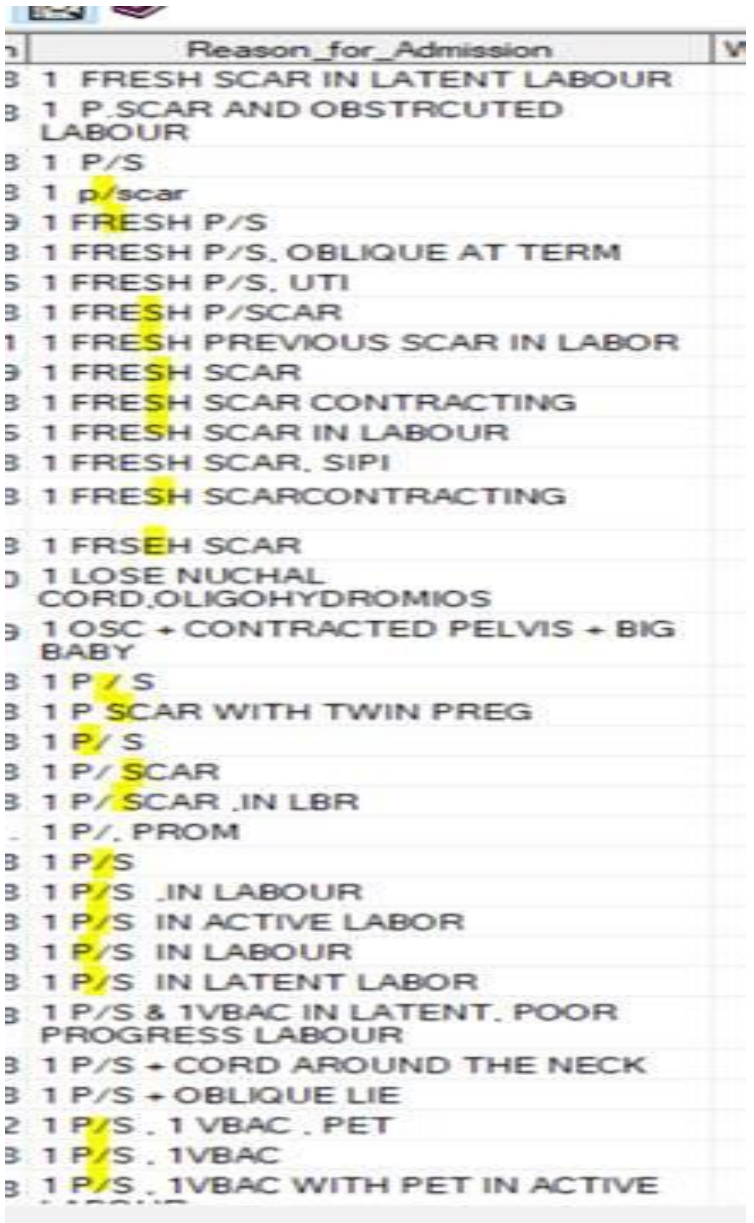
IROC data in the workbench

- Data curation support by **MMS Holdings Inc. USA. ICODA curation partner**
  - Curation done outside the workbench
  - Another data processing agreement signed
  - Supported Improvement of the study meta-data
- Statistical support/advise from ICODA's Statistical Expert Group.
- Further interactive meetings/training with ICODA/Workbench team on use of the workbench tools including export and use of the analysis modules on virtual machines.



	Reason_for_Admission	V
3	1 FRESH SCAR IN LATENT LABOUR	
3	1 P.SCAR AND OBSTRCUTED LABOUR	
3	1 P/S	
3	1 p/scar	
9	1 FRESH P/S	
3	1 FRESH P/S. OBLIQUE AT TERM	
5	1 FRESH P/S. UTI	
3	1 FRESH P/SCAR	
1	1 FRESH PREVIOUS SCAR IN LABOR	
9	1 FRESH SCAR	
3	1 FRESH SCAR CONTRACTING	
5	1 FRESH SCAR IN LABOUR	
3	1 FRESH SCAR. SIPI	
3	1 FRESH SCARCONTRACTING	
3	1 FRSEH SCAR	
0	1 LOSE NUCHAL CORD,OLIGOHYDROMIOS	
9	1 OSC + CONTRACTED PELVIS + BIG BABY	
3	1 P / S	
3	1 P SCAR WITH TWIN PREG	
3	1 P/ S	
3	1 P/ SCAR	
3	1 P/ SCAR .IN LBR	
	1 P/. PROM	
3	1 P/S	
3	1 P/S .IN LABOUR	
3	1 P/S IN ACTIVE LABOR	
3	1 P/S IN LABOUR	
3	1 P/S IN LATENT LABOR	
3	1 P/S & 1VBAC IN LATENT. POOR PROGRESS LABOUR	
3	1 P/S + CORD AROUND THE NECK	
3	1 P/S + OBLIQUE LIE	
2	1 P/S . 1 VBAC . PET	
3	1 P/S . 1VBAC	
3	1 P/S . 1VBAC WITH PET IN ACTIVE	

Benefits using the TRE

- The Aridhia service desk was very **supportive in guiding the team:** on uploading data onto the workspace; using the exported modules and in resolving user challenges.
- Single secure data storage accessible **remotely** by only **accredited** study team members.
- **Secure file storage** and sharing for large files – removed the burden of sharing data files and related meta data with team members.
- **Analytics and tools** to model data more efficiently were available for use.

Benefits using the TRE

- While using the VM, there is restricted access to external resources such as the web, **reassuring on data security.**
- Using the **airlock provision**, team members can only download datasets after authorization from the workspace administrator.
- Improved collaboration as team members contributed directly on the data analysis codes and other inputs as the analysis progressed

Challenges

- Used tools/modules outside of the environment – The team was not able to optimally use them.
- Using data from routine service delivery, containing text data fields- The team worked collaborating with MMs to complete the data curation.
- Using the R Markdown modules in the VM environment, required familiarity with R program
- Working in the environment needing large bandwidth, hence patience to run and re-run scripts

Stakeholder engagement session

Acknowledgements

- ICODA workbench team/engineers
- ICODA SEG,
- MMS, ICODA data curation partner

- Ministry of Health, Uganda
- Kawempe National Referral Hospital
- Study participants


感謝你
Danke
Gracias
Grazie
Merci
Thanks!
THANK
YOU!

The University Of Sheffield.

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The PRIEST (Pandemic Respiratory Infection Emergency System Triage) Study for Low and Middle-Income Countries

The role of the Trusted Research Environment and Work Bench

ICODA
International COVID-19 Data Alliance

PLOS ONE

RESEARCH ARTICLE

Derivation and validation of a clinical severity score for acutely ill adults with suspected COVID-19: The PRIEST observational cohort study

Steve Goodacre[1]*, Ben Thomas[1], Laura Sutton[1], Matthew Burnsall[1], Ellen Lee[1], Mike Bradburn[1], Amanda Loban[1], Simon Waterhouse[1], Richard Simmonds[1], Katie Biggs[1], Carl Marincowitz[1], Jose Schutter[1], Sarah Connelly[1], Elena Sheldon[1], Jamie Hall[1], Emma Young[1], Andrew Bentley[2], Kirsty Challen[3], Chris Fitzsimmons[4], Tim Harris[5], Fiona Lecky[1], Andrew Lee[1], Ian Maconochie[6], Darren Walter[7]

1 School of Health and Related Research (ScHARR), University of Sheffield, Sheffield, United Kingdom, **2** Intensive Care, Manchester University NHS Foundation Trust, Wythenshawe Hospital, Manchester, United Kingdom, **3** Emergency Department, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, United Kingdom, **4** Emergency Department, Sheffield Children's NHS Foundation Trust, Sheffield, United Kingdom, **5** Emergency Department, Barts Health NHS Trust, London, United Kingdom, **6** Emergency Department, Imperial College Healthcare NHS Trust, London, United Kingdom, **7** Emergency Department, Manchester University NHS Foundation Trust, Wythenshawe Hospital, Manchester, United Kingdom

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OPEN ACCESS

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Abstract

Objectives

We aimed to derive and validate a triage tool, based on clinical assessment alone, for predicting adverse outcome in acutely ill adults with suspected COVID-19 infection.

Methods

We undertook a mixed prospective and retrospective observational cohort study in 70 emergency departments across the United Kingdom (UK). We collected presenting data from 22445 people attending with suspected COVID-19 between 26 March 2020 and 28 May 2020. The primary outcome was death or organ support (respiratory, cardiovascular, or renal) by record review at 30 days. We split the cohort into derivation and validation sets, developed a clinical score based on the coefficients from multivariable analysis using the derivation set, and the estimated discriminant performance using the validation set.

BMJ Open

Potential solutions for screening, triage, and severity scoring of suspected COVID-19 positive patients in low-resource settings: a scoping review

Sarah Hirner,[1] Jennifer Lee Pigoga ,[2] Antoinette Vanessa Naidoo,[2] Emilie J Calvello Hynes ,[3] Yasein O Omer,[2,4] Lee A Wallis,[2] Corey B Bills [3]

To cite: Hirner S, Pigoga JL, Naidoo AV, *et al*. Potential solutions for screening, triage, and severity scoring of suspected COVID-19 positive patients in low-resource settings: a scoping review. *BMJ Open* 2021;**11**:e046130. doi:10.1136/bmjopen-2020-046130

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-046130).

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Accepted 25 June 2021

[1]University of Colorado Denver

ABSTRACT

Objectives Purposefully designed and validated screening, triage, and severity scoring tools are needed to reduce mortality of COVID-19 in low-resource settings (LRS). This review aimed to identify currently proposed and/or implemented methods of screening, triaging, and severity scoring of patients with suspected COVID-19 on initial presentation to the healthcare system and to evaluate the utility of these tools in LRS.

Design A scoping review was conducted to identify studies describing acute screening, triage, and severity scoring of patients with suspected COVID-19 published between 12 December 2019 and 1 April 2021. Extracted information included clinical features, use of laboratory and imaging studies, and relevant tool validation data.

Participant The initial search strategy yielded 15 232 articles; 124 met inclusion criteria.

Results Most studies were from China (n=41, 33.1%) or the United States (n=23, 18.5%). In total, 57 screening, 23 triage, and 54 severity scoring tools were described. A total of 51 tools—31 screening, 5 triage, and 15 severity scoring—were identified as feasible for use in LRS. A total of 37 studies provided validation data: 4 prospective and 33 retrospective, with none from low-income and lower middle-income countries.

Conclusions This study identified a number of screening, triage, and severity scoring tools implemented and proposed for patients with suspected COVID-19. No tools were specifically designed and validated in LRS. Tools specific to resource limited contexts is crucial to reducing mortality in the current pandemic.

Strengths and limitations of this study

- ► We provide the first review of COVID-19 screening, triage, and severity scoring tools both proposed and implemented among initial patient presentations to the healthcare system.
- ► Many screening, triage, and severity scoring tools have been proposed and implemented, but none are specific to low-resource settings (LRS).
- ► We identified 51 tools—31 screening, 5 triage, and 15 severity scoring—that have variables feasible for collection in LRS.
- ► Feasibility, however, does not predict that a tool will be accurate or effective, and no tools from this review were validated in LRS.
- ► It is likely that many tools being used in healthcare systems worldwide are not published and thus cannot be described in this review.

healthcare systems worldwide by increasing demand for personal protective equipment (PPE), diagnostics, oxygen and mechanical ventilators.[6] Low-resource settings (LRS) have limited access to these resources and remain disproportionately challenged during the COVID-19 pandemic.[7 8] Even in regions where viral transmission remains low, patients with suspected COVID-19 require precautions, and confirmed cases require

Aims

Primary objective: develop clinical risk stratification tools to predict need for inpatient admission from the ED for patients with suspected COVID-19 infection applicable to LMIC settings.

S**econdary objectives**:

- consult with patient and clinical stakeholders to develop clinically usable and contextually appropriate risk stratification tools.
- externally validate new and previously developed risk-stratification tools in different income settings and waves of the pandemic
- identify the optimal cut-off points for the risk stratification tools and compare their performance with existing triage methods (e.g. National Early Warning Scores and the WHO hospitalisation algorithm for pneumonia).

Research team and collaboration

The University Of Sheffield.

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- Clinical researchers (Myself, Dr Fuller and Professor Goodacre)
- Statistical and Machine Learning Expertise (Information School, Professor Bath, Dr Hassan and Dr Sbaffi)
- Clinical and data expertise (Professor Wallis, Professor Hodkinson and Dr McAlpine)
- Collaboration Sudan (led by Dr Omer)

Data sets

UK, PRIEST study

N = 20,698 (adults)

26th March and 28th May 2020

Western Cape, South Africa

N = 446,084 (adults)

27th August 2020 to 11th March 2022

Sudanese Multi-centre study

N = 2583 (adults)

3rd January 2020 to 17th December 2021

Outputs (Achieved and Projected)

- Validation of existing (including PRIEST) clinical risk-stratification tools in Western Cape (including Omicron sub-group)
- Development new modified version of PRIEST tool applicable to LMICs using Western Cape dataset
- Validation of new and existing tools in Sudanese population
- Comparison of Machine Learning tools to traditionally developed clinical risk-stratification tools

Role of the TRES/Workbench

UK, PRIEST study

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26th March and 28th May 2020

Western Cape, South Africa

N = 446,084 (adults)

27th August 2020 to 11th March 2022

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TRES/Workbench

Advantages for PI

UK, PRIEST study

N = 20,698 (adults)

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Sudanese Multi-centre study

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TRES/Workbench

Advantages for analysis

Access for our team anywhere in the world (in theory!)

TRES/Workbench

Suite of simple descriptive applications

Good for linux and python

Useful for collaboration across teams for analysis

Caveats

At the start of the project and for a while after, the opened terminals did not last for long and disappeared very quickly, even in less than 2 minutes upon moving to another tab or window. This problem was resolved later.

Some of the frequent and normal keyboard shortcuts (such as ctl+c, ctl+v) can't be used when working on the terminals or writing scripts, which causes lots of delays in the work.

Needs very large internet bandwidth to maintain connection.

Hard to access/install external libraries. This also applies to famous providers like IBM.

Not having the permission for copying results from the workspace to some files outside the workspace introduces more manual work. Trying to print every single result to a file then asking for permission to airlock is not an optimal solution, especially if the results will come from different scripts.

Conclusions

- TRES/Workbench- key for pooling and managing our datasets
- Due to restrictions on use of some datasets (Sudanese)-analysis had to occur on TRES
- Probably possible to conduct all analyses on TRES but due practical limitations some analysis conducted in UoS secure environment

Additional resources

Privacy Enhancing Technologies (PETs). Draft anonymisation, pseudonymisation and privacy enhancing technologies guidance
- Information Commissioner's Office (ICO)
https://ico.org.uk/media/about-the-ico/consultations/4021464/chapter-5-anonymisation-pets.pdf

Repository of PET Use Cases
- Centre for Data Ethics and Innovation
https://cdeiuk.github.io/pets-adoption-guide/repository/

Building Trusted Research Environments - Principles and Best Practices; Towards TRE ecosystems (paper)
- UK Health Data Research Alliance, NHSX
https://zenodo.org/record/5767586#.YyM_2uzML0o

An Introduction to Privacy Enhancing Technologies (online course)
- Health Data Research UK Futures
https://hdruklearning.csod.com/ui/lms-learning-details/app/course/cec9fd53-df0b-4821-aaec-ba73019f75ab

Thank you, any questions?

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