When faced with a fever of uncertain origin, healthcare workers currently lack the diagnostic tests they need to correctly identify the underlying disease and take an informed clinical decision. As a result, many fall into the habit of prescribing antibiotics “just in case”, even though the cause of the infection may be viral and the antibiotics would therefore be ineffective. The COVID-19 virus has further exacerbated this challenge for healthcare workers since it also presents with fever.

This massive diagnostic gap, coupled with the resulting misuse of antibiotics, is causing avoidable morbidity and mortality. Moreover, the problem is fuelling the growth of antimicrobial resistance (AMR), a global health security challenge that threatens individuals’ health and the stability of healthcare systems both now and in the future.

"The centre receives about 500 patients per month, and about 70% of the cases present with fever”.

– Hellen Auma, Senior Clinical officer
Nagongera Health Center IV, Uganda

“When a patient presents with fever, the physician prescribes antibiotics without completing a diagnostic test”.

– Veronica Apetorgbor,
Deputy Director of Nursing Services (PH)
Dodowa Health Research Centre, Ghana

ACUTE FEBRILE ILLNESSES AT A GLANCE

AFIs ARE A SIGNIFICANT CAUSE OF MORBIDITY AND MORTALITY
Acute febrile illnesses (AFIs) are common among adults and children in primary care settings. In low- and middle-income countries (LMICs), most cases go undiagnosed and tend to be inappropriately treated. In 2019, 5.2 million children died before the age of five. Nearly half of these deaths were due to infectious diseases, with fever being the single most common symptom.

DIAGNOSING THE CAUSE OF FEVER IS CHALLENGING, ESPECIALLY IN LMICs
Many AFIs, especially in children, present with highly non-specific, overlapping signs and symptoms that are difficult to distinguish clinically. Causes vary geographically and seasonally, and there are few pathogen-specific tests (malaria and SARS-CoV-2 rapid diagnostic tests being notable exceptions) and no validated all-age syndromic guidelines to inform clinical decision-making.
To correctly diagnose and appropriately treat AFIs, healthcare workers in LMICs need better diagnostic tools and more reliable clinical algorithms to inform their clinical decision-making. Furthermore, to generate insights applicable to real life, any trial investigating new approaches must also account for the behaviours of healthcare workers and patients.

The AMR Dx Use Accelerator has been created to identify practical solutions for LMICs to tackle AMR and provide better healthcare to people presenting in primary care facilities with AFIs.

**The project will achieve this using a two-pronged approach:**

**01 CLINICAL INTERVENTION:** The project will address critical steps in the decision-making process by studying the effects of an intervention package (including a set of available point-of-care diagnostic tests [POCTs] and clinical algorithms) designed to help healthcare workers reach a case-management decision.

**02 BEHAVIOUR:** Through a better understanding of the factors that promote or hinder adherence to prescriptions, the project aims to ensure that informed case-management decisions result in improved health outcomes. It will also focus on gaining a better understanding of the factors that promote or hinder the uptake of diagnostics and associated prescribing by healthcare workers.

Overall, the project vision is to adapt implemented solutions to local contexts and needs, which is why the project will move through specific phases. The first phase, initiated in 2018, focused on common AFIs reflecting prevailing causes of infections in the study countries. In response to the COVID-19 pandemic and to account for subsequent changes in local needs at primary care facilities, a second phase will be launched in 2021 that introduces COVID-19 tests to the POCTs package in a number of countries.

“We can deliver better than what we have been doing until now, diagnostic kits will help us make proper diagnoses for our patients”.

– Hellen Auma, Senior Clinical officer Nagongera Health Center IV, Uganda

“This project is going to positively impact how people are taking antibiotics”.

– Ernestina Baaba Sam, Nurse/Health Promotion Officer Shai-Osudoku District Health Directorate, Ghana
To generate evidence, we have enrolled almost 22,000 patients in what may be the largest study ever conducted on improving point-of-care diagnostic use to positively impact AMR and improve fever-patients’ health outcomes. In a unique design combining a qualitative exploration of behaviours with a quantitative two-arm, clinic-based randomized controlled trial, we are conducting studies with harmonized protocols across eight sites in five countries. This approach will enable us to draw both locally relevant and generally applicable conclusions on how to improve AFI patient management.

THE AMR DX USE ACCELERATOR APPROACH: A LARGE-SCALE, MULTI-COUNTRY PROJECT INCORPORATING A NESTED SOCIAL SCIENCE COMPONENT INTO A CLINICAL STUDY

STUDY PARTNERS: EIGHT CENTRES IN FIVE COUNTRIES

UGANDA
Infectious Diseases Research Collaboration (IDRC)

NEPAL
Oxford University Clinical Research Unit-Nepal

GHANA
Dodowa Health Research Centre

BURKINA FASO
IRSS-DRCO/Clinical Research Unit of Nanoro (CRUN)

INDIA
CHHATTISGARH
Jan Swasthya Sahyog

CHANDIGARH
Post Graduate Institute of Medical Education & Research (PGIMER)

MADHYA PRADESH
RD Gardi Medical College

WEST BENGAL
National Institute of Cholera and Enteric Diseases (NICED)

EVIDENCE-BASED PRACTICE: PICO FRAMEWORK

PATIENTS: Children and adolescents with undifferentiated febrile illness presenting to outpatient clinics or peripheral health centres

INTERVENTION: Available diagnostic tests; diagnostic algorithms and aids; clinic process flow; training and communication for healthcare workers and patients and caregivers

CONTROL: Current practice

OUTCOMES: Improved case management of AFIs; targeted use of antibiotics and reduced antibiotic prescriptions
KEY FACTS ON STUDY DESIGN

CLINICAL STUDY WITH SOCIAL SCIENCE COMPONENT: The project incorporates both qualitative contextual and quantitative empirical outcomes to address the various aspects of the core research question.

HARMONIZED PROTOCOL WITH LOCAL ADAPTATIONS: All study sites have adopted a standard protocol template adapted to reflect regional differences in infection patterns and behaviours at each site and geographical area.

TARGET POPULATION: The project primarily targets children and adolescents as a recognized vulnerable group. Some sites have also included adults for broader population representation.

PROJECT PERIOD: The extended study period accounts for seasonal variations in infectious diseases in the study countries.

CLINICAL INTERVENTION STUDY

The clinical intervention study’s objective is to assess the impact of a package of interventions on clinical outcomes and antibiotic prescriptions compared with standard care practices.

After a pre-screening for fever, eligibility criteria assessment and consent collection, we use 1:1 randomization to enrol patients in either the control or the intervention arm of the study. Patients assigned to the control arm will follow their clinic’s standard AFI diagnostic and treatment procedures. Meanwhile, those assigned to the intervention arm will follow the test protocol, including the intervention package described below. We will follow up with all patients in both the intervention and control arms on day 7 (±2) to reassess their health status and prescription adherence.
**Intervention package**

- **Diagnostics available at the point of care**
  This study will not introduce any new tests. Instead, it will examine the positive impact of existing tests that may not be used locally at present. These include generic tests that indicate whether the fever has a viral or bacterial cause and (depending on clinical presentation and the prevailing causes of infections at the study site) some pathogen-specific tests performed at point-of-care to inform the clinical decision.

- **Decision trees and diagnostic algorithms**
  Considering the specific tests to be used at the site, healthcare workers will follow diagnostic algorithms to support their clinical decision-making process.

- **Improved clinic patient flows**
  Standardized patient flows will ensure that all patients receive the care they need.

- **Training and communication**
  Based on the intelligence gathered during the social study, healthcare workers will deliver predefined prescription adherence messaging to patients and caregivers along with their prescription. We will train healthcare workers on how to deliver these communications.

![Diagram of clinical decision process]

**SOCIAL SCIENCE BEHAVIOURAL ACTIVITIES**

The behaviours of healthcare workers, patients and caregivers have a tremendous influence on treatment practices. Therefore, understanding these behaviours is vital if we are to overcome potential barriers to the adoption of any new approach to the diagnosis and treatment of AFI.

**Pre-intervention: focused on prescription adherence to develop relevant training and communication intervention**

In the initial stage, we are using qualitative methods and behavioural approaches to explore behavioural determinants that affect:
- healthcare workers’ effective communication of prescription messages
- patients’ and caregivers’ adherence to prescriptions

**Generate recommendations for future behavioural interventions**

In parallel with the enrolment of patients in the clinical study, we will use qualitative methods and behavioural approaches to explore behavioural factors that affect healthcare workers’ uptake of diagnostics. Finally, we will use behavioural frameworks to guide an investigation of a broader behaviour change strategy and formulate recommendations for future behavioural change interventions. This will cover both healthcare workers’ uptake of diagnostics and patients’ and caregivers’ prescription adherence.
The AMR Dx Use Accelerator will generate evidence on the impact of the provision of diagnostic tools, that accounts for the behaviours affecting their adoption, thereby ensuring real-life applicability. In turn, this evidence will inform policy changes and lay the groundwork for a robust route to diagnostic uptake that improves patient care globally.

**KEY TAKEAWAYS AND CONCLUSIONS**

**GENERATING DEMAND FOR BASIC DIAGNOSTIC–TRIAGE BUNDLES**
The AMR Dx Use Accelerator sits under an umbrella of initiatives that empower countries to implement innovative testing services and thus improve primary healthcare.

**BUILDING AN ECONOMIC ASSESSMENT**
We want to build a convincing case that:
- it is worth investing in better practice
- when it comes to accelerating pathways for the uptake of new diagnostics and improved clinical decision-making, the benefits outweigh the costs.

**CONTRIBUTING TO THE DUAL GOAL OF FIGHTING AMR AND ACHIEVING UHC**
The project will provide evidence to inform improved policies and practices that combine diagnostic tools, clinical algorithms and strategies to create positive social and behavioural change. In so doing, we hope to improve the management of AFIs, reduce the unnecessary antibiotic use that drives AMR, and contribute to UHC.

**PAVING THE WAY FOR THE INTRODUCTION OF NEW DIAGNOSTICS**
The AMR Dx Use Accelerator will promote the deployment of existing diagnostics that may not be used locally at present. While the creation of new diagnostics is ongoing, there remains no clear path to deployment. To that end, this project aims to inform best practice around the introduction of new diagnostics and interventions, as well as the modification of behaviours that hinder the effective management of AFIs.