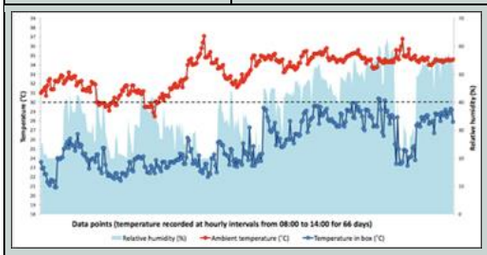
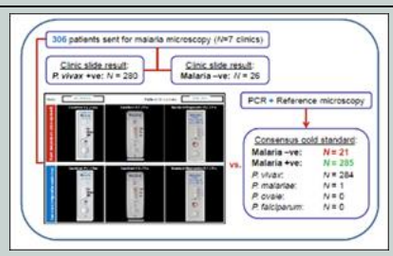
Project:	Performance evaluation of 3 Plasmodium vivax rapid diagnostic tests with and without a cold chain in mid-summer
Donor:	This study is part of the ACT consortium project portfolio. The ACT consortium is funded by the Bill and Melinda Gates Foundation and grants are administered by the London School of Hygiene and Tropical Medicine.
Duration:	June 2009 - September 2009
Objectives:	Accurate parasitological diagnosis of malaria is essential for targeting treatment where more than one species coexist. In this study, three rapid diagnostic tests (RDTs) (AccessBio CareStart (CSPfPan), CareStart PfPv (CSPfPv) and Standard Diagnostics Bioline (SDBPfPv)) were evaluated for their ability to detect natural Plasmodium vivax infections in a basic clinic setting. The potential for locally made evaporative cooling boxes (ECB) to protect the tests from heat damage in high summer temperatures was also investigated.
Design:	Venous blood was drawn from P. vivax positive patients in Jalalabad, Afghanistan and tested against a panel of six RDTs. The panel comprised two of each test type; one group was stored at room temperature and the other in an ECB. RDT results were evaluated against a consensus gold standard based on two double-read reference slides and PCR. The sensitivity, specificity and a measure of global performance for each test were determined and stratified by parasitaemia level and storage condition.
Findings:	Of the three RDTs, the CSPfPan test was the most consistent and reliable, rendering it appropriate for this P. vivax predominant region. The CSPfPv test proved unsuitable owing to its reduced sensitivity at a parasitaemia below 5,000/µL (affecting 43% of study samples). Although the SDBPfPv device was more sensitive than the CSPfPv test, its invalid rate was unacceptably high. ECB storage reduced the proportion of invalid results for the SDBPfPv test, but surprisingly had no impact on RDT sensitivity at low parasitaemia.
Publication/Links:	Amy FW Mikhail, Toby J Leslie, Mohammad I Mayan, Rohullah Zekria, Nader Mohammad, Mohammad A Hasanzai, Najibullah Safi, Christopher JM Whitty and Mark Rowland, Field trial of three different Plasmodium vivax-detecting rapid diagnostic tests with and without evaporative cool box storage in Afghanistan; Malaria Journal 2011, 10:169





Project:	Evaluation of the role of malaria rapid diagnostic tests (RDT) for the treatment of malaria and non-malarial fever in Afghanistan.
Donor:	This study is part of the ACT consortium project portfolio. The ACT consortium is funded by the Bill and Melinda Gates Foundation and grants are administered by the London School of Hygiene and Tropical Medicine.
Duration:	October 2008 to October 2010
Objectives:	In Afghanistan, most malaria is caused by the less serious species, Plasmodium vivax. Far fewer cases (less than 10%) of malaria are caused by the more deadly P.

	falciparum malaria. Since treatment for these two diseases differs, diagnostic and treatment accuracy is paramount for patient care. We aimed to evaluate how well malaria treatment is targeted at those with malaria in Afghanistan's health system. To do this, we aimed to measure the: • Accuracy of clinic-based diagnosis using either microscopic examination of blood smears or clinical diagnosis based on symptoms of the patient alone • Accuracy of the treatment provided by the clinician who treated the patient at the study clinics • The accuracy of treatment using Artesunate Combination Therapy (ACT) for P. falciparum malaria • Factors which determine the accuracy of treatment, for example the patient's age, gender and symptoms; or the clinician's qualifications
Design:	The study was conducted in 22 clinics in 2 provinces of Afghanistan. We asked the clinicians to note the diagnosis and treatment that was given to each patient and we measured the accuracy of each diagnosis and treatment against a reference diagnosis that was given by HPRO's expert laboratory staff. This was confirmed by reading the malaria slide twice to give a "gold standard" result. The study was approved by the Ethics Board of the Afghan Public Health Institute, Ministry of Public Health and the London School of Hygiene and Tropical Medicine. Using this observational study design we examined the accuracy of the diagnosis and the accuracy of the clinicians' response to the diagnosis. The study involved more than 4000 patients in the 22 clinics between June and September 2009.
Findings:	The study found that when there is no diagnosis available for patients, clinicians are unable to accurately prescribe malarial drugs because patient symptoms are not specific to malaria – most patients do not have malaria, but almost all are given an antimalarial drug. When diagnosis is available, there is a loss of accuracy of about 40% in the process of diagnosing and treating patients. Although the majority of those with malaria received a malaria drug, so did around 40% of those who did not have malaria – meaning that they were not correctly treated. Around ½ of the inaccuracy (20%) can be tracked to inaccurate diagnosis (which tends to over diagnose malaria leading to false positive results) and around ½ (the additional 20%) is attributed to the clinician's response to a negative diagnosis, where they tend to provide treatment anyway. Treatment for the few cases of the more severe P. falciparum malaria was not well applied – microscopic examination of blood slides was not accurate for detecting the very few cases seen in the study cohort. The study results will now be applied to policy by concentrating on expansion of diagnostic services to include clinics which do not currently have any way of accurately diagnosing malaria, and on training of clinicians for improved targeting of antimalarial drugs.
Publication/Links:	ACT Consortium, Afghanistan Project: http://www.actconsortium.org/pages/project-6.html

Project:	Evaluation of the role of malaria rapid diagnostic tests (RDT) for the treatment of malaria and non-malarial fever in Afghanistan.
Donor:	This study is part of the ACT consortium project portfolio. The ACT consortium is funded by the Bill and Melinda Gates Foundation and grants are administered by the London School of Hygiene and Tropical Medicine.
Duration:	September 2009 - ongoing
Objectives:	A new generation of diagnostic tools has the potential to revolutionise access to diagnosis for malaria. However, there are many aspects of this intervention that require operational research to define their role in providing accurate and timely diagnosis and treatment for fever. We aimed to evaluate whether malaria Rapid Diagnostic Tests (RDT) improve treatment of malaria and non-malarial fever in patients at clinics in Afghanistan. To do this, we aimed to measure the: Accuracy of clinic-based diagnosis using either microscopic examination of blood smears or RDT or clinical diagnosis based on symptoms of the patient alone Accuracy of the treatment provided by the clinician who treated the patient at the study clinics The accuracy of treatment using Artesunate Combination Therapy (ACT) for P. falciparum malaria Factors which determine the accuracy of treatment, for example the patient's age, gender and symptoms; or the clinician's qualificiations Economic costs-effectiveness of each of the diagnostic methods
Design:	The study was conducted in 22 clinics in 2 provinces of Afghanistan. Patients who came to the clinic with a history of fever which was suspected to be caused by malaria were enrolled. They were randomly assigned to be diagnosed with either the RDT or the microscopy. We measured the accuracy of each diagnosis and treatment against a reference diagnosis that was given by HPRO's expert laboratory staff using blood slide reading and advanced molecular diagnostic methods (PCR) to give a "gold standard" result. The study was approved by the Ethics Board of the Afghan Public Health Institute, Ministry of Public Health and the London School of Hygiene and Tropical Medicine. Using this randomised control trial design we examined the accuracy of the diagnosis and the accuracy of the clinicians response to the diagnosis. The study involved more than 4000 patients in the 22 clinics between June and September 2009.
Findings:	To be published soon
Publication/Links:	ACT Consortium, Afghanistan Project: http://www.actconsortium.org/pages/project-6.html The problems of diagnosis of malaria: http://www.malariajournal.com/content/7/S1/S7 Clinical Trial Registration: http://clinicaltrials.gov/ct2/show/NCT00935688
Project:	Evaluation of the role of malaria rapid diagnostic tests (RDT) for the treatment of malaria and non-malarial fever by Community Health Workers in Afghanistan.

Donor:	This study is part of the ACT consortium project portfolio. The ACT consortium is funded by the Bill and Melinda Gates Foundation and grants are administered by the London School of Hygiene and Tropical Medicine.
Duration:	August 2011 - October 2012
Objectives:	A new generation of diagnostic tools has the potential to revolutionise access to diagnosis for malaria. However, there are many aspects of this intervention that require operational research to define their role in providing accurate and timely diagnosis and treatment for fever. One potential use is to deploy them through community health workers, who are often the first port of call for people with fever, especially where access to healthcare centres is restricted or not possible. We aimed to evaluate whether malaria Rapid Diagnostic Tests (RDT) improve treatment of malaria and non-malarial fever in patients seen by community health workers in Afghanistan. To do this, we aimed to measure the: • Accuracy of community-based diagnosis using either RDT or clinical diagnosis based on symptoms of the patient alone • Accuracy of the treatment provided by community health workers • The accuracy of treatment using Artesunate Combination Therapy (ACT) for P. falciparum malaria • Factors which determine the accuracy of treatment, for example the patient's age, gender and symptoms; or the community health workers qualifications • Economic costs-effectiveness of each of the diagnostic methods.
Design:	The study is conducted as a cluster randomized control trial in 22 clinics in 2 provinces of Afghanistan. It includes around 400 community health workers. Patients who are seen by a CHW with a history of fever which was suspected to be caused by malaria are enrolled. The clinic is the unit of randomization and so all CHWs attached to the clinic either receive RDTs or no diagnostic tool. We are measuring the accuracy of each diagnosis and treatment against a reference diagnosis that was given by HPRO's expert laboratory staff using advanced molecular diagnostic methods (PCR) to give a "gold standard" result. The study is approved by the Ethics Board of the Afghan Public Health Institute, Ministry of Public Health and the London School of Hygiene and Tropical Medicine. Using this cluster randomized control trial design we examined the accuracy of the diagnosis and the accuracy of the CHWs response to the diagnosis. The study will involve more than 6000 patients enrolled through the 400 CHWs at 22 clinics between August 2011 and October 2012
Findings:	To be published soon
Publication/Links:	ACT Consortium, Afghanistan Project: http://www.actconsortium.org/pages/project-6.html The problems of diagnosis of malaria: http://www.malariajournal.com/content/7/S1/S7 Clinical Trial Registration: http://clinicaltrials.gov/ct2/show/NCT00935688

Project:	Identifying the causes of non-malaria febrile illness in a malaria endemic area of Afghanistan (CONFIA)
Donor:	This study is part of the ACT consortium project portfolio. The ACT consortium is funded by the Bill and Melinda Gates Foundation and grants are administered by the London School of Hygiene and Tropical Medicine.
Duration:	June 2010 - September 2010
Objectives:	In 2010, the World Health Organization published revised guidelines for the treatment of malaria which stipulate that only patients with laboratory confirmation of malaria parasites in their blood should be treated with an antimalarial drug. Not treating malaria negative patients with an antimalarial raises an uncomfortable question for attending physicians. The patients are clearly febrile and unwell, but if they do not have malaria, what is the cause of their illness and what should it be treated with? In this study, the causative pathogens of non-malaria febrile illness (NMFI) in Afghanistan will be identified. The results will then be compared with those from two parallel NMFI studies being conducted in Tanzania and Lao-PDR, respectively.
Design:	Out-patients from Kama District Hospital in Nangarhar will be recruited when the attending physician has suspected malaria but the patients' blood slide is negative for malaria parasites. Upon enrolment, a detailed history will be taken from the patient and a medical exam will be performed. Haemoglobin, C-reactive protein, lactate and pro-calcitonin levels, a full differential blood count and urine analysis will be performed for all enrolled patients. In addition, venous blood and respiratory samples will be collected for blood culture, serological and molecular testing, respectively. The samples will be tested with a series of assay panels for pathogens known to cause febrile illness. Patients will also be followed-up on days 7 and 14 post-enrolment to check on recovery and to take a convalescent blood sample.
Findings:	The identified pathogens and indicators of infection will be used to improve guidelines for the diagnosis and integrated management of childhood and adult illness (IMCI and IMAI).
Publication/Links:	ACT Consortium: http://www.actconsortium.org/pages/project-6.html
Project:	Improving the radical cure of vivax malaria: A multicenter randomized, placebo-controlled comparison of short and long course of primaquine regimens
Donor:	Sponsor: University of Oxford, UK Funder: Medical Research Council, U.K.
Duration:	2014 to 2017
Objectives:	• To determine whether a 7-day primaquine regimen is safe and not inferior to the standard 14-day regimen (total dose of 7mg/kg in both arms) in preventing P. vivax relapse in G6PD normal patients. • To assess the absolute risks and benefits of radical treatment regimens in different endemic settings. • To provide data on the safety of a weekly dose of primaquine (0.75 mg base/kg) in patients with G6PD deficiency.

	• To identify the most cost-effective strategies for the management of P. vivax with respect to the use of G6PD tests, the dosing schedule and the epidemiological context.
Design:	This was a randomized, double-blind, placebo-controlled, non-inferiority trial in G6PD normal patients with uncomplicated vivax malaria in seven participating study sites in Indonesia (two sites), Vietnam, Ethiopia (two sites), and Afghanistan (two sites). Patients presenting to a participating treatment center with uncomplicated vivax malaria and fulfilling the enrolment criteria were randomly assigned to one of three treatment arms: Intervention 1: Standard blood schizontocidal therapy plus 14 days of supervised primaquine/placebo (7mg/kg total dose) administered once per day (0.5 mg/kg). Intervention 2: Standard blood schizontocidal therapy plus 7 days of supervised primaquine/placebo (7mg/kg total dose) administered once per day (1.0 mg/kg OD) followed by 7 days of placebo. Control arm: Standard blood schizontocidal therapy plus 14 days placebo.
Findings:	To be published.
Publication/Links:	Publication will be released by University of Oxford, UK