Methodology

Creation of a database of the current research in Highly-Sensitive Point of Care Tests

In order to review the current landscape of research in Highly-Sensitive Point of Care Tests, we systematically collected data of funded and current research projects.

Following the MESA terminology[1], a project was defined as a research or development study with defined objectives that contributes to the malaria elimination and eradication agenda.

Eligibility criteria

The inclusion criteria for the projects were the following:

- ✓ Funded research projects
- ✓ Active in 2012 and onwards
- ✓ Projects that included research (development and manufacturing, clinical evaluation & technical support) of highly sensitive point of care tools to detect low-density infections, specially Highly-Sensitive Rapid Diagnostic Tests (hsRDTs, uRDTs)
- ✓ Keywords: *Alere, HRP2, highly-sensitive, uRDT, hsRDT, ultrasensitive, sensitivity, sensitive, RDT, asymptomatic, low-density*

Systematic data collection

From December 2017 to May 2018, we systematically compiled information on research projects and grants. We pursued the information, as a first step, from public sources such as institutional websites or annual reports and through direct contact with the researchers and principal investigators.

All the projects were collected from:

- ❖ Research grants databases:
  - Bill & Melinda Gates Foundation (BMGF)
  - Clinicaltrials.gov
  - Clinton Foundation
  - Department for International Development UK (DFID)
  - Europe PMC Grant Finder
  - FIND
  - Grand Challenges
  - Grantome.com
  - Medical Research Council of the United Kingdom (RCUK)
  - National Institutes of Health (NIH)
  - National Science Foundation
  - PATH
  - President's Malaria Initiative (PMI)
  - Research Council Norway
  - Swiss National Science Foundation

[1] http://www.malariaeradication.org/mesa-track/methodology-definitions

- The Global Fund to Fight AIDS, Tuberculosis and Malaria
- The Rockefeller Foundation
- UNITAID
- USAID
- Wellcome Trust

❖ Research institutions:

- Harvard T.H. Chan School of Public Health (HSPH)
- London School of Hygiene and Tropical Medicine (LSHTM)
- Malaria Consortium
- QIMR Medical Research Institute
- Shoklo Malaria Research Unit (SMRU), Mahidol Oxford Tropical Medicine Research Unit (MORU)
- Swiss Tropical and Public Health Institute (Swiss TPH)
- University of California San Francisco (UCSF)
- UT Southwestern Medical Center
- Others

❖ Other sources of information:

- 7th MIM Pan-African Malaria Conference abstracts
- Abbot
- American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting abstracts
- Consulted institutions on the MESA Track database
- European Commission

❖ Contact via e-mail with expert researchers with projects related to highly-sensitive diagnostic tools

As a second step, we produced a draft portfolio of the projects collected and reached out the principal investigators of the projects via e-mail. We provided them with the link to the project in the MESA Track database or an excel file with the information compiled enabling them to validate the information collected, fill in any gaps and provide additional projects or information.

Publication in the MESA Track database

We published the results obtained in the MESA Track database, they can be consulted here[2].

Categorization of Projects

With reference to the key use case scenarios identified – **malaria surveillance, malaria elimination and malaria in pregnancy** - and to be discussed at the *WHO Technical Consultation on research requirements to support policy recommendations on highly sensitive malaria diagnostic tests,* the following illustrates the association of these scenarios to sub-categories used in the database:

- *Diagnosis, Risk maps, Border, and HH Surveys* to be considered as sub-categories under the main topic of *malaria surveillance*
- *MSAT-FSAT*, *ACD in risk groups*, *RACD*, and *ISTp-SSTP* to be considered as sub-categories under the main topic of *malaria elimination*

[2] http://www.malariaeradication.org/mesa-track/advanced-search?keywords=highly-sensitive

- *MiP* is the acronym for *malaria in pregnancy*

As well, *Other POC* refers to other research projects on development and/or testing of a diagnostic tool other than that manufactured by Alere (Abott) with similar premise of highly sensitively detection of malaria parasites at point-of-care setting.

With reference to the categorization of the projects compiled in the different potential use case scenarios, we charted the projects according to the following definitions:

- Diagnosis: Confirmation of malaria cases and malaria surveillance
- Risk maps: Projects aiming at identifying foci that meet criteria for elimination interventions
- Border: Projects using highly-sensitive point of care tests as screening tools in border areas
- MSAT/FSAT[3]: Mass Screen and Treat/ Focal Screen and Treat
- ACD in risk groups[3]: In risk groups, detection by health workers of malaria cases at community and household levels
- Reactive case detection (RACD)[3]: Response to a confirmed case or cluster, in which a population potentially linked to such cases is screened and tested
- Household surveys: Routine health information systems
- MiP: Malaria in pregnancy
- ISTp/SSTp: Intermittent Screening and Treatment in pregnant women/ Single Screening and Treatment in pregnant women

Definitions used

- Intensity of transmission[4]
    - High transmission: Annual parasite incidence of about 450 or more cases per 1000 population and a *P. falciparum* prevalence rate of ≥35%
    - Moderate transmission: Annual parasite incidence of 250-450 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* malaria of 10-35%
    - Low transmission: Annual parasite incidence of 100-250 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* of 1-10%.
- Low-density infection[5]: When parasitaemia is quantified, infections with <100 parasites/µL accompanied by a description of the method of quantification. In studies that do not quantify parasitaemia, infections identified through highly-sensitive methods but not detected using conventional diagnostics (microscopy or RDT).

[3] WHO Malaria Terminology (http://apps.who.int/iris/bitstream/handle/10665/208815/WHO_HTM_GMP_2016.6_eng.pdf;jsessionid=187BC1155548261C6EA5A79E8C28C6FA?sequence=1)
[4] A framework for malaria elimination (http://www.who.int/malaria/publications/atoz/9789241511988/en/)
[5] Outcome of the WHO Evidence Review Group on malaria low density infections, MPAC October 2017 (http://www.who.int/malaria/mpac/mpac-oct2017-erg-malaria-low-density-infections-session2-presentation.pdf?ua=1)