A Malaria Elimination Guide to Targeted Surveillance and Response in High-Risk Populations

Module 2: Identifying Risk Factors Using Case-control Studies

The Malaria Elimination Initiative

shrinkinthemalariamap.org
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## Acronyms and Key Terms

<table>
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<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td><strong>Active case detection (ACD)</strong></td>
<td>Detection by health workers of malaria cases at community and household levels, sometimes in population groups that are considered at high risk. Active case detection (ACD) can consist of screening for fever followed by testing of all febrile patients or as testing of the target population without prior screening for fever.</td>
</tr>
<tr>
<td><strong>Case, imported</strong></td>
<td>Malaria case in which the infection was acquired outside the area in which it is diagnosed. The origin of imported cases can be traced to a known malarious area outside of the area to which the case has travelled.</td>
</tr>
<tr>
<td><strong>Case, index</strong></td>
<td>A case of which the epidemiological characteristics trigger additional active case or infection detection. The term “index case” is also used to designate the case identified as the origin of infection of one or a number of introduced cases.</td>
</tr>
<tr>
<td><strong>Case, locally acquired</strong></td>
<td>A case acquired locally by mosquito-borne transmission. Note: Locally acquired cases can be indigenous, introduced, relapsing or recrudescent; the term “autochthonous” is not commonly used.</td>
</tr>
<tr>
<td><strong>Confirmed malaria case</strong></td>
<td>Malaria case (or infection) in which the parasite has been detected via a diagnostic test, i.e. microscopy, a rapid diagnostic test or a molecular diagnostic test.</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>A subject (person) who does not have the outcome of interest and is therefore a member of a comparison group to which those with the outcome (the ‘cases’) are compared. For the example of case control studies to understand risk factors for malaria, a control is a person who tests negative for malaria.</td>
</tr>
<tr>
<td><strong>Exposure</strong></td>
<td>A term used to indicate that a study subject has a particular risk factor. For example, exposure to cross-border travel was defined as travelling internationally within the past 30 days.</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>A general term for the endpoint of a study, such as occurrence of a disease. In this case, the outcome is malaria status.</td>
</tr>
<tr>
<td><strong>Passive case detection (PCD)</strong></td>
<td>Detection of malaria cases among patients who, on their own initiative, visit health services for diagnosis and treatment, usually for a febrile illness.</td>
</tr>
<tr>
<td><strong>RACD (reactive case detection)</strong></td>
<td>A form of active case detection (ACD): screening and testing provided to a subset of a population in a given area in response to the detection of an infected person (i.e. the index case). Traditionally carried out among index case household members and households within a given radius. response to the detection of an infected person. Typically carried out around the index case household within a given radius.</td>
</tr>
<tr>
<td><strong>RDT</strong></td>
<td>Rapid Diagnostic Test</td>
</tr>
<tr>
<td><strong>Source population</strong></td>
<td>Population that would have been included in a cohort study (if cases were to arise prospectively) and which gives rise to the cases.</td>
</tr>
</tbody>
</table>

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Definitions were reproduced from WHO malaria terminology unless referenced otherwise.  

Overview of the HRP Guide

The High-Risk Population (HRP) Guide provides a set of approaches for NMCPs and NMEPs to:

- Review transmission patterns and surveillance gaps
- Gather detailed epidemiological evidence on risk factors and behaviors of populations likely at high-risk for malaria
- Adapt surveillance activities
- Track epidemiological trends in HRPs
- Improve targeting of interventions

The HRP Guide contains four modules that, when used in sequence, aim to incorporate evidence, tracking, and targeting of HRPs in broader surveillance and response strategies.

**Module 1:** Planning Targeted HRP Surveillance and Response

**Module 2:** Identifying Risk Factors Using Case-control Studies

**Module 3:** Monitoring Malaria Transmission and Intervention Coverage

**Module 4:** Adapting Reactive Case Detection

This guide is designed to be used by National Malaria Program Managers, Monitoring and Evaluation officers, and their implementing partners, including non-governmental organizations, and researchers in countries with low malaria transmission. For more details on the broader HRP Guide, read *A Malaria Elimination Guide to Targeted Surveillance and Response in High-Risk Populations: Introduction.*
Overview of Module 2: Identifying Risk Factors Using Case-control Studies

What is Module 2?
Module 2 provides instructions to conduct an assessment of malaria risk factors and collects data on a core set of essential indicators. Module 2 uses the Malaria Elimination Risk Factor Assessment Tool (MERFAT) that includes a questionnaire administered to malaria cases and a comparison group of controls identified at health facilities. This module provides a way to identify and quantify the importance of key actionable risk factors to guide program surveillance and response.

How to Use Module 2
Module 2 is designed to guide project staff during the design and implementation of a case-control study for malaria by providing detailed documentation and standardized operating procedures (SOPs). The MERFAT standardized questionnaire is provided separately for download as a paper-based or tablet (Open Data Kit) form.

The Module 2 guide covers MERFAT study design, how to adapt the MERFAT materials, procedures for recruitment and enrollment, procedures for study participation, roles and responsibilities of staff and study communication, documentation and data management and forms for field work.

Figure 1: Generating and using evidence: steps in the surveillance cycle for targeting HRPs
The ‘MERFAT Study Data Collection Phase’ section in this guide provides detailed SOPs. These SOPs should be adapted as needed and carefully reviewed during staff training.

Other Helpful Tips

- It is helpful for each staff member to carry a copy of the SOPs (based on procedures outlined in the ‘MERFAT study data collection phase’ section) with them while in the field. For an editable version of this section in Word, please email Tiese.mei@ucsf.edu.
- Any procedural changes should be documented in writing and attached to the SOPs.
- Regular practice sessions and refresher courses help maintain quality of data.
- The field staff should be regularly given the opportunity to request clarifications about the implementation of the SOPs.
Introduction to MERFAT

What is MERFAT?

The Malaria Elimination Risk Factor Assessment Tool (MERFAT) is a tool to help identify specific risk factors associated with malaria infection and gaps in interventions to inform programmatic action.

The MERFAT uses a case-control methodology that compares people with malaria (cases) to those without malaria (controls) and can be nested within the existing surveillance system for cost-effective and continuous assessment.

The tool consists of guidelines, example protocols and questionnaires to help programs and partners to design and implement the study and interpret the findings. In addition, there is an online component which provides an interactive platform to calculate the sample size, clean, map and analyze core data collected using the standard MERFAT ODK questionnaire.

Who Should Use MERFAT?

This toolbox is for health decision makers, malaria program managers, nongovernmental organizations, and researchers who wish to improve surveillance and response for populations at increased risk for malaria, with the ultimate aim of eliminating and preventing reintroduction of malaria.

MERFAT is for national malaria control programs, nongovernmental organizations, academics and other researchers who wish to provide evidence to support targeted intervention strategies.

The design and interpretation of these studies may require technical assistance from a technical partner such as UCSFs Malaria Elimination Initiative. Please contact mei@ucsf.edu if you are seeking technical support to implement MERFAT.
MERFAT Study Design

A case-control study is a classic epidemiological study design that is used to study a wide variety of diseases, although it is best known for its use in outbreak scenarios like cholera, Ebola or Zika virus. In its simplest form, a malaria case-control study compares the characteristics of malaria cases to the characteristics of a population without malaria (controls).

The MERFAT uses a health-facility based case-control study design, in which both cases and controls are selected from individuals presenting at a health facility. This design is simple, easy to carry out and is designed for resource poor places with little malaria. In most settings, it will provide a valid comparison group for passively detected malaria cases.

In certain settings the MERFAT study design may be adapted in order to better inform programmatic aims or when treatment seeking behavior in malaria at-risk populations is very low. We discuss adapting these methods and materials in a later section. MERFAT will require some technical assistance to design, implement and analyze.

Study Area

A first step to implementing this Module is to determine the geographical area that the study will cover and how many health facilities are needed. This will be dictated by:

- The number of cases per facility per month in the study area
- The minimum sample size needed to determine risk factors
- Budget resources available for health facility staff
- The populations for which the program requires information

Case Definition and Selection

The standard MERFAT design uses symptomatic malaria cases that are passively detected at health facilities through the existing surveillance system, although this may be adapted to include actively detected cases in some settings. By extrapolation, the source population is the entire health catchment population who, if they were infected with malaria and had symptoms, would be tested at the health facility.

The case definition should include only confirmed malaria cases, i.e. cases that have been diagnosed with a Plasmodium infection and confirmed by microscopy, RDT or some more sensitive diagnostic test. It is worth bearing in mind that some tests (like RDTs) have low sensitivity and may miss cases with lower density infections. However, test sensitivity and specificity are likely to be high in a clinical setting, as malaria parasite density is expected to be high in symptomatic individuals.

Control Definition and Selection

The primary aim of control selection is to provide a valid comparison to the cases by ensuring that controls have the same exposure distribution as the source population for cases. MERFAT controls are recruited from febrile individuals testing negative for malaria at health facilities, This ‘test-negative’ design implicitly conditions on healthcare-seeking practices, and eliminates an important source of selection.
bias. However, investigators should be aware that non-malarial febrile illnesses may share some risk factors with malaria (such as socioeconomic status). Malaria risk associated with such shared factors will be underestimated but most actionable risk factors will not be affected. All interviews should be carried out on site, as follow-up may be difficult for highly mobile populations.

The definition of the "control" population should include only people who are confirmed not to have malaria, i.e. controls that were confirmed negative for a *Plasmodium* infection by microscopy, RDT or some more sensitive diagnostic. It is worth bearing in mind that some tests (like RDTs) have low sensitivity and some cases with lower burden infections may be mistakenly classified as controls. Using health facility controls should minimize this misclassification, however carrying out confirmatory testing with a more sensitive and specific test, such as LAMP or PCR can help to correctly classify cases and controls for the analysis.

Given that calendar time could be related to malaria exposures, controls should be recruited in fixed numbers throughout the study period, rather than matching by date of diagnosis. This will allow an estimate of how risk varies throughout the year in relation to environmental (rainfall, vegetation and IRS) and behavioral (travel patterns, outdoor work, or bednet use) factors.

Note: If a more detailed examination of specific occupations or behaviors is needed, then the recruitment of a second set of community-based controls is encouraged. This set of controls can be recruited during reactive case detection (RACD) and include controls from the same village or neighborhood of cases. These controls are likely to have similar health access as cases (i.e. live the same distance from a health facility) but are not currently ill, so may provide a better comparison for treatment seeking and behaviors that may be affected by any illnesses. However, controls living in close proximity to index cases are also likely to be more similar in terms of education, socioeconomic status, and housing and so will underestimate any associated risk with these broader risk factors. Finally, this design will add cost and require additional technical assistance to carry out an analysis incorporating matching at the village or neighborhood level. Therefore, we only recommend including this control series when RACD is routinely carried out or when a highly focused risk factor study is the primary objective.
Inclusion and Exclusion Criteria

Inclusion criteria are those characteristics that all participants must have to be included in the study, while individuals meeting specific exclusion criteria are disqualified from participation. The same inclusion and exclusion criteria should generally apply to both cases and controls, as the objective is to ensure that the controls are a representative background population (i.e. a control would be detected and included as a case if he/she was infected with malaria). Recommended inclusion and exclusions are described below and in a protocol accompanying this document (available for download).

### Inclusion criteria

1. **Attending a selected health facility with suspected malaria:**
   - In order to minimize selection bias and costs, we recommend that both cases and controls are recruited from individuals attending a selected health facility and presenting with fever, thus triggering malaria screening.
   - Where reactive case detection is routinely carried out around index cases, a second community control set may be recruited. This control set is likely to be more similar in regards to selection factors (i.e. distance to health facility) but also may share other characteristics, like socioeconomic status, intervention coverage and occupation. This control set is more appropriate where a very targeted risk factor analysis is of interest, for example when there are several malaria cases reported from one or two geographically close villages.

2. **Confirmed diagnosis:**
   - Both cases and controls should have tested positive or negative by RDT, microscopy and/or other diagnostic test.

### Exclusion criteria

1. **Prior diagnosis with malaria in the past 30 days:**
   - Cases that have received a diagnosis of malaria within the past month are likely to have a relapsed, rather than incident, infection. Individuals who test negative for malaria, but have recently recovered, can arguably be considered part of the case population.
   - It may be necessary to modify criteria by extending the period to 60 days where *P. vivax* transmission is dominant, in order to allow for the higher probability of relapse infections.

2. **Malaria chemoprophylaxis or treatment in the past 14 days:**
   - Individuals testing positive for malaria infection, but reporting recent chemoprophylaxis or treatment, may be more likely to be a relapsed/uncured infection than a newly incident infection. This is due to the potential inhibition of the parasite’s development due to treatment with an antimalarial drug or lack of efficacy of treatment.
   - Individuals testing negative for malaria infection, but reporting chemoprophylaxis or treatment, are either not susceptible to infection (and therefore not at risk of being a case) or have recently been infected.

### 3. Willing and available to participate in the study:

- All participants in the study should be fully informed on the aims, risk and benefits of the study, and have agreed to participate.
Matching Controls to Index Cases

Due to variation in healthcare seeking behaviors, health facility populations are largely pregnant women and young children. To ensure that the controls are representative of a comparable population, we recommend that control recruitment is restricted to reflect the expected age range and gender distribution of cases. For example, if all cases are males and over the age of 15 years, then the controls recruited from health facilities should also be males over the age of 15 years. If 1/3 of cases are female, then a similar ratio can be recruited. These numbers can be based on historical data. This strategy is termed “restriction” or “frequency matching” and will not complicate the analysis. However, it does mean that the effect of age or gender cannot be estimated from these data and require that census data are used instead as a comparison (i.e. how age influences the risk of malaria).

In contrast, matching on individual case characteristics (i.e. matching each control to a specific index case in terms of age, gender, time of diagnosis, etc.) in a programmatic setting and for studies of malaria is discouraged for four key reasons:

- Individual matching on a given factor will preclude investigation of their effect or any interaction. While we can still use census data to estimate the effect of age or gender (i.e. how age influences the risk of malaria), we cannot determine whether the risk of an exposure differs according to age or gender (i.e. how does the effect of travel on malaria vary with gender).
- **Age and gender can be measured and controlled for easily** in the analysis using logistic regression or stratification, thus eliminating any need to individually match on these characteristics.
- Successfully matching controls to individual cases will require a more complex type of analysis, called conditional logistic regression that may be too technically demanding for program staff.
- Matching cases and controls by calendar time (and other characteristics) may be operationally difficult and leave a large number of cases unmatched.

Where a focused risk factor analysis for specific occupational or behavioral characteristics is the priority, it may be convenient to select a second set of community controls where RACD is routinely carried out. This design effectively matches controls to cases by village or neighborhood, has specific advantages and disadvantages outlined under ‘Control definition and selection’ and will require a more complicated analysis.

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**Figure 3. Conceptual diagram of factors influencing risk of exposure to malaria**

- **Location-related**
  - Residence/travel locations
  - Rainfall
  - Vegetation
  - IRS coverage

- **Behavioral-related**
  - Net use
  - Travel to endemic areas
  - Outdoor activities (occupational, recreational)

- **Vector-related**
  - Vector density
  - Breeding sites

- **Risk of exposure**
  - High biting times
  - Vector species
  - Vector behaviors
Exposures

The core MERFAT questionnaire components cover a broad range of potential risk factors. Conceptually, factors can be related to behavioral risk (i.e. forest work, occupational or leisure activities, intervention use, etc.) and location-related risk (i.e. environmental factors associated with home or travel locations), which usually vary by socio-demographic characteristics. Malaria risk is determined by these characteristics, together with vector-related factors in the area where transmission takes place (residence or travel/work destination). If resources and entomological capacity are available, vector assessments around case and control households can be added to understand differences in peri-domestic transmission between these two populations.²

When considering risk factors, it is important to take into consideration the incubation period of the various malaria species, which in most cases varies from 7 to 30 days but can be longer in the case of *Plasmodium vivax*. In MERFAT, both cases and controls must have a date of diagnosis associated with them and the recommended period of exposure to assess for risk factors will usually be 30 days prior to diagnosis. If there is transmission of *P. vivax* in the study area, consider adapting the questionnaire to cover a 60 day period of exposure for particular risk factors.

Calculating the Sample Size

In the analysis, risk factors for malaria will be expressed as associations between an exposure and being a case or a control. This is quantified through an odds ratio (OR). For example, if 40% of cases have a risk factor but only 20% of controls do, we would say that the cases have a 2.67 times greater odds of the risk factor than the controls. In order to say this with an acceptable level of certainty, we need to have a large enough number of cases. In this scenario, a reasonable minimum sample size will be 92 cases in order to have adequate power (80%) to distinguish an OR of 2.67, assuming a 20% prevalence of a risk factor in controls and 40% prevalence in cases.

In elimination settings, there are likely to be few cases and reaching the target sample size may be difficult, especially when there are low prevalence risk factors and your required sample size is higher. In this situation you should recruit more controls (up to 4) per case in order to increase your power and decrease the number of cases required to ~65 and/or extend your study so that it covers several years in order to reach your sample size. Table 1 demonstrates how adding controls can reduce the number of cases required when the prevalence of the exposure of interest is 20% in the controls and 40% in the cases. A larger sample size will be needed when the prevalence of the exposure of interest is lower.

Where the study covers multiple health facilities over a non-contiguous area, you will need to add a design effect to inflate your sample size in order to account for the fact that many exposures (such as travel behaviors) may cluster geographically. We recommend a minimum design effect of 1.5 and its effect on sample size can be explored in the Online MERFAT Sample Size Calculator. If controls are matched on some factor (for example, village residence), then you should use a higher design effect to help account for added correlation between cases and controls.

### Table 1. Sample size calculations for unmatched cases control studies, assuming 20% prevalence of exposure of interest (cases) and 40% prevalence (controls), with 80% power and alpha = 0.95. Community controls are assumed to come from the neighborhood of cases, and have a correlation of 0.3.

<table>
<thead>
<tr>
<th>Cases: control Ratio</th>
<th>Odds ratio</th>
<th>Sample size</th>
<th>Total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cases</td>
<td>Health facility controls</td>
</tr>
<tr>
<td>1:1</td>
<td>2.67</td>
<td>92</td>
<td>92</td>
</tr>
<tr>
<td>1:2</td>
<td>2.67</td>
<td>72</td>
<td>144</td>
</tr>
<tr>
<td>1:3</td>
<td>2.67</td>
<td>65</td>
<td>195</td>
</tr>
</tbody>
</table>

Respective number of cases needed are 125, 86, and 72 in the matched design.

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The first MERFAT pilot was conducted in Zambezi Region, northern Namibia between January 2015 and June 2016. Zambezi Region borders several countries with higher malaria transmission, including Angola and Zambia, and so the Malaria Control Program was particularly interested in defining cross border movement and high-risk populations.

The first malaria transmission season was low (96 cases and 199 controls), while there was a large malaria outbreak in the second transmission season (674 cases and 442 controls). Overall, indoor residual spray (IRS) coverage was low amongst both cases (44%) and controls (56%), but IRS did appear to be protective in this context. The case-control study identified that males of all ages and children aged 5–14 years were more likely to be malaria cases.

After adjusting for education and socioeconomic status, there were a large number of programmatical risk factors identified, including cross-border travel and migration early in the transmission season.

In addition, higher risk of malaria was related to housing (sleeping in tents or traditional housing), intervention use (low bednet use or lack of IRS), and specific outside behaviors at night (studying outside and cow herding).

Using an analysis technique to group high-risk characteristics, preliminary analyses have identified three key populations:

1. **Students**: Children aged 0–15 years, often males, who studied outside at night. Tended to have very low levels of intervention coverage and slept in tents or traditional houses. More common in later in the transmission season (local).

2. **Mobile and migrant populations**: Characterized by high mobility and cross-border travel, this group included more adult males and cow herders. More likely to sleep outdoors or in tents and were often not covered by IRS campaigns. More common early in season.

3. **Rural and remote residents**: Adults of both genders tended to live further from health facilities and with lower education and socioeconomic status. These populations were likely to be missed by IRS campaigns and had very low net use, lived in traditional houses, and frequently did agricultural work outside at night.

**Figure 1. Recruitment of cases and controls from February 2015 to June 2016**

**Figure 2. Intervention types and access strategies to address specific risk factors and high-risk populations**
MERFAT Study Planning Phase

The following materials provide an example to guide you in creating a protocol, data collection instruments, and budget for your study. You can download editable versions of these documents here. Begin by reading through the entire protocol, questionnaire and other documents, and marking sections that you can use or adapt and sections that you need to create.

Tips and resources for writing sections of the protocol are included as footnotes.

Throughout the materials, instructions to you are in brackets and italicized, e.g. [INSERT name here].

We have used the following terms to represent the sample target population, location and language. These terms should be changed to reflect your own context:

- Nibia (we used this as a generic country name)
- Bezi (we used this as a generic town/region name)
- Language X

Once you have finished a draft of your protocol and other materials, make sure to edit sections from this example to reflect your study. You can use the Find and Replace functions in Word to help you with this task, for example to find every instance of “Nibia” and replace it with the name of the relevant country.

Adapting the Study Design

All materials will need to be adapted to a particular study area and in some settings, the study design may be adapted to focus on particular populations or purposes. We recommend adapting the study design with technical assistance from UCSF MEI or another technical partner, but all changes should follow the steps below.

Step 1: Review existing case data and compile information on high-risk populations

The first step in adapting the design is to review available information from:

- Monthly data from health information management systems (HMIS)
- Patient registers, and
- Local malaria experts at the community level (i.e. health facility level or lower)

This can be done as a part of Module 1: Planning Targeted HRP Surveillance and Response.

Figure 4 (next page) outlines the key questions and data inputs that should be considered, which will help to tailor the design of MERFAT and staffing decisions.

Step 2: Review MERFAT study aims

While the standard MERFAT design captures a broad range of risk factors, it may be useful to modify the study aims if there are known characteristics of high-risk populations, based on prior studies or expert knowledge. Programs also may wish to:

- Ensure that environmental risk factors can be investigated and geographical clustering explored
- Confirm a suspected high-risk group (and remove other exploratory questions), or
- Focus investigation into behavioral risk factors or intervention gaps in a known high-risk group (such as mobile and migrant populations).

Some tailored designs based on specific risk factors of interest are outlined in Table 2 (page 14). However, it is best to utilize support from technical partners in making major changes to the MERFAT design to ensure that the study is unbiased and will provide useful information to the program.
## Figure 4. Key questions and inputs for organizing design of MERFAT

<table>
<thead>
<tr>
<th>Activities</th>
<th>Decision points</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMIS</strong></td>
<td>Calculate number of cases, by:</td>
<td>• How many health facilities need to be included to reach the minimum sample size?</td>
</tr>
<tr>
<td></td>
<td>• Health facility</td>
<td>• Determine the study area</td>
</tr>
<tr>
<td></td>
<td>• Month</td>
<td>• Propose timeline for data collection</td>
</tr>
<tr>
<td></td>
<td>• Species</td>
<td>• Set minimum sample size calculation for all species or separately</td>
</tr>
<tr>
<td></td>
<td>• Travel &amp; Importation status (if available)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• How many health facilities need to be included to reach the minimum sample size?</td>
<td></td>
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<tr>
<td></td>
<td>• How long does the study need to extend to reach the minimum sample size?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Are there sufficient cases to analyze the results by species?</td>
<td></td>
</tr>
<tr>
<td><strong>Registry review</strong></td>
<td>Calculate number of individuals tested and cases per month, by:</td>
<td>• What is the historical age and gender distribution of cases?</td>
</tr>
<tr>
<td></td>
<td>• Age</td>
<td>• Based on the above distribution, will you be able to meet monthly control recruitment</td>
</tr>
<tr>
<td></td>
<td>• Gender</td>
<td>targets at health facilities?</td>
</tr>
<tr>
<td></td>
<td>• Occupation (if available)</td>
<td>• What are expected importation rates and from where?</td>
</tr>
<tr>
<td></td>
<td>• Location (if available)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Travel &amp; Importation status (if available)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• What is the historical age and gender distribution of cases?</td>
<td>• Set monthly control recruitment targets for each health facility based on age and</td>
</tr>
<tr>
<td></td>
<td>• Based on the above distribution, will you be able to meet monthly control</td>
<td>gender-specific caseload</td>
</tr>
<tr>
<td></td>
<td>recruitment targets at health facilities?</td>
<td>• If occupation, travel and/or location data available, use to inform study aims and</td>
</tr>
<tr>
<td></td>
<td>• What are expected importation rates and from where?</td>
<td>questionnaire design</td>
</tr>
<tr>
<td><strong>Expert opinion</strong></td>
<td>• Are there known high-risk populations? How common are they?</td>
<td>• Increase the sample size in order to detect small groups, if needed.</td>
</tr>
<tr>
<td></td>
<td>• Do they vary across the proposed study area?</td>
<td>• Split the study area into homogenous zones if groups vary</td>
</tr>
<tr>
<td></td>
<td>• What levels of access do different groups have to treatment?</td>
<td>• Consider using TLS or a peer referral method to access specific hard-to-reach populations</td>
</tr>
<tr>
<td></td>
<td>• Is &lt;10% of the population likely to fall into a high risk category?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Are high risk groups likely to vary across the study area?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Are there likely to be high risk groups who do no attend health facilities</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Increase the sample size in order to detect small groups, if needed.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Split the study area into homogenous zones if groups vary</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Consider using TLS or a peer referral method to access specific hard-to-reach</td>
<td></td>
</tr>
</tbody>
</table>

- Consolidate steps 2–5
- Solicit technical input
- Adapt proposal/SOP
- Adapt questionnaire
### Module 2: Identifying Risk Factors Using Case-control Studies

#### Step 3: Decide on the study area

The catchment population of selected health facilities will typically determine the study area, and so selecting specific districts and all health facilities (or a sample) within them is recommended. Consider the questions below to ensure that the selected study area meets programmatic needs, will capture the required sample size and is operationally feasible.

- **Over what area is programmatic information needed and is it important to look at environmental risk factors?** If resources or strategies will be decided at the health district level, then the source population should be representative of this area. If a smaller area (for example border areas) are targeted, then the study area can be reduced.

- **How many confirmed cases of malaria are there in this area per year?** How many health facilities does this include? Fill out the table found in Appendix III with information for each health facility in your initial study area and compare to your required sample size. Does the study need to be larger or can the period of the study be extended?

- **What are the resource constraints in implementing MERFAT?** Will it be more efficient or cost-effective to expand the geographical study area to increase the number of cases or extend the study over several transmission periods?

- **How large is the area?** Do environmental factors like rainfall and vegetation vary across the study area? Do you expect the area to have similar or very different high-risk populations?

---

#### Table 2. Overview of potential MERFAT design options for specific risk factors for interest

<table>
<thead>
<tr>
<th>Risk factors of interest</th>
<th>Programmatic relevance</th>
<th>Study design options</th>
</tr>
</thead>
</table>
| Environmental factors    | Malaria may cluster into geographical ‘hotspots’ that are related to topography, vegetation and other environmental factors. These may influence vector habitat availability and density, and resulting foci extent. | If more than one health facility is included in the study, there are two options to ensure that you can carry out a spatial analysis:  
1. Use the standard study design together with a risk mapping software like DISARM, which will model risk factors and predict malaria incidence using information on the underlying population distribution instead of a control series.  
2. Assign controls to health facilities based on probability proportional to size. This will help ensure that the distribution of the control population in space matches the true population distribution. |
| Forest malaria           | When all malaria transmission is forest related, the objective may be to identify whether there are high-risk groups or behaviors within forest-going populations. | Restrict the study population (both cases and controls) to individuals reporting forest or forest-fringe exposure.  
In this scenario, it may be advisable to include 1) a set of community controls matched at the village level and/or 2) include cases identified through active screening activities and a wider source population for controls (i.e. a random selection of those included in the active screening).  
Focus the questionnaire on forest-related exposures and defining activities, evening and early morning behaviors and travel patterns within the forest. |
| Cross border travel      | A higher proportion of cases are imported in pre-elimination settings. Identifying specific patterns of human movement and reasons for travel associated with higher risk will be important for targeting screening procedures. | Restrict the study population to cross border travelers.  
In this scenario, it may be advisable to include cases identified through active screening activities and a wider source population for controls (i.e. a random selection of those included in the active screening).  
Focus the questionnaire on cross-border travel patterns (specific destinations and travel routes), reasons for travel and defining high-risk behaviors in that context. |
• Is the area contiguous? If the study area is comprised of several districts or enumeration areas (EAs) that are separated in space, consider the implications. Are the populations likely to differ and should they be analyzed separately or powered for subgroup analyses?

Note that the geographical catchment area of a health facility does not always correspond to the true catchment area. For example, health facilities located near border posts may capture MMPs who are in transit.

Step 4: Decide on the sample size
In some circumstances, the recommended sample size may need to be inflated, including for:

• Sub-group analyses: If you are planning to do sub-group analysis by malaria species or occupational group, you will need to increase your sample size. To achieve the same power (80%) for each sub-group, you will need to capture the total sample size in each sub-group.

• Low prevalence exposures: If you suspect that the prevalence of some high-risk characteristics (i.e. occupational groups or travel) is less than 20% in the general (health-seeking) population, you will need a higher sample size.

• Focal risk factors: If your study area is large, and you expect high-risk characteristics to only be present in certain areas, then you may want to split your study area into homogenous strata and ensure you reach your sample size in each area.

Use the Online MERFAT Sample Size Calculator to explore the effect of changing these assumptions on the required sample size.

Step 5: Decide on the duration of the study
This will have budget implications and will depend on whether one transmission season will be sufficient to achieve the minimum sample size, given the proposed study area. Given potential variation in transmission between years, be prepared to seek funding if data collection needs to be extended to meet the sample size.

Step 6: Decide what type of ethical review is needed
MERFAT may be integrated into regular programmatic data collection or conducted more as a research activity. Whether this activity requires ethical review, and what type of review is required, will depend on national guidelines from the Ministry of Health as well as any requirements from implementing or technical partners. If this is required, a section should be included in the protocol that details what type of review will be obtained as well as procedures around informed consent and data confidentiality.

Steps for Adapting the Questionnaire to Your Context

The ODK (.xls) and paper form (formatted for printing in Excel) provide a core set of questions that we recommend using in all MERFAT studies. However, users will need to adapt the questionnaire to fit their setting and may also choose to remove or alter questions. Modifications should be done with technical assistance.

Step 1: Review all questions in the core components
For the most part, these questions should remain unchanged but the language may need to be modified to fit the setting.

If *P. vivax* is dominant, consider extending the period of exposure for key risk factors from 30 to 60 days.

Step 2: Review all responses in the core components
The response sets will need to be tailored to each setting. For example: nearby countries, health facilities and typical materials used in housing construction.

In particular, it is important to develop a very detailed list of occupations in each setting, particularly those suspected to be common or potentially high risk. This can be informed during a formative review as described in the guide to Module 1, Planning for HRP Surveillance and Response, which includes speaking to community members and reviewing registry data.

Step 3: Replace all administrative lists with their own country sub-divisions (ODK only)
The standard ODK questionnaire is developed to filter responses by administrative levels 1 (region/province), 2 (district), 3 (sub-district), 4 (village). However, for this to work, a .csv file needs to be made that specifies these levels, as shown in Villages.csv. This form should be adapted, keeping the column headers titled exactly as they are.
Please seek technical assistance with this aspect of the ODK questionnaire if required.

**Step 4: Add or remove additional modules**

Additional modules have been generated to gather additional information on forest travel where transmission in this setting is suspected or confirmed.

**Step 5: Translate questions into the local language**

Translate questions in the paper questionnaire and text in the ‘label’ and ‘hint’ columns in the ODK form into the local language (‘label::X’, ‘hint::X’). This should be translated as closely as possible by two separate translators and then compared. The final version should be back translated to English and compared against the original text. In the ODK form, you can switch between languages.

**Step 6: Generate a photobook for each interviewer**

For different types of housing (i.e. construction materials of walls), household environmental questions (i.e. presence of long grass) or specific species of monkeys, it is recommended to have pictures for interviewers to show respondents. This will improve the reliability of self-reported data for these questions.

**Step 7: Pilot questionnaire**

The questionnaire should be piloted on at least 5 people of the same background as potential participants in the study. This will help to ensure that questions are understandable and the correct data is being collected.
MERFAT Study Data Collection Phase

Following study planning and IRB approval (if required), the data collection phase can begin. Data collection should be planned to cover at least one full transmission season, but may be extended (or carried out regularly) to increase the sample size or inform ongoing surveillance.

All activities will be carried out on an ongoing basis, as the target is to include all malaria cases that arise within the study area and a sufficient number of eligible controls.

The study will be successful only if each team member understands and follows correct data collection procedures. The steps below describe the staffing and procedures for data collection.

Staff Roles and Responsibilities

Project staff must adhere to the ethical principles and standards when conducting the survey. Most importantly, they must respect and protect the privacy, confidentiality, and autonomy of participants. In addition, project staff should conduct themselves in a professional manner when interacting with participants, fellow staff members, and the general public.

The field staff include the following positions:

- Field coordinator
- Interviewers
- Health facility nurse

Size of field teams:

- Low burden health facility: In this setting, existing health facility staff (either nurses or designated malaria officers) can usually act as interviewers.
- High burden health facility: It may be necessary to hire a designated interviewer to be based at high burden health facilities where the burden of malaria is too high for existing staff to take on the role of interviewer.

The time needed for one interviewer to enroll one survey participant is likely to be about 45 minutes, including eligibility screening, informed consent, survey interview and malaria testing.

The roles and responsibilities of these positions are described below and listed in Figure 5 (page 19).

Table 3. Key steps and staff responsible during the Data Collection Phase

<table>
<thead>
<tr>
<th>Before data collection</th>
<th>Each participant</th>
<th>Daily</th>
<th>Weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Visit all health facilities to be included and orient all nurses/existing staff to their role in the study</td>
<td>• Potential participant is tested for malaria according to national guidelines (RDT or microscopy)</td>
<td>• Upload data to central server from tablet (if applicable)</td>
<td>• Data checks to summarize recruitment numbers and any refusals</td>
</tr>
<tr>
<td>• Prepare materials</td>
<td>• Forward participant to interview area</td>
<td>• Daily planning and debriefing call</td>
<td>• Pick up of all laboratory samples and transport to a centralized storage unit</td>
</tr>
<tr>
<td>• Set up interview area</td>
<td>• Check eligibility status</td>
<td>• Review all records of each participant, separate information sheets and blood samples and store in a safe location</td>
<td>• Pick up of documents/forms and transport to centralized storage unit</td>
</tr>
<tr>
<td></td>
<td>• Assign participant ID</td>
<td>• Store all survey equipment and documents/forms in a secure, restricted-access location</td>
<td>• Double enter paper questionnaires (if applicable)</td>
</tr>
<tr>
<td></td>
<td>• Administer informed consent</td>
<td>• Charge tablet (if applicable)</td>
<td>• Field Coordinator</td>
</tr>
<tr>
<td></td>
<td>• Administer the questionnaire</td>
<td></td>
<td>The Field Coordinator will be responsible for the day-to-day management of all survey activities, including data collection (interviews and biological specimens), quality assurance and correct management of data and records. The Field Coordinator will also</td>
</tr>
<tr>
<td></td>
<td>• Create slides and DBS</td>
<td></td>
<td>provide prevention materials (if applicable) and thank participant</td>
</tr>
<tr>
<td></td>
<td>• If malaria positive, administer treatment according to national guidelines</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
be responsible for direct supervision of other field staff, leading regular debriefing calls, and developing progress reports. Extensive in-person supervision of field staff is critical in the first several months to ensure adherence to protocols and high quality data collection.

**Interviewer**
As Interviewers will be responsible for interviewing all cases of malaria and eligible controls, he/she must coordinate closely with the nurse to ensure that every person tested is screened for eligibility. If eligible, Interviewers will administer informed consent and conduct the interview using the tablet. They are responsible for storing all biological samples and documentation, as well as ensuring the quality of the interview data. Interviewers must report any problems to the Field Coordinator. In low burden areas, this role can usually be taken on by health facility nurses.

**Health facility nurse**
Nurses are responsible for testing individuals presenting to a health facility with symptoms of malaria, according to their national guidelines. The results of this test create the pool of potentially eligible cases (positive for malaria) and controls (negative for malaria). In addition, nurses are responsible for creating DBS for further testing and coordinating with Interviewers to ensure correct labeling and storage of DBS. Nurses will treat and refer individuals testing positive for malaria according to national guidelines.

**Implement Data Collection at Selected Health Facilities**
An overview of the data collection procedures is shown in Figure 6 (page 20).
Figure 5. Field staff responsibilities

Field Coordinator
- Ensure that field personnel are punctual and have a professional demeanor
- Support the health facility staff to ensure that there is a secure place to store materials and equipment
- Manage expenses
- Ensure the availability of all survey materials
- Based on supervision of recruitment and interview at health facilities, provide feedback to the interviewers and nurses to improve procedures for data collection and fix problems found by the team
- Store samples and documents (consent forms, field notes, enumeration and other forms) in a safe, secure place
- Ensure proper documentation of all survey activities, using the tablets, spreadsheets and forms
- Review, tabulate, and reconcile questionnaires, forms and logs used in the field. Review errors with field staff
- Write weekly progress reports used by the field team and PI to monitor recruitment
- Conduct daily debriefings by phone or in person to assess the procedures for data collection, challenges, and how to improve data quality
- Conduct weekly meetings with the larger survey team (including investigators) to communicate and discuss progress and adjust the planning of the survey, as necessary
- Supervise and monitor the work of the field teams, particularly early in data collection (interviewers and nurses)
- Assign a unique participant ID and ensure that the participant ID entered in the questionnaire matches the participant ID put on the malaria tests and blood samples
- Conduct informed consent
- Conduct interviews
- Ensure that all questionnaires are completed and uploaded at the end of the day
- Organize and store all malaria tests and blood samples collected by the nurse, to be picked up by the Field Coordinator
- Organize and store all study documentation (i.e., informed consent and line listings) for review and pick up by the Field Coordinator
- Maintain data integrity (i.e., all data collected accurately represents the information provided by participants)
- Comply with guidelines for maintaining safety, data security, and participant confidentiality
- Implement local safety procedures and report field incidents to the Field Coordinator immediately
- Conduct daily inventory of all supplies, and communicate with the Field Coordinator when any supplies are low or need to be replenished

One staff member may assume the role of both the interviewer and nurse if health facility burden allows.

Interviewers
- Ensure that all forms, DBS cards and other supplies are prepared for each day
- Promptly assess eligibility and complete the eligibility screening form of any individual tested for malaria by the nurse
- Recruit participants for interviews and enter details into line listing
- Take blood samples from participants using venipuncture and finger-sticks
- Create DBS for analysis
- Coordinate with Interviewers to properly store and transport the samples
- Provide treatment and referrals according to regular test results and national guidelines

One staff member may assume the role of both the interviewer and nurse if health facility burden allows.
Figure 6. A systematic flowchart of case/control classification and data collection procedures

1. **Does patient have symptoms of malaria?**
   - **yes**
     - Test for malaria by RDT or microscopy (according to national guidelines)
   - **no**
     - Diagnose and treat according to national guidelines

2. **Test for malaria by RDT or microscopy (according to national guidelines)**
   - **yes**
     - Does the case/control meet eligibility criteria?
   - **no**
     - Is the monthly control recruitment target unmet?
   - **yes**
     - Does the patient meet age/gender requirements?
   - **no**
     - Does patient test positive by RDT/microscopy

3. **Does patient test positive by RDT/microscopy**
   - **yes**
     - Complete informed consent procedures
     - Add case/control to the line list
     - Assign unique case/control ID to the patient
     - Collect a DBS for future testing and label with ID
     - Complete MERFAT questionnaire
     - Store DBS sample and upload questionnaire
     - Report case details to Field Coordinator
   - **no**
     - Does the case/control meet eligibility criteria?
   - **yes**
     - Does the case/control provide informed consent to participate in the study?
   - **no**
     - Diagnose and treat according to national guidelines
   - **yes**
Prepare the Necessary Materials

**Staff member: All staff members**

Interviewers and nurses must always have the necessary materials on hand to complete their daily tasks. The Field Coordinator will be responsible for replenishing these supplies during routine supervision and check-in visits. Materials are listed in Figure 7. It is recommended to provide a cold drink and/or small snack to participants as they will likely feel ill at the time of interview.

### Case selection and eligibility screening

**Staff member: Interviewer**

Upon arrival to the health facility, patients with suspected malaria will be tested according to country-specific National Guidelines by nurses, which typically includes all febrile individuals. All people who test positive for malaria by RDT or microscopy (confirmed cases) at any of the participating health facilities should be assessed against the eligibility criteria laid out in Appendix IV.

#### Material required
- Participant folder (containing two copies of the Informed Consent form and eligibility screening form)
- Pen

#### Procedures
1. Complete the paper-based case notification form (if applicable), answering questions accordingly.
2. Complete the eligibility screening form to determine if the case is eligible to participate in the study.
3. If case is eligible to participate in the study, enter his/her name and details on the ‘Health facility case line list.’

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**Figure 7. Checklist of materials required for MERFAT**

<table>
<thead>
<tr>
<th>Survey Coordinator</th>
<th>Nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Master case recruitment line list</td>
<td>□ Dried Blood Spot (DBS) cards</td>
</tr>
<tr>
<td>□ Master control recruitment line list</td>
<td>□ Gloves</td>
</tr>
<tr>
<td>□ Extra DBS cards</td>
<td>□ Alcohol swabs</td>
</tr>
<tr>
<td>□ Extra paper questionnaires</td>
<td>□ Lancets, syringes, needles</td>
</tr>
<tr>
<td>□ Extra pens</td>
<td>□ Cotton or gauze</td>
</tr>
<tr>
<td>□ Extra forms (line lists, screening, informed consent, refusal)</td>
<td>□ Biohazard plastic bag (red)</td>
</tr>
<tr>
<td>□ Extra tablet (charged) and charger</td>
<td>□ Plastic bag for other trash (black)</td>
</tr>
<tr>
<td>□ Coolbox with ice to transport samples to centralized location</td>
<td>□ Sharps container</td>
</tr>
<tr>
<td>□ Extra refreshments (if applicable)</td>
<td>□ Pencils, pens, and permanent markers (sharpies)</td>
</tr>
<tr>
<td>□ Eligibility screening forms</td>
<td>□ Clear plastic zip bags for samples</td>
</tr>
<tr>
<td>□ Informed consent forms</td>
<td>□ Desiccant for zip bags</td>
</tr>
<tr>
<td>□ Refusal forms</td>
<td>□ Drying racks for slides and DBS</td>
</tr>
<tr>
<td>□ Copies of approval letters from the bioethics committee and administrative approval</td>
<td>□ Refrigerator (in health facility)</td>
</tr>
<tr>
<td>□ Refreshments for participants</td>
<td></td>
</tr>
</tbody>
</table>
Control selection and eligibility screening

*Staff member: Interviewer*

Upon arrival to the health facility, patients with suspected malaria will be tested according to National Guidelines, which typically includes all febrile individuals. All people who test negative for malaria by RDT or microscopy at any of the participating health facilities should be assessed against the control eligibility criteria laid out in Appendix IV.

**Material required**
- Participant folder (containing two copies of the Informed Consent form and eligibility screening form)
- Pen
- Health Facility Control Line List
- Monthly Control Recruitment Tracker

**Procedures**
1. Complete the eligibility screening form to determine if the control is eligible to participate in the study. Note that this includes a question whether recruitment targets for his/her specific age and gender have been met for the current month.
2. If control is eligible to participate in the study, enter his/her name and details on the ‘Health facility control line list.

Administer informed consent

*Staff member: Interviewer*

It is important that each eligible individual invited to participate fully understands all procedures and how their samples and data will be used. The process of informed consent is a necessary ethical procedure preceding any data collection and no samples or data should be analyzed if consent is not available. Even when MERFAT is performed as part of routine surveillance, as opposed to by a research institution, it is important that participants have a clear understanding of these activities.

**Material required**
- Participant folder (containing two copies of the Informed Consent form and eligibility screening form)
- Pen

**Procedures**
1. Take out two copies of the informed consent.
2. Following the script on the case/control informed consent form (see Appendix VIII), explain the purpose of this study and invite the patient to participate in blood testing and a survey questionnaire. Note that the informed consent form should be tailored to organizational/institutional requirements.
3. For youth under the age of 18 years, informed consent will be obtained from a parent or guardian.
4. Have the patient sign both copies of the case/control consent form.
5. Add a tick in the appropriate box on the ‘Health facility case line list’ (cases only) or the ‘Health facility control line list’ (controls only).
6. Affix a barcode to one copy of the informed consent (as described below). Keep this copy and write in the ID number on the second copy to give to the participant.
7. Write the participant ID on the case (or control) line list.
8. Add a tick next to the appropriate age and gender category in the ‘Monthly Control Recruitment Tracker’ [Controls only].

Participants who decline to participate

If the participant declines to be interviewed in the study during the informed consent process, they will not be allowed to participate in the study. Thank them for their time.

Assign Participant ID and label materials

*Staff member: Interviewer*

If the patient agrees to participate in the study, he/she will need to be assigned an identification (ID) code. This code will be used to link blood samples to epidemiological data. Therefore, it is critical that codes are unique and entered correctly. The best practice is to use barcode IDs, which can be pre-printed before the study and scanned into the tablet to avoid mistakes in data entry.

More details on the creation and printing of these IDs is available in Appendix I.

**Material required**
- Pre-printed barcode IDs
- A felt tip pen to mark any samples missing a sticker

**Procedures**
1. Use the next available participant ID, specific to a case or a control, and place barcodes as follows:
   a. Place a single barcode on the informed consent form, and write the barcode identifier and date the patient presented on the second copy.
b. Place a single barcode on the case or control line listing (see Appendix VI and Appendix VII).

c. Write the barcode ID or place a single barcode sticker on the positive microscopy slide/RDT to indicate that the slide is now tracked within the study. Ensure that the pen is permanent.

d. Place the double barcode on the outside of a dried blood spot sample.

Administer the survey questionnaire

*Staff member: Interviewer*

The survey questionnaire is the main data collection tool for the case-control study. Training materials and tips on how to conduct interviews are available from MEI and other sources, in order to ensure good quality data collection. Always try to move through the interviews at a good pace, while avoiding making the respondent feel pressured or uncomfortable.

**Material required:**
- Tablet (make sure the battery is charged)
- Paper copy of questionnaire and pen as back-up
- Participant folder (containing two copies of the Informed Consent form and eligibility screening form)
- Photobook with pictures of relevant housing/environmental variables (i.e. construction materials, different types of vegetation)

**Procedures**
- Complete the interview on tablet or on paper-based questionnaire.
- When asking the participant about specific construction materials for walls of their house and different types of vegetation, have them verbally respond and also pick out the (correct) picture. This will confirm their understanding of what is/is not each type (i.e. long grass vs other types of vegetation).
- At the end of the interview, thank the participant and escort him/her to the nurse to take a DBS.

It is important to be mindful that in the MERFAT study, people who are invited to participate in the study as cases or controls have sought treatment because they feel ill. If individuals are clearly unwell, they should be prioritized. If an individual is critically ill, then he/she should not be interviewed until well enough to participate.

Collect blood sample and laboratory procedures

*Staff member: Nurse*

**Material required:**
- Dried Blood Spot (filter paper and envelope)
- Lancet
- Gloves
- Alcohol swab
- Slides

**Procedures**
1. Collect the following: 1) dried blood spot (DBS) sample; 2) slide. Detailed procedures for these activities are available in Appendix II.

**Review survey forms and upload**
Upon completing the above procedures, immediately do a full review of all forms to ensure that:
1. Participant IDs are correct on the tablets/paper questionnaire, blood samples, line listing and informed consent forms
2. Informed consent forms are signed by the participant or guardian (if under age)
3. Tablet/paper questionnaire is completely filled out

Upon checking all forms, the tablet form should be uploaded to a centralized server. This may be done immediately or at the end of the day.

All paper forms should be stored together in the Participant Folder. As soon as the DBS is dry, it should be organized in a labeled plastic bag with desiccant and stored in a freezer. A complete protocol for creation and storage of DBS can be found in Appendix II.
Data Analysis

Analysis of the data collected from MERFAT should follow clear steps to define recruitment patterns, map patterns of malaria, characterize cases and controls, and identify key actionable risk factors. Steps 1 and 2 should be conducted on a regular (i.e. biweekly) basis in order to check recruitment of controls is on target and to identify any emerging risk factors. A more complex and multivariate analysis of risk factors, or analysis to account for matching in the study, can be conducted with technical assistance.

A MERFAT Online Analysis Tool is under development, hosted on the same platform as the MERFAT Online Sample Size Calculator (screenshots in Figure 8). This will aid in carrying out steps 1–3 if you have used the standard MERFAT questionnaire for data collection. This Online Tool currently includes functionality to generate a map of cases and controls (reviewed in Step 4), and future versions will automate detection of geographical hotspots.

**Figure 8. Screenshots of the MERFAT Online Analysis Tool**

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**Step 1. Recruitment tracking**

Calculate the number of cases and controls recruited into the study to date and compare them against the recruitment target.

Generate a histogram to observe the number of cases and controls (separate bars) recruited by week within the study period. You will notice that the number of cases will fluctuate with malaria transmission (as well as any other temporal factors influencing treatment seeking like holidays), while the number of controls should remain relatively stable. A comparison of the patterns of case and control recruitment should identify when the case burden is higher and malaria transmission is more intense.

**Step 2. Characterize cases and controls**

Calculate the number and proportion of cases and controls that have specific characteristics that are of interest in either profiling populations (age, gender, residence location) or that point to specific high-risk behaviors or activities (occupation, travel/forest exposures, housing, sleeping outdoors, etc.). A selection of these factors are available on the MERFAT Analysis Tool and these numbers and statistics can be visualized using histograms.
### Table 4. Key risk factors profiled by the MERFAT Online Analysis Tool

<table>
<thead>
<tr>
<th>Category</th>
<th>Variable Name</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Socio-demographics</td>
<td>• Age</td>
<td>Profile sub-populations</td>
</tr>
<tr>
<td>• Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Citizenship</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Main occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk activities</td>
<td>• Outdoor activities at night</td>
<td>Identify risk behaviors to target</td>
</tr>
<tr>
<td>• Slept outdoors in past 30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Slept within 20m of cattle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housing and malaria prevention</td>
<td>• Net use (frequency)</td>
<td>Identify intervention gaps</td>
</tr>
<tr>
<td>• Net slept under prior night</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• IRS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Traditional vs Modern housing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Open vs Closed housing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Travel and mobility</td>
<td>• Intervention use</td>
<td>Profile sub-populations/Identify risk behaviors/Identify intervention gaps</td>
</tr>
<tr>
<td>• Duration lived at residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Second residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Domestic travel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Cross-border travel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Worked/slept in forest</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Step 3. Identify key actionable risk factors

In order to identify key risk factors to inform programmatic action, the odds (or risk) of exposure in cases is compared to controls. If cases are more likely to have been exposed to a particular behavior or activity than controls, then we consider that it might be important in malaria transmission.

If the distribution of any factors have been restricted by design in controls (i.e. age, gender, or by setting a health facility recruitment target), then they must be controlled for at this stage. That is because they are not representative of the population and may change observed risk factor associations. The standard analysis will control health facility where recruitment took place, age and gender while calculating the odds ratios for all of the above key risk factors and an indication of whether this odds ratio is likely to be associated with increased or decreased risk of malaria.

There are likely to be additional, potentially important, risk factors that cannot be analyzed using the MERFAT Online Analysis Tool. A complete analysis can be conducted using this same approach with standard statistical software packages, such as STATA, SPSS or R. Please seek technical assistance with the statistical analysis as needed.

### Step 4 Map patterns of malaria

The standard MERFAT questionnaire will collect information on the residence of cases and controls, down to the village level. These village locations can be geolocated – i.e. assigned to a specific longitude and latitude. Village coordinates may already be available from the census or other databases (like school databases or from malaria program RACD activities), or you may have to go out with a GPS enabled device like a smartphone, tablet or tracker to capture these coordinates. Remember: each village that is the same should be assigned exactly the same coordinates in the database.

The number of cases and controls, village name and coordinates can be entered into the template available to download on the MERFAT Online Mapping Tool, and then uploaded to automatically generate a map of cases and controls. Future iterations of this Tool will also identify any areas of elevated risk (i.e. where cases are much more likely to be located based on the distribution of controls). This analysis can also be done in other GIS programs with technical assistance.
Documentation and Data Management

Table 5. Description and storage of key MERFAT documentation

<table>
<thead>
<tr>
<th>Name</th>
<th>Format</th>
<th>Description</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility forms</td>
<td>Paper</td>
<td>* Eligibility decision tree for cases/controls. Should be completed for each individual tested for malaria.</td>
<td>* Kept in the participant folder. If the person is NOT eligible to participate, will be stored in a separate folder.</td>
</tr>
<tr>
<td>Informed consent</td>
<td>Paper</td>
<td>* Informed consent forms to explain the study. Each participant should have two signed copies.</td>
<td>* One copy (with the barcode ID) will be kept in the participant folder. The other copy (with ID written on it) will be given to the participant.</td>
</tr>
</tbody>
</table>
| Case line lists    | Paper               | * Health facility case line lists list all eligible cases each participating health facility.  
                     * Master case line lists include all eligible cases at all participating health facilities. | * Health facility case line lists must be maintained in the study binder at the health facility.  
                     * Master case line lists are maintained by the study coordinator and entered into an excel sheet on a weekly basis. |
| Control line lists | Paper               | * Health facility control line lists list all eligible controls at each participating health facility.  
                     * Master control line lists are maintained by the Field Coordinator, and include all eligible controls at all participating health facilities. | * Health facility control line lists must be maintained in the study binder at the health facility.  
                     * Master control line lists are maintained by the study coordinator and entered into an excel sheet on a weekly basis. |
| Survey Questionnaire| Tablet (or paper)   | * Data collection instrument                                                | * All completed forms must be uploaded to a centralized server at the end of each day. |

Data Management and Storage

The following general procedures should be followed in order to ensure proper management and storage of all data and samples:

1. Interviewers must save the original slide/RDT, the DBS, the case notification form (if applicable), eligibility screening form and the informed consent form to be collected by the Field Coordinator.
   a. Blood samples should be stored as outlined in Appendix II as soon as they are dry.
   b. All paper documents should be stored together in a Participant folder, so that they can be checked and collected.

2. The Field Coordinator will copy entries from the health facility case line listing into the master case line listing weekly.

3. The Field Coordinator will pick up the slides/RDT and DBS weekly and transport to a centralized location for further testing.

Close coordination between the Field Coordinator and all Interviewers is essential. The Field Coordinator is responsible for reconciling all survey questionnaires submitted electronically with paper line lists from the health facilities and collected samples.

The following table outlines the data management procedures that the Field Coordinator should carry out regularly.
<table>
<thead>
<tr>
<th><strong>Table 6. Regular MERFAT data management procedures conducted by the Field Coordinator</strong></th>
</tr>
</thead>
</table>
| **Study start up** | • Extensive (at least week-long) piloting of the survey questionnaire to ensure that translated questions are collecting the correct data and any errors are resolved  
• Regular on-site supervision to ensure that SOPs are followed and all samples and data collected and are stored correctly |
| **Daily** | • Check in with all study staff by telephone for debrief on case and control recruitment.  
• Resolve any outstanding issues with data collection or uploading data to the server.  
• Ensure study staff have a sufficient stock of all supplies. |
| **Weekly** | • In person visit to all participating health facilities to add to master case and control line lists and replenish diminished supplies  
• Collect blood samples and participant folders and do a full inventory to ensure none are missing.  
• Reconcile online data with master case and control line listings.  
• Summarize recruitment and key demographics and/or enter data from paper questionnaires into a database. |
| **Monthly** | • Check whether monthly control recruitment targets were met at each health facility and the time period over which controls were recruited.  
• Summarize recruitment and conduct interim analysis for key socio-demographic and behavioral risk factors. Online tool available for this, based on the standard MERFAT questionnaire.  
• Monthly (if not more frequent) batches of LAMP or PCR from DBS; any positive controls reclassified as cases |
| **End of the study** | • Complete all LAMP or PCR analysis of DBS.  
• Carry out a full risk factor analysis. |
Appendix I. Participant Identification Codes

In order to keep each participant’s information confidential, we have created codes that will be used in place of the participant’s names. The code is 6 digits long and correspond to a barcode/sticker that will be used on all forms associated with the participants (health facility notification log, informed consents, survey questionnaire, participant tracking forms), in addition to all the biological samples (slide, dried blood spot, RDT, whole blood). When you return your completed forms to the Field Coordinator, be sure to keep all those with the same code together and stapled. Each digit within the code has a significant meaning that corresponds to the study site, study component and a unique number corresponding to that individual.

The breakdown of the code is as follows:

<table>
<thead>
<tr>
<th>Subdistrict code</th>
<th>Interview type</th>
<th>Unique ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1 digit)</td>
<td>(2 digits)</td>
<td>(3 digits)</td>
</tr>
</tbody>
</table>

The first digit of the code is based on your study location, or subdistrict. If there are two study locations with the same initials or name, make sure that they are coded differently. An example of the digits for this code is as follows:

<table>
<thead>
<tr>
<th>Subdistrict</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>KG</td>
<td>1</td>
</tr>
<tr>
<td>LH</td>
<td>2</td>
</tr>
<tr>
<td>SA</td>
<td>3</td>
</tr>
<tr>
<td>RG</td>
<td>4</td>
</tr>
</tbody>
</table>

The second and third digits in the code are for the study component participant type that is being enrolled into the study. Depending on the study component, use one of the following codes:

<table>
<thead>
<tr>
<th>Participant type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index case</td>
<td>01</td>
</tr>
<tr>
<td>Health facility control</td>
<td>02</td>
</tr>
<tr>
<td>Community control</td>
<td>03</td>
</tr>
</tbody>
</table>

Lastly, the final 3 digits are unique to each individual and will be between 001 and 999. Each participant is to have a different number so no two providers or patients will have the same final 2 digits. Here are some examples of codes you will write on each form used for each participant.

An index case in KG1 would have the following code:

1 01 001

Using Barcodes

The barcodes should be pre-printed onto stickers for ease of use. Barcode sheets allowing at home printing (Avery 5428) include four barcode stickers for each participant. The three left columns contain single barcodes and the right column contains double barcodes. The double barcode will enable the sample to be cut in half so that two spots are available for analysis at each of several facilities. The use of these barcodes is as follows:

- Column 1: Case/Control line list
- Column 2: Informed Consent Form (one copy kept for study files)
- Column 3: RDT slide
- Column 4: (double barcode) place on dried blood spot

Note: the date and identifier will need to be hand written on the other copy of the informed consent for the patient to keep.
Appendix II: Sample Collection and Storage

Background

Scientists have over many years collected and stored various kinds of samples for processing at a later stage. In their quest to understand diseases and their causative agents, medical scientists have often prepared blood samples from both exposed and non-exposed individuals. Samples were normally collected in the field or at a health facility, stored within a specified range of temperature, and then transported to a well-equipped laboratory for the screening of target organisms or parts thereof. Samples are important for both preclinical and clinical research.

Malaria is caused by parasites from the *Plasmodium* genus. There are 5 other species that are known to cause Malaria in humans. In Namibia, *Plasmodium falciparum* is the most predominant species, although *P. vivax* cases have also been recorded. These parasites infect human red blood cells, and thus, live in the human blood. For this reason, malaria-causing parasites can be isolated from blood samples.

If blood samples are not stored properly, the malaria parasites may not be able to be identified. This means that even if a person really does have malaria, their tests may be negative. It is therefore important that the blood samples are collected and stored properly in order for them to be kept intact and so that people with malaria can be reliably identified.

Key Terminology

**Sampling:** The process of obtaining biological specimens such as blood, sweat, urine, skin tissue by venipuncture or use of swabs from a source individual within a defined population.

**Sample/Specimen:** This includes whole blood, urine, cheek tissue, feces, plasma, skin and hair from human or animals. There are also instances where water, air or soil maybe termed a “sample” if it is being analyzed/screened for the presence of a particular agent.

**Storage and Preservation:** A manner by which samples are bottled or placed in a bag, with the main aim of ensuring that its not subjected to damage due to the surrounding environmental condition, i.e. temperature, pH, chemicals etc. The samples in the bag, should be kept away from moisture and direct sunlight.

**Coding:** Is a method of assigning unique identifiers, comprised of characters. This identification codes, may be a link to identify the person; the area; their treatment etc.

**Rapid Diagnostic Testing (RDT) cassette:** A cassette that detects parasite antigens/antibodies depending on the working principle. Results are readily available and can be read through a screen by the presence or absence of a line.

**Dry Blood Spot (DBS):** A folded paper containing a filter paper with equally sized, stamped rings on which finger-prick blood is collected on the circles, this blood is allowed to dry and the paper is subsequently folded to close.

Sample Collection

In most countries, blood samples will be drawn from patients by a qualified health practitioner, who may be an Enrolled/Registered Nurse or Medical doctors. This may vary in different contexts but should always align with National Guidelines.

A malaria test using a slide or RDT cassette will have already been conducted to diagnose all eligible participants for the MERFAT study. The interviewer will need to ask the nurse to conduct a DBS for all consenting MERFAT participants.

Sample Coding

It is critical that we are able to link each and every blood sample to the correct person, so that the malaria test results can be matched to the completed questionnaire. This is done using the unique Participant ID that are printed on the barcode labels. After a person has gone through the informed consent process, you will assign them a Participant ID and use the barcode labels.
Sample barcodes (top) and placement of barcode stickers on DBS and RDT (below)

Three labels have been printed, which should be put on the 1) informed consent form, 2) RDT and 3) DBS. The label with two barcodes should be put on the DBS, as shown on the pictures above.

Example: If Patient X has consented to be in the study, then the informed consent form, the RDT and the DBS from Patient X should all have the same barcode label with the same Participant ID. e.g. An RDT and DBS from Patient Simon Jackson will be labeled with corresponding code CJYW.

- **DBS**: DBS cards will need to be labeled prior to giving them to the nurse so that she/he may take the blood sample. It is best to request this sample at the end of the interview so that you can move on to interviewing the next person.

- **RDT**: If the person has already been tested for malaria and is included in the study as a case or a control, they will already have an RDT or slide. You must ask for this from the nurse and then label it with the barcode label.

Sample Handling

Although the nurses will be responsible for conducting the malaria test and collecting the DBS, Interviewers will need to handle the samples in order to dry them and store them. The following protocol should be followed.

1. Samples should be left to dry in an area that has good ventilation and is protected from the wind or people touching them. They should not be in the sun. Leave them to dry until the blood spot appears brown (approx. 10 minutes).

2. After they are dry, fold the flap down to cover the blood spots.

You should never touch the white filter paper, and only touch the yellow cardstock cover. It is also mandatory to wear gloves when handling samples for coding and examination purposes. It is also good practice to always disinfect your hands with methylated spirits after handling samples, even if you have not come in direct contact with it.

Barcode placement on DBS

Sample Organization and Storage

After they are dry, DBS and RDTs should be neatly stacked into trays for organization and storage. Ideally, stacks of filter paper cards should remain stable and organized, and not shift within a box. Samples should be sorted in order of the Participant ID, with the DBS and RDT with the same code stored next to each other.

The tray of samples should be placed in a zip lock bag, containing a humidity sponge/desiccant. Two trays should be able to be fit into a zip lock bag. Before the bag is sealed, squeeze out excess air. The zip lock bags should be clearly labeled (using...
a Sharpie pen) with the dates of the week in which samples were collected as well as the health facility name. Immediately store in the cool box to preserve sample.
Appendix III: Confirmed Cases by Health Facility

<table>
<thead>
<tr>
<th>#</th>
<th>Health Facility Name</th>
<th># tested RDT/Mic.</th>
<th>Total</th>
<th>Gender</th>
<th>Age Group (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5–14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15–29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30–44</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45+</td>
</tr>
</tbody>
</table>

Note: Disaggregating this table by month may help to plan for control recruitment targets.
Appendix IV: Eligibility Screening Form

Participant ID (if applicable): ______________________________________________________

Instructions: Complete the entire screening form for every individual tested for malaria. Only questions that are not in brackets should be made to the participant. Circle the answer to each criteria. If the person is eligible to participate, enter the person into the line list and continue with informed consent.

Date: __ __ / __ __ / __ __ __ __
(DD/MM/YYYY)

Health Facility:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Must be ‘YES’ to be eligible</td>
<td>[RDT result]</td>
<td>Positive result</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative result</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YES / NO</td>
</tr>
<tr>
<td>Must be ‘NO’ to be eligible</td>
<td>[Clinical Diagnosis only?]</td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td>Have you had a malaria diagnosis in the last four weeks?</td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td>Have you taken malaria treatment in the last 14 days?</td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YES / NO</td>
</tr>
<tr>
<td></td>
<td>[Monthly recruitment target met?]</td>
<td>Not applicable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YES / NO</td>
</tr>
<tr>
<td>Is the candidate eligible?</td>
<td>YES / NO</td>
<td></td>
</tr>
</tbody>
</table>

If NO, why is candidate not eligible? [mark all that apply]

☐ Has an invalid test or diagnosed clinically?
☐ Has had a prior malaria diagnosis in preceding month?
☐ Has taken malaria prophylaxis or treatment in preceding 14 days?
☐ Is present at the clinic because he/she was accompanying someone with fever
☐ Is critically ill and is excluded from the study
☐ Is unable to communicate in understood language
☐ Other: ____________________________________________
## Appendix V: Monthly Control Recruitment Tracker

**Instructions:** Monthly control recruitment targets should be set based on the expected total number of cases in the study area and the number of controls needed for acceptable statistical power, divided by 12. The proportion of males/females recruited should match the case distribution. Age ranges should be restricted to 15 years and up if all cases are adults, or frequency matched based on the expected case distribution.

NB: If the number of individuals tested for malaria every month far exceeds the number of expected controls (based on the formative review), use a skip pattern.

**Month:** __________  **Year:** __________  **Health Facility:** ________________________

**Previous Month Rollover:** Enter the number of individuals in each control category that could not be recruited in previous months. These individuals should be recruited before the current month recruitment begins.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age category</td>
<td>0–14</td>
<td>15+</td>
<td>0–14</td>
</tr>
<tr>
<td>Number to Rollover</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

**Current Month Recruitment:** enter the number of individuals in each control category to be recruited at each health facility in the current month in the first row. A tally mark should be made for each participant recruited in this category. Recruitment for the month can cease after the target has been met.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age category</td>
<td>0–14</td>
<td>15+</td>
<td>0–14</td>
</tr>
<tr>
<td>Target Recruitment</td>
<td>5</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>
### Appendix VI: MERFAT Case Line List

**Instructions:** Enter all eligible cases into the line list and assign a participant ID to those who provide informed consent.

<table>
<thead>
<tr>
<th>Date Diagnosed</th>
<th>Health Facility</th>
<th>Individual Details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Name</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Informed Consent?</th>
<th>Interview?</th>
<th>DBS?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td></td>
<td>□</td>
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<td>□</td>
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<tr>
<td></td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
Appendix VII: MERFAT Control Line List

**Instructions:** Enter all eligible controls into the line list and assign a participant ID to those who provide informed consent.

<table>
<thead>
<tr>
<th>Date Diagnosed</th>
<th>Health Facility</th>
<th>Individual Details</th>
<th>Participant ID</th>
<th>Informed Consent?</th>
<th>Interview?</th>
<th>DBS?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
<td>Interview?</td>
<td>DBS?</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td>Health Facility</td>
<td>Individual Details</td>
<td>Participant ID</td>
<td>Informed Consent?</td>
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Appendix VIII: Informed Consent Form

Name: ________________________________
Study ID: ______________________________

Malaria Elimination Risk Factor Assessment Tool (MERFAT)
Consent to Participate in Research

Study Title: Identification of risk factors for malaria in Bezi: a case-control study

My name is ____________________ and I am working on a study with ____________________ (program name/organization), funded by ____________________ (name of funder). This study will help to understand the causes of malaria in Bezi and gather information that will help to eliminate malaria here. You/your child are/is being asked to take part in the study because either you have been diagnosed with malaria or you have tested negative and can provide a comparison for those with malaria. If the patient is legally defined as a child (under 18 years of age), we also need to obtain consent from a parent or guardian.

Confidentiality and Consent

If you agree to participate in this study, I am going to take an additional fingerprick blood sample and ask some questions to understand your exposures to malaria, including where you live, your travel history and malaria knowledge and protection. The questions are not sensitive and your answers are completely confidential. You do not have to answer the questions if you do not want to, and you can finish this interview anytime. Participation or refusal to participate will not affect you or your child's medical care or access to public health services. However, your honesty in answering these questions will help us understand what behaviors and kinds of activities might lead to malaria in Bezi. The information we put together will be useful for helping the malaria program to develop strategies to prevent and respond to malaria in this area.

We appreciate your help responding to this interview which will take about 45 minutes.

Consent

Do you agree to provide a blood sample to be used for current and future malaria testing? □ Yes □ No
Do you agree to participate in the questionnaire? □ Yes □ No

If you wish to be in this study, please sign or provide a thumb print below.

____________________  ________________________________________________________________________
Date    Participant’s signature/thumb print for consent

____________________  ________________________________________________________________________
Date    Witness signature (if participant does not speak/read English) or Parent or Guardian signature if participant is under 18 years, if participant is over 10 the child’s signature must also be obtained above.

____________________  ________________________________________________________________________
Date     Interviewer’s signature

Note: The Informed Consent form should be adapted to meet any organizational/institutional requirements.
Successful interviewing is an art and should not be treated as a mechanical process. Each interview is a new source of information, so make it interesting and pleasant. Follow general guidelines below on how to build rapport with the contact and conduct a successful interview.

**Building Rapport**

The contact’s first impression of you will influence her/his willingness to cooperate. Be friendly, respectful and smile as you introduce yourself. You will also be given a letter (and an identification badge to wear at all times) that states that you are working with the [name of institution or organization] on malaria surveillance.

**Assure Confidentiality**

If the person is hesitant about responding or asks what the data will be used for, explain that the information you collect will remain confidential, their name will not be used for any purpose, and all information will be grouped together for statistical analysis and reports about malaria by the [name of institution or organization]. This information will help them to prevent malaria.

Never mention information from other interviews or show completed interview forms in front of a contact or anyone else.

**Interview the Contact Alone**

The presence of other people during an interview can prevent you from getting frank, honest answers. It is, therefore, very important that the individual interview be conducted privately and that all questions be answered by the interviewee.

**Answer Questions Frankly**

Before agreeing to be interviewed, the contact may ask you about the interview or why he/she was selected to be interviewed. Be direct and pleasant when you answer.

The person may also be concerned about the time or length of the interview. If they ask, tell them that the interview usually takes about 30 to 60 minutes.

Individuals who work in the forest may be concerned that you will ask them about illegal activities or testing for drug use. Explain to them that:

- Testing is for malaria, not illegal drug use, or other diseases
- They will not be asked about illegal activities, only forest work; if the forest work they are engaging in is illegal, they will not be asked any of those details and they can choose not to provide any details at any time.
- Remind the respondent that the interview is completely confidential and you will not be sharing any of the information with anyone outside of the surveillance team.

Interviewees may ask questions or want to talk further about the topics you bring up, such as indoor residual spraying or how to use a mosquito net. It is important not to interrupt the flow of the interview, so tell them that you will be happy to answer their questions or to talk further after the interview. After the interview is over, if you feel comfortable doing so, you may answer basic health or other questions to the best of your ability while informing the person that you are not a nurse, doctor or expert on the topic. Give the person the health information materials and refer them to local health staff for more information.

**Maintain a Neutral Attitude**

Interviewers should be sympathetic listeners and avoid giving the impression of having strong views on the subject under discussion. Neutrality is essential because some contacts, trying to be polite, will say what they think the interviewer wants to hear.

If the respondent gives an unclear answer, try to probe in a neutral way, asking questions such as the following:

- “Can you explain a little more?”
- “I did not quite hear you. Could you please tell me again?”
- “There is no hurry. Take a moment to think about it.”
Never Suggest Answers
If a contact’s answer is not relevant to a question, do not prompt her/him by saying something like “I suppose you mean that...Is that right?” In many cases, she/he will agree with your interpretation of her/his answer, even when that is not what she/he meant. Rather, you should probe in such a manner that the respondent herself/himself comes up with the relevant answer. You should never read out the list of coded answers to the respondent, even if she/he has trouble answering.

Do Not Force Participants to Answer Questions
If the respondent is reluctant or unwilling to answer a question, explain once again that the same question is being asked of many respondents and that the answers will all be merged together. If the respondent is still reluctant, select the “Refused to answer” option on the question and proceed as if nothing had happened. Remember, the respondent cannot be forced to give an answer.

Phrase Questions Carefully
Avoid questions that can be answered by a simple yes or no. For example, questions such as “Please tell me about malaria prevention?” are better than “Do you know about malaria prevention?”

Use Probing Techniques
Encourage informants to detail the basis for their conclusions and recommendations. For example, an informant’s comment, such as “The malaria program has really changed things around here,” can be probed for more details, such as “What changes have you noticed?” “Who seems to have benefitted most?” “Can you give me some specific examples?”