5.2 Study area/ setting

The study will be undertaken in the provinces of Romblon and Oriental Mindoro. These provinces were purposively sampled to include one province that is potentially rabies-free, but in which the risk of incursions remains high, and one province in which rabies remains endemic.

5.3 Recruitment and Participants

Governors of both Romblon and Oriental Mindoro will be requested to officially authorize implementation of IBCM in their Province and for staff within the Provincial Health Office, ABTCs and the Provincial Veterinary Office. Likewise, the Mayors of all municipalities will be requested to authorize the staff from the Municipal Health Offices and the Municipal Agriculture Offices to be trained in its delivery in two phases.

During Phase 1, all public health and animal health workers within the selected ABTCs and their catchment municipalities will be trained to implement IBCM. In phase 2 all public health and animal health workers within the remaining ABTCs and their catchment municipalities will be trained to implement IBCM. In the event of any staff missing training or of staff transfers into the catchment area, additional training sessions will be offered.

In Phase 1a, in which we develop and optimize IBCM, we will invite all public health and animal health workers associated with the 2 ABTCs and associated health/veterinary services in catchment municipalities to participate in the training, delivery of IBCM and associated data collection for its evaluation (see Table 1). We will also seek consent from a sample of adult patients or carers to observe consultations to assess rabies risk and form animal owners to investigate animals (See Table 1).

In Phase 2a we will ask all public health and animal health workers associated with the remaining ABTCs and their catchment municipalities in Romblon and Oriental Mindoro to participate in training and associated data collection (as in Phase 1a). We will also seek consent from all to observe interactions of the peer support group interactions/messages, to complete an acceptability, appropriateness and adoption questionnaire. A sample will be asked for permission to observe their practice and to participate in a semi-structured interview. Finally, as for Phase 1, we will seek consent from a sample of adult patients or carers to observe consultations to assess rabies risk and from animal owners to observe animal investigations (See Table 1).

5.4 Study sample and sampling technique/selection criteria

The Provinces of Romblon and Oriental Mindoro were purposively selected for inclusion to include one province that is potentially rabies-free but in which the risk of incursions remains high (Romblon) and one province in which rabies remains endemic (Oriental Mindoro).

Romblon previously suffered a rabies incursion at a time when the province was likely free from rabies [13]. As a result, PEP use rose dramatically, and is now at unsustainable levels, even though dog rabies has since been controlled and incidence is thought to be very low [6]. However, the risk of incursions from nearby Mindoro and surrounding islands remain high. Hence, Romblon provides an ideal location for this study given the very costly expenditure on PEP and that lack of sensitive surveillance needed to verify freedom and to facilitate rapid response should an incursion occur.

The study aims to address the generalizability and wider benefits of IBCM, therefore we also wished to implement IBCM in a more endemic setting, ideally epidemiologically connected

to Romblon, to make the surveillance data generated as informative as possible. Oriental Mindoro provides a more challenging endemic province. It is the closest island to Romblon presenting an incursion risk and is contiguous with the province of Occidental Mindoro where rabies also circulates endemically. Oriental Mindoro was therefore selected for implementation given the potential for considerable transferrable lessons to be gained.

Phase 1 Study Sites and Participants: During the development and optimization study (Phase 1) IBCM will be introduced to 1 ABTC and the catchment municipalities that refer patients to that ABTC in each of Romblon and Oriental Mindoro provinces – specifically San Jose in Romblon and Roxas in Oriental Mindoro. These centers and their catchments have been pre-selected for practical reasons and guided by local knowledge. San Jose on Romblon was selected because it is recognized locally for its good practice. Roxas on Oriental Mindoro was selected for its accessibility, as it can be reached within a day from Romblon.

All 10 public health and designated animal workers associated with the 2 ABTCs and catchment municipalities will be requested to complete a pre-post-training questionnaire, and a questionnaire on adoption of IBCM two weeks and 12 weeks after training. We will also ask their permission to observe training sessions. Any staff not consenting to observation of training will be excluded from mention in the observation notes. With the support of the Provincial Health and Veterinary Office we expect a 100% response rate to the pre-post training questionnaire. The response to the questionnaire on adoption of IBCM will inform retention strategies for Phase 2a. We will also ask all 10 health and animal workers for permission to observe the peer support group they will set up using Facebook messenger, to take part in a semi-structured interview, and ask up to 5 pairs of public health workers and patients, and 5 pairs of animal health workers and animal owners per ABTC for permission to observe the interactions.

Phase 2a Study Sites and Participants: The implementation study (Phase 2a) will take place in all remaining ABTCs and their catchment municipalities in Romblon and Oriental Mindoro.

All 61 health and designated animal workers associated with each ABTC and its catchment areas in Romblon and Oriental Mindoro who participate in training for delivery of IBCM will be requested to consent to observation of training, to complete a pre-post training questionnaire, for permission to observe the peer support group they will set up using Facebook messenger, and to complete a questionnaire on adoption of IBCM two weeks and 6 months after training. Because some may need to leave training early we expect a 90% response rate to the post-training questionnaire. Because our fieldworker staff will have pre-existing relationships with animal and health workers, and because of our proposed procedures (see section 6), we expect a high (at least 80%) response rate to the request to observe peer support interactions and to the adoption questionnaire.

We will ask permission to observe up to 5 interactions between public health workers and patients, and animal health workers and animal owners associated with each ABTC. The observations will be a convenience sample of a) consultations taking place on 5 different days of observation, b) animal investigations as they arise.

We will recruit a purposive sample of 5-6 staff from each ABTC and its catchment municipalities for semi-structured interviews. The purpose of sampling is to observe the practices of staff with different responsibilities in the delivery of IBCM and will include each of chief of hospital/medical officer/doctor, nurse, animal health workers, and Barangay public health workers if involved. If there are more than one sort of potential participant

associated with each ABTC we will assign each a random number and approach each to participate until the purposive sample is achieved.

5.5 Sample size estimation

In Phase 1, in the two participating ABTCs and catchment municipalities, we seek to train and collect data from all 10 public health and animal health workers who will be involved in delivering IBCM. Since this is a whole population implementation study, questionnaires will be undertaken in all ABTCs and staff involved in delivering IBCM in Phase 1.

In Phase 2, we also seek to train all 61 public health and animal health workers and will request them all to complete a pre-post-training questionnaire, and two week and six month adoption questionnaires.

We estimate that a sample of 5 observations of patient consultations and of animal investigations per ABTC and its catchment area will be enough to capture variations in practice in the ABTC. If we find more variation than expected we will seek to observe more consultations and investigations until data saturation is achieved.

We estimate a purposive sample of 5-6 public health and animal health workers to include each of each of chief of hospital/medical officer/doctor, nurse, animal health workers, and Barangay public health workers if involved is practical and feasible in terms of data collection and analysis but also likely to be sufficient to give us insight into acceptability, appropriateness and adoption of IBCM from different perspectives. If we find that perspectives of staff in the same roles vary greatly, we will seek to interview additional staff until we reach data saturation.

5.5 Intervention – Integrated Bite Case Management (IBCM)

The World Health Organisation (WHO) technical guidance for IBCM [10] has two components: risk assessment of biting animals undertaken at the point a bite patient presents to a clinic and epidemiological investigation of the biting animals. IBCM will be delivered within a platform comprising of these two components, together with several tools to support implementation and augment existing practice.

Current procedures for managing bite victims and for epidemiological investigations are outlined in Figure 1 and described as follows:

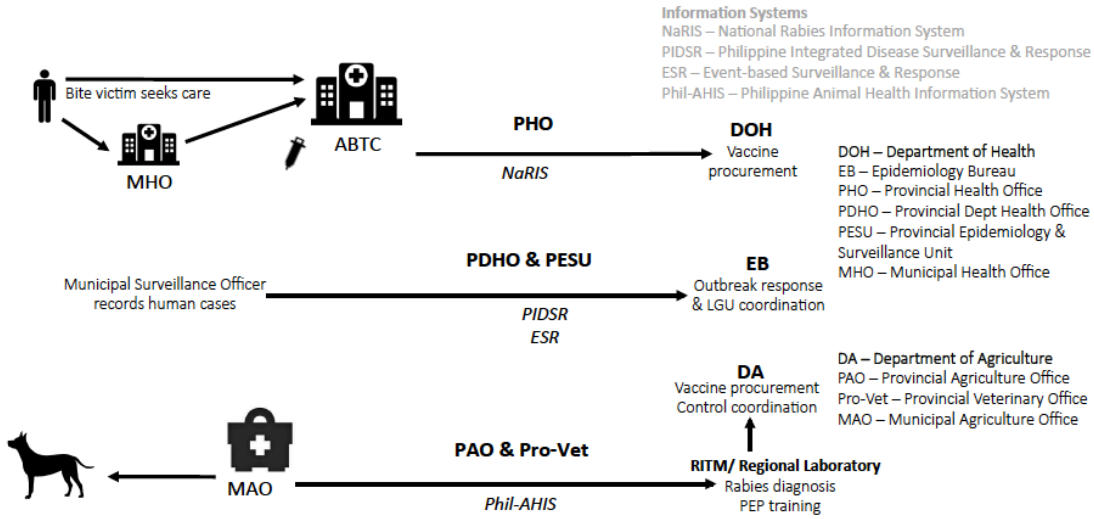
Bite victims typically present to a Rural Health Unit (RHU) where a nurse interviews them, assesses the wound (according to WHO categories I-III), provides wound cleaning and, if necessary, administers tetanus toxoid injection. Patients with either category II or III wounds are referred to an Animal Bite Treatment Centre (ABTC) for post-exposure prophylaxis (PEP); patients with category I wounds are not offered PEP.

At the ABTC the rabies nurse (RN) registers the patient before the Medical Doctor (MD) prescribes PEP and refers the patient back to the RN who administers PEP, completes the National Rabies Information System (NaRIS) form and rabies registry and provides the patient with health education. The patient is required to return to the ABTC according to their PEP regimen to complete their PEP course.

The updated Thai Red Cross Intradermal Regimen was formerly the recommended PEP regimen in the Philippines [13], but a recent administrative order updated this to the one-week 2-site ID regimen according to the latest WHO position [14].

If a patient presents to an RHU, an ABTC or a hospital with signs and symptoms of rabies, palliative care is provided and an investigation is conducted by the Provincial Rabies Coordinator, typically involving staff from both the Provincial Health Office (PHO) and the Provincial Veterinary Office (PVO), and recording the case in the Philippines Integrated Disease Surveillance and Response (PIDSR). If the dog/animal has been killed the veterinarian is expected to collect a sample and submit it to the regional laboratory for diagnostic services.

Figure 1. Outline of current procedures for patient management and epidemiological investigations



In line with the latest WHO technical guidance [15], our study investigates the implementation of refined IBCM procedures (Figure 2, italicized red font and arrows indicating communication channels) as described below.

Risk assessment undertaken by Public Health Worker at the ABTC

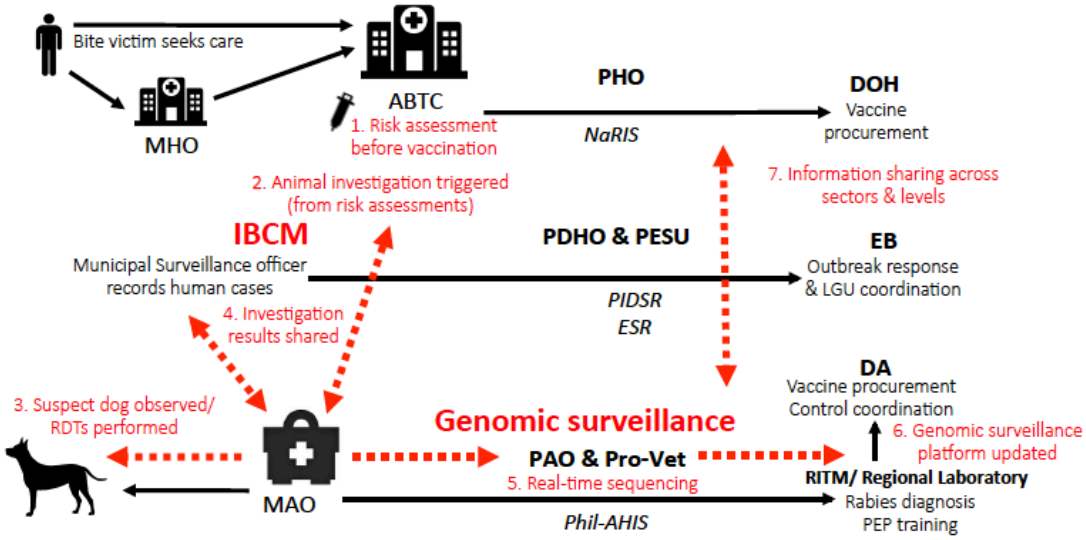
When a bite patient presents to an ABTC the nurse should first carry out a risk assessment based on the status of the biting animal before the MD reviews the risk assessment to confirm the status and prescribe PEP. The risk assessment comprises of questions to assess the biting animal's vaccination history, if known; the animal's outcome (alive or dead or disappeared) following the bite and its health status, as well as the category and severity of the bite (Risk Assessment form, Appendix 5.3). The nurse should complete the risk assessment using a tailored mobile phone-based application to ensure rapid and accurate information recording and standardization of criteria, and to facilitate real-time alerts to trigger investigations (see below). According to the risk assessment 'high-risk' bites involve animals that die, are killed, disappear or show signs of illness after the bite.

In the event of a high-risk bite, the nurse is expected to immediately alert the designated animal health worker (Livestock Technician or Barangay Health Worker) at the Municipal Agriculture Office (MAO), using the application.

The automatically generated alert from the risk assessment will detail information required for the investigation. The public health worker should follow up the alert with a direct phone call to the animal health worker to confirm that they will investigate. For animals available for observation that are considered no/low risk, the patient should still be requested to observe the animal for 10 days and to immediately report back via the ABTC hotline number if any changes in health are observed. Vaccination certificates should be issued to patients

indicating the ABTC hotline number that they should use in the event of observing any signs of illness in the dog, or for other advice on first aid and PEP. All other aspects of the patient consultation remain the same.

Figure 2. Refined procedures for patient management and investigations (steps shown in red) with risk assessments based on the biting animal status. Refinements to current procedures shown in red.



Animal investigation undertaken by designated Animal Health Worker

When a Designated Animal Health Worker receives an alert of a high-risk bite, they should investigate immediately and always within 24 hours. The Designated Animal Health Worker should first follow up via the patient's phone number and address, provided in the alert and, where possible, identify the owner of the biting animal. The Designated Animal Health Worker should visit the dog owner, undertake a visual check of the biting animal, record the circumstances of the bite and details of the animal behavior and health according to criteria following the investigation form (Animal Investigation Form, Appendix 5.4), administered via the tailored mobile phone-based application. In the event that an animal is suspected to have rabies and displays clinical signs compatible with rabies the Provincial Veterinary Officer should be notified and requested to immediately euthanize the animal according to current procedures in the Philippines [13].

If the animal is already dead or following euthanasia, and if the Designated Animal Health Worker is qualified to do so, a sample should be collected following current RITM protocols and sent to the regional laboratory for testing [13], with whole genome sequencing (WGS) completed for positive cases. If the Designated Animal Health Worker is not qualified to collect a sample they should alert the PVO immediately of the need for a sample to be taken. When a sample is taken, the Designated Animal Health Worker or PVO will also perform a rapid diagnostic test (RDT) on site. Following the manufacturers' instructions, the animal health worker should insert a swab of brain homogenate into the specimen tube containing the 1ml of assay diluent that is provided in the RDT kit. They should mix the swab sample with the assay diluent well. The test device should be removed from the foil pouch, and placed on a flat and dry surface. Using the disposable dropper provided, four drops of the mixed assay diluent from the specimen tube should be added into the sample hole. If the migration has not appeared after 1 minute, on more drop should be added. A test

readout should be made between 5-10 minutes afterwards, as recommended by the manufacturers. The test result should be recorded in the investigation using the application.

The Designated Animal Health Worker should conduct further interviews with the bite victim (or witnesses to the bite) and any other persons or animals that were bitten to complete the investigation form, even if the biting animal cannot be found. For all other bitten persons/ animals, contact details should be recorded in the investigation form and advice provided on the need for PEP. This may identify other bite victims who have not sought care and is therefore of critical importance.

If the biting animal is alive and not vaccinated, the owner is requested to ensure the dog is home quarantined for 10 days and the Animal Health Worker should issue a quarantine notice to confirm the animal's condition and ensure adherence to the home quarantine. If at any point during the home quarantine the dog shows signs of illness the owner should immediately contact the Designated Animal Health Worker for further follow up.

On completion of the animal investigation, the investigation form should be submitted via the mobile phone-based application. The Animal Health Worker should call the corresponding public health worker to notify them of the investigation result. A summary will automatically be sent via the application to the RHU and ABTC to enable appropriate patient management and to the PVO and PHO to guide subsequent control effort. In the event of a probable rabies case, the Animal Health Worker should also call these officers directly to notify them of the case. The Animal Health Worker should immediately send any samples to the Provincial Veterinary Office, and the PVO should submit the sample to RITM or RADDL for laboratory confirmation and sequencing. Viruses from all positive samples should be sequenced using the MinION, the minor virus lineage identified and most recent common ancestor estimated and source attribution assigned.

Tools and training

Prior to implementation, training will be provided to practitioners required to implement the refined IBCM procedures as part of their routine duties. The training will comprise of an orientation meeting bringing all practitioners together from both the public health and veterinary sectors, followed by joint training and practical simulation exercises.

A training package will be provided with the materials and tools for practitioners to implement IBCM, including a field operations manual, accompanying checklists, guides and algorithms to assist them while undertaking animal investigations and risk assessments and IEC for bite victims, animal owners and community members. For Animal Health Workers the package will include sample collection kits with personal protective equipment, rapid diagnostic tests and quarantine notices. For each head of ABTC, a helpline register will also be provided. The ABTC staff will be instructed to complete the register for all calls received that relate to animal bites and potential rabies exposure or rabies cases.

A peer support group will be established (provisionally a facebook page and messenger chat), that Public Health and Animal Health Workers will be asked to join during the training. These practitioners will be encouraged to use this peer support group to share their experiences, including challenges, and to solicit peer support to address them. All the practitioners will also be encouraged to call the designated research team members in case of any difficulties during their work through the contact details provided in the field operations manual.

The IBCM application (App) that will be used to guide and record risk assessments and animal investigations will be installed onto phones for use in the field. The forms for risk assessments and for animal investigations that will be completed via the application are provided as Appendices (5.3 and 5.4) and will used as a contingency measure if any challenges are encountered using the App/phone.

A password protected dashboard for the App will be accessible via the web or mobile phone interface. Feedback will be provided to practitioners via the dashboard including data summary tables, time series and maps of bites indicating risk status and of investigations undertaken and their outcomes. Regular reports summarizing the surveillance data generated by the IBCM (including categorization of exposures and cases according to WHO case definitions) will be shared routinely and presented at stakeholder meetings to discuss their interpretation.

The two days of training will be delivered to participants following a schedule of lectures, and participatory sessions, including simulations of patient consultations and animal investigations. At the start of the training each participant will be requested to complete the pre-training test and an initial situation analysis will be undertaken with the public health and animal health workers from each ABTC and their catchment municipalities. The purpose of the situation analysis will be to understand the local context in which IBCM will be delivered and whether any aspects of training need to be tailored accordingly. For instance, in Municipalities lacking a Municipal Animal Health Worker, who amongst the Barangay Health Worker should instead be designated as the Animal Health Worker responsible for undertaking animal investigations as part of IBCM and will be given appropriate training. Similarly, where laptop or desktop computers are available, for example at Municipal Offices or Provincial Hospitals, more emphasis in the training will be given to recording of risk assessments via the web interface.

At the end of the first day of training, all participants will be registered to the IBCM application, will join the peer support network and Animal Health Workers will be administered their first dose of rabies Pre-Exposure Prophylaxis, with the second and final dose to be delivered on day 3, by their assigned ABTC counterparts.

On the second day of training each participant will receive the remaining components of their training package and the IBCM application will be downloaded to the designated phones. Officials from the PHO, the PVO, the MAOs and the MHOs will also be introduced to the dashboard, given a virtual tour of the dashboard and provided with instruction to enable them to fully use the dashboard. Before departure, each participant will complete the post-training questionnaire and will be given a certificate of training in IBCM.

A one-week training course on genomic surveillance will be carried out at RITM with national and regional laboratory staff. The objective of the workshop will be to train staff in the rabies MinION sequencing protocol, which is adapted and available via the ARTIC network (http://artic.network/). The training will comprise of 3 days of practical laboratory sessions and sequencing interspersed with accompanying lectures, followed by 2 days of computer-based practicals and lectures. The practical laboratory sessions will cover RNA extraction, cDNA preparation, PCR, library preparation and MinION sequencing. The computer-based practicals will cover command-line basics, bioinformatics pipelines, sequence data management, analysis and reporting. The RITM special pathogens laboratory will be equipped with the complete lab-in-a-suitcase platform and required reagents and consumables. As part of the training archived samples will be sequenced at RITM to ensure

laboratory scientists are proficient in protocols and to provide baseline coverage of rabies virus diversity across the Philippines. Additional subsequent sequencing should focus on areas which may represent incursion risks to and within Region IVB MIMAROPA, and where existing genomic coverage is low.

5.6 Study variables and outcome measures

The variables and outcome measures, and qualitative data collected, will be the same for Phase 1 and Phase 2a. Although variables are the same, their analysis will be different to address different objectives. We will collect the following process and outcome variables

Process variables

- Proportion of correct answers to pre-post knowledge questionnaire
- Items on IBCM acceptability, appropriateness and adoption questionnaire will be summarized from scores for each of four NPT constructs (coherence, cognitive participation, collective action and reflexive monitoring) **as described in section 7.2.3**.
- Cost per training session, per patient consultation and per animal investigation.

Outcome variables

- Percentage of patients presenting at clinics who have risk assessments of bite events undertaken by health workers
- Percentage of biting animals investigated following classification that they are high-risk
- Percentage of patients bitten by a high-risk animal who receive PEP promptly and who complete PEP regimens
- Animal rabies cases detected from investigations, discriminating outcomes in terms of not a case, suspect case or probable case, as well as rapid diagnostic test results and rabies virus lineage and most recent common ancestor (from phylogenetic analysis)
- Number of bite victims identified from animal investigations who are recommended to seek PEP but who had not previously sought care
- Frequency of calls to ABTC helplines by patients and providers and categorized by themes

We will also examine trends in rabies case detection to determine the relative risk status of each province [16], with further phylogenetic analysis of confirmed cases to distinguish endemic transmission from incursions and to identify sources of risk. From an operational perspective, we will examine the trends in quality of patient care and surveillance, which will be triangulated with the summative process evaluation.

Analyses of qualitative data in both phases will be guided by Normalisation Process Theory (NPT) [17]. NPT suggests that for a new approach to be implemented sustainably it is necessary that: a) it makes sense to staff (a concept called Coherence within NPT); b) staff engage with each other about the new approach and understand each others' role (a concept called Cognitive Participation within NPT); c) all team members have the resources they need and then actually do the work under the new system and delivers their role within the new system (a concept called Collective Action within NPT); d) staff can monitor the effects and make amendments to improve delivery (a concept called Reflexive Action within NPT).

6. Study Procedures

6.1 Phase 1 – development and optimization study (objective 1)

As described in section 5.2, in Phase 1a we will invite all public health workers and animal health workers associated with the 2 ABTCs and associated health services in catchment municipalities to participate in a pre-post-training questionnaire, a questionnaire on adoption of IBCM two weeks and 12 weeks after training. We will also ask their permission to observe peer support group interactions, training sessions and to take part in semi-structured interviews. In effect, this is an initial implementation of IBCM to allow us to try out and improve our full processes prior to wider implementation and refine data collection.

6.1.1 Training

The ten staff responsible for IBCM in the two ABTCs and associated municipalities will be invited to take part in training. Training will be scheduled at a time agreed upon by the managers and project staff. Training will be delivered over 2 days by project staff on all aspects of IBCM (see section 5.5). At the start of training the research will be introduced and all staff given an Information Sheet (Appendices 2.17 and 2.18). They will also be asked for consent to observation while being trained (Appendices 2.5 and 2.6) and to complete a pre post questionnaire (Appendix 15.16).

Before and after the training those staff who consented to do so will complete the pre-training and post-training questionnaire to assess what they have learnt (Appendix 15.16). The research team will observe the training to assess delivery and staff members' response (Appendices 5.10, 2.5 and 2.6). Notes will be taken only on those staff who have consented. A structured observation proforma will cover quality of training delivery, interactions between trainers and staff and staff responses (Appendix 5.11).

6.1.2 Observation of IBCM consultations and animal health investigations

Patient consultations: our research staff will spend between 3-5 days in ABTCs to observe consultations with patients. Prior to observation, an information sheet will be provided to patients/carers (Appendices 2.19 and 2.20) and consent sought to record and conduct the observation (Appendices 2.13 and 2.14). We seek to observe at least five patient consultations in each ABTC. Researchers will seek to observe consultations led by 5 different staff. Observation notes will include details on how the protocol was administered, and how patients responded. Care will be taken to avoid noting any details that might identify patients. If a child is involved in the consultation we will not take notes on anything about them. We seek to include notes only about the extent to which the protocol was delivered with fidelity involving only adult patients, adult carers of patients and public health workers. The audio recording will be used only as an aide-memoir for detailed note taking. When notes have been finalized audio-recordings will be deleted.

Animal Investigations: on identification of a high-risk animal during a risk assessment undertaken by a public health worker, a research staff member will, with permission, accompany the Designated Animal Health Worker during the investigation. The animal owner will be given an information sheet (Appendices 2.11 and 2.12) and consent to record and observe the interaction will be sought (Appendix 2.9 and 2.10). We seek to observe at least 5 investigations of high-risk animals. Observation notes will include details in how the protocol was administered, animal owners' response. Care will be taken to avoid noting any details that might identify the animal owner. The audio recording will be used only as an aide-memoir for detailed note taking. When notes have been finalized audio-recordings will be deleted.

Logs from the peer support group: Prior to using the digital peer support group, staff will be asked for permission to log, observe and analyse interactions (Appendices 2.15 and 2.16). The logs will be anonymised and analyzed to review the experiences and challenges encountered including self-reported solutions.

Registers from the ABTC hotline: Queries recorded in the ABTC hotline registers will be transcribed anonymously according to the role of each caller (patient, animal owner, community member, animal health worker, public health worker, other), and quantified thematically. The queries will be analyzed to review the experiences and challenges encountered and solutions provided. An FAQ information sheet will be prepared to be included with IEC based on popular questions.

6.1.3 Questionnaire on acceptability, appropriateness and adoption of IBCM

We will conduct a survey of all the trained participants within two weeks of training and 12 weeks following training to investigate acceptability, appropriateness and adoption of IBCM. The survey questionnaire is designed using the NPT-informed NoMAD tool [18, 19]. It will be delivered by a member of our field staff during pre-arranged visits to the ABTCs. Prior to completing the questionnaire staff will be given another copy of the Information Sheet (Appendices 2.17 and 2.18) and asked for permission to conduct the survey (Appendices 2.3 and 2.4). If staff are not available for face to face interview there will be an option to complete the questionnaire vis a link to a web-based version of the questionnaire which can be completed using their mobile phone.

6.1.4 Semi-structured interviews

At the end-point of the implementation study phase, a member of the research team will conduct a semi-structured interview with each member of the public health and animal health workers trained in IBCM. The interview will probe for more in-depth insights, seeking especially to understand how IBCM implementation activities interact with local context. The topic guide is informed by NPT, Appendix 15.7) Prior to the interview staff will be provided with another version of the Information Sheet (Appendices 2.3 and 2.4) and asked to complete a consent form (Appendices 2.1 and 2.2). All interviews will, with permission, be digitally recorded, transcribed and translated into English for analysis.

6.1.5 The IBCM database

The IBCM database will be organized with tables for users (role, ABTC, Municipality, Province), risk assessment information submitted by public health workers and animal investigation information submitted by animal health workers. These data will be downloaded every quarter and summarized by patient presentations (high/low risk, PEP initiated and completed) and animal investigations (not a case/ suspect/ probable, required actions: PVO support, sample collection and RDT result, home quarantine, case closed).

6.1.6 ABTC register summaries

Every quarter data will be transcribed from ABTC registers for comparison to data from the IBCM database to determine ease of comparison and alignment of key indicators. Specifically, numbers of patients presenting with animal bites will be summarized, according to bite category and PEP provision.

6.1.7 Laboratory Record summaries

Records of samples collected, tested and test outcomes from the two provinces will be transcribed from the RITM and RADDL laboratory books on a quarterly basis for comparison

to data from the IBCM database. Laboratory reports of confirmed rabies cases and sequencing results will be compiled quarterly for review.

6.1.7 Describing costs

Costs of IBCM implementation: Public health and designated Animal Health Worker time for risk assessments and animal investigations will be recorded during observations of patient consultations and animal investigations (see section 6.1.2). The number of risk assessments and animal investigations conducted will be extracted from the IBCM database and used to determine costs per task. Resources required for IBCM implementation will be recorded and distinguished from those for research activities. The implementation budget will subsequently be audited to confirm these costs.

Costs of IBCM training: All resources used for training will be carefully recorded ensuring that they apply only to IBCM training delivery and not research activities. The training budget will subsequently be audited to confirm these costs.

6.1.8 Debriefing by researchers for purpose of refining data collection tools

After each data collection procedure is completed, the researchers will take debriefing notes on the performance of each data collection instrument, in order to document whether and how the data collection instruments need to be refined.

In the last 2 months of phase 1 we will analyze all data descriptively (see section 7) to inform the conduct of Phase 2a.

6.2 Phase 2a) - Implementation of IBCM, its impact and the processes through which outcomes are achieved

We will adapt all intervention and data collection materials on the basis of findings from Phase 1. Nevertheless, the process of delivering training, implementing and evaluating IBCM across all ABTCs and associated municipalities in Phase 2a) will be very similar to Phase 1. **We envisage refining rather than changing data collection tools and do not refer again to specific data collection tools, information sheets and consent forms.**

6.2.1 Training

The training process will be the same as for Phase 1, with materials amended as appropriate. Blocks of training will be conducted, by geographical location, bringing together Municipality catchments and ABTCs by island, with 3 training blocks in Oriental Mindoro to keep group sizes practical.

6.2.2 Observation of IBCM consultations, animal health investigations, peer support group interactions and registers from ABTC hotlines

Observations will be conducted as for Phase 1, with materials amended as appropriate. Logs from the peer support group and registers from the ABTC hotlines will continue to be compiled and reviewed regularly, as for Phase 1.

6.2.3 Questionnaire on adoption of IBCM

The questionnaire (amended as appropriate) will be administered in the same way as for Phase 1, except the second questionnaire will be conducted 6 months rather than 12 weeks to give the IBCM approach more time to bed down.

6.2.4 Semi-structured interviews

Around six months after training, we will conduct semi-structured interviews with a purposive sample of staff in each ABTC and associated municipalities (see section 5.4). The

approach to data collection will be the same as for Phase 1, using a topic guide amended as appropriate.

6.2.5 The IBCM database

These data will be continue to be downloaded each quarter and summarized by patient presentations and animal investigations, as per Phase 1.

6.2.6 ABTC register summaries

These data will continue to be transcribed from ABTC registers for comparison to data from the IBCM database each quarter.

6.2.7 Laboratory Record summaries

As for phase 1, records of samples collected, tested and test outcomes from the two provinces will be transcribed every quarter from the RITM and RADDL laboratory books as well as laboratory reports of confirmed rabies cases and sequencing results.

6.2.8 Describing costs

All costs will be recorded as for Phase 1 (see Section 6.1.7)

7. Data Analysis / Statistical Consideration

7.1 Phase 1

All data analysis for Phase 1 will be focused on what needs to change in relation to all aspects of the implementation of IBCM and data collection to optimize delivery of Phase 2a).

Qualitative data (observation notes, transcripts of interviews) will be managed in Nvivo 11. In relation to what needs to change to the IBCM protocol, the data will be analysed thematically with a coding frame informed by NPT. The codes will focus not so much on content as on what needs to change for Phase 2.

In relation to what needs to change to the data collection instruments, in stage 1 we will analyse debriefing notes taken by research staff on the performance of data collection instruments. We will also investigate consent rates, response rates and the willingness of staff to engage in qualitative data collection and the resources it takes to collect data to consider feasibility of qualitative data collection.

Quantitative data analysis will be descriptive and focused on how well data collection instruments and processes performed in relation to response rates, quality of data entered in the App, missing data, and inconsistencies between reports from public health and animal health workers in relation to the same incident. In addition the logs from the peer support group interactions and the queries from the helpline registers will be analyzed thematically and quantified. These data will be used to review the experiences and challenges encountered during IBCM and how training and support can be adapted to improve delivery and implementation in Phase 2.

The downloaded and summarized data from IBCM database will be reviewed to determine whether the IBCM App design is sufficient to capture key outcomes and for comparison to the ABTC register summaries to ensure they are compatible for comparison and that key outcome measures align. Analysis of all data will be descriptive and focused on what needs to change in training and delivery of IBCM between Phase 1 and Phase 2a and whether and how the data collection instruments need refining.

Before starting Phase 2a we will adapt IBCM protocols and data collection instruments as required. However, as described in Section 6.2 we envisage refining rather than changing data collection tools and will resubmit any change to the IBCM protocol or data collection tools as an amendment to protocol for approval by IRB.

7.2 Phase 2a

Analyses for Phase 2a will be structured around addressing 5 research objectives and will test whether the hypothesized improvements in outcomes measures (see 4) are realized.

7.2.1 Coverage achieved by IBCM and its impact (objectives 2 and 3)

We will estimate the coverage achieved in terms of completed risk assessments and high-risk animals investigated over 24 months (objective 2) using the IBCM outcome measures (listed in 5.6) collected through the risk assessments and investigations detailed in 6.7 and 6.8 (percentage of bite patient presentations where a risk assessment is conducted; and percentage of biting animals investigated following classification that they are high-risk). We will examine temporal trends and geographic coverage of these outcome measures across ABTCs, and municipalities in each province, using generalized linear mixed models (GLMMs) to test for the hypothesized improvements in these outcome measures. Operational performance outcome measures (coverage achieved in terms of completed risk assessments and high-risk animals investigated over 24 months) will also be checked to determine whether they meet WHO and OIE verification and validation criteria [10].

We will evaluate the impact of IBCM in terms of appropriate patient care and rabies detection over 24 months (objective 3) using the IBCM outcome measures (listed in 5.6) collected through the risk assessments and investigations detailed in 6.7 and 6.8 (percentage of patients bitten by a high-risk animal who receive PEP promptly and who complete PEP regimens; animal rabies cases detected from investigations, investigation outcomes, and bite victims identified who had not previously sought care; patient and provider helpline use categorized thematically). As per Objective 2, we will examine temporal trends and geographic coverage of outcome measures across ABTCs, and municipalities in each province, using GLMMs to test for the hypothesized improvements.

From an epidemiological perspective trends in rabies case detection will be used to determine the relative risk status of each province [7], with further phylogenetic analysis of confirmed cases to distinguish endemic transmission from incursions and to identify sources of risk [20]. Trends and geographic patterns in these outcome measures will be summarized and presented to stakeholders.

7.2.3 The quality of training, acceptability, appropriateness and adoption of IBCM (objective 4)

Data are collected to address objective 4 using both qualitative and quantitative data. Each data set will be analyzed separately in the first instance.

7.2.3.1 Quantitative data

***Training*: Quantitative data from pre-/post training questionnaires will be analysed descriptively to examine whether knowledge increased before and after training. The variables described in section 5.6 will be summarized visually using spider diagrams of the overall extent to which IBCM has been adopted in each ABTC and overall. We will also derive scores for acceptability, appropriateness and adoption as described below.**

***Acceptability*: Acceptability is the perception among implementation stakeholders that a given treatment, service, practice, or innovation is agreeable, palatable, or satisfactory.**

The operational definition of acceptability is the extent to which Animal and Public Health Workers:

1. **Understand how IBCM differs from their usual way of working**
2. **Share an understanding with colleagues about the purpose of IBCM**
3. **Understand how IBCM will affect the nature of their own work**
4. **See the potential value of using IBCM in their own work**

This operational definition is derived from the main NPT constructs of 'Coherence'. This will be measured using the responses in C1.1.1 and C.1.2.1 in the IBCM questionnaire (appendices 5.6 and 5.7). IBCM can be considered acceptable if more respondents answer at least agreeable (ie., 'Agree' and 'Strongly Agree') to the questions (C1.1.1 and C.1.2.1 i.e. not 'Neither agree nor disagree', 'Disagree' and 'Strongly disagree').

***Appropriateness*: Appropriateness is the perceived fit, relevance, or compatibility of the intervention for a given practice setting; and perceived fit of the innovation to address the problems. The operational definition of appropriateness is the extent to which Animal and Public Health Workers:**

1. **See the potential value of using IBCM in their own work**
2. **Can integrate IBCM into their existing work**
3. **Have confidence in their own and other's ability to do IBCM**
4. **Think that they and others have the relevant skill set and training to do IBCM**
5. **Think that IBCM is sufficiently resourced and supported in their setting**

This operational definition is derived from the main NPT constructs of 'Coherence' and 'Cognitive Participation'. This will be measured using responses in C1.1.3 and C.1.2.3 in the IBCM questionnaire. IBCM is considered appropriate if more respondents answer at least agreeable (ie., 'Agree' and 'Strongly Agree') to the questions (C1.1.3 and C.1.2.3 i.e. not 'Neither agree nor disagree', 'Disagree' and 'Strongly disagree').

***Adoption*: Adoption is the intention, initial decision, or action to try or to employ an innovation. The operational definition of adoption is the extent to which Animal and Public Health Workers:**

1. **Are willing and able to engage others in the implementation of IBCM**
2. **Have the capacity and willingness to organise themselves in order to collectively contribute to the work involved with IBCM**
3. **Think that IBCM should be part of their work**
4. **IBCM remains a concern for participants beyond its initial initiation**
5. **Can integrate IBCM into their existing work**
6. **Have confidence in their own and other's ability to do IBCM**
7. **Think that they and others have the relevant skill set and training to do IBCM**
8. **Think that IBCM is sufficiently resourced and supported in their setting**

This operational definition is derived from the main NPT constructs of 'Cognitive Participation' and 'Collective Action'. This will be measured using responses in C1.1.2 and C.1.2.2 in the IBCM questionnaire. IBCM is considered appropriate if more respondents answer at least agreeable (ie., 'Agree' and 'Strongly Agree') to the questions (C1.1.2 and C.1.2.2 i.e. not 'Neither agree nor disagree', 'Disagree' and 'Strongly disagree').

7.2.3.2 Qualitative data

Qualitative data (observations of training, semi-structured interviews with staff) will be entered in Nvivo 11 for analysis. The main analytical approach used to analyze qualitative and process evaluation data in SPEEDIER is the Framework approach [18]. Briefly these stages are:

1. Data management – becoming familiar with the data (reading and re-reading); identifying initial themes/categories; developing a coding matrix; assigning data to the themes and categories in the coding matrix.
2. Descriptive accounts – summarising and synthesising the range and diversity of coded data by refining initial themes and categories; identify association between the themes until the 'whole picture' emerges.
3. Explanatory accounts – developing associations/patterns within concepts and themes; reflecting on the original data and analytical stages to ensure participant accounts are accurately presented and to reduce the possibility of misinterpretation; interpreting/finding meaning and explaining the concepts and themes; seeking wider application of concepts and themes.

Training: Qualitative data from observations of training will summarized thematically with a coding frame structured in the first instance by the observation proforma and second, allowing for any unanticipated themes to emerge. We will interrogate summaries for any possible response difference by doctors, nurses, animal health workers and Barangay health workers (if involved). We will manage data using NVIVO, and analyse it using the 3-stage Framework approach information by NPT.

*Acceptability and appropriateness **and adoption***: Qualitative data from the semi-structured interviews will be coded in relation to acceptability, appropriateness, **and adoption based on operational definitions above**. Data will be analysed in relation to the context in which each ABTC is delivering IBCM, that is, features such as staffing profile, local population structure, extent of public health messaging on rabies in the local area and other features of what helps and hinders implementation gathered during semi-structured interviews.

7.2.3.3 Data synthesis

Once qualitative and quantitate analyses are complete, we will compare and integrate findings from different data sources to consider the quality of training, and the extent to which IBCM is acceptable, appropriate and easily adopted. The integration will be guided by the 'triangulation protocol' [21], which suggests researchers assess degrees of agreement and dissonance across the datasets and also to identify areas of 'silence' i.e. where a given

Training: the descriptive qualitative and quantitative data on training will be compared to assess the quality of training from different perspectives.

Acceptability, appropriateness and adoption: A convergence coding matrix, summarising findings for feature (*acceptability, appropriateness and adoption)* will be constructed. Data summaries in relation to each of the concepts of acceptability, appropriateness and adaptation from different data sources compared to one another in a matrix to assess the extent of convergence, divergence or silence. The analysis will then be guided by what O'Cathain *et al* describe as 'following a thread' whereby convergence and divergence or silence may require further data analysis in each data set to provide explanations [22].

7.2.4 The fidelity of implementation of IBCM

Indicators of fidelity include description of the percentage of patients presenting at clinics who have risk assessments of bite events undertaken by health workers and the percentage of biting animals investigated following classification that they are high-risk (see section 7.2.1). We will also examine the trends in coverage over time as implementation beds in and the extent of variation in fidelity between ABTCs and between types of worker

Qualitative data from observations of IBCM consultations and investigations of high-risk animals will be summarized in relation to the extent to which they adhere to the protocols. Using the framework approach any explanations for adherence or lack of adherence in context will be sought. Using the 'following the thread' approach [22], the qualitative data will be interrogated in particular to explain (or not) the quantitative indicators.

7.2.5 The costs of implementing IBCM

The total costs of implementing IBCM will be summarized in terms of resources used for implementation (public health and animal health worker time for risk assessments and animal investigations, IBCM training and training package costs). These costs will be carefully recorded for subsequent cost-effectiveness analyses in Phase 2b. However, for Phase 2a, only the costs will be measured over time and across settings (Municiaplities, ABTCs and provinces).

8. Limitation of the study (if there are any)

This is an observational implementation study of IBCM as recommended by WHO. Because WHO have already recommended use of IBCM, a randomized controlled trial of IBCM itself was not seen as appropriateness. Nevertheless the study is limited by the inability of observational studies to establish cause and effect.

9. Ethical Considerations

9.1 Compliance with Declaration of Helsinki

The research protocol will be developed in full compliance with the principles enunciated in the Declaration of Helsinki.

9.2 Risks

The partners are fully aware that a research project of the scale and ambition of this study will have a number of inherent risks. The multidisciplinary approach mitigates the risk by bringing together partners with extensive track records of successfully conducting programmes of work involving the key techniques in the project. The table below presents a summary of the risks we have identified in the project and the strategies identified to ensure the successful conduct of SPEEDIER should these risks occur.

We see two types of risk to the study. Risks to implementation of IBCM (our intervention) and risks to participants. Table 2 summarises both types of risk and their mitigation.

Table 2 Summary of risks and mitigation strategies in the implementation of the study

Risk	Mitigation Strategy
Implementation of ICM	
Difficulties in recruiting ABTCs to the study	Because IBCM has such high level support within the Provinces in which we work we think this is low risk Nevertheless, he IBCM development and optimization stage of the study (Phase 1) will aim to identify challenges to attendance of staff at training, identifying an appropriate designated animal health worker and other aspects of delivery. At the end of Phase 1 we will adapt IBCM protocols accordingly. .
IBCM application or digital device will fail or not be available for use due to battery or system faults or infrastructure limitations	Staff will be trained to use a checklist and alternative communication and action plan in the event of such events. A paper form will be completed and subsequently uploaded to the system when available.
High numbers of suspect rabid animals make investigation completion challenging	One objective of the study is to quantify numbers of rabid animals. However, under high incidence of rabies completion of all investigations might not be possible and this would be an important finding of the study. This is unlikely to be the case on Romblon where rabies may be absent at least from some municipalities, however in Mindoro Oriental incidence is expected to be high. During the feasibility study if this situation is encountered protocols will be refined to be more manageable in high incidence settings for the implementation study.
Few numbers of suspect rabid animals mean criteria for identifying a high-risk situation is not encountered.	This is not expected to be the case, since high incidence of rabies and recent cases have been reported from Mindoro Oriental. Nonetheless, several criteria for triggering investigations are not rabies specific and therefore expected to be encountered. If this situation is encountered during the feasibility study, further criteria will be added to ensure investigations are encountered and simulations will also be undertaken to assess frontline worker proficiency for discriminating high-risk situations.
Research staff and government personnel may be exposed to rabies during epidemiological investigations and sample collection	Measures will be taken to minimize risks of exposure and to protect staff members as follows: Proficiency training in safe animal handling, sample collection and storage will be given to all government staff. The team will work closely with the national authorities responsible for this training and following the latest international guidelines. If encountered, rabid animals will be restrained and muzzled by vaccinated personnel and government veterinarians will humanely euthanize the animals. Experience suggests that local communities usually kill rabid animals and therefore live rabid animals are very rarely encountered. Although the aim of IBCM is to trace suspicious animals as soon as possible to improve chances of sampling or to confirm through observation that the animal is actually healthy. All field officers will provided with personal protective equipment including masks, goggles and gloves. To minimize risk to staff members involved in animal investigations, pre-exposure prophylaxis will be provided. PEP stocks will also be checked monthly to ensure availability if required.

Animal bite victims identified during investigations will not respond to advice to seek PEP	Records of patients reporting with animal-bite injuries will be used to trigger epidemiological investigations that may reveal victims of bites by suspicious animals who did not seek care. The identities of affected individuals will be kept confidential in all reports and analyses, however this information will be essential to conducting animal investigations and providing appropriate advice. In such circumstances, identifying the animal and taking measures to minimize further risks is an ethical imperative. By working with locally trusted government personnel and where required also involving provincial level authorities the project will aim to reduce the risks of poor health seeking behavior and it is expected that this risk will be reduced compared to under standard operating procedures.
Genuinely rabid animals test negative for rabies due to poor sample storage/testing and inappropriate measures will be taken.	Training will be provided to field officers in appropriate sample storage and testing using rapid diagnostic tests. However, emphasis will be placed on ensuring preventative measures are implemented upon clinical suspicion of rabies (in the absence of laboratory testing).
Risk	**Mitigation Strategy**
To public health workers and animal health workers participating in the research	
The IBCM dashboard summarises data on percentage of risk assessments of bite events undertaken by individual health workers and percentage of biting animals classified as high-risk investigated. If it is apparent that they are performing poorly, it may be seen as a risk by participants.	Managers will be trained to support staff who may be performing poorly and staff will be encouraged to use the digital peer support group to seek solutions to problems identified.
ABTCs can sometimes operate in very busy and cramped circumstances and private space for individual interviews may be in short supply. This may risk a lack of confidentiality for individual interviews	The interview time and place will be arrange to suit the staff member and all efforts made to identify a quiet space to conduct the interview without risk of overhearing. This may be outside if preferred
Public and Animal Health workers are very busy and they may perceive that data collection required by the study gets in the way of routine care.	Every effort will be used to arrange data collection at a time that least inconveniences staff members.
Staff may be worried that data collection will be used to feedback to others about what they do.	The information sheet makes explicit that all data are confidential and anonymized.
To patients and animal owners	
The main risk may be a lack of confidentiality for observations performed.	As described in section 9.7, all efforts are in place to ensure complete confidentiality of all data collection and analysis.

9.3 Benefits

We expect the research to generate important benefits:

- Improve the engagement and performance of public health and animal health workers, including intersectoral working and communication and sharing of surveillance information within and across the geographic settings and with national stakeholders.
- Improve the quality of care provided to patients including the adherence to the latest WHO guidance on PEP administration
- Improve the detection of rabies that is required by provincial and national stakeholders to monitor the impacts of control efforts and improve their ability to implement control informed by these surveillance data

9.4 Risk-Benefit Ratio

The risks to participants in SPEEDIER (both public health and animal health workers and bite victims and communities in the provinces) are deemed minimal, while benefits could be considerable in terms of improving control efforts and patient care for those exposed to rabies. No specific risk-benefit is calculated because it is not appropriate to an implementation study of this nature.

9.5 Informed Consent

9.5.1 Who will obtain consent

IBCM Training: Dr Jobin Maestro will obtain authorization from Mayors of all Municipalities to train public health and animal health workers in IBCM.

Research data collection: Research workers will obtain consent for all data collection with staff, from patients and animal health workers.

9.5.2 How consent will be obtained

IBCM Training: Dr Jobin Maestro will contact Mayors of Municipalities by email or letter followed up by a phone call. He will be supported administratively by field staff.

Research data collection: Research workers will provide participants with an information sheet and having given them time to read it, will seek written informed consent

9.5.4 When and where consent will be obtained

IBCM Training: Authorization from Mayors of Municipalities will be sought in advance of training by email or letter.

Research data collection: Consent will be requested in advance of data collection at the ABTC (for public health staff and patients), before reaching the location of a high-risk animal (for animal health workers) or at the home of the animal owner (for animal owners).

9.5.5 How comprehension of the information sheet will be assessed

We do not expect human and animal health staff to have literacy problems. However, some patients and animal health workers may not be literate. When asking for consent to observe consultations or animal health investigations research staff will offer to read information sheets and consent forms.

9.6 Indemnification, Incentives and Payments for Study Participation

Patients will not receive any payment for participation in the study. Public health and Animal Health workers will be provided with remuneration to cover the expenses of travel for training, and all expenses will be provided to cover accommodation (if required) and subsistence during the training.

9.7 Confidentiality

All evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. All records will be kept in a secure storage area with limited access by appropriate staff only. The PI and staff involved with the study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. The ethics approval and all relevant documentation will be available on request after approval.

9.8 Persons to Contact

The Principal Investigator in the Philippines, Dr Elizabeth Mary Miranda will be the primary contact for national and regional level stakeholders and enquiry. Dr Jobin Maestro, the local Field Epidemiologist will be the primary contact for field issues and local concerns. Their contact details are as follows:

Dr Elizabeth Mary Miranda, FETPAFI, Quezon City, Mobile 02-2812465; email: megmiranda@fetpafi.org

Dr Jobin Maestro, MHO, Alcantara, Romblon Province, Mobile 09491513837 email: maestromd79@gmail.com

10. Role/Responsibilities of each collaborating institutions, if applicable

SPEEDIER is a partnership between the UK (Universities of Glasgow and Cambridge) and the Philippines (Field Epidemiology Training Program Alumni Foundation, Inc.; Research Institute for Tropical Medicine, RITM).

Researchers from all the institutions will work collectively to develop and implement the research. However, RITM will be responsible for the development of the training package for IBCM with a focus on PEP and for laboratory diagostics. FETPAFI will be responsible for delivering and evaluating the training package and the dissemination of research findings. The University of Glasgow will be responsible for the evaluation design and analysis and will provide supervisory oversight for research activities.

10.1 Authorship (Rights to publication)

The co-Investigators on the grant will all be co-authors on any resulting publications from the research. Prior to the development of any draft manuscripts all co-Is will be consulted to determine the appropriate authorship structure and inclusion of all appropriate team members.

10.2 Plans for publication

Two publications are initially anticipated from the study: 1) A Randomised Controlled Trial Protocol (guided by Phase 1 - the Development and Optimization study) and 2) Guidance on

the implementation of IBCM. Potential for other publications will be considered during annual progress reviews.

10.3 Timeline

Year	Month	Phase		IBCM	Data Collection	Analysis & reporting
2019	May	1 DEVELOPMENT & OPTIMIZATION STUDY		Phase 1 preparation: develop IBCM training package; laboratory training		
	Jun			IBCM training & training evaluation	Pre-post training questionnaire, observation of training; 2 week post-training questionnaires & semi-structured interviews	
	July			IBCM implementation in 2 catchments	Observations (patient consultations & animal investigations);	
	Aug				Compile IBCM & ABTC data	*Submission of Phase 2B Ethics*
	Sep				12 week post training questionnaires & semi-structured interviews	Refinement of training materials & data collection instruments
	Oct			Preparation for Phase 2a delivery (amend protocol as required)	Observations (patient consultations & animal investigations). Compile IBCM & ABTC data	Summarize data (ABTC registers & helpline; IBCM; peer support logs; lab records)
	Nov	2A IBCM IMPLEMENTATION STUDY	*Wedge*	IBCM training & training evaluation		*Preparation of judicious PEP training*
	Dec	2B Embedded Stepped Wedge RCT of Rationalized PEP	I	IBCM implementation across 2 provinces	2-week post training questionnaires & semi structured interviews	
2020	Jan				Compile IBCM & ABTC data	
	Feb		II		Observation (patient consultations & animal investigations)	Summarize data & share with stakeholders
	Mar					Summative evaluation of Phase 2A
	Apr		III		Compile IBCM & ABTC data	
	May				6-month post training questionnaires & semi structured interviews	Summarize data & share with stakeholders
	Jun		IV			
	July				Compile IBCM & ABTC data	
	Aug		V		Observation (patient consultations & animal investigations)	Summarize data & share with stakeholders
	Sep					
	Oct		VI		Compile IBCM & ABTC data	Mid-study analysis
	Nov				Observation (patient consultations & animal investigations)	Summarize data & share with stakeholders
	Dec		VII			
2021	Jan				Compile IBCM & ABTC data	
	Feb		VIII		Observation (patient consultations & animal investigations)	Summarize data & share with stakeholders
	Mar					
	Apr		IX		Compile IBCM & ABTC data	
	May				Observation (patient consultations & animal investigations)	Summarize data & share with stakeholders
	Jun		X			
	July				Compile IBCM & ABTC data	
	Aug		XI		Observation (patient consultations & animal investigations)	Summarize data & share with stakeholders
	Sep					
	Oct		XII		Compile IBCM & ABTC data	
	Nov					End-of-study analysis. Summarize data & share with stakeholders
	Dec					Synthesis of Phase 2a and 2b data

This provisional plan for Phase 2B is indicated but may be amended with learning from Phase 1 prior to submission of the Phase 2B protocol for ethical approval.

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