



University  
of Glasgow



**SPEEDIER:**  
Surveillance integrating Phylogenetics and Epidemiology for  
Elimination of Disease:  
Evaluation of Rabies Control in the Philippines



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**STUDY PROTOCOL**

## Glossary

Acceptability	Extent to which implementation stakeholders perceive IBCM to be agreeable, palatable, or satisfactory. <b>See section 7.2.3.1 for an operational definition of how we will evaluate acceptability based on qualitative and quantitative data.</b>
Adoption	Intention, initial decision, or action to try or to employ IBCM. Also called “uptake.” <b>See section 7.2.3.1 for an operational definition of how we will evaluate acceptability based on qualitative and quantitative data.</b>
Animal Investigation	An investigation undertaken by designated animal health worker triggered by assessment of animal being of high risk by health worker.
Animal Health Worker (AHW) (see also Designated Animal Health Worker)	Workers who provide frontline animal health services such as vaccinations and treatment and surveillance activities.
Application (App)	The ‘App’ is an application that can be installed onto phones or used via a web-interface. The application is for use by public health workers and animal health workers to record risk assessments and investigations.
Appropriateness	Perceived fit, relevance, or compatibility of the IBCM for a given practice setting; and perceived fit of IBCM to address the problems. <b>See section 7.2.3.1 for an operational definition of how we will evaluate acceptability based on qualitative and quantitative data.</b>
Cognitive Participation	The relational work that participants do to build and sustain a community of practice around IBCM.
Coherence	The sense-making work that participants do individually and collectively when they are faced with the problem of operationalising some set of practices for IBCM.
Collective Action	This is the operational work that participants do to enact IBCM.
Coverage	Extent to which risk assessments are completed by public health workers and high-risk animals are investigated by animal health workers
Dashboard (IBCM App Dashboard)	A web-based information management tool that visually tracks and displays key performance indicators (KPI), metrics and data to monitor IBCM implementation and outcomes of risk assessments and animal investigations.

Designated Animal Health Worker	Workers or other individuals tasked with conducting IBCM animal investigations (See Animal Investigations).
Feasibility	Extent to which IBCM can be successfully used or carried out within a given agency or setting.
Fidelity	Degree to which IBCM is delivered as prescribed in the protocol.
Information, Education and Communication materials (IEC)	Information, Education and Communication materials are public health information for distribution to the public and communities which attempts to change or reinforce a set of health behaviour.
Integrated Bite Case Management (ICBM)	Integrated Bite Case Management is an approach advocated by the World Health Organisation (WHO) to reduce the costs of PEP once rabies has been controlled. It is a strategy that formally engages the medical and veterinary sectors (a 'One Health' approach) to assess the risk of genuine exposure to rabies and the subsequent need for PEP.
MinION	A portable device for DNA and RNA sequencing in real-time.
NoMAD	A validated instrument containing implementation assessment items reflecting the constructs of NPT.
Normalisation Process Theory (NPT)	Normalisation Process Theory provides a conceptual framework for understanding and evaluating the processes by which new health technologies and other complex interventions are routinely operationalized in everyday work, and sustained in practice.
One Health	An approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes.
Patient Consultation	Patient consulting with health worker as a result of interaction with animal (eg. bite, scratch, lick).
Peer Support Group	A group formed to focus on providing mentoring, emotional and social support, information, education, and practical help to group members, in this case, public health and animal health workers.
Personal Protective Equipment (PPE)	Personal Protective Equipment are materials that are part of standard precautions for all healthcare or animal health workers to prevent skin and mucous membrane exposure

	when in contact with blood and body fluids.
Phylogenetic Analysis	A computational approach to analysing sequence data to determine the evolutionary history and relationships of organisms, in this case of rabies viruses.
Post-exposure prophylaxis (PEP)	Rabies post-exposure prophylaxis comprises wound washing, vaccine given after an exposure or suspected exposure to rabies has occurred and immunoglobulin if indicated.
Pre-Exposure Prophylaxis (PrEP)	Rabies pre-exposure Prophylaxis consists of a course of rabies vaccination given to high-risk individuals such as Animal Health Workers
Public Health Worker (PHW)	Individuals responsible for providing essential services of public health regardless of the organization in which they work.
Rapid Diagnostic Test (RDT)	Rapid Diagnostic Tests are medical diagnostic tests used for quickly detecting pathogens of animals.
Reflexive Monitoring	The appraisal work that participants do to assess and understand the ways that IBCM affect them and others around them.
Risk Assessment (Algorithm)	Risk assessment performed by human health workers on potential rabies exposure.
Routine implementation	The operationalization of IBCM in everyday work and sustained in practice.
Training package	All the collaterals that AHWs and PHWs will receive to perform their duties, such as PPE, Sample Collection Kits, Rapid Diagnostic Tests (RDT), Visual Guides, Data collection tools, IEC tools and the Field Operations Manual.

## 1. Introduction

Rabies, a horrific but preventable disease, kills over 200 people annually in the Philippines. Recently, a global campaign was launched to eliminate human deaths from dog-mediated rabies by 2030 [1] and ASEAN member states have committed to take action against rabies [2]. The Philippines Government set a goal of elimination of rabies by 2020 through a national program of mass dog vaccination and prompt administration of post-exposure prophylaxis (PEP) to bite victims [3-5]. This program has catalyzed control efforts and some provinces are now aiming to declare freedom from rabies.

SPEEDIER is a three-year project jointly funded by the UK Medical Research Council and the Philippine Council for Health Research and Development. The primary aim of SPEEDIER is to deliver a cost-effective, epidemiologically robust, enhanced surveillance and response package to guide and sustain the elimination of rabies from the Philippines.

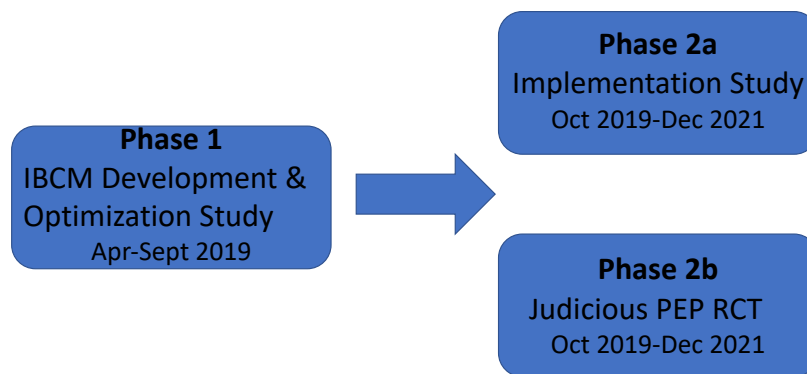
The objectives of SPEEDIER are to:

1. Assess the impact of Integrated Bite Case Management (IBCM) on increasing case detection of rabies and thereby enabling rapid and effective outbreak responses to maintain rabies freedom;
2. Assess the potential for IBCM to improve patient care, by identifying and treating persons bitten by suspect rabid dogs who would otherwise be overlooked by the health system;
3. Assess the impact of judicious protocols for administration of rabies post-exposure prophylaxis (PEP) and therefore the potential for generating cost savings, including the timeframe over which benefits are achieved;
4. Determine whether IBCM and judicious PEP can be implemented as intended in different local contexts, identifying facilitators and barriers to successful implementation and sustainable roll out;
5. Develop best practices for delivering enhanced surveillance to support rabies elimination, bridging research to policy and implementation;
6. Develop decision support tools and guidance for risk assessment, outbreak response and maintaining rabies freedom in the Philippines.

The study design comprises an initial period of development and optimization of materials followed by an implementation study of IBCM with an embedded stepped-wedge randomized controlled trial of rationalized use of PEP.

The study will be delivered in two phases. In Phase 1 we will develop and optimize IBCM for the Philippines context. In Phase 2 we will, a) implement IBCM and, b) conduct an embedded stepped-wedge randomized controlled trial (RCT) of rationalized use of PEP.

**This ethics application covers the development and optimization of materials (Phase 1) and the implementation study (Phase 2a). We will submit a second ethics application for the Phase 2b stepped-wedge RCT of rationalized use of PEP.**



**Figure 1 SPEEDIER Phases of work (2019-2021)**

## 2. Rationale/Significance

The Philippines National Rabies Prevention and Control Program has catalyzed control efforts and some provinces are now aiming to declare freedom from rabies. However, the problem is that incursions and outbreaks continue [6, 7] and PEP is so expensive that it strains local and national healthcare budgets.

Bite incidence in the Philippines is extremely high, exceeding 800/100,000 annually in some provinces, mostly due to bites from healthy dogs [8]. PEP is given to almost all dog bite victims if available. As a result, PEP use has continued to rise, despite mass dog vaccination substantially reducing the circulation of rabies in some provinces [7] and the likelihood is that most bites are from dogs that are not rabid. As one Chief of Hospital said, *“We urgently need to rationalize PEP.... We cannot afford to keep vaccinating patients ... we vaccinate so many that we run out and then have to send people away and ask the mayor for more vaccines”*.

Meanwhile, routine rabies surveillance in the Philippines has shortcomings and is not sufficiently sensitive for international agencies to verify rabies-free areas. This is because surveillance is largely passive with limited sharing of information between sectors. Human and animal rabies are reported through two information systems (PIDSR and Phil-AHIS), and a third (NaRIS) records vaccine use. Investigations are only initiated after a human fatality, which is too late to detect the responsible rabid dog or for effective preventative action for other exposed persons or animals. Population-based sampling is ineffective for rabies due to the low incidence of infection and short time window for diagnosis [9], so it is no longer recommended [10]. Passive reporting of suspicious animals is typically rare because it depends on community awareness, motivation and ability to detect and report a rabid dog. Hence, current surveillance detects only a very small proportion of circulating animal rabies cases. Sometimes human cases are recorded even in the absence of animal rabies, highlighting the inadequacy of the current system for detecting rabies and for verifying freedom.

Integrated Bite Case Management (IBCM) is advocated by the World Health Organisation (WHO), to reduce the costs of PEP once rabies has been controlled [10]. IBCM is a strategy that formally engages the medical and veterinary sectors (a ‘One Health’ approach) to assess the risk of genuine exposure to rabies and the subsequent need for PEP.

The key components of IBCM are, a) risk assessments of exposure events by public health workers based on the clinical history of the animal involved and circumstances of the exposure and, b) linking exposure from animals deemed high-risk to investigations of the animal. Clear communication between human and animal health sectors on the outcomes of these two components are critical to ensuring exposed victims are treated appropriately, necessary control measures are undertaken, and accurate surveillance information is reported.

The implementation of IBCM in Haiti, a resource poor endemic setting, has been shown to improve patient care by identifying and treating those at risk [11], whilst reducing PEP use by 40-60% [12]. In endgame settings, as in some Philippines provinces, where rabies incidence is very low or potentially absent, PEP savings are expected to be even higher.

IBCM has also been identified as a potential strategy that can sufficiently enhance surveillance to enable verification of rabies freedom [9]. IBCM could therefore have immediately beneficial applications within the Philippines and is of critical importance for the global campaign to eliminate human rabies deaths by 2030. However, there is currently no guidance on the operationalization of IBCM for local contexts or on best practice for implementation.

### 3. Objectives

#### 3.1 General

The overall objective of the SPEEDIER IBCM Implementation Study is to evaluate the impact of IBCM in the Philippines and the processes through which outcomes are achieved.

#### 3.2 Specific

Before IBCM can be implemented and evaluated, we need to develop and optimize the materials to support its use. Thus, in Phase 1 we will deliver an operational objective to develop and optimize the materials for operationalizing IBCM in the Philippine context. In Phase 2a) we will deliver five research objectives by implementing IBCM and assessing its impact and the processes through which outcomes are achieved. Specific objectives are:

Phase 1) Operational objective:

1. To develop and optimize IBCM to be delivered in the Philippines

Phase 2a) Research objectives:

2. To estimate the coverage achieved by IBCM in terms of completed risk assessments and investigations of high-risk animals
3. To evaluate the impact of IBCM in terms of appropriate patient care and rabies detection
4. To assess the quality of training in IBCM and the acceptability, appropriateness and adoption of IBCM
5. To evaluate the fidelity of implementation of IBCM
6. To estimate the costs of implementing IBCM

### 4. Hypotheses

We hypothesize that, compared to current practice, IBCM will result, over 24 months, in:

- 1) health workers undertaking risk assessments of bite events for >90% of bite patients presenting to clinics

- 2) designated animal health workers investigating >90% of biting animals classified as high-risk
- 3) PEP administered promptly to, and regimens completed by, 100% of patients bitten by high-risk animals
- 4) at least a doubling of rabies cases detected in settings with current human cases
- 5) confirmation that animals classified as high-risk are not rabid in settings with no current human cases
- 6) IBCM proving acceptable and appropriate and being adopted in everyday practice
- 7) IBCM protocols being implemented with high fidelity.

## 5. Materials and Methods

### 5.1 Study design

Observational study of the implementation of IBCM in the Philippines using mixed methods delivered in two phases.

In Phase 1 we will deliver operational objective 1. We will develop and optimize IBCM and the training package for its delivery. We will do this by a) developing and delivering a training package tailored to local contexts, b) implementing IBCM in 1 ABTC and the health services within catchment municipalities that refer patients to that ABTC in each of Romblon and Oriental Mindoro provinces, d) assessing the success of the training and how IBCM and training to deliver it needs to change prior to Phase 2a), e) assessing the extent to which public health and animal health workers can implement IBCM (reviewing all components in terms of their ease of use, acceptability, appropriateness, adoption and the fidelity with which they are delivered), so as to identify refinements for Phase 2 delivery and, f) assess the feasibility of data collection as planned. **Using the understanding gained on the context and provision of PEP in the two Provinces we will fully develop the protocol for the stepped-wedge RCT of rationalized PEP use (Phase 2b) and submit our ethics application for Phase 2b mid-way through Phase 1 (see Timeline 10.3).**

In Phase 2a we will deliver research objectives 2-6. We will deliver training for IBCM in remaining ABTCs and their catchment municipalities, evaluate the impact of its implementation and the processes through which outcomes are achieved. **Once ethical approval for Phase 2b has been secured we will undertake the stepped-wedge RCT of rationalized PEP across the two provinces. Our provisional design for the embedded stepped wedge RCT is for each ABTC catchment to be randomly assigned to a wedge and to implement training in the first wedge three months after completion of IBCM training across the two provinces at the start of Phase 2a. Training and implementation of rationalized PEP in each subsequent wedge will be undertaken every second month until complete. This provisional plan is indicated in the Timeline (10.3) but may be amended with learning from Phase 1 prior to submission of the Phase 2b protocol for ethical approval.**

Table 1 summarises the objectives, criteria through which we will know whether we have achieved objectives and information required, the data collected methods and population to which methods are applied.