# Combining genomics and epidemiology to investigate rabies outbreaks in the Philippines

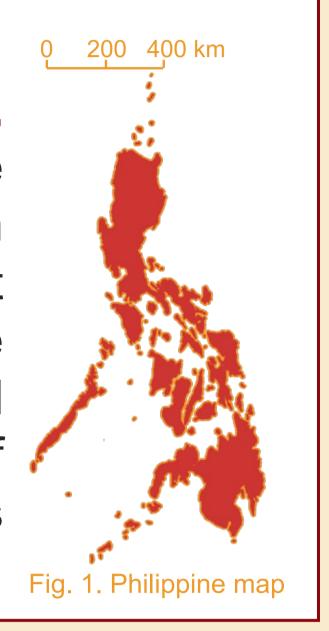


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Enhanced surveillance through Integrated Bite Case Management (IBCM) and genomic sequencing enabled us to detect a canine rabies outbreak in a rabies-free island in the Philippines, which we traced from at least 3 separate introductions from other provinces.

## BACKGROUND

Rabies kills 200-300 people in the Philippines (Fig. 1) annually, and is mainly transmitted by dogs. The province of Romblon was declared rabies-free in 2019, but through Integrated Bite Case Management (IBCM) and whole genome sequencing (WGS), we investigated the transmission dynamics of a local outbreak in late 2022, demonstrating the value of using a One Health approach for tracking rabies outbreaks in real time.



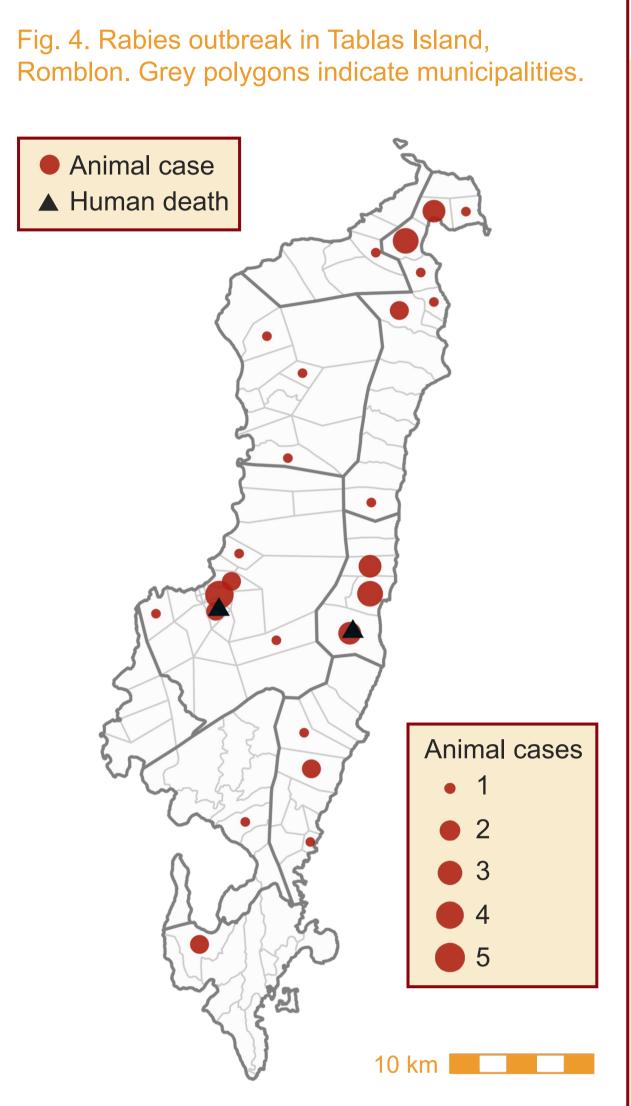
## METHODS Fig. 2. Integrated Bite Case Management (IBCM) step-by-step process ANIMAL HEALTH WORKERS HEALTHCARE WORKERS ···· 3 Perform <u>animal investigation</u> 1 Interview bite patient **2** Conduct bite <u>risk assessment</u> Test for rabies □□□ ⊕ using RDT\* Intersectoral Send to lab for communication confirmation & W wgs

Rabies surveillance data have been collected implementation of IBCM in 2020. Epidemiological data collected from human exposures and animal investigations (Fig. 2) increased case detection, enabling whole genome sequencing of confirmed rabies-positive samples using an established samplesequence-interpretation workflow. 48 consensus sequences were obtained, supplemented by publicly available data (n=664), and an ongoing Philippine-wide sequencing study (n=162). Phylogenetic analysis, including tree dating and ancestral character reconstruction, was conducted to estimate the dates and locations of geographic dispersal events. Transmission trees for the Romblon outbreak were reconstructed, ensuring consistency with phylogenies.

43 dog rabies cases were confirmed in Tablas Island from September 2022-2023. Despite increased case detection by IBCM, considerable transmission went undetected, resulting in two human deaths (Fig. 3).

Fig. 3. Romblon rabies cases (September 2022 – September 2023) Confirmed (animal) Probable (animal) Human death 06/23 03/23 Month/Year

Rabies cases were reported in all except one municipality in Tablas Island (Fig. 4). An estimated 75 undetected cases occurred average and detection delays ranged from 4-14 months. Integrating human bite cases and animal investigations in conjunction with viral genome data vastly improved transmission chain resolution, revealing orphaned cases and unsampled transmission chains indicative of undetected cases in locations where transmission was occurring. Phylogenetic analysis showed at least three independent introductions to Tablas Island based on three clusters of lineages (Fig. 5). The resulting cases were found to be closely related to lineages from



northern provinces, implying human-mediated movement of dogs into Romblon as the likely source of the outbreak, facilitated by pandemic-induced lapses in dog vaccination from 2020 to 2021.

Fig. 5. Time-scaled phylogenetic subtrees from the current outbreak Lineages 1 2 3 4 5 Provinces Batangas Bulacan Laguna Metro Manila Quezon Romblon 2012 2014 2016 2018 2020 2022 1995 2000 2005 2010 2015 2020 2025 2030 2012 2014 2016 2018 2020 2022

Our results indicate that human-mediated introductions to geographically isolated areas occur frequently and maintaining dog vaccination coverage together with strict border control will limit incursions. This investigation demonstrates the value of IBCM, WGS and RDTs for inferring the source and spread of rabies outbreaks.

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