1	Disentangling fine-scale effects of environment on malaria detection and infection to design risk-
2	based disease surveillance systems in changing landscapes
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#### 25 Abstract:

26

27	Landscape changes have complex effects on malaria transmission, disrupting social and
28	ecological systems determining the spatial distribution of risk. Within Southeast Asia, forested
29	landscapes are associated with both increased malaria transmission and reduced healthcare access.
30	Here, we adapt an ecological modelling framework to identify how local environmental factors influence
31	the spatial distributions of malaria infections, diagnostic sensitivity and detection probabilities in the
32	Philippines. Using convenience sampling of health facility attendees and Bayesian latent process models,
33	we demonstrate how risk-based surveillance incorporating forest data increases the probability of
34	detecting malaria foci over three-fold and enables estimation of underlying distributions of malaria
35	infections. We show the sensitivity of routine diagnostics varies spatially, with the decreased sensitivity
36	in closed canopy forest areas limiting the utility of passive reporting to identify spatial patterns of
37	transmission. By adjusting for diagnostic sensitivity and targeting spatial coverage of health systems, we
38	develop a model approach for how to use landscape data within disease surveillance systems. Together,
39	this illustrates the essential role of environmental data in designing risk-based surveillance to provide an
40	operationally feasible and cost-effective method to characterise malaria transmission while accounting
41	for imperfect detection.
42	
43	Background:

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Malaria transmission is highly variable spatially, driven by the geographical distribution of human
populations, mosquito vectors and the environments in which these populations interact (1).
Surveillance systems aim to identify these high-risk locations and populations in order to effectively
plan, implement and evaluate control policies and measures. As control programmes reduce incidence

49	and transmission decreases, spatial heterogeneity becomes more pronounced, necessitating
50	increasingly higher resolution data to detect foci of infection (2). This becomes increasingly critical in
51	rapidly changing environments, where changing human populations and vector habitats may cause
52	significant shifts in transmission patterns (3). However, despite extensive research linking landscape
53	with malaria transmission, landcover data rarely informs malaria surveillance systems.
54	
55	For passive surveillance systems relying on reported malaria case data, understanding spatial
56	distributions of risk is further challenged by underreporting due to health-seeking behaviour or
57	asymptomatic infections present in the community. Increasing evidence suggests the proportion of
58	asymptomatic malaria infections not detectable by standard diagnostics increases in low transmission
59	settings, resulting in large numbers of infections not detected by passive surveillance systems (4, 5).
60	These asymptomatic infections are commonly seen in older age groups, with potentially different risk
61	factors and spatial distributions from clinical malaria cases (6, 7). Population-based community surveys
62	remain the gold standard for assessing spatial patterns of infection; however, these sampling
63	approaches are highly resource intensive and may require very large sample sizes in low transmission
64	settings. Alternatively, more operationally feasible surveys of easy access groups, such as health facility
65	attendees or school children, are used to increase probability of detecting infections within the
66	community (e.g. (8-11)). However, both approaches targeting clinical cases and easy access groups are
67	inherently biased and do not fully capture the spatial distribution of infections.
68	
69	Within ecology, estimates of species distribution or abundance are similarly challenged by imperfect
70	detection and spatially biased observation processes (12). Occupancy models are widely used to

estimate the probability that a species occupies a geographic location within a specified time period

while accounting for possible non-detection (13). This method partitions observation processes

73	determining detection probability and biological processes determining occupancy probability, each
74	associated with potentially overlapping spatial and environmental covariates. This makes the simple
75	assumption that a species cannot be detected if it is not present; however, if present, the species may or
76	may not be detected during sampling. In addition to allowing estimation of true occupancy states as a
77	latent variable, this method allows quantification of uncertainty in the observation process under
78	different sampling scenarios (14-16).
79	
80	Here, we combine occupancy models with practical health facility surveys and molecular
81	diagnostics to evaluate the spatial coverage of surveillance approaches and their ability to detect
82	locations with recent malaria transmission. By estimating a spatially explicit sensitivity of different
83	diagnostic methods, we illustrate how environmental data can be used to develop operationally feasible
84	risk-based surveillance systems to increase the probability of detecting areas of infection while
85	rationalising scarce resources. This provides an adaptable framework to integrate convenience sampling
86	approaches into existing disease surveillance systems to target control measures and characterise
87	spatial and environmental drivers of infection from opportunistically collected data.
88	
89	Using rolling cross-sectional health facility-based surveys in which all attendees regardless of
90	patient status or symptoms were screened for malaria using routine and molecular diagnostics, with
91	residences geolocated in real-time using tablet-based applications, we apply this approach to describe
92	the spatial distribution of malaria infections in Rizal, Palawan, The Philippines (Figure 1 (11)). While the
93	Philippines has made substantial progress towards malaria elimination, with 50 provinces declared
94	malaria free, Palawan contributes over 95% of malaria cases nationally, including 2718 cases from the
95	municipality of Rizal in 2018 (17). Deforestation rates have increased markedly within Rizal; of the 24%
96	decrease in forest cover between 2000 – 2018, over 50% of deforestation occurred after 2015, largely

97	driven by agricultural expansion (18). Within this region, malaria risks are strongly associated with
98	proximity to forested areas due to both vector ecology and occupational risks (19). Described as
99	"frontier malaria," factors associated with increased malaria risks, such as proximity to forest edges and
100	recent deforestation, are also associated with reduced healthcare access, resulting in potentially
101	complex interactions between detection bias and infection risks (20).
102	
103	Our results illustrate that enhanced health facility-based surveys increase the probability of
104	detecting locations with malaria infections by markedly increasing the spatial coverage of the
105	surveillance system in addition to simply increasing the numbers of individuals screened. By comparing
106	locations of infections detected by routine diagnostics (microscopy and/ or rapid diagnostic tests (RDTs))
107	with sub-patent infections only detectable by molecular methods, we show the sensitivity of routine
108	diagnostics decreases in highly forested areas, with many locations of malaria transmission only
109	detectable by molecular methods. We demonstrate how these findings can be used to develop
110	operationally feasible and cost-effective environmentally targeted risk-based surveillance methods and
111	prioritise locations with high probabilities of infection not captured by existing surveillance systems.
112	
113	Figure 1. Study area and forest cover in 2017
114 115	
116	Results:
117	
118	Impact of survey method on detection probability
119	
120	We conducted monthly rolling cross-sectional surveys at 27 health facilities across Rizal,
121	Palawan over a one-year period (Figure S1). All consenting individuals, regardless of symptoms or

122	patient status, were screened for malaria using microscopy or RDTs and polymerase chain reaction (PCR)
123	as described by (21). As multiple malaria species are present in this area and over 75% of infections were
124	with <i>Plasmodium falciparum</i> , we classified malaria as positive for any <i>Plasmodium</i> species. Using this
125	data, we initially compared two surveillance approaches: 1. Standard - passive case detection (PCD),
126	including febrile patients screened using routine diagnostics (RDTs or microscopy) as per current
127	national surveillance guidelines; 2. Enhanced – standard PCD plus screening all health facility attendees
128	with both routine and molecular methods.
129	
130	Between June 2016 – June 2017, 5767 individuals were enrolled in this study, including 1914
131	(33.2%) febrile patients screened for malaria by existing passive surveillance systems (21). Of these, 801
132	individuals (13.9%) were positive for malaria by molecular methods and 498 were positive by RDT or
133	microscopy. We geolocated all residences in Rizal (n=7313), identifying individuals screened by PCD from
134	698 unique locations while enhanced surveillance screened individuals from 2201 locations (Table S2).
135	Malaria infections were detected at 352 household locations using enhanced surveillance and 117
136	locations by standard PCD.
137	
138	As control measures are targeted based on reported locations with malaria infection and over
139	80% of infected locations had only one infected individual detected, we chose to model whether malaria
140	infection was present or absent in a specific location (occupancy) rather than incidence. Detection
141	probabilities, the probability of screening at least one individual from a location during the study period,
142	varied geographically, with travel time to the nearest health facility negatively associated with detection
143	probability by both PCD and enhanced surveillance methods (Table 1). Enhanced surveillance increased

detection probabilities over three-fold compared to standard PCD (mean probability 3.34, 95%BCI: 1.03

- 145 8.27) in addition to markedly increasing spatial coverage of surveillance, particularly in rural
- 146 populations living in forested areas (Figure 2A, 2B).

148 149 150 151 152 153 154 155 156	<b>Figure 2.</b> Posterior probability of infection under different sampling scenarios adjusted for detection probabilities: A. detection probability using routine passive case detection; B. detection probability using health facility-based surveys; C. probability of infection estimated from passive case detection using routine diagnostics; D. probability of infection estimated from active case detection using molecular diagnostics
157	
158	
159	Spatial distribution of infection
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161	Incorporating these detection probabilities into hierarchical occupancy models revealed a much
162	wider spatial distribution of malaria detected by enhanced surveillance compared to PCD alone,
163	identifying areas of infection not captured by existing surveillance systems (Figure 2C, 2D). We identified
164	a range of differing spatial and environmental risk factors for infections detected by different diagnostic
165	methods; however, all infections were associated with proximity to closed canopy forests in more rural
166	populations (Table 1). For joint models for each surveillance scenario, incorporating a shared spatial
167	random effect between detection and infection probability improved model performance, suggesting a
168	common spatial process driving healthcare access and disease risks (Table S3).
169	

#### **Table 1.** Posterior estimates of fixed effects and spatial range for joint models of A. standard PCD and B.

171 enhanced surveillance

172 173

Α.			
	Mean	SD	95% BCI
Probability of detection			
Distance to roads	0.226	0.125	-0.020, 0.227
Travel time to clinic	-0.317	0.120	-0.561, -0.090
Distance to forest	-0.112	0.053	-0.217, -0.009
Spatial range (km)	8.140	2.500	4.319, 14.050
Probability of infection			
Distance from roads	0.094	0.101	-0.109, 0.287
Population density	-0.603	0.145	-0.894, -0.322
Precipitation of wetness month	0.212	0.107	-0.006, 0.420
Distance from closed canopy forest	-0.222	0.156	-0.537, 0.078
Spatial range (km)	1.752	1.096	0.493, 4.643
Scaling parameter for shared spatial effect	0.590	0.163	0.282, 0.921

174 \*\* All covariates mean-centred and scaled

176

В.			
	Mean	SD	95% BCI
Probability of detection			
Population density	-0.533	0.085	-0.701, -0.368
Travel time to clinic	-0.511	0.107	-0.729, -0.309
Aspect	0.094	0.039	0.017, 0.171
Spatial range (km)	15.804	6.130	7.212, 30.957
Probability of infection			
Distance from roads	0.285	0.071	0.145, 0.423
Upslope area	0.181	0.111	-0.038, 0.399
Topographic wetness index	-0.243	0.120	-0.481, -0.011
Temperature annual range	0.236	0.098	0.043, 0.428
Distance from closed canopy forest	-0.326	0.111	-0.548, -0.112
Spatial range (km)	0.897	0.232	0.532, 1.438
Scaling parameter for shared spatial effect	1.216	0.177	0.887, 1.179

177 \*\* All covariates mean-centred and scaled

- 178
- 179

180 To explore the factors determining these differing distributions of infections, we estimated the

181 probability of patent malaria detectable by RDT or microscopy in all malaria infections we identified.

182 Malaria infected individuals were identified from 435 locations and over one third of infected individuals

183 (37.8%, 95% CI: 34.5-41.3%) could only be detected by molecular methods. Subpatent malaria was

substantially more common in forested areas with the odds of patent infections increasing 1.23 (95%BCI

<sup>175</sup> 

- 185 1.03-1.47) with every kilometre distant from closed canopy forested areas (Table 2). Using data from all
- 186 residence locations identified within Rizal, we predicted a location-specific probability of patent malaria,
- 187 equivalent to the sensitivity of routine diagnostics (RDT and/or microscopy) (Figure S2).
- 188
- **Table 2.** Posterior estimates of fixed effects for malaria positive households detected by routine
   diagnostics (RDT and microscopy) compared to molecular methods

	Mean	SD	95% BCI
Distance from closed canopy forest*	0.225	0.112	0.036, 0.476
Annual precipitation*	-0.318	0.121	-0.620, -0.145
Precipitation of wettest month*	0.256	0.085	0.091, 0.422
Population density <sup>2</sup> *	0.093	0.087	-0.078, 0.263

191 \* Mean-centred and scaled

192

193 Evaluating surveillance systems

194

195 As our primary aim was to identify all locations of malaria infection, we evaluated surveillance 196 approaches against estimates of true infection status using molecular diagnostics and all available 197 spatial data. Accounting for spatial bias of collection data, we estimated 11.4% (95%BCI: 4.6%-21.9%) of 198 all locations in Rizal had malaria infections during the sampling period. While no surveillance method 199 identified all areas of infection perfectly, enhanced surveillance using molecular methods identified 200 38.7% (95% BCI: 33.6-43.8%) of infected locations while PCD only identified 5.7% (95% BCI: 0.1 – 11.9%). 201 Including molecular diagnostics in PCD only slightly improved the probability of detecting infections 202 while conducting health facilities using only routine diagnostics increased the number of infected 203 locations identified slightly more (Figure 3A, Figure S4). We additionally identified 247 locations with a 204 very low (<0.05% probability) of detection by any health facility-based surveillance. 205 206 Based on distributions of malaria infections and probability of detection by routine diagnostics,

207 we additionally explored the use of environmentally-stratified risk-based surveillance approaches. We

208	defined high-risk areas based on distances from closed canopy forest (Figure S3). Evaluating costs of
209	each surveillance system relative to baseline costs of standard PCD (Methods, SI), we estimated the total
210	cost per location with malaria infection identified (Figure 3B). As the cost per infection detected was
211	most sensitive to inclusion of molecular diagnostics, we defined a risk-based surveillance approach using
212	health facility surveys in all areas and only applying molecular diagnostics to locations within 100m of
213	closed canopy forest areas (Table 3, Figure S5). This risk-based surveillance approach almost halved the
214	cost of detecting a location of infection compared to enhanced surveillance, from USD 603.10 (95% BCI:
215	530.02 – 690.82) to USD 370.00 (95% BCI: 313.18- 444.04) while detecting almost as many locations of
216	infections.

217

## 218 Table 3. Surveillance methods assessed

219

	Survey method		Diagnostic method		Total cost
	Passive case	Health facility	Routine (RDT/	Molecular	(USD)
	detection	surveys	microscopy)		
1: Standard PCD	Х		X		-
2: Enhanced surveillance	Х	Х	Х	Х	193,547.70
3: PCD + molecular	Х		Х	Х	56,654.40
4: Health facility surveys + routine	Х	Х	X		22,844.50
5: Risk-based surveys + diagnostics	Х	Risk zone only	X	Risk zone only	

220

Figure 3. Evaluation of surveillance methods described in Table 3 by A. estimated numbers of locations

with malaria infections not detected, and B. estimated additional costs per location with malaria

223 infections detected (relative to standard PCD)

- 224
- 225

226

### 227 **Discussion**

- 229 The spatial distribution of malaria is driven by a complex interplay of environmental and social
- 230 factors influencing both disease transmission and identification by health systems. Statistical methods

231 enabling examination of processes driving infection and detection provide an invaluable tool to evaluate 232 the roles of environmental factors and develop targeted surveillance approaches. Here, we demonstrate 233 a convenience sampling approach using health facility surveys markedly increases spatial coverage of 234 surveillance systems; incorporating these surveys with satellite-derived remote sensing data allows 235 estimation of the underlying distribution of infection not captured by passive surveillance. We 236 additionally show higher proportions of subpatent malaria infections in forested areas, highlighting the 237 limited utility of routine diagnostics within these regions. Applying these findings, we develop a cost-238 effective and operationally feasible risk-based surveillance approach using environmental data and 239 illustrate how landscape data can be incorporated into disease surveillance systems. 240 241 Despite extensive research identifying proximity to forests as risk factors for malaria infection in 242 Southeast Asia (e.g. (3, 22-27)), landscape data are not routinely used to design or inform surveillance 243 systems. Malaria control programmes typically conduct community-based active case detection in 244 response to reported malaria cases (2); however, we show this may miss a substantial proportion of 245 active malaria foci due to biases in health-seeking behaviour and increased prevalence of subpatent 246 malaria within higher transmission areas. Although mechanisms driving this relationship between forest 247 cover and subpatent malaria are not known, patent malaria infections are more common in children in 248 this area and settlements in closer proximity to forests may have different demographic compositions 249 (e.g. logging and plantation camps) (21). Previous studies have also suggested a role for immunity in 250 high transmission areas, with individuals repeatedly exposed to malaria commonly having lower parasite 251 densities (4). Despite lower parasite densities, these subpatent infections can lead to infections in 252 mosquitoes and may have a critical role in sustaining transmission in elimination settings, highlighting 253 the importance of identifying and treating these individuals (28).

255 While screening entire populations may be prohibitively costly and intensive, the increasing 256 availability of satellite-based remote sensing data provides new opportunities to use environmental data 257 to target surveillance activities (29). Surveillance systems for malaria, as well as for other low incidence 258 or emerging diseases, are challenged by the need to identify relatively rare events with shifting spatial 259 patterns. Widely used in veterinary epidemiology, risk-based surveillance uses known risk factors to 260 focus intensive surveillance activities on the populations where rare events are most likely to occur (30). 261 Integrating remote-sensing derived environmental data into this approach provides an adaptable 262 framework which can be easily updated in changing landscapes. Further, quantifying the detection 263 probabilities associated with these surveillance approaches allows estimation of biases in data and 264 identification of populations not captured by opportunistic sampling and can be used to plan active case 265 detection. For this example, using health facility surveys, this enables evaluation of spatial patterns of 266 health seeking behaviour as well as populations outside health system coverage. Screening all 267 individuals attending health facilities, including those accompanying patients or for nonfebrile illnesses, 268 vastly increases the spatial coverage of surveillance. The improved performance of models including a 269 common spatial term for both infection and detection suggests processes determining healthcare 270 coverage also influence infection risks, demonstrating the multiple utilities of measuring health seeking 271 behaviour in this context.

272

Within this study, remote sensing data was used not only as covariates but also to define the populations at risk. The application of machine learning approaches to identify building footprints from very high resolution satellite imagery has produced increasingly accurate estimates of household distributions and allows estimation of spatial distribution of the populations (31). Development of tablet-based methods including population data and satellite imagery enabled near real-time identification of the residences of health facility attendees in a rural population with no formal

279 addresses and limited internet connectivity (11). These tools and datasets can be further expanded to 280 create accessible interfaces for local health workers to use environmental and spatial data and 281 incorporate risk-based decision pathways on screening procedures and diagnostic tests based on 282 household locations and travel history. This approach can also be easily modified to include multiple 283 diseases with different underlying environmental risk factors and updated to include new environmental 284 data, such as near real time deforestation alerts (32). Despite advances in using meteorological data to 285 forecast vector-borne disease epidemics, landscape data is rarely used operationally and may provide 286 more actionable information within rapidly changing environments. While we have focused on malaria, 287 this is additionally relevant for targeting risk-based surveillance of emerging diseases, such as by 288 detecting rare spillover events in changing habitats. 289 290 Despite the utility of these methods, there were several limitations to this study. As this study 291 was designed to identify spatial locations of malaria infections within the sampling year, we did not 292 explore temporal patterns of infection or health seeking behaviours. However, the modelling approach 293 used is easily extendable to incorporate dynamic state-space models of changes in infection over time 294 (12). If health facility surveys were collected over longer periods of time, this could additionally be 295 expanded to incorporate seasonally varying meteorological data to further refine risk stratifications. 296 While populations at risk were defined using multiple datasets, this is likely to have limited coverage of 297 highly mobile indigenous populations not residing in permanent structures. Future work could explore 298 the utility of satellite imagery to identify these populations, such as through monitoring of forest 299 disturbance or modelling movement patterns. Within this study, the numbers of infections with 300 different Plasmodium species precluded species-specific analyses. As all species are transmitted by the 301 same mosquito vectors, environmental risk factors are expected to be similar; however, future work 302 could examine differences between spatial distribution by malaria species. Additionally, while molecular

303	approaches for malaria are not easily applied in rural settings, new diagnostics, such as lateral flow
304	assays and serological tests, may facilitate point of contact testing in the future (33, 34).
305	
306	Even with these limitations, this provides a novel and adaptable surveillance approach for
307	environmentally driven diseases and demonstrates the role of landscapes in driving malaria infection
308	and detection within this region. Incorporation of forest data enables identification of cost-effective risk-
309	based surveillance approaches which increase probabilities of detecting malaria infections and can be
310	applied to support elimination efforts. Additionally, the process-based ecological modelling method
311	used provides a flexible framework to quantify detection probabilities and estimate the true spatial
312	distribution of infection using biased data from convenience-based sampling approaches.
313	
314	Methods:
314 315	Methods: Survey approaches
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<ul> <li>314</li> <li>315</li> <li>316</li> <li>317</li> <li>318</li> </ul>	Methods:         Survey approaches
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<ul> <li>314</li> <li>315</li> <li>316</li> <li>317</li> <li>318</li> <li>319</li> <li>320</li> <li>321</li> <li>322</li> <li>323</li> </ul>	Methods:         Survey approaches         We conducted cross-sectional health facility-based surveys at 27 facilities, including at one         Regional Health Unit (RHU), 9 Barangay Health Stations (BHS) and 17 RDT centres based in community         health worker households, established to increase access to malaria diagnosis and treatment (Figure S1).         For one week every month between June 2016 – June 2017, all individuals attending the health facility,         regardless of symptoms or patient status, were asked to participate in this survey. For consenting         individuals, malaria status was assessed using either microscopy or rapid diagnostic tests (RDTs), with         finger-prick blood samples collected on Whatman 3MM filter paper for subsequent polymerase chain

325 species were *P. falciparum* and all malaria species are transmitted by common vectors in this area.

- Household locations were identified on offline maps and basic demographic information was recorded
   using GeoODK on Android tablets (11).
- 328
- 329 Spatial and environmental covariates
- 330

331 To define the locations of all households within Rizal, we extracted information on household 332 structure locations from the Facebook High Resolution Settlement Layer, a 30m resolution satellite-333 based remote sensing derived dataset on all inhabited structures (35). This dataset was combined with 334 all reported households identified by survey participants and geolocated households from the 2015 335 Philippine census (36). We resampled all datasets to 50m resolution and removed duplicate locations to 336 account for spatial resolution of datasets and inaccuracies of reported household locations. To estimate 337 detection probabilities, we classified households included by a surveillance scenario if one or more 338 individuals were sampled. Similarly, households were classified as infected if one or more individuals 339 were identified as infected by diagnostics used by the surveillance approach. 340 341 Plausible covariates used to model detection or infection probabilities were assembled (Table 342 S1). Handheld GPS devices (Garmin, USA) were used to record locations of all sampled clinics and roads 343 within the region. Travel time to the nearest sampled clinic was calculated as accumulated cost from 344 friction surfaces extracted from (37). Additional environmental and spatial covariates included 345 population density (38), Euclidean distance from roads and bioclimatic variables (39). Elevation and 346 topographic measures, including topographic wetness index (TWI), upslope area and aspect, were 347 calculated from the ASTER Global Digital Elevation Model (40). Forest cover was classified as over 50% 348 canopy cover based on (18) and Euclidean distance was calculated to the forest edge, recent 349 deforestation within the past year and historical deforestation within the previous five years. We

- additionally included closed canopy forest, defined as canopy cover over 90% with a minimum area of0.5ha (41).
- 352
- 353 Occupancy modelling
- 354

355	Covariates were extracted for all identified household locations and Pearson correlation analysis
356	was used to assess multicollinearity between variables. To select variables for inclusion, nonspatial
357	binomial generalised linear models were fit separately for detection probabilities and infection
358	probabilities for each surveillance scenario using backwards stepwise model selection with a five-point
359	threshold for improvement in deviance information criteria (DIC) to minimise overfitting (42). Residual
360	spatial autocorrelation was assessed using Moran's I and performance assessed by area under the
361	receiver operating curve (AUC). Weakly informative priors of Normal (0, 1/0.01) were used for all
362	intercepts and coefficients. All models were implemented in Integrated Nested Laplace (INLA), with
363	10,000 posterior samples generated from the approximated posterior distribution to include uncertainty
364	in these estimates (43). Final models had an AUC of 85% for both surveillance approaches.
365	
366	We modelled the distribution of infections under each surveillance scenario separately using
367	occupancy models in which the probability of detecting an infection $(y_i)$ in location $i$ is dependent on the
368	probability of detection ( $p_i$ ) and presence of infection ( $\omega_i$ ) (13), modelled as:
369	

$$y_i \sim \begin{cases} 0, & \omega_i = 0\\ \text{Bernoulli}(p_i), & \omega_i = 1 \end{cases}$$

370

371 Where the linear predictor determining the probability of detection is modelled as:

$$logit(p_i) = \alpha_0 + X_i \alpha + u_i$$

373

374 Where  $\alpha_0$  represents the intercept,  $X_i \alpha$  represents a vector of covariate effects and  $u_i$  is the spatial 375 effect modelled as a Matern covariance function using the stochastic partial differential equations 376 approach to represent the spatial process by Gaussian Markov random fields as implemented in INLA 377 (43, 44). The process determining the true state of malaria presence  $\omega$  is determined by the true 378 probability of infection  $\psi$ :  $\omega_i \sim \text{Bernoulli}(\psi_i)$ 379 380 With the linear predictor for the Bernoulli model specified as: 381  $logit(\psi_i) = \beta_0 + X_i \beta + \gamma_i + Z u_i$ 382 Where  $\beta_0$  represents the intercept,  $X_i \beta$  represents a vector of covariate effects and  $\gamma_i$  represents the 383 384 spatial effect, modelled as described above. As processes influencing probability of detection 385 (healthcare access) additionally may impact infection, we include a shared spatial component  $Zu_i$  with 386 scaling parameter Z (45). 387 388 Patent malaria distribution 389 390 To explore factors affecting the distribution of locations of patent malaria infections (detected 391 by RDT or microscopy) compared to all infections, we subset all malaria infected locations. For  $J_i$  malaria 392 infected individuals identified in each location, the number of patent infections observed  $(m_i)$  is 393 modelled as:

$$m_i \sim \text{Binomial}(J_i, s_i)$$
394395With the linear predictor determining the probability of patent infections (s\_i) modelled as:396 $\log it(s_i) = \kappa_0 + X_i \kappa$ 397398Where  $\kappa_0$  represents the intercept and  $X_i \kappa$  represents a vector of covariate effects. Using data from all399locations included in the study site, we then predicted a location specific sensitivity of routine400diagnostics. Based on these results, we used environmental data to define an area with higher401probabilities of malaria infections only detectable by molecular diagnostics.402403Evaluation of surveillance systems404405405406407408409409400401402403404405405406407408409409409400401402403404405405406407408409409409409400401402403404405405406407408409409409409409409409409409

$$\sum_{i=1}^i \omega_i (1-p_i) + \omega_i p_i (1-s_i)$$

Where p<sub>i</sub> is the probability of detection using different survey methods and s<sub>i</sub> represents diagnostic
sensitivity, with PCR considered the gold standard. We additionally included risk-based surveillance
methods, using health facility surveys and molecular diagnostics in high risk areas defined by proximity
to closed canopy forest. All derived quantities were estimated using 10,000 posterior samples.

413	To evaluate the cost effectiveness of different surveillance approaches, we estimated the
414	additional costs to health systems of including different survey and diagnostic approaches (Table S4).
415	This excluded capital costs and costs already covered by existing health systems (e.g. RDT and
416	microscopy diagnostics for febrile patients). Health facility survey costs included additional payments to
417	personnel, training, equipment, RDT and microscopy for non-febrile participants, sample collection and
418	molecular diagnostics for all attendees and salary for a technician to support data management and
419	sample analysis. The costs of molecular diagnostics included DNA extraction and PCR reagents, assuming
420	all DNA extraction was completed using Chelex with 10% of samples verified using a commercial Qiagen
421	kit. To account for varying numbers of samples screened from each location, we estimated the mean
422	cost of molecular diagnostics per location as the total cost of molecular diagnostics divided by the total
423	number of locations included. We evaluated these against the estimated number of locations correctly
424	identified as a measure of cost effectiveness. All analysis was completed in R statistical programming
425	language (v 3.6), with maps visualised in R or ArcGIS (ESRI, Redlands, USA).
426	
427	Ethics approval
428	This study was approached by the Institutional Review Board of the Research Institute for Tropical
429	Medicine, Department of Health Philippines (IRB:2016-04) and the Research Ethics Committee of the
430	London School of Hygiene and Tropical Medicine (11597). Written informed consent was obtained from
431	all participants or parents or guardians and assent obtained from children under 18.
432	
433	Data availability
434	Data is available upon reasonable request and with permission of ethics committees in the Philippines

435 and United Kingdom. All R code needed to conduct these analyses will be available at

436 <u>https://github.com/kfornace</u>

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- 554
- 555 Author contributions
- 556 KMF, FE, JRCH and CJD designed this study. KMF analysed the data and wrote the manuscript. KMF and
- 557 RAR collected and analysed spatial and remote sensing data. RAR, MLMM, APNB and JSL collected the
- health data and analysed samples. All authors read and approved the final manuscript.



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