


Estimating the effectiveness of vaccine programs in dog populations

R.M. Wallace¹ , E.A. Undurraga^{1,2}, A. Gibson^{3,4}, J. Boone⁵, E.G. Pieracci¹, L. Gamble³ and J.D. Blanton¹

Original Paper

Cite this article: Wallace RM, Undurraga EA, Gibson A, Boone J, Pieracci EG, Gamble L, Blanton JD (2019). Estimating the effectiveness of vaccine programs in dog populations. *Epidemiology and Infection* **147**, e247, 1–12. <https://doi.org/10.1017/S0950268819001158>

Received: 29 October 2018

Revised: 5 April 2019

Accepted: 9 May 2019

Key words:

Modelling; rabies (animal); vaccination (immunisation); zoonoses

Author for correspondence:

R.M. Wallace, E-mail: euk5@cdc.gov

¹Centers for Disease Control and Prevention, Atlanta, GA; ²Escuela de Gobierno, Pontificia Universidad Católica de Chile, Santiago, Chile; ³Mission Rabies, Cranborne, UK; ⁴University of Edinburgh, Royal Dick School of Veterinary Medicine, Edinburgh, Scotland and ⁵Humane Society International, Washington DC, United States

Abstract

Dogs harbor numerous zoonotic pathogens, many of which are controlled through vaccination programs. The delivery of these programs can be difficult where resources are limited. We developed a dynamic model to estimate vaccination coverage and cost-per-dog vaccinated. The model considers the main factors that affect vaccination programs: dog demographics, effectiveness of strategies, efficacy of interventions and cost. The model was evaluated on data from 18 vaccination programs representing eight countries. Sensitivity analysis was performed for dog confinement and vaccination strategies. The average difference between modelled vaccination coverage and field data was 3.8% (2.3%–5.3%). Central point vaccination was the most cost-effective vaccination strategy when >88% of the dog population was confined. More active methods of vaccination, such as door-to-door or capture-vaccinate-release, achieved higher vaccination coverage in free-roaming dog populations but were more costly. This open-access tool can aid in planning more efficient vaccination campaigns in countries with limited resources.

Introduction

The domestic dog has been a companion of man for over 10 000 years [1, 2]. Dogs perform numerous important roles within communities, including companionship, security, disability assistance services and livestock protection. Dogs also play host to at least 60 zoonotic pathogens, diseases that can spread from dogs to humans, which has resulted in the development of numerous canine health interventions applied for the ultimate objective of reducing dog-mediated human disease [3]. Interventions that are commonly practiced include surgical sterilisation, routine vaccinations, vector control and vaccinations for zoonotic pathogens.

Delivery of these health interventions has been optimised in many high-income countries through the development of veterinary and public health infrastructure. These efforts have led to the elimination of diseases such as canine-variant rabies virus in many countries and reduction of other zoonoses such as leptospirosis, parvovirus, canine distemper virus and tick-borne diseases. Veterinary and public health infrastructure in many middle- and low-income countries has not been extensively developed and a propensity to allow domestic dogs to roam freely further compounds poor animal health and facilitates transmission of zoonotic pathogens [4].

Rabies lyssavirus (RABV) is considered the deadliest of all zoonotic pathogens, responsible for over 2 million human infections and at least 59 000 deaths annually [5, 6]. Nearly all human deaths are the result of infection from the bite of a RABV-infected dog [7]. Practical experiences, as well as predictive modeling techniques, have shown that RABV transmission can be interrupted when herd-immunity is maintained above 50% in the susceptible dog population [8–11]. Due to population turnover, annually applied dog vaccination campaigns reaching >70% of the susceptible population have proven adequate to eliminate RABV in dogs [12–15].

While the challenge of canine rabies elimination may be more difficult in low and middle-income countries, several programs have shown that successes can be achieved under such conditions [16–19]. Learning from successful programs and taking advantage of new technology could accelerate time to elimination for countries that are committed to the goal [20]. Limited understanding of the epidemiology of dog and dog-mediated diseases, lack of community awareness, shortages of trained vaccination personnel and insufficient planning capabilities to project needed resources are among the main barriers to conduct effective animal disease prevention interventions [11, 16, 21–24]. Here, we describe a model to help reduce the period between research and application of successful dog vaccination interventions.

Methods

In order to develop a dynamic model to estimate the effectiveness of a health intervention in a dog population, we partitioned the process of canine vaccination into five elements: *allocation of*

© The Author(s) 2019. This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike licence (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the same Creative Commons licence is included and the original work is properly cited. The written permission of Cambridge University Press must be obtained for commercial re-use.

vaccines, *accessibility* of dog populations, vaccine *efficacy*, *vaccination* effectiveness and *summation* of distributed vaccines. A set of equations are used to calculate estimated vaccination coverage according to dog confinement status and vaccination method used. User-defined values include: the total number of dogs in the vaccination area and their proportional makeup by confinement status (Step 1); number of vaccine doses procured and allocated by vaccination method (Steps 2 & 3), efficacy of the vaccines (Step 4) and the effectiveness of vaccination method in reaching target dog populations (Step 5). The user's confidence in their responses is also recorded to develop confidence levels around the model outputs (scale 1–10, higher indicating more confidence) (Fig. 1).

Vaccination methods considered in this analysis included central point vaccination (CP), door to door vaccination (DD), capture-vaccinate-release (CVR) and oral rabies vaccination (ORV). Vaccination by the CP method involves prior community awareness of the campaign and notification of the location where it will be held. Vaccinators set up a clinic in a convenient location and wait for dog owners to bring dogs to them. Vaccination by DD involves vaccination teams walking through a community and asking dog owners to present their dogs for vaccination. Vaccination by CVR requires a trained and properly equipped staff to move through a community vaccinating accessible (through owner presentation) and inaccessible (through nets and control poles) dogs. Vaccination by ORV involves the distribution of oral rabies baits to free-roaming dogs (owned or unowned).

Allocation

The model begins by defining the dog population structure.

$$d_i = D_T \times p(C_i), \quad \text{where } \sum p(C_i) = 1$$

where D_T is the user-defined total dog population and $p(C_i)$ is defined as the proportion of the dog population in each confinement status category: always under owner confinement (C), sometimes confined (SC) and never confined (NC).¹

A similar process is used to allocate the procured vaccine supply to each distribution method used in the campaign.

$$s_j = S_T \times p(m_j), \quad \text{where } \sum p(m_j) = 1$$

where S_T is the user-defined total number of vaccine doses procured and $p(m_j)$ is defined as the proportion of vaccine doses allocated to each distribution method in the campaign: CP, DD, CVR and ORV (see footnote 1).

Accessibility

The next step in the model determines the number of dogs in each confinement category that is accessible by a given vaccination method, using vaccination method efficacy estimates provided by the user. Users are able to directly define the expected proportion of dogs that can be reached in each segment of the population

¹The GDREP describes a framework in which novice dog vaccination programs will scale-up activities to eventually reach 70% coverage and eliminate rabies. The framework assumes that in Phase I countries will begin vaccination pilot programs and evaluate methods that work with their dog populations. Phase II involves scaling up those effective vaccination strategies. Phase III considers that those effective campaigns need to be maintained until elimination is reached.

by each distribution method (i.e. accessible). Alternatively, pre-defined effectiveness matrices are provided based on a country's current vaccination coverage levels and data obtained from the previously published global dog rabies elimination pathway (GDREP) (Box 1) [25].

$$a_{ij} = d_i \times p(i|j)$$

where $p(i|j)$ is defined as the probability of vaccinating a dog in confinement category i using method j (see footnote 1).

Vaccination

An iterative set of equations are used to define the number of vaccinated dogs in each confinement category by vaccination method, using the number of allotted vaccines for the campaign. A pre-defined rank order is defined to determine which population category would be most accessible for a given vaccination method and allocated vaccines are applied to that population category first, before applying the remainder of vaccines to the next confinement category and so on, until all vaccine is utilised. If the iterative process is complete and vaccines remain, they are classified as wastage (w). If vaccines are depleted before the iterative processes is completed, no vaccines will be allocated to the remaining dog populations.

$$V_{ji}(x) = \begin{cases} \min [s_j, a_{ij}], & x = 1 \\ \min [(s_j - V_j(1)), a_{ij}], & x = 2 \\ \min \left[\left(s_j - \sum_{i=1}^2 V_j(x) \right), a_{ij} \right], & x = 3 \\ \max \left[0, \left(s_j - \sum_{i=1}^3 V_j(x) \right) \right], & x = 4 \end{cases}$$

where x defines the rank order for allotting the vaccine doses as outlined below (see footnote 1).

	CPV	DDV	CVR	ORV
C	1	1	3	3
SC	2	2	1	2
NC	3	3	2	1
w	4	4	4	4

Summation

A final summation of the number of vaccinated dogs by confinement category is completed and used for calculating all other summary statistics (e.g. vaccination coverage).

$$V_i = \sum V_{ji}$$

To provide an estimated confidence range around each point estimate of the vaccination coverage, users are asked to indicate their confidence in their provided inputs on a scale from one to ten (one being not confident and ten being very confident). The confidence rank (CR) is used to approximate a measure of variance for calculating confidence intervals for results related to vaccination coverage.

$$DS_{ij} = \sqrt{100} \times (UC/3.92)$$

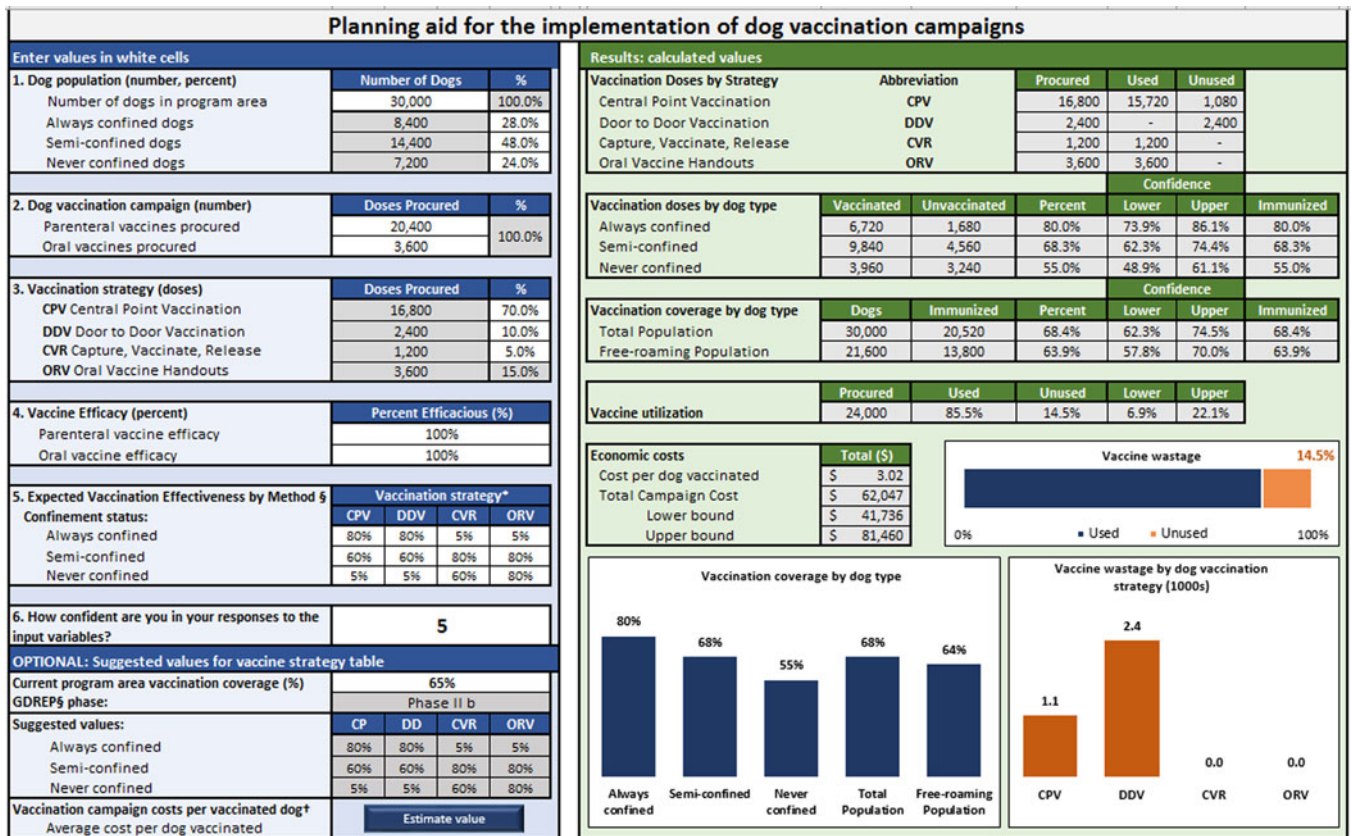


Fig. 1. User-interface for planning dog vaccination campaigns.

Box 1. Global dog rabies elimination pathway vaccination effectiveness by strategy and phase

VACCINATION STRATEGY		CENTRAL POINT (CP)			DOOR TO DOOR (DD)			CAPTURE-VACCINATE-RELEASE (CVR)			ORAL RABIES VACCINATION (ORV)		
		I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)
CONFINEMENT	GDREP* PHASE												
	CONFINED	20	80	95	20	80	95	5	5	5	5	5	5
	SEMI-CONFINED	20	60	80	20	60	80	20	80	95	20	80	95
	NEVER CONFINED	5	5	5	5	5	5	20	60	80	20	80	95

where

$$UC_{ij} = d_i \times CR, \quad 0.05 \leq CR \leq 0.15$$

The CR is a user provided value. A weighted deviation is calculated for the number of dogs vaccinated in each population group according to the proportion of vaccines used by each distribution method. The weighted deviation score was used as a proxy for standard deviation to calculate confidence intervals by the standard method.

Cost estimates

Costs commonly encountered during a rabies vaccination campaign were derived from subject matter experience and published articles [18, 19, 26–29]. Costs were validated through

international workshops with vaccination program managers. Cost data used for this analysis were provided from the Haiti Ministry of Agriculture and are reflective of true costs incurred by their dog rabies vaccination program during 2015–2017. While these costs were fixed for the analysis, they are user-defined values in the tool to reflect the costs and efficiencies for limitless variations of vaccination campaigns.

Validation

We evaluated the model by comparing real-program field outcomes to model-predicted outputs. We developed a standardised data collection tool which was distributed to vaccination program managers in Haiti, Ethiopia, Malawi, India and Sri Lanka (see Supplemental 1). These programs were selected based on the recent publication of vaccination activities or through

collaboration networks [30, 31]. Up to four respondents familiar with the program were selected from each vaccination campaign. Furthermore, we included publications from 2010–2017 that reported the input data necessary to run the model, as well as post-vaccination evaluation results derived from either dog-marking or household survey methods [18, 19, 25–29, 32, 33]. Respondents were neither given access to the vaccination tool nor were they allowed to alter input data based on model output. Coverage estimates for each campaign were also modelled using input values derived from the GDREP (Box 1) [20].

We compared the model-derived vaccination coverage (predicted) to the coverages obtained from field post-vaccination evaluations (observed) and provide the results as the mean and absolute differences in coverage. We calculated the aggregate differences between predicted and observed values and corresponding 95% confidence interval (CI). Predicted vaccination coverage rates were plotted against observed coverages. Correlations were calculated by the Pearson product-moment correlation coefficient (r), coefficient of determination (r^2) and 2-tailed P -value ($\alpha = 0.05$).

Intra-class correlations were used to evaluate consistency in the respondent's input values using a one-way random effects model to measure consistency between raters within a single campaign and consistency in responses between campaigns [34]. The Shrout-Fleiss reliability score was used to calculate correlation scores for dog population groups and vaccine accessibility by distribution methods [35]. Correlations scores <0.4 were considered poor, between 0.4 and 0.59 fair, between 0.6 and 0.74 good and >0.74 excellent. Only campaigns with three or more respondents were analysed for consistency.

Sensitivity analysis was conducted to explore two primary vaccination outcomes: impact of dog confinement rates on vaccination coverage and impact of vaccination method on campaign cost (see Supplemental 2).

Results

Data derived from four published and nine unpublished dog vaccination campaigns that satisfied the inclusion criteria were used to evaluate the vaccine model (13 total campaigns evaluated) (Table 1). Campaigns used in this analysis were conducted in eight countries located in North America, Central America, East Africa, North Africa and Asia. Eighteen unique respondents completed the data collection tool (Table 1). Of the 67 entries used to evaluate the vaccination model, field-derived (i.e. observed) free-roaming dog vaccination coverage was available for 31 (46.3%) and total dog vaccination coverage was available for 67 (100.0%).

Respondents reported an average confidence level of 5.9 out of 10, with 10 as the most confident response. The intraclass correlation for dog population distribution and vaccine distribution efficiency reflected some of this uncertainty. Overall, there was poor to fair correlation between users on these values (Table 2). Respondents were fairly consistent when assessing the accessibility of semi-confined dogs. There was generally poor consistency in values provided for the accessibility of all vaccine distribution methods for never-confined dogs.

The mean difference between the estimated and observed free-roaming dog vaccination coverage was 0.5% (95% CI –2.4%, 3.4%) (Table 3). Among the 31 respondent-derived estimates, this mean difference was 0.4% (95% CI –3.3%, 4.1%) and among the eight GDREP-derived estimates the mean difference was 0.7% (95% CI –3.8%, 5.2%). The absolute difference between

the estimated and observed free-roaming dog vaccination coverage was 6.7% (95% CI 4.9%, 8.4%). Among the 31 respondent-derived estimates, the mean absolute difference was 6.8% (95% CI 4.4%, 9.2%) and among the eight GDREP-derived estimates the mean difference was 6.2% (95% CI 4.8%, 7.7%). Overall, there was high linear correlation between the observed and predicted free-roaming dog vaccination values ($r^2 = 0.84$, slope = 1.01, P -value <0.0001) (Fig. 2)

The mean difference between the predicted and observed total dog vaccination coverage was –1.7% (95% CI –3.5%, 0.1%) (Table 3). Among the 54 respondent-derived estimates the mean difference was –1.9% and –1.4% among the 13 GDREP-derived estimates. The mean absolute difference was 3.8% (95% CI 2.3%, 5.3%); among respondents, this absolute difference averaged 4.3% and for the GDREP-derived estimates was 2.7%. Overall, there was high linear correlation between the observed and predicted total dog vaccination values ($r^2 = 0.96$, slope = 1.00, P -value <0.0001) (Fig. 2).

Sensitivity analysis

The sensitivity analysis for dog confinement showed that predicted vaccination coverage among the free-roaming dog population is heavily influenced by the vaccination strategy and proportion of dogs that are always under owner confinement. The CP strategy is expected to achieve >70% coverage in free-roaming dogs, but only when the confined dog population exceeded 88% (Fig. 3). Vaccination coverage among the total dog population in the CP strategy is expected to achieve >70% when more than 30% of the dog population is confined. The CVR and ORV strategies are both expected to achieve >70% coverage in the free-roaming dog population regardless of the proportion of confined dogs. Using the respondent-provided mean values for dog confinement (28% confined, 48% semi-confined, 24% never confined), the expected cost-per-dog-vaccinated would be \$3.26 for CP campaigns, \$3.62 for CVR campaigns and \$4.09 for ORV campaigns to achieve 63%, 95% and 95% vaccination coverage in free-roaming dogs, respectively, under the specific parameters used for analysis.

Projections from the dog confinement sensitivity analysis suggest that the majority of costs-per-dog-vaccinated under the CP strategy are allocated to campaign awareness (\$0.78 USD), followed by vaccines (\$0.69 USD) and vaccination equipment (\$0.54 USD) (Fig. 3). Under the CVR strategy, the majority of costs-per-dog-vaccinated were allocated to equipment (\$0.93 USD), followed by awareness (\$0.75 USD) and dog vaccines (\$0.66 USD). Under the ORV strategy, the majority of costs-per-dog-vaccinated were allocated to vaccines (\$1.94 USD), followed by awareness (\$0.72 USD) and equipment (\$0.61 USD). The CVR strategy is expected to result in 40 vaccinator bite events per campaign, resulting in an estimated cost to the campaign of \$0.18 USD per dog vaccinated, compared to an estimated 12 vaccinator bite events for the CP strategy (\$0.06 per dog vaccinated) and three vaccinator bite events for the ORV strategy (\$0.01 per dog vaccinated).

Figure 4 shows the results from the ORV and CVR sensitivity analysis. For this analysis, we assumed that GDREP phase I, II and III vaccination strategy effectiveness values were equivalent to programs with poor, moderate and high levels of veterinary capacity. However, since the ORV strategy does not require direct handling of the animal, we fixed the values of ORV strategy effectiveness at GDREP phase III values across the poor, moderate, and

Table 1. Respondent and literature-derived data describing canine rabies vaccination programs across four continents

Campaign location (role)	Dog population	Dog confinement			Vaccine procured	Vaccine distribution method				Respondent confidence score ^e	Free-roaming dog population		Total dog population	
		Confined (%)	Semi-Confined (%)	Never confined (%)		CP ^a (%)	DD ^b (%)	CVR ^c (%)	ORV ^d (%)		Estimated coverage (confidence)	Observed coverage	Estimated coverage (confidence)	Observed coverage (%)
Eddy County, AZ, USA (GDREP III)	10 750	80	15	5	10 000	95	5	0	0	5	61 (55, 67)	na	88 (82, 94)	86
Chad 2012 (GDREP II)	24 500	70	20	10	35 000	90	10	0	0	5	42 (36, 48)	na	69 (62, 75)	71
Mali (GDREP I)	3500	40	50	10	3000	100	0	0	0	5	18 (10, 25)	na	19 (11, 26)	19
Chad 2013 (GDREP II)	30 074	70	20	10	35 000	90	10	0	0	5	42 (36, 48)	na	69 (62, 75)	71
Ethiopia 2016 (Epidemiologist)	14 300	5	65	30	3000	75	25	0	0	5	15 (9, 21)	8%	16 (9, 22)	12
Ethiopia 2016 (Field assistant)		40	40	20		70	30	0	0	5	8 (4, 12)		21 (16, 26)	
Ethiopia 2016 (GDREP I)		23	53	25		73	28	0	0	5	15 (9, 21)		17 (10, 23)	
Ethiopia 2016 (Coordinator)	140 000	15	45	40	7500	10	70	20	0	5	1 (0, 5)	na	5 (2, 9)	5
Ethiopia 2016 (Epidemiologist)		5	65	30						5	3 (0, 7)		5 (1, 10)	
Ethiopia 2016 (Field assistant)		25	65	10						5	1 (0, 7)		5 (0, 11)	
Ethiopia 2016 (Field assistant)		40	40	20						5	2 (0, 6)		5 (1, 10)	
Ethiopia 2016 (GDREP I)		21	54	25						5	2 (0, 6)		5 (1, 10)	
Haiti 2015 (Coordinator)	1 100 000	35	50	15	460 000	100	0	0	0	5	43(38, 48)	36%	42 (37, 47)	42
Haiti 2015 (Field assistant)		20	45	35						5	37 (28, 48)		42 (36, 48)	
Haiti 2015 (Field assistant)		15	80	5						8	35 (31, 39)		42 (38, 46)	
Haiti 2015 (Epidemiologist)		15	75	10						8	35 (31, 39)		42 (38, 46)	
Haiti 2015 (GDREP II)		21	63	16						5	32 (27, 37)		42 (37, 47)	
Haiti 2016 (Coordinator)	11 687	35	50	15	8340	35	37	21	7	5	51 (45, 57)	66%	54 (48, 60)	71
Haiti 2016 (Field assistant)		20	45	35						5	50 (44, 56)		52 (46, 58)	
Haiti 2016 (Field assistant)		15	80	5						8	70 (66, 74)		71 (67, 76)	
Haiti 2016 (Epidemiologist)		15	75	10						8	70 (66, 74)		71 (61, 75)	
Haiti 2016 (GDREP II)		21	63	16						5	70 (64, 76)		71 (65, 77)	

(Continued)

Table 1. (Continued.)

Campaign location (role)	Dog population	Dog confinement			Vaccine procured	Vaccine distribution method				Respondent confidence score ^e	Free-roaming dog population		Total dog population	
		Confined (%)	Semi-Confined (%)	Never confined (%)		CP ^a (%)	DD ^b (%)	CVR ^c (%)	ORV ^d (%)		Estimated coverage (confidence)	Observed coverage	Estimated coverage (confidence)	Observed coverage (%)
Goa, India (Coordinator)	73 039	25	55	20	55 000	0	60	40	0	5	69 (63, 75)	62%	75 (69, 81)	73
Goa, India (Epidemiologist)		14	28	58						8	72 (68, 76)		75 (71, 79)	
Goa, India (Field assistant)		10	20	70						8	60 (56, 64)		64 (60, 68)	
Goa, India (Field assistant)		14	28	58						8	60 (56, 64)		65 (61, 69)	
Goa, India (GDREP III)		16	33	51						5	70 (64, 76)		74 (68, 80)	
Blantyre, Malawi (Epidemiologist)	45 526	10	75	15	35 500	66	30	4	0	8	73 (69, 77)	73%	74 (70, 78)	77
Blantyre, Malawi (Coordinator)		30	50	20		60	39	1	0	5	54 (48, 60)		62 (56, 68)	
Blantyre, Malawi (Field assistant)		40	40	20		66	30	4	0	5	60 (54, 66)		74 (68, 80)	
Blantyre, Malawi (GDREP III)		27	55	18		64	33	3	0	5	65 (59, 71)		73 (67, 79)	
Zomba, Malawi (Coordinator)	29 298	25	50	25	30 000	44	56	0	0	8	53 (49, 57)	58%	64 (60, 68)	70
Zomba, Malawi (GDREP III)		25	50	25						5	55 (49, 61)		65 (59, 71)	
Zomba, Malawi (Coordinator)	6647	40	50	10	8000	72	28	0	0	8	77 (73, 81)	74%	84 (80, 88)	82
Zomba, Malawi (GDREP III)		40	50	10						5	68 (61, 74)		79 (72, 85)	
Sri Lanka (Coordinator)	7610	40	40	20	5000	0	75	25	0	8	49 (45, 53)	67%	61 (57, 65)	60
Sri Lanka (Field assistant)		30	60	10						5	60 (54, 66)		54 (48, 60)	
Sri Lanka (Field assistant)		20	50	30						5	60 (54, 66)		52 (55, 58)	
Sri Lanka (Epidemiologist)		40	40	20						5	60 (54, 66)		60 (54, 66)	
Sri Lanka (GDREP II)		33	47	20						5	59 (53, 65)		66 (60, 72)	

^aProportion of vaccines allocated to Central Point vaccination method.

^bProportion of vaccines allocated to Door to Door vaccination method.

^cProportion of vaccines allocated to Capture-Vaccinate-Release vaccination method.

^dProportion of vaccines allocated to Oral Rabies vaccination method.

^eThe user's self-reported confidence in the values provided for the model, with 1 being least confident and 10 most confident.

Columns are merged when all respondents from the same campaign provided the same parameter value. Estimated coverage values in bold are within the confidence limits of the field-measured value.

Table 2. Inter-operator variability for respondent-provided subjective input variables^a

Dog Population Demographics		Shrout-Fleiss Reliability Score			
Confined	0.08				
Semi-confined	0.03				
Never confined	0.48				
Vaccination Strategy Effectiveness		Shrout-Fleiss Reliability Score			
	Central point	Door to door	Capture-vaccinate-release	Oral rabies vaccination	
Confined	0.21	0.52	0.12	0.07	
Semi-confined	0.47	0.58	0.19	0.4	
Never confined	0.21	0.07	0.05	0.29	

^aIntra-class correlations were used to evaluate consistency in the respondent's input values using a one-way random effects model with single rater. The Shrout-Fleiss reliability score was used to calculate correlation scores for dog population groups and vaccine accessibility by distribution methods. Correlations scores <0.4 were considered poor, between 0.4 and 0.59 fair and >0.6 good/excellent.

Table 3. Comparison of observed and estimated dog vaccination coverage for free-roaming dogs and the total dog population

FREE-ROAMING DOG POPULATION COVERAGE ESTIMATES									
	Average difference (%)	Standard deviation	95% confidence interval	Absolute difference (%)	Standard deviation	95% confidence interval	Correct	Over-estimated	Under-estimated
Total	0.5	0.08	3.4%, -2.4%	6.7	0.05	8.4%, 4.9%	14 (45.2%)	6 (14.6%)	11 (35.5%)
User average	0.4	0.09	4.1%, -3.3%	6.8	0.06	9.2%, 4.4%	10 (43.5%)	4 (17.4%)	9 (39.1%)
GDREP average	0.7	0.07	5.2%, -3.8%	6.2	0.02	7.7%, 4.8%	4 (50.0%)	2 (25.0%)	2 (25.0%)
TOTAL DOG POPULATION COVERAGE ESTIMATES									
	Average Difference (%)	Standard Deviation	95% Confidence Interval	Absolute Difference (%)	Standard Deviation	95% Confidence Interval	Correct	Over-estimated	Under-estimated
Total	-1.7	0.06	0.1%, -3.5%	3.8	0.05	5.3%, 2.3%	30 (75%)	1 (2.5%)	9 (22.5%)
User average	-1.9	0.07	0.6%, -4.4%	4.3	0.05	6.4%, 2.3%	19 (70.4%)	0 (0.0%)	8 (29.6%)
GDREP average	-1.4	0.03	0.3%, -3.1%	2.7	0.02	3.8%, 1.5%	11 (84.6%)	1 (7.7%)	1 (7.7%)

high capacity scenarios; this decision was made based on author experience with ORV campaigns in Haiti, Bangladesh and India. This analysis shows that programs with low capacity for handling dogs (GDREP phase I) are unlikely to achieve >70% vaccination coverage in free-roaming dog populations regardless of the number of vaccine doses allocated to the CVR strategy. Conversely, programs with low capacity were able to achieve >70% vaccination coverage when >50% of the vaccination effort was allocated to ORV. The most cost-effective strategy for low-capacity programs, defined as the lowest cost strategy that achieved >70% coverage in the free-roaming dog population, occurred when 70% of the vaccines were distributed by ORV (cost per 1% increase in coverage of \$936, free-roaming vaccination coverage of 95%). Adequate coverage (>70%) in moderate animal handling capacity programs (GDREP phase II) was only achieved by the ORV strategy and only when ORV encompassed >40% of the total vaccination effort. Under the high-capacity program setting (GDREP phase III), allocating 10% of vaccines to ORV or 20% to CVR achieved >70% coverage at a cost of \$1009 USD and \$971 per 1% increase in coverage, respectively.

Discussion

Campaigns considered in this analysis reflected heterogeneous populations of dogs and campaigns: dog confinement rates varied from 15% to 80%, vaccination strategies included CP, DD, ORV and CVR and programs had varying levels of vaccination experience [20]. Despite this heterogeneity, the tool gave accurate predictions of dog vaccination coverage, often within 6% of the field-derived vaccination coverage estimates. Prior studies suggest that under ideal circumstances it will take a novice rabies control program approximately 6 years to develop capabilities to reach 70% dog vaccination coverage. Tools that aid vaccination campaign managers to design more cost-effective and efficient campaigns, such as what is described here, can minimise the time and cost to achieve canine rabies elimination [23, 36, 37].

This model more accurately estimated vaccination coverage among total dog populations than free-roaming dog populations (Table 3). Population and vaccination coverage estimation methods for free-roaming dogs often have a high degree of error, as the methods are fraught with uncertainty and require a substantial

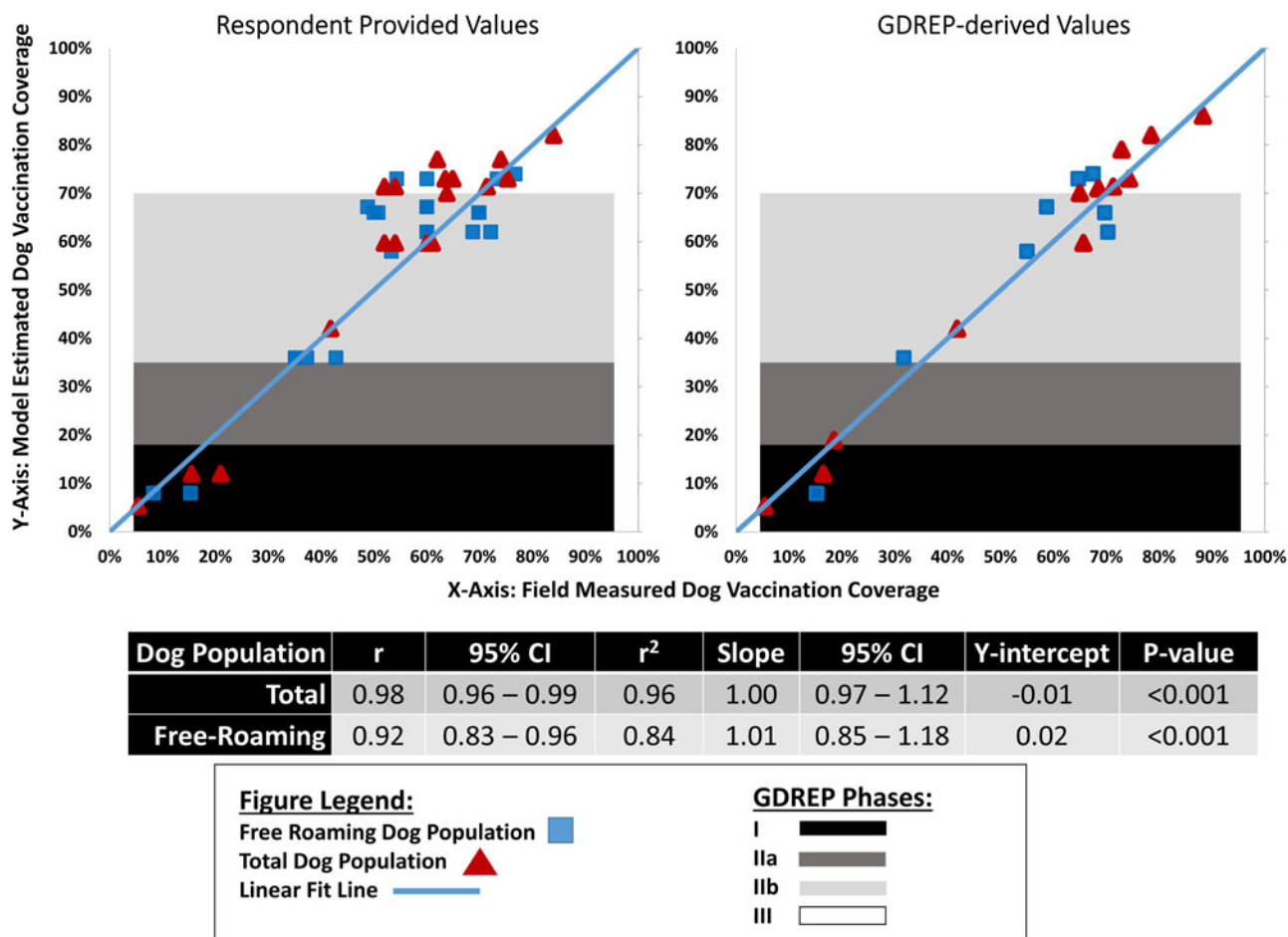


Fig. 2. Field-measured vaccination coverage compared to the model-derived estimated coverage among the free-roaming and total dog populations using respondent and GDREP-derived model input values.

Field-measured vaccination coverage was obtained from campaign managers or published literature (Table 1). Expected vaccination coverage was estimated from the vaccination calculator tool (Table 1). The solid blue line represents a slope of 1.0, which is an indicator of perfect agreement. Blue squares are the free-roaming dog value and red triangles are total dog population values. Values located above the blue line represent under-estimated vaccination coverage per the vaccination tool. Values located below the blue line represent over-estimated vaccination coverage per the vaccination tool.

GDREP = Global Dog Rabies Elimination Pathway (Box 1, reference 14).

r² = the linear correlation value for the field-measured and estimated vaccination coverages based on respondent-provided parameters.

number of assumptions [38]. As a result, post-vaccination coverage estimates in free-roaming dogs can be difficult to assess with any degree of certainty. The reduced accuracy of this tool for free-roaming dogs may be partly due to decreased accuracy in the field-derived vaccination coverages reported from the campaigns in this study. There may also be other variables influencing free-roaming dog population vaccination coverage that are either unaccounted for or inadequately represented in our model assumptions. Despite slightly less accurate predictions, the model was still reasonably accurate at predicting the vaccination coverage in free-roaming dogs and could be useful in planning effective intervention strategies.

When the observed vaccination coverage was outside of the range of the model's predictions, model values more frequently erred on under-estimating field-derived vaccination coverages (Fig. 2). This is reassuring, as the majority of campaigns, had they utilised this tool to plan their campaign, would have achieved greater vaccination coverage than predicted. This tool is intended to aid in more efficient planning of campaigns when limited data are available. However, every dog vaccination

program should incorporate routine and representative post-vaccination evaluation to ensure that the anticipated vaccination goals are met [19].

Evaluation of respondent-provided input data revealed a large degree of uncertainty and disagreement among respondents regarding their input values for dog confinement and vaccination strategy effectiveness (Table 2). These are characteristics of dog populations and vaccination campaigns that are often difficult to measure, even for experienced vaccination program managers. This may indicate that when the tool is used to strategise new methodologies it may be prone to less accurate user input values and less accurate results. The GDREP-recommended values for vaccination strategy effectiveness resulted in more accurate coverage predictions when compared to respondent-provided values, suggesting that when users lack confidence in their responses GDREP values should be considered (Table 2).

It is well recognised that, where effective, CP vaccination is relatively inexpensive and more easily implemented compared to other vaccination strategies. However, CP vaccination may not be effective for certain dog populations. In this analysis,

Impact of dog confinement on expected vaccination coverage and cost per dog vaccinated by three vaccination methods: Central Point, Capture-Vaccinate-Release, and Oral Rabies Vaccination

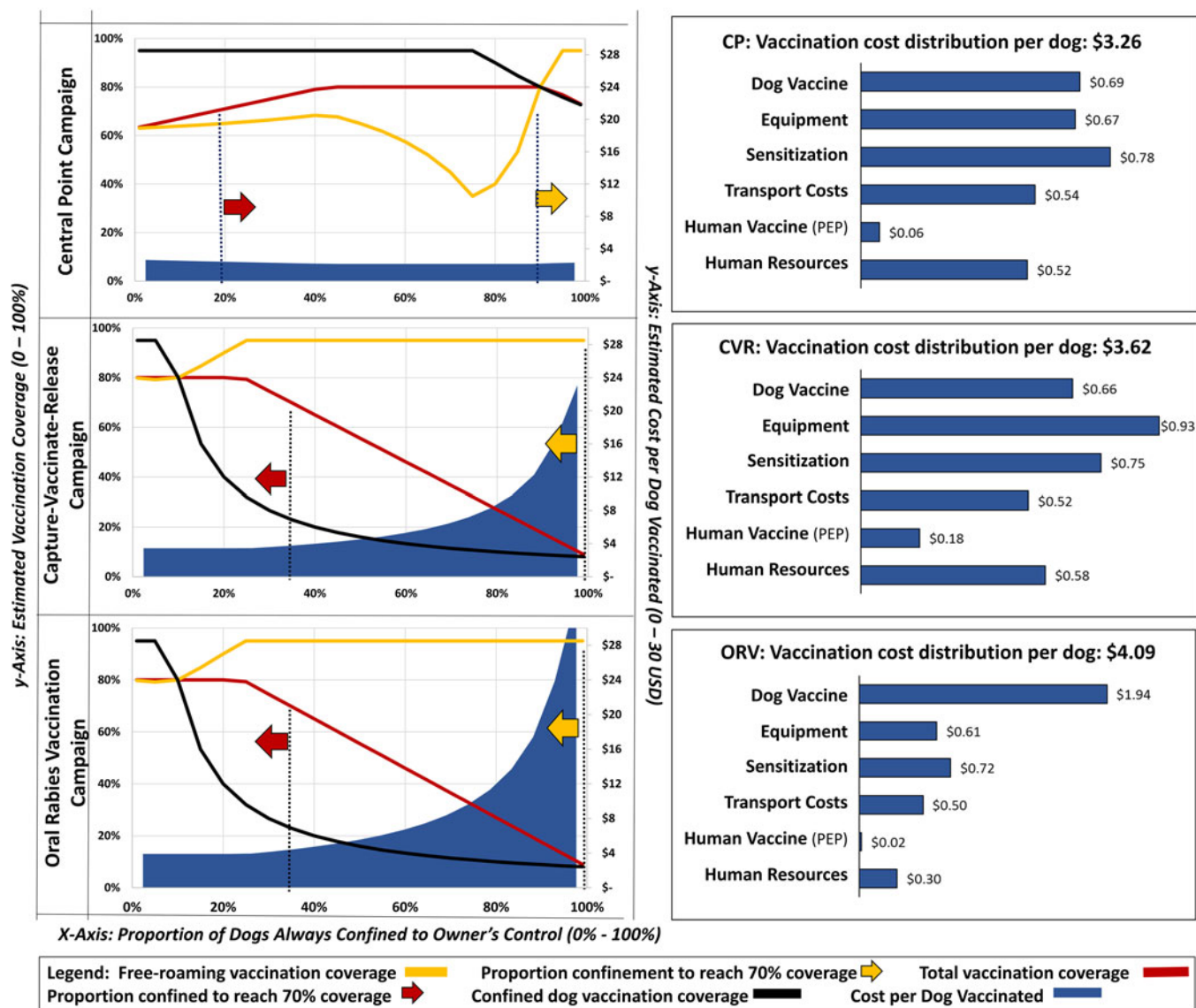


Fig. 3. Sensitivity analysis showing the impact of dog confinement on expected vaccination coverage and cost-per-dog-vaccinated by three vaccination strategies. All three scenarios assumed GDREP phase III vaccination strategy effectiveness levels (Box 1). Each scenario assumed a population of 30 000 dogs and a campaign for which 24 000 vaccine doses were procured and distributed as follows: Central Point: 90% CP, 5% DD, 5% CVR // Capture-Vaccinate-Release: 5% CP, 5% DD, 90% CVR // Oral Rabies Vaccination: 5% CP, 5% DD, 5% CVR, 85% ORV. Summary costs for each scenario are provided in the right column; cost summary results assumed a fixed confinement population distribution of 28% confined, 48% semi-confined and 24% never confined. Average cost horizontal bars reflect the intra-method relational distribution of costs. Confinement proportions were obtained by the formulas: semi-confined = 1 - (confined × 0.66) and never confined = 1 - (confined × 0.33). Red arrows indicate the scenarios in which >70% total dog vaccination coverage is expected to be achieved. Yellow arrows indicate scenarios in which >70% free-roaming dog vaccination coverage is expected to be achieved.

introducing CVR or ORV into a CP-focused strategy was shown to improve both cost-savings and vaccination coverage, assuming a heterogeneous dog population (Fig. 4). In high-performing, experienced vaccination programs, allocating 10% of vaccines to ORV or 20% to CVR reduced the cost of the campaign by 12% and 8%, respectively, and brought the free-roaming vaccination coverage above 70%. Where vaccinator experience is limited, the only scenario examined in this study that achieved >70% free-roaming dog coverage was when >50% of the vaccines were distributed by ORV. This is largely a reflection of the limited vaccinator training that was assumed to be required for staff

distributing oral rabies vaccines. While ORV was found to result in a higher cost-per-dog-vaccinated under the majority of scenarios explored in this study, vaccination program managers should consider the long-term cost of using less-expensive methods that do not achieve effective vaccination levels in the susceptible dog population. The cost analysis in this study is only representative of the specific scenarios used to evaluate this model; any program considering incorporating alternative vaccination methods into their program should use this tool or a similar process to determine the likely cost and effectiveness of the intervention for their unique setting.

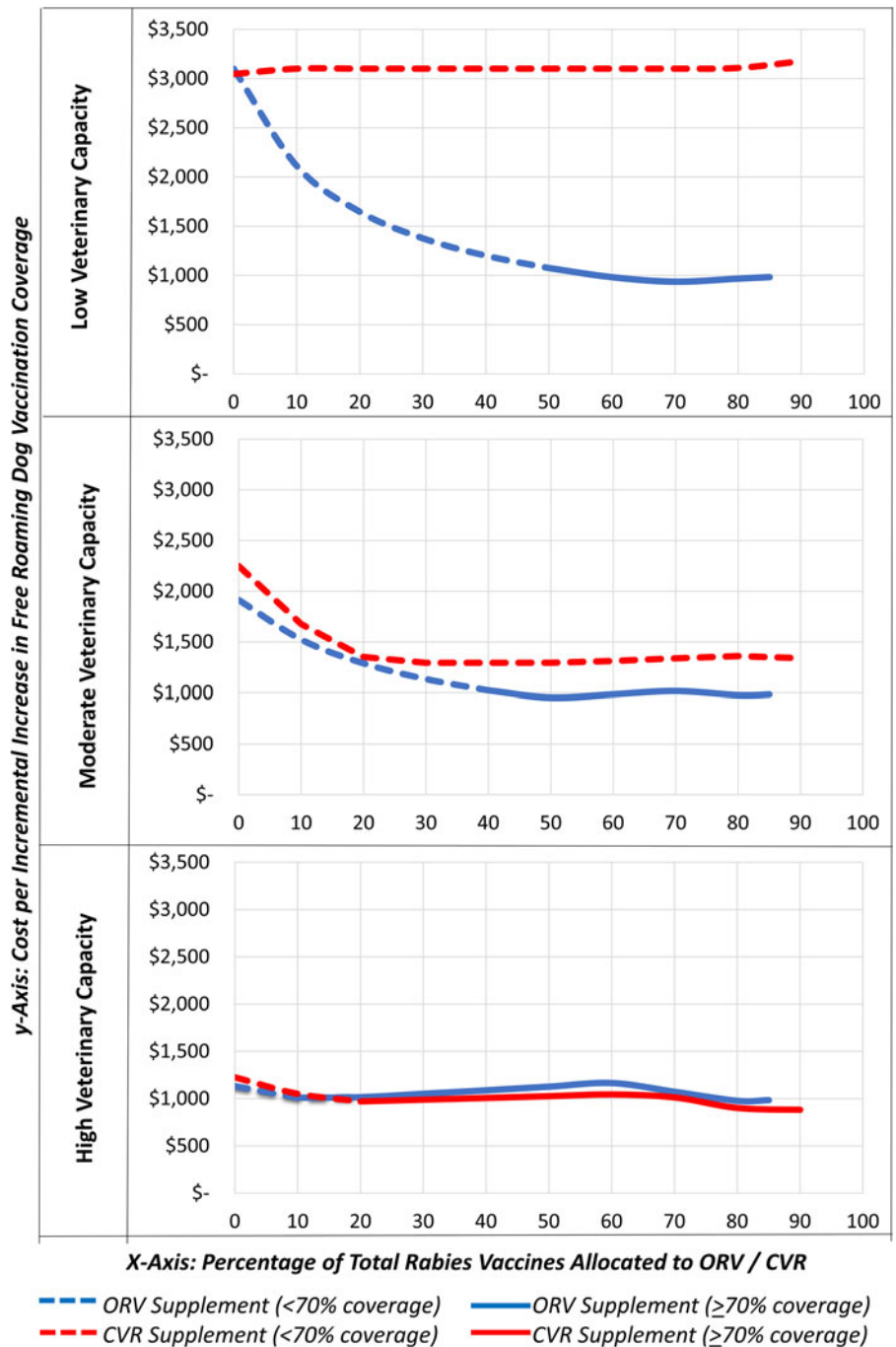


Fig. 4. Sensitivity analysis showing the impact on cost per marginal increase in vaccination coverage as vaccines are transitioned from CP to CVR and ORV strategies.

High, moderate and low veterinary capacity refers to GDREP vaccination strategy effectiveness phases of III, II and I, respectively. ORV was assumed to be at GDREP phase III levels for all three scenarios since no animal handling is required per this method. Each scenario assumed a population of 30 000 dogs of which 28% are confined, 48% semi-confined and 24% never confined. 24 000 vaccine doses were procured and distributed to strategies shown on the x-axis.

Transitioning vaccination strategies from CP towards CVR is expected to increase coverage among the free-roaming dog population, but it comes with additional costs and considerations. The majority of CVR strategy costs comes from the procurement of specialised equipment, such as nets, control-poles and protective gloves (Fig. 3). Additional costs resulted from PEP provided to vaccinators bitten in the line of duty, which was estimated to increase 2.5-fold under the CVR strategy. Transitioning from CP to an ORV strategy had similar benefits for increasing vaccination coverage among free-roaming dogs, but resulted in far fewer vaccinator bite events. The sensitivity analysis conducted in this study supports that the CP strategy should be a primary component of the most-any vaccination program, but also emphasises

the importance of utilising a mixed-methods approach to improve coverage among free-roaming dogs when vaccinator experience is limited or when there are numerous free-roaming dogs. This vaccination tool provides a method for vaccination coordinators to devise a tailored mixed-methods vaccination approach while considering costs, effectiveness and the risk of injury and possible rabies exposures to their staff.

Inter-method cost comparisons are limited in this analysis, as very little data exist for CVR and ORV campaigns. For example, WHO and OIE recommend that ORV be used only under settings where the community has been sensitised to the risks and benefits of oral vaccines and where surveillance systems are capable of detecting unintended vaccine exposures and can provide

appropriate post-exposure care [19]. Costs for these additional requirements were not considered in this study, and may limit where ORV can be appropriately incorporated into a vaccination program. Another limitation of the cost analysis presented here is the lack of analysis around the rate of dogs vaccinated per person (vaccinator capacity). Published data related to vaccinator capacity is uncommon and there are numerous external variables that can influence this value. Users of this tool should carefully consider this input parameter and recognise that it could have significant impacts on campaign costs and the expected duration of the campaign. As with any model, the predictions are only as accurate as the data provided by the user. The vast heterogeneity in dog populations and community acceptance of dog-centred health interventions may lead to scenarios that were not considered in this analysis.

Conclusion

We identified five key steps to successful vaccination of dogs and from this built a dynamic model to estimate the effectiveness of a user-defined vaccination campaign (Fig. 1). The model was validated using data and experience from multiple international vaccination campaign managers and results suggest that the model is highly accurate at estimating vaccination coverage outcomes. The sensitivity analysis highlighted how the inclusion of alternative vaccination methods under most scenarios would result in reduced costs and increased effectiveness. We probed which vaccination methods may be most appropriate under differing dog population dynamics and found that inclusion of ORV strategies into programs with less-developed veterinary infrastructure may improve the likelihood of eliminating canine rabies, but programs with high levels of animal handling experience and communities with high levels of confined dogs can achieve this goal without relying upon ORV. Further studies examining the cost-effectiveness of programs utilizing alternative vaccination methods would allow for additional validations of this model. Optimistically, use of this tool by rabies vaccination coordinators (be they national governments or local non-governmental organisations), may help to conduct more cost-effective, successful campaigns, thereby accelerating canine rabies elimination efforts.

Disclaimer. The findings and conclusions presented here are reflective of the authors and do not necessarily represent the policy of the Centers for Disease Control and Prevention.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0950268819001158>

An online version of the vaccination campaign planning tool can be found at: <https://rabiestaskforce.com/toolkit/vaxplan/>

Acknowledgements. Haiti Ministry of Agriculture and Rural Natural Development: Fleurinord Ludder, Pierre Dilius. Christian Veterinary Mission: Kelly Crowdis

Mission Rabies: Julie Corfmat, Stacy Daniella Sequeira, Gowri Yale, Paul Grossman, Jordana Burdon-Bailey, Samantha Green, Mark Green, Dananjaya Karunaratna, Waruna Hewa Vitharana

Global Alliance for Rabies Control: Daniel Stewart

Centers for Disease Control and Prevention: Sylvia Murphy

Ohio State University: Alexandra Medley

References

1. Montagu MF (1942) On the origin of the domestication of the dog. *Science* **96**, 111–112.
2. Ovodov ND *et al.* (2011) A 33,000-year-old incipient dog from the Altai Mountains of Siberia: evidence of the earliest domestication disrupted by the Last Glacial Maximum. *PLoS One* **6**, e22821.
3. Chomel BB (2014) Emerging and re-emerging zoonoses of dogs and cats. *Animals (Basel)* **4**, 434–445.
4. Fahrion AS *et al.* (2017) The road to dog rabies control and elimination—what keeps us from moving faster? *Frontiers in Public Health* **5**, 103.
5. Hampson K *et al.* (2015) Estimating the global burden of endemic canine rabies. *PLoS Neglected Tropical Diseases* **9**, e0003709.
6. Coleman PG, Fèvre EM and Cleaveland S (2004) Estimating the public health impact of rabies. *Emerging Infectious Diseases* **10**, 140.
7. World Health Organization. (2013) *WHO Expert Consultation on Rabies*. Second Report. Geneva, Switzerland: World Health Organization.
8. Tierkel ES *et al.* (1950) Effective control of an outbreak of rabies in Memphis and Shelby County, Tennessee. *American Journal of Public Health and the Nations Health* **40**, 1084–1088.
9. Shimada K (1971) The last rabies outbreak in Japan. In Y N, FM D (eds), *Rabies*. Baltimore: University Park, 11–28.
10. Bögel K (2002) Control of dog rabies. In Jackson A, Wunner W (eds), *Rabies*. San Diego, USA: Elsevier Academic Press, 429–443.
11. Dodet B *et al.* (2008) Rabies awareness in eight Asian countries. *Vaccine* **26**, 6344–6348.
12. Coleman PG and Dye C (1996) Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* **14**, 185–186.
13. Cleaveland S *et al.* (2003) A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* **21**, 1965–1973.
14. Zinsstag J *et al.* (2009) Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proceedings of the National Academy of Sciences* **106**, 14996–15001.
15. Borse RH *et al.* (2018) Cost-effectiveness of dog rabies vaccination programs in East Africa. *PLoS Neglected Tropical Diseases* **12**, e0006490. doi: <https://doi.org/10.1371/journal.pntd.0006490>.
16. Clavijo A *et al.* (2013) Gains and future road map for the elimination of dog-transmitted rabies in the Americas. *The American Journal of Tropical Medicine and Hygiene* **89**, 1040–1042.
17. Vigilato MAN *et al.* (2013) Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philosophical Transactions of the Royal Society of London B: Biological Sciences* **368**, 20120143.
18. Kayali U *et al.* (2006) Cost-description of a pilot parenteral vaccination campaign against rabies in dogs in N'Djaména, Chad. *Tropical Medicine & International Health* **11**, 1058–1065.
19. Lapiz SMD *et al.* (2012) Implementation of an intersectoral program to eliminate human and canine rabies: the Bohol Rabies Prevention and Elimination Project.
20. Wallace RM *et al.* (2017) Elimination of dog-mediated human rabies deaths by 2030: needs assessment and alternatives for progress based on dog vaccination. *Frontiers in Veterinary Science* **4**, 9. doi: [10.3389/fvets.2017.00009](https://doi.org/10.3389/fvets.2017.00009).
21. Wallace RM *et al.* (2015) Establishment of a canine rabies burden in Haiti through the implementation of a novel surveillance program. *PLoS Neglected Tropical Diseases* **9**, e0004245.
22. Dodet B (2009) The fight against rabies in Africa: from recognition to action. *Vaccine* **27**, 5027–5032.
23. Undurraga EA *et al.* (2017) Tool for eliminating dog-mediated human rabies through mass dog vaccination campaigns. *Emerging Infectious Diseases* **23**, 2114–2116.
24. Mulipukwa CP, Mudenda B and Mbewe AR (2017) Insights and efforts to control rabies in Zambia: evaluation of determinants and barriers to dog vaccination in Nyimba district. *PLoS Neglected Tropical Diseases* **11**, e0005946.
25. McNeil CS *et al.* (2015) Community rabies knowledge and pet vaccination practices after a skunk rabies outbreak in Eddy County, New Mexico. *Journal of the American Veterinary Medical Association* **246**, 1242–1247.
26. Kaare M *et al.* (2009) Rabies control in rural Africa: evaluating strategies for effective domestic dog vaccination. *Vaccine* **27**, 152–160.
27. Hatch B *et al.* (2017) Towards canine rabies elimination in South-Eastern Tanzania: assessment of health economic data. *Transboundary and Emerging Diseases* **64**, 951–958.

28. **Knobel DL *et al.*** (2005) Re-evaluating the burden of rabies in Africa and Asia. *Bulletin of the World Health Organization* **83**, 360–368.
29. **Tenzin WK and Ward MP** (2012) Human and animal rabies prevention and control cost in Bhutan, 2001–2008: the cost–benefit of dog rabies elimination. *Vaccine* **31**, 260–270.
30. **Gibson AD *et al.*** (2016) The vaccination of 35,000 dogs in 20 working days using combined static point and door-to-door methods in Blantyre, Malawi. *PLoS Neglected Tropical Diseases* **10**, e0004824.
31. **Wallace R *et al.*** (2017) The health impact of rabies in Haiti and recent developments on the path toward elimination, 2010–2015. *American Journal of Tropical Medicine and Hygiene* **97**(4_Suppl), 76–83.
32. **Lechenne M *et al.*** (2016) Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine* **34**, 571–577.
33. **Muthiani Y *et al.*** (2015) Low coverage of central point vaccination against dog rabies in Bamako, Mali. *Preventive Veterinary Medicine* **120**, 203–209.
34. **Koo TK and Li MY** (2016) A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *Journal of Chiropractic Medicine* **15**, 155–163.
35. **Shrout PE and Fleiss JL** (1979) Intraclass correlations: uses in assessing rater reliability. *Psychology Bulletin* **86**, 420–428.
36. **Tozzi AE *et al.*** (2016) Can digital tools be used for improving immunization programs? *Frontiers in Public Health* **4**, 36.
37. **Tago D *et al.*** (2017) VacciCost - A tool to estimate the resource requirements for implementing livestock vaccination campaigns. Application to peste des petits ruminants (PPR) vaccination in Senegal. *Preventive Veterinary Medicine* **144**, 13–19.
38. **Belo VS *et al.*** (2015) Population estimation methods for free-ranging dogs: a systematic review. *PLoS One* **10**, e0144830.