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Oral bait handout as a method to access roaming dogs for rabies vaccination in Goa, India: A proof of principle study

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ABSTRACT

Rabies has profound public health, social and economic impacts on developing countries, with an estimated 59,000 annual human rabies deaths globally. Mass dog vaccination is effective at eliminating the disease but remains challenging to achieve in India due to the high proportion of roaming dogs that cannot be readily handled for parenteral vaccination.

Two methods for the vaccination of dogs that could not be handled for injection were compared in Goa, India; the oral bait handout (OBH) method, where teams of two travelled by scooter offering dogs an empty oral bait construct, and the catch-vaccinate-release (CVR) method, where teams of seven travel by supply vehicle and use nets to catch dogs for parenteral vaccination. Both groups parenterally vaccinated any dogs that could be held for vaccination.

The OBH method was more efficient on human resources, accessing 35 dogs per person per day, compared to 9 dogs per person per day through CVR. OBH accessed 80% of sighted dogs, compared to 63% by CVR teams, with OBH accessing a significantly higher proportion of inaccessible dogs in all land types. All staff reported that they believed OBH would be more successful in accessing dogs for vaccination. Fixed operational team cost of CVR was four times higher than OBH, at 127 USD per day, compared to 34 USD per day. Mean per dog vaccination cost of CVR was 2.53 USD, whilst OBH was 2.29 USD. Extrapolation to a two week India national campaign estimated that 1.1 million staff would be required using CVR, but 293,000 staff would be needed for OBH.

OBH was operationally feasible, economical and effective at accessing the free roaming dog population. This study provides evidence for the continued expansion of research into the use of OBH as a supplementary activity to parenteral mass dog vaccination activities in India.

1. Introduction

The rabies virus remains endemic across much of Africa and Asia, with India estimated to suffer one third of the global burden, costing the country an estimated 20,000 human lives and 2.3 billion USD annually [1,2]. Efforts to improve access to human post exposure prophylaxis are underway to reduce human rabies deaths, however the virus is maintained in the free-roaming dog population reservoir.

Mass dog vaccination is advocated by the WHO and OIE as a cost-effective method of rabies elimination, with many examples of rapid decline in both canine and human rabies deaths following annual vaccination of 70% of the dog population [3,4]. Nevertheless, examples of large scale dog vaccination activities in India remain scarce, attributing for less than 0.5% of the estimated economic burden from the disease [1].

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The dog population can be accessed for parenteral rabies vaccination through a variety of practical approaches including static point (SP), door-to-door (DD) and catch-vaccinate-release (CVR) methodologies. SP-only approaches have the potential to achieve 70% coverage in settings where the community is engaged with the vaccination campaign and a high proportion of the roaming dog population can be brought to SP vaccination clinics by their owners [5]. In areas where 70% is not achieved through the SP approach, the addition of DD vaccination teams moving house-by-house makes it possible to increase coverage by vaccinating dogs that can be handled by their owners, but were not brought to SP clinics [5,6]. The SP and DD approaches rely on owners presenting their dogs for parenteral vaccination and their success at scale has only been reported in Latin America where most dogs are responsibly owned [4]. SP and DD approaches are less likely to achieve adequate coverage in regions with a high proportion of inaccessible roaming dogs and so the addition of more intensive methods is required to consistently achieve over 70% vaccination coverage, as is the case in many parts of Asia [7–9]. The 'catch-vaccinate-release' (CVR) approach involves roaming vaccination teams using butterfly nets to catch and restrain dogs for parenteral vaccination before marking and release [10]. A combination of DD and CVR methods have been reported to achieve adequate coverage in urban settings [10], however there are limited examples where this approach has been successfully applied on a scale that could expand to a national level in India.

Mission Rabies, an international NGO working with international partners and local governments to develop effective approaches to rabies control, has been working in Goa State, India, since 2013. In 2017 the campaign vaccinated over 97,000 dogs throughout the state using a combination of DD and CVR vaccination approaches. Although the use of teams catching dogs with nets can achieve high coverage [10], their widespread sustained use has several limitations, including difficulty catching dogs in open areas, roaming dogs becoming increasingly cautious of net catching teams with repeated use and the requirement for a large number of skilled catchers per vaccination team. Therefore, there is a need for investigation of alternative approaches which can vaccinate free roaming dogs at high coverage.

Oral rabies vaccination is used in Europe and North America to control rabies in wildlife reservoir species [11,12]. Oral vaccination of dogs, as a supplementary tool to parenteral vaccination, has been shown to increase dog vaccination coverage in various field studies, especially of ownerless and poorly supervised owned dogs [13–16]. The use of the oral bait 'handout' method (OBH) involves offering a bait to owned and unowned dogs that cannot be held for parenteral vaccination. Any bait or remnants that are not consumed are recollected by the vaccination staff and disposed of safely [17]. Studies to assess OBH have been conducted in settings in the Americas, Africa, Europe and Asia [16,18–22], however its use has not been studied in India and no studies have compared the operational practicalities with CVR methods. WHO and OIE advocate for the evaluation of this approach as a supplementary measure to increase vaccination coverage in areas where a sufficient proportion of dogs cannot be accessed for parenteral vaccination [17,23,24].

This study compares two vaccination approaches for inaccessible dogs, CVR and OBH, on the basis of effectiveness at accessing the target population for vaccination, operational feasibility and cost. Both approaches were used in conjunction with parenteral vaccination of dogs that could be held for vaccination. There are no oral rabies vaccines (ORVs) currently licensed for use in India and so no ORV was used in this study, instead a prototype bait containing an empty PVC sachet was used to assess the OBH method. This study aimed to explore the proportion of dogs that could be accessed by each method, with further optimization of the bait construct required.

2. Methods

2.1. Study site

Goa is one of India's smallest states, with a human population of 1.5 million [25]. The state has a growing urban population (62% of total population) and tourism is a significant contributor to the economy. The state is divided into two districts, North and South, which are further divided into a total of 12 administrative regions (Talukas). The Government of Goa has been supporting Mission Rabies to intensify mass dog vaccination and rabies education activities in Goa since 2015. The campaign now vaccinates approximately 97,000 dogs throughout the state on an annual basis and delivers rabies education classes to over 150,000 children in schools every year.

The study was conducted over two weeks in February 2018. The sampling frame was dogs within the Ponda Taluka due to it being a convenient location alongside the ongoing vaccination schedule at the time of the study and also away from the coast, where dog populations are influenced by fluctuations in tourism throughout the year. The Taluka was stratified by land type (urban, sub-urban, village housing, sparse housing and forest-agriculture) according to appearance on Google satellite images (Fig. 1, Section 3 in "Supplementary materials") [6]. Forest areas were omitted from the study due to the absence of dogs (known from previous campaigns). The remaining strata were divided into working zones based on subjective assessment of the Google satellite images to produce an area that would take the vaccination teams 1–3 days to vaccinate. Working zones were randomly assigned to either CVR or OBH study arms within each stratum.

Permission for the study was granted by the Department of Animal Husbandry & Veterinary Services, Government of Goa. Dogs were parenterally vaccinated in accordance with the Memorandum of Understanding between Mission Rabies and the Government of Goa as part of a non-research public health campaign. Ethics approval was provided by University of Edinburgh R(D)SVS Veterinary Ethical Review Committee (Reference number 113.18).

2.2. Comparison of CVR and OBH

Four vaccination teams were included in the study, with all teams having approximately the same levels of experience and ability. Two teams performed CVR for the first week, followed by OBH the second week and the other two teams performed OBH in the first week followed by CVR in the second week. All staff had received pre-exposure rabies vaccination.

Because no ORV was used, all OBH regions were revisited immediately following the study to catch, vaccinate and mark roaming dogs that were not already marked as parenterally vaccinated in accordance with the standard campaign protocol.

For both study arms, dogs that could be handled either by an owner or by the team were manually held and vaccinated parenterally. An inaccessible dog was defined as any dog which could not be readily handled and restrained for parenteral injection of vaccine. In the CVR study arm, an attempt was made to catch inaccessible dogs using nets, to enable parenteral vaccination. In the OBH study arm, inaccessible dogs were offered a bait (Fig. 2). An information leaflet containing an explanation of the study in English and Hindi, with contact details for further information, were distributed to members of the public by all teams (Section 4 in "Supplementary materials"). In cases where owners refused vaccination, were not available to give consent or reported that the dog

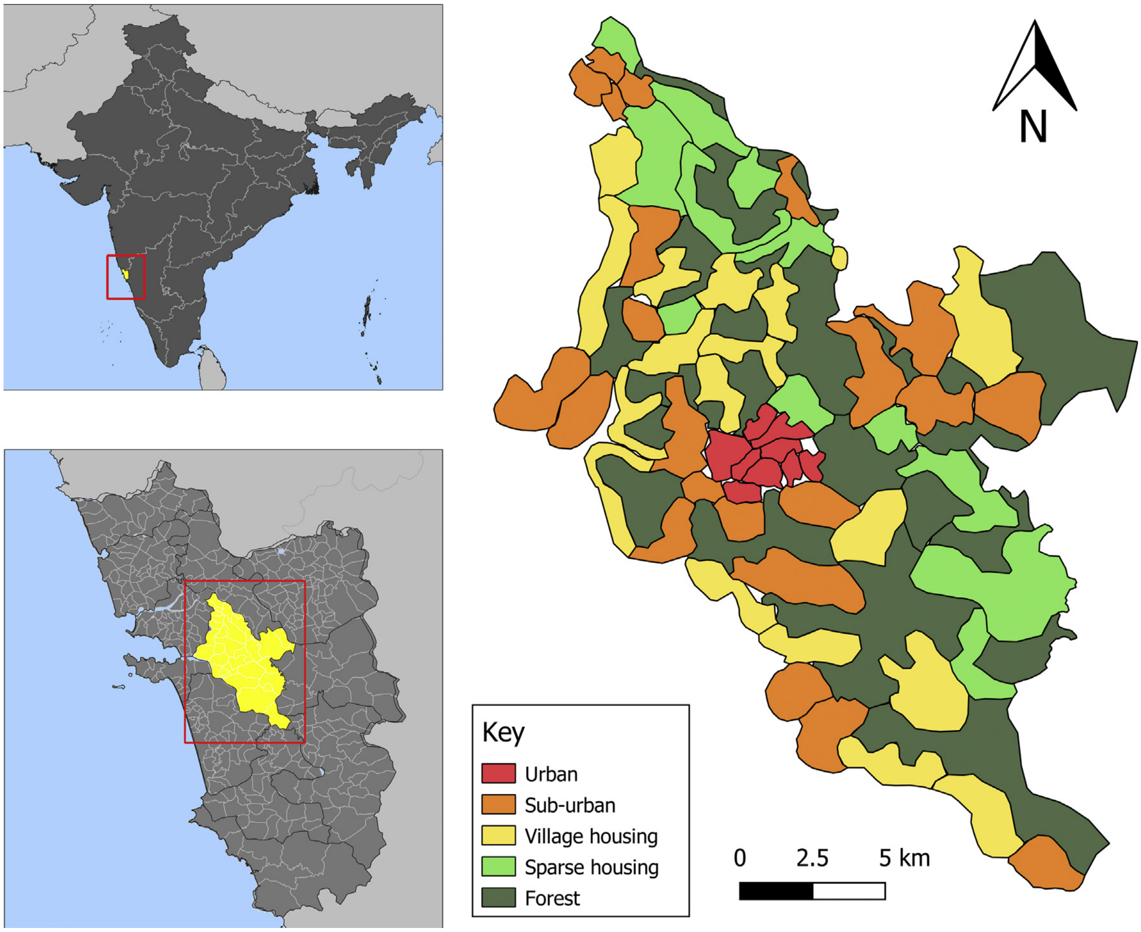

Fig. 1. Map of the Ponda Taluka showing working zones coloured by land type. Inserts show maps of India and Goa state indicating region of Ponda Taluka (red boxes). "Forest" regions were not included in the sampling frame for the study due to the absence of dog populations in these areas. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

was already vaccinated, the dogs were recorded as sighted, but were removed from analysis in both arms as they were not available to attempt vaccination in either group.

Existing methods of estimating coverage in CVR, by marking all vaccinated dogs and conducing post-vaccination dog sight surveys to count the proportion of marked sighted dogs could not be used to assess OBH because it was not possible to physically mark all dogs consuming baits. The use of biomarkers within baits has been described to evaluate coverage [26–28], however this was not considered acceptable for use in the dogs of unknown ownership status in this study.

2.3. Oral Bait Handout method (OBH)

Empty vaccine capsules made of PVC ($3\ \text{cm} \times 6.5\ \text{cm}$) and sealed with aluminium foil were used to replicate the mechanical presence of the capsule in the bait. The capsule was placed inside a collagen casing with a section of blanched pig skin to encourage chewing (Section 1 in "Supplementary materials"). The capsule was tied at both ends and frozen until the morning of distribution. Each morning baits were packaged into zip-lock bags and transported in cooler boxes. At the start of the vaccination session, a sachet of commercial meat dog food and gravy (Chicken & Vegetable 100 g pouches) was poured into each zip-lock bag to coat all 15 baits in each bag.

OBH teams were comprised of two people riding a two-wheel scooter. Roles within the OBH teams were a team leader, responsible for vaccinating dogs parenterally and distributing baits, and one assistant, who was responsible for navigation, data entry and public communication. The total training period was a full day the day before beginning OBH vaccination which consisted of a verbal training and afternoon supervised practical session. Where an owned dog could not be held for vaccination, verbal consent was requested to offer a bait. They were informed that their dog had not been vaccinated and that teams would return with equipment to help vaccinate their dog within the same week. Where accessible, all puppies were parenterally vaccinated, however puppies under approximately 5 kg that could not be caught were not offered a bait.

2.4. Catch Vaccinate Release method (CVR)

CVR teams contained seven people travelling in a supply vehicle [10]. Roles within the team were one team leader, one assistant, one driver and four animal handlers/ butterfly-net catchers (Section 1 in "Supplementary materials"). The CVR method requires at least four catchers working as a team to capture dogs in nets. The process is dynamic and requires physical strength, agility and teamwork as well as an understanding of dog behaviour and movement. All four teams were experienced in the CVR method and are employed by Mission Rabies to conduct this method across Goa state throughout the year. The mean number of months working experience in the CVR method per team member was 14 months. CVR teams received the same briefing as in the OBH

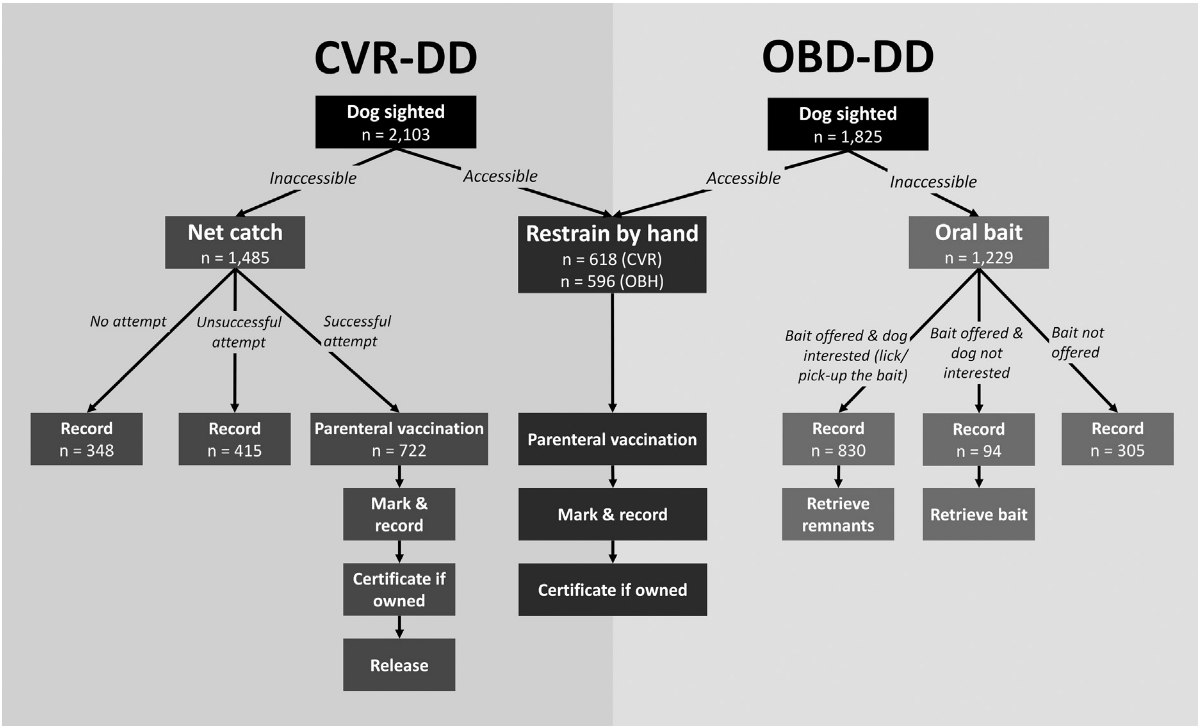

Fig. 2. Flow diagram for action taken for sighted dogs in each intervention arm. CVR = Catch-vaccinate-release, DD = Door-to-door, OBH = oral bait handout. Dogs which were reported by the owner as already vaccinated or refused vaccination were not included in the counts or analysis for either group.

training and were given training on the study data collection protocol, followed by an afternoon of supervised vaccination.

2.5. Data collection

Both study arms entered data about every dog sighted in the WVS App, a tailor made smartphone-web system designed to direct vaccination teams and monitor campaign outputs [29]. The data structure is summarised in Section 2 of "Supplementary materials", however in brief, the dataset for every dog sighted included (i) whether the dog was vaccinated and if not, why, (ii) for dogs not parenterally vaccinated by hand, whether the alternative method was attempted. For OBH, information about bait acceptance, swallowing and capsule/bait retrieval were also recorded. For the purpose of the evaluation of the OBH method's potential, a dog was considered to have been 'mock vaccinated' by the bait if the dog made direct contact through licking or consuming the bait, with the assumption that the rudimentary bait used in this study would be optimised for palatability to achieve vaccination of these dogs. Throughout the manuscript references to the number of dogs 'vaccinated' includes those mock vaccinated using the bait constructs. The ownership status, confinement, sex, neuter status, age and health of every dog vaccinated was also recorded.

2.5.1. Spatial analysis

Convex Hull polygons were drawn around the GPS locations within each working zone recorded in each vaccination session using QGIS [30]. Anomalous GPS locations outside of the general working area resulting from variation in GPS signal were removed based upon time stamp and GPS accuracy records available for each entry. The polygon boundaries were adjusted to the nearest border of the assigned working zone so that the final polygon represented the proportion of the working zone that had been covered (Section 5 of "Supplementary materials"). The area of polygons was used to calculate the density of dog vaccinations and sightings by each team and land type.

2.5.2. Statistical analysis

Data were exported from the WVS app database in CSV format. Further analysis was then performed in R statistical software environment [31].

Multivariable logistic regression was used to estimate the difference in vaccination coverage achieved by each arm of the study adjusting for other factors including land type and team. Three different models were built; the first estimating the proportion of total dogs vaccinated, the second estimating the proportion of inaccessible dogs vaccinated (dogs unable to be vaccinated by hand) and the third estimating the proportion of sighted dogs vaccinated by hand. All predictors were considered for inclusion in the model and all possible combinations of interaction between predictors. The model with lowest Akaike information criterion (AIC) was chosen as the final model.

To estimate the difference between the numbers of dogs vaccinated per hour a multivariable quasipoisson model was used. All combinations of predictor variables and interactions were considered using the model averaging approaches implemented in the package *MuMIn* [32]. The model with the lowest quasi-likelihood AIC (QAIC) was chosen as the final model. Estimated marginal means [33] of the overall predicted vaccination coverage/rate of dogs vaccinated by each vaccination method and for each land type were calculated using the *emmeans* package [34]. Results were plotted using package *ggplot2* [35]. Model selection procedures for each model are shown in (Section 6 in "Supplementary materials").

Given variable reported rates of seroconversion in dogs consuming ORV, estimates were calculated to compare the proportion of sighted dogs expected to seroconvert following the two methods. The proportion of dogs estimated to seroconvert from parenteral vaccination was 98% [36], whilst scenarios for seroconversion in 60, 70, 80 and 90% of dogs that accessed bait by the OBH method were included [16,37].

2.5.3. Cost comparison

All operational costs associated with implementing each method were recorded based on expenditure during the study or review of monthly project expenditure. This figure does not include costs of post-exposure rabies prophylaxis for staff, training, publicity, community awareness activities, bite surveillance, cold chain storage or vaccine transport. Costs reported in this paper are stated in US dollars at a currency exchange rate of 72.2 rupees per dollar. Operational costs were defined as either fixed or variable costs. Fixed costs were constant regardless of the number of dogs vaccinated (e.g. salaries, staff pre-exposure vaccination, vehicle purchase, equipment). In contrast, variable costs changed with the number of dogs vaccinated (e.g. vaccine cost, needles, syringes). Itemised fixed costs that span months or years were converted into a daily operational cost (Section 8 of Supplementary Materials). Variable costs were calculated per vaccine administered, at a parenteral vaccine dose cost of 0.45 USD (32 Rupees), 0.05 USD per parenteral dose for consumable equipment (needle, syringe, vaccine certificate) and 2.77 USD (200 Rupees) per oral bait dose delivered. The mean daily variable cost was calculated for each method using the parenteral and oral vaccine per-dose costs, multiplied by the mean daily doses of each vaccine type administered.

$$\text{Mean variable daily cost} = (\text{Per}\textit{dose parenteral vaccine cost} \times \textit{mean parenteral doses per day}) + (\textit{per dose oral vaccine cost} \times \textit{mean oral vaccine doses per day})$$

The cost per vaccine administered was then compared for each approach using the following formula:

$$\text{Cost per vaccine administered} = \left(\frac{\text{Fixed daily cost} + \text{Mean variable daily costs}}{\textit{Mean total vaccinations administered per team per day}}\right)$$

2.5.4. Staff survey

A survey to explore the opinions of staff members was conducted immediately following completion of the field study, consisting of a face-to-face questionnaire with each Team Leader and Assistant (Section 9 in "Supplementary materials").

2.5.5. Estimation of scalability

The approximate number of teams and staff that would be required to vaccinate 50,000 dogs (district level estimate from historic data) and 100 million dogs (national level estimate used in previous studies [38,39]) was estimated for two campaign durations; a two week period (10 working days) or a one year period (288 working days). The number of team-days required was calculated by dividing the number of dogs to be vaccinated by the mean vaccinations per team per day for each method. This was divided by the number of working days in the campaign duration to give the number of teams that would be required. The total number of staff required was calculated by multiplying the number of teams by the number of staff in each method (2 per team for OBH, 7 per team for CVR). The estimate was compared with current project structure in Goa (three CVR teams, approximately 21 staff vaccinating over a 12 month period) to assess reliability at the district level.

Table 1
Table of aggregate and means from team-day data by method and land type. The mean figures refer to the proportions for each team-vaccination-day averaged over method and land type. Calculations of the total row refer to the proportions for each team day averaged by method. Numbers in brackets indicate 95% confidence intervals.

Land type	Method	Team vacc days	Total available dogs sighted	Total dogs vacc*	Total dogs hand vacc	Total dogs alternate method vacc (bait/net)*	Mean daily output (vacc/team/day)*	Mean proportion sighted dogs vacc (%)*	Mean sighted dogs vacc by hand (%)	Mean area covered (km^2)	Mean sighting density ($dogs/km^2$)	Mean vacc density ($vacc/km^2$)*	Mean vacc rate (vacc/hour)*
Urban	CVR	5	523	342	134	208	68	64	24	0.38	345	189	13
	OBH	4	407	319	71	248	80	79	18	0.45	259	187	13
Sub-urban	CVR	8	793	453	209	244	57	59	27	1.39	94	51	12
	OBH	8	722	548	261	287	69	79	40	1.19	121	80	14
Village housing	CVR	7	563	408	221	187	58	72	41	1.46	65	43	11
	OBH	6	521	410	193	217	68	81	38	1.48	98	67	12
Sparse housing	CVR	3	224	137	54	83	46	61	25	2.95	36	21	9
	OBH	4	175	149	71	78	37	85	42	3.07	25	18	7
Total	**CVR**	**23**	**2103**	**1340**	**618**	**722**	**58**	**64**	**30**	**1.39**	**132**	**75**	**11**
(95% CI)							**(49–67)**	**(60–68)**	**(26–35)**	**(0.95–1.84)**	**(76–188)**	**(43–106)**	**(10–13)**
	OBH	**22**	**1825**	**1426**	**596**	**830**	**65**	**80**	**35**	**1.47**	**123**	**85**	**12**
							(56–74)	**(76–85)**	**(27–44)**	**(0.83–2.13)**	**(80–166)**	**(55–115)**	**(11–13)**

* Vaccination figures include dogs that were 'mock vaccinated' by accepting a bait, however no oral rabies vaccine was used in the study.

3. Results

In total 45 working zones were included in the study (23 CVR, 22 OBH) in which teams sighted a total of 3,928 available dogs (Table 1). A further 467 dogs were sighted, but were not eligible for attempted vaccination. The mean estimated by the regression model was 10.43 and 11.48 vaccinations per team per hour for CVR and OBH respectively (Section 6 in Supplementary Materials), equating to 1.5 vaccinations per person per hour for CVR and 5.7 vaccinations per person per hour for OBH. For a working day consisting of 6 h of vaccination time (1 h travel to/from vaccination site), the CVR teams vaccinated 63 dogs per day as compared to OBH teams vaccinating 69 dogs per day. Given the difference in team size for each approach, the CVR method results in 9 dog vaccinations per person per day, compared to 35 dogs per person per day for OBH. Teams using the OBH method had a higher vaccination output per hour compared to CVR in all land types, however this difference was not statistically significant.

OBH teams were able to access a significantly higher proportion of sighted dogs for vaccination than CVR teams. The predicted proportion of sighted dogs vaccinated, adjusted for other factors, was 63% (CI 61–66) for CVR and 80% (78–82) for OBH ($P < 0.001$) (Fig. 3A). Estimates for the proportion of dogs that would seroconvert for the two methods are given in Section 7 of "Supplementary materials".

The proportion of sighted dogs that could be captured by hand was similar for both methods after adjusting for other factors, at 30% (CI 27 – 32) for CVR and 31% (CI 29 – 34) for OBH. Of all dogs that were 'vaccinated' by each method, the mean proportion that could be held for parenteral vaccination was 47% for CVR and 43% for OBH (Table 1).

Of dogs that could not be restrained by hand for parenteral vaccination (inaccessible dogs), OBH was able to access 69% (CI 66–72) through baits, as compared to 46% (CI 43–49) by CVR. The difference between the proportion of inaccessible dogs 'vaccinated' was significantly different between methods for each land type (Fig. 3B).

Overall OBH teams vaccinated a larger area than CVR at 1.47 km^2 compared to 1.39 km^2 and at a higher vaccination density at 85 dogs per km^2 compared to 75 dogs per km^2 by CVR (Table 1).

In total, 924 baits were dropped during the study. Of the 94 baits that were not picked up by dogs, only one (0.1% of all baits) could not be retrieved. Of the 830 baits that were picked up by dogs, the capsules of 133 could not be retrieved because the dog carried it away, of which the perforation status of 124 baits was unknown. This represents 13% of all baits distributed that were carried away by dogs to an unknown location and it is unknown whether the capsule was perforated or swallowed.

The number of people bitten per day was recorded for 17 of 22 vaccination sessions for CVR and 19 of 22 sessions for OBH. Three staff members were bitten during CVR work, and there were no bites reported from OBH teams.

3.1. Staff survey

Eight staff (team leader and data collector for each of the four teams) were interviewed. The full responses to questions are included in Section 9 of "Supplementary materials". All eight staff responded that they believed that the OBH method could reach more dogs than CVR. Seven staff responded that they preferred the OBH approach, with all seven giving the reason that more dogs can be reached and three additionally reporting the method is easier. The one staff member who preferred the CVR method gave the reason that there is less fear of dog bite when using the nets.

3.2. Cost

The costs associated with the two methods are summarised in Table 2. The itemised breakdown of fixed costs is provided in Section 8 of "Supplementary materials". The mean cost per vaccine delivered through CVR teams was 2.53 USD, whilst per dog vaccinated through OBH teams was 2.29 USD (Table 2). The CVR method had high fixed costs at 127 USD per day, representing 80% of the mean cost per dog vaccinated, but low variable vaccine costs (Fig. 4A). The fixed cost of running an OBH team was 34 USD per team per day, almost a quarter of the cost of CVR, however variable costs were considerably higher due to the cost of ORV (Fig. 4A). The high fixed cost of CVR resulted in increasing per dog vaccinated costs in lower density areas where fewer dogs were vaccinated each day, whereas OBH costs rose in areas with a greater number of inaccessible dogs (Fig. 4B).

3.3. Extrapolation of resources to a district and national vaccination campaign scale

Extrapolating the pilot study vaccination efficiencies for each method to district and national dog vaccination campaign sizes revealed large differences in the manpower and vehicle require-

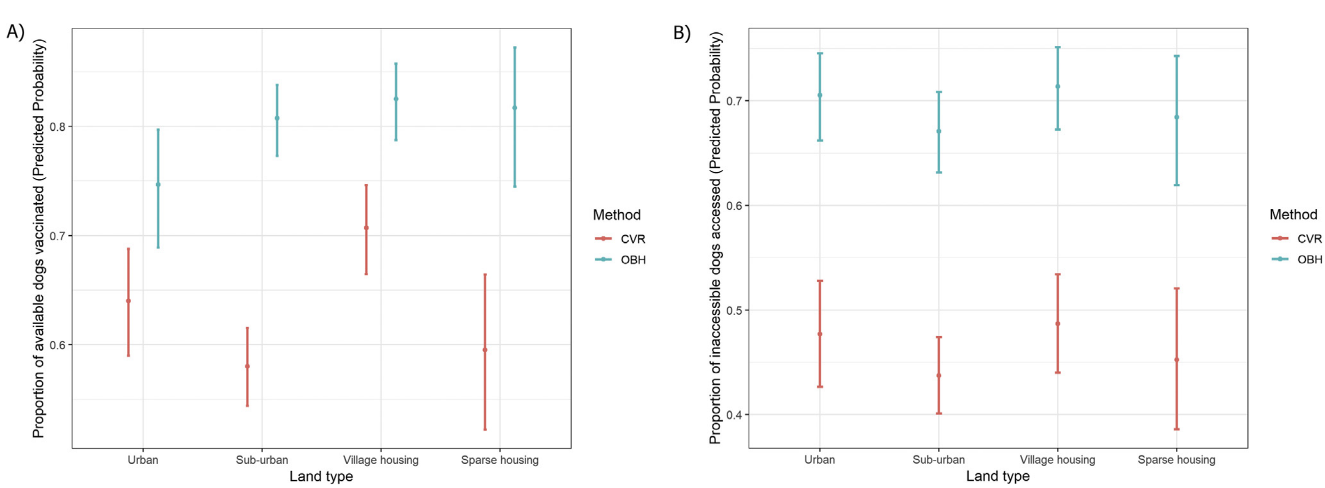

Fig. 3. (A) Point graph of predicted proportion of sighted dogs vaccinated for each method by land type. Error bars show 95% confidence intervals. (B) Point graph of predicted proportion of inaccessible dogs that could be accessed for vaccination using the alternative method (oral bait or net catching) for each method by land type. Error bars show 95% confidence intervals.

Table 2
Table showing calculation of cost per dog 'vaccinated' by land type (USD). Numbers in brackets for totals are the confidence interval calculated using the 95% confidence limits for the rate of vaccination for each method.

Land type	Method	Parenteral			Oral			Total variable cost/team	Fixed cost	Total cost/team/day	Total vacc/day	Per dog cost
		Parenteral cost/ dose	Parenteral doses/day	Total parenteral cost/team/day	Oral cost/dose	Oral doses/ team/day	Total oral cost/team/day					
Urban	**CVR**	0.5	75.23	37.57	2.77	0.00	0.00	37.57	127.113	164.67	75.23	2.19
	OBH	0.5	18.80	9.39	2.77	64.04	177.40	186.78	34.41	221.19	82.84	2.67
Sub-urban	CVR	0.5	70.49	35.20	2.77	0.00	0.00	35.20	127.11	162.31	70.49	2.30
	OBH	0.5	37.54	18.75	2.77	40.08	111.02	129.77	34.41	164.18	77.62	2.12
Village housing	CVR	0.5	63.50	31.71	2.77	0.00	0.00	31.71	127.11	158.82	63.50	2.50
	OBH	0.5	32.14	16.05	2.77	37.79	104.68	120.73	34.41	155.14	69.93	2.22
Sparse housing	CVR	0.5	45.53	22.74	2.77	0.00	0.00	22.74	127.113	149.84	45.53	3.29
	OBH	0.5	24.93	12.45	2.77	25.20	69.82	82.27	34.41	116.67	50.13	2.33
TOTAL	**CVR**	**0.5**	**62.57 (57.3–68.3)**	**31.25 (28.6–34.1)**	**2.77**	**0**	**0**	**31.25 (28.6–34.1)**	**127.11**	**158.36 (155.7–161.2)**	**62.57 (57.3–68.3)**	**2.53 (2.36–2.72)**
	OBH	**0.5**	**29.83 (27.5–32.4)**	**14.90 (13.7–16.1)**	**2.77**	**39.08**	**108.24**	**123.14 (113.3–133.7)**	**34.41**	**157.55 (147.7–168.1)**	**68.90 (63.4–74.8)**	**2.29 (2.25–2.33)**

ments (Table 3). To vaccinate 50,000 dogs in two weeks using CVR would require 560 staff, compared to 146 staff using OBH, whereas at the estimated national level would require 1.1 million staff using CVR and 293,000 staff for OBH. The extrapolation accurately estimated the current campaign structure at district level.

4. Discussion

This study reports the first field evaluation of a combined door-to-door parenteral vaccination and oral bait handout (OBH) method for accessing dogs on a large scale for rabies vaccination in India. OBH was superior to CVR in terms of the proportion of roaming dogs accessed for vaccination, mean cost per dog vaccinated and human resource efficiency.

Under the direction of the Government of Goa, there has been success through the current state-wide mass dog vaccination campaign using catch-vaccinate-release and door-to-door vaccination, however the method has limited potential for sustained national implementation. The large team sizes required in the CVR method resulted in low per-person vaccination efficiencies (9 vaccinations/person/day), in contrast to the OBH method, which was able to vaccine three times as many dogs per person per day (35 dogs/person/day). When extrapolating these methods to the district and national scale this would result in a dramatic difference in the human resource requirement of the campaign [39]. A national two week campaign using CVR would require and estimated 1.1 million staff and 160,000 trucks, compared to 300,000 staff and 150,000 scooters using OBH. In 2015 there were reported to be 70,767 veterinarians and veterinary *para*-professionals in India, highlighting that an intensive short campaign using either method would need additional staff to be trained [40]. Experience from multi-national dog vaccination efforts in Latin America demonstrate a number of benefits to synchronizing large campaigns over short timeframes, such as combining resources from multiple government and NGO sectors and in maximising public/political awareness through mass media [41], however this would be infeasible with the CVR method. From a logistical and human resource perspective, OBH would be a more feasible approach for conducting mass dog vaccination over a short timeframe at the national scale.

The mean operational cost per vaccine delivered for the CVR and OBH methods was 2.53 USD and 2.29 USD respectively, however this varied with land type. The high fixed daily operating cost of each CVR team at 127 USD meant that acceptable cost-efficiency relied on a high number of dogs being vaccinated every day. In low density areas the CVR cost per dog vaccinated rose to 3.29 USD in contrast to 2.33 USD for OBH. The higher vaccine cost of ORV in comparison to high quality parenteral vaccine increases the cost of OBH in regions where large numbers of inaccessible dogs require vaccination by ORV. The only other study evaluating the cost of different methods was conducted in Tunisia, comparing door to door or central point distribution of bait to dog owners and transect line distribution [42], which would not be considered acceptable methods of bait distribution in Goa. The cost per dog vaccinated for both methods here are comparable to reports from other mass dog vaccination campaigns in Africa ranging from to 1.73 to 7.3 USD, however these campaigns only accessed owned dogs that could be handled for parenteral vaccination [43–45].

The OBH method of bait distribution has a number of advantages to public safety and campaign efficiency over other methods such as distributing to dog owners to administer and the wildlife-immunisation model (WIM). A study in Tunisia distributed baits to dog owners at central collection points [42], however this approach could not be applied in most countries due to the unacceptable risk of human exposure to the vaccine. Additionally,

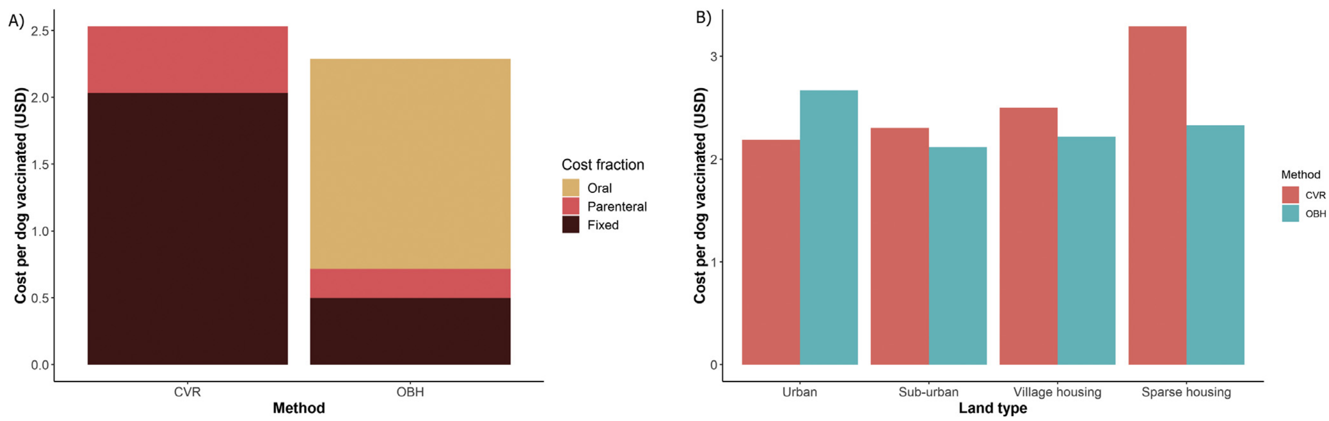

Fig. 4. (A) Graph showing a breakdown of mean Fixed and Variable (oral/parenteral) cost per dog vaccinated based on the mean number of dogs vaccinated per team per day in each method. (B) Bar graph of cost per dog vaccinated by land type and method in USD.

Table 3
Extrapolation of mean team 'vaccination' output for CVR and OBH methods to the district level in Goa.

Approx. Scale	Method	Campaign duration	Dog vacc	Number staff per team	Vacc/ team/day	Working days	Number of team days	Number of teams	Number teams (LCI)	Number teams (UCI)	Total staff	Total Staff (LCI)	Total Staff (UCI)
District	CVR	2 weeks	50,000	7	62.6	10	799	80	74	88	560	518	616
District	ORV	2 weeks	50,000	2	68.9	10	726	73	67	79	146	134	158
District*	CVR*	1 year*	50,000*	7*	62.6*	286*	799*	3*	3*	4*	21*	21*	28*
District	ORV	1 year	50,000	2	68.9	286	726	3	3	3	6	6	6
National	CVR	2 weeks	101,067,346	7	62.6	10	1,615,157	161,516	147,975	176,297	1,130,610	1,035,825	1,234,079
National	ORV	2 weeks	101,067,346	2	68.9	10	1,466,815	146,682	135,034	159,334	293,363	270,068	318,668
National	CVR	1 year	101,067,346	7	62.6	286	1,615,157	5647	5174	6165	39,532	36,218	43,155
National	ORV	1 year	101,067,346	2	68.9	286	1,466,815	5129	4722	5572	10,257	9444	11,144

* Indicates the estimated number of teams and manpower requirement for the method and timeframe that is currently being conducted in Goa across two districts (therefore double the capacity stated here).

parenteral vaccination should be prioritized for these owned dogs whose owners can hold them for injection [17,24]. The use of WIM may be of use for vaccination of dogs that cannot be approached, which is often the case in garbage dumps [18,46,47]. The widespread use of the WIM would be unfavourable in residential areas, particularly due to the risk of children coming into contact with baits and the increased risk of uptake or re-distribution by non-target species such as crows, rats and cats [48]. Coverage achieved by OBH in this study is comparable with studies conducted elsewhere [19–22], likely due to roaming dogs generally being accustomed to the presence of humans, albeit not comfortable enough to be held.

Estimation of vaccination coverage using oral bait approaches is challenging because the dogs cannot be easily marked and therefore conventional post-vaccination surveys counting marked dogs are not possible [6,10]. In the current study the recording of all dogs sighted enabled estimation of the proportion of all dogs sighted that could be vaccinated, however this does not equate to the vaccination coverage in the population. The proportion of sighted dogs vaccinated may be influenced by the likelihood of sighting dogs between the two methods. Many staff reported that dogs are more likely to run away from the net catching teams and alert dogs in the area by barking, therefore potentially making it less likely for dogs that could not be vaccinated to be sighted. This may have resulted in over-estimating the proportion of vaccinated dogs in the CVR group in contrast to OBH teams, which did not carry nets, and so were less likely to alert dogs prior to sighting. In contrast, OBH teams reported that dogs were often attracted to the baits and would gather around them. This not only has benefits in the chances of vaccinating dogs, but would also be of benefit to the sustainability of repeat vaccination campaigns.

Parenteral vaccination will continue to be the primary choice for animals that can be readily handled because of the greater control over the certainty of administration and high rates of protection in dogs of different ages and immunocompetence [49]. With the use of live-modified or live-attenuated oral rabies vaccines, lower rates of immunoconversion are often seen [37]. A field study of oral vaccination using SPBN GASGAS reported that 78% of dogs that consumed the bait had detectable rabies binding antibodies measured by blocking enzyme linked immunosorbent assay (ELISA) [16]. Challenge studies have shown high levels of protection using a number of oral rabies vaccines [37,50–52], and that evaluation of the presence of rabies binding antibodies using ELISA is likely to be a better predictor of immunity in vivo than serum neutralization tests [53]. Estimates of possible proportion of sighted dogs successfully seroconverting following the two methods in this study remained comparable even at rates as low as 60% of dogs accessing ORV.

Ultimately the cost-effectiveness of a campaign hinges on the successful elimination of rabies, and for this to occur it must be feasible to achieve sustained, high vaccination coverage across land types [54]. OBH was able to consistently access a higher proportion of inaccessible dogs for vaccination across land types in comparison to CVR (Fig. 3B). The challenges in catching dogs through CVR in open areas, as well as dogs becoming fearful of nets over time, creates the potential for pockets of low vaccination coverage and therefore regions where sustained endemic transmission may occur [55].

The impact on the welfare and safety of the dogs, staff and general public as a result of any intervention must be considered and weighed against the consequence of not conducting the intervention. Action to minimise the risk of injury or suffering to these groups should be taken at every opportunity. Both CVR and OBH methods present potential risks due to the fact that dogs are often roaming freely in public areas and can behave unpredictably, however this must be weighed against the suffering that would be prevented for future generations through rabies virus elimination. The selection of an ORV that is safe in both target and non-target species, including humans, is essential [56]. More than 270 million doses of recombinant, modified-live and attenuated-live oral rabies vaccines have been used in wildlife in Europe and North America with minimal adverse events in target and non-target species [23,24,57,58], and the handout distribution method reduces the chances of human exposure to vaccine by removing a large proportion of the unconsumed bait and capsule material from the environment. In the current study it was possible to recover 99.9% of unconsumed intact baits, however the outcome of 13% of baits was unknown. This compares to a study in Haiti, where the fate of 4.8% of the baits offered was unknown [16]. This could be because roaming dogs in Goa may be more likely to take the bait away to eat, however may have also been influenced by the prototype bait construct used. The potential higher rate of non-retrieval will need to be considered when evaluating the chances of human exposure to vaccine material remaining in the environment. The lower staff bite rate for OBH suggests that there may be benefits to staff safety, project administration and cost, however the occurrence was too low to evaluate significancebetween the two approaches. The rate of staff dog bites in this study was too low to evaluate significance between the two approaches, however warrants further study.

The results of the staff opinion survey in this study indicate that staff preferred the OBH method and felt that they were able to 'vaccinate' more dogs with this as compared to the CVR method. The limitations of small sample size and possible bias for a novel method must be considered, however this survey found that experienced vaccination staff endorsed the OBH method as a feasible supplement to door-to-door parenteral vaccination to reach inaccessible dogs. Training of catchers using nets is difficult, requiring novice catchers to work within teams of experienced catchers for several weeks or months to become competent. This presents limitations to the rapid up-scaling of CVR in larger states. In the current study, the comparison was between teams highly experienced in CVR, compared to having had one day of field training using the OBH method. Despite this limitation, OBH was still comparable in the number of dogs 'vaccinated' per team per day with CVR. The OBH method still requires good training and strict adherence to standard operating procedure, however this study suggests that OBH can be successful, given good training over a short time period.

There is no universally successful bait due to differences in local culture, dog ecology and food preference between countries [13,23,59,60]. The lack of a quality bait construct in this study is likely to have affected the proportion of dogs 'vaccinated' through the OBH approach. It is expected that more attractive baits will be developed with time, however there were limited options at the time of the study. It is important to note that the OBH 'vaccination coverage' in this study includes all dogs that were interested in the bait, as opposed to dogs that perforated the capsule. Studies using intestine baits in Haiti and Philipines both reported that 93% of baits offered to dogs resulted in the capsule being perforated [16,21] and so with bait optimisation for use in Goa, it is expected that similar outcomes could be achieved.

5. Conclusion

The development of efficient, scalable methods to repeatedly vaccinate a high proportion of the roaming dog population is the only way to avoid the indefinite provision of post-exposure prophylaxis, suffering caused by rabid dog bites and detrimental impact on tourism and agriculture industries in developing countries [24]. The lack of a licenced ORV means that capture of dogs for parenteral vaccination is the only method of increasing coverage in inaccessible dog populations. This study indicates that should ORV be available, it would likely benefit both operation efficiency and vaccination coverage in the free roaming dog population and therefore may be of considerable benefit to rabies control activities in Goa and similar settings.

Declaration of interest

Ad Vos is a full-time employee of a company that manufactures oral rabies vaccine bait. Alasdair King is a full-time employee of a company that manufacture parenteral rabies vaccine. Other authors have no conflict of interests.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvacx.2019.100015.

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